

DEVELOPMENT OF THE COMPOSITION OF THE BALM-MASK FOR TREATMENT APPLICATION SEBOREIC DERMATITIS OF THE SCALP

Cherkasova A.O., Konovalenko I.S.

National University of Pharmacy

Kharkiv, Ukraine

ilonakovalenko1601@gmail.com

Резюме. На сьогоднішній день себорейний дерматит є частою проблемою серед усіх дерматологічних захворювань. Саме екстемпоральне виготовлення ліків набуває нового значення і сьогодні позиціонується як виготовлення ліків для потреб кожного конкретного пацієнта. Перевагою екстемпоральних лікарських засобів є індивідуалізація медичної допомоги для кожного хворого, вибір найбільш раціонального співвідношення інгредієнтів, варіювання дозування, зважаючи на генетичні, вікові, статеві особливості організму людини. Але, нажаль, більшість асортименту екстемпоральних прописів застаріли, враховуючи темпи розвитку сучасної фармації та виробництво нових субстанцій. Метою нашого дослідження було провести аналіз лікарських препаратів фармацевтичного ринку України та на основі отриманих результатів розробити склад та опрацювати алгоритм створення нового лікарського засобу у формі маски-бальзаму для лікування себорейного дерматиту шкіри голови. Об'єктами дослідження було обрано такі активні фармацевтичні інгредієнти: цинк-пірїтїон, азелаїнова кислота, гліколева та молочна кислота. Визначено оптимальний склад емульсійної основи та готової м'якої лікарської форми.

Abstract. Today, seborrheic dermatitis is a common problem among all dermatological diseases. The extemporaneous production of medicines takes on a new meaning and today is positioned as the production of medicines for the needs of each specific patient. The advantage of extemporaneous medicines is the individualization of medical care for each patient, the choice of the most rational ratio of ingredients, variation of the dosage, taking into account the genetic, age, and sex characteristics of the human body. But, unfortunately, most of the range of extemporaneous prescriptions are outdated, taking into account the pace of development of modern pharmacy and the production of new substances. The purpose of our research was to conduct an analysis of drugs on the pharmaceutical market of Ukraine and, based on the results, to develop a composition and develop an algorithm for creating a new drug in the form of a mask-balm for the treatment of seborrheic dermatitis of the scalp. The following active pharmaceutical ingredients were chosen as the subjects of the study: zinc pyrithione, azelaic acid, glycolic and lactic acid. The optimal composition of the emulsion base and the finished soft dosage form was determined.

Keywords: seborrheic dermatitis, composition, technology, active ingredients.

Introduction: Seborrheic dermatitis (DS) is a chronic recurrent skin disease associated with increased secretion of skin sebum, a change in its qualitative composition, and is characterized by localization in areas of accumulation of sebaceous glands - on the scalp, face, upper body, folds. Peeling of the scalp, accompanied by

itching, creates not only medical, but also social and psychological problems for patients.

The French microbiologist Louis Charles Malassez first suggested that dandruff could be caused by *Malassezia* fungi about a hundred years ago, when he first discovered a yeast-like substance in the dandruff of a patient with seborrheic dermatitis. Currently, the leading role of *Malassezia* in the pathogenesis of dandruff and seborrheic dermatitis has been confirmed by numerous clinical and laboratory studies. It is believed that at least 90 % of the population has these yeast fungi as part of the permanent or temporary microbiota of the skin [1, 2].

Mushrooms of the genus *Malassezia* are imperfect yeast-like lipophilic fungi that colonize a significant number of zones characterized by increased secretion of sebum, since the presence of a sufficient amount of lipids is required to support the vital activity of these microorganisms. At the same time, it has been proven that at least five species of *Malassezia* (*M. furfur*, *M. globosa*, *M. sympodialis*, *M. restricta*, *M. obtusa*) can play the role of a pathogen in the development of seborrheic dermatitis [3, 4].

Modern knowledge about the nature of the appearance of dandruff and seborrheic dermatitis allows us to state that dandruff is a mild clinical form of seborrheic dermatitis and can transform into it under a combination of three conditions (Table 1):

- increased sensitivity of the skin to the formation of inflammatory reactions to the action of oleic acid due to an innate predisposition.
- the presence of sebum as a nutrient medium for fungi;
- the presence of *M. globosa* in the microflora of the scalp [5, 6].

Table 1

Causes of seborrheic dermatitis

Basic	Additional
– Relative or absolute hyperandrogenism, or increased sensitivity of sebocytes to the action of androgens (with a normal general hormonal background). – Excessive amount and activity of <i>Malassezia</i> fungi (<i>M. globosa</i>). – Individual high sensitivity to the action of free fatty acids [7].	- Genetic predisposition – Endocrine diseases – Pathology of the gastrointestinal tract - Stress - Nature of nutrition – Chronic infections – Hypovitaminoses (especially A and C) – Improper or insufficient scalp care [8, 9].

Aim: The purpose of our research was to conduct an analysis of drugs on the pharmaceutical market of Ukraine and, based on the results, to develop a composition and develop an algorithm for creating a new drug in the form of a mask-balm for the treatment of seborrheic dermatitis of the scalp.

Materials and methods: The following active pharmaceutical ingredients were chosen as the subjects of the study: zinc pyrithione, azelaic acid, glycolic and lactic acid.

Research methods. Information retrieval, information analytical, organoleptic, physicochemical, pharmacotechnological.

Results and discussion: Directed relief of clinical symptoms of the disease with the help of antifungal drugs. In this regard, medical management includes the use of etiotropic and pathogenetic agents that help to relieve inflammation, itching, regulate sebum secretion, provide a fungicidal and fungistatic effect, and normalize desquamation of the epidermis [10].

A promising medicinal form are balms and masks to be applied to clean scalp after shampooing and application for 10–15 minutes. Thus, it can be concluded that the creation and research of new drugs from active pharmaceutical substances of synthetic and natural origin and the development of a line of drugs for the treatment of seborrheic dermatitis of the hairy part of the scalp is a promising and urgent task of the Ukrainian industry.

In the literature search, we selected the following active pharmaceutical ingredients that exhibit fungicidal (on *Malassezia* fungi), antibacterial, wound-healing, and anti-inflammatory effects and can be used in the treatment of seborrheic dermatitis of the hairy part of the scalp (Table 2).

Table 2

Characterization of active pharmaceutical ingredients used in the development of new drugs for the treatment of seborrheic dermatitis of the hairy part of the scalp

Name	Physicochemical properties	Pharmacological activity
Zinc-pyrithion	Appearance: white amorphous powder, odorless. pH: (5 % suspension): 6.5 – 9.0. Solubility parameters: in water - 8 mg/dm at pH 7.0. % input – 0.1–0.2 %.	Fungicidal agent, exhibits bacteriostatic effect, high activity against yeast-like fungi, able to eliminate superficial skin irritation
Azelaic acid	Appearance: white crystalline powder or flakes. Solubility parameters: perfectly soluble in hot water, as well as in ethanol. % input – 5–20 %	Anti-inflammatory, antibacterial, keratolytic action. Reduces the fraction of free fatty acids in the surface lipids of the skin
Solution glycolic acid 70 %	Appearance: transparent liquid with a specific smell. Solubility parameters: well soluble in water. % input – 5–15 %	Improves the condition of the epidermis, evens out the relief of the skin, narrows the pores, prevents clogging of the sebaceous ducts with horny plugs
Solution lactic acid 80 %	Appearance: transparent, colorless and odorless liquid. Solubility parameters: well soluble in water. % input – 5–20 %	Exfoliating, light astringent action. Moisturizes and deeply penetrates the skin, normalizes the process of epithelization, carries out collagen synthesis

When creating the balm-mask recipe, a whole complex of auxiliary substances is used, which ensures the physical, chemical and microbiological stability of the product over a certain period of time. The cream chosen by us belongs to the emulsion

type1 (oil in water), therefore the following components can be included in the composition of auxiliary substances: oil phase (fatty oils, silicone and synthetic oils, natural or synthetic waxes), emulsifiers, structure formers, humectants, preservatives, etc.

In the development of new medicinal products, excipients approved for medical use, which are presented in the table, were used in table 3.

Table 3

Excipients that were used in the development and research of new medicines

Name of excipient	Regulatory documentation	Purpose
Purified water	SPhU	Dispersion medium, solvent
Ethyl alcohol 95%		Extract agent, co-solvent
Concentrated sulfuric acid	Ph.Eur. standart–Sigma	Reagent
Emulsion wax	SPhU	Emulsifier
Emulfarma 1000	Ph.Eur. standart–Sigma	Emulsifier
PEG 100		Emulsifier, moisturizer
Monostearol glyceride 40		Emulsifier
Olivem 1000		Emulsifier
Glycerin	SPhU	Co-solvent
Propylene glycol		Co-solvent
Potassium sorbate		Preservative
Benzoic acid		Preservative
Phenoxyethanol		Preservative

All components are physically and chemically compatible when mixed with each other and exhibit the declared pharmacological effect. The combination of acids potentiates the effect of each other, and zinc-pyrithion does not enter into chemical interaction with the active substances listed above.

According to the results of previous studies of the rheological properties of balsam samples, it was established that the optimal structural and mechanical parameters are possessed by samples with structural viscosity values in the range of (2000 – 10000) mPa·sec at 20 rpm, samples with Emulfarma 1000.

Conclusions. 1. The conducted informational and analytical analysis made it possible to establish that currently combined medicinal preparations for the treatment of seborrheic dermatitis of the scalp of extemporaneous production are presented in insufficient quantities.

2. The development of new multifunctional cosmeceutical preparations for application in the form of a balm-cream containing active substances with complex therapeutic activity (anti-inflammatory, wound healing, antibacterial and mild exfoliating effect) is an urgent task of modern pharmacy.

3. A brief description of the objects of research is given: active pharmaceutical ingredients and auxiliary substances that were used in the development of the balm-mask.

4. Methods of experimental research were developed, namely: physical and physicochemical, pharmacotechnological and statistical, which allowed to objectively evaluate the properties of medicinal products for external use during the development of their composition and technology.

5. The selection of concentrations of zinc-pyrithione, azelaic, glycolic and lactic acids active substances, which would show the claimed effect, was carried out.

6. A study was conducted on the selection of auxiliary substances and their concentration. It was determined that the optimal emulsifier is Emulfarma 1000.

References

1. Clark GW, Pope SM, Jaboori KA. Diagnosis and treatment of seborrheic dermatitis. *Am Fam Physician*. 2015 Feb 1;91(3):185-90. PMID: 25822272.
2. Schwartz RA, Janusz CA, Janniger CK. Seborrheic dermatitis: an overview. *Am Fam Physician*. 2016 Jul 1;74(1):125-30. PMID: 16848386.
3. Tucker D, Masood S. Seborrheic Dermatitis. 2023 Feb 16. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan–. PMID: 31869171.
4. Dall'Oglio F, Nasca MR, Gerbino C, Micali G. An Overview of the Diagnosis and Management of Seborrheic Dermatitis. *Clin Cosmet Investig Dermatol*. 2022 Aug 6;15:1537-1548. doi: 10.2147/CCID.S284671. PMID: 35967915; PMCID: PMC9365318.
5. Naldi L, Diphorn J. Seborrheic dermatitis of the scalp. *BMJ Clin Evid*. 2015 May 27;2015:1713. PMID: 26016669; PMCID: PMC4445675.
6. Li J, Feng Y, Liu C, Yang Z, de Hoog S, Qu Y, Chen B, Li D, Xiong H, Shi D. Presence of *Malassezia* Hyphae Is Correlated with Pathogenesis of Seborrheic Dermatitis. *Microbiol Spectr*. 2022 Feb 23;10(1):e0116921. doi: 10.1128/spectrum.01169-21. Epub 2022 Jan 12. PMID: 35019692; PMCID: PMC8754105.
7. Sei Y. [Seborrheic dermatitis--clinical diagnosis and therapeutic value of different drugs]. *Nihon Ishinkin Gakkai Zasshi*. 2022;44(2):77-80. Japanese. doi: 10.3314/jjmm.44.77. PMID: 12748587.
8. Barak-Shinar D, Green LJ. Scalp Seborrheic Dermatitis and Dandruff Therapy Using a Herbal and Zinc Pyrithione-based Therapy of Shampoo and Scalp Lotion. *J Clin Aesthet Dermatol*. 2018 Jan;11(1):26-31. Epub 2018 Jan 1. PMID: 29410727; PMCID: PMC5788265.
9. Sobhan M, Gholampoor G, Firozian F, Mohammadi Y, Mehrpooya M. Comparison of efficacy and safety of atorvastatin 5% lotion and betamethasone 0.1% lotion in the treatment of scalp seborrheic dermatitis. *Clin Cosmet Investig Dermatol*. 2019 Apr 29;12:267-275. doi: 10.2147/CCID.S196412. PMID: 31118730; PMCID: PMC6503294.
10. Parham S, Kharazi AZ, Bakhsheshi-Rad HR, Nur H, Ismail AF, Sharif S, RamaKrishna S, Berto F. Antioxidant, Antimicrobial and Antiviral Properties of Herbal Materials. *Antioxidants (Basel)*. 2020 Dec 21;9(12):1309. doi: 10.3390/antiox9121309. PMID: 33371338; PMCID: PMC7767362.