Local Bischofite Therapy: Monograph. Edited by Head of the Pharmacology department of the Volgograd State Medical University, professor A.A. Spasov; Volgograd: FGUP IPK “Tsaritsyn”, second edition with corrections, 2003 - 160 p.

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The monograph deals with the medical aspects of administering the magnesium-containing mineral of bischofite for the local treatment of musculoskeletal diseases, inflammatory pathology of mucous membranes of the mouth and ENT organs as well as its application in dermatological practice. The information on the geochemistry of magnesium minerals is provided, pharmacological properties of bischofite such as its anti-inflammatory, immunotropic and anti-microbial effects, its effects on infected and non-infected ulcerous defects of mucous membranes and skin are described.

Pharmacological and toxicological properties of bischofite are also described in the book. A pharmacological profile of the agents containing bischofite such as balneological bischofite, bischofite solution (purified from technogenic impurities), bischofite in the form of paste such as Bischolin, Bischal, dry (scaly) bischofite; balneological ointments of Polycatan, Polcatan-forte, analgetic Polycatan for local therapy in dentistry, Polycatan solution in ENT-practice is presented. Much consideration is given to the clinical effectiveness of the agents and the tactics of their administration in mono- and complex therapy of inflammatory diseases of joints, mucous membranes and skin in this monograph.

The book caters to physicians, pharmacistists and pharmacologists.

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(THE PROSPECTS OF BISCHOFITE ADMINISTRATION IN MEDICAL PRACTICE)

BIBLIOGRAPHY
Preface

Despite considerable achievements in producing agents for treating inflammatory diseases of joints, mucous membranes and skin, the problem of this therapy effectiveness is still not readily solvable. First of all, it is conditioned by the fact that steroidal and non-steroidal agents, though highly efficient, have a great number of adverse effects (gastropathies, immunodepression, etc.) and do not have any antimicrobial effect. As a rule, antibacterial agents administered for the local treatment of infected inflammatory diseases produce various antimicrobial effects causing dysbacteriosis, immunodepression, etc. This accounts for the revival of the researchers’ interest in natural balneological agents obtained from magnesium-containing minerals (salts of the Dead Sea, White Sea coast natural brine, etc.) Though they do not produce any marked anti-inflammatory effect, their moderate antibacterial and immunomodulating properties may be exploited to ensure the effective local therapy without any serious adverse effects. In addition, well adapted pharmacological forms of balneological agents (pastes, ointments, solutions and dried agents obtained from salts) make this treatment possible both at home and in outpatient clinics.

One of these natural agents is the mineral of bischofite, whose deposits were discovered in a depression near the Caspian Sea. Primarily, bischofite brine was traditionally administered as a folk remedy for treating arthritis. Consequently, it was experimentally and clinically studied by the researchers from Volgograd Medical Institute and registered as a balneological agent in the Pharmacology Committee. Afterwards, the scientists of Volgograd Medical Academy studied the mechanisms of the anti-inflammatory effect of bischofite, its immunomodulating and antibacterial properties were revealed and finally, medicinal agents and balneological agents (including preformed ones), whose effectiveness had been put through clinical trials were made up. The authors of this monograph want to share their experience in administering bischofite brine, the agent of Polycatan and balneological agents such as Bischolin, Bischal, etc. in the clinical practice of
rheumatologists, dentists, otolaryngologists, and dermatologists, they also describe the rational forms of both monotherapy and complex therapy.

This research is of fundamental value, as the conducted pharmacological and toxicological investigation of bischofite enabled the authors to reveal the new property of this magnesium-containing mineral, namely, the ability to decrease the phlogistic properties of inflammation mediators such as histamine and serotonin, to establish its stimulating effect on different stages of phagocytosis, on the inhibition of the growth of opportunistic fungi and pathogenic microorganisms. These data gave grounds for registering the discovery of “The property of bischofite to inhibit the growth and propagation of pathogenic and opportunistic microorganisms” (Спасов А. А. и др., 1988).

The reliable results of the research as well as high social value of developing bischofite deposits for medical purposes have equipped Volgograd Medical Academy supported by the administration of the Volgograd region to launch the project “Russian Magnesium”, which will enable not only to produce agents to be administered in local therapy, but also process the mineral to produce pharmacopeal organic and non-organic magnesium salts and agents derived from them having a resorptive effect (Максюта Н. К., 2001).

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Rector of Volgograd State Medical University,
Academician of the Russian Academy of Medical Sciences V. I. Petrov
INTRODUCTION

The second half of XX century witnessed the emergence of powerful anti-inflammatory agents (of steroid and non-steroidal structure), which entail both success and failures in the struggle against the anti-inflammatory syndrome. The struggle is successful as molecular aspects in the pathogenesis of inflammation have been established, and, primarily, the role of eicosanoids (prostaglandins, prostacyclins, leukotrienes, etc.) has been revealed (Серов В. В., Паукова В. С., 1995; Brestel Е. Р., K. Van Dyke K., 1992). Unfortunately, today’s anti-inflammatory agents blocking the synthesis of these agents produce a great number of adverse effects. These complications are also conditioned by decreased synthesis of eicosanoids outside the site of inflammation (Петров В. И., 2002; Насонов Е. Л., 1999). Even the local therapy of the inflammation process especially with the help of glucocorticoid ointments may entail such complications as thinning of skin, haemorrhages (ecchymoses), acne and hirsutism, decreased tissular resistance to infections, depressed local immunity (Насонов Е. Л., 1999; Зборовский А. Б., 2001; Kvan D. C., Swingle K. F., 1992).

The persistant interest in natural agents applied in balneotherapy can be easily explained. First of all, magnesium-containing minerals (carnallite, kieserite, bischofite, etc) which are the components of the Dead Sea water, Pomorian natural brine, Crimean natural brine and continental saline lakes (such as the lake of Elton) are of interest. Though, the salt composition of these brines is complex, the factor which is common for them is high magnesium concentration.

The agents derived from magnesium-containing minerals are traditionally administered as anti-inflammatory agents in balneology and cosmetology. It has been established, that decreased magnesium concentration in tissues results in the development of inflammatory processes. The neuropeptide, substance P, released at the same time is the earliest pathological sign indicating the stimulation of inflammatory cytokines such as interleukin-1, interleukin-6, the agent of tumour
necrosis, which can stimulate free radical mechanisms of inflammatory degeneration of tissues (Weglicki W. B., Phillips T. M., 1992). The antiphlogistic effect may be caused (Nigam S. et al., 1986) by the ability of magnesium to depress cyclooxygenase activity, as well as its antagonistic interaction with inflammation mediators, i.e. serotonin, histamine, prostaglandins (Спасов А. А., 2000).

It has been established that magnesium not only builds up tissular resistance to alteration and decreases the manifestations of the inflammatory process exudation, but also stimulates the processes of the final stage of inflammation, that of proliferation. It has been demonstrated that this cation stimulates the biosynthetic functions of fibroblasts (Galland L. D. et al., 1986) and stabilizes energy metabolism (Dyckner T., Webster P. O., 1984), eliminates lymphohistocytic infiltration (Galland L. D. et al., 1986) and stimulates phagocytosis (Спасов А. и др., 1956).

Some scientists believe that the mechanism of the anti-inflammatory effect of hypertonic magnesium salts involves osmotic dehydration of tissues and increased local blood flow. For example, Сатоскар Р. С. and Брандоскар С. Д. (1986) showed that the glycerin-based saturated solution of magnesium sulphate (25-50%) has a local anti-inflammatory effect. On the other hand, other researchers (Голосова Л. О. и др., 1993) proved that even hypotonic solutions (1 and 3%) of the mineral known as bischofite (MgCl₂6H₂O) have an anti-inflammatory effect when bischofite is administered by means of electrophoresis which prevents osmotic dehydration of tissues and ensures that the focus of the disease is immediately affected. It is apparent that magnesium in tissues and especially in skin and in mucous membranes not only stabilizes energy metabolism and local immunoreactivity, but also determines their anti-inflammatory potential. When there is local and systemic magnesium deficiency, the latter effect may be caused by decreased generation of the so-called inflammation anti-mediators (Серова В. В., Пауков В. Г., 1995) and the activation of the above mentioned inflammation agents.
The experimental studies revealed that acute magnesium deficiency results in the development of a systemic inflammatory reaction associated with skin hyperemia, hyperalgesia, leukocytosis, elevated number of inflammatory cytokines (IV-VI), proteins of acute stage (α2-macroglobulins, α1-glycoproteins, fibrinogen) (Malpuech-Brugere C. et al., 2000). It was established that this inflammatory reaction can be pharmacologically corrected with the help of glucocorticoids and by eliminating magnesium deficiency while it can not be corrected by means of non-steroidal anti-inflammatory agents and anti-histamine agents (Begon S. et al., 2002). The study showed that hyperalgesia induced by magnesium deficiency is not associated with an inflammatory reaction and it is blocked by the antagonists of NMDA-receptors or by restored magnesium concentration (Dubray C. et al., 1997; Chutkow J. G., Grabow D., 1972).

Some scientists believe that the admixtures of more than 30 microelements whose concentration in some cases may be as high as several per cent, can be of great importance for the mechanism of anti-inflammatory effect of natural magnesium minerals and brines (Бачев С., Писарев Ю., 1970). However, it should be noted that there have been no publications proving the role of microelements in the anti-inflammatory effect of natural brines of magnesium minerals. However, taking into account the data on the role of some microelements in immunological tolerance regulation in the activity of adhesion molecules and cytokines (Кудрин А. В. и др., 2000), it is too early to ignore the importance of these admixtures in the anti-inflammatory effect of the brines of the Dead Sea salts, bischofite salts, Pomorian natural brine, etc.

Magnesium salts are administered in dental practice for treating stomatitis, paradontosis and gingivitis. For example, the agent of Polyminerol obtained from Pomorian natural brine (its dry extract contains up to 76% of magnesium chloride) produces an anti-inflammatory effect decreasing the exudation phase. Polyminerol stimulates immunological defense reactions of mucous membranes (Бачев С., Писарев Ю., 1970). Natural brines containing mainly magnesium salts are used for producing toothpastes (e.g. Pomorin, Zhemchug, etc) which are recommended
as remedies for preventing gingivitis and stomatitis. Vulnusan ointment containing the extract of Pomorian saline lakes of Bulgaria is administered to treat the inflammatory pathologies of mucous membranes and skin.

With their immunologic and antiphlogistic effects taken into account, magnesium minerals are in wide use in balneology and cosmetology. Various body creams (nourishing, moisturizing), lotions, shaving creams, gels, salts for baths are obtained from the Dead Sea salts.

Balneotherapy with the salts of the Dead Sea, Pomorian natural brine or the remedies derived from them is effective in patients with inflammatory pathologies of the locomotor apparatus and fibromialgia, with skin diseases (psoriasis, eczema) with the syndrome of chronic fatigue. In some countries sea water (irrigation, aerosols, drops) containing a wide range of magnesium salts and other macro- and microelements is used for preventing and treating non-aggravated inflammatory diseases of the mucous membranes of the eyes, oral cavity and upper respiratory tract. The concentration of magnesium salts in sea water is highest as compared to other elements.

Nowadays magnesium-containing minerals are actively used in three spheres - balneology, cosmetology and in agent production (Спасов А. А., 2001). It should be noted that modern pharmaceutical forms of balneological agents and balneological preformed agents not only enhance the effectiveness of their therapeutic effect but also enable to use this kind of therapy in out-patient clinics and at home much wider. The similar therapeutic properties which were described as early as late XIX century are inherent to bischofite. The discovery of unique deposits of this mineral in a depression near the Caspian Sea in 1930-50s (Ермаков Е. А., Самойлов В. Ю., 2001) and the production of the brine of this mineral called the researchers’ attention to its therapeutic properties in treating joint inflammation. Since late 80s of XX century single and later systemic studies of the pharmacological properties of bischofite have been carried out. At present scientific data proving the therapeutic properties of balneological, cosmetological and medicinal agents produced from bischofite have been obtained. It has also
been proved that the pharmacological activity of bischofite is higher than that of Pomorian natural brine and the brine of the Dead Sea.

This book contains the most important information on the nature of bischofite, its pharmacological and toxicological properties. It also describes balneological and medicinal agents derived from it. Special emphasis is put on the practical application of bischofite therapy in medical practice.
# ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>AlAt</td>
<td>alanin transaminase</td>
</tr>
<tr>
<td>SMD</td>
<td>Strümpell-Marie disease (Bekhterev’s disease)</td>
</tr>
<tr>
<td>GCs</td>
<td>glucocorticoids</td>
</tr>
<tr>
<td>DMSO</td>
<td>dymethyl sulfoxide</td>
</tr>
<tr>
<td>ED&lt;sub&gt;50&lt;/sub&gt;</td>
<td>the dose which is effective in 50% of cases</td>
</tr>
<tr>
<td>CD</td>
<td>coronary disease</td>
</tr>
<tr>
<td>IH</td>
<td>index of oral cavity hygiene</td>
</tr>
<tr>
<td>IHC</td>
<td>index of oral cavity hygienic condition</td>
</tr>
<tr>
<td>LD&lt;sub&gt;50&lt;/sub&gt;</td>
<td>lethal dose resulting in the death of animals in 50% of cases</td>
</tr>
<tr>
<td>LD&lt;sub&gt;50&lt;/sub&gt;/ED&lt;sub&gt;50&lt;/sub&gt;</td>
<td>index of therapeutic range</td>
</tr>
<tr>
<td>LDG</td>
<td>lactate dehydrogenase</td>
</tr>
<tr>
<td>TE</td>
<td>therapeutic exercises</td>
</tr>
<tr>
<td>MAC</td>
<td>membrane attacking complex</td>
</tr>
<tr>
<td>MDH</td>
<td>malate dehydrogenase</td>
</tr>
<tr>
<td>NSAID</td>
<td>non-steroidal anti-inflammatory agents</td>
</tr>
<tr>
<td>NBT</td>
<td>nitroblue tetrazole test</td>
</tr>
<tr>
<td>OA</td>
<td>osteoarthritis</td>
</tr>
<tr>
<td>PRI</td>
<td>parodontal index</td>
</tr>
<tr>
<td>BSP</td>
<td>brachioscapular polyarthritis</td>
</tr>
<tr>
<td>PCR</td>
<td>polymerase chain reaction</td>
</tr>
<tr>
<td>ESR</td>
<td>erythrocyte sedimentation rate</td>
</tr>
<tr>
<td>UA</td>
<td>urogenous arthritis</td>
</tr>
<tr>
<td>COG</td>
<td>cyclooxygenase</td>
</tr>
</tbody>
</table>
CHAPTER I

MAGNESIUM CONTAINING MINERALS

Magnesium is a microelement. It is widespread in nature and makes up about 2.35% of the weight of the earth’s crust (Деревягин В. С. и др., 1989). Pure magnesium is a light transparent, silver white mineral, whose density is 1.74 g/cm$^3$ and the melting point is 651° C. In the air it gets covered with oxide protective film. Natural magnesium is a component of different minerals, it does not exist independently.

1.1. Magnesium Geochemistry

Among 200000 natural minerals containing magnesium, there are about one hundred hypergenous ones (table 1). Magnesium is found both in deep layers of the earth’s crust and in hypergenesis area where it accumulates mainly in oceans, seas, lakes. Natural magnesium migrates being a component of easily solvable sulphates and chlorides.

The main source of magnesium that is in sea water (1.3 g/l) which makes up 0.13% is the dust that formed as a result of the continental rocks being weathered by wind.

In the seas of the earlier geological epochs magnesium concentrated in dolomites and magnesium silicates (Высоцкий Э. Л., Кислик В. З., 1986). Nowadays, dolomite and magnesium silicates concentrate only in continental saline lakes. When sulphate lakes evaporate heavily, the sediment of magnesium sulphates and the basic salt of magnesium carbonate start to deposit. In sea lagoons getting saline the sedimentation of magnesium salts occurs at the late stages of their development with the sedimentation of magnesium sulphates preceding that of magnesium chlorides.
<table>
<thead>
<tr>
<th>Mineral Type</th>
<th>Mineral</th>
<th>Chemical Composition of a Mineral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Silicates</td>
<td>Olivine</td>
<td>$(\text{Mg, Fe})_2 [\text{SiO}_4]$</td>
</tr>
<tr>
<td></td>
<td>Talc</td>
<td>$\text{Mg}_3 [\text{Si}<em>4\text{O}</em>{10}] ,(\text{OH})_2$</td>
</tr>
<tr>
<td></td>
<td>Serpentine</td>
<td>$\text{Mg}_6 [\text{Si}<em>4\text{O}</em>{10}] ,(\text{OH})_8$</td>
</tr>
<tr>
<td>Carbonates</td>
<td>Magnesite</td>
<td>$\text{MgCO}_3$</td>
</tr>
<tr>
<td></td>
<td>Dolomite</td>
<td>$(\text{Ca, Mg}),(\text{CO}_3)_2$</td>
</tr>
<tr>
<td>Sulphates</td>
<td>Kieserite</td>
<td>$\text{MgSO}_4 \cdot \text{H}_2\text{O}$</td>
</tr>
<tr>
<td></td>
<td>Kainite</td>
<td>$\text{MgSO}_4 \cdot \text{KCl} \cdot 3\text{H}_2\text{O}$</td>
</tr>
<tr>
<td></td>
<td>Langbeinite</td>
<td>$\text{MgSO}_4 \cdot \text{K}_2\text{SO}_4$</td>
</tr>
<tr>
<td></td>
<td>Schoenite</td>
<td>$\text{K}_2\text{SO}_4 \cdot \text{MgSO}_4 \cdot 6\text{H}_2\text{O}$</td>
</tr>
<tr>
<td></td>
<td>Epsomite</td>
<td>$\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$</td>
</tr>
<tr>
<td></td>
<td>Sakiite</td>
<td>$\text{MgSO}_4 \cdot 6\text{H}_2\text{O}$</td>
</tr>
<tr>
<td></td>
<td>Leonite</td>
<td>$\text{K}_2\text{SO}_4 \cdot \text{MgSO}_4 \cdot 4\text{H}_2\text{O}$</td>
</tr>
<tr>
<td></td>
<td>Polygallite</td>
<td>$\text{K}_2\text{SO}_4 \cdot \text{MgSO}_4 \cdot 2\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$</td>
</tr>
<tr>
<td></td>
<td>Astrakhanite</td>
<td>$\text{Na}_2\text{SO}_4 \cdot \text{MgSO}_4 \cdot 4\text{H}_2\text{O}$</td>
</tr>
<tr>
<td>Chlorides</td>
<td>Carnallite</td>
<td>$\text{KCl} \cdot \text{MgCl}_2 \cdot 6\text{H}_2\text{O}$</td>
</tr>
<tr>
<td></td>
<td>Bischofite</td>
<td>$\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$</td>
</tr>
<tr>
<td></td>
<td>Tachyhydrite</td>
<td>$2\text{MgCl}_2 \cdot \text{CaCl}_2 \cdot 12\text{H}_2\text{O}$</td>
</tr>
<tr>
<td>Borates</td>
<td>Ascharite</td>
<td>$2\text{MgO} \cdot \text{B}_2\text{O}_3 \cdot \text{H}_2\text{O}$</td>
</tr>
<tr>
<td></td>
<td>Hydroboracite</td>
<td>$\text{MgO} \cdot \text{CaO} \cdot 3\text{B}_2\text{O}_3 \cdot 6\text{H}_2\text{O}$</td>
</tr>
<tr>
<td>Oxides</td>
<td>Periclase</td>
<td>$\text{MgO}$</td>
</tr>
<tr>
<td>Hydroxides</td>
<td>Brucite</td>
<td>$\text{Mg(OH)}_2$</td>
</tr>
</tbody>
</table>
It should be noted that the concentration of magnesium in underground and river waters is the second highest with that of calcium being the highest (Деревягин В. С. и др., 1989). The main sources of magnesium compounds are still the deposits of dolomites and magnesites, sea water, saline deposits with carnallite and the brines of saline lakes.

Sea water is an inexhaustible source of magnesium compounds. Every cubic metre of sea water contains nearly 4 kg of magnesium. The concentration of magnesium is highest in the brines of saline lakes such as Crimean and Pomorian lakes, the lakes of Elton, Baskunchak, of the Kulundin steppe, Sivash, The Caspian Sea and the Dead Sea.

1.2. The World’s Bischofite Formations

Bischofite was named after the German chemist and geologist G. Bischoff, who was the first to discover it in Zehnstein saline deposits of Germany. Bischofite deposits are not normally large. It is quite hygroscopic, and easily solvable in water and alcohol and bitter. The texture of bischofite rock is massive, stratified and spotted. Bischofite had been considered to be a rare mineral for a long time until rich bischofite beds were discovered in a depression near the Caspian Sea on the saline tops of Osinka and Chelkar in 1930-50s (Казанцев О. Д. и др., 1974). The unique thick and pure bischofite formations were found in the territory of the Volga region (fig. 1). Bischofite deposits as unique as the above mentioned ones were discovered in mid 60s in Brazil, Gabon and Congo (fig. 2).
Fig. 1. Bischofite Deposits in Saline Formations of the World.

Nomenclature:

1. The Caspian Sea basin (Volgograd deposit);
### Bischofite in the World’s Saline Formations of Different Geological Ages

(Деревягин В. С. и др., 1989)

<table>
<thead>
<tr>
<th>Geological Age</th>
<th>Deposit, location</th>
<th>Expansion character, segregation form</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quaternary</td>
<td>Lake of Zarhan (Zaidam basin, China)</td>
<td>Several cm large bands</td>
</tr>
<tr>
<td></td>
<td>Danakil depression</td>
<td>Mineral admixture</td>
</tr>
<tr>
<td></td>
<td>Kaidak deposit</td>
<td>Bischofite admixture in kieserite-gallite-carnallite beds (up to 70m)</td>
</tr>
<tr>
<td>Lower Cretaceous</td>
<td>Congo, Brazil, Gabon</td>
<td>Rich deposits of tachyhydrite with bischofite bands and enclosures</td>
</tr>
<tr>
<td>Cretaceous</td>
<td>Thailand</td>
<td>Tachyhydrite beds with bischofite</td>
</tr>
<tr>
<td>Triassic</td>
<td>Hemisset (Morocco)</td>
<td>Bischofite show in carnallite rocks Cretaceous</td>
</tr>
<tr>
<td>Late Permian</td>
<td>Zehschtain of West Europe, Stassfurt series (Germany)</td>
<td>Dispersed bischofite enclosures, pockets, irregularly shaped piles (Stassfurt bed)</td>
</tr>
<tr>
<td></td>
<td>Leine series (Holland)</td>
<td>Rich bischofite deposit including large horizon (Ronnenberg bed)</td>
</tr>
<tr>
<td>Early Permian</td>
<td>Dneeper-Donetsk depression (Ukraine)</td>
<td>Horizon of potassium and magnesium salts with bischofite rock enclosures</td>
</tr>
<tr>
<td></td>
<td>Pripyat trough (Byelorussia)</td>
<td>2m thick bischofite bed</td>
</tr>
<tr>
<td></td>
<td>Depression near the Caspian Sea (Russia, Kazakhstan)</td>
<td>Beds, bands, enclosures of other saline rocks</td>
</tr>
<tr>
<td></td>
<td>Monocline of the Volga river basin</td>
<td>Massive extensive beds (from 20 to 60m thick)</td>
</tr>
</tbody>
</table>
Prospecting for oil and gas in 1960 by the geological organizations “Nizhnevolezhskneft”, “Nizhnevolezhskgeologia” and “Saratovneftegas” in the depression near the Caspian Sea in the Volga basin territory resulted in the discovery of unique bischofite formations in the western and north-western parts of the depression framework. The productive beds in the section of saline mass in the territory of the Volga Region were first discovered in 1958-59s when oil prospecting holes were drilled in Kachalin aquare (the Volgograd Region).

The composition of these beds is quite varied (silvinites, polygallites, carnallite and bischofite rocks, boron mineralization, etc.) and the area of their spread is very vast (more than 300 km) (Борисенко В. И. и др., 1986; Бондаренко Я. Н., 2001; Баталин Ю. В., Свидзинский С. А., 2001).

Thick bischofite beds, 20-60 m in width which had never been found in any other saline basins, called the researchers’ attention. The first of them were V. A. Ermakov (“Volgogradneftegeophysica”) and N. P. Grebennikov (“VolgogradNIPIneft”). In 1966 N. P. Grebennikov worked out the technologies of selecting core from bischofite horizons as well as a reliable method of bischofite rock preservation. In June 1969 Nizhnevolezhsk Geological Department of the Ministry for Geology of the USSR received an application to issue a patent for the discovery of Volgograd bischofite deposit.

1.3. The Technology of Mining and Processing Bischofite

Some time ago bischofite which had been extracted from the brine of the Caspian Sea bay at the factory of Karabogassulphate was used for industrial purposes. The process of extracting bischofite involved multi-stage natural evaporation of the brine in special basins. This kind of bischofite production is affected by weather conditions and changes in the hydrogeological mode of the bay. At the final stage of evaporation chlorine and magnesium brine forms, which later evaporates to a hard salt in the apparatus of immersion combustion. Bischofite which had been obtained in this way, was packed in air-tight
polyethylene bags. At present the production of bischofite in Turkmenistan has been suspended.

Bischofite beds in the Volga basin monocline are deposited at the depth ranging from 1000 to 2000 m (Борисенко В. И. и др., 1986, Ермаков В. А., Самойлов В. Ю., 2001). The world practice of exploiting saline deposits proves that these salts can be mined as deep as 1500 m. But this way of mining bischofite is not applicable as bischofite is highly hygroscopic. The most profitable way of mining bischofite, the method of its underground dissolution, was prompted by its high solubility (fig. 2).

In 1974-75s the researchers from “Nizhnevolzhskneft” and VNIIgalurgia worked out and suggested a method which enables to extract 75-85% of bischofite in the form of brine. Tubing strings were submerged over 1000 m below the ground level. The brine was obtained as a result of the hole irrigation with fresh water.

The Gorodishe hole is the most productive hole. In the open-cast of the Gorodishe hole 6040 at the depth of 1597-1630m a productive bischofite bed was opened. Its central part is filled with bischofite rock which is practically monomineral; its lower and upper parts are rich in carnallite (17-69%) and gallite (16-55%). In the open-cast of Narimanov hole 1 two beds containing bischofite were opened at the intervals of 1706,5-1724,5 m and 1600-1621,5m. The most massive layer of nearly monomineral bischofite rock (12 m) is deposited in the lower bed. Magnesium oxide, basic magnesium carbonate and magnesium sulphate are pharmacopeal agents in Russia. In foreign pharmacopoeias one can also find magnesium chloride, magnesium hydroxide and magnesium organic salts (aspartate, orotate, citrate, etc.) Though many magnesium nonorganic salts occur in the form of natural minerals (magnesite, kieserite, periclase, brucite, etc.) they are not used for producing agents for non-parenteral and parenteral administration.
Fig. 2. The diagram demonstrating mining of bischofite with the method of underground dissolution.
The research carried out by the all-Russian N. M. Feodorovsky Scientific Research Institute revealed that balneological bischofite contains up to 73 elements (table 3). The content of many microelements is below the threshold sensitivity of the applied equipment and probably is of no balneological value.

Some components, iron in particular, are technogenous admixtures and penetrate bischofite brine as a result of corrosion of the metalwork of the equipment used for producing and storing the mineral brine. The method of cleaning bischofite developed by Озеров А.А. и др. (2002) enables to reduce the concentration of iron, calcium, bromine and microelements such as Zn, Se, Ba, Al, Si, Bi, Ni in the mineral brine.

1.4. Chemical Composition of Bischofite from the Lower Volga Basin

The chemical composition of bischofite deposits of the Lower Volga basin was detailedly described by Деревягин В. С. и др. (1889). When mined with the method of underground dissolution, the composition of bischofite depends on many factors: the age and the location of the saline basin, the depth of mining and technogenous admixtures (admixtures added to water to dissolve bischofite and those emanating from the metalwork of the installation and the tanks for storing the brine). Though the concentration of bischofite in the deposits of the Lower Volga basin is from 67 to 99,7%, its rock may contain the admixtures of carnallite and kieserite. These magnesium salts are carriers of a number of chemical elements (Деревягин В. С. и др., 1989), which are of value as far as their pharmacological and toxicological properties are concerned.
The Report on the Trials of the Chemical Composition of Balneological Bischofite in the Feodorovsky Analytical Licensing and Trial Centre of all-Russian Research Institute of Mineral Raw Materials of February 27, 2001

<table>
<thead>
<tr>
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</thead>
<tbody>
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<td>Sample selection</td>
<td>is carried out by the Client</td>
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<tr>
<td>Methods of analysis</td>
<td>Mass spectral method with inductively connected plasma (ICP-MS), the method of atom-emission with inductively connected plasma (ICP-AES), titrimetric analysis</td>
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<tr>
<td>Equipment</td>
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<tr>
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</tr>
<tr>
<td>1</td>
<td>Magnesium*</td>
</tr>
<tr>
<td>2</td>
<td>Chlorine*</td>
</tr>
<tr>
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<tr>
<td>5</td>
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<td>6</td>
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</tr>
<tr>
<td>8</td>
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<td>16</td>
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<td>17</td>
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</tr>
<tr>
<td>18</td>
<td>Iron</td>
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<tr>
<td>19</td>
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</tr>
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</tr>
<tr>
<td>25</td>
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</tr>
<tr>
<td>26</td>
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<td>Element</td>
<td>Symbol</td>
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<tr>
<td>-----------------</td>
<td>--------</td>
</tr>
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</tr>
<tr>
<td>Rubidium</td>
<td>Rb</td>
</tr>
<tr>
<td>Strontium</td>
<td>Sr</td>
</tr>
<tr>
<td>Yttrium</td>
<td>Y</td>
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<td>Zirconium</td>
<td>Zr</td>
</tr>
<tr>
<td>Niobium</td>
<td>Nb</td>
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<td>Molybdenum</td>
<td>Mo</td>
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<td>Ruthenium</td>
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<td>Thulium</td>
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<td>Symbol</td>
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<td>Ytterbium</td>
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<td>Ir</td>
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<td>Thorium</td>
<td>Th</td>
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<tr>
<td>Uranium</td>
<td>U</td>
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</table>

* - concentration, g/l

So far it has been established that bromine, rubidium, caesium, boron and strontium accumulate in saline rocks of bischofite. The data of the research carried out by the department of geochemistry of MSU (Валяшко М. Г. и др., 1976, 1979; Жеребцова И. К. и др., 1986) were used to determine the concentration of these elements in different bischofite samples of the Volga basin monocline. These researchers believe that the concentration of lithium, caesium and rubidium in the water-soluble portion of bischofite brine is low and ranges (depending on the sensitivity of the method applied to determine it) from the threshold concentrations up to 0.00010-0.0003%. The concentration of boron is higher ranging from 0.003 to 0.740%. The concentration of bromine in bischofite is considerably higher ranging from 0.36 to 0.78%.
Table 4

The Concentration of Bischofite Brine
(according to Деревягин В. С. и др., 1989)

<table>
<thead>
<tr>
<th>Salts</th>
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</thead>
<tbody>
<tr>
<td>1 MgCl₂</td>
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</tr>
<tr>
<td>2 MgSO₄</td>
<td>0,11</td>
</tr>
<tr>
<td>3 KCl</td>
<td>0,78</td>
</tr>
<tr>
<td>4 CaSO₄</td>
<td>0,8</td>
</tr>
<tr>
<td>5 NaCl</td>
<td>0,25-0,30</td>
</tr>
<tr>
<td>6 MgBr₂</td>
<td>0,58</td>
</tr>
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</table>
CHAPTER 2
PHARMACOLOGICAL PROPERTIES OF BISCHOFITE

This chapter informs about the results of the studies of pharmacological properties of bischofite (standardized brine according to ВФС (temporary pharmacopeal standard) 42-2950-97), its balneological forms such as Bischolin liniment (bischofite with carboxymethylcellulose), Bischal paste (bischofite in the form of aerosol), Polycatan ointment (bischofite in polyethylene glycol) and Polycatan, the agent for local administration obtained from bischofite (ВФС 2952-97) (Машковский М. Д., 1997) when bischofite solution is administered locally and when it produces a resorptive effect on the body.

2.1. The Anti-inflammatory Effect

To study the anti-inflammatory effect of bischofite (Спасов А. А. и др., 1998) standardized solution (the density is 1.268 g/ml) containing 95-96% of magnesium chloride as dry residue was used. The experiments were performed on 224 nonlinear white rats weighing 150-180 g, and 110 nonlinear white mice weighing 18-20 g.

The edema of the rats’ legs was induced by phlogogenic agents (2% solution of formalin and carragenin, 0,5% solution of histamine and 0,01% solution of serotonin) administered intraplantarly. The size of the leg edema and the extent of the anti-edematous effect of bischofite brine were determined according to Тринус Ф. П. и др. (1975). The experimental group of animals had an hour bischofite solution application. To draw a comparison Polyminerol (Bulgaria) obtained from Pomorian natural brine was chosen. The size of the leg was measured again in rats with formalin and carragenin-induced edema 4 hours later, in rats with histamine and serotonin-induced edema 1 hour after phlogogenic agents were administered. The experimental first-degree skin burn was induced in mice who were dipped into the water heated to have the temperature of 54° C as deep as their costal arch. (Тринус Ф. П. и др., 1975). A dose of 0,02 ml/kg of 5% bischofite brine solution
was given to the animals from the experimental group by hypodermic injection until a thermal injury set in. The survivability of the mice was the evidence of the protective effect of the mineral.

The data on the influence of bischofite and Polyminerol on the phlogogenic effect of the agents causing an inflammatory edema are presented in fig. 3.

Fig 3. The Effect of Bischofite Brine and Polyminerol on the Size of the Edema of the Rat’s Hind Leg Induced by Phlogogenic Agents (Formalin, Carragenin, Serotonin, Histamine)
* - the data are statistically relevant as to the control (P<0,05)

The research showed that both bischofite and Polyminerol compared to it have an anti-inflammatory effect. In addition, it should be noted that bischofite was more active than Polyminerol in mice with the inflammation induced by formalin and carragenin, the differences are less marked in mice with the edema caused by serotonin and histamine. If the absolute value of their anti-inflammatory effect is taken into account bischofite and Polyminerol were most active in mice with
serotonin and histamine-induced edemas, when the leg edema decreased more than by 50%.

The additional set of experiments (Мазанова Л. С., Черников М. В., 2002) on rats with a formalin-induced edema of the hind leg proved the anti-inflammatory properties of balneological pharmaceutical forms of bischofite such as Bischolin liniment and Polycatan ointment (table 5). As far as the force of their anti-inflammatory effect is concerned these agents were practically twice as effective compared to the agent of Vulnusan. It was proved that the antiphlogistic effect of the balneological ointment of Polycatan persists when bischofite concentration in the agent decreases to 1% (fig 4). Dimexide enhances the anti-inflammatory effect of Polycatan.

87.5% of the mice with an extensive first-degree skin burn died in the first four days. When administered preventively, bischofite and Polyminerol decrease the death rate of mice to 50% and 57.5% respectively.

Table 5

<table>
<thead>
<tr>
<th>Agent</th>
<th>The change of the leg size as to the control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3 hours later</td>
</tr>
<tr>
<td>Polycatan</td>
<td>-47,96**</td>
</tr>
<tr>
<td>Bischolin</td>
<td>-43,28*</td>
</tr>
<tr>
<td>Vulnusan</td>
<td>-16,90</td>
</tr>
</tbody>
</table>

* - true when P<0,05
** - true when P<0,001
Therefore, the described research established that bischofite brine has an anti-inflammatory effect which in some cases exceeds that of Polyminerol compared to it. These data prove the clinical observations of the anti-inflammatory effect of bischofite and glycerine solution of magnesium sulphate in treating rheumatic polyarthritis (Зборовский А. Б., 1993; Сатоскар Р. С., Брандоскар С. Д., 1986).

Balneological agents containing bischofite also produce a noticeable antiphlogistic effect, which is much stronger as compared to Vulnusan, whose active ingredient is Pomorian natural brine. We believe that such marked differences in the antiphlogistic effect of bischofite agents are conditioned not only by the differences in the chemical composition of Pomorian natural brine and bischofite brine (in Pomorian natural brine in contrast to bischofite brine the concentration of magnesium chloride is lower with their mineralization being similar) but also in mass-forming compounds: in the production of Vulnusan lanoline and castor oil are used; in the production of balneological bischofite...
agents water-soluble bases such as carboxymethylcellulose, aerosil, ethylene glycols, etc. are used.

Therefore, the tested agents containing bischofite and Pomorian natural brine produce an antiphlogistic effect which is especially marked in the models of tissular edema induced by serotonin and histamine. Thus, the agents had an antagonizing effect on the classical mediators of inflammation and consequently, one may assume that they can enhance the anti-inflammatory potential of tissues. Taking into consideration the fact, that bischofite mainly consists of hexahydrous magnesium chloride one may assume that the well-known properties of magnesium and hyperosmotic solutions of the mineral are exploited in the mechanism of its anti-inflammatory effect. The role of hyperosmotic solutions of bischofite is probably especially important when studying the agents with a high concentration of magnesium chloride (up to 30-34%).

In our research bischofite in iso- and hypoosmotic concentrations (less than 5%) (fig.4) also decreases the edema of tissues. It is probable that magnesium is the agent responsible for the anti-inflammatory effect of natural minerals. In this connection, the data obtained by Weglicki W. B. and Phillips T. M. (1992), Nigam S. et al. (1986) proving that decreased magnesium concentration in tissues induces an inflammatory process increasing the excretion of the substance P, interleukin-1 and interleukin-6, the factor of tumour necrosis, prostaglandins, the activation of free radical processes and the development of tissue degeneration are worth considering.

The study conducted by Chutkow J. G. and Grabow D (1972) showed that acute magnesium deficiency results in the development of a marked inflammatory reaction associated with skin redness and hyperthermia. Besides, the data obtained by Malpuech-Brugere C. et al. (2000) revealed marked growth of the number of leukocytes, an increase in the size of the spleen as well as elevated concentration of cytokine IL-6, α2-macroglobulins, α1-glycoproteins and fibrinogen. This enabled to make an assumption that this immunopathologic reaction contributes to the
development of atherosclerosis, dysplasia of connective tissue and results in the mitral valve prolapse, increased joint motility and arthropathia.

2.2. The Immunotropic Effect

45 white common mice weighing 18-20 g were used to study the effect of bischofite on the phagocytic activity of blood polynuclears. Daily for 6 days running the mice had hypodermic injections of standardized bischofite solution (10%). The phagocytic activity of neutrophils was estimated on 3\textsuperscript{rd} and 6\textsuperscript{th} days according to the phagocytic index and NBT-test determined with the help of the method of Исин Ж. М. and Сулейбино Б. М. (1987).

To study the immunotropic effect a dose of 1 ml/kg of standardized bischofite solution (in the form of sterile nonpyrogenic water-based 10% solution) was given to 20 non-lineal white rats weighing 150-170 g into their femoral area by hypodermic injections daily for 6 days running. The immunological indices were determined 3 days after the infusion of bischofite solution had stopped. The control group included animals who received the same amount of a solvent. Peripheral blood and the spleen of the animal subjects were studied. The following indices were determined: the number of lymphocytes in the spleen, the percentage of the main populations of lymphocytes in the rosette reaction with rabbit erythrocytes (T-lymphocytes) and the particles of opsonized zymozan (B-lymphocytes) (Сановский И. В., Фоменко В. Н., 1979), the number of antibody-forming cells (AFC) in the spleen with the help of the method of local hemolysis (Клемпарская Н. Н., 1969), the proliferative activity of lymphocytes using phytohemagglutinin (PHA) (“Flow Laboratoris”) and mitogen laconos (ml) (“Flow Laboratores”). The radiometric method (Константинова Н. Р., 1985) considering $[^3]$H-methylmethyline inclusion into ribonucleic acid registered on the liquid scintillation counter “Mark-III” (Delta Medical) was used to calculate the stimulation index (SI) according to the formula:

$$SI = \frac{\text{the number of impulses in the cells with mitogen}}{\text{the number of impulses in the cells without mitogen}}$$
In the blood serum of the animals the concentration of lysozyme was investigated with the help of turbidimetric method using the sets and techniques of scientific industrial association of “Reacomplex”.

The results of the investigations were statistically processed, the reliability of the differences was estimated with the help of Student’s t-test.

The data presented in fig. 5 show that the bischofite solution subject to the administered dose 1,5-1,8 times increased the phagocytic index of neutrophils (percentage of microbial cell absorption) for more than 3 days, the index of the test with nitroblue tetrazole (NBT-test) became 3 times higher at the maximum which is the evidence of increased myeloperoxidase, release of free oxygen and the completion of phagocytosis stage.

The effect of bischofite solution on the cellular composition of spleenocytes and their proliferative activity is shown in table 6. These data are sufficient to claim that the mineral effect on the cellular composition of spleen lymphocytes and their proliferative activity is insignificant. The concentration of T- and B-lymphocytes is within the range of control values. Being affected by bischofite solution, the proliferative activity of lymphocytes (in the reaction of blast transformation to PHA and mitogen laconos) practically did not change, therefore, the agent does not produce an immunodepressive effect and probably it did not disturb the synthesis of lymphokines - IL-1 and IL-2.

The stimulating effect of bischofite in the concentration range of 10g/l on the phagocytic activity of human monocytes and neutrophils (in the experiments in vitro) was demonstrated in the studies of Дзяк Г. В. и др. (1997). The authors also established that bischofite enhances redox metabolism in the stimulated and non-stimulated phagocytes under study. Most probably, these changes may be interpreted using the results of the research performed by Park J. et al. (1992) on the role of magnesium ions in generating NADP-oxidase complex in the outer cell membrane and the data of De Valk H. W. et al. (1933) on the magnesium deficiency in the neutrophils of the patients with bronchial asthma.
Fig. 5. The Effect of Bischofite on the Phagocytic Activity of the Neutrophils of Mice Blood:
A - the phagocytic index PI (the number of neutrophils per 100 cells of phagocytic bacteria); B - NBT-test (percentage of neutrophils containing the granules of diformozane).
Table 6

The Effect of Bischofite Standardized Solution on the Cellular Composition of Spleenocytes, their Functional Activity, the Stimulation of Antibody Formation and the Concentration of Lysozyme (M±m)

<table>
<thead>
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<th>№</th>
<th>Indices</th>
<th>Control group n=6</th>
<th>Experimental group n=6</th>
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</thead>
<tbody>
<tr>
<td>1</td>
<td>The concentration of lymphocytes in the spleen, mln cells</td>
<td>33,5±3,2</td>
<td>26,5±3,4</td>
</tr>
<tr>
<td>2</td>
<td>The concentration of T-lymphocytes in the spleen, % of the total number of lymphocytes</td>
<td>39,2±3,8</td>
<td>40,2±3,4</td>
</tr>
<tr>
<td>3</td>
<td>The concentration of B-lymphocytes in the spleen, % of the total number of lymphocytes</td>
<td>23,2±2,8</td>
<td>28,9±4,5</td>
</tr>
<tr>
<td>4</td>
<td>Transferative activity of lymphocytes on phytohemagglutinin (PHA), stimulation index (SI)</td>
<td>25,7±8,8</td>
<td>19,6±8,0</td>
</tr>
<tr>
<td>5</td>
<td>Proliferative activity of lymphocytes on mitogen laconos (ML) and stimulation index (SI)</td>
<td>12,2±3,6</td>
<td>13,8±4,2</td>
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<tr>
<td>6</td>
<td>The number of antibody-forming cells (AFC) in the spleen, AFC/mln lymphocytes</td>
<td>35,3±7,7</td>
<td>93,7±20,2*</td>
</tr>
<tr>
<td>7</td>
<td>The number of antibody-forming cells (AFC) in the spleen, AFC/spleen</td>
<td>1103,7±202,1</td>
<td>2623,7±673,4*</td>
</tr>
<tr>
<td>8</td>
<td>The concentration of lysozyme in blood serum (mkg/ml)</td>
<td>4,52±0,63</td>
<td>6,73±0,77*</td>
</tr>
</tbody>
</table>

* - the data are true as to the control p<0,05

n - the number of animals in the group
Bischofite caused a substantial increase in the number of antibody-forming cells in the spleen. One may make an assumption that in case of infected animals bischofite is to intensify antibody formation. The antibodies interacting with antigenic determinants of bacterial surface contribute to the formation of the membrane attacking complex (MAC) causing the damage of bacterial cell (Соколов Е. И., 1998). Taking into account the fact, that the C3b complement is magnesium dependent (Ройт А., 1991) we may assume that MAC is more active under the effect of bischofite.

One of the factors of local nonspecific immunity is lysozyme, which is an enzyme, disintegrating muramilic acid within the coat of gram-positive microorganisms up to a microbial cell lysis (Соколов Е. И., 1998). Being affected by bischofite solution, lysozyme concentration in blood serum actually increases by 48%, which is of great importance for building up antimicrobial defense of the body.

2.3. Antimicrobial Effect

Antimicrobial effect of bischofite was studied in experiments in vitro. Standardized bischofite brine was investigated as a component of liquid and dense nutrient medium with the concentration ranging from 0,01% to 50%. The reference strains of pathogenic microflora were involved in the experiments (Staphilococcus Aureus, Streptococcus Mutans, Candida albicans). Agar and Hottinger’s broth with pH of 7,4 were used as a nutrient medium for Staphilococcus and Streptococcus, agar and Saburo’s broth with pH of 6,8 were used as a nutrient medium for Candida albicans. 48-hour suspensions (grown up at a temperature of 37° and 28° respectively) of agar cultures of microorganisms with the concentration of 10², 10⁴ and 10⁶ m.b.(microbial bodies)/ml according to the turbidity standard of ГКИ (State Monitoring Institute) for bacteria were employed. Goryachev’s chamber was used to calculate the yeast cells of Candida albicans. When studying the bacterial properties of the agent in dense and liquid nutrient media the ultimate concentration of microorganisms was 10⁶ m.b./ml of the medium which appeared
to be an epidemiologically important value according to the order № 535 of the Ministry of Public Health of April 22, 1985 on the unification of microbiological (biological) methods of investigation applied in clinicodiagnostic laboratories of patient care and prophylactic institutions. Lower concentrations of microorganisms ($10^2$ and $10^4$ m.b./ml of the medium) were used to estimate the bacteriostatic effect of the agents. The growth of colonies was the criterion of the agent effectiveness: very scarce growth - growth of single colonies (up to 10); scarce growth - from 10 to 25 colonies; moderate growth - more than 50 colonies; intensive growth - incalculable colonies. Polyminerol (Bulgaria), standardized solution of Pomorian natural brine (the concentrate of sea water containing magnesium chloride) was chosen as a comparable agent. The growth of colonies or its absence testified to the effectiveness of the antimicrobial action of bischofite and the other agent.

The results of the investigations (tables 7,8) were statistically processed, parametric methods of study involving the use of Excel 5.0 computer software were employed.

It was established that bischofite brine with 50% concentration fully inhibits the growth of the strains of Staphilococcus Aureus, Streptococcus Mutans and Candida albicans, bischofite brine with the concentration of 20-30% moderately inhibits Staphilococcus Aureus and with the concentration of 5-30% it inhibits Candida albicans both in liquid and solid nutrient media. Polyminerol with the concentrations of 5-50% did not produce any antimicrobial effect.

The research shows that bischofite inhibits the growth of microorganisms when the inoculation dose is $10^6$ m.b./ml of the medium only with the concentration of 30% which proves the fact that a bactericidal effect sets in only when bischofite concentration is high. When the inoculation dose is $10^2$ and $10^4$ m.b./ml bischofite had a bacteriostatic effect on Staphilococcus and Streptococcus with the concentration of 20% and on Candida with the concentration of 10%.
Table 7

**Bischofite Effect on the Growth of Opportunistic Microorganisms in Liquid Nutrient Media**

<table>
<thead>
<tr>
<th>Concentration in the medium, %</th>
<th>The growth of microorganisms with the inoculation dose of, m.b./ml of the medium</th>
<th>Staphilococcus Aureus</th>
<th>Streptococcus Mutans</th>
<th>Candida albicans</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>$10^6$</td>
<td>$10^4$</td>
<td>$10^2$</td>
</tr>
<tr>
<td>Control</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>30</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td></td>
<td>+</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>+</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Nomenclature: + - growth in the broth

0 - absence of growth in the broth
### Bischofite Effect on the Growth of Opportunistic Microorganisms in Dense Nutrient Media

<table>
<thead>
<tr>
<th>Concentration in the medium, %</th>
<th>The growth of microorganisms with the inoculation dose of, m.b./dish</th>
<th>Staphilococcus Aureus</th>
<th>Streptococcus Mutans</th>
<th>Candida albicans</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>The number of colony-forming units (CFU) of microorganisms per dish</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>10⁶</td>
<td>10⁴</td>
<td>10²</td>
<td>10⁶</td>
</tr>
<tr>
<td>Control</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>30</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>+</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>10</td>
<td>+++</td>
<td>+++</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>5</td>
<td>+++</td>
<td>+++</td>
<td>++</td>
<td>+++</td>
</tr>
</tbody>
</table>

Nomenclature: x - the number of colony-forming units (CFU) of microorganisms per dish

Evaluation criteria:

+ - absence of the growth

+ - growth from 10 to 50 CFU/dish

++ - growth more than 50 CFU/dish

+++ - growth more than 100 CFU/dish
Bischofite in vitro had a bacteriostatic effect on Streptococcus pyogenes and Clostridium perfringens diluted 1/32, on Pseudomonas aeruginosa and Proteus vulgaris diluted 1/16, on E. coli diluted 1/8, on Bacillus subtilis and Streptococcus aureus diluted 1 (Поверенный А. М. и др., 1991). Bischofite had a bactericidal effect on Streptococcus pyogenes diluted 1/8, on Pseudomonas aeruginosa and Proteus vulgaris and colon bacillus only no more than twice diluted. It should be noted that the mineral is highly active in relation to the anaerobic infection of Clostridium perfringens.

The minimal concentration of bischofite producing a bacteriostatic effect in vitro in anaerobic conditions was 0.315-1.25%. Bischofite did not produce any bactericidal effect on Bacillus subtilis and Streptococcus aureus. In a number of cases it was possible to inoculate single colonies of these microorganisms in the concentrated brine of the mineral. The study on 3 strains of the yeast: two strains of Saccharomyce cerevisiae (haploid and diploid) and that of Candida albicans (Поверенный А. М. и др., 1991) proved the fungicidal effect of bischofite when its brine is 50% diluted. With the concentration of 25% bischofite had a powerful mycostatic effect and with the concentration from 4% to 12.5% it reduced the rate of proliferation and the viability of the yeast strains under study.

2.4. The Effect on the Thermal Ulcers of Nasal and Oral Mucous Membranes

The research (Спасов А. А. и др., 1999 а,б) was carried out on 41 rabbits of Shinshilla and Russian Giant breeds. Mucous membranes were damaged in rabbits under anaesthetics (diethyl ether by inhalation or 30 mg/kg of thiopental sodium intravenously) with the help of a red hot stomatological tool, namely, a stopfer (5 mm in diameter). The stopfer was placed on the lateral wall of nasal cavity within 0.5 cm from its vestibule and on the mucous membrane of the oral cavity in the area of the frenulum labii superioris to the left and the right of upper incisors for 20 seconds.
24 hours after the thermal injury the defect was surrounded by inflammatory swelling dominating above the surface of the injured mucous membrane. The defect bottom was covered with fibrinous incrustation and was bleeding. In the group of the animals not undergoing treatment edema and suppuration increased as well as grey incrustation and sphacelous submucous layer persisted in the oral cavity up to 8-10th days, and in the nasal cavity up to 5-7 days. Subsequently, edema and hyperemia of the adjacent tissues decreased. By 20-23d days in the oral cavity and by 10-12th days in the mucous membrane of the nose a white nodule filled with serous fluid formed at the site of the injury. Besides, fibrous incrustation and tissular edema were no longer there. Wounds on the nasal mucous membrane healed completely in the control group by 15th day and in the oral cavity by 33d day.

The treatment of the ulcerous defect with Polycatan started on 2nd day after the thermal injury. The treatment involved a ten minutes’ irrigation of the wound with 5%, 10%, 20% Polycatan solution and 20% Polyminerol solution (Pharmachim, Bulgaria). In the control group animals were irrigated with distilled water. The defects of mucous membranes were examined and measured daily.

In the experimental group of animals after Polycatan irrigation the clinical presentation was greatly different from that in the control group. In the first days of Polycatan treatment the inflammatory reaction decreased sharply, the wounds cleansed of fibrinous incrustation and pus.

Fig. 6 shows the dynamic of the changes in the area of ulcerous defects of the nasal mucous membrane when irrigated with Polycatan solution. The analyzed data demonstrate that 5% solution of Polycatan makes the 50% reduction of the ulcerous area and complete epithelization of the nasal mucous membrane defect approximately twice as fast. Complete epithelization of the thermal ulcer of oral mucous membrane was over by 33d day (Table 9). 5% Polycatan solution and 20% Polyminerol solution accelerated wound healing approximately on 6-7th days. 20% Polycatan solution had a maximal therapeutic effect.
Fig. 6. The Effect of Polycatan on the Thermal Ulcer of the Nasal Mucous Membrane

Table 9

The Effect of Polycatan and Polyminerol on the Healing of Thermal Wounds of the Rabbits’ Oral Mucous Membrane (M±m)

<table>
<thead>
<tr>
<th>№</th>
<th>Agent</th>
<th>Concentration</th>
<th>Terms of healing, days</th>
<th>Relative acceleration of healing, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Control</td>
<td>-</td>
<td>33.33±1.80</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Polycatan</td>
<td>5%</td>
<td>26.16±1.80</td>
<td>21.51</td>
</tr>
<tr>
<td></td>
<td></td>
<td>20%</td>
<td>19.00±3.06*</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Polyminerol</td>
<td>20%</td>
<td>27.16±1.26</td>
<td>18.51</td>
</tr>
</tbody>
</table>

*- the differences are statistically relevant as to the control (p<0.05)
The daily application of this solution reduced the ulcerous area by half by 8-10th days, complete epithelization set in by 19th day of treatment. The results of the research showed the positive effect of Polycatan on thermal ulcers of nasal and oral mucous membranes. The power of anti-ulcerous effect of Polycatan on oral mucous membrane is greater than that of the Bulgarian agent of Polyminerol.

2.5. The Effect on the Experimental Gastric Ulcers

In the experiments on the rats anesthetized with nembutal (40mg/kg) ulcer was induced by irrigating gastric serous tunic with icy acetic acid (Okabe S. et al., 1986), which was followed by the introduction of 1 ml of bischofite diluted 1:10 and 1:20 into the stomach. The same amount of distilled water was introduced to the control group (Тютенко И. Н. и др., 1993). The authors established that in the control group of animals an ulcerous defect was revealed in all the animals with its area being 17,75±2,60mm and in 26% of the control animals a perforated ulcer was revealed. In the experimental group of the animals who received bischofite diluted 1:10 to produce a therapeutic effect, the area of the ulcerous defect was 2,55±0,45mm; in 57% of cases neither ulcerous defect nor perforated ulcers were revealed in the animals of this group.

Bischofite had a marked anti-ulcerous effect in 1:10 solution, this effect, though less marked persisted in 45% of animals when bischofite was 1:20 diluted (Рогова Л. Н., 1993). The comparative investigation of anti-ulcerous activity of bischofite, Almagel and gastrocepine using the model of “acetate” ulcer in rats showed that the ulceration area of gastric mucous membrane in rats who had been treated with bischofite was 2,55±0,45 mm (p<0,01), in those who had been treated with gastrocepine it was 4,67±0,67 (p<0,05) and in those treated with Almagel it was 5,50±0,43 (p<0,05). A half of the experimental animals on bischofite had no ulcerous defect while in the group of animals on Almagel ulcerous defects of gastric mucous membrane were registered. In rats on bischofite and gastrocepine no cases of perforated ulcer were revealed and in 20% of the experimental animals treated with Almagel perforated ulcer was revealed (Тютenko И. Н. и др., 1993).
The authors of this research believe that the recovery of magnesium concentration to a normal one in the gastric mucous membrane underlies the anti-ulcerous effect of bischofite (in case of acetate ulcer) (Porova L. N., 2000). There is also an evidence of anti-ulcerous activity of magnesium asparaginate (Ivashkin V. T., 1981). One may assume that magnesium ions in experimental gastric ulcers stimulate the reparative processes in the mucous membrane.

2.6. The Effect on the Process of Eye Cornea Cicatrization

The researchers of the Volgograd branch of MNTC “Eye Microsurgery” Фокина В. П., Райхлина Н. Т., Посыльных И. А. (1993) studied the effect of 10% solution of bischofite on the process of cornea cicatrization after a radical keratotomy (RKT) in the experiment on rabbits.

The operation of radical keratotomy was done on both eyes and employed standard techniques. After the operation 0,01% solution of citral, 20% solution of chloramphenicol and physiological saline were instilled into the right eye of the animals; 0,01% solution of citral, 20% solution of chloramphenicol and 10% aqueous solution of bischofite were instilled into the left eye (experiment). The material (enucleated eyes) was sampled successively from 3d to 35th days after the operation.

While processing the material the researchers carried out a comparative morphological analysis of the changes of corneal tissues at the histological level. To study the ultrastructural changes the ultrathin sections of the material were prepared and then examined under the electronic microscope JAM - 1200 EX.

On 3d day after the radical keratotomy both in the experimental and control group of the animals in the section area there was an intensive proliferation of stratified scaly epithelium. On 6th day in the experimental group the number of dark epithelial cells having marked signs of ultrastructural differentiation (developed desmosomes, apical microvilli) was greater than that in the control group. From 10th day of the experiment the corneal insection was completely covered with highly differentiated cells. In the experimental group there was a
decrease in the number of the layers of epithelial cells in the cornea and a noticeable activation of fibroblast cells in the stroma as compared to the control group. In the subsequent period synchronous smoothing of the defect and gradual thinning of stratified scaly epithelium were revealed.

Bischofite produced a stimulating effect on the process of corneal cicatrization which manifested itself in the formation of a thinner layer of ultrastructurally mature epithelial cells, in the acceleration of the maturation of light basal epithelial cells filling in the corneal defect, and in the considerable activation of the cells of fibroblast type, situated in the area of corneal stroma defect.

2.7. The Treatment of Septic Wounds of the Skin

The experiments to study the effect of the agents on septic wounds (Гусева Т. Н. и др., 1999) were performed on white common female rats weighing 160-200 g and employed the technique by Скопинцев В. Б. (1992). The animals whose skin had been prepared in the back area received standard flat skin wounds having the area of 200,0 mm$^2$ under anesthesia (sodium pentobarbital 40 mg/kg). $1\cdot10^9$ microbial bodies of bacterial suspension containing a 24-hour culture of Staphilococcus aureus 209p ATCC 6538p were placed into the wounds. The material was inoculated on 3, 5, 7, 10, 12 days after the wounds had been infected. The wounds of the animals in the experimental group were either bathed with 10% Polycatan solution or given daily applications of Polycatan ointment, a balneological agent.

The dynamic of the healing process was estimated according to the following clinical signs: the terms when granulations and edge epithelization appeared; when the wounds cleansed of purulent and sphacelous tissues and complete epithelization set in; the quantitative composition of intratissular microflora in the tissue sampled from the edge of the wound (the quantity of microbial bodies in the bacterial suspension containing a 24-hour culture of Staphilococcus aureus).
Wound planimetry was carried out using the method of Фенчин К. М. (1979). To carry out bacterial control the quantity of microbial bodies in 1 g of tissue was calculated on 3, 5, 5, 10, 12 days after the wound had been infected using the technique of Кузин М. И. (1980). The criterion showing that the wound cleansed of bacterial seeds was the number of microbial bodies under $10^5$ per 1 g of tissue. The histologic sections were hematoxylin and eosin stained using the technique described by Лилли Р. (1969).

**The Experiment with Polycatan Solution**

The results of the study on the effect of Polycatan (Спасов А. А. и др., 2001) on the size, reduction rate and terms of epithelization of septic wounds in the control and experimental groups of animals are presented in fig 7. In the control group of the animals there was marked inflammation around the skin defect with the edema of surrounding tissues, infiltration, hyperemia, the crusts were knobby with white incrustation; there was edge swelling.

The area of the wounds in the control group of animals reduced as a result of the retraction of the wound edges; a day later the wound area reduced by 7.34% as compared to the original wound area. 2 days later the wound area reduced by 42.4%, 4 days later the wound area reduced by 79.9%. The reduction rate of the wound area was the most marked two days after the culture of Staphilococcus aureus was placed on the wound surface. In the next three days the wound area was reducing at a steady rate. On 12-15 days the wound eschar came off. Complete epithelization involving rough cicatrical modifications took place 15 days later.

Macroscopic purulent inflammatory phenomena, especially the stage of hydration were less marked in the experimental group of animals treated with the solution of Polycatan. From the first days the wound edges were moderately hyperemic with small edema. The wound area began to reduce on 1st day after the treatment.
Fig. 7. The Effect of Polycatan on the Dynamic of the Area Reduction (A), The Reduction Rate (B) and the Terms of Epithelization (C) of Septic Wounds.

Vs = (S-Sn)·100 / (S·t), t – time, days, S – the original area of the wound, Sn – the area of the wound on the day of testing.
The most marked effect of the wound area reduction was registered 2 days later similarly to the control group, but the rate of the wound area reduction was more marked. Thus, in the experimental group two days later the wound area reduced by 71.9% as compared to the original wound area while in the control group the wound area reduced by 42.4% at the same period. In the next three days the wound area in the experimental group was reducing at a steady rate. After 5 days of treatment the wound area in the animals of the experimental group reduced sharply (by 94%). It should be noted that in the experimental group of animals it took the wounds less time to cleanse of purulent and phacelous masses and by 3-4th days they appeared look like a clean granulated surface with proper edge epithelization. The wounds were covered with thin dry crusts. After the wound eschar came off on 8-9th days, the wound bottom became clean and pink. There was a great and reliable difference between the acceleration of the healing process in the experimental group and that in the control group. The number of microbial bodies in the suspension and from the imprint (table 10) enabled to estimate the effect of Polycatan on the cleansing of the wounds of bacterial seeds. A day after the wounds were bathed with Polycatan solution there was a decrease in the number of microbial bodies in the wound. In the experimental group the number of microbial bodies from the imprint 10 times decreased and in the suspension it more than 300 times decreased as compared to the control group. 3 days later in the experimental group the number of microbial bodies from the imprint 10 times decreased and in the suspension it 5 times decreased as compared to the control group. On 5 day after the treatment started there was a sharp decrease in the number of bacterial seeds in the wound in the experimental group. The number of microbial bodies from the imprint 10 times decreased and in suspension it 100 000 times decreased. In the following days – 7,10,12 days after the treatment started the growth of microbial bodies was not registered in the experimental group.
Table 10

The Effect of Polycatan on the Period Required for the Wounds to Cleanse of Bacterial Seeds

<table>
<thead>
<tr>
<th>The period of observation after the treatment started</th>
<th>The number of microbial bodies per 1 g of tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
</tr>
<tr>
<td>1 day</td>
<td></td>
</tr>
<tr>
<td>Imprint</td>
<td>$1 \cdot 10^7$</td>
</tr>
<tr>
<td>Suspension</td>
<td>$1 \cdot 10^9$</td>
</tr>
<tr>
<td>3 day</td>
<td></td>
</tr>
<tr>
<td>Imprint</td>
<td>$1 \cdot 10^4$</td>
</tr>
<tr>
<td>Suspension</td>
<td>$7 \cdot 10^7$</td>
</tr>
<tr>
<td>5 day</td>
<td></td>
</tr>
<tr>
<td>Imprint</td>
<td>$1 \cdot 10^2$</td>
</tr>
<tr>
<td>Suspension</td>
<td>$2 \cdot 10^7$</td>
</tr>
<tr>
<td>8 day</td>
<td></td>
</tr>
<tr>
<td>Imprint</td>
<td>$1 \cdot 10^1$</td>
</tr>
<tr>
<td>Suspension</td>
<td>$8 \cdot 10^4$</td>
</tr>
<tr>
<td>10 days</td>
<td></td>
</tr>
<tr>
<td>Imprint</td>
<td>—</td>
</tr>
<tr>
<td>Suspension</td>
<td>$7 \cdot 10^2$</td>
</tr>
</tbody>
</table>
In the control group the wounds cleansed of microbial bodies to meet the specified criterion ($10^5$) on 8th day. The decrease in the number of bacterial seeds in the experimental group was conditioned by the effect of Polycatan on the growth of opportunistic microorganisms. The comparison of the planimetry data and the effect of the agent on the growth of opportunistic microorganisms revealed a correlation between them. Thus, Polycatan solution has a marked necrolytic healing effect on the infected wounds in the experiment.

**The Experiments with Polycatan Ointment**

The macroscopic purulent inflammatory phenomena especially, the stage of hydration were less marked in the experimental group of animals treated with Polycatan ointment (Спасов А. А. и др., 2002). From the first days the wound edges were moderately hyperemic with small edema. On 4-7th days after the treatment started the wound area was reducing in a more marked way than it was doing under the effect of Vulnusan ointment and in the control group (table II, fig. 8A). Thus, being treated with Polycatan ointment the wound area reduced by 41%, under the effect of the comparable agent, Vulnusan ointment, it reduced by 27,6%.

The most marked effect of the wound area reduction in the course of the treatment of septic wounds with Polycatan ointment was registered 7 days after the treatment started. At this time the wound area diminished by 85,5%, while in the control group the wound area diminished by 29,26% and when treated with Vulnusan ointment it reduced by 42,38%. In the next days the wound area under the effect of Polycatan ointment was diminishing at a steady rate. On 9th day the wound area reduced by 91,59% and on 11th day it reduced by 95,56%. In the control group and under the effect of Vulnusan ointment the wound area reduced by 63,95% and 83,3% respectively; and in the control group it reduced by 57-74%. The comparison of the anti-inflammatory and regenerative activity of Polycatan ointment and Vulnusan ointment in relation to the control group revealed that the activity of Polycatan ointment considerably exceeds that of the other agent.
Table 11
The Effect of Polycatan Ointment on the Period Required for the Wounds to Cleanse of Bacterial Seeds

<table>
<thead>
<tr>
<th>Periodicity of measuring the indices</th>
<th>Control group</th>
<th>Vulnusan Ointment</th>
<th>Polycatan Ointment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>imprint smear from the wound</td>
<td>imprint smear from the wound</td>
<td>imprint smear from the wound</td>
</tr>
<tr>
<td>beginning of the treatment</td>
<td>$1 \times 10^7$ solid growth</td>
<td>$1 \times 10^7$ solid growth</td>
<td>$1 \times 10^7$ solid growth</td>
</tr>
<tr>
<td>2 day</td>
<td>$1 \times 10^6$</td>
<td>$3 \times 10^8$</td>
<td>$1 \times 10^6$</td>
</tr>
<tr>
<td>4 day</td>
<td>$1 \times 10^6$</td>
<td>$4,4 \times 10^7$</td>
<td>$1 \times 10^5$</td>
</tr>
<tr>
<td>7 day</td>
<td>$1 \times 10^5$</td>
<td>$8 \times 10^3$</td>
<td>$1 \times 10^5$-$10^3$</td>
</tr>
<tr>
<td>9 day</td>
<td>$1 \times 10^3$</td>
<td>$3 \times 10^3$</td>
<td>$1 \times 10^3$</td>
</tr>
<tr>
<td>11 day</td>
<td>$1 \times 10^2$</td>
<td>$1 \times 10^6$</td>
<td>$1 \times 10^2$</td>
</tr>
</tbody>
</table>
Fig. 8. The Effect of Polycatan Ointment on the Dynamic of the Area Reduction (A), the Reduction Rate (B) and Terms of Epithelization (C) of Septic Wounds.

\[ \text{Vs} = \left( \frac{S - Sn}{S} \right) \times 100 / t \]

where, t - time, days, S- original area of the wound on the day of testing.
Thus, on 2-4 days after the treatment started Polycatan was twice as effective as Vulnusan and on 7-9 days it was 4-5 times as effective as Vulnusan (table 11).

The reduction rate of the septic wound area under the effect of Polycatan ointment was distinctly marked on 2 day after the treatment and was 11% (fig.8B). The highest rate of the wound reduction in the experimental group under the effect of Polycatan ointment was registered on 7 day after the treatment started (12,2%). In the subsequent period the rate of the wound area reduction was gradually decreasing and on 9th day it was 10-8,7%. The reduction rate of the area of the wounds under the effect of Vulnusan ointment was lower than that in the experimental group of animals treated with Polycatan ointment. The most marked reduction rate of the area of the wounds under the effect of Vulnusan was registered on 2-4th days (7-8%). 7 days after the treatment started the reduction rate of the wound area reduced to 6%. On 9-11th days this index was gradually rising up to 7-7,5% but still was lower than it was under the effect of Polycatan ointment. In the control group the dynamic of the reduction rate of the wound area was similar to that under the effect of the other agent, still the reduction rate was most marked on 4th day (6,8%).

It took the wounds less time to cleanse of purulent and sphacelous masses when they were treated with Polycatan ointment and by 7th day they looked like clean granulated surface without any signs of acute inflammation with proper edge epithelization. The wounds were covered with thin dry crusts. After the wound eschar came off, the wound bottom became clean and pink. In the control group marked inflammation associated the edema of adjacent tissues, infiltration, hyperemia, intensive exudation was registered. Affected by Vulnusan the edema of the adjacent tissues and hyperemia were less marked than those in the control group. In the control group and that under the effect of the agent of Vulnusan wound epithelization with rough cicatrical changes made up 80% 15 days later, while in the experimental group epithelization entailed the formation of delicate, soft cicatrix, complete epithelization took place on 13th day. The agents under
study accelerated the cleansing of the wound of microorganisms (table 11). The tested Polycatan ointment had a maximal effect by 9th day while the other agent had such an effect much later.

Comparing the data on the effects of Polycatan solution and the balneological ointment of Polycatan on reparative processes in the conditions of experimental infiltrated ulcer it is important to emphasize that the soluble form of bischofite has the most marked therapeutic effect. It is possible to assume that this is conditioned by closer contact of the agent solution with the wound area and by better absorption of magnesium ions from the liquid therapeutical form of Polycatan.

**Experiments with Bischolin**

The experiments were carried out on 38 rabbits of Shinshilla breed and on 80 sexually mature rats of Wistar line (Поверенный А. М. и др., 1991). 10% solution of calcium chloride was introduced to the rabbits intradermally and 2 days later an infecting agent (1ml of bacterial suspension) was inoculated into the area where necrosis started.

The mixture of goldish Staphilococcus ATCC 25923 (F-49) (1bn CFU) and the bacilli of blue and green pus ATCC 27853 (F-51) (2 bn CFU) recommended as reference strains in determining antibiotic susceptibility was used as an infecting agent. 3 days after the animals had been infected, they all had suppurative inflammatory foci comparable in size with clearly marked edema, infiltration and perifocal inflammation. These foci contained sphacelous tissues and a considerable amount of purulent and serous exudate.

To estimate the healing process the following indices were used:

a) clinical criteria (changes in the body weight, thermometry data, dynamic of the development and the elimination of the perifocal edema and the infiltration of the wound edges, the amount and character of exudate, terms of wound cleansing);

b) laboratory blood tests;
c) microbiological investigation of a septic wound comprising the estimation of types of microbial causative agents and the quantitative analysis of intratissular microflora.

The most stable and informative microbiological index correlating closely with the character of a purulent inflammatory process is the method of quantitative analysis of microflora per 1g of tissue taken for biopsy (Колкер И. И., 1989). The number of bacterial seeds on the wound surface may fluctuate considerably and is of lower diagnostic and prognostic value.

In the experiments to study the specific activity of Bischolin 3 days after being infected the septic wound was surgically opened and cleaned, then the animals had a course of treatment with the agent. A thin layer of the ointment (2mm) was applied directly on the wound surface. The treatment continued for one week with the dressing being changed daily.

A comparative evaluation of the effectiveness of the pharmacopeal agent of Vulnusan containing castor oil and lanoline-based standardized solution of the natural brine of Pomorian lake (Bulgaria) and administered for treating septic wounds was made, the effect of the liniment base (physiologic saline-based 6% carbomethylcellulose with glycerine) used to produce Bischolin on the main clinical and microbiological indices of the healing process at the stage of inflammation was studied.

Therefore, the liniment obtained from bischofite possesses marked dehydrating activity, decreases perifocal inflammation, edema and infiltration of the septic wound edges, accelerates its cleansing of exudate and the remains of sphaelous tissues (Поверенный А. М. и др., 1991). When Bischolin was administered the necrotic type of cytogram changed into the degenerative inflammatory one earlier than in non-treated animals. Bischolin dressings applied once a day do not stick to the wound and the wounds do not bleed when they are changed or applied. One of the most important and beneficial effects of Bischolin is its marked bactericidal and bacteriostatic effect on Ps. aeruginosa. The administration of Bischolin results in a statistically relevant decrease in the extent
of wound infiltration in the first 3-5 days. The therapeutic effect of the agent according to the criterion of purulent exudate content became apparent by the end of 1st week. In control animals the wound cleansed by 7th day in 29% of cases and in the animals treated with Bischolin it cleansed in 89% of cases. In the experimental group wounds healed by 9th day, and in non-treated animals they healed by 12-13th days. The dehydrating and antipseudomonad activity of Bischolin exceeds that of the Bulgarian agent of Vulnusan, which is an ointment with similar basic properties.

The results obtained in vitro and proving the antibacterial effect of the agent on Streptococcus pyogenes, Proteus vulgaris and Clostridium perfringens suggest that Bischolin when administered for treating wounds, primarily infected with the above mentioned causative agents of wound infection may have antimicrobial effects.

The conducted trial enables us to recommend Polycatan and Bischolin for the local treatment of initial septic wounds (the wounds which formed as a result of lancing, abscesses, phlegmons, mastitis and pulling apart the edges of incisional wounds due to suppuration) at the stage of inflammation. They may be administered both independently in case of small size injuries and together with surgical treatment in case of extensive septic wounds and when approximation primary delayed and secondary sutures can not be applied.

2.8. The Prevention of the Ototoxic Effect of Kanamycin

Sensorineural deafness was simulated in 32 guinea-pigs weighing from 400 to 650 g who had been previously classified according to the motor reaction to the sound. Deafness was caused with the help of the antibiotic of kanamycin (Moschimpharmpreparat). A dose of 100 mg/kg was introduced intraperitoneally for 10 days running (Лобзов М. С., 1998). The state of the sound-perceiving apparatus of the animals was estimated according to Pfeifer’s symptom implying that an animal turns its head and body in the direction of a sound stimulus. The investigation was carried out in a room isolated from external and internal sound
and light signals, it was poorly lit with red light. The tested animals were brought into the room one at a time and after a 5-minute adaptation the experiment started. Barani’s ratchet which was placed at the distance of 1m from the animal made a sound signal, which was 81dB strong. The sound continued for 5 minutes. Bone conduction was estimated according to Pfeifer’s symptom when the animal reacted to the bump of a pencil weighing 5g against the cage frame (the pencil was dropped on the cage wall from the height of 50 cm, the pencil was screened from the animal with a partition).

All the animals were divided into 4 groups: 1st group included intact animals (control); 2nd group included animals who received kanamycin; 3d group included animals to whom 5% Polycatan solution was introduced into the retroauricular area by means of electrophoresis (the electrophoretic device was Potok-1, the strength of the current was 2mA, the negative electrode was fixed on the skin of the retroauricular area; the hair was previously removed, the length of electrophoretic exposure was 10 min.) for 10 days; 4th group comprised the animals who received Polycatan and kanamycin. From 9th till 19th day the animals of 2nd and 4th groups were given 100 mg/kg of kanamycin intraperitoneally. On 20th day of the experiment the animals were slaughtered which was followed by the histological study of the cochlea based on K. Wittmaack’s method (1912). In our country this method was described by Ямпольский Л.Н. (1933).

The statistic processing of the data employed the Quatro Pro computer software. The reliability of the differences was estimated with the help of Student’s t-test.

The data (Спасов А. А., Лобзов М. С. и др., 1999) presented in fig. 9 show that kanamycin has an ototoxic effect starting from 13th day. The maximal depression of the sensory and neural apparatus of the guinea-pig ear was observed by 20th day of the experiment. Moreover, it should be noted that both test-indices of sound and bone conduction were changing synchronously under the effect of kanamycin.
Fig. 9. The Effect of Polycatan on the Hearing Sensibility of Guinea-pigs (the Turn of the Head and Body) Intoxicated with Kanamycin

Polycatan considerably decreased the depression of the animals’ reaction to the sound caused by the antibiotic: the first animals with negative Pfeifer’s reaction were revealed on 4\textsuperscript{th} day and later. The total number of the animals in the experimental group was 3 times as small as that in the control group. The introduction of Polycatan to the intact animals did not have any impact on Pfeifer’s reaction in guinea-pigs.

The analysis of ear labyrinth sections made when the histological block was oriented in the sagittal plane showed that no changes of either inner or outer hair cells both in the control group of animals and in the group of guinea pigs on Polycatan were revealed. Inner hair cells were arranged in one line with their nuclei closer to the basal part, outer hair cells were arranged in 2-4 lines with small vacuolar lumps along the cell periphery. In the animals on kanamycin the changes occurred mainly in inner hair cells and manifested themselves as metachromasia or basophylic degeneration of the cytoplasm of some cells.
In guinea-pigs on Polycatan and kanamycin the histologic changes involved mainly the vascular component: hyperemia of the vascular stria and adjacent blood vessels.

Thus, the magnesium-containing agent of Polycatan protects inner hair cells from the harmful effect of kanamycin. It also enhances the trophism of the spiral organ by increasing the secretory function of the vascular stria generating endolymph. The similar data on magnesium sulphate were obtained by Крюкова Н. А. и др. (1984) in model studies. The vascular component of the effect of magnesium-containing agents may be explained by the fact that they compete with calcium ions by blocking their effect. Therefore, the local change of blood microcirculation under the effect of Polycatan and resulting in hyperemia of the vessels of the sound-perceiving organ is probably of positive significance in the conditions of kanamycin intoxication.

Aminoglycoside antibiotics cause kidney injury, which disturbs the concentration of electrolytes including magnesium ions in blood plasma. Though, the phenomenon of hypomagnesiemia is not correlated with hearing impairment the metabolic importance of magnesium ions for hair cells can not be underestimated. This is conditioned by the fact that, firstly, the basic enzymes of energy metabolism are magnesium dependent. This fact was proved by the experimental data of Крюкова Н. А. и др. (1984) on the increased excitability and intensified respiration of Recius neurons of the medicinal leech under the effect of magnesium. One should also bear in mind that Polycatan has an anti-inflammatory effect and stimulates the phagocytic reaction of macrophages. These effects are also determined by the effect of magnesium salts on the generation of prostaglandins and the complement of C3b.

Thus, the experiments on guinea-pigs showed that the preceding introduction of Polycatan (standardized solution of magnesium-containing mineral of bischofite) into the retroauricular area by means of electrophoresis reduces the ototoxic effect of the aminoglycoside antibiotic of kanamycin. Polycatan prevents
degenerative changes of ear labyrinth hair cells induced by kanamycin and ameliorates local blood flow.

2.9. The Effect on Gastrointestinal Motility

The effect of bischofite on the motor function of the gastrointestinal tract was studied in comparison with the agent of Karlovy Vary geiser salt. The experiments were carried out on both 50 white non-lineal rats. The method of “tracers” was used (Ходжай А. и др., 1966), the animals were on a standard vivarium diet. 5ml of 10% activated charcoal suspension was introduced perorally to the rats to serve as a tracer. 10 minutes before the activated charcoal suspension was introduced, 2,5ml/100g of bischofite standardized brine diluted 1:100, 1:70, 1:50, 1:40, 1:30, 1:25 was introduced to the experimental group. Distilled water was introduced to the control group of animals.

It was established that bischofite intensified the motor function of the gastrointestinal tract depending on the dose. For example, 1:100 and 1:70 bischofite solution practically had no effect on the intestinal motor activity. 1:50 bischofite solution increased the advancement of the charcoal suspension by 24% and 1:30 and 1:25 bischofite solution was conducive to complete bowel emptying of the contrast medium. Karlovy Vary geiser salt intensified intestinal motor function depending on the dose too. But as far as absolutely effective dose which accelerates the advancement of the “tracer” along the intestine by 50% is concerned, bischofite is 2,43 times less active than Karlovy Vary geiser salt, but as far as the index of therapeutic range (LD<sub>50</sub>/ED<sub>50</sub>) is concerned it 1,25 times exceeds the latter.

The obtained data prove the thesis that in medical practice magnesium salts are widely used as purgatives (M. D. Mashkovsky, 1997). Salt purgatives in the gastrointestinal tract dissociate, generating ions which are difficult to be absorbed; osmotic pressure increases in the intestine which results in the fact that water accumulates in the intestine and softens its contents. In this connection, intestinal peristalsis increases. Salt purgatives act along the whole length of the intestine.
They increase the release of cholecystokinin accelerating intestinal peristalsis by the cells of the mucous membrane of the small intestine, intensify the secretion of digestive juices, make Oddi’s sphincter relaxed.

2.10. Local Warming Effect on the Skin

The clinical experience of administering brines of magnesium-containing minerals for treating inflammatory diseases of locomotor system enables to make an assumption that they have a local warming effect on the skin (Дзяк Г. В. и др., 1996). This effect is probably exploited in producing some cosmetic creams and lotions obtained from the salts of Pomorian natural brine and the Dead Sea.

We devised bischofite plaster which is cotton cloth impregnated with standardized brine of bischofite and dried at room temperature (Мазанова Л. С. и др., 1993). It was studied as a warming agent and a local irritant in comparison with mustard paper.

The study of the bischofite plaster effect on the intensity of erythema and body temperature changes was carried out on 10 white guinea-pigs weighing 250-300g. Bischofite plaster was put through trials according to “Methodological Guide on Revealing Skin Hypersensitivity in Experiment” approved by the Central Institute of Dermatovenerology (Москва, 1976). The irritant action was studied for 10 days. Bischofite plaster was applied daily on a site of the skin 3x3 cm in area situated in the right back segment of the lateral surface of the animal’s body. Similarly, a site of the skin was shorn off in the left lateral segment to register the reflex change of the animal’s body temperature. One day later bischofite plaster was removed and the intensity of erythema in the right lateral segment was visually estimated from 0 to 5 points using the calorimetric ruler of Суворова С. В. (1975).

The experiments to reveal the irritant action of bischofite plaster on the skin of 10 white rats were performed. 12 hours before the experiment started 1% solution of methylene blue was intraperitoneally introduced to the animals at a rate of 1ml of the solution per 100g of the animal weight. Bischofite plaster was
applied on a clean shorn lateral surface in the right back segment. One hour later
the plaster was removed and the intensity of colour of this skin area was
determined. A similar clean shorn area of the skin in the left back segment of the
lateral surface of the white rats’ bodies was a control one.

In guinea-pigs and white rats bischofite plaster was fixed with the help of
elastic tubular bandage. Skin temperature of the guinea-pigs was taken with the
help of an electrometer before the experiment and then 5,15,30,45 and 60 minutes
after bischofite plaster was applied.

In guinea-pigs and white rats bischofite plaster did not induce any clearly
marked erythema and edema during the whole experiment. In guinea-pigs a poor
and insufficiently clear-cut erythema corresponding to the estimate of 1 point (the
average point was 0,8±0,13) was registered. In white rats the irritant effect of the
bischofite plaster caused the blood vessels at the site of the plaster application to
dilate and the colour intensity of this skin area of the white rat to increase. The
results of the experiment on the rats proved the results of erythema intensity in
guinea-pigs (0,8 ± 0,5 pints) completely.

The study of the effect of bischofite plaster on the guinea-pigs’ skin
temperature was carried out immediately at the site of plaster application and at the
opposite lateral surface of the animals’ body. During the experiment the
fluctuations of the guinea-pigs’ skin temperature were determined as to their
original temperature measured before the experiment (fig. 10).

In the first 15 minutes after bischofite plaster was applied there was an
increase in guinea-pigs’ skin temperature then skin temperature gradually
decreased to the original level. The maximal increase of guinea-pigs’ skin
temperature was registered 5 minutes after bischofite plaster was applied;
immediately under the plaster it increased by 0,4°C; its effectiveness (Dt%) was
1,0%, on the opposite lateral surface it increased by 0,2%, its effectiveness was
0,5%. The increase in the skin temperature on the opposite lateral surface is the
evidence of reflex dilation of blood vessels under the effect of bischofite plaster
which may be considered an objective estimate of their effect.
A comparative study of the effect of mustard paper on the erythema intensity and the increase in the laboratory animals’ skin temperature was carried out. It was established that after the application of mustard paper on the lateral surface of guinea-pigs’ bodies erythema was clearly marked and according to the ruler of Суворова С. В. it was 2 points (the average point was 2,1±0,1).

The effect of the irritant action of mustard paper on the increase in the guinea-pigs’ skin temperature immediately under the mustard paper and on the opposite lateral surface of the animals’ bodies was studied. It was found that the warming effect manifests itself 15 minutes after mustard paper is applied. The maximal increase in the guinea-pigs’ skin temperature was registered 30 minutes later; on the lateral surface under the mustard paper it was +0,7°, on the opposite lateral surface it was +0,8°.

Therefore, bischofite quickly produced a warming and insignificant irritant effect on the skin of the guinea-pigs. Mustard paper has a warming and marked
irritant effect by 30th minute after it is applied. The warming effect of bischofite is probably associated with increased local blood flow as blood vessels are affected by magnesium ions. Increased local blood flow at the sites of bischofite application was demonstrated in clinical conditions (Щавелева Л. А., 1995).
CHAPTER 3

PHARMACOKINETIC PROPERTIES OF BISCHOFITE

Some pharmacokinetic properties of standardised bischofite solution and Bischolin liniment were studied in their local action on the skin and mucous membranes and in intragastric introduction of bischofite solution (Смирнова Л.А. и др., 1991; 1992; 1993; 1194; 1995). Magnesium, the main constituent of bischofite, was chosen as marker for the evaluation of bischofit kinetics.

Experiments were carried out on 160 waking common male rats with a weight 160-180 g. The study was carried out in accordance with Guidelines on Preclinical Study of Agent Pharmacokinetics (1991). 5% bischofite solution was introduced intragastrically in the dose 0.2 ml/kg. After a certain time period the animals were decapitated to make blood tests, investigate the liver, kidneys, spleen, muscles and omentum. To investigate excretion urine and faeces were collected for 72 hours. In 5 control animals tests for background content and daily fluctuations of magnesium in blood were made at certain time intervals.

The ability of bischofite to permeate through the skin, mucous membranes of the mouth, stomach, small and large intestine was studied with dialysis chamber. The experiments were made on narcotised (50 mg/kg of pentobarbital intraperitoneally) common white rats of both sexes. A skin flap was removed from the animal’s sides, the hair being removed in advance. The mucous membrane of the oral cavity was taken from the rat’s cheek. The contents of the stomach, small and large intestine were washed away preliminarily with normal saline. The object under study was then placed into a dialysis chamber consisting of a hollow glass cylinder, a lid with two openings. One opening was intended for fixing the skin flap, mucous membrane of intestine and application of 0.05 ml of the investigated preparation on it; the other – for taking test materials from the cylinder with the help of an eye dropper. The cylinder was filled with 10 ml of Krebs-Hänseleit solution until contact with the inner surface of the skin flap. The dialysis compartment was kept at the constant temperature of 37°C, continuously stirred.
The penetration of bischofite through the skin, mucous membrane of the oral cavity and intestine of rats was assessed with the constant value of dialysis rate which is calculated in the following way:

\[ K = \frac{2.303}{t} \cdot \log \frac{C_0}{(C_0 - C_t)} \]

where

- \( C_0 \) = the initial amount of substance
- \( C_t \) = the amount of substance remaining by the dialysis time,
- \( t \) = dialysis time.

The time of half-transition of the substance through the membrane was calculated with the formula \( T_{1/2} = \frac{0.693}{K} \).

The permeability index characterising the rate of penetration of magnesium through a unit of membrane area can be calculated as the quotient

\[ P = \frac{C}{t} \cdot \frac{10}{60} \cdot A \cdot C_0 \]

where:

- \( \frac{C}{t} \) - the change of concentration per time unit,
- 10 - the capacity of dialysis chamber,
- A - the area of the membrane,
- \( C_0 \) - the initial concentration,
- 60 - the coefficient for time translation.

The content of bischofite in the samples was assessed judging by the change of magnesium concentration in the samples under study. The assessment was made photometrically with the wavelength 500-600 nanometres in colour reaction with titanium yellow according to the technique described by Menshikov V.V. (Меньшиков В.В., 1998).

To increase ingestion of magnesium ions from the 5% bischofite solution or Bischolin liniment 10% dimethyl sulfoxide was used.

The experimental data were processed with the help of Student’s distribution.
Table 12

**Pharmacokinetic characteristics of bischofite in peroral administration**

(in the dose of 0.2 ml/kg of 5% solution)

<table>
<thead>
<tr>
<th>AUC - Area under pharmacokinetic curve, (mMol/l*hour)</th>
<th>Half-life T(_{1/2}), hour</th>
<th>Apparent clearance CI, l/hour</th>
<th>Retention time for 1 molecule of preparation MRT, hour</th>
<th>Renal clearance CI(_R), l/hour</th>
<th>Extrarenal clearance CI(_{NR}), l/hour</th>
</tr>
</thead>
<tbody>
<tr>
<td>65.55</td>
<td>17.37</td>
<td>2.06(\times10^{-4})</td>
<td>13.22</td>
<td>0.17</td>
<td>0.20</td>
</tr>
</tbody>
</table>

The examination of the pharmacokinetic curve of bischofite made it possible to establish that the concentration of magnesium ions begins to increase by the second hour reaching the peak and then decreases from the second to the fourth hour. During the following 12 hours the concentration does not change which corresponds to the control level. The pharmacokinetic curve looks like a single chamber model. The calculation of the area under the pharmacokinetic curve was performed with the model-independent method of statistic points.

The area under the pharmacokinetic curve (table 12) was found to be 65.55 mMole/l*hour. Upon extravascular introduction of the agent apparent clearance is assessed which reflects the rate of agent release from a unit of volume of blood due to excretion as the relation of dose to the area under the pharmacokinetic curve which amounted to 2.06\(\times10^{-4}\) l/hour. The average retention time characterising the dwelling time of the preparation molecule in the body equals 13.22 hours. The stationary volume of distribution amounts to 2.72\(\times10^{-3}\) l. This parameter characterises the extent of distribution of the agent around the body. The duration of half-life period reflecting the time when the concentration of the agent in blood decreases twofold was found to be 17.37 hours.
The investigation of distribution of bischofite in organs and tissues revealed that the mineral does not affect magnesium content in the organs under study.

Investigating the excretion of bischofite it was noted that magnesium concentration in urine increased during the second to ninth hour, and then the concentration gradually decreased during the ninth to 48th hour. The excretion of bischofite through the intestine proceeded in the same way.

The intensity of excretion of a agent is characterised by excretory clearance. The excretion of bischofite with urine was assessed as renal clearance determined as the relation of cumulative agent excretion with urine to the area under the pharmacokinetic curve; it was found to be 0.17 l/hour. Extrarenal clearance amounted to 0.230 l/hour. That is, 47% of magnesium chloride introduced into the stomach of a rat was excreted by the body through the kidneys, 53% being excreted through the gastrointestinal tract.

The investigation of permeability of magnesium ions through various biological barriers revealed that the rate of ingestion depends on bischofite concentration in the solution under study (table 13). Through the skin of rats a concentrated bischofite solution is ingested 70 times faster than its 20% solution. We were not able to determine kinetic characteristics of 5% bischofite solution or Bischolin liniment. To increase the rate of ingestion of magnesium ions from 5% bischofite solution or Bischolin liniment 10% dimethyl sulfoxide solution was added to the solution. Through the mucous membrane of the mouth of rats 20% bischofite solution is ingested about 100 times more intensively than through the skin of rats. 5% bischofite solution easily penetrates through the mucous membrane although the rate of ingestion is 50 times lower than that of 20% bischofite solution.

The evidence of ingestion rate of magnesium ions from bischofite solutions through the mucous membranes of the mouth and gastrointestinal tract is represented in Table 14. The investigation of ingestion of bischofite through the intestinal tube revealed that it was the small intestine that was most permeable for magnesium ions, though both the stomach and large intestine are permeable for
magnesium ions, too. Magnesium ions from 20% bischofite solution and 5% bischofite solution permeate through the small intestine at an approximately similar rate, although in the stomach and small intestine the rate of ingestion decreases along with the decrease in bischofite concentration.

On the basis of the represented evidence of bischofite kinetics one can note that upon local application to the skin and mucous membranes the ingestion rate of magnesium is in direct proportion to its content in bischofite solution. It seems interesting that the ingestion rate of magnesium can be regulated with the help of dimethyl sulfoxide, so as to increase it; and with the help of carboxymethylcellulose, so as to reduce it. Upon internal introduction of bischofite solution magnesium is excreted through the kidneys and intestine in about the same amount.

Table 13

<table>
<thead>
<tr>
<th>PREPARATION</th>
<th>The constant of dialysis rate, mMole/hour</th>
<th>$T_{1/2}$, hour</th>
<th>Permeability factor, mMole/hour/cm$^2$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standardised bischofite solution</td>
<td>7.16*10^{-4}</td>
<td>19.83</td>
<td>2.43*10^{-4}</td>
</tr>
<tr>
<td>20% bischofite solution</td>
<td>1.158*10^{-5}</td>
<td>1222</td>
<td>1.35*10^{-5}</td>
</tr>
<tr>
<td>20% bischofite solution+10% dimethyl sulfoxide solution</td>
<td>1.51*10^{-2}</td>
<td>7.23</td>
<td>4.79*10^{-2}</td>
</tr>
<tr>
<td>5% bischofite solution</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5% bischofite solution+dimethyl sulfoxide solution</td>
<td>6.21*10^{-4}</td>
<td>1.45</td>
<td>2.14*10^{-3}</td>
</tr>
<tr>
<td>Bischolin liniment</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Bischolin liniment+10% dimethyl sulfoxide solution</td>
<td>3.73*10^{-4}</td>
<td>1.5</td>
<td>1.16*10^{-3}</td>
</tr>
</tbody>
</table>
Table 14

Permeability of magnesium ions from bischofite solutions through the stomach, small and large intestine

<table>
<thead>
<tr>
<th>Bischofite concentration, %</th>
<th>Organ</th>
<th>Constant of dialysis rate, mMole/hour</th>
<th>T_{1/2}, hour</th>
<th>Permeability factor, mMole/hour/cm^2</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>Mucous membrane of the mouth</td>
<td>0.00155</td>
<td>9.6</td>
<td>0.00128</td>
</tr>
<tr>
<td></td>
<td>Stomach</td>
<td>0.054</td>
<td>12.76</td>
<td>2.32</td>
</tr>
<tr>
<td></td>
<td>Small intestine</td>
<td>0.059</td>
<td>11.68</td>
<td>2.49</td>
</tr>
<tr>
<td></td>
<td>Large intestine</td>
<td>0.0037</td>
<td>181.7</td>
<td>0.156</td>
</tr>
<tr>
<td>5</td>
<td>Mucous membrane of the mouth</td>
<td>0.000316</td>
<td>37.5</td>
<td>0.000296</td>
</tr>
<tr>
<td></td>
<td>Stomach</td>
<td>0.0259</td>
<td>26.71</td>
<td>0.011</td>
</tr>
<tr>
<td></td>
<td>Small intestine</td>
<td>0.073</td>
<td>9.5</td>
<td>2.82</td>
</tr>
<tr>
<td></td>
<td>Large intestine</td>
<td>0.0288</td>
<td>24.02</td>
<td>0.018</td>
</tr>
</tbody>
</table>
CHAPTER 4

TOXICOLOGICAL PROPERTIES OF BISCHOFITE

Investigation of toxicity of natural minerals is impeded by their multicomponent composition and different solubility. So bischofite was standardised in accordance with VFS 42-2950-97. Toxicity testing of this mineral was carried out in accordance with the guidelines by Pharmacological Committee under the Ministry of Public Health (Фисенко В.П. и др., 2001).

4.1. Acute toxicity

Acute toxicity of pharmacopeic and balneological bischofite brine and their derivatives was tested in experiments on common white rats of both sexes with a weight of 150-180 g. Bischofite brine, dry bischofite, Polycatan as 20% solutions, and pastes that dissolve upon warming were introduced intragastrically through a tube. The animals’ death was registered for 2 weeks. The data obtained are represented in table 15.

Upon introduction of the investigated salt preparations the animals first presented signs of increased motion activity with its subsequent suppression; death occurred due to respiratory arrest. Upon autopsy of dead animals hyperaemia and erosion of the mucous membrane of the stomach were noted.

Taking into consideration that in clinical practice the preparations are administered locally, within the range of values of acute toxicity they can be classified as substances of low toxicity.

Methods of investigation

Acute toxicity testing of Polycatan was carried out on common white rats with a weight of 120-150 g. The substance to be investigated was introduced intragastrically with a tube. After a single introduction of the substance the animals were observed for two weeks. No death of animals was registered. The appearance of the animals was within the norm, there were no deviations in behavioural reactions or motor activity.
Acute toxicity testing of Polycatan revealed that the solution in 5% and 20% concentrations does not cause the death of rats. The value of acute toxicity fluctuated from 11 to 30 ml/kg which indicates low toxicity of Polycatan.

Table 15
Acute toxicity (LD50) of bischofite and its derivatives upon its intragastric administration to rats

<table>
<thead>
<tr>
<th>Preparation</th>
<th>LD50 value (ml/kg/~mg/kg of dry residual)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Females</td>
</tr>
<tr>
<td>Pharmacopeic bischofite (20% solution)</td>
<td>55.0/~4950.0</td>
</tr>
<tr>
<td>Balneological bischofite purified from technological admixtures (20% solution)</td>
<td>30.6/~2666.5</td>
</tr>
<tr>
<td>Crystallised bischofite</td>
<td>1412±227.0**</td>
</tr>
<tr>
<td>Dry bischofite</td>
<td>2200.0±500.0**</td>
</tr>
<tr>
<td>Polycatan (20% solution)</td>
<td>11.0/~840.4</td>
</tr>
<tr>
<td>Bischolin</td>
<td>11.5</td>
</tr>
<tr>
<td>Polycatan ointment</td>
<td>13.5</td>
</tr>
<tr>
<td>Polycatan forte ointment</td>
<td>8.9</td>
</tr>
<tr>
<td>Polycatan analgesic ointment</td>
<td>8.1</td>
</tr>
</tbody>
</table>

** in mg/kg

According to the evidence cited by Bulgarian company Farmchim the preparation Polyminerol caused the death of animals in the dose 6-7 ml/kg. Acute toxicity testing of Polycatan ointment, Polycatan forte and Polycatan analgesic ointment revealed that Polycatan ointments do not cause the death of rats; the value of acute toxicity fluctuating from 8 to 13 ml/kg which indicated low toxicity of the preparation.
Acute toxicity testing of Polycatan ointment, Polycatan with dimexide and Polycatan analgesic ointment was carried out on common white rats of both sexes upon peroral administration. After a single administration of the preparation the animals were observed for 2 weeks. No death of rats occurred. The appearance of the animals was within the norm, there were no deviations in the behavioural reactions or motor activity. The calculation was made with Lichfield-Wilcoxon and regressive statistics methods (Microsoft Excel) which enables one to calculate the value on the basis of results of pharmacological trials of the compounds with the help of alternative reaction test. No sex-related sensitivity was revealed.

On the strength of the obtained LD\textsubscript{50} value and guided by the classification of toxicity levels by Sanotsky I.V. and Ulanova I.I. (1975) one can classify Polycatan ointment, Polycatan with dimexide ointment and Polycatan analgesic ointment as preparations of moderate toxicity.

4.2. Cumulation

The ability to accumulate bischofite was studied on white nonlinear rats of both sexes with a weight of 180-220 g. The preparation was administered intragastrically for 28 days in doses 0.1 - 1.12 LD\textsubscript{50} with Lym’s technique. It was established that bischofite does not have a cumulative effect (cumulation factor > 20). Insignificant death of animals occurred from 14\textsuperscript{th} day of administration of the mineral in the total dose over 10 LD\textsubscript{50}. 2-4 days prior to the death of animals their hair lost its lustre and fell out in patches. Upon autopsy of dead animals multiple erosions and ulcers of the mucous membrane of the stomach and plethora of internal organs were noted.

4.3. Chronic toxicity

Chronic harmlessness of bischofite (upon 30-day administration) was studied in experiments on rats and dogs. Bischofite was administered intragastrically once a day in three doses: therapeutic dose of 0.2 ml/kg of 5\% bischofite solution (equalling bischofite content in the therapeutic dose in
Polycatan), intermediate dose of 2 ml/kg of 5% bischofite solution, subtoxic dose of 20 ml/kg of 5% bischofite solution. Every 10 days control weighing of animals was performed; in 4 weeks the animals’ condition was assessed on the basis of their behaviour and biochemical, functional and blood tests.

Examination of peripheral blood included erythrocyte and leukocyte numbers, haemoglobin concentration, colour index, erythrocyte sedimentation rate, blood clotting time. Cytomorphological examination of peripheral blood cells was performed by Romanovsky-Gimsa technique. The condition of the nervous system was assessed judging the motor activity in the open field test. The condition of the cardiovascular system was assessed with electrocardiogram evidence in the second standard lead. To assess the functional status of the liver, kidneys and other organs a complex of biochemical indexes of blood serum was used. Biochemical examination of blood serum included the determination of protein in biuret reaction, the transaminase activity by Rightman-Frenkel method, urea by diacetyl monoxyme method, creatinine in Jaffe colour reaction, thymol test by Huergo-Popper method, glucose test by Gultman’s orthotoluidine method. The tests for transaminase activity, creatinine, urea, and thymol tests were carried out with the help of Bio-la-test diagnostic sets (Czech Republic).

Chronic toxicity testing of bischofite revealed a weight gain in the animals which exceeded weight gain in control group 2-3 times. After withdrawal of bischofite the anabolic action in experimental animals decreased (3 weeks after the withdrawal of bischofite the weight of experimental animals approximated that of animals in the control group).

In the group of animals receiving heavy doses of bischofite a reversible psychosuppressing action was noted, depending on duration and dose of administration.

The data of cytological and biochemical examinations of peripheral blood did not change. The data of function study of the liver, kidneys and cardiovascular system activity were within the range of due values. Pathologoanatomical and histological examination of the experimental animals revealed a local irritating
effect of bischofite on mucous membranes of gastrointestinal tract. The changes were reversible, dependent on the dose.

4.4. Allergenic action

The ability of bischofite to affect the course of allergic reactions and its ability to cause local irritation were studied in accordance with the guidelines for evaluation of allergenic properties of pharmaceuticals passed by Pharmacological Committee under the Ministry of Public Health (1988). The standardised bischofite brine was investigated as a 20% solution in the dose of 0.2 ml/kg (the dose equalling the content of bischofite in Polycatan used in dental practice) and in doses 10 and 100 times as large. Examining the local irritating effect of bischofite solutions of increasing concentrations were made from the standardised brine.

The data obtained enable one to suppose (Лиходеева В.А. и др., 1993) that the mineral under study does not have anaphylactogenic effect in general or active anaphylactic reactions. Examination of the effect of the mineral upon delayed-type hypersensitivity on guinea pigs and mice did not reveal any effect on this pathological process. Bischofite did not change anaphylactic activity in the reaction of immune complexes in experiments on guinea pigs.

Large concentrations of the mineral had a local irritating effect. Thus in experiments on guinea pigs the standardised bischofit brine only caused erythema to develop upon intradermal administration; in conjunctival tests the irritating effect was noted at 50% concentration.

4.5. Mutagenic activity

The investigation of mutagenic activity recorded recessive, sex-linked and lethal mutations in Dr. Melanogaster flies, analysed dominant lethal mutations in germ cells of F1 (CBA x C57BL16) crossbreed of mice, and registered chromosomal anomalies in the cells of spinal cord of the C57BL16 line of mice. The investigation was carried out on Dr. Melanogaster male flies of wild type (line D-32). Bischofite was added to the food medium in the ratio 0.1 ml of standardised
bischofite brine per 1 cm³ of feedstuff. This amount of the mineral caused death of 50% males of line D-32 after a 3-day inoculation period. In the second and third series of experiments on mice the 20% standardised bischofite brine in the dose 12.5 ml/kg (1/2 LD50) was administered once intragastrically (Середенин С.Б и др., 1991). The investigation was carried out in accordance with the guidelines by Pharmacological Committee under the Ministry of Public Health “Assessment of mutagenic activity of new medicinal agents” (1990).

The investigations undertaken did not reveal any property of bischofite to induce genetic or chromosomal mutations in sex and somatic cells of eukaryotic organisms.

4.6. Transplacental activity

The tocolytic effect of magnesium ions is well known and is made use of in medical practice. However, deficiency of this mineral leads to disorders of physiological progress of pregnancy.

Within the study of transplacental activity of the mineral experiments were carried out on 60 white nonlineal rats with a weight of 120-160 g in accordance with methodological recommendations by Pharmacological Committee under the Ministry of Public Health of Russian Federation concerning investigations of embryotoxic action of pharmacological agents and their impact on the reproductive function (Дыхабын А.П. и др., 1986).

Pregnant females receiving bischofite (5% solution) perorally in doses 0.2; 2.0 and 20 ml/kg at various stages of pregnancy ate well, they were tidy, the hair was smooth and glossy, the general condition and behaviour of female rats did not change; no gross anomalies of foetus development were noted. The weight gain of pregnant rats did not depend on the dose of the preparation, being somewhat less than in animals of the control group, however. Bischofite in the therapeutic dose (0.2 ml/kg of 5% solution) had practically no effect on the birth and development of the progeny. The new-born rats displayed some sedation and sluggishness at the
beginning of their development (15-21 day), these signs, however, were within normal physiological parameters.

One should note, however, the embryotoxic action of bischofite. Bischofite caused preimplantational and postimplantational foetal death at all stages of pregnancy in all three doses. Thus, in the dose of 0.2 ml/kg of 5% solution the rate of preimplantational and postimplantational foetal death was 2.4 times higher than in the control group; haemorrhage into body cavities of foetuses occurred 1.5 times more often than in the control group. Less pronounced changes were noted upon administration of bischofite in the dose 2.0 ml/kg of 5% solution. Haemorrhages caused by bischofite can be attributed to the antiaggregant action of magnesium ions.

Thus, bischofite can have a foetotoxic action in resorptive activity in large doses.

4.7. Local irritating effect

In clinical practice the local irritating effect was noted in some cases upon local epicutaneous administration of bischofite (Машковский М.Д., 1996).

The mucous membranes of gastrointestinal tract, eyes and vagina are more sensitive to the irritating action of bischofite solutions. Diluted 1:10 and more bischofite brine did not damage the mucous membrane of the eye (Фокин В.П., Блинкова Е.С., 1995). A similar threshold was established for mucous membranes of the nose, nasopharynx and external auditory passages in patients and animals (Темкин Э.С. и др., 1995; Санжаровская Н.К. и др., 1995). Diluted 1:50 and more bischofite brine did not have a damaging effect on mucous membranes of the stomach, oesophagus, intestine and vagina of animals after prolonged administration (Тюренков И.Н. и др., 1993). Histological tests established that in weak solutions bischofite salts cause oedema and hyperaemia of mucous membranes; petechiae, erosions and ulcerations are noted as well as dystrophic changes: swelling of epithelium cells, ectopy of cellular nuclei, and their contraction (Тюренков И.Н. и др., 1993).
Conclusion

The obtained acute toxicity value of the standardised bischofite brine $LD_{50}$ enables one to classify bischofite as a substance of low toxicity. Bischofite does not accumulate in the body; it does not have an allergenic or mutagenic action. Upon a 30-day daily intragastric administration of bischofite brine to rats its anabolic effect was revealed. Upon a 30 day administration of the therapeutic dose (0.2 ml/kg of 5% solution) corresponding to the content of bischofite in Polycatan dose for a single gargle or application to oral mucosa no pathological changes were revealed. Bischofite in doses exceeding the therapeutic dose 10 and 100 times had a psychosuppressing action, an irritating effect on mucous membranes of gastrointestinal tract. One should note that bischofite in all investigated doses increased the rate of preimplantational and postimplantational foetal death, increasing the occurrence and size of subcutaneous haemorrhages in foetuses.
CHAPTER 5

BALNEOLOGICAL AND MEDICINAL AGENTS CONTAINING BISCHOFITE

Over recent years considerable progress has been made in the development and introduction into practice of various balneological and medicinal agents based on bischofite mineral.

The first experimental administration of bischofite in the 80-90s showed that the mineral is to a large extent contaminated with iron salts. This component has nothing to do with bischofite itself; it is probably included in bischofite brine as a result of technological contamination – corrosion of metal structures during bischofite salt extraction and storing. Another no less important aspect was the development of criteria for standardisation of bischofite salt for the content of MgCl$_2$•6H$_2$O, macro- and microelements. The investigations undertaken revealed that the local anti-inflammatory effect of bischofite can be determined by the content of its main component, MgCl$_2$•6H$_2$O rather than the admixtures in the form of macro- and microelements (Спасов А.А., 2000). The third aspect of standardisation of bischofite salt consisted in reducing admixture content (especially that of heavy metals) in accordance with СанПиН and Pharmacopoeia of Russian Federation. Unfortunately, technical documentation with its stringent requirements to the composition of brine of this mineral is not always given due consideration.

At present a technology for obtaining naturally occurring balneological bischofite from technological bischofite brine by removing technological and toxic admixtures is developed with the assistance of Volgograd Medical Academy. Volgograd Pharmaceutical Factory manufactures a balneological preparation “Bischofite brine” (purified from technological admixtures) (ТУ 3918-004-01896777-2001, valid since August 27, 2001) and a pharmaceutical composition “Bischofite” (ВФС 42-2950-97; registration certificate № 98113316, date of registration April 23, 1998).
Clinical practice has long made use of the following balneological preparations: paste of Volgograd bischofite, Bischolin (ТУ 461-4721933-07-90, valid since 1.12.90, developed by interindustrial research and manufacturing group Bischofite in Volgograd) and bischofite paste, Bischal (ТУ 461-10500666-01-91, valid since 1.09.92, Marketing Service enterprise, Volgograd). The content of bischofite (magnesium chloride concentration) is virtually the same in the paste and salt solution. Such substances as carboxymethyl cellulose, aerosil, polyethylene glycol and others are used as paste base.

Dry bischofite is very convenient for transportation and use. It is manufactured under the name “Sol’ drevnego Moria’ (ancient sea salt) (ТУ-2152-002-53561075-00), developed by Avangard Bischofite enterprise, Moscow, and Volgograd Medical Academy. Another brand of dry bischofite, “Svetlyi yar” (ТУ № 9158-002-38960719-01) was developed by Mineral Cosmetic enterprise and Volgograd Medical Academy. Upon dissolution of 340-360 g of dry bischofite in water to achieve 1 kg a natural saturated bischofite solution is obtained.

Since 2002 Volgograd Pharmaceutical Factory has started manufacturing balneological preparations: Polycatan ointment (based on natural bischofite) (ТУ 9318-001-01896777-200, valid since August 23, 2001, developed by Volgograd Medical Academy and Piatigorsk Pharmaceutical Academy), Polycatan forte ointment (based on natural bischofite and dimexide ) (ТУ 9318-002-01896777-2001, valid since August 23, 2001, the same developers), Polycatan analgesic ointment (based on natural bischofite and local anesthetic agent (ТУ 9318-003-01896777-2001, valid since August 27, 2001, the same developers). The content of bischofite (magnesium chloride) in the series of balneological ointments Polycatan amounts to 34%. Bischofite plaster is known to be developed (Машковский М.Д., 1997; Спасов А.А., 1992); it is a strip of dry paper or cotton fabric impregnated with bischofite brine. Poly Service-M enterprise (Moscow) manufactures “Tigrovy glaz” (tiger’s eye) gel containing bischofite, clay and extracts of silicon-containing herbs (ТУ 64-19-162-92).
Medicinal preparation Polycatan (ВФС 42-2952-97; registration certificate №98/133/15, registration date April 23, 1998) was developed for local administration in dental and ENT practice. The preparation was developed by Volgograd Medical Academy and Medek company (patent № 2053774); it consists of pharmacopoeic bischofite with the addition of flavors, sweetener, antiseptic agent and detergent.

In accordance with the recommendations by Pharmacological State Committee under the Ministry of Public Health of Russian Federation of October 24, 1988, Order № 778MZ, balneological bischofite brine and dry bischofite are administered in the form of baths. They have the following indications:

- sleeplessness, nervous strain;
- diseases of the musculoskeletal system (arthrosis deformans, rheumatoid arthritis, spinal osteochondrosis, radiculitis, lumbodynia, muscular contraction, trauma consequences, consolidating fracture of extremities and spinal column, sprain and rupture of ligaments, tendons and muscles, calcaneal spul, bone production and foot deformity, some types of contracture.

Balneological pasty forms of bischofite – Bischolin and Bischal ointment – are indicated for administration in cases of

- diseases of the musculoskeletal system (arthrosis deformans, rheumatoid arthritis, osteoarthritis, vertebrogenic diseases of the nervous system: radiculitis, lumbodynia;
- muscular contracture in children suffering from cerebral paralysis;
- minor purulo-inflammatory skin lesions;
- in geriatric practice;
- in a relatively grave course of the disease when general mineral baths, including bischofite baths are contraindicated.

Balneological preparation Polycatan ointment is analogous to balneological preparations Bischolin and Bischal ointments as to bischofite content so it is administered according to the same indications. Balneological preparation
Polycatan forte ointment (containing natural bischofite and dimexide) has a more pronounced anti-inflammatory action.

Balneological preparation Polycatan analgesic ointment is indicated for administration in the same diseases with a more pronounced pain syndrome.

In accordance with recommendations by Pharmaceutical State Committee under the Ministry of Public Health of 9.10.1997 the pharmaceutical composition Polycatan (registration certificate № 98/133/15) is administered in inflammatory diseases of the oral cavity, accessory sinuses of the nose and pharynx (gingivitis, stomatitis, rhinitis, maxillitis, acute and chronic tonsillitis).
CHAPTER 6

CLINICAL ADMINISTRATION OF BISCHOFITE AND BISCHOFITE-BASED PREPARATIONS

6.1. Diseases of the musculoskeletal system

6.1.1. Introduction

Diseases of the musculoskeletal system present a serious problem for medicine and the society. Diseases of the joints, such as rheumatoid arthritis, osteoarthritis account for a considerable portion of all cases of rheumatic diseases (28-56% of patients). This group of diseases is one of the leaders in the structure of temporary and permanent disability. One should emphasize that in recent years local therapy of these diseases has been preferable which is quite justified both from the point of view of the mechanism of development of osteoarticular and muscular lesions and in relation to the prevention of numerous complications of agent therapy (Зборовский А.Б., 2001).

Rheumatic processes of both inflammatory and degenerative-dystrophic nature are the most common diseases of the musculoskeletal system. Rheumatic diseases include processes associated with a local or systemic connective tissue lesion; the most common clinical manifestation of these diseases is the articular syndrome.

The prevailing rheumatic diseases are lesions of the joints, spinal column, extraarticular soft tissues. As for other nosological types (diffuse connective tissue diseases, systemic angiitis, rheumatism etc.), their proportion is much smaller than that of articular lesions or lesions of extraarticular soft tissues.

Diseases of the musculoskeletal system were the first cases where bischofite was used spontaneously, at first purely empirically. The first clinical trials of bischofite at Volgograd Medical Academy and Rheumatology Research Institute under Russian Academy of Sciences were carried out on a group of patients with osteoarthritis and rheumatoid arthritis. These trials confirmed the strong therapeutic effect of bischofite in these diseases (Зборовский А.Б. и др., 1991,
New antirheumatic agents come to the world pharmaceutical market every year, but the results of treating rheumatoid diseases are not satisfactory enough. That is why a search for new pharmaceutical and other agents helping to relieve the patients’ suffering is well justified. Continuous intake of anti-inflammatory agents, steroid and nonsteroid ones, leads to various side effects (Насонова В.А., Сигидин Ю.А., 1985). Complex therapy of rheumatoid arthritis has recently begun to employ natural bischofite and balneological bischofite-based preparations (Bischal, Polycatan, Bischolin). Although these preparations are inferior to glucocorticoids in what concerns their anti-inflammatory action, they have an advantage over synthetic chemical compounds or physiotherapy. They cause much fewer complications (in most cases) and are more attractive from the financial point of view.

6.1.2. Effectiveness of bischofite in musculoskeletal diseases

Administration of bischofite in the treatment of inflammatory and degenerative diseases of the joints and extraarticular soft tissues is well-founded from the point of view of various pharmacological effects of bischofite established by numerous trials (see chapter 2).

Biological action of bischofite can be to a large extent determined by the content of magnesium ions which act on various organs modifying metabolism on the cellular and molecular level of the body’s systems.

Clinical use of bischofite in the treatment of rheumatoid arthritis relies on the known mechanism of action of magnesium chloride and salt solutions. First of all, magnesium stimulates defence and restorative processes in the skin and adjacent tissues; its anti-inflammatory action is due to the activation of cellular immunity, antagonism with inflammation mediators and antibacterial effect. Administration of bischofite in complex therapy with nonsteroid anti-inflammatory agents is especially effective.
Thus, the effectiveness of complex therapy with nonsteroid anti-inflammatory agents in combination with bischofite (bischofite baths and compresses) was studied on 340 people 125 of whom were patients with osteoarthritis (Сидорова Е.А., 1995, 1996, Зборовский А.Б., 1997; Мартемьянов В.Ф. и др., 1997). It was established that the effectiveness of such complex therapy is considerably higher than that of therapy with only nonsteroid anti-inflammatory agents. Thus, after complex therapy the result classified as “improvement” and “considerable improvement” was achieved in 68-72% of cases while the therapy with only nonsteroid agents yielded this result in 53% of cases.

The undertaken investigation established that bischofite brine can be administered to patients with rheumatoid arthritis in the form of baths (local and general ones) and compresses in combination with nonsteroid anti-inflammatory agents. No significant difference between the effectiveness of bischofite bath treatment and that of bischofite compresses was established for the patients with rheumatoid polyarthritis, so the form of bischofite administration (baths or compresses) is chosen by the doctor depending on the amount of affected joints, type of lesion, the patient’s age and the presence of concomitant diseases.

It is noteworthy that bischofite procedures (especially baths) are contraindicated to patients with acute infectious diseases, high arterial blood pressure, exacerbation of coronary heart disease, cardiac decompensation, lung tuberculosis, renal insufficiency and other conditions where even regular baths of this duration are contraindicated. To control the effectiveness of treatment of patients with rheumatoid polyarthritis it is expedient to determine the dynamics of indices, range of motions and the circumference of inflamed joints, as well as the dynamics of erythrocyte sedimentation rate and isoenzymes (Lactate Dehydrogenase and Malate Dehydrogenase). A marked clinical effect of bischofite therapy sets on after 3-4 procedures (baths or compresses). When there is no therapeutic effect after 5-6 procedures bischofite therapy should be withdrawn.
In osteoarthritis a progressing capillary circulatory failure occurs which inevitably leads to an increased resistance of microcirculatory bloodstream. The opening of arteriovenous shunts followed by pathological shunt into the venous network and an increase of pressure is a compensatory reaction. As a result, the volume velocity of maximum venous outflow increases. Administration of bischofite and bischofite-based preparation Bischolin to patients with osteoarthritis led to a statistically reliable reduction of the stroke volume index and range of motion index around knee joints and digital joints. Such changes are associated with decrease in pulse fluctuations of the arterial wall in periarticular tissues and reduction of arterial flow. The proportion of arterial flow and venous outflow decreased in all joints, and the stroke volume index was reliably decreased which indicates an increase in venous outflow (Щавелева Л.А., 1995).

Examination of coagulogram in patients with osteoarthritis receiving bischofite baths in combination with nonsteroid anti-inflammatory agents revealed that before treatment patients had a shorter blood coagulation time, slower retraction and fibrinolysis time, decreased clot density which is indicative of hypercoagulation. Hypercoagulation and fibrinolysis suppression which are in direct correlation with the extent of inflammatory process were revealed in patients with osteoarthritis accompanied by reactive synovitis. Bischofite baths contributed to the reduction of hypercoagulation manifested by an increased clotting time, acceleration of the onset of retraction and increase in clot density (Щавелева Л.А. и др., 1994, 1995).

The investigation of bischofite administration in the treatment of extraarticular soft tissues diseases was carried out on two groups of patients: the first group received bischofite applications or local baths, as well as nonsteroid anti-inflammatory agents; the other group of patients only received nonsteroid anti-inflammatory agents.

The inclusion of bischofite in the therapy of extraarticular soft tissues diseases contributes to the achievement of better pronounced improvement of clinical presentations (mitigation of pain, increase in the range of motion of the
joint, the strength of hand constriction) and laboratory findings (reduced levels of glycosaminoglycans and their antibodies). These results enable us to draw the conclusion that bischofite has a good therapeutic effect and can be recommended for local therapy of extraarticular soft tissues diseases (Бабаева А.Р. и др., 1993).

Positive results were noted upon administration of electrophoresis with 1% and 3% bischofite solution in the therapy of patients with osteoarthritis and rheumatoid arthritis (Голосова Л.О. и др., 1993). The procedures had an analgesic, moderate anti-inflammatory action, a stimulating effect on the trophic processes in tissues which was due to the combined effect of various chemical components of bischofite and direct current. The procedures are well tolerated by patients, no skin changes are noted. The effectiveness of treatment of patients with osteoarthritis and rheumatoid arthritis was 78-85%. Besides, the procedures had a favourable action on the indices of arterial pressure in patients with the concomitant essential arterial hypertension. Thus, electrophoresis with 1-3% bischofite solution can be administered both in combination with other treatment modes, and as a monotherapy.

Combined administration of bischofite and acupuncture in a complex therapy of arthrological patients is of interest (Грехов Р.А и др., 1993). The effectiveness of the therapy was assessed by a number of clinical indicators (general pain assessment, pain index, articular, inflammatory and functional index, the amount of inflamed joints and their range of motion, the strength of hand constriction) and laboratory findings (ESR, C-RP, seromucoid, rheumatoid factor, antibodies to type II collagen, activity and isoenzyme range of LDH and MDH). The administered treatment showed considerable improvement in 15% of patients with rheumatoid arthritis, and a less pronounced improvement – in 52% of patients. Among the patients with osteoarthritis considerable improvement was noted in 20% of cases, improvement – in 58%, laboratory findings showing positive changes, too.

Administration of bischofite baths and Bischolin phonophoresis in combination with nonsteroid anti-inflammatory agents contributed to clinical
improvement in 78% of patients with rheumatoid arthritis (reliable reduction of pain syndrome and inflammatory syndrome, reduction of articular indices, of morning stiffness in the joints) (Щавелева Л.А., 1995).

46 patients with primary osteoarthritis received bischofite compresses (diluted 1:1) on the affected joints and low-intensity helium-neon laser. Laser therapy consisted in skin irradiation of the affected joints and biologically active points (Mamasaidov A.T. et al., 1993). The assessment of therapy effectiveness was based on the dynamics of clinical indicators, pain and articular indices, length of stay in hospital. On the basis of the undertaken investigation (Мамасаидов А.Т. и др., 1993) one can draw the conclusion that complex therapy with bischofite and low-intensity helium-neon laser is more effective than monotherapy with nonsteroid anti-inflammatory agents which was expressed in a more pronounced and fast improvement, and the shortening of hospital stay by 6-8 days. No side effects were noted.

Patients with rheumatoid arthritis and osteoarthritis receiving Bischolin in corporal reflex therapy on biologically active points showed better improvement than those receiving an isolated action of Bischolin on biologically active points (Чернов А.С. и др., 1993).

Summing up many years’ experience of treating patients with rheumatoid arthritis and osteoarthritis with bischofite baths and compresses at the Experimental and Clinical Rheumatology Institute under Russian Academy of Medical Sciences, academician Zborovsky (Зборовский А.Б., 2001) pointed out the effectiveness of this approach from the financial point of view: shortening of treatment period and, accordingly, of inability to work.

The effect of Bischolin paste was investigated on arthrological patients at Kalmyk Republic hospital (Badmaev V.A.), at the rheumatology department of Stavropol City hospital (under the guidance of Prof. Arushanian), at the rheumatology department of Ryasan Regional hospital (Lukina I.M., head of rheumatology department, Prof. Nogaller A.M., research supervisor), at the
Dnepropetrovsk City clinical hospital (Prof. Dziak G.V., research supervisor). In total 120 patients with diseases of the musculoskeletal system were examined.

It was established that the anti-inflammatory and analgesic action of Bischolin manifested itself according to the stage of disease and the nature of its course. Thus, in patients with rheumatoid polyarthritis the analgesic effect was noted in 83% of cases, reduction of articular edema – in 69%, increased range of motion in the joints – in 34%. A more pronounced action of Bischolin ointment manifested itself in patients with osteoarthritis and osteochondrosis. Thus, in this group the analgesic action was noted in 93% of cases, reduction of articular edema – in 78%, increased range of motion in the joints – in 90%; stiffness in the joints

6.1.3. Complex therapy of arthropathy with bischofite administration

In accordance was noted to reduce in virtually all patients (Спасов А.А. и др., 1993).

Elaboration of dry bischofite plaster has made it possible to streamline bischofite transportation considerably. Dry bischofite plaster, Bischoplast is manufactured from cotton fabric or paper by impregnating it with bischofite brine and drying. The plaster has an anti-inflammatory and analgesic action in diseases of the musculoskeletal system, radiculitis, osteochondrosis, rheumatoid arthritis (Мазанова Л.С. и др., 1993).

Dry bischofit is a convenient form of balneological preparation; after dilution with warm water it is effective against the diseases mentioned above (Спасов А.А., Оробинская Т.А., 2002).

The effectiveness of bischofite therapy of patients with diseases of the musculoskeletal system increases upon combining it with anti-inflammatory agents, acupuncture and laser therapy, percutaneous administration of bischofite in electrophoresis, phonophoresis and enhancers.with the effective classification and nomenclature of rheumatic diseases, this group of diseases includes the following nosological types:

1. Rheumatoid arthritis;
2. Juvenile rheumatoid arthritis;

3. Ankylosing spondyloarthritis (Strümpell-Marie disease);

4. Arthritis combined with spondylarthitis:
   - psoriatic arthritis,
   - Reiter’s disease,
   - arthritis in Crohn’s disease, nonspecific ulcerative colitis.

5. Arthritis associated with infection:
   - infectious arthritis (septic, gonococcal, brucellous, tuberculous, syphilitic etc.),
   - reactive or associated with infection (postenterocolitic, urogenital, arthritis secondary to immunisation, etc.).

6. Microcrystal arthritis:
   - gout,
   - chondrocalcinosis,
   - hydroxyapatite arthropathy;

7. Osteoarthritis:
   - primary,
   - secondary.

8. Other joint diseases (palindromic rheumatism, hydrarthrosis intermittens, synovioma, etc.);

9. Arthropathy in nonrheumatic diseases:
   - in allergic diseases,
   - in metabolic disorders,
   - in congenital defects of connective tissue metabolism,
   - in endocrine diseases,
   - in nervous system lesions,
   - in systemic blood diseases,
   - in malignant newgrowth (paraneoplastic syndrome)
   - in occupational diseases,
   - in other diseases (chronic viral hepatitis, sarcoidosis, periodic peritonitis).
Speaking about arthropathy in general, one can divide all pathological processes into inflammatory and degenerative-dystrophic ones. The most common inflammatory diseases as well as those with the most social impact are rheumatoid arthritis and seronegative spondyloarthritis, the latter group including Strümpell’s disease, psoriatic arthropathy, Reiter’s disease and other urogenital arthrites. As for degenerative-dystrophic processes, the most common diseases in this group are osteoarthritis and gout. In this respect, considering the problem of bischofite administration in arthrology, let us dwell on some articular diseases that are of a great medical and social importance.

6.1.3.1. Osteoarthritis

Osteoarthritis is the most common articular disease. Osteoarthritis is caused by primary degeneration and destruction of articular cartilage with the subsequent proliferation of underlying osseous tissue. Inflammatory changes of the synovial membrane (synovitis) are not constant and are of a secondary nature. Epidemiological investigation indicates that osteoarthritis occurs in 10-12% of all adult population, and in the age group over 50 30% of people suffer from osteoarthritis.

Osteoarthritis is a multi-factor disease whose development is determined by the following etiological factors: heredity, overuse of the joints, chronic microtraumas, acute trauma, incorrect posture, dysplasia of the joints, inflammatory lesion of the joint, metabolic disorder, endocrinopathy.

Degeneration of articular cartilage in osteoarthritis occurs due to two major reasons: overuse of the healthy cartilage and reduced resistance of the cartilage to a regular physical exertion. These two factors lead to a disorder of cartilage metabolism and a loss of its main constituent, proteoglycan which results in substitution of cartilaginous ground substance (matrix) with connective tissue. The cartilage becomes less flexible and elastic, it is fissured, defibrated and ulcerated in the area of most mechanic load.
Osteoarthritis treatment consists in restoring cartilaginous metabolism and controlling the secondary inflammatory process. The pathological process in articular cartilage can be treated locally or generally. Modern pathogenetic therapy of osteoarthritis calls for a complex administration of systemic and local methods.

The main objectives of treatment are to prevent the progress of degenerative process, to relieve pain and reactive synovitis, to improve the function of the joint.

Basal therapy calls for methods aimed at prevention of cartilage degeneration. The agents used in basal therapy are mucopolysaccharides (glycosaminoglycans) that are administered parenterally (intramuscular or intraarticular administration). This group of agents includes rumalon, chonsurid, vitreous body, hyaluronic acid agents (alflutol). Components of glycosaminoglycans, hexosamines, are used as a means of basal therapy, too; these agents can be administered enterally. The therapeutic effect of glycosaminoglycans is determined by their ability to stimulate fibroblast proliferation and production of articular cartilage components by these cells, rather than by their substitution effect.

Removal of functional load on the joint should be regarded as a means of basal therapy, too. At the same time one should bear in mind that an abrupt limitation of movement in the joint contributes to circulatory disorders in the affected structures resulting in a progressive degeneration of articular cartilage. In this respect the importance of physical therapy as a basal means of treatment in the treatment of osteoarthritis is apparent. It is desirable that patients with osteoarthritis should lose weight (in obesity), avoid prolonged immobility, and have permissible physical exercise.

As for anti-inflammatory therapy, it is aimed at controlling pain syndrome and reactive synovitis. The main means of achieving the goal are nonsteroid anti-inflammatory agents which can be administered enterally, parenterally, locally, rectally. Along with a powerful anti-inflammatory and analgesic action these agents have undesirable side effects, especially upon prolonged administration.
These are, first of all, gastropathy and a negative impact on cartilaginous metabolism which aggravates the degenerative change in cartilaginous matrix.

In a severe course of osteoarthritis accompanied by synovitis resistant to nonsteroid anti-inflammatory agents glucocorticosteroids can be administered. These agents, however, can only be administered in a short course of parenteral – intramuscular, periarticular, intraarticular – injections. One should bear in mind that a prolonged glucocorticosteroid therapy leads to degeneration and destruction of articular cartilage.

Methods of physiotherapy and remedial exercises are widely used in the treatment of osteoarthritis. A complex therapy of osteoarthritis calls for combination of various methods to achieve an optimal effect.

*Bischofite in the therapy of osteoarthritis*

Biological action of bischofite makes it an expedient agent for the treatment of osteoarthritis. This action to a large extent depends on the content of magnesium chloride (see chapter 2).

All the techniques of bischofite administration described above can be used in the treatment of osteoarthritis (see chapter 6.1.4). The choice of a technique depends on the clinical type of osteoarthritis, the number of affected joints, the involvement of the spinal column, the presence of signs of reactive synovitis, functional deficiency of the joint.

In polyosteoarthritis progressing with a multiple affection of the joints and generalised osteochondrosis of the spinal column preference should be given to general bischofite baths. If there are signs of vertebral compression or radicular syndrome, bischofite baths with spinal traction are indicated. Various forms of traction can be administered: vertical traction, horizontal traction, traction with one’s own weight.

In polyosteoarthritis with a prevailing affection of lower extremities sitting baths, local baths, compresses and ointment applications with bischofite can be recommended.
If minor articulations of hands and feet are affected, local baths with 5-10% bischofite solution, electrophoresis with 1-3% bischofite in chamber baths are indicated. Compresses with bischofite, ointment applications with Bischolin, Bischal, Polycatan can be administered, too.

In mono- and oligoarthrosis local baths, compresses, ointment applications, bischofite plaster can be recommended for administration; electrophoresis and phonophoresis with bischofite are indicated. The presence of signs of reactive synovitis is not a contraindication to bischofite administration. However, upon augmentation of exudative manifestations the therapy should be temporarily withdrawn. Bischofite therapy should be resumed when the inflammatory process has subsided.

6.1.3.2. Gout

It is a metabolic disease accompanied by a considerable increase in the uric acid content in the body and urate deposition in the tissues of the musculoskeletal system and internal organs. Clinically gout is manifested by acute joint inflammation and formation of gouty tophuses.

This condition is determined by constitutional dyspurinism – disorder of purine metabolism due to a genetic defect leading to hyperuricemia (normally, the uric acid content should not exceed 0.36 mmole/l in females, and 0.42 mmole/l – in males). The mechanism of development of hyperuricemia is determined both by the hyperproduction of uric acid and its decelerated excretion by the kidneys.

The following stages of the disease are distinguished: asymptomatic hyperuricemia, acute arthritis, periods between attacks, chronic arthritis.

The diagnosis of gout is based on the following criteria:
A) acute arthritic attacks coming on suddenly, with complete clinical remission in 1-2 weeks;
   b) increased uric acid content in blood serum;
   c) gouty tophuses;
   d) sodium urate crystals in synovial fluid.
The treatment of gout is aimed at rapid relief of symptoms and prevention of urate deposition in tissues.

In an acute attack of gout the treatment begins with nonsteroid anti-inflammatory agents (indometacine, diclofenac, etc.). Maximal daily doses with a subsequent reduction are administered. To advance the action nonsteroid anti-inflammatory agents can be administered parenterally.

Colchicine is most effective within the first day after the onset of the attack. The treatment regimen is as follows: 1 mg for the first intake, then 0.5 mg every 1-2 hours until the attack is arrested or side-effects set on. The total dose should not exceed 6 mg.

If nonsteroid anti-inflammatory agents and colchicines prove ineffective, or if there are contraindications to them, glucocorticosteroids are administered to control the attack. 40-60 mg of prednisolone are administered a day, quickly reducing the dose after a relief of arthritic symptoms.

In the time period between attacks hypouricemic agents are administered. These include xanthine oxidase inhibitor – allopurinol, and uricosuric agents – probenecid, ethamid, sulfinpyrazone and others. Uricosuric agents are combined with an adequate amount of alkaline fluid intake to prevent an attack of renal colic.

Physiotherapy and spa cure are important factors in the treatment of gouty arthritis as they have a beneficial action on metabolic processes, contribute to improvement of microcirculation, have a resolving and anti-inflammatory effect. Patients with gout are administered diathermy, therapeutic electrophoresis, phonophoresis with hydrocortisone, mud and paraffin applications, laser therapy, massage, remedial exercises, radon and sulfurat ed hydrogen baths.

*Bischofite in the treatment of gouty arthritis*

Administration of bischofite to patients with gout can include bischofite compresses, general and local baths, ointment application, bischofite plaster, electrophoresis and phonophoresis with bischofite.
Bischofite compresses are indicated in oligo- and monoarthritis in the period of remission. In this situation local bischofite baths can be administered to provide an anti-inflammatory effect.

In the periods of remission general baths, ointment applications, electrophoresis and phonophoresis with bischofite are indicated.

6.1.3.3. Rheumatoid arthritis.

Rheumatoid arthritis is a systemic inflammatory disease of connective tissue characterised by a chronic progressing erosive polyarthritis. Its incidence rate is 0.5-1%, females suffering from it 3-4 times more often than males.

Clinical presentations of rheumatoid arthritis include articular syndrome, intoxication (at an advanced stage), and extraarticular manifestations due to immunocomplex disorder.

Making diagnosis and differential diagnosis of rheumatoid arthritis one should take into consideration the following important signs and symptoms: persistent polyarthritis with symmetric affection of metacarpophalangeal and proximal interphalangeal joints, gradual progressing of the disease affecting more joints, the presence of osseous erosion on radiograph, the presence of rheumatoid factor in blood, detection of rheumatoid nodules.

Making the diagnosis of rheumatoid arthritis one should assess its clinical-anatomical type (articular type or rheumatoid arthritis with systemic manifestations), stage of the disease (1, 2, 3), course (progressing fast or slowly), radiographic stage (1\textsuperscript{st} – 4\textsuperscript{th}), functional deficiency of the joint. These parameters are necessary to determine the policy of treatment in each particular case.

The treatment of rheumatoid arthritis depends on the clinical-anatomical type of the disease, its stage, character of its course, the presence of complications.

In the absence of systemic clinical manifestations the therapy begins with nonsteroid anti-inflammatory agents. By administering one agent after another the most effective and best tolerated agent is chosen. Nonsteroid anti-inflammatory agents are administered virtually continuously in combination with other
antirheumatic agents. In oligo- and monoarthritis which progresses with a high activity one can administer glucocorticosteroids intraarticularly for a rapid relief of exudative manifestations in the joint.

Systemic administration of glucocorticosteroids is only possible in the presence of affection of internal organs, rheumatoid vasculitis, severe anaemia. It is noteworthy that a high rheumatoid factor titre (1:1280 and more) can be regarded as a sign of the systemic nature of rheumatoid arthritis. The agent of choice is prednisolone in the daily dose 20-40 mg. An alternating treatment regimen (administration of prednisolone every other day) is preferable as it makes it possible to reduce side effects of hormone therapy.

A progress of the disease in spite of nonsteroid anti-inflammatory agents therapy is an indication for slowly acting antirheumatic or basal agents. The agents of this group are characterised by high toxicity; the therapeutic effect comes on several months after the beginning of therapy. The mechanism of action is associated with the inhibition of immunopathological processes that lead to synovitis and destruction of articular cartilage.

Basal agents for the treatment of rheumatoid arthritis are:

- aminocholine agents (delagil, plakvenil, resochin),
- gold agents (tauredon, auranofin),
- D-penicillamine (cuprenil, metalcaptase),
- sulfonamides (sulfasalazine, salazopyridasine),
- immunosuppressants (methotrexate, azatioprin, cyclophosphamide).

The most powerful basal agents are immunosuppressants – azatioprin and cyclophosphamide. They are administered in a high activity of the pathological process, in the presence of grave systemic manifestations of rheumatoid arthritis when the therapy with glucocorticosteroids and other immunosuppressive agents is ineffective or is poorly tolerated.

Local therapy methods – percutaneous administration of nonsteroid anti-inflammatory agents, glucocorticosteroid preparations (ointments, gels), dimethyl sulfoxide applications, electrophoresis, phonophoresis, balneotherapy, mud
therapy, remedial exercises – are of great importance in the treatment of rheumatoid arthritis.

*Bischofite in the treatment of rheumatoid arthritis*

Inclusion of bischofite into the complex treatment of rheumatoid arthritis makes it possible to enhance the effectiveness of treatment and to reduce side effects of pharmaceutical agents. Bischofite can be administered both during exacerbation (in a minimal or moderate activity of the process) and clinical remission of rheumatoid arthritis. Maximal activity of rheumatoid arthritis, grave systemic manifestations, vasculitis, renal amyloidosis, infectious complications, pseudoseptic syndrome impose limitations upon its administration.

In mono- and oligoarthritis local baths, compresses, ointment applications, electrophoresis with bischofite and phonophoresis with Bischal or Bischolin paste are administered. It is desirable to continue courses of bischofite therapy (ointments, compresses, baths, plaster) in the period of clinical remission at home.

In polyarthritis with a prevailing affection of articulations of the hand local baths and electrophoresis with bischofite in chamber baths can be administered.

Polyarthritis with multiple affection of major and minor joints presents indications for the administration of general bischofite baths. Besides, electrophoresis with 1-3% bischofite solution can produce a general effect on the body. It is administered according to two techniques:

1) Vermel electrophoresis;
2) Electrophoresis in 4-chamber baths.

The latter technique is preferable as it allows a direct action on minor joints of the extremities. The intensity of current in this procedure is up to 40 mA. The duration of the procedure is 15-30 min., the course of treatment consisting of 15-20 procedures.
6.1.3.4. Seronegative spondyloarthropathy

Seronegative spondyloarthropathy is a group of diseases including spondylitis, sacroileitis, enthesopathy (inflammation of a portion of a tendon in the spot of its fixation to the bone), asymmetric oligoarthritis. In spondyloarthropathy typical extraarticular manifestations are observed: inflammatory affection of the eyes (conjunctivitis, iritis, iridocyclitis), urethritis, lesion of the skin and mucous membranes. The rheumatoid factor of blood is not revealed. The patients are usually carriers of histocompatibility antigen HLA B27.

6.1.3.5. Ankylosing spondyloarthritis (Strümpell-Marie disease)

Ankylosing spondyloarthritis is a chronic ankylosing disease of articulations of axial skeleton. The incidence rate of this condition is 1-2 per 1000 people, with predominantly young people suffering. The ratio males to females is 9:1.

The disease is mainly manifested by inflammation and ossification of ligaments of the spinal column and sacrococcygeal joints with affection of peripheral joints (mostly major ones) and costovertebral joints.

For reliable diagnosis of ankylosing spondyloarthritis the following criteria are used:

a. lumbar pain of more than 3 month duration, not relieved by rest;

b. pain and stiffness in the thorax;

c. limited respiratory movements;

d. limited movement in the lumbar part of the spine;

e. iritis revealed upon examination or in past history;

f. radiographic signs of bilateral sacroileitis;

g. radiographic signs of syndesmophytosis.

The main component of the treatment of Strümpell-Marie disease is nonsteroid anti-inflammatory agent therapy. Derivatives of indoleacetic acid (indometacin) often prove most effective. The choice of a particular nonsteroid anti-inflammatory agent is made by consecutive administration of different agents.
The criterion for preference of a agent is its therapeutic effectiveness along with good tolerance.

Local administration of nonsteroid anti-inflammatory agents (ointments, sprays, gels, emulsions) is widely used along with enteral administration.

A short course of glucocorticosteroids is administered in a high activity of the process, ineffectiveness of nonsteroid anti-inflammatory agents, the presence of systemic manifestations. In active arthritis of peripheral joints intraarticular administration of glucocorticosteroids of durable action (kenalog, depomedrol, diprosan) is indicated. Among basal agents sulfasalazine is preferable when administered in the regimen described above (see the section Rheumatoid arthritis).

In grave systemic manifestations in the rare cases when glucocorticosteroids are ineffective one should resort to immunosuppressive therapy (methotrexate, azatioprin, cyclophosphamide).

Along with agent therapy intensive physiotherapy is undertaken aimed at controlling pain syndrome, inflammatory process and prevention of ankylosis development. Doing remedial exercises is an indispensable condition for the prevention of joint immobility. When there is no exacerbation swimming and daily exercise are recommended.

Bischofite in the treatment of Ankylosing spondyloarthritisis

The importance of bischofite in the treatment of Ankylosing spondyloarthritisis can hardly be overestimated. A torpid progressive treatment requires a prolonged administration of agents able to produce an anti-inflammatory and analgesic effect, to improve the functional condition of the spinal column without causing side effects. Bischofite answers these requirements to a great extent.

As in most cases of Ankylosing spondyloarthritisis disease it is the spine that is predominantly affected. It is necessary to treat the corresponding parts of the spine and the entire spinal column. Treatment with general bischofite baths is recommended; baths with traction and sitting baths are indicated in radicular
syndrome. Bischofite compresses on the lumbosacral part and peripheral joints are used. Bischofite can be administered with electrophoresis on the lumbosacral part, cervical and thoracic parts of the spine, with phonophoresis with Bischal or Bischolin ointments or Polycatan. Application of bischofite plaster or rubbing-in ointment balneological forms of bischofite is recommended overnight.

6.1.3.5. Urogenous arthritis

Rheumatologists of many countries have noted the increase in the incidence of reactive arthritis associated with urogenital infection in recent years. According to the data collected by the Institute of Rheumatology at RAMS, patients with reactive arthritis constitute about 10% of all patients at rheumatoid clinics, 50-75% of all cases of reactive arthritis being of the urogenous type. This fact is due to a high incidence of sexually transmitted diseases, on the one hand, and to the emergence of new methods of laboratory diagnostics of urogenital infections, on the other hand, which enables one to make a correct etiological diagnosis and to avoid overdiagnosis of rheumatoid arthritis.

*Chlamydia trachomatis* is recognised to be the most significant etiological factor in the development of urogenous arthritis nowadays. According to various sources, 70-80% of cases of urogenous arthritis are associated with Chlamydia infection. This causative agent was detected in the cytogram or urethral and cervical smears of patients with urogenous arthritis. When anogenital or orogenital contacts have taken place, Chlamydia can be detected in rectal and pharyngeal swabs.

Mycoplasma is another causative agent of urogenital infections, *Ureaplasma urealyticum* and *Mycoplasma genitalium* being of most importance as the genitals and urinary tract are the primary site of their inhabitation.

Urogenous arthritis is manifested as seronegative oligoarthritis associated with enthesopathy, lesion of mucous membranes and skin. This type of rheumatoid arthritis is seronegative spondyloarthritis: the rheumatoid factor is not revealed in the patient’s blood, asymmetrical sacroileitis being a frequent manifestation.
The combination of arthritis with urethritis, conjunctivitis, skin lesion is referred to by clinicians as Reiter’s syndrome (Reiter’s triad or Reiter’s tetrad depending on the intensity of the manifestations of the syndrome). The question whether urogenous arthritis should be regarded as synonymous with Reiter’s syndrome is still debatable. Researchers at the Rheumatology Research Centre of RAMS have suggested that the term Reiter’s syndrome should be applied to urogenous arthritis which is due to Chlamydia infection.

The following points are important in diagnosis of urogenous arthritis, besides clinical features of the disease:

a) chronological association with an acute urogenital infection in the past;
b) presence of chronic diseases of urogenital tract;
c) detection of Chlamydia antigens and (or) its antibodies;
d) detection of the HLA B27 gene.

The problem of effective therapy for urogenous arthritis is one of great importance for a practicing rheumatologist. The principles of therapy for arthritis associated with infection result from the mechanism of development of the articular syndrome.

First, sanation of the nidus of infection in the urogenital tract is necessary. Second, pathogenetic therapy of arthritis should be undertaken, including anti-inflammatory therapy, use of basal agents, immunomodulators, local therapy methods.

Broad spectrum antibiotics are used to sanate the nidus of infection in the urogenital tract. Tetracyclines, macrolides, azalides, fluoroquinolones, and to a lesser extent, chloramphenicol, riphampicine are active against Chlamydia. As for ureaplasma, the most effective agents against them are macrolides, azalides and tetracyclines. The choice of antibiotic is determined by the type of causative agent, individual tolerance, considerations of economy.

Pharmacotherapy of the articular syndrome in urogenous arthritis should begin with nonsteroid anti-inflammatory agents. There is no unambiguous answer to the question, which of the huge amount of NSAID is preferable in the therapy of
urogenous arthritis. The choice of this or that agent is based on individual susceptibility and tolerance. Well-reputed agents for the therapy of urogenous arthritis are derivatives of indoleacetic acid (indometacin, sulindac, etodolac). They have a high anti-inflammatory activity and are regarded as agents of the first line in the therapy of seronegative spondyloarthropathy.

Other NSAID are used in the therapy of urogenous arthritis: derivatives of propionic acid (ibuprofen, naproxen, ketoprofen, flugalin, surgam), derivatives of arylacetic acid (diclofenac, fentiazac), oxycam (pyroxcam, tenoxycam) in standard daily doses.

Glucocorticosteroids are administered when the process is very intensive and the effectiveness of NSAID is poor. It is noteworthy that glucocorticosteroids should be introduced locally – intraarticularly or periarticularly. Enteral administration of glucocorticosteroids is indicated only in the presence of systemic manifestations, such as carditis, meningoencephalitis, and polyneuritis.

To control the inflammatory process in the joints and periarticular tissues one can use local hydrocortisone injections, methylprednisolone, betametasone (diprospan), triamcinolone. One should bear in mind, however, that prolonged administration of glucocorticosteroids contributes to the persistence of infective agent and leads to articular destruction due to the negative action on cartilage metabolism.

If the course of urogenous arthritis is chronic and recurrent, administration of basal agents used in therapy of rheumatoid arthritis is indicated:

a) aminochinoline agents – chloroquine, plakvenil;
b) sulfonamides – sulfasalazone, salazopyridazine;
c) gold preparations – crinazole, auranofine, tauredone;
d) immunodepressants – azathioprin, methotrexate.

Most researchers outside Russia believe that sulfasalazone is expedient for basal therapy of urogenous arthritis. It is advisable to use this agent in protracted course of arthritis to prevent the process from becoming chronic. Sulfasalazone therapy in the daily dose of 2 g should take 3-6 months until a clinical effect is
achieved with a gradual reduction of dose. Control of thrombocyte, erythrocyte and leukocyte levels is required.

An important role in the therapy of articular syndrome is assigned to physiotherapy methods, exercise therapy, massage, sanatorium-and-spa treatment.

*Bischofite in the therapy of urogenous arthritis*

Biological action of bischofite renders important among therapeutic factors in the complex therapy of urogenous arthritis. Its combination of anti-inflammatory, antimicrobial and immunomodulatory effects enables us to recommend it for wide use for treating patients with Reiter’s syndrome. It is noteworthy that bischofite therapy is indicated in both acute and chronic course of urogenous arthritis, high intensity of arthritis does not limit administration of bischofite.

Since oligoarthritis is typical of urogenous arthritis, the most applicable methods of bischofite therapy are local baths and compresses, electrophoresis, phonophoresis with Bischolin and Bischal paste, Polycatan, use of bischofite plaster.

In moderate or minimum activity of the process rubbing-in Bischolin and Bischal paste, Polycatan is possible. In high activity a local bath with 5-10 % bischofite solution, compress with 50 % bischofite solution are more effective.

In multiple affection of the joints, typical of a chronic recurrent course it is expedient to use a general bath with 2-3 % bischofite solution. If sacroileitis and lumbar spondyloarthritis symptoms predominate a warm hip sedentary bath is possible together with general baths. In some cases with pronounced radicular syndrome traction of the spine in bischofite bath is indicated.

During remission it is advisable to continue procedures of bischofite therapy at home (compress, paste, plaster, foot and hand bath) for prevention of repeat exacerbation of arthritis. A course of bischofite treatment should be undertaken once every three months.
6.1.3.6. Diseases of extraarticular soft tissues

Diseases of extraarticular soft tissues take a prominent place in the structure of rheumatic diseases among out-patients. They include a group of rheumatic processes of degenerative or inflammatory nature developing both directly in periarticular tissues (tendons, ligaments, tendinal vaginas, fasciae, aponeuroses, articular bursae) and at some distance from the joints (muscles, subcutaneous fat, neurovascular formations). Outside Russia these diseases are included into the general term non-articular rheumatism or soft-tissue rheumatism. According to various sources, a disease of extraarticular soft tissues can be revealed in 15-25% of patients who sought ambulatory aid.

Lesion of extraarticular soft tissues comprises another large group of rheumatic processes. These processes are comprised in division 13 of working classification and nomenclature of rheumatic diseases.

Diseases of extraarticular soft tissues:

a) muscle diseases (myositis, myositis ossificans);

b) diseases of periarticular soft tissues (periarthritis, tendonitis, tendovaginitis, bursitis, ligamentitis);

c) diseases of fasciae and aponeuroses (fascitis, aponeurosis);

d) diseases of subcutaneous fat (erythema nodosum, painful lipomatosis, panniculitis);

e) polyosteoarthralgia (fibromyalgia).

In recent years we have witnessed an increase in the amount of patients with chronic muscular pain of local or diffuse nature: it is usually a pain in the lower region of the back – or diffuse muscular pain – fibromyalgic syndrome. We deem it important to classify the diseases of extraarticular soft tissues into local and diffuse lesions, as the mechanism of their development is different which entails different therapeutic tactics.

The prevalence of this pathology is due to not only high morbidity rates but also to inefficient treatment of extraarticular pathology, and the incidence of protracted and recurrent types of soft tissue diseases is growing, as a result. One
third of patients with various types of articular lesion demonstrate a chronic course, many of them having sought medical advice and received therapy whose effect usually proved short-term.

This situation is apparently due to the belief commonly held by clinicians that the main objective in treating such patients is arresting the pain syndrome and improving dysfunction. And all the time the fact is overlooked that the process of periarticular structure regeneration is a prolonged one requiring a rehabilitation complex including correction of metabolic imbalance.

Most often, degenerative and inflammatory processes in the soft tissue region of musculoskeletal apparatus develop secondary to physical overwork or recurrent microtrauma. Microtrauma can take place as a result of occupational, sportive or domestic accident due to the surface location of periarticular structures and their high functional loading. It has been determined that frequently repeated stereotype movements lead to the development of degenerative process.

Depending on the extent of tissue vascularisation the outcome of pathological process varies. In poorly vascularised tissues ruptures of separate fibrillae with the formation of necrotising foci, hyalinization and calcification of collagen fibres develops which is due to constant tension and microtrauma. In each particular case the anatomical structure of tissues modifies pathological and clinical picture of the lesion. Why lesions of periarticular tissues are localised predominantly in the shoulder region is quite understandable: the short rotating muscles of the shoulder and the tendons of the biceps muscle are constantly under great functional strain, often under compression as the tendons are located in a narrow space.

Diagnostics of periarticular soft tissue pathology is mainly based on clinical presentations. Laboratory findings are, as a rule, without variance. Radiographic evidence in the form of tendon and ligament calcification is discernible only after a prolonged chronic course of the process. Ultrasonography and MR-imaging are quite informative diagnostic methods; however, they cannot be widely used in ambulatory rheumatologic practice for reasons of economy.
Main clinical manifestations of some common periarticular soft tissue
diseases are given below.

**Tendonitis, tendovaginitis, ligamentitis**

*De Quervain’s disease* – tendovaginitis of the short extensor muscle and the
long abductor muscle of thumb, or stenotic ligamentitis of the first tunnel of dorsal
carpal ligament.

*Carpal tunnel syndrome* – tendovaginitis of flexor muscles of fingers and
hand or stenotic ligamentitis of the transverse carpal ligament.

*“Jerk finger”* – tendovaginitis of superficial flexor muscles of finger,
stenotic ligamentitis of orbicular finger ligaments.

*Dupuytren’s contracture* – palmar aponeurosis. It is a chronic
inflammatory disease of the ulnar part of palmar aponeurosis where tendons of 4<sup>th</sup>
and 5<sup>th</sup> fingers are involved in the fibrous cicatricial process with the formation of
tendogenic contracture of these fingers. No pains are felt. Induration of palmar
aponeurosis at the base of 4<sup>th</sup> and 5<sup>th</sup> fingers, induration and shortening of these
fingers can be detected.

**Bursitis and tendobursitis**

Clinical presentations depend on the localisation and depth of articular
bursa. In superficial bursitis there are painful, clearly confined round swellings that
are sometimes hyperemic, with skin hyperthermia above them. In profound bursitis
diagnostics is difficult; there are symptoms of muscle or tendon compression, some
movements are limited and painful.

*Humeral bursitis* – subacromial bursitis develops most often. It is a
component part or a variation of Duplay’s disease.

*Ulnar bursitis* usually develops in people whose occupational activities
involve constant pressure on the ulnar region. Pain and tumour-like formation in
the olecranon region develops. Flexing in the elbow is limited.
Trochanteric bursitis is localised in the region of the greater trochanter. It is a variation of hip joint periarthritis. Abduction of the hip typically yields maximum painfulness.

Ischiadic bursitis is localised between the ischiadic tuber and gluteus maximus muscle. It is manifested by pains in the region of ischiadic tuber with aggravation upon flexing the hip.

Prepatellar bursitis is inflammation of the synovial bursa localised between the skin and patella. A clear confined swelling over the patella is visible.

Baker’s cyst can be both a disease per se and a consequence of gonarthritis as in 50 % of cases the popliteal bursa is connected to the articular cavity. Pains in the popliteal region are typical, full extension in the knee joint is difficult and painful; a tumour-like formation can be detected in the popliteal region whose puncture yields synovial-like fluid.

**Periarthritis**

Scapulohumeral (shoulder) periarthritis falls into three types depending on the severity of affection: simple, acute (acute painful shoulder), chronic ankylosing scapulohumeral periarthritis (locked or “frozen” shoulder).

- Periarthritis of elbow, or external humeral epicondylitis (“tennis elbow”);
- Internal humeral epicondylitis, or epitrochleitis (“golfer’s elbow”);
- Hip joint periarthritis (trochanteritis);
- Knee joint periarthritis;
- Foot periarthritis (talalgia, achillodynia, subcalcaneal bursitis, heel spur).

**Myositis, myofascial pain syndrome**

Clinical manifestations depend on anatomical features of the affected muscles. There are, however, common features typical of this condition:

a) local pain aggravating upon energetic movement;

b) pain on palpation in the area of affected muscles;

c) hyperemia and hyperthermia in the affected area in acute myositis;
d) induration of muscle, uneven “ropelike” consistency of muscle;

e) forced position of the body or limbs;

f) limited movement of the limbs, spine, respiratory excursion due to pain;

g) reduced muscular strength in dynamometry;

h) formation of solid nodules and bands;

i) increased muscle tone;

j) muscular atrophy, decreased muscle tone in an acute course of the disease;

k) vegetative polyneuropathy and Raynaud’s syndrome upon compression of neurovascular fascicle.

First of all, we would like to dwell on the therapy of periarticular tissue diseases: periarthritis, tendonitis and tendovaginitis, bursitis, ligamentitis. We find it necessary to consider this problem in detail as extra-articular pathology does not receive its due attention, unfortunately.

Conventional therapy of these diseases begins with administration of non-steroid anti-inflammatory agents (NSAID). This choice is quite justified because patients who take initiative in seeking medical aid usually display reactive inflammation in the affected area. Pain at rest or night pain is an important clinical sign of the extent of a marked inflammatory process.

One should bear in mind, however, that administering NSAID we only affect the tip of the iceberg which is reactive inflammation while the main mechanism is the degenerative-dystrophic process in the connective tissue. Besides, prolonged NSAID therapy has a negative effect on connective tissue metabolism aggravating degenerative disorders.

The mechanism of anti-inflammatory action of non-steroid agents is the same for all preparations in this group; it is based on suppression of synthesis of inflammation mediators (prostaglandins) by inhibiting the activity of cyclooxygenase enzyme. Suppressed prostaglandin synthesis, however, results in disruption of protective properties of gastric mucosa and development of gastropathy.
The choice of NSAID is made empirically considering the extent of analgesic and anti-inflammatory effect, duration of the effect, individual tolerance of the agent. If there is no effect within a week a agent of another chemical group of NSAID should be administered.

To reduce side effects local NSAID therapy is used. Nowadays there is a variety of medicinal forms for external use. Anti-inflammatory ointments, gels, sprays, plasters with NSAID as an active component are widely used in clinical practice. Besides, NSAID can be administered in the form of rectal suppositories used once a day, usually before night-time. After local NSAID therapy the incidence of side effects is reduced several times.

In spite of a wide choice of these agents and variety of their forms, they may prove ineffective in severe periarticular lesions. In this case local glucocorticosteroid therapy is considered necessary. Numerous clinical observations demonstrate high effectiveness of this group of agents in the therapy of scapulohumeral periarthritis, epicondylitis, tendonitis, bursitis of varying localisation in acute course of these processes. Local injections of glucocorticoids are usually administered in combination with local anesthetics (Novocain, lidocain). Periarticular injection of anesthetics without glucocorticosteroid agents can be used for a quick control of pain syndrome; use of anesthetics, however, does not affect the outcome of treatment significantly.

Practicing therapists should be warned against over-indulgence in local glucocorticosteroid therapy. The fact is that acute shoulder periarthritis can last for up to 18 months! In chronic types of the disease the recurrent process can last for many years. Multiple injection of glucocorticosteroids leads to local soft tissue atrophy, sclerosis of periarticular structures, and development of neurodystrophic syndrome in the affected limb.

In this respect one should give preference to methods that enable one to achieve more favourable, if deferred, results. Use of chondroprotectors is one of such methods.
Chondroprotectors are currently believed to be basic agents in the therapy of osteoarthritis considering the modulatory action of these agents on cartilage metabolism. Agents of this group are rumalon, artheparon, alflutop, chonsurid. Besides having proven anti-inflammatory action due to stabilisation of cellular membranes and reduced activity of cellular hydrolase, hyaluronidase and glucuronidase in particular, these agents slow down degradation of connective tissue structure and stimulate the activity of chondrocytes and fibroblasts producing the main connective tissue components.

Research carried out at the laboratory of soft tissue diseases at the Clinical and Experimental Rheumatology Research Centre of RAMS has established pronounced therapeutic effect of agents containing glycosaminoglycan (artheparon, alflutop) in common types of periarticular lesions: periarthritis and tendonitis.

Besides, an ointment containing artheparon, dimethyl sulfoxide and voltaren was developed for local therapy of periarticular lesions. Administration of the ointment yielded pronounced improvement of clinical manifestations and laboratory tests which demonstrate the extent of connective tissue lesion. The therapeutic effect of the therapy of ointment application with artheparon, dimethyl sulfoxide and voltaren did not differ significantly from that of the method of periarticular artheparon injection. The preparation chondroxid containing dimethyl sulfoxide and chondroprotector chonsurid made in Russia is an analog of this ointment.

It has been established that application of 30-50 % dimethyl sulfoxide solution in combination with NSAID leads to considerable reduction in such manifestations of extra-articular soft tissue diseases as pain on movement and at rest, stiffness, limited movement, swelling and hyperthermia in the affected area.

The repertory of complex therapy of extra-articular soft tissue diseases is not confined to pharmacological treatment. This complex therapy also includes various electrotherapy, magnitotherapy, ultrasound, low-level laser irradiation methods which enhances the effectiveness of patients’ rehabilitation.
Bischofite administration in local types of extra-articular soft tissue diseases

Bischofite administration in the therapy of extra-articular soft tissue diseases makes it possible to achieve several objectives of pathogenetic therapy: to reduce pain syndrome due to secondary inflammation, to reduce stiffness and movement constraint in the joints by relaxing the muscles, to check the development of secondary compression syndrome, to prevent severe sclerotic processes in a chronic course of the disease, to stimulate regeneration of affected structures.

Clinical tests have shown that inclusion of bischofite into the therapy of various types of extra-articular soft tissue diseases contributes to the reduction of pain, stiffness, increases the volume of active movements at earlier stages. Besides, laboratory tests that reflected the extent of periarticular structure affection showed improvement, too. Methods of bischofite application depend mainly on clinical characteristics of the disease.

Bischofite in the therapy of periarthritis

In periarthritis of the shoulder compresses with 30-50 % bischofite solution are administered. In the initial procedure 30 % solution is used (diluted 1:2), duration 30 minutes. Then bischofite concentration is raised to 50 % (diluted 1:1), duration of the procedure can be up to several hours. Before applying the compress the skin is warmed with a sun wave lamp. After removing the compress the skin is washed with warm water and covered with flannel or wool. The course should include up to 20 procedures 2-3 hours each.

Bischofite compresses are indicated in various types of shoulder periarthritis. In acute painful shoulder bischofite compresses can be combined with application of bischofite plaster or paste Bischolin, Bischal, Polykatan. In adhesive capsulitis of humeral joint several courses of compress therapy are indicated, each course consisting of 10-20 procedures. Repeat courses are administered with a 2 month interval. If the course consists of 10 procedures, repeat courses begin in 1 month. Another alternative is bischofite electrophoresis course therapy, or
Bischolin phonophoresis course therapy. Afterwards rubbing-in of bischofite paste or application of bischofite plaster is recommended.

In periarthritis of the elbow (epicondylitis and epitrochleitis) bischofite compresses are also effective. 8-10 procedures usually suffice to achieve a therapeutic effect. Bischofite electrophoresis in the ulnar joint region or Bischolin phonophoresis is indicated, the course consisting of 10-12 procedures. These procedures can be combined with rubbing-in Bischolin or Bischal at home.

In the therapy of foot periarthritis local bischofite baths are indicated, the concentration increasing from 5 % to 20 % (on condition that there are no signs of dermatitis). The duration of the procedure can be up to 1 hour, the course of treatment consisting of 10-20 procedures. Bischofite compresses are an alternative to local baths. Ointment forms of bischofite can also be used.

_Bischofite in therapy of tendonitis, tendovaginitis, and ligamentitis_

In De Quervain’s disease the most effective method is electrophoresis with 3-5% bischofite solution, current intensity up to 10 mA. The duration of the procedure should be up to 20 min, the course of treatment consisting of 10-15 procedures. Electrophoresis can be carried out in a one-chamber bath with bischofite concentration 2-3 %. An alternative treatment regimen would be compress application with 30-50 % bischofite solution as described above. Compresses can be combined with ointment application.

Ligamentitis, carpal tunnel syndrome in particular, also requires a course of bischofite compresses, or bischofite administration through electrophoresis or phonophoresis. There can also be a course of baths with 5-10 % bischofite solution (one can use contrast baths, bischofite temperature being 10-16°C and 40-42°C. The wrist and the region of radiocarpal joint should be immersed in the bath completely. Contrast baths are indicated in manifestations of vegetative polyneuralgia, Raynaud’s syndrome. Ointment application and bischofite plaster are also a possibility.
In Gouillon canal syndrome bischofite should be applied to the entire ulnar surface of the forearm covering elbow and radiocarpal joints. A therapy with local baths is a possibility, but the arm should be immersed up to the lower third of the shoulder. Phonophoresis with Bischolin produces a favourable effect (applying it to the internal surface of elbow joint and shoulder to the hand).

_Bischofite in therapy of bursitis_

Baker’s cyst and achillobursitis are the most common clinical varieties of bursitis. Subacromial bursitis is a type of scapulohumeral periarthritis.

In Baker’s cyst the treatment should start with warm compress with 50 % bischofite solution, the concentration being 30 % at the initial procedure only. Before applying the compress the popliteal area should be warmed with dry heat. The duration of procedure is 1-3 hours, the course of treatment consisting of up to 20 procedures. In poor tolerance of strong bischofite concentrations the alternative is administration of electrophoresis with 1-3 % bischofite solution, current intensity 10-15 mA. The duration of the procedure is 20 min., the course of treatment consisting of up to 20 procedures. Ointment forms of bischofite can be used; however, one should avoid intensive rubbing-in; use of Bischoplast is preferable.

In achillobursitis treatment regimen is the same as in foot periarthritis.

_Bischofite in therapy of myositis and myalgia_

In diffuse myalgia, myositis of back muscles and lumbosacral region general baths are indicated, the method being as described in chapter 6.1.4. In local affection of skeletal cervical muscles, extremities of lumbosacral region bischofite compresses are effective. For the compresses on the extremities and lumbar region 30-50 % solution is used, for compresses on the neck – 10 % bischofite solution. Treatment response usually becomes apparent after 5th or 6th procedure, the course of treatment consisting of 10-20 procedures. An alternative to compresses would be bischofite electrophoresis or Bischolin phonophoresis. Ointment applications or
bischofite plaster are a possibility. The application of bischofite paste combines well with therapeutic massage.

**Primary fibromyalgia**

Since primary fibromyalgia is regarded as a psychosomatic disorder, it is psychotropic agents that constitute the basis of pharmacotherapy. It is well known that aside from muscle pain patients often complain of disturbance of sleep, irritability, undue fatigability. These symptoms, as a rule, justify administration of tranquillisers – benzodiazepine. At the same time clinical observations and electrophysiological investigation shows that benzodiazepine therapy aggravates psychological disorders and does nothing to relieve muscular pain in patients with primary fibromyalgia as this agent has a negative effect on deep sleep. Considering this, benzodiazepine should be avoided in this syndrome. Psychological disorders are managed with the help of antidepressants, using tricyclic antidepressants.

Non-steroid anti-inflammatory agents are traditionally used in fibromyalgic syndrome management. At the same time we should point out that the therapy of this disease should be a prolonged one, and it often produces undesirable side effects. Monotherapy with NSAID in patients with primary fibromyalgia should be avoided. It is expedient to combine nonsteroid agents, predominantly those with analgesic effect, with basic antidepressant therapy. Combination of antidepressants with local NSAID therapy is indicated. This combination can be supplemented with local dimethyl sulfoxide applications.

As in other clinical types of extraarticular soft tissue diseases, methods of agentless therapy are of great importance: physiotherapy, exercise therapy, acupuncture, and also psychotherapy whose objective is psychological rehabilitation and social adaptation of patients.

**Bischofite in therapy of fibromyalgia**

Bischofite therapy of primary fibromyalgia is aimed at achieving two objectives:
1. impact on muscular system

2. general impact on the body.

In fibromyalgia general bischofite baths should be used as this method fully covers the above mentioned objectives. It is noteworthy that this condition is often combined with the syndrome of chronic fatigue whose origin is to a great extent due to reduced levels of intracellular magnesium. The reduction of chronic fatigue symptoms upon exposure to bischofite seems to be associated with the diffusion of magnesium salts in the tissue.

In an acute condition a course of 20 daily procedures is administered. A repeat course can be recommended in 1-2 months. Bischofite therapy is combined with antidepressant and NSAID therapy.

After a course of baths one can administer paste applications on the skin in the region of algesia. The paste can be applied 2-3 times a day, the course of treatment lasting for 10-20 days.

If the pain syndrome predominates in the lower part of the back and lower extremities, one can recommend sitting baths with bischofite, or electrophoresis in the lumbar, femoral and crural region.

Overall impact on the body can be achieved with the help of bischofite electrophoresis. In this case one electrode is placed on the interscapular region, and the other two – on posterior surface of shins in the lower third. 3 % bischofite solution is used; the duration of the procedure is 20-30 min., the course of treatment consisting of 20 procedures. Bischofite electrophoresis with four-chamber baths as described in chapter 6.1.4. can also produce an overall impact on the body.

Another way of managing fibromyalgia is combination of bischofite applications with irradiation of pain spots with infrared laser.

We should point out, in conclusion, that management of primary fibromyalgia is a difficult task of which bischofite therapy is an indispensable part.
6.1.4. Recommendations on practical application of bischofite

The balneotherapeutic use of bischofite calls for general, local and sitting baths, traction of the spine in bischofite baths (Зборовский А.Б. и др., 1997; Сулим Н.И., Спасов А.А. и др., 1999).

**General baths with bischofite**

Bischofite brine is poured into a bath full of water in the ratio 1:50 (i.e. 2 l of solution per 100 l of water). Recommended water temperature should be 36-37°C. The contents of the bath are carefully stirred. The patient takes a general bath for 15-20 min., duration of the initial procedure can be 5-10 min. While the patient is in the bath, his condition should be monitored, the pulse rate, arterial blood pressure, respiratory rate are taken. After the bath bischofite is washed away with warm water. If there are no side effects, the course should include 10-12 procedures taken daily or every other day. If side effects develop, or articular syndrome exacerbates, the procedures are cancelled.

**Sitting baths with bischofite**

Bischofite solution in water is prepared in the ratio 1:50. The patient sits down in the bath immersing his pelvis, abdomen and legs. Sitting baths can be warm (36-37°C) lasting for 15-30 min., or hot (40-41°C) lasting for 10-15 min. After the bath the patient takes a warm shower. The course of treatment is 10-15 procedures provided there are no side effects.

**Local baths with bischofite**

2-3 % bischofite solution is made with bischofite brine and water in the ratio 1:50-1:30. The resulting solution is warmed to the desired temperature and poured into a basin, then the legs (or feet) or arms (hands) are immersed into it. The baths can be warm (36-37°C) or hot (40-41°C). The duration of warm local baths is up to 30 min., that of hot baths – up to 20 min. The course of treatment is 10-15 procedures.
**Traction of the spine in bischofite baths**

There are several techniques of traction of the spine in baths.

- **vertical traction** is performed in vertical baths or pools filled with 1-2 % bischofite solution. The patient puts on a belt with traction weight on the pelvis. Leaning against the headrest and armrests the patient stays in the bath for 15-20 min. The weight is gradually increased from 2 to 20 kg. The course of treatment is 10-12 procedures.

- **horizontal traction** is performed in a bath with 1-2 % bischofite solution. The patient is laid on a board; his shoulder and pelvic girdle are fixed with special supports. The weight is attached to the lower end of the support with a pulley system. The traction starts from 5 kg, increasing the weight to 30 kg. The duration of the procedure is 15-20 min.; the course of treatment is 10-12 procedures.

- **traction with one’s own weight** is performed by fixing the patient’s shoulder girdle with a bracket attached at the head end of the bath. The feet are fixed with cuffs at the opposite end of the bath. The traction is performed in a warm water (36-37°C) containing 1-2 % of bischofite salt. The duration of the initial procedure is 5 min., and then it is extended to 15 min. The course of treatment is 10-12 procedures.

**Bischofite compresses**

Bischofite aqueous solutions can be used in treatment with compresses. For compresses higher bischofite concentrations, from 10% to 50%, are used. In good tolerance of the procedure 30 % - 50 % solutions can be recommended. The technique of applying bischofite solution is as follows: prior to the procedure the affected joint is heated with an ultraviolet lamp or dry heat. A cloth saturated with bischofite solution warmed to 40°C and wrung out is placed on the joint, covered with cellophane and wrapped warmly. The compress is left for 1-2 hours, the initial procedure lasting for 15-20 min.

After removing the compress the skin is washed with warm water, the joint is wrapped with dry flannel or wool. Compresses can be applied to 2-3 joints.
simultaneously. The course of treatment is 15-20 procedures. The procedures are easy to carry out at home.

**Electrophoresis with bischofite solution**

1-3 % solution of bischofite salt is used for electrophoresis.

Gauze saturated with bischofit solution is placed under the anode so that the distance between electrode edges exceeds their size. The electrodes are usually placed on the anterior and posterior surface of the joint or on the medial and lateral surfaces. If it is smaller joints of hands and feet that are affected, a chamber bath with 1-3 % bischofite solution (36-37°C) serves as an electrode, the second electrode is placed as a cuff on the hand or foot. In multiple affection of hands and feet it is expedient to use two-, three- or four-chamber baths. The intensity of current when handling the spine and greater joints is 10-15 mA. The duration of the procedure is 15-20 min., the course of treatment is 10-20 procedures taken daily or every other day.

In affection of small joints **chamber baths** are preferable. In this procedure the patient immerses the affected limb into the bath with 1-3 % bischofite solution; the cathode is placed on the limb on the more proximal surface. The intensity of current can be up to 30 mA, the duration of the procedure is 15-20 min., the course of treatment is 12-15 procedures.

When **four-chamber baths** are used, the entire body feels the impact rather than just the joints of extremities. The patient is sitting on a chair, the limbs immersed in baths with 1-3 % bischofite solution of 36-37°C. Each bath is connected to the positive pole of the device. Each bath has a second electrode, carbon one, covered from direct contact with the patient’s body. The procedure is carried out at current intensity up to 30 mA. During the procedure the patient should not remove the limbs from the baths. The duration of the procedure is 15-30 min., the course of treatment is 10-15 procedures.
Application of bischofite pastes Bischolin, Bischal and Polycatan

Bischofite paste is applied in a thin layer on the affected area and is rubbed in with light motions for 2-3 min. The paste can be applied 3-4 times during a day. The course of treatment is 10-20 days; a repeat course should start in 2-4 weeks.

Bischofite phonophoresis

The affected area is covered with the paste. A 4 cm vibrator is moved along the surface of the joint maintaining good contact in a pulsed or continuous mode, the radiated power 0.4-0.6 W/cm. The duration of the procedure 5-10 min., the course of treatment is 6-10 procedures taken daily or every other day.

Bischofite plaster

Bischofite plaster is moistened with warm water and applied inside to the affected area, wrapped warmly and left for 8-10 hours (overnight). After the procedure bischofite is washed away with warm water. The plaster can be applied to 2-3 areas simultaneously. The course of treatment is 10-20 procedures taken daily or every other day.

Application of dry bischofite

The salt is diluted with warm water (340-360 g is poured into 1 litre of water) and is used as balneological bischofite brine.
6.2. Application of bischofite mineral in dentistry

6.2.1. Introduction.

Periodontopathy is one of the most common and complicated diseases of the faciomandibular area. According to the evidence of World Health Organisation (WHO) up to 90 % of world population suffer from periodontopathy; at the age over 40 up to 80 % tooth extractions are due to periodontopathy.

In the structure of periodontal diseases inflammatory diseases prevail: gingivitis, periodontitis. About 90 % of gingivitis cases are catarrhal gingivitis (Курякина Н.В., Кутепова Т.Ф., 2000).

According to the International WHO classification, 5 main groups of periodontal diseases are recognised: gingivitis, periodontitis, parodontosis, tumorous and tumour-like lesions (Дмитриева Л.А. и др., 1997).

Specialists in Russian Federation use the classification adopted at the XVI Plenary meeting of Russian Dentists’ Society in 1983. It is based on the nosological principle used by WHO. According to this classification the following diseases are distinguished:

1. Gingivitis – gum inflammation due to the adverse effect of local and general factors; its course does not affect odontogingival juncture.
   i) Types: catarrhal gingivitis, necrotising ulcerative gingivitis, hypertrophic gingivitis.
   ii) Severity: mild, medium, grave.
   iii) Course: acute, chronic, aggravated.
   iv) Localisation: localised, generalised.
2. Periodontitis – inflammation of periodontal tissues characterised by progressing destruction of periodontium and bones of alveolar process of the jaws.
   i) Severity: mild, medium, grave.
   ii) Course: acute, chronic, aggravated, remission.
   iii) Localisation: localised, generalised.
i) Severity: mild, medium, grave
ii) Course: chronic, remission.
iii) Localisation: generalised.

4. Idiopathic diseases with progressing lysis of periodontal tissue (periodontolysis): Papillon-Lefevre syndrome, granulocytopenia, agammaglobulinemia, decompensated diabetes, histiocytosis X, etc.

5. Parodontome – tumours and tumour-like processes in the periodontium.

Rapidly progressing types of periodontitis have come to be recognised in recent years:

- localised juvenile periodontitis;
- generalised juvenile periodontitis;
- rapidly progressing post-juvenile periodontitis;
- rapidly progressing periodontitis of the adults.

**6.2.2. Effectiveness of bischofite administration**

Experimental evidence (Спасов А.А., Островский О.В. и др., 1999; Спасов А.А., Темкин Э.С. и др., 1999) of anti-inflammatory, antibacterial, immunostimulating action of bischofite, stimulation of epithelisation of oral mucosal lesions, and also evidence of how important magnesium is for dental tissue formation were the reasons for using bischofite in dentistry.

One can name the following aspects of bischofite administration in dental practice (Помойницкий В.Г., 1996):

1. Use of bischofite in dressings used in the therapy of periodontopathy; instillation in periodontal pockets due to its pronounced anti-inflammatory effect;
2. Dry bischofite can be used as one of the components in manufacture of biological pastes for treatment of incomplete pulpiteis and deep caries;
3. Due to high mineralisation of bischofite the latter can be used as remineralising solution in treatment and prevention of initial caries stages;
4. Manufacture of improved dental products for filling carious cavities and fixing orthopedic devices. As research data show, the addition of bischofite accelerates the silicon-forming process which improves physical and mechanical properties of dental cement;
5. Use of bischofite in the currently developed dental treatment pastes; dental rinses and other articles of oral hygiene.

6.2.2.1. Inflammatory diseases of oral mucosa

A clinical study of bischofite brine approved for dental practice under the name Polycatan included 335 patients of both sexes (113 men, 232 women) aged 18-65. The study was carried out at preventive dentistry department (Prof. Zekovsky V.P.) of Arkhangelsk Medical Academy, preventive dentistry department at the advanced training faculty (Prof. Segen I.T.) and preventive dentistry department (Prof. Temkin E.S.) of Volgograd Medical Academy, Dentistry clinic of Medical Association of Voronezh region (Ziborova G.M., head doctor), propedeutic preventive dentistry department (Prof. Maximovsky Y.M.) of Semashko Dental Institute in Moscow, Central Research Institute for Dentistry (Prof. Borovsky E.V.), preventive dentistry department (Prof. Tsarinsky M.M.) of Kuban Medical Academy, and preventive dentistry department of Stavropol Medical Academy (Prof. Grechishnikov V.I.)

Table 16 represents the distribution of patients with diseases of oral mucosa.

The diagnosis was made on the basis of complex clinical trials and instrumental examination including, apart from physical examination, examination of periodontal index, hygiene index, and oral hygiene index.
Table 16

Distribution of patients according to the nature of disease

<table>
<thead>
<tr>
<th>№</th>
<th>Diagnosis</th>
<th>Number of patients</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>study group</td>
<td>control group</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Generalised mild periodontitis</td>
<td>45</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Medium periodontitis</td>
<td>194</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Grave periodontitis</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Gingivitis</td>
<td>61</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Allergic stomatitis</td>
<td>6</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Ulcerative necrotising stomatitis</td>
<td>6</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Chronic recurrent aphthous stomatitis</td>
<td>9</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Lichen ruber planus</td>
<td>5</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Trauma of oral mucosa</td>
<td>5</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Total</strong></td>
<td><strong>335</strong></td>
<td><strong>43</strong></td>
<td></td>
</tr>
</tbody>
</table>

Clinical effectiveness of the preparation was determined on the basis of the patients’ subjective sensations, examination of oral cavity, a complex estimation of the above indexes before and after therapy, depth of periodontal pockets, the presence of discharge from them, tooth mobility. The amount of gingival fluid was determined with the technique of G.M. Barer (Г.М. Барер, 1996). The patients were treated with Polycatan in the setting of dental clinic; in several cases the preparation was given to the patient to use at home. In this case the patient received instruction on using Polycatan, with a follow-up examination in 5-7 days. During Polycatan therapy use of any other preparations with a similar effect was avoided.

Besides applications, Polycatan and Polyminerol baths, the therapy always included removal of dental deposit and dental calculus. Polycatan was diluted 1:10. If there were complaints about a stinging sensation, the dilution was increased to 1:15.
After 5-8 procedures with Polycatan the inflammatory manifestations subsided, the wound surface was cleared from necrotic patches, the wounds began to granulate, and the existing erosions were in the process of active epithelisation. After 4-5 procedures purulent discharge from the pockets stopped; in mild periodontitis the pockets disappeared in most patients. In medium periodontitis the pockets decreased by 1-2 mm, the amount of gingival fluid decreased by 13.1 %, gingival hemorrhage subsided or ceased. When Polyminerol was used, the onset of the anti-inflammatory effect was 2-3 days later than in Polycatan therapy; and it was less pronounced. In patients with gingivitis the amount of gingival fluid decreased by 23.9 %.

Exposed to the action of Polycatan, the necrotic patches came off quickly, the wound surface cleared and epithelised. The evidence of therapeutic effectiveness of Polycatan is represented in table 17.

On the basis of this evidence one can state that the complex effect of the tested preparation Polycatan is stronger than that of Polyminerol. Thus, a persistent stabilisation of the process took place in 127 out of 335 patients in the study group, improvement – in 206 patients. No patient showed deterioration of the process.

In Polyminerol therapy stabilisation of the process was achieved in 10 patients, improvement – in 20 out of 40. The preparation had no effect on the course of the disease in 12 people; in two cases aggravation of the pathological process was observed.

The dynamic change of some indexes (periodontal index, hygienic index, gingivitis index) obtained during clinical trials of the preparation is an objective criterion of the favourable effect exercised by Polycatan on periodontal tissues and oral mucosa. The data presented in Table 18 enable us to draw the conclusion about high effectiveness of Polycatan as an anti-inflammatory agent in diseases of periodontium and oral mucosa. It illustrates the reduction of hygienic index from 3.5 to 1.3 in medium periodontitis, and the positive change of hygienic and periodontal indices in diseases of oral mucosa.
## Table 17

**Comparative evidence of the effect of Polycatan and Polyminerol therapy**

<table>
<thead>
<tr>
<th>№</th>
<th>Diagnosis</th>
<th>Effect of therapy with Polycatan and Polyminerol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Stabilisation</td>
</tr>
<tr>
<td>1.</td>
<td>Gingivitis</td>
<td>19</td>
</tr>
<tr>
<td>2.</td>
<td>Mild periodontitis</td>
<td>18</td>
</tr>
<tr>
<td>3.</td>
<td>Medium periodontitis</td>
<td>78</td>
</tr>
<tr>
<td>4.</td>
<td>Grave periodontitis</td>
<td>6</td>
</tr>
<tr>
<td>5.</td>
<td>Allergic stomatitis</td>
<td>5</td>
</tr>
<tr>
<td>6.</td>
<td>Ulcerative necrotising stomatitis</td>
<td>2</td>
</tr>
<tr>
<td>7.</td>
<td>Chronic recurrent aphthous stomatitis</td>
<td>-</td>
</tr>
<tr>
<td>8.</td>
<td>Lichen ruber planus</td>
<td>-</td>
</tr>
<tr>
<td>9.</td>
<td>Trauma of oral mucosa</td>
<td>-</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>127</td>
</tr>
</tbody>
</table>
Table 18

**Dynamics of change of periodontal indices in Polycatan therapy**

<table>
<thead>
<tr>
<th>№</th>
<th>Diagnosis</th>
<th>Periodontal index</th>
<th>Hygienic index</th>
<th>Oral hygiene index</th>
</tr>
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<tr>
<td></td>
<td></td>
<td>A</td>
<td>B</td>
<td>A</td>
</tr>
<tr>
<td>1</td>
<td>Gingivitis</td>
<td>2.8</td>
<td>1.3</td>
<td>3.8</td>
</tr>
<tr>
<td>2</td>
<td>Mild periodontitis</td>
<td>3.2</td>
<td>1.6</td>
<td>2.75</td>
</tr>
<tr>
<td>3</td>
<td>Medium periodontitis</td>
<td>4.7</td>
<td>2.5</td>
<td>3.15</td>
</tr>
<tr>
<td>4</td>
<td>Diseases of mucosa</td>
<td>1.6</td>
<td>1.1</td>
<td>3.8</td>
</tr>
</tbody>
</table>

A – periodontal indices before treatment
B – periodontal indices after treatment

The time required for homeostasis was 30% less than in patients using Polyminerol; halitosis disappeared; discharge from the pockets ceased.

Patients showed good tolerance of the preparation, only 6 out of 335 patients complained of a stinging sensation which disappeared within 5 minutes.

Another positive effect of Polycatan revealed during the trial was reduced hypersensitivity of teeth to thermal irritation, especially in patients with strong dental abrasion.

6.2.2.2. **Filling of teeth**

Zorina М.А. (Зорина М.А., 1996) has developed the following filling material: zinc phosphate cement – 74%, orthophosphoric acid solution – 20%, and bischofite – 6%. Trial results show that strength properties of this filling material are 1.1 – 1.3 times higher than the standard ones. This phenomenon seems to be due to Sorel’s effect typical of magnesium chloride (Кенпе Н.И. и др., 1975). This filling material did not produce toxic effects; it had a stable antimicrobial action against various microorganisms of constant and incidental microbial flora of the oral cavity, and mixed microbial flora of root canals.
Clinical trials of the material (34 fillings) show that “bischofite-phosphate-cement” fillings used in pediatric dentistry are stronger mechanically than “phosphate-cement” fillings, and setting time is shorter which is important considering children’s salivation. In all cases of odontodiagnostic control there was no pathologic reaction of the pulp.

6.2.2.3. Objects of oral hygiene

Tooth pastes and mouth washes with seawater, brine and Dead Sea salts have been used as articles of oral hygiene for quite a long time (“Pomorin” and “Balsam” toothpaste etc).

Dnepropetrovsk Medical Academy and Zaporozhie Medical Institute have developed Bischofitnaya toothpaste. Clinical trials have confirmed therapeutic and preventive properties of this toothpaste (Дзяк Г.В. и др., 1996)

6.2.3. Use of bischofite in complex therapy

Principles of treating inflammatory periodontal diseases (gingivitis, periodontitis) are closely associated with the notion of genesis and development of inflammation in periodontal tissues.

Most researchers consider local reasons to be one of the leading factors of etiology and pathogenesis of periodontal diseases. The inflammatory process in periodontal tissues is a complex of microcirculatory, hematological reactions and those of connective tissues. There is a supposition that if an inflammatory reaction is limited to formation of inflammation mediators, an acute inflammation develops while the addition of immunological reactions leads to the development of a prolonged chronic inflammatory process (Дмитриева Н.И., 1997).

While ascribing the leading role in the onset of periodontal inflammatory process to the microbial factor, Lemetskaia T.I. (Лемецкая Т.И., 1988) considers it wrong to reduce the etiology of the disease solely to it. Development of gingivitis and periodontitis should be regarded as a result of interaction between the microbial factor and the patient’s body which, according to many authors,
justifies the use of the following in the therapy of inflammatory periodontal
diseases: antibacterial therapy, pathogenetic therapy, therapy enhancing defensive
and adaptive mechanisms, rehabilitation therapy.

In clinical practice of treating the inflammatory diseases of periodontium
and oral mucosa monotherapy with anti-inflammatory and antibacterial agents does
not always prove effective. That is why combination therapy or agents combining
these effects has been used in recent years (Holroyd S.V., Wynn R.L., 1983).

A new medical product Polycatan developed in Volgograd Medical
Academy on the basis of bischofite is of considerable interest in this respect. As
experimental and clinical trials have shown, Polycatan has an anti-inflammatory,
antimicrobial and immunostimulating effect.

**Gingivitis** is inflammation of the gum which is the most common disease
among diseases of periodontium. The inflammation can develop in marginal
periodontium of 1-2 teeth or be generalised. Inflammatory manifestations in the
gum are evaluated against the following signs: hyperemia, swelling, hemorrhage,
ulceration, hypertrophy, acute or chronic course.

Examination of oral cavity of a patient with acute catarrhal gingivitis
(mostly young people) reveals strong hyperemia of gingival mucosa; the gingival
surface is smooth, glistening, edematous, easily bleeds upon contact.

People over 30 usually have chronic catarrhal gingivitis characterised by a
prolonged subacute course. The patients complain of gingival hemorrhage upon
brushing, halitosis, gingival itching. Upon exacerbation of the chronic course noted
in spring and winter seasons gingival pains upon eating grow worse.

Objective examination of catarrhal gingivitis cases shows congestive
hyperemia of the gum, swelling, cyanosis, looseness of gingival tissue, it bleeds
easily. Confined desquamation foci are noted. The strength of capillaries is
decreased which is characterised by shorter time of hematoma formation. The teeth
show increased amounts of dental deposit.

The presence of ulcerative gingivitis with typical gingival hyperemia and
swelling and gray necrotic patches along the gingival margin indicate a grave
disorder of the body’s reactivity. Upon removal of necrotic patches ulcerative hemorrhagic painful surface is revealed. Ulcerative gingivitis occurs mostly in young age after some diseases (grippe, angina, and acute respiratory viral infection) or supercooling resulting in reduced immune protection of the body.

Severity of ulcerative gingivitis is due to both the duration of inflammatory process and the extent of clinical manifestations. The patients complain of high body temperature, gingival bleeding, pain in gums, especially while eating. One should bear in mind that ulcerative gingivitis can be observed in systemic blood diseases.

**Hypertrophic gingivitis** is a chronic inflammatory process where proliferation processes prevail, localised mostly in the area of frontal teeth of maxilla and mandible. This disease mostly occurs in young people. Two types of the disease are distinguished – edematous and fibrous. Important factors of the etiology of hypertrophic gingivitis are hormonal changes (juvenile gingivitis, pregnancy gingivitis, vitamin C deficiency, blood diseases, intake of phenytoin by patients with epilepsy). Among local reasons are deep overbite, tooth replacement of low quality.

The patients complain of gingival enlargement, itching, hemorrhage upon brushing the teeth or biting solid food, gingival desquamation, halitosis. In mild cases the hypertrophy covers 1/3 of tooth crown, in severe cases – 2/3 or the whole crown. Due to considerable gingival enlargement false periodontal pockets are revealed; odontogingival junction, however, is not disturbed.

Periodontitis is an independent nosological type of periodontal disease where all the periodontal tissues are typically involved: gums, periodontium, alveolar bone and the tooth.

The development of the disease is determined by processes of exudative-alterative inflammation with pronounced progressing manifestations of destruction of alveolar bone, dental cement and periodontal tissue. Localised periodontitis develops under the impact of local factors: mechanical trauma, chemical and
physical injuries (overhanging edges of fillings, faulty tooth replacement, contact of arsenous acid with interdental spaces, etc).

Generalised periodontitis develops in prolonged chronic course of the process as a result of disorder of barrier function of periodontium and immune reactivity of the body.

A chronic type of periodontitis when the inflammatory process lasts for years and sometimes decades is common in clinical practice. When the body’s reactivity is reduced, concomitant general diseases are present and a secondary infection develops, the inflammatory process in periodontal tissues exacerbates. In the dynamics of the development of the process the odontogingival juncture is damaged, dental ligamentous apparatus is destroyed, resorption of bone takes place.

Patients complain of gingival hemorrhage, tooth mobility of various degrees, hyperesthesia of dental necks, and purulent discharge from periodontal pockets.

Objective investigation reveals gingival hemorrhage, deposits of subgingival tartar and dental plaque, tooth mobility, discharge of pus upon pressing with an instrument on gingival margin at an advanced stage, a positive Schiller-Pisarev test. However, it is odontogingival pockets of varying depth depending on the stage of the process that is the main sign of periodontitis.

Mild periodontitis is characterised by a periodontal pocket up to 3.5 mm deep. In medium periodontitis the typical depth of the pocket is up to 5 mm; grave periodontitis is characterised by many clinical manifestations, periodontal pocket being 5-6 mm.

6.2.3.1. Treatment of inflammatory periodontal diseases

Since periodontitis develops due to the impact of both general and local factors, treatment calls for the use of general and local therapeutic measures.

Primary objectives of general therapy are: stimulation of the body’s reactivity, anti-inflammatory, desensitising and general health-improving therapy.
Local therapy is aimed at elimination of local etiological factors, anti-inflammatoriy effect, stimulation and activation of periodontal vessels.

Anti-inflammatory therapy is the basis of local therapy. A great variety of agents are available for this purpose. Using agents that spare periodontal tissues is considered to be the main principle of local therapy.

In clinical practice of treating inflammatory diseases of oral mucosa monotherapy with anti-inflammatory or antibacterial agents is not always effective. That is why lately preference has been given to combination therapy, or agents combining these effects are used. Cases of negative outcomes or adverse side effects of synthetic and semi synthetic agents prompted an interest in phytotherapy. However, the applied prescriptions and formulations of decoctions and tinctures were created empirically, without an adequate pharmacological and clinical substantiation, so they require an in-depth study.

In this respect, we believe it justified to use preparations based on natural mineral salts containing numerous macro- and microelements in complex therapy of inflammatory periodontal diseases. A great importance is attached to environmental purity of crude agents.

Thus, the mineral bischofite whose deposits are found at a great depth in the Low Volga region is of certain interest. This interest is justified by the rather well known biological effect of magnesium salts, availability of bischofite source, its environmental purity and the economy of processing it. A number of studies show that bischofite has an anti-inflammatory, antimicrobial and immunostimulating action.

Polycatan preparation based on bischofite was developed at Volgograd Medical Academy for the treatment of inflammatory periodontal diseases. The composition of Polycatan is a standardised bischofite solution with the addition of flavouring agents and aromatisers.

Experimental and clinical study has shown that Polycatan has an anti-inflammatory, antimicrobial, anesthetising action; it enhances phagocytic activity of neutrophils and speeds up regeneration of tissues.
Use of Polycatan is authorised by Ministry of Public Health Decree №133 of April 23, 1998. Registration certificate №98/133/15.

6.2.4. **Recommendations for practical application of bischofite and bischofite-based preparations**

Indications for administration of Polycatan in dental practice are as follows:

- gingivitis;
- periodontitis;
- aphthous stomatitis.

**Therapy of gingivitis:**

a. Sanation of oral cavity;

b. Removal of dental calculus, deposit;

c. Administration of vitamins C, P, B, A, E;

d. **Technique of Polycatan administration:** 1 fraction of Polycatan is diluted in 10 fractions of warm boiled water, carefully stirred; applications are made on gums with cotton swabs for 30 min. replacing the swabs every 5 min. The course of treatment depending on the extent of clinical manifestations – 3-4 days.

e. Careful observation of oral hygiene with the use of therapeutic pastes.

Therapy of gingivitis in the presence of hormone imbalance begins with sanation of oral cavity irrespective of the stage of the process. General treatment of gingivitis is undertaken with consideration to the underlying disease (hormone disturbance in hypertrophic gingivitis, blood disease, disturbance of vitamin balance, etc) jointly with an endocrinologist, hematologist, allergist etc.

**Therapy of periodontitis:**

a. Sanation of oral cavity;

b. Removal of dental calculus and deposit;

c. **Technique of administration:** in mild periodontitis Polycatan is administered diluted with water 1:8; cotton swabs are applied from the
vestibular and oral sides for 30 min. replacing them every 5 min.; the course of treatment 5-7 days;

d. Administration of vitamins C, P, b, A, E;
e. Careful observation of oral hygiene (brushing the teeth twice a day, in the morning and evening for 5-10 min.).

General treatment of mild periodontitis is undertaken with consideration to the patient’s condition and the presence of systemic and background diseases.

In medium periodontitis Polycatan is recommended to be used undiluted with introduction of wick drains into the gingival pocket. Wick drains, saturated with Polycatan, are introduced into the gingival pocket from the approximating side of each affected tooth. A slight stinging sensation which wears off quickly is felt at this moment. The drains remain in the oral cavity for 20 min. It is desirable to replace the drains every 5 min. The course of treatment is 7-10 days.

Another beneficial property of Polycatan is its anesthetising action on hard dental tissues.

Therapy of aphthous stomatitis:

a. Sanation of oral cavity;
b. Removal of dental calculus and deposit;
c. Technique of Polycatan administration: Polycatan is diluted with water 1:15, cotton swabs saturated with diluted Polycatan are applied to the affected areas of oral mucosa for 20-30 min., replacing the swabs every 5 min. The course of treatment is 4-5 days.
6.3. Use of bischofite in otorhinolaryngological practice

6.3.1. Introduction

ENT diseases are those of most common occurrence in medical practice. Seasonal diseases (in cold time of the year) are very common, especially in children and debilitated patients with impaired immunity. It is, as a rule, anti-inflammatory and antimicrobial agents that are administered in the therapy of acute and chronic tonsillitis, rhinitis, pharyngitis, sinusitis. Various balneological preparations have come into use for the treatment of ENT diseases recently. Prof. Sanzharovskaia and Dr Martynova of ENT-diseases clinic at Volgograd Medical Academy used Polycatan in the treatment of patients with various ENT problems (Спасов А.А., Санжаровская Н.К. и др., 1999; Мартынова Л.А. и др., 1996; Мартынова Л.А, Шахова Е.Г., 1999; Мартынова Л.А, Лобзов М.С., 1997; Мартынова Л.А, 1998).

6.3.2. Effectiveness of bischofite

Therapy of acute and chronic tonsillitis, rhinitis, pharyngitis, sinusitis and other ENT diseases calls for the use of anti-inflammatory, antimicrobial agents. In recent years good results have been obtained by employing natural bischofite mineral and bischofite-based preparations in the treatment of ENT diseases.

6.3.2.1. Acute, chronic rhinitis and sinusitis

84 patients with acute or chronic rhinitis and sinusitis (40 females, 44 males aged 15-60) received Polycatan therapy. The patients had signs of inflammation of mucous membrane of the nose and accessory nasal sinuses. The patients’ main complaints were about stuffiness in the nose, laboured breathing through the nose, discharge from the nose of varying nature. Most patients with chronic rhinitis and sinusitis commented upon unsatisfactory results of earlier treatment.

The duration of disease was from 3-6 months to 20 years. Before and after treatment all patients underwent anterior and posterior rhinoscopy, investigation of
respiratory and olfactory function of the nose, pH of mucous membrane of the nose, mucociliary clearance; 20 patients’ nasal cultures were taken for bacteriological analysis.

The findings of radiological and ultrasound investigation as well as those of exploratory puncture verified the type of maxillary sinusitis: catarrhal or purulent. The treatment often included puncture of maxillary sinuses and trepanopuncture of frontal sinuses; the sinuses being irrigated with Polycatan solution diluted with distilled water 1:20. Patients with chronic polypous maxilloethmoiditis first had polyps removed from nasal cavity, in case of purulent polyps maxillary sinuses were punctured and irrigated with Polycatan solution diluted 1:20 until clear lavage fluid was obtained. In 2-3 days phonophoresis with Polycatan was administered. In chronic rhinitis Polycatan diluted 1:20 was introduced by the method of endonasal electrophoresis from the positive pole.

The results of treatment were estimated as “clinical recovery”, “improvement”, “no effect”, “aggravation”. Patients in the “clinical recovery” group showed the absence of both objective and subjective signs of the disease, the findings of function study and laboratory examinations were normal. The result was classified as “improvement” when the patient’s condition improved, the discharge from the nose decreased, nasal breathing was restored. Absence of positive changes in the course of the disease or temporary insignificant improvement in the condition was labelled as “no effect”. In case of “aggravation” there were no positive changes in the course of the disease.

The therapeutic effect of administered treatment (Table 19) in patients with catarrhal types of sinusitis came on on 4th day; in case of purulent sinusitis pathological discharge from the nose decreased after 2-3 irrigations with Polycatan solution, on 5-6th day it ceased altogether. By that time catarrhal signs in nasal cavity had subsided altogether.

Bacteriological investigation of nasal contents revealed different microflora, mostly opportunistic pathogens of the genus *Staphylococcus epidermalis*, pathogens *Staphylococcus aurens*, and intestinal group of bacteria. Some tests
detected several infecting agents (*Staphylococcus epidermidis*, *Staphylococcus aurens*, and *Escherichia coli*). After Polycatan therapy the pathogens were no longer present, saprophytic organisms prevailing.

The study by Martynova L.A. and Shakhova E.G. (Мартынова Л.А., Шахова Е.Г., 1999) demonstrated the effectiveness of Polycatan in allergic rhinitis. The study was carried out on 25 patients aged 18-60. The patients received therapy consisting of endonasal electrophoresis with Polycatan diluted 1:20 or phonophoresis (6-8 procedures). Between procedures the patients received Polycatan as nose drops. The administered therapy resulted in general health improvement of the patients, considerable decrease of edema of mucous membrane of nose, restoration of nasal breathing, stabilisation of serum immunoglobulin A and M.

<table>
<thead>
<tr>
<th>№</th>
<th>Diseases</th>
<th>№ of patients</th>
<th>Outcome of treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Abs</td>
<td>%</td>
</tr>
<tr>
<td>1</td>
<td>Acute maxillitis</td>
<td>11</td>
<td>100</td>
</tr>
<tr>
<td>2</td>
<td>Chronic maxillitis</td>
<td>26</td>
<td>11.5</td>
</tr>
<tr>
<td>3</td>
<td>Chronic frontitis</td>
<td>7</td>
<td>14.2</td>
</tr>
<tr>
<td>4</td>
<td>Chronic hyperplastic maxilloethmoiditis</td>
<td>18</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>Chronic rhinitis</td>
<td>22</td>
<td>18.2</td>
</tr>
</tbody>
</table>

Table 19

**Effectiveness of Polycatan therapy of inflammatory diseases of nasal mucosa and paranasal sinuses**
6.3.2.2. Sensorineural hearing loss

The study was carried out by Prof. Sanzharovskaia and Dr Lobzov of ENT-diseases clinic at Volgograd Medical Academy (Лобзов М.С., 1997; 1998; Спасов А.А., Санжаровская Н.К. и др., 1999). 159 patients with acute and chronic sensorineural hearing loss were treated. The patients’ age varied from 3 to 70, 65 people having suffered from hearing loss for less than a year, 55 people – over 5 years.

The examination of patients (otoscopy, tympanometry, tonal liminal audiometry) helped to diagnose the localisation and extent of hearing loss and the presence of concomitant diseases. 93 patients had sensorineural hearing loss, 37 – unilateral hearing loss. Chronic purulent inflammation of middle ear was detected in 20 patients, salpingootitis with dysfunction of auditory tube – in 5 patients. 25 patients had hearing loss of first degree, 78 – second degree, 43 – third degree, 13 – fourth degree.

The main cause of hearing loss in these patients, in adults and children likewise, was viral infection which accounted for 52 cases. Inflammatory processes in the middle ear accounted for 33 cases. The authors observed a chronic course of the disease in 132 patients, an acute course – in 27 patients. In 19 patients the patency of tympanic cavity and auditory tube was investigated. Tympanometric curve of type A was registered in 6 patients, flattened A – in 8 patients, type C – in 5 patients which indicated a disorder of patency of the middle ear in patients with sensorineural hearing loss.

Rheovasography of the basin of vertebrobasilar artery was administered to 28 patients, in 28 of them reduced venous tone was detected, increased arteriole tone was detected in 24, normal venous tone – in 2, normal arteriole tone – in 4.

Depending on the administered method of treating hearing loss all the patients under observation were divided into 2 groups. Group 1 (35 people) received Polycatan therapy administered with endoaural electrophoresis. The procedure was administered with Potok-1 apparatus: intensity of current was 2
mA, the negative electrode was fixed in retroaural area, the positive electrode was introduced into external auditory passage with a wick drain saturated with 5% Polycatan solution, the duration of electrophoresis was 10 min., the course of treatment was 10 procedures. Patients of the control group (30 people) received therapy with potassium iodide administered with endoaural electrophoresis.

The results of treatment were estimated according to the approach of Tokarev O.P.: a three-point scale was used in relation to air conduction of the less impaired ear in a bilateral process. The case was rated as first degree when tonal threshold remained on the same level, second degree – when auditory sensitivity improved by 15 decibel, third degree – by 20 decibel and more.

The investigations performed helped to establish that patients of the study group revealed improvement against the background of better auditory sensitivity (2nd and 3rd degree of therapeutic effectiveness) while there was no positive effect in the control group (1st degree).

The patients who received endoaural electrophoresis with Polycatan revealed lower auditory sensitivity threshold at the following frequencies: 500 hertz (by 15 decibel), 1000 hertz (by 13.7 decibel), 2000 hertz (by 11.4 decibel), and 4000 hertz (by 10 decibel).

Improved patency of the tympanic cavity and auditory tube after Polycatan therapy was observed in 52.6% of patients; it was manifested by normalisation of curve A and absence of curve C on the tympanogram.

The findings of rheovasoencephalography showed that after complex therapy venous tone normalised in 82.1% of patients while initially it had been decreased; in 57.1% of patients arteriole tone normalised while initially it had been increased which confirms the favourable effect of fluctuating current and Polycatan on blood circulation in the system of vertebrobasilar artery.

Thus, the results of tonal liminal audiometry, tympanometry, and rheovasoencephalography prove therapeutic effectiveness of Polycatan in the treatment of patients with sensorineural hearing loss.
6.3.3. *Technique of administering Polycatan*

Main indications for using Polycatan in ENT practice are:
1. sensorineural hearing loss;
2. chronic tonsillitis;
3. acute pharyngitis;
4. chronic pharyngitis (catarrhal and hypertrophic types);
5. acute and chronic rhinosinusitis.

6.3.3.1. *Sensorineural hearing loss*

Sensorineural hearing loss is a polyetiological disease whose main subjective and objective manifestations are disorder of speech intelligibility and high tonal threshold of bone sound conduction to sound frequencies above 1-2 kilohertz, mainly.

Sensorineural hearing loss is caused by individual susceptibility of structures and functional interrelation of auditory receptor and analyser to the damaging effect of endogenous and exogenous pathological factors.

The types of hearing disorder determined by degeneration of hair cells, fibres of acoustic nerve and ascending passages of auditory analyser in the brain can be regarded as **primary sensorineural hearing loss**. There is no medical rehabilitation for this type of hearing loss nowadays. The only method of rehabilitation for such patients is supportive agent therapy and use of hearing aid to prevent further progressing of degeneration of functioning portions of hair cells and axons of cells of the spiral organ. In case when the disturbance of intelligible speech perception and higher threshold of tonal signals in bone sound conduction (disturbance of sound perception) is only due to the effect of pathogenic etiological factors on the structures of sound analyser while hair cells and ascending afferent passages of the brain remain intact, this type of resulting sensorineural hearing loss can be regarded as **secondary**. Secondary sensorineural hearing loss if untreated can eventually result in degeneration of hair cells and fibres of acoustic nerve, i.e. in primary sensorineural hearing loss.
Patients with sensorineural hearing loss present problems with impaired hearing in one or both ears, subjective ear noise (tinnitus), sometimes dizziness of unclear nature, unsteady and teetering walk.

Depending on the course of the disease acute, subacute and chronic sensorineural hearing loss is distinguished.

INTERNATIONAL CLASSIFICATION OF HEARING LOSS:

1st degree – mean value of audibility threshold at speech frequencies 26-40 (decibel);

2nd degree – 41-55 (decibel);

3rd degree – 56-70 (decibel);

4th degree – 71-90 (decibel)

Deafness > 91 (decibel).

The clinical course of sensorineural hearing loss has its peculiarities depending on etiological factors.

Substantiation of Polycatan therapy in the treatment of hearing loss.

Magnesium ions whose deficiency is noted in different types of hearing loss acting upon neuroepithelial hair cells of cochlea increase the activity of intracellular processes, excitability and intensity of neuron respiration, whole protein and nucleic acids content in perilymph, and the formation of action potentials. (Крюкова Н.А. и др., 1984).

It has been proved experimentally that in the treatment of hearing loss induced by aminoglycoside antibiotic kanamycin its damaging effect on inner hair cells is deterred. The signs of plethora and thickening of vascular stria and adjacent blood vessels are noted at the same time. Apparently, Polycatan contributes to better trophism of the spiral organ due to increased secretory function of the vascular stria producing endolymph (Лобзов М.С., 1998).

6.3.3.2. Chronic tonsillitis

Chronic tonsillitis is a chronic inflammation of palatine tonsils developing in children and adults secondary to recurrent quinsy or acute infectious diseases with
the involvement of pharyngeal lymphoid tissue (scarlet fever, measles, diphtheria and others). The change of immunological status is of primary importance in the development and course of chronic tonsillitis.

**Chronic tonsillitis classification** (I.B. Soldatov)

1) Non-specific:
   a. Compensated type;
   b. Decompensated type.

2) Specific: in infectious granuloma – tuberculosis, syphilis, scleroma.

**Symptoms.** Patients complain of bad breath, an awkward sensation or sensation of a foreign body in the pharynx, neuralgic pains irradiating to the ear or neck. Evening temperature can rise to subfebrile values; flaccidity, undue fatigability, low physical efficiency and headaches are noted. Some patients present no problems.

Some patients’ case histories report frequent quinsy which is usually a repeat exacerbation of chronic tonsillitis. The course of chronic tonsillitis does not always include quinsy (nonanginal chronic tonsillitis).

Local signs of chronic tonsillitis:
   a. hyperaemia and cushion-like thickening of palatine arch margin;
   b. cicatrical adhesions between tonsils and palatine arches;
   c. loose or cicatrical and indurated tonsils;
   d. caseous-purulent plugs or fluid pus in tonsil crypts;
   e. regional lymphadenitis – enlargement of retromandibular lymph nodes.

The presence of two or more local signs above makes it possible to diagnose chronic tonsillitis.

Two clinical types of chronic non-specific tonsillitis are distinguished, compensated and decompensated ones. These two types have clear clinical definitions; they are regarded with respect to the main factors of genesis of the disease: reactivity of the body and barrier function of the tonsils. In the first type only local signs of chronic tonsil inflammation are present, the barrier function of the tonsils and reactivity of the body are still able to counterbalance the condition.
of local inflammation; they compensate for it so a pronounced general reaction does not develop.

In the second type the local signs of chronic tonsil inflammation are supplemented by decompensation manifestations in the form of recurrent acute tonsillitis (quinsy), paratonsillitis, paratonsillar abscess, various pathological reactions, diseases of distant organs and systems.

6.3.3.3. Pharyngitis

**Acute pharyngitis.** Acute inflammation of pharyngeal mucous membrane is rarely isolated. More often, it develops as descending acute catarrh of nose and pharynx.

*Symptoms.* Acute pharyngitis can be accompanied by subjective symptoms like dryness, slight tenderness or tension in the pharynx, cough or scratchy feeling. Painful sensations in the area of lateral wall can irradiate into the ear upon swallowing. Empty swallowing (swallowing saliva) is more painful than upon swallowing food.

Objective symptoms: the mucous membrane is red with patches of mucous-purulent secretion. On the surface of mucous membrane of pharyngeal posterior wall separate follicles stand out as red grains. Redness and a slight swelling of the uvula are noted, too. Sometimes the inflammatory process goes over to the larynx. The temperature is usually normal or slightly feverish. The general condition is not much impaired.

**Chronic pharyngitis,** a chronic disease of mucous membrane of pharynx.

Chronic pharyngitis classification.

1. Catarrhal
2. Hypertrophic.
3. Atrophic.

*Symptoms.* In case of simple or hypertrophic type of catarrh of the pharynx patients complain of accumulation of viscous mucous discharge in large amounts which irritates and causes a constant need to clear one’s throat and to expectorate.
Expectoration is most pronounced in the morning, it can be accompanied by nausea and sometimes vomiting. In chronic catarrhal pharyngitis the mucous membrane of the pharynx is hyperaemic and thickened; superficial branching congested veins often stand out. Mucus discharge is increased. In the hypertrophic type all these manifestations are more pronounced. The mucous membrane is more hyperaemic; the posterior wall is often oedematous and covered with mucous-purulent secretion flowing down from the nasopharynx. The soft palate and uvula are oedematous and thickened. Hyperplasia of separate follicle groups forming separate red grains dispersed on posterior pharyngeal wall (granular pharyngitis) is noted. In some cases hypertrophy of adenoid tissue in lateral pharyngeal folds which bulge as bright red bands behind posterior palatine arches develops (lateral pharyngitis). In some cases markedly hypertrophic follicles on posterior pharyngeal wall or palatine protuberances can induce reflex cough due to the irritation of trigeminal nerve.

6.3.3.4. Chronic inflammatory diseases of nasal cavity and paranasal sinuses

**Rhinitis** is inflammation of mucous membrane of the nose accompanied by the following (one or more) symptoms: stuffiness of the nose, rhinorrhea, sneezing and itching.

International classification of rhinitis:

1. Allergic rhinitis:
   - seasonal,
   - all-year.
2. Infectious rhinitis:
   - acute,
   - chronic,
   - specific,
   - non-specific.
3. Other types:
   - vasomotor;
- hormonal;
- medicamentous;
- induced by irritants;
- induced by food;
- induced by emotional factors;
- atrophic.

*Russian classification of rhinitis:*

1. Catarrhal rhinitis
2. Hypertrophic rhinitis:
   a. limited;
   b. diffuse.
3. Atrophic rhinitis:
   a. simple - limited, diffuse;
   b. ozena
4. Vasomotor rhinitis:
   a. allergic type;
   b. neurovegetative type.

In chronic *catarrhal rhinitis* the complaints are typical: constant mucous or mucous-purulent discharge from the nose, alternate stuffiness in one or the other side of the nose, laboured nasal breathing in horizontal position of the body which subsides upon change of position or physical exertion.

Rhinoscopy reveals hyperemia, profuse moisture of mucous membrane in nasal cavity; inferior and superior nasal conchas are swollen, the lumen of common nasal passage is narrowed. After irrigation of mucous membrane with 3% ephedrine solution and 0.1% adrenaline solution nasal conchas tighten completely which differentiates catarrhal rhinitis from hypertrophic one. There is mucous or mucous-purulent discharge in the nasal cavity, mostly on the bottom.

The following symptom triad is typical of *idiopathic* (vasomotor) *rhinitis*: laboured nasal breathing, profuse mucous or serous discharge from the nose,
sneezing attacks. Rhinoscopy reveals cyanosis of mucous membrane; blue-grey spots (Voyatchek’s spots) are often detected against this background.

**Paranasal sinusitis**

This disease is determined by an inflammatory process in the mucous membrane lining paranasal sinuses.

The inflammatory process in sinusitis can involve any of paranasal sinuses: maxillary sinus (maxillitis), ethmoid sinus (ethmoiditis), frontal sinus (frontitis), sphenoid sinus (sphenoiditis). A combined disease of maxillary and ethmoid sinuses or frontal and ethmoid sinuses often occurs in adult patients. All sinuses on one side can be affected which is diagnosed as hemisinusitis; if both sides are affected pansinusitis is diagnosed.

Depending on the course of the disease *acute* and *chronic* sinusitis are distinguished.

**Classification of acute sinusitis.**

1. Catarrhal
2. Exudate
3. Purulent.

**Classification of chronic sinusitis (by Preobrazhenskaia B.S.):**

1. Purulent
2. Polypous
3. Parietal-hyperplastic
4. Catarrhal
5. Serous
6. Cholesteatomous
7. Atrophic
8. Combined.

**Symptoms.** Headaches in acute and chronic sinusitis are usually located in the frontal area irrespective of which sinus is affected – frontal, maxillary or
ethmoid. In sphenoiditis the headache is usually projected onto frontal area with irradiation of pain into temporal, retroorbital and occipital area.

The general symptoms are: stuffiness in the corresponding half of the nose, one-sided purulent rhinitis, hyposmia, detection by rhinoscopy of purulent streak or purulent accumulation in the middle or upper nasal passage. In case of chronic sinusitis one can also detect polyps in the middle or upper nasal meatus.

In acute sinusitis or exacerbation of chronic sinusitis the following signs are noted: elevated body temperature, changed haemogram, there can be a swelling in the buccal area (in maxillitis), in the area of root of nose (in ethmoiditis), in the frontal area (in frontitis), edema of eyelids (of the lower eyelid in maxillitis, of the upper one - in frontitis), tenderness of facial walls of the corresponding sinus upon palpation.

Such methods of investigation as ultrasound sinusoscopy, radiography and computer tomography provide valuable evidence for diagnostics and especially for adjustment of process localisation.

Polycatan can be used in complex therapy of acute and chronic rhinitis (catarrhal and vasomotor types), acute and chronic sinusitis as it has an antiinflammatory and bacteriostatic effect; it acts as a biostimulating and immunomodulating agent.

**6.3.4. Practical recommendations for administration of bischofite and bischofite-based preparations**

**6.3.4.1. Sensorineural hearing loss**

The preparation Polycatan can be used in a complex therapy of patients with sensorineural hearing loss by administering it via endoaural electrophoresis (Potok-1 apparatus) from the positive pole. The solution is prepared before the procedure by diluting Polycatan with distilled water in the ratio 1:20.

Immediately before the procedure the skin of outer auditory passages is sponged with alcohol, the patient lying supine. The negative electrodes with gauze turundas saturated with Polycatan solution are introduced into outer auditory
passages until the bone wall is touched. The positive electrode with a gauze pad saturated with tap water is placed on the occipital area. The intensity of current is 0.5-2.0 mA, duration of the procedure is 10 min. The course of treatment consists of 8-10 procedures and it is repeated in 6-12 months.

**Contraindications:**
- tumours;
- infectious diseases;
- acute inflammatory diseases of the brain and spinal cord;
- pustular diseases of the skin of outer auditory passage;
- eczema of outer auditory passage;
- acute purulent otitis media;
- exacerbation of chronic purulent otitis;
- chronic purulent epitympanitis complicated by cholesteatoma, caries, polyps;
- organic diseases of the heart, kidneys, liver or lungs;
- blood diseases;
- pregnancy;
- extreme emaciation;
- epilepsy;
- instability of arterial blood pressure;
- individual hypersensitivity to Polycatan.

6.3.4.2. *Chronic tonsillitis*

Polycatan is recommended for use in combined treatment of chronic tonsillitis as it has an antiinflammatory and bacteriostatic effect; it acts as a biostimulating and immunomodulating agent. There are four techniques of administering Polycatan in chronic tonsillitis.

**Technique one.**

5% Polycatan solution (in distilled water) is used for systematic irrigation (gargling) of the mucous membrane of the pharynx 3-4 times a day.
**Technique two.**

Irrigating lacunae with 5% Polycatan solution (in distilled water) daily or every other day, the course consisting of 8-10 procedures; if necessary, the course can be repeated in 2-4 months.

**Technique three.**

Therapy with Tonsillor apparatus with 5% Polycatan solution (in distilled water or 0.9% NaCl).

This technique includes the following steps: patient preparation, apparatus preparation, pretreatment of tonsils with a fluid agent. Patient preparation consists in local application of anesthesia of the pharynx with anesthetic solution (1-2% tetracaine, 2-5% cocaine, 10% lidocaine solution) to suppress the pharyngeal reflex.

The apparatus is turned on by pressing on the pedal. The surfaces of acoustic units, generator, suction device and cables, applicators with funnels, waveguides and tubes are disinfected twice with a coarse calico pad saturated with 3% hydrogen peroxide and 0.5% detergent or 1% chloramine solution. To sterilise the applicator with funnels, waveguides and tubes for feeding and venting the agent 6% hydrogen peroxide solution is used (immersing for 6 hours).

Pretreatment of the tonsils with fluid agent is performed in the following way: the applicator valve is closed; the applicator with a funnel of required size is placed on the tonsil, the applicator valve is opened, the vacuum suction device is turned on to create negative pressure of 0.3-0.5 kg/cm in the applicator system (the suction device operates independently from the generator), and the fluid agent, Polycatan solution is sucked into the funnel. Then the apparatus is turned on and the tonsils are processed with the energy of high-frequency fluctuations through the circulating agent in the waveguide whose end face is tilted at 30°. The procedure lasts for 90-120 sec. The processing of tonsils with Polycatan solution is carried out in the otorhinolaryngological or dentist’s chair with the patient in a semisitting position, his head facing the apparatus. After processing the tonsil the applicator valve is closed, the generator and suction device are turned off. The
applicator is taken off while the patient holds his breath which prevents aspiration of the agent remaining in the funnel.

The course of treatment consists of 8-10 procedures once a day or every other day. A repeat course is in 3 months, 3-4 times a year if required.

If there are any cysts, suppurating follicles, they should be opened before the procedure.

After several procedures some patients may develop pronounced signs of exacerbation of chronic tonsillitis manifested subjectively by a slightly sore throat, a scratchy feeling in the throat; pharyngoscopy can detect slight hyperemia and edema of the tonsils and palatine arches. The general condition of the patient is not impaired. In this case the ultrasound therapy should be suspended for 2-3 days; gargling with 5% Polycatan solution should be administered until exacerbation is controlled.

**Technique four.**

**Regional lymphotropic therapy with Polycatan.**

The technique under discussion, regional lymphotropic therapy with Polycatan is based on treating chronic tonsillitis by lymphotropic introduction of Polycatan or Bischolin ointment with ultraphonophoresis in the area of lymph collector and regional lymph node (the area of jugulodigastric lymph node, the node of the first order for palatine tonsils). The high penetration power of ultrasound signal helps the antiseptic agent to penetrate into the lymph stream bringing the antibacterial action closer to the inflammation focus. At the same time ultrasound has the power to stimulate lymph circulation (Мальцев М.В., 2000).

The technique is as follows. Bischofite ointment or a pad saturated with Polycatan is applied daily to the projection of regional lymph nodes for palatine tonsils, that is on the border of the upper and middle third of sternocleidomastoid muscle along its anterior margin on both sides. Ultrasound is applied in a labile pulse mode for 10 min., with the power of 0.4 W/cm² for 5 min. on each side. The course consists of 10-15 procedures depending on the patient’s age and the extent of clinical manifestations.
**Contraindications** (for technique 3 and 4)
- tumours;
- acute infectious diseases;
- organic diseases of the heart, kidneys, liver or lungs;
- blood diseases;
- pregnancy (the first trimester and 9th month);
- extreme emaciation;
- epilepsy;
- iodine or bromine intolerance;
- instability of arterial blood pressure;
- individual hypersensitivity to Polycatan.

6.3.4.3. Acute and chronic pharyngitis

Polycatan is recommended for use in the form of inhalation in the treatment of acute and chronic pharyngitis (catarrhal and hypertrophic type).

**Technique of administration.** Polycatan is diluted with distilled water or 0.9% NaCl and poured into the chamber of Akhtuba ultrasound inhaler in the indicated amount. The lid of the chamber is placed on the bowl so that the notch on the lid fits into the lateral notch on the bowl. A fitting is placed into the opening in the lid. When the power is switched on, there will be a fountain of fluid in the centre of the chamber and aerosol will come out of the fitting in a stream. The inhaler with the fitting is held by the hand at 0.5-2.0 cm from the mouth. The recommended temperature of water is 22-36°C. Duration of the procedure is 5-10 min, 1-3 times a day. The course of treatment is 10-15 procedures.

**Contraindications.** Pregnancy. Individual Polycatan intolerance.

6.3.4.4. Acute and chronic rhinitis

4 techniques of Polycatan therapy in rhinitis have been developed at the ENT clinic of Volgograd Medical Academy.
Technique one.

5% Polycatan solution (in distilled water) is taken in the form of drops intranasally, 3-4 drops thrice a day; or by introducing wick drains saturated with the agent solution for 5-10 min. 2-3 times a day.

Technique two.

5% Polycatan solution (in distilled water) is used to irrigate paranasal sinuses by puncturing with Kulikovsky’s needle or through post-operative anastomoses.

Technique three.

5% Polycatan solution (in distilled water) is administered by electrophoresis endonasally from the positive pole; intensity of the current 0.5-2.0-5.0 mA, duration of the procedure 10-15 min., the course of treatment consisting of 6-8 procedures. In 3-6 months the course is repeated if required.

Technique four.

5% Polycatan solution (in distilled water) is administered endonasally with wick drains by phonophoresis with LOR-2, LOR-3 ultrasound apparatus. The intensity of current is 0.2-0.4 W/cm², duration of the procedure is 5-10 min., the course of treatment consisting of 6-8 procedures. In 3-6 months the course is repeated if required.

Contraindications (to technique 3 and 4):
- tumours;
- acute infectious diseases;
- organic diseases of the heart, kidneys, liver and lungs;
- blood diseases;
- pregnancy (first trimester and 9th month);
- extreme emaciation;
- epilepsy;
- intolerance to iodine, bromine;
- instability of arterial blood pressure;
- individual hypersensitivity to Polycatan.
6.4. Administration of bischofite in dermatology

6.4.1. Introduction

The main principle underlying the treatment of patients with dermopathy is that any skin lesion is not only a local pathological process but one that is determined, to a lesser or greater extent, by general changes in the body. At the same time, medicamentous therapy administered externally does not only have a local effect in many cases as it also produces a general effect on the patient’s body. Subjective and objective changes taking place under the impact of local treatment (the relief of itching, stinging, tenderness, resolution of pathological skin changes) acts on the patient’s condition and emotional state beneficially which in itself is conducive to recovery.

The action of agents administered locally is determined by the effect on the receptor apparatus of skin, by antimicrobial, antiinflammatory and antiparasitic effect.

One should bear in mind that normal skin, and, to a lesser extent, skin that is pathologically changed has poor restoration power. That is why agent forms in various concentrations are used to enhance the therapeutic effect; on the other hand, one can control the depth of skin penetration by using active ingredients added to the base which simplifies application of the agent to skin. Choosing a agent base one should take into consideration the solubility of the active ingredient in it, the rate of its release, the ability of the base to hydrate the corneal layer thus increasing the penetrability of the therapeutic agent.

Nowadays ointment bases of new synthetic compounds are coming into common use. They easily penetrate the skin and are easily released from the added pharmacological substances. These are hydrophile bases: ethylene oxide polymers, cellulose derivatives, sorbitane esters and esters of higher fatty acids. These synthetic ointment bases are not oxidised, do not degrade; they are easily tolerated and removed from the skin surface.

Natural minerals carnalithe, talcum, dolomite, bischofite and bischofite-based preparations are used in the treatment of skin diseases, too.
It has been established that bischofite has a bacteriostatic and bactericidal effect (depending on its concentration) on streptococci and staphylococci (Spasov A.A. et al., 1998). Its immunomodulating effect in complex therapy including the ability to increase phagocytic activity in tissues has been established, too.

Experiments and clinical practice have proved its anti-edematous effect. The antiinflammatory effect of magnesium salts has been detected (perhaps due to the inactivation of cyclooxygenase and inflammatory mediators). A moderate keratolytic effect of bischofite and its derivatives has been established in clinical conditions (Родин А.Ю., 2000). Vasodilating properties of bischofite and the ability to increase phagocytic activity in tissues underlie the mechanism of action of bischofite (Спасов А.А. и др., 1998). Its ability to improve the reparative activity due to stimulation of biosynthetic function of fibroblasts and activation of local circulation has been established, too.

**Indications** for the administration of bischofite and its derivatives in complex treatment of patients with dermopathy are as follows:
- extensive or limited vulgar psoriasis in the steady or steady-regressive state;
- psoriatic arthropathy (except for acute inflammatory processes);
- superficial pyoderma (streptococcal impetigo, impetigo vulgaris, osteofolliculitis and folliculitis);
- chronic scleroderma (morphea guttata, scleroderma striata, Csillag’s disease)
- systemic lupus erythematosus (discoid lupus).

**Contraindications** to bischofite administration are as follows:
- progressive state of vulgar psoriasis, pustular psoriasis, psoriatic erythroderma;
- epidermolysis bullosa (pemphigus vulgaris, pemphigus vegetans, pemphigus foliaceus, seborrheal pemphigus);
- During’s herpetiform dermatosis;
- eczema;
- atopic dermatitis;
- contact dermatitis;
- acne rosacea, perioral dermatitis, demodicosis;
- ulcerative skin defects (ulcerative pyoderma, necrotising vasculitis etc.);
- therapeutic contraindications: pronounced organic diseases of the heart, kidneys, liver, lungs, blood diseases, pregnancy, neoplastic disease.

6.4.2. Effectiveness of bischofite in dermopathy

The study was carried out on patients using Bischolin paste consisting of bischofite solution and carboxymethylcellulose (Машковский М.Д., 1997) at the Dermatology clinic of Volgograd Medical Academy by Prof. Rodin and Dr. Shava.

The effectiveness of the paste was assessed on 124 patients (Table 20) with various dermatoses: psoriasis (56 patients), streptostaphyloderma (20 patients), scleroderma (6 patients), atopic dermatitis (6 patients), acne rosacea (7 patients), pemphigus vulgaris (8 patients), eczema (4 patients), ulcerative pyoderma (4 patients), lichen planus ruber (4 patients), lupus erythematosus (3 patients), acne conglobata (3 patients).

49 patients received Bischolin as monotherapy, 75 patients - as local therapy included into complex in-hospital treatment. Bischolin paste was applied to affected areas 2-3 times a day for 1-2 weeks. The effectiveness of treatment was judged by clinical presentations. After the end of treatment the patients were divided into the following groups:

1. **clinical recovery** - complete resolution of the skin process: resorption of patches, detachment of streptodermal crust, absence of hyperaemia or oedema in erysipelatous inflammation, absence of subjective sensations;

2. **considerable improvement** of the skin process - incomplete resolution of the skin process: considerable flattening and shrinking of patches, abatement of subjective sensations;

3. **improvement** - positive changes assessed quantitatively as to the reduction of the extent of skin manifestations of dermatoses. In psoriasis cases the
quantitative assessment of patches in points was applied (Владимиров В.В. и др., 1992). In cases of scleroderma the stage of the process and thermographic evidence was assessed (Смирнов А.В., Кошечкин С.В., 1988). In cases of discoid lupus erythematosus reduction of hyperaemia and patch infiltration, decrease of local temperature was assessed.

4. **no effect** - absence of improvement. The patches remained of the same size and density, subjective sensations did not change.

**Control group** comprised 24 people who received analogous therapy, however, with 2% salicylic ointment as local therapy. The extent of manifestations of psoriasis before treatment did not differ in both groups; it was 2.6 points.

The group of patients receiving local Bischolin therapy showed a reduction in the extent of disease manifestations by the end of the course of treatment. The extent of manifestations in this group was 1.1 points, while in the group receiving local salicylic acid therapy it was 1.8 points.

The administration of Bischolin proved effective in 73.2% out of 56 patients with psoriasis (Table 20), including clinical recovery in 33.9% of cases, considerable improvement - 26.8%, improvement - 12.5%. The treatment was of no effect in 26.8% of patients including 8.9% of cases where the skin process was aggravated as manifested by the development of hyperaemia, oedema, stinging sensation.

Bischolin was administered to 20 patients with streptostaphyloderma including 15 patients with streptococcal impetigo, 3 cases of impetigo vulgaris, 2 - of erysipelatous inflammation). In streptostaphyloderma only local therapy was administered: aniline dyes and Bischolin paste. 2 patients with erysipelatous inflammation received antibiotic therapy.

Detachment of crust and complete epithelisation after bischofite administration was noted on 8-9th day, on average; upon administration of tetracycline paste - on 10-11th day. Clinical recovery was observed in 12 patients with streptococcal impetigo, in 1 patient with impetigo vulgaris, in 2 patients with erysipelatous inflammation.
In scleroderma Bischolin was administered to 6 patients. All the patients had morphea guttata. The complex treatment included antibiotics, lidase, vitamins, ultrasound. The control group comprised 5 patients who received the same conventional therapy with hydrocortisone paste as local therapy. In all patients thermal imaging registered increased temperature in the foci, the gradient averaging 1.67°C.

After treatment the patients showed a reduced density and size of focus, regress of the inflammatory crown, absence of new eruptions. Clinical improvement was accompanied by the reduction of temperature gradient which averaged 0.83°C and 0.97°C in patients receiving Bischolin and hydrocortisone paste, respectively.

A three-month follow-up observation showed considerable improvement in patients with scleroderma and discoid lupus erythematosus.

Local Bischolin therapy proved ineffective in patients with atopic dermatitis, rosacea, pemphigus vulgaris, eczema, acne conglobata, Devergie’s lichen.

Assessing the obtained evidence one can draw the conclusion that Bischolin, perhaps due to its vasodilating properties, causes aggravation of a skin process and exacerbation of exudation; it has a local irritating effect in eczema, rosacea, pemphigus vulgaris, atopic dermatitis. For this reason administration of Bischolin is ineffective at the progressing stage of psoriasis and lichen ruber planus.

6.4.3. Technique of administration of bischofite and bischofite-based preparations

In various types of dermatopathy - in patients with psoriasis, scleroderma, lupus erythematosus and other dermatoses - the technique of treatment with administration of bischofite and bischofite-based preparations has its peculiarities.
## Clinical effectiveness of Bischolin paste in dermatoses

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<th>№</th>
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<th>Number of patients</th>
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<th>Considerable improvement</th>
<th>Improvement</th>
<th>No effect</th>
<th>Aggravation</th>
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Psoriasis (psora, alphos) is one of the most common dermatoses, presumably genetically determined. Up to 2-3% of population develop this disease. The disease is manifested by characteristic flat rose-red papules from pin-size to massive patches covered with abundant silvery laminar scales.

The onset or regular exacerbation usually develops after stressing situations, exacerbation of focal infection or depending on the season, usually in autumn or winter. The prevailing number of cases are patients with vulgar psoriasis. To administer adequate therapy one should differentiate between the stages of inflammatory skin process so as to avoid exacerbation, an irritation causing new eruptions.

One of the central links in the pathogenesis of psoriasis is disorder of the immune system manifested by an increase in the level of serum circulating complex, disproportion between T-lymphocytes and B-lymphocytes, disorder of cellular and humoral components of the immunity.

The clinical presentations are determined by the disorder of epidermal proliferation manifested by its acceleration due to a shorter time of cellular cycle of keratinocytes, accelerated cell turnover rate, increased permeability of vascular walls.

* A contraindication to bischofite administration would be the progressive stage of psoriasis manifested by:
  - new eruptions;
  - ill-defined desquamation on the surface of papules;
  - the presence of peripheral rim of growth (hyperaemic rim on the periphery of papules);
  - positive Kobner’s isomorphous reaction (new eruptions in response to mechanical injury of skin due to contact with clothes, injections, bruises etc.).

Another contraindication to bischofite administration is pustular psoriasis and psoriatic erythroderma which are regarded as malignant varieties of psoriasis.
For the treatment of patients with vulgar psoriasis techniques 1, 2 are used (see chapter 6.4.4.).

For the treatment of patients with psoriatic arthropathy (subacute and, especially, chronic stages of joint affection) techniques 2, 3, 4 are used. Application of compresses or rubbing-in into skin integuments around the joints in the presence of psoriatic eruptions in this area (techniques 3, 4) is to be avoided.

6.4.3.2. Administration of bischofite in the treatment of patients with superficial pyoderma

Impetigo is a contagious disease, especially for children. The infecting agent is staphylococcus, in some cases (impetigo vulgaris) - a symbiosis of staphylococci and streptococci.

Impetigo is manifested by quickly opening flaccid vesicles with serous-purulent exudate (phlyctenules). Upon opening the integument loose stratified yellowish crust is quickly formed in the area of erosion. This crust is the main clinical presentation of the disease.

To enhance the effectiveness of treatment with bischofite and bischofite-based preparations with technique 1 (see chapter 6.4.4.) the crust can be softened and removed with warm vegetable oil prior to the procedure. The oil is then carefully wiped away and the affected area is treated with aniline dyes (brilliant green, methylene blue, fucorcine).

To preclude autoinoculation the periphery of the foci is sponged with alcohol solution.

6.4.3.3. Administration of bischofite in the treatment of patients with scleroderma

Scleroderma is a disease with systemic connective tissue lesion, fibrous-sclerotic and vascular disorders in the skin and subcutaneous fat prevailing. In the systemic type of disease there are grave changes of internal organs like in obliterating arteriolith with the subsequent sclerosis of tissues, the outcome is often
fatal. The modern view is that scleroderma belongs to the group of diseases of immunocomplex pathology. It has been revealed that various autoantibodies are present, along with a lower T-lymphocyte level, decreased suppressor activity, increased immunoglobulin concentration etc.

The disease develops secondary to a disorder of connective tissue metabolism in the form of accelerated biosynthesis of collagen by fibroblasts and its maturation. The autoimmune nature of the disease is manifested, in particular, in the interaction between antibodies and lymphoid cells. Thus, T-helpers activated by exogenous and endogenous factors produce lymphoquins stimulating fibroblasts to synthesise anomalous collagen fibres.

It is expedient to administer bischofite and its derivatives only in limited types of scleroderma (morphea guttata, scleroderma striata, Csillag’s disease). At the stage of inflammatory oedema technique 1 is used; at the stage of induration - technique 4 (see chapter 6.4.4.).

6.4.3.4. Administration of bischofite in the treatment of patients with lupus erythematosus

Lupus erythematosus is an autoimmune dermatosis accompanied by the destruction and homogenising of fibrous structures and interstitial tissues; in case of systemic lesion the internal organs undergo dystrophic lesion. Like scleroderma, this disease belongs to the group of “diseases of immune complexes”.

Autoimmune lesion is manifested by the formation of specific antinuclear factor appertaining to immunoglobulins and directed against corpuscular elements of blood, vascular endothelium and some cell components.

Bischofite is administered in complex therapy of patients with chronic discoid lupus erythematosus. At the stage of inflammatory edema and hyperkeratosis technique 1 (see chapter 6.4.4.) is administered.
6.4.3.5. Administration of bischofite in the treatment of patients with other dermatoses

Preliminary clinical study of the effectiveness of bischofite in the form of Bischolin ointment as part of complex therapy of some uncommon dermatoses has been carried out.

The data obtained show that a certain therapeutic effect after Bischolin administration was noted in patients with erysipelatous inflammation, Darier’s keratosis follicular, lupus vulgaris, acne vulgaris, erythema multiforme and some other diseases. However, as the evidence about these conditions is still insufficient, the data need further elaboration and investigation.

6.4.4. Practical recommendations for bischofite administration in dermatological practice

Administration technique. In dermatological practice one can administer balneotherapy with bischofite or local baths. However, balneological ointment or paste forms of bischofite - Bischolin, Polycatan, Bischal - are more convenient for practical use.

Technique one. The affected skin area is cleared of crust and purulent discharge, if required. Bischolin is applied to the focus in a thin layer twice a day. In good tolerance a slight rubbing-in is acceptable. Most patients experience a slight stinging sensation that soon subsides. In case of an intensive prolonged stinging sensation the preparation is withdrawn.

Technique two. Bischofite brine is poured into a bath filled with warm water (36-37°C) in the ratio 1:50 (2 litres of bischofite solution per 100 litres of water). The water is carefully stirred for 5 min. to avoid precipitation of the salt. Then a general bath is taken of 15-minute duration. If the tolerance is good, the therapy is administered daily or every other day, the course of treatment consisting of 10-12 procedures. Two hours after the bath the patient should take a warm
shower. If the disease is exacerbated by hyperaemia develops, the procedures are withdrawn.

**Technique three.** A flannel cloth is immersed into an enamelled bowl with bischofite brine warmed to 36-37°C. The cloth is slightly wrung out and then placed on the affected area, and covered with wax-paper or cellophane for 20-30 min. Then the cloth is removed and the affected area is wrapped with a warm towel for 2-3 hours. To avoid irritation by magnesium salts the affected area is lavishly washed with warm water. The course of treatment consists of 12-15 procedures.

**Technique four.** Bischolin ointment is warmed to 38-39°C and then rubbed in intensively into the skin integuments in the area of joints, muscles and the spine for 10-15 min. Then the affected area is wrapped up for 6-8 hours. After the procedure the ointment is washed away with warm water and soap. Rubbing-in is made daily or every other day, the course of treatment consisting of 10-15 procedures.
CONCLUSION

(THE PROSPECTS OF BISCHOFITE ADMINISTRATION IN MEDICAL PRACTICE)

The study of bischofite carried out over the last 15 years as experimental investigations (Мазанова Л.С. и др., 1993; Тюренков И.Н. и др., 1993; Фокин В.П. и др., 1993; Смирнова Л.А. и др., 1991; Смирнова Л.А., 1995; Спасов А.А. и др., 1998, 199-b; Гусева Т.Н. и др., 1999; Спасов А.А. и др., 2001-a, 2001-b) and clinical trials (Зборовский А.Б. и др., 1991; Дзяк Г.В. и др., 1993; Бабаева А.Р. и др., 1993; Щавелева Л.А., Багирова В.В., 1994; Мартынова Л.А. и др., 1996; Лобзов М.С., 1997, 1998; Сулим Н.И., 1999; Щава С.Н., 2001) have proved that bischofite possesses anti-inflammatory, antibacterial, immunotropist properties as well as a stimulating effect on reparative processes in infected and noninfected conditions. Quite probably, the anti-inflammatory effect of bischofite is first of all due to its action on the anti-inflammatory potential of tissues – the ratio between inflammatory mediators and antimediators (Серова В.В., Пауков В.Г., 1995) in addition to tissue dehydration. The action on anti-inflammatory potential of tissues is typical of local magnesium deficiency in tissues as it has been established (Weglicki W.B., Philips Т.М., 1992) that in this case cytokine activation – interleukine-2, -6, tumour necrosis factor – takes place, and the inflammatory-degenerative changes in tissues are intensified. The fact that virtually 95-99% of bischofite consist of magnesium chloride seems to confirm the supposition.

At the exudative stage of inflammation bischofite reduces the phlogistic action of serotonin and histamine; at the proliferation phase it stimulates fibroblast and histiocyte activity (Бачев С., Писарев Ю., 1970; Спасов А.А. и др., 1998). The anti-inflammatory effect of bischofite is quite probably mediated by phagocyte stimulation and antibacterial activity (Спасов А.А. и др., 1998), and by the role of magnesium in the regulation of energy metabolism (Durlach J., 1993).

Nowadays a technique of obtaining balneological and pharmacopeic bischofite purified from contaminants is available. On the basis of this
environmentally appropriate raw material a new generation of balneological preparations has been developed – dry bischofite, bischofite brine, paste and ointment forms Bischolin, Polycatan, Polycatan forte, analgesic Polycatan. The effectiveness of these preparations has been proved by arthrological and dermatological clinical practice. Indications and contraindications to their administration in local therapy have been determined. Like many other balneological preparations bischofite has a moderate anti-inflammatory action so it can be combined with steroid and nonsteroid anti-inflammatory agents in a complex therapy of diseases of musculoskeletal system. In their anti-inflammatory action bischofite-based balneological preparations proved more effective than analogous preparations based on Dead Sea salts and Bulgarian Pomorian natural brine. The superior effectiveness of bischofite can be ascribed to its optimum chemical composition. At the same time one should note that medical practice does not make a wide use of bischofite balneotherapy in the treatment of neurological diseases, especially so in case of chronic fatigue syndrome (neurasthenia). It has been established that it is magnesium deficiency that underlies this condition (Fehlinger R., 1990), so transdermal introduction of magnesium into the body while taking bischofite baths is practicable.

Polycatan preparation developed for dental and ENT practice comprises pharmacopeic bischofite brine. It is the anti-inflammatory, antibacterial and immunomodulating properties of bischofite that determine the effectiveness of Polycatan in inflammatory diseases of mucous membranes of the mouth and nasopharynx (Мартынова Л.А. и др., 1996, 1998; Спасов А.А. и др., 1999).

The problem of Polycatan administration in gynaecological and proctological diseases has not been investigated as yet.

Considering magnesium deficiency in the cochlea in sensorineural hearing loss (Крюкова Н.А. и др., 1998) the effectiveness of electrophoretic introduction of Polycatan in experimental aminoglycoside hearing loss in guinea pigs has been proved (Лобзов М.С., 1998; Спасов А.А. и др., 1999). Analogous evidence was

The system of bischofite purification developed by Prof. Ozerov and colleagues (2002) at Volgograd Medical Academy makes it possible to remove technological contaminants, heavy metal salts and other microelements, and to achieve pharmacopeic purity of the preparation. This achievement lays grounds for the development of bischofite-based agent forms and balneological supplements for internal intake to meet the physiological need of the body in magnesium ions, or for treatment of various conditions associated with magnesium deficiency.
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