Clinical studies of Shilajit. Publication 1: History of the introduction to domestic medical practice

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Clinical research of Mummy (Shilajit)
Publication 1. The History of introduction in the official domestic medical practice

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RESUME

The results of the information analytical study of archival materials Pharmacological Gosudarstvennogo Committee, Russian Ministry of Health on clinical trials of mummies, harvested in different parts of the former USSR in the 60-90-ies of the last century.

Keywords: mummy, mummy asil, mummy Central Asian, Caucasian mummies, pharmacological activity.

SUMMARY

The results of an information and analytical study of archival materials of the Pharmacological State Committee of the Ministry of Health of the Russian Federation, devoted to clinical trials of mummy, harvested in various regions of the USSR in the 60s-90s of the last century, are presented.

Keywords: mummy, asil mummy, Central Asian mummy, mummyCaucasian, pharmacological activity.

Despite a significant amount of information on various types of pharmacological activity of mummy [4, 13–27, 29–31], so far none of the dosage forms of this natural organomineral complex [10] is used in domestic clinical practice as medicines. ... This is the reason for the need for this information and analytical research, in particular, analysis and generalization of the results of the use of mummy in domestic clinical practice, both unpublished and published in numerous publications, but actually not available to the practitioner. At the same time, dry mummy extract is an ingredient in a number of official medicines and biologically active food additives. There is no modern evidence base for its scientifically based clinical use.

This publication opens a series of articles containing the results of information and analytical studies devoted to the analysis of specific clinical trials of mummy conducted in the Russian Federation with the aim of

study of its effectiveness and safety in various diseases.

The purpose of this work: information and analytical researchunique archival materials of the FGK MH USSR, dedicated to the history of pre-registration clinical trials of domestic mummy, harvested in various regions of the USSR in the 60s – 90s of the XX century.

Research methods: historical, informational and analytical. Research objects:

1) the official documentation of the archives of the FGK Ministry of Health of the USSR, provided by the Ministry of Health of Russia to the employees of the Department of Medicinal Products of Natural Origin in 1993–96. for the purpose of carrying out this research; 2) the results of our own experimental research, published in the open press and protected by RF patents.

I. Analysis of the results of pre-registration clinical trials Central Asian mummy-asil

For the first time, the Pharmacological Committee (FC) of the Ministry of Health of the USSR allowed the clinical study of a thick extract of mummy in surgical practice for bone fractures on June 18, 1965. The Central Institute of Traumatology and Orthopedics (CITO), the Department of Traumatology of the Central Institute for Advanced Medical Studies (CIU) and Department of Surgery, Tashkent Institute of Advanced Medical Education. Later, clinical trials were allowed in the orthopedic and traumatological clinic of the Tashkent Medical Institute (Protocol No. 7 dated 04/15/1966) and the Moscow Orthopedic Hospital (Protocol No. 3 dated 07/01/1966).

The FC of the USSR Ministry of Health (November 28, 1969) reviewed the presented research results on mummy and recommended that the Uzbek Research Institute of Regional Medicine carry out additional chemical and biological studies of mummy, in particular, a detailed study of its composition, the development of a dosage form and methods for controlling its quality, determination of microbiological purity and carcinogenicity, study of pharmacological properties.

As a result of the experimental studies of the Central Asian mummy carried out at the Institute, despite the advisory support from the Federal Committee of the USSR Ministry of Health, no scientifically substantiated data were obtained confirming the feasibility of a wide clinical use of the mummy.

On September 28, 1973 (Minutes No. 17), at a meeting of the FC of the USSR Ministry of Health, additional materials on the drug mumiyo-asil, presented by the Scientific Medical Council of the Uzbek Ministry of Health, were considered. SSR and AN Uzbek. SSR, and noted the failure to comply with the decisions of the FC from 18.06.65, and from 28.11.69, on the conduct of clinical trials of thick extract of mummy. In accordance with the research protocol, it was supposed to approbate mummy as a means of promoting bone fusion in 9 medical clinics: in 6 clinics - for the treatment of burns and in 4 - for dental diseases. However, the dosage form was not developed, the drug was provided in insufficient quantities and not to all designated clinical sites. The results of studies carried out on the basis of 2 clinics were contradictory and did not allow to reliably assess the effectiveness of the drug.

(Protocol No. 1 of 21.02.75 and Protocol No. 4 of 28.02.75) was the decision to terminate the clinical study of mummy (Protocol No. 1 of 21.02.75) due to the lack of grounds for its use as a medicinal means (Protocol No. 4 dated 02.28.75): its advantages over other methods of treating fractures have not been revealed and effectiveness in the treatment of periodontal disease has not been shown.

According to the conclusion of the reviewers - the Research Institute for Biological Testing of Chemical Compounds and the State Research Institute for Standardization and Control of Medicines - the volume of experimental studies of the specific activity and harmlessness of the drug is not sufficient, and the standardization methods in the developed regulatory documents (ND) for the Central Asian mummy are not specific. Therefore, ND on the mummy was not recommended for approval, and the Presidium of the FC of the USSR Ministry of Health made a decision to apply to the Higher Attestation Commission with a letter about the inadmissibility of using materials on the clinical use of mummy as a substance that has not received permission for medical use in dissertations.

The modified materials on the Central Asian mummy and the developed dosage form - mummy tablets, 0.1 g each, were presented to the FC of the USSR Ministry of Health on September 5, 1979. After a comprehensive review of these materials, including, from the point of view of assessing the completeness of the study of toxicity, specific pharmacological activity , as well as the quality and standardization of mummy tablets, additional data were requested on acute toxicity, the effect of mummy on the blood coagulation system, local irritating effect on the gastric mucosa, as well as statistically reliable data on efficacy in bone fractures and the results of a comparative study of the specific activity of mummy and other biostimulants. And only after the provision of all the necessary materials, the FC of the Ministry of Health of the USSR on May 16, 1980 (Protocol No. 11) clinical trials of the drug mumiyo asil in 0.1 g tablet dosage form as a means of accelerating bone tissue regeneration were allowed. Clinical trials were completed in 1982. Reports of clinical trial results obtained from clinical sites were inconsistent.

The developed ND for the drug did not allow to control its quality, and, consequently, its effectiveness and safety. In this regard, at a meeting of the FC of the Ministry of Health of the USSR on April 10, 1987 (Protocol No. 7), it was decided that it was not advisable to recommend the drug for medical use due to the lack of sufficient volume, evidence of the effectiveness, standard and stability of the dosage form of the mummy tablet. At this stage, official correspondence with the USSR Ministry of Health, which lasted for almost a quarter of a century, was terminated, and the drug mumiyo Asil was not registered in the prescribed manner.

II. Pre-registration clinical trials of the Caucasian mummyAlmost simultaneously with the Central Asian in the North Caucasus, a study of the mummy of local origin was carried out.

In 1967, the Stavropol Medical Institute asked the FK of the USSR Ministry of Health to authorize the clinical study of the Caucasian mummy for ulcerative

diseases of the stomach, radiculitis and other diseases, but the FC provided the results of an experimental study of samples in an insufficient volume. Therefore, the FK Ministry of Health of the USSR instructed the Pyatigorsk Pharmaceutical Institute and the Pyatigorsk Institute of Balneology and Physiotherapy to continue the experimental study of the Caucasian mummy. After revision, the volume and results of the materials provided, as before, did not meet the requirements of the Federal Code of the Ministry of Health of the USSR, therefore, permission for clinical trials of the Caucasian mummy drug was not received.

III. Clinical trials of mummy of various origins

In June 1969, the Burn Center of the Institute of Surgery named after V.I. Vishnevsky (Moscow) with a request to authorize clinical trials of mummy, providing preliminary results of treatment of burns in humans with mummy preparations. The volume and results of the materials provided did not meet the requirements of the Federal Code of the Ministry of Health of the USSR, and the clinical study of the mummy was not allowed.

The Leningrad Chemical and Pharmaceutical Institute The Leningrad Sanitary and Hygienic Institute appealed in 1971 (Protocol No. 15 of September 24, 1971) to the FK of the USSR Ministry of Health with a request to authorize clinical trials of the dry extract of mummy developed by them. However, the FC of the USSR Ministry of Health (Protocol No. 11 dated 09.06.72) rejected the appeal due to the lack of specific methods for identifying and monitoring the biological activity of the drug (substance).

The Pharmacological Committee of the USSR Ministry of Health resumed consideration of the issue of permission for the clinical study of the mummy extract, developed by scientists at the Leningrad Institute of Chemical Physics, on April 13, 1973 (Protocol No. 7). The conclusion of the Pharmacological Committee of the USSR Ministry of Health indicates the absence in the documents of data on adequate methods for identifying the substance, confirming the constant qualitative composition of raw materials and mummy extract. In this regard, the FC recommended the development of an ND for raw materials and mummy extract, which guarantees the constancy of the qualitative and quantitative composition of the drug, as well as adequate methods for controlling its quality.

The appeal to the FC of the Ministry of Health of the USSR Research Institute of Oncology and Radiology of the Ministry of Health of the Kyrgyz SSR with a package of documents for drugs: sublimated mummy, mumidez, mumidelis ointment with a request to authorize their clinical trials was rejected due to the fact that the documents were provided in an incomplete volume and did not correspond to the existing ones. requirements.

Thus, the main problem that hindered the conduct of clinical trials of the substance and various dosage forms of mummy in the period from 1965 to 1993 was the lack of standard samples for conducting such tests. In addition, adequate methods for identification and quality control of mummy were lacking. Information about its nature and chemical composition was contradictory and incomplete [34].

Therefore, in 1993, the Ministry of Health of Russia instructed the Research Institute of Traditional Methods of Treatment of the Ministry of Health of the Russian Federation (since 2000 - the Federal Scientific Clinical and Experimental Center for Traditional Methods of Diagnostics and Treatment of the Federal Public Health Service - FNCEC TMDL) -

the only scientific institution in the country dealing with the problems of studying and substantiating the experience of folk and traditional medicine in different countries, to conduct a comprehensive study of domestic and foreign mummy (in a comparative aspect); substantiate the feasibility of its use in clinical practice; develop methods for its identification and standardization.

IV. Modern research on the standardization of mummy

In accordance with the instructions of the Ministry of Health of the Russian Federation, we were the first to develop unique methods for identifying dry mummy extract (substance) and raw materials. In particular, we studied the composition and determined the quantitative content of fatty acids, free amino acids and the amount of amino acids after acid hydrolysis in mummy raw materials of various mummy provinces (Gorno-Altai, Pamir-Altai, Central Asian, Mongolian) and mummy preparations: dry mummy extract, tablets dry mummy extract. The similarity of the qualitative fatty acid and amino acid composition of the samples of different mummy provinces was established. Using GLC and HPLC, a method for the quantitative determination of fatty acids, free and bound amino acids has been developed. The limits of fluctuations in the content of the total fatty acids,

The spectral characteristics of mummy were studied: UV-, IR-spectra and fluorescence spectra. The specificity of fluorescence spectra for mummy has been shown [11, 12, 32, 34].

The characteristics of the authenticity and quality indicators of mummy raw materials, dry mummy extract, dry mummy extract tablets have been developed [7, 9, 12, 32, 33, 34].

The effect of a standardized extract of dry mummy on the morphology and directed migration of fibroblast-like and epithelial cells, spontaneous and ADP-stimulated platelet adhesion, and intracellular pH of fibroblasts and platelets was studied using cell models. It was shown that under the experimental conditions, dry mummy extract does not cause changes in the morphology of fibroblast and epithelial cells and does not lead to accelerated wound healing, does not affect spontaneous and ADP-stimulated platelet adhesion, intracellular pH of fibroblast connective tissue cells, and causes an increase in the intracellular pH of platelets. The use of these biological tests as biological criteria for assessing the quality of mummy is not advisable [5, 8, 28].

The specific pharmacological activity (antitoxic, antioxidant, choleretic) of a standardized dry mummy extract was studied. The pronounced antitoxic properties of the drug, combined with choleretic activity, have been established [4, 29, 30, 31].

The results of the research were used to develop VFS 42-3082-98 "Mumiyo" [1], VFS 42-3084-98 "Mummy dry extract" [2], VFS 42-3083-98 "Dry mummy extract tablets 0.2" [3], as well as “Instructions for the preparation of raw mummy”.

The priority of the research results is confirmed by two RF patents for the invention "Method for the identification of mummy-like substances" (No. 2042948) [11] and "Hepatoprotective agent of natural origin" (No. 2114626) [4]. In the course of research in the field of synonymy and etymology of mumiyo, we compiled a terminological dictionary containing 127 mumiyo terms. It is included in the Methodological Recommendations of the Ministry of Health of the Russian Federation "Application of the terms naturotherapy and naturofarmation in practical health care" [10].

Conclusion

The results obtained in the course of this study of available domestic bibliographic sources, as well as unpublished archival data of the Pharmacological State Committee of the USSR Ministry of Health, are the basis for choosing promising areas of modern clinical research of standardized dosage forms and the substance of mummy.

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