

## UTILIZATION OF HIVE PRODUCTS FOR DRUG PRODUCTION, A PRESENT TASK FOR PHARMACY

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Taking into consideration the present stage of researches carried out on raw materials used for drug production, the apicultural products – propolis, honey, pollen etc. represent an increasing interest as very accessible sources. Large amounts of biologically active products, having wide possibilities of application in the various fields of the national economy, including medicine, are produced on their basis.

We have studied, analysed and synthesized the use of apicultural products as prophylactic and therapeutic means in treating various diseases, from different points of view: apicultural, botanic, chemical, microbiological, pharmacological.

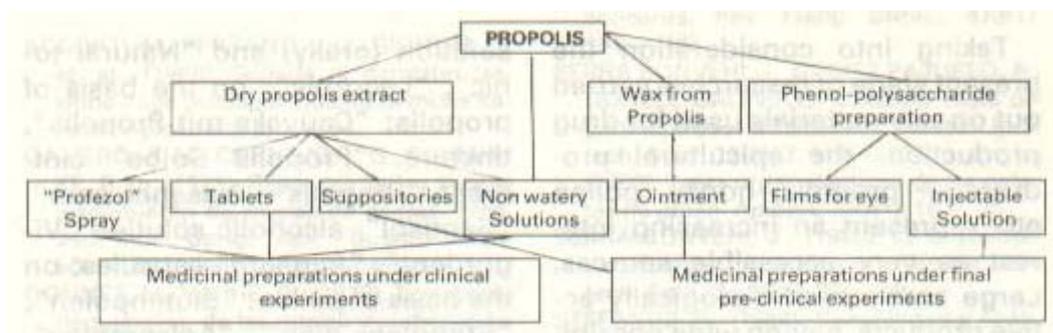
The apitherapeutical products, produced by specialized units in the USSR, France, FRG, Canada, Spain, Japan, Bulgaria, Romania, China, Chekoslovakia etc. are widely appreciated. Let's take for example those prepared on the basis of royal jelly: "Apilac" tablets, polyvitamines in capsules "Apifortil", phials containing "Royal jelly" solution (orally) and "Natural tonic", "Lac-Apis"; on the basis of propolis: "Cauvaks mit Propolis", tincture, "Propolis Solbe" ointment, "Propolis – Nasenbalsam", "Sentisol", alcoholic solution "Vigordent", "Aagaard" capsules; on the basis of pollen: "Blutenpollen", "Stimulans-diab", "Apicomplex", "Vitapol", the "Aptopolen" tonic product; on the basis of bee venom: "Apitrit", "Verapin", "Forapin p" emulsion, solutions "Apicur", "Apiver", "Immenin".

Mention should be made that several of the drugs prepared on the basis of initial raw material are not always standardized, thus limiting their utilization and validity.

The opportuneness of making a serious study of propolis as raw material used in drugs' preparation, with the help of the present methods of physical and chemical analysis, is conditioned by the necessity of solving out the problem linked to the possibility of extracting biologically-active fractions.

By applying mathematical planification in our experiments, we have carried out differentiated methods for the extraction of biologically-active substances deriving from dry propolis extract and the phenol-polysaccharidic complex. We have then worked out, on their basis, the compositions and technology of the various medicinal forms: tables, spray, ointments, solutions (see diagram).

**Technological Diagram of Producing Drugs Based on Propolis**



The dry propolis extract represents a sum of biologically-active substances. Its composition includes phenolic compounds (oxycumarine, phenolcarbonic acids), polysaccharides, terpenes and microelements.

From the physical point of view it is a brownish-yellow dust, having specific smell and a bitter taste. It is soluble in 80-95% alcohol, acetic ether; it is practically insoluble in water and light petroleum.

A series of technological properties (friability, pourable sealing compound, volume density, pressing degree, humidity content) were studied in order to utilize dry propolis extract for the creation of several solid medicinal products. The results obtained were used as basis for establishing the optimal composition and technology of tablets used as drugs in the treatment of ulcer and liver protection.

At present all preclinical tests of this kind of drug have come to an end. The reports have been forwarded to the Pharmacological Committee of the Health Ministry of the USSR, in order to get the approval to carry out clinical researches.

Based on the above mentioned biologically-active substance we have worked out the composition and technology for other two products – spray with film and spary with foam. The conventional denomination is “Profezol”. We have studied their physical-chemical characteristics. The results obtained allowed us to establish the optimal concentration of propolis extract, under this drug form, by establishing the critical concentration of micella formation (CCM), found within the limits of 1%.

The study on aerosol's stability in the case of storage at various temperature conditions, as well as depending on the kind of package (we have determined the pH, specific electric conductivity, superficial tension, stickiness, refractory index, quantitative amount of phenolic coumpounds) pointed to the following optimal conditions: storage temperature of 6-10 °C, package – aerosolic glass tube covered by polymer.

The results obtained after the preclinical experiments allowed us to recommend the spray for the treatment and prophylaxy of various skin diseases, of mucous membranes and body cavities. The documentation was presented to the Pharmacological Committee of the Health Ministry in the USSR, in order to obtain the approval to carry out clinical tests.

For NPHE, stomatology, dermatology we recommend the use of several unwatery propolis solutions having antimicrobial, antiinflammatoty, recovery properties. However, these products are also based on dry propolis extract, dissolved in alcohol mixtures-water with 80% ethanol content; polyethyleneoxid 400; alcohol and glycerine solutions. Propolis substance concentration is in all the cases 1-10%, 20%, 30%. The solutions obtained were submitted to physical and chemical researchers.

The analysis of the results: dependency between the refractory index, stickiness, specific electro-conductibility, pH, superficial tension of unwatery dry propolis extract solutions and its concentration allowed for the determination of optimal correlations between the raw material and the solvent. The CCm of propolis extract combined with water and alcohol represents 5.4%, whereas in polyethyleneoxid solution it is of 400-3%.

At present, according to the decision of the Pharmacological Committee of the Health Ministry in the USSR, the unwatery propolis solutions are under clinical research.

This substance was used to work out the composition and technology of the ointments used in sport medicine and characterized through antiinflammatory properties, anaesthetic action, resorbtion, noncatching disease, in the treatment of microtraumatism and rheumatic disease prophylaxy. The drugs created for this aim are still under preclinical tests.

Based on another substance – phenol – polysaccharide complex of propolis, we have elaborated the technology for a freeze dried product having an antihypoxic, biostimulating, highly adaptable action. We have studied the qualitative composition through thin layer paper cromathography. We have established the macro and microelements (calcium, phosphorus, magnesium, potassium, sodium, cobalt, manganese, iron, zinc). At present this product is in the final preclinical testing phase, under the form of solution and injections.

In parallel our research work is headed towards other hive products which can also be used in the drug industry: floral pollen and honey. Researchers are carried out for the extraction of biologically-active fractions of these products, for their use in peditry and narcology departments. We have studied the content in aminoacids (qualitative and quantitative) applying the Spakmann, Moore and Stein metod and using the device AAA 881 (automatic analyser for aminoacids). We established the presence of unreplaceable aminoacids: lysine, threonine, valine, methionine, leucine, isoleucine, phenilalanine; and of semisubstituible aminoacids: histidine, arghinine tyrosine, and the presence of aminosuccinic acid, serine, glutamic acid, proline, glycine, alanine, cystine.

Using FLAPHO-4 devices (photometer with flame – produced by Karl Zeiss Jena, GDR), AAS – 1 (atomic spectrophotometer with absorption-produced by Karl Zeiss Jena, GDR), we established the quantitative content in macroelements (sodium, potassium, phosphorous, calcium) and microelements (zinc, manganese, copper, cobalt, iron).

On the basis of pollen and honey we worked out for the first time, for drug production, a technology for freeze dried products: watery extract of pollen and honey. We have established the period, freezing and drying temperature, depth of vacuum.

Thus the researches carried out in the USSR and the results obtained point to a novelty in the scientific orientation as regards the production of efficient drugs, on the basis of biologically-active substances, out of apicultural products, which are on their way to be widely introduced in medical practice.

#### REFERENCES

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