

## ОРГАНІЗАЦІЯ ТА ЕКОНОМІКА ФАРМАЦІЇ

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### ANALYSIS OF OROMUCOSAL MEDICINAL PRODUCTS IN SOLID DOSAGE FORMS FOR THERAPEUTIC DENTISTRY

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*Key words: dental medicinal products with the local action; solid dosage forms; marketing research; pharmaceutical market*

*In order to determine the necessity of creating dental medicinal products the oromucosal dosage forms of the Ukrainian pharmaceutical market have been analysed. Tablet drugs are increasingly used in the treatment of periodontal diseases. Based on the results of the analysis of 35 drugs it has been found that the share of drugs produced in Ukraine (23%) ranks second after Germany (31%) among manufacturer countries. According to the data of the marketing research 54.3% of solid dosage forms are tablets, 25.7% – lozenges and 20% – pastilles. It has been determined that 34.3% of drugs are two-component products, 25.7% – three-component, 20% are one-component and 20% are multi-component. Distinguishing the concept of active substances it has been shown that 77.1% of drugs contain antiseptics, 14.3% – antibiotics, 20% – essential oils, 17.1% – anesthetics. Natural substances as a component are in 8.6% of medicinal products, e.g. phenolic hydrophobic propolis preparation in “Proalor” (LLC “Pharmaceutical company “Zdorovie”, Ukraine), a thick sage extract in “Shavlia” (Natur Product Europa BV, Netherlands) and a solid chlorophyllipt extract in “Chlorophyllipt” tablets (LLC “Pilot Plant “State Scientific Centre on Medicinal Products”, Ukraine). It has been found that there is dominance of combined drugs and a small share of drugs based on natural substances; therefore, creation of oromucosal herbal medicinal products in a solid dosage form is expedient.*

One of the most pressing problems in Ukraine is the health status of the population, including such component as dental health, which low level has a negative impact on the general health condition during all periods of life [4]. Dental service is growing rapidly in Ukraine. Physicians prescribe drugs to patients in different dosage forms for therapeutic purposes [5]. Scientific works of domestic and foreign researchers focus on pharmacotherapeutic issues of oral inflammatory diseases outlining the ways to create new drugs for dental practice, defining the prospects for new research based on the assessment of the range of dental drugs at the Ukrainian pharmaceutical market, etc. [6, 8, 11].

Dental medicinal products can be solid (tablets, lozenges, pastilles, herbal teas), soft (pastes, gels) or liquid (solutions for rinsing the mouth, tinctures) drugs.

Pharmacotherapy of inflammatory periodontal diseases increasingly offers solid dosage forms, such as orally disintegrating (mouth dissolving) tablets, sublingual tablets, lozenges or pastilles that are easy to administer and have pleasant organoleptic properties for a patient [7, 14]. Each of these solid dosage forms has its own specific characteristics. This is primarily due to the advantages in use, dosage of this form, the absence of difficulties with swallowing or discomfort of passage through the gastrointestinal tract, the possibility of combining

several active substances with addition of flavouring agents to enhance organoleptic properties, and it is achieved by the technology of manufacturing the abovementioned medicinal form [3]. Oral pills are usually represented by uncoated tablets with the composition providing slow release and the local action of the active substance or substances, or release and absorption of the active substance or substances in certain parts of the mouth [9, 12, 13]. Lozenges and pastilles are solid single-dose drugs dissolving in the mouth for the local effect, containing one or more active ingredients; they are usually aromatic or sweet-based. They are prescribed for slow dissolution or dispersion in the oral cavity as a result of disintegration, i.e. they are at the site of inflammation for a long period of time, and it allows prolonging the local exposure of active substances [1].

The aim of the research is to carry out the comprehensive assessment of the range of solid drugs used in dental practice in treating diseases of the oral cavity and to determine the expedience of developing new dental products of this dosage form.

#### Materials and Methods

The study involved medicinal products for dental practice of the following groups according to the ATC classification [1]: AA01 – Stomatological preparations (A01AB53 – Chlorhexidine, combinations; A01A D – Other agents for

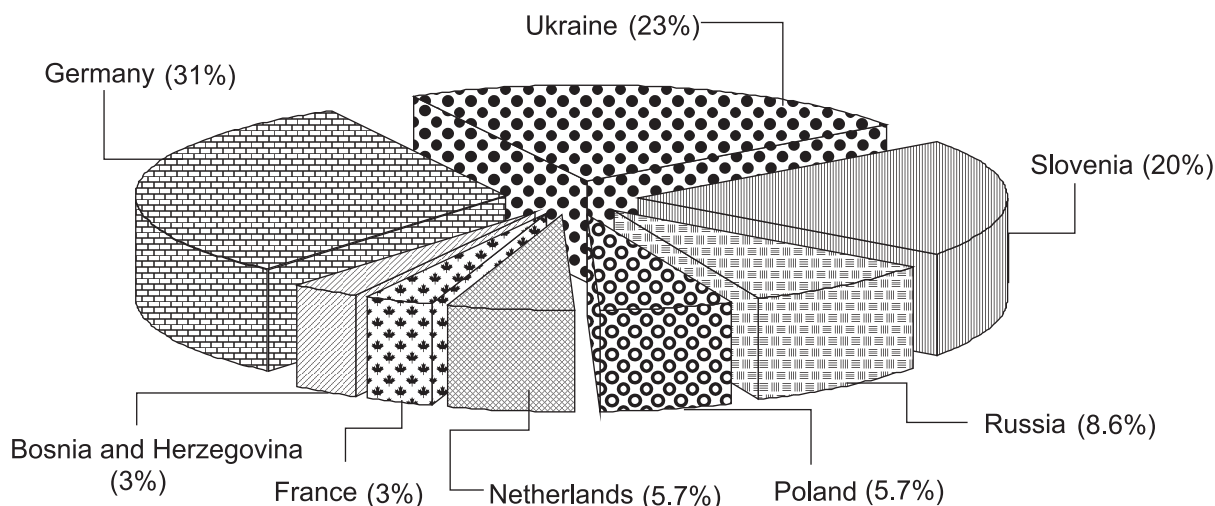


Fig. 1. Manufacturer countries of medicinal products for dentistry in solid dosage forms.

local oral treatment, including group A01A D11 – others); R02 A – Throat preparations (R02A A – Antiseptics: R02A A05 – Chlorhexidine, R02A A06 – Cetylpyridinium, R02A A20 – Various antiseptics, R02A A50\*\* – Chlorhexidine, combinations; R02A B – Antibiotics: R02A B30 – Gramicidin, R02A B52 – Tyrothricin, R02A B53\*\* – Other preparations) and D08 – Antiseptics and disinfectants (D08A X – Other antiseptics and disinfectants: D08A X10 – other preparations).

Using the concentric method the information search was conducted, and 35 drugs labeled for “inflammation of gums and oral mucosa, periodontitis, stomatitis, gingivitis” in the solid dosage form were analysed [2].

### Results and Discussion

A detailed analysis of drug manufacturers has shown that Ukraine as a supplier of medicinal products for dental practice ranks second after Germany since the number of solid dosage forms produced by this country amounts for almost one third (31%) of the total amount. The rest of drugs are supplied by such manufacturer countries as Slovenia, Russia, Poland, Netherlands, France and Bosnia and Herzegovina. It is shown in Fig. 1.

Fig. 2 shows distribution of solid drugs in therapeutic dentistry. It has been determined that among the medicinal products studied pills (including orally disintegrating tablets, oral tablets) are 54.3%, lozenges – 25.7% and pastilles – 20%.

A separate study was performed to assess the amount of active drug substances: 34.3% of the segment under research belonged to two-component drugs, 25.7% – three-component, 20% – one-component and 20% – multi-component. Most of the drugs are combined (Fig. 3). They comprise several antimicrobial components with different mechanisms of action and include the following combinations: antiseptic + vitamin, antiseptic + anesthetic, antiseptic + vitamin + anesthetic, antibacterial component + antiseptic, antiseptic + essential oils, antiseptic + extracts of medicinal plants, products of the natural origin + vitamin.

### Number of medicinal products, %

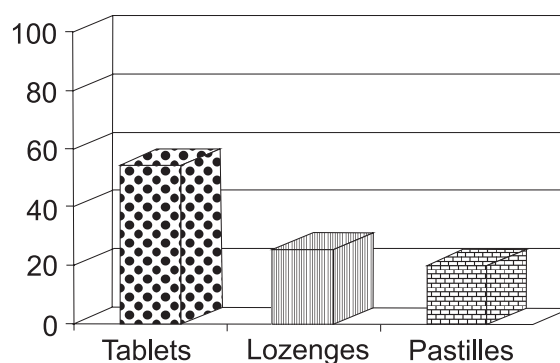


Fig. 2. The types of solid dosage medicinal products for therapeutic dentistry.

### Number of medicinal products, %

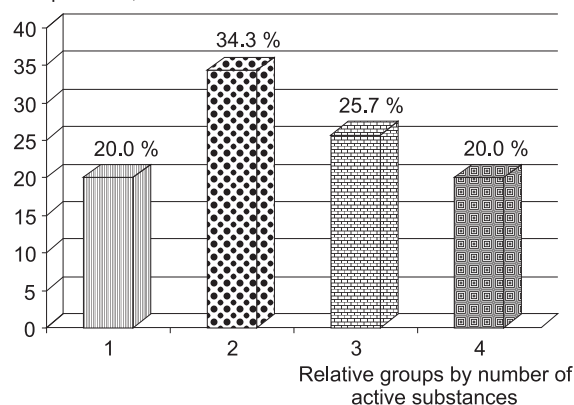


Fig. 3. The number of components in solid medicinal products used for treating inflammatory periodontal diseases, where: 1-4 – groups by the number of active substances. 1 – one-component drugs; 2 – two-component drugs; 3 – three-component drugs; 4 – multi-component drugs.

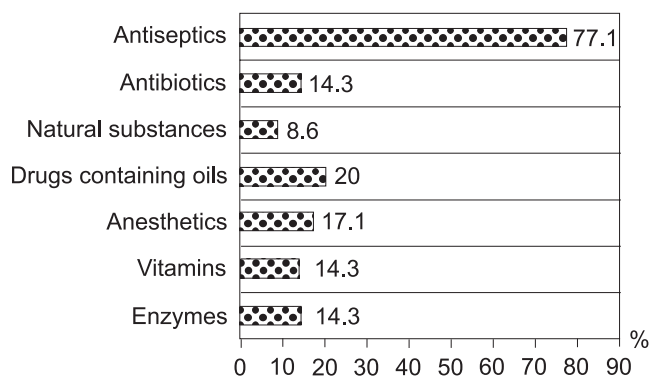


Fig. 4. The active components of solid medicinal products for dental practice.

Such combinations allow obtaining the desired therapeutic effect. Addition of various components of essential oils (menthol, anethole, thymol, etc.) to the antimicrobial component gives a mild local anaesthetic effect, while essential oils or extracts of medicinal plants (peppermint, sage, eucalyptus) enhance the antimicrobial and anti-inflammatory effect.

Medicinal products with a strong anesthetic action contain local anesthetics (benzocaine hydrochloride, lidocaine hydrochloride, oxybuprocaine chloride, etc.). Drugs for ulcerative necrotic lesions of the oral mucosa are found to contain enzyme components, such as lysozyme hydrochloride with antibacterial properties and ability to stimulate the body's non-specific reactivity by splitting necrotic tissues.

The total number of drugs includes 77.1% of drugs with antiseptics as the main components (Fig. 4), namely chlorhexidine, dichlorobenzyl alcohol, cetylpyridinium, decamethoxin, dequalinium, benzalkonium, amylmetacresol, biclotymol. Some drugs (Neo-angin® sugar-free, Neo-angin, Neo-angin® Sage, Neo-angin® Cherry (Divapharma GmbH Klosterfrau Berlin GmbH, Germany) combine several antiseptics, such as amylmetacresol and dichlorobenzyl alcohol. Antibiotics are components of 14.3% of drugs. These are such active ingredients as tyrothrisin Trachisan (Engelhard Arzneimittel GmbH & Co.KG, Germany), dorithricin (RIEMSER Specialty Production GmbH, Germany) and gramicidin (Grammidin® with anesthetic Neo, Grammidin® Neo) and Grammidin® (JSC "Valenta Pharmaceuticals", Russian Federation).

Natural substances as a component are in 8.6% of medicinal products, e.g. phenolic hydrophobic propolis preparation in "Proalor" (LLC "Pharmaceutical company "Zdorovie", Ukraine), a thick sage extract in "Shavlia"

(Natur Product Europa BV, Netherlands) and a solid chlorophyllipt extract in "Chlorophyllipt" tablets (LLC "Pilot Plant "State Scientific Centre on Medicinal Products", Ukraine).

The antibacterial agent and lysozyme are contained in 14.3% of drugs (Hexalyse (Laboratoires BOUCHARA-RECORDATI, France) Lysobact® (Bosnalijek dd, Bosnia and Herzegovina), Lizak® (3 names) JSC "Farmak", Ukraine), and 14.3% of drugs, e.g. (Septalor (LLC "Ternopharm", Ukraine), Lysobact (Bosnalijek dd, Bosnia and Herzegovina), Proalor (LLC "Pharmaceutical company "Zdorovie", Ukraine), Sebodin and Sebodin Plus (Glaxo SmithKline, Poland), etc., have vitamin components (ascorbic acid and pyridoxine hydrochloride) in their composition. More than 50% of the abovementioned drugs contain ascorbic acid in combination with chlorhexidine. It has been noted that 20% of drugs combine components of essential oils (menthol, levomenthol, anethole, thymol) or essential oils themselves (peppermint oil, eucalyptus oil) with antiseptics (benzalkonium chloride – Septotele, Septotele D (KRKA, Slovenia), dichlorobenzyl alcohol – Angi-Sept (5 names) Dr. Theiss Naturwaren GmbH, Germany).

The anesthetic component (active substances – benzocaine, oxybuprocaine chloride, tetracaine hydrochloride, lidocaine hydrochloride) are in 17.1% of the drugs under study (Septotele® Plus Menthol, Septotele® Plus Honey and Lime (KRKA, Slovenia) Anti-Angin Formula (HERKEL BV, Netherlands), Grammidin® with anesthetic Neo (JSC "Valenta Pharmaceuticals", Russian Federation) Trachisan (Engelhard Arzneimittel GmbH & Co.KG, Germany), Dorithricin (RIEMSER Specialty Production GmbH, Germany)).

#### CONCLUSIONS

The range of solid medicinal products that are available at the domestic pharmaceutical market and used in dental practice in the treatment of inflammatory periodontal disorders and oral diseases has been analysed.

Medicinal products have been characterized depending on the manufacturer country, the type of a solid dosage form and structured according to the amount and content of active components and their combination.

It has been found that the segment of natural oromucosal drugs for therapeutic dentistry is too small.

It has been determined that creation of a new oromucosal herbal medicinal product in a solid dosage form is based on natural substances can be considered to be a relevant and up-to-date task for pharmaceutical technology.

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#### **АНАЛІЗ ОРОМУКОЗНИХ ПРЕПАРАТІВ ДЛЯ ТЕРАПЕВТИЧНОЇ СТОМАТОЛОГІЇ У ВИГЛЯДІ ТВЕРДИХ ФОРМОВАНИХ ЛІКАРСЬКИХ ФОРМ**

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**Ключові слова:** стоматологічні препарати місцевої дії; тверді лікарські форми; маркетингові дослідження; фармацевтичний ринок

З метою визначення необхідності створення стоматологічних лікарських засобів (ЛЗ) проаналізовані оромукозні лікарські форми (ЛФ) фармацевтичного ринку України. При лікуванні захворювань пародонту дедалі частіше застосовують таблетовані ЛЗ. За результатами аналізу 35 ЛЗ зазначеного сегменту встановлено, що частка препаратів вітчизняного виробника (23%) поступає серед країн-виробників лише Німеччині (31%). Маркетинговим аналізом твердих формованих ЛЗ визначено, що 54,3% – це таблетки, 25,7% – льодяники, 20% – пастилки. Підраховано, що за кількістю компонентів 34,3% ЛЗ є двокомпонентними, 25,7% – трикомпонентні, по 20% – одно- та багатокомпонентні препарати. Розмежовуючи поняття про діючі субстанції, ми виявили, що антисептична складова зустрічається у 77,1% препаратів, антибіотики – у 14,3%, ефірні олії – у 20%, анестетики – у 17,1%. Природні субстанції є у складі у 8,6% ЛЗ. Це фенольний гідрофобний препарат прополісу у ЛЗ «Проалор» (ТОВ «Фармацевтична компанія «Здоров'я», Україна), екстракт шавлії сухий у ЛЗ «Шавлія» (Natur Product Eurora B.V., Нідерланди) та хлорофіліпту екстракт густий у складі таблеток «Хлорофіліпт» (ТОВ «Дослідний завод «ДНЦЛЗ», Україна). Вивченням підкреслено домінування комбінованих ЛЗ і замалу частку ЛЗ на основі природних субстанцій, що підтверджує доцільність створення оромукозних рослинних ЛЗ у вигляді твердих ЛФ для стоматологічної практики.

#### **АНАЛИЗ ОРОМУКОЗНЫХ ПРЕПАРАТОВ ДЛЯ ТЕРАПЕВТИЧЕСКОЙ СТОМАТОЛОГИИ В ВИДЕ ТВЕРДЫХ ФОРМИРУЕМЫХ ЛЕКАРСТВЕННЫХ ФОРМ**

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**Ключевые слова:** стоматологические препараты местного действия; твердые лекарственные формы; маркетинговые исследования; фармацевтический рынок

С целью определения необходимости создания стоматологических лекарственных средств (ЛС) проанализированы оромукозные лекарственные формы (ЛФ) фармацевтического рынка Украины. При лечении заболеваний пародонта все чаще применяют таблетированные ЛС. По результатам анализа 35 ЛС вышеупомянутого направления установлено, что доля препаратов отечественного производителя (23%) уступает среди стран-производителей только Германии (31%). Маркетинговым анализом твердых формируемых ЛС отмечено, что 54,3% – это таблетки, 25,7% – леденцы, 20% – пастилки. Подсчитано, что по количеству компонентов 34,3% ЛС являются двухкомпонентными, 25,7% – трехкомпонентные, по 20% – одно- и многокомпонентные препараты. Разграничивая понятия о действующих субстанциях, выявлено, что антисептическая составляющая встречается у 77,1% препаратов, антибиотики – у 14,3%, эфирные масла – у 20%, анестетики – у 17,1%. Природные субстанции есть в составе 8,57% ЛС. Это фенольный гидрофобный препарат прополиса в ЛС «Проалор» (ООО «Фармацевтическая компания «Здоровье», Украина), экстракт шалфея сухой в ЛС «Шалфей» (Natur Product Eurora B.V., Нидерланды) и хлорофиллипта экстракт густой в составе таблеток «Хлорофиллипт» (ООО «Опытный завод «ГНЦЛС», Украина). Изучением подчеркнута доминирование комбинированных ЛС и малая доля ЛС на основе природных субстанций, что подтверждает целесообразность создания оромукозных растительных ЛС в виде твердых ЛФ для стоматологической практики.