

STUDY OF EUCALYMIN AS AN ACTIVE PHARMACEUTICAL INGREDIENT FOR THE DEVELOPMENT OF SOFT DOSAGE FORMS

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Introduction. The choice of rational therapy of inflammatory skin diseases requires a deep understanding of the mechanisms of inflammation and the causes of their occurrence. For example, non-infectious exogenous factors of physical and chemical nature cause violations of the epithelial integrity of the skin, accompanied by the formation of wounds, the pathology of which for many years remains a complex clinical problem of doctors in everyday practice due to complications that are common cause of morbidity and mortality [1].

To prevent and reduce possible complications, much attention is paid to the study of the physiology of wound healing, as well as to new therapeutic approaches to treatment [2].

Due to the high prevalence of wounds in the general population and the increasing incidence in the adult population, this pathology has a great socio-economic impact.

The development of a new herbal medicine is often associated with difficulties associated with the influence of pharmaceutical factors (particle size, solubility, dosage form, production technology, etc.), which provide stable quality indicators, such as uniform distribution of the active substance and pharmacological effect. In this regard, the rationale for the choice of method of administration, excipients, technological scheme of production allows to take into account the critical points at each stage and as a result.

It is necessary to know the composition of a substance of plant origin, containing a complex of biologically active substances capable of chemical transformation under the influence of aggressive environments and high temperatures. The above arguments are the basis of further research in examining the possibility of a method of introducing eucalymin into the placebo of medical pencils.

Substances of various chemical nature, synthesized by plants, are a rich source of drugs and prophylactics with bactericidal and fungicidal properties. The peculiarity of extracts from medicinal plants is a certain ratio of biologically active substances that contribute to the optimal effect on the human body, and the ability to use them for a long time. The chemical structure of many natural compounds is similar to the physiologically active substances of microorganisms (hormones, vitamins, enzymes, etc.), which allows them, in contrast to synthetic drugs or antibiotics, to be more actively involved in biochemical processes. In this case, given the similarity in cell structure, there is no abrupt change in the chemical reaction systems of living cells of higher animals and humans, as well as no side effects and toxicity of substances of plant origin, which allows adequate replacement of antimicrobial drugs of synthetic origin.

In this regard, the search for new antimicrobials of natural origin and the development of drugs based on them is necessary and timely.

Among the known drugs of plant origin should be noted preparations of eucalymin, macelia, sage, yellow cubes. Biological activity of substances eucalymin, sanguiritrin, lutenurin, 7-hydroxyroyleanone show antibacterial activity against the most common pathogens.

The substances have a wide range of antimicrobial activity and have a high bacteriostatic effect against a number of laboratory strains of pathogenic and opportunistic microorganisms. The activity is due to both individual compounds – alkaloids (sanguiritrin, lutenurin, 7-hydroxyroyleanone) and the purified amount of terpenoid phenolaldehydes of the phloroglucin series (euglobals) and triterpenoids. Along with them in the literature there is information about the use as drugs for the prevention and treatment of inflammatory diseases of the skin of chamomile, St. John's wort, spruce, etc.

According to the EF definition, medical pencils in the form of a cylindrical or conical pencil with a rounded end, intended for external use to provide local action and consisting either only of active substances (one or more), or represented by a suitable base in which evenly distributed active substances. It is known that excipients have a significant effect on the quality of medical pencils, such as: stability, hardness, plasticity, homogeneity, and others.

The aim of the study was to conduct research on the solubility of the active pharmaceutical ingredient eucalymin to create a soft dosage form in the form of medical pencils.

Materials and research methods. Eucalymin is an original domestic phytopreparation isolated from the leaves or shoots of *Eucalyptus viminalis* Labil family (*Myrtaceae*), is a purified amount of terpenoid phenol aldehydes of the phloroglucin series (eupeglobals) and eupeglobals.

The drug has a broad spectrum of antimicrobial activity and has a high bacteriostatic effect against a number of laboratory strains of pathogenic and opportunistic microorganisms, inhibiting the growth of gram-positive bacteria such as *Staphylococcus aureus*, *Streptococcus pyogenes*, *Bacillus subtilory Bacillus*, *Bacillus subtilory Bacillus. tuberculosis* (MIC: 0.24 – 62.5 µg / ml).

Eucalymin is weakly active against mycelial fungi (genus *microsporum* and *Trichophyton*) and yeast-like fungi (genus *Candida*), and at a dose of 500 µg / ml and below does not show activity against gram-negative microorganisms of the genus *Escherichia* and *Pseudomonas*.

Results. Eucalymin is practically insoluble in water, soluble in 95 % alcohol, chloroform, benzene. It should be noted that in the development of dosage forms with substances of plant origin, the use of aggressive solvents is impractical given the possible destruction of the complex of biologically active substances that are part of the substances. Eucalymin is practically insoluble in purified water, little in glycerin, propylene glycol, ethyl oleate, chloroform; moderately soluble in PEG-400 and 95 % ethyl alcohol at a temperature of 20 °C, soluble in ethyl alcohol at a temperature of 50 °C. Eucalymin is soluble in systems of dispersion media ethyl alcohol – PEG in a ratio of 1: 1 and 1: 2 [4]. However, in this work, as solvents for eucalymin, excipients of placebo are of interest, in particular peach oil / castor oil. From a biopharmaceutical point of view, determining the particle size of the substance is necessary to determine

the rate and completeness of penetration through the skin. Therefore, the study of the influence of the nature of the solvent on the particle distribution is an important stage in the development of drugs.

From a biopharmaceutical point of view, determining the particle size of a substance determines its penetration through the skin.

In this regard, the study of the shape and size of eucalymin particles and its distribution in different dispersion media (Fig. 1).

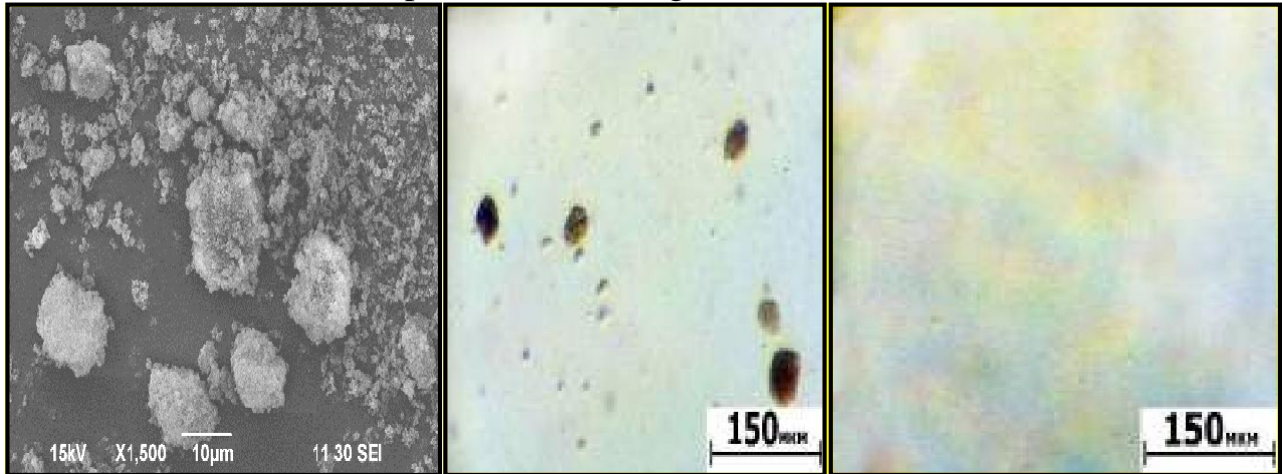


Fig. 1 Eucalymin particles (lens x 1.5); in ethyl alcohol 95 % (20 °C) (lens x 10); in the system of solvents peach oil: castor oil in a ratio of 1: 2 (lens x 10)

The results of microscopic analysis showed that eucalymin is soluble in the system of solvents peach oil – castor oil in a ratio of 1: 2. In 95% ethyl alcohol at a temperature of 20 ° C there are individual particles ranging in size from 20 to 60 µm. However, ethyl alcohol belongs to class 3, subclass 3.2 of toxic substances and has dehydrating properties, which limits the possibility of its use. Eucalymin is soluble in dimethyl sulfoxide, however, its use as a solvent is undesirable because this solvent extracts lipoproteins from the surface layers of the skin and causes structural changes in the stratum corneum, by increasing the rate of absorption of drugs and the likelihood of infection [5].

Dissolution of eucalymin in a system of solvents peach oil – castor oil in a ratio of 1: 2 provides a uniform distribution of the substance in dosage forms (fig. 2).

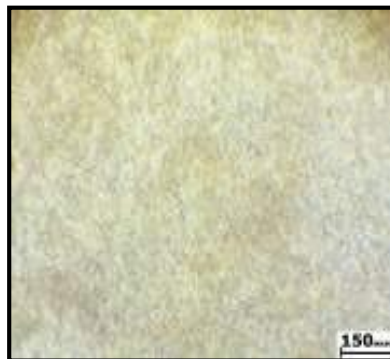


Fig. 2 Micrograph of a medical pencil with eucalymin (lens x 4)

The use of peach oil and castor oil as a solvent, due to the high content of glycerides of unsaturated acids contributes to the atraumatic application of castor oil on the skin.

To establish the homogeneity and uniform distribution of eucalymin in medical pencils, a microscopic study of an experimental sample of a medical pencil was performed.

Conclusions. A photomicrograph of a medical pencil with eucalymin on a longitudinal section, shows the absence of particles, air rod or funnel-shaped depression and is a homogeneous mass with a greenish-gray hue with a faint specific odor of the substance. In this regard, peach oil with subsequent solubilization with castor oil was selected as the solvent for eucalymin.

References

1. Пантюхина, Е. В. Разработка состава, технологии мази и медицинского карандаша антимикробного действия с полиэтиленоксидным экстрактом травы донника лекарственного: дис. канд. фарм. наук: 15.00.01. Пантюхина Елена Валерьевна. Пятигорск, 2018. 157 с.

2. Плешков, В. Г. Лечение хронических ран. В. Г. Плешков, В. В. Привольнев, А. В. Голуб. Вестн. Смоленской гос. мед. акад. 2015. Т. 14, № 2. С. 58–65.

3. Вичканова, С. А. Новые аспекты применения эвкалимина. С. А. Вичканова, Н. М. Крутикова. Вопросы биологической, медицинской и фармацевтической химии. 2012. Т. 10. № 1. С. 214–220.

4. Алешникова, К. Ю. Технологические аспекты разработки карандашей лекарственных с эвкалимином. К. Ю. Алешникова, М. А. Джавахян. Вопросы биологической, медицинской и фармацевтической химии. 2019. Т. 22, № 3. С. 37–41.

5. Современные основообразующие вещества в технологии мягких лекарственных форм. М. А. Джавахян, А. В. Давыдова, С. П. Комкова, Т. А. Сокольская. Фармация. 2015. № 6. С.53–56.