

ISSN 2518-1483 (Online),  
ISSN 2224-5227 (Print)

2020 • 5

ҚАЗАҚСТАН РЕСПУБЛИКАСЫ  
ҰЛТТЫҚ ҒЫЛЫМ АКАДЕМИЯСЫНЫҢ

# БАЯНДАМАЛАРЫ

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## ДОКЛАДЫ

НАЦИОНАЛЬНОЙ АКАДЕМИИ НАУК  
РЕСПУБЛИКИ КАЗАХСТАН

## REPORTS

OF THE NATIONAL ACADEMY OF SCIENCES  
OF THE REPUBLIC OF KAZAKHSTAN

PUBLISHED SINCE 1944



ALMATY, NAS RK

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ISSN 2518-1483 (Online),

ISSN 2224-5227 (Print)

Меншіктенуші: «Қазақстан Республикасының Ұлттық ғылым академиясы» Республикалық қоғамдық бірлестігі (Алматы қ.).

Қазақстан Республикасының Ақпарат және қоғамдық даму министрлігінің Ақпарат комитетінде 29.07.2020 ж. берілген № KZ93VPY00025418 мерзімдік басылым тіркеуіне қойылу туралы куәлік.

Тақырыптық бағыты: *наноматериалдар алу, биотехнология және экология саласындағы бірегей зерттеу нәтижелерін жариялау.*

Мерзімділігі: жылына 6 рет.

Тиражы: 500 дана.

Редакцияның мекенжайы: 050010, Алматы қ., Шевченко көш., 28; 219, 220 бөл.; тел.: 272-13-19, 272-13-18,  
<http://reports-science.kz/index.php/en/archive>

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Типографияның мекенжайы: «NurNaz GRACE», Алматы қ., Рысқұлов көш., 103.

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**Доклады Национальной академии наук Республики Казахстан»**

**ISSN 2518-1483 (Online),**

**ISSN 2224-5227 (Print)**

Собственник: Республиканское общественное объединение «Национальная академия наук Республики Казахстан» (г. Алматы).

Свидетельство о постановке на учет периодического печатного издания в Комитете информации Министерства информации и общественного развития Республики Казахстан № **KZ93VPY00025418**, выданное 29.07.2020 г.

Тематическая направленность: *публикация оригинальных результатов исследований в области получения наноматериалов, биотехнологии и экологии.*

Периодичность: 6 раз в год.

Тираж: 500 экземпляров

Адрес редакции: 050010, г. Алматы, ул. Шевченко, 28; ком. 219, 220; тел. 272-13-19, 272-13-18,

<http://reports-science.kz/index.php/en/archive>

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Owner: RPA "National Academy of Sciences of the Republic of Kazakhstan" (Almaty).

The certificate of registration of a periodical printed publication in the Committee of information of the Ministry of Information and Social Development of the Republic of Kazakhstan **No. KZ93VPY00025418**, issued 29.07.2020.Thematic scope: *publication of original research results in the field of obtaining nanomaterials, biotechnology and ecology.*

Periodicity: 6 times a year.

Circulation: 500 copies.

Editorial address: 28, Shevchenko str., of. 219, 220, Almaty, 050010, tel. 272-13-19, 272-13-18,

<http://reports-science.kz/index.php/en/archive>

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Address of printing house: «NurNaz GRACE», 103, Ryskulov str, Almaty.

**REPORTS OF THE NATIONAL ACADEMY OF SCIENCES  
OF THE REPUBLIC OF KAZAKHSTAN**

ISSN 2224-5227

<https://doi.org/10.32014/2020.2518-1483.113>

Volume 5, Number 333 (2020), 13 – 18

UDC 61.339.13; 61.659.1;616.9

**E.G. Tolokonnikov<sup>1</sup>, A.S. Adekenova<sup>2</sup>, O.V. Maslova<sup>2</sup>**<sup>1</sup>LLP «Karaganda Pharmaceutical Plant», Karaganda, Kazakhstan;<sup>2</sup>JSC «International Research and Production Holding «Phytochemistry», Karaganda, Kazakhstan.E-mail: [etolokonnikov@krgpharm.kz](mailto:etolokonnikov@krgpharm.kz); [info@phyto.kz](mailto:info@phyto.kz)**PHARMACOECONOMICAL ANALYSIS  
OF ANTI-PERIODONTOSIS DRUGS**

**Abstract.** In this work, a retrospective analysis of anti-periodontosis drugs is carried out using the methods of pharmacoeconomic analysis: analysis of the "cost of disease" (direct costs), "cost-effectiveness" for promoting the original drug "Matripin-Dent" on the pharmaceutical market.

In the clinic of the Dental Institute of Kazakh National Medical University named after S.D. Asfendiyarov (Almaty), clinical trials of a new domestic phytopreparation "Dental gel Matripin-Dent" were carried out. The gel preparation was used in the complex therapy of periodontal diseases of an inflammatory and inflammatory-destructive nature. As a result of the experimental studies, it was found that "Matripin-Dent", due to the original composition of the gel composition, provides high adhesion to mucous surfaces, ensures reliable fixation of the drug on the gums, contributes to a better distribution of active components due to good absorption of the ointment base composition.

It has been proven that the developed dosage form "Matripin-Dent" based on pharmacologically active compounds of *Populus balsamifera* L. buds and flowers, leaves, buds of *Matricaria chamomilla* L. has a number of advantages in comparison with the drugs existing on the pharmaceutical market used in dental practice.

**Key words:** Parodontosis, Matripin-Dent, "Kamistad", pharmacoeconomics.

**Introduction.** According to the World Health Organization, published in the annual news-bulletin, the most common dental diseases include caries, periodontitis, congenital and traumatic oral pathologies, diseases of an infectious nature.

To date, the pharmaceutical market is represented by a fairly wide range of therapeutic and prophylactic agents used for the treatment and prevention of periodontitis, containing extracts of medicinal plants as active ingredients. The main active ingredients in therapeutic and prophylactic agents used in dental practice are biologically active substances of medicinal plants: *Matricaria chamomilla* L., *Potentilla erecta* (L.) Hampe., *Hypericum perforatum* L., *Achillea millefolium* L., *Salvia officinalis* L., *Acorus calamus* L., *Arnica*, *Mentha piperita* L., *Eucalyptus viminalis* Labill. Based on the results of studying the chemical composition and pharmacological properties of medicinal plants, there is a unique opportunity to use plant substances as an active ingredient in the development of the composition and technology of new drugs used for the treatment and prevention of infectious and inflammatory diseases of the oral mucosa [1-2].

Numerous studies have shown that the introduction of plant extracts into the composition of dosage forms can increase the effectiveness of therapy for various inflammatory diseases of the gums, especially of an infectious nature. In this regard, the development of new, more effective and safe agents for the treatment of this disease is urgent.

In dental practice, the following pharmacopoeial preparations based on plant raw materials are used with great efficiency: maraslavin, sangviritrin (liniment, alcohol and water solutions), novoimaninum, chlorophyllipt and others [3-4].

Globally, 70-90% of school-age children and 95-99% of the adult population have caries. Severe periodontitis is found in 20% of people aged 35 to 45 years. Globally, 30% of elderly people aged 65 and over have a complete absence of natural teeth. The prevalence of dental pathologies is higher and tends to increase among populations from disadvantaged groups and in countries with a low level of living.

For the treatment of inflammatory periodontal diseases, antioxidants and antihypoxants (mexidol, vitamins of group E and others) are actively used, which have a wide range of therapeutic action, low toxicity, increasing the adaptive capabilities of the body, including compensatory ways of maintaining peripheral homeostasis. These preparations have anti-inflammatory and anti-edematous effects, enhance the regeneration processes.

The possibilities of using drugs based on plant substances for the treatment of dental diseases are very relevant. In the modern pharmaceutical industry, there is a wide range of medicinal preparations from plant raw materials used for diseases of the oral cavity, however, the treatment of periodontal diseases is largely empirical in nature, due to the lack of convincing evidence of the advisability of using certain drugs in the treatment of periodontal diseases. Therefore, the development of anti-parodontosis drugs based on plant raw materials that meet modern requirements for proper manufacturing practice is a promising direction.

Pharmacologically active compounds of poplar species (*Populus* L.) are a promising source for obtaining antimicrobial, anti-inflammatory and wound-healing drugs [5].

A significant role in the development of the inflammatory process in the parodontosis is played by the microbial factor. Complex therapy should also provide a specificity of the effect of drugs on a specific type of microorganism. A high level of inflammatory periodontal diseases (IPD) is observed at the age of 20-44 (65-95%) and 15-19 years (55-89%) [6-13].

Therefore, the developed drug "Matripin-Dent" based on the plant substances of *Populus balsamifera* L. and *Matricaria chamomilla* L. has a number of advantages in comparison with the drugs existing on the pharmaceutical market used in dental practice [14].

Firstly, the drug "Matripin-Dent" allows you to expand the range of complex phytopreparations for the treatment of inflammatory diseases of the oral mucosa, get rid of the purchase of expensive imported drugs of similar pharmacological action. Secondly, it shortens the treatment time for patients.

A positive aspect when creating a gel dosage form is the provision of a pharmacological action due to the presence of a combined effect of the extracts of biologically active substances, which affects technological factors such as the accuracy of dosing, the constancy of the concentration of biologically active substances for a long time, strong fixation to damaged tissues of the oral mucosa.

**The aim of the study:** to carry out a pharmacoeconomical analysis of the use of anti-parodontosis drugs using the analysis of "cost of disease" and "cost-effectiveness".

**Materials and methods:** A retrospective analytical review was carried out using the methods of pharmacoeconomical analysis: analysis of the "cost of disease" (direct costs), "cost-effectiveness" with the definition of competitive advantages, life cycle, target audience, ultimate consumer, links of strong and weak influence on the marketing promotion of the drug on the pharmaceutical market. SWOT analysis of drug, Sell-in, Sell-out analysis, Porter's Five Forces methodology, which allows to visually consider the market in a competitive environment.

#### **Study results.**

In the clinic of the Dental Institute of Kazakh National Medical University named after S.D. Asfendiyarov (Almaty), clinical studies of a new domestic phytopreparation "Dental gel Matripin-Dent" were carried out. The gel preparation was used in the complex therapy of periodontal diseases of an inflammatory and inflammatory-destructive nature.

As a result of experimental and clinical studies, it was found that "Matripin-Dent", due to the original composition of the gel composition, provides high adhesion to mucous surfaces, ensures reliable fixation of the drug on the gums, promotes a better distribution of active components due to the good absorption of the ointment base composition.

The results obtained indicate the effectiveness of the drug in a complex of therapeutic measures in the treatment of gingivitis and parodontosis.

Based on the processed data and information on the state of the pharmacological market in Kazakhstan and the countries of the Eurasian Economic Union (EAEU), the following conclusions can be drawn - at the moment is the most favorable time for the development and launch of drugs on the market. The policy of the EAEU countries is aimed at creating a self-sufficient pharmaceutical industry, ousting imported drugs from the market and increasing healthcare costs. The state policy of countries and market participants is facing strong resistance from importing companies with strong market positions and possibly a strong lobby in the government (for example, the Russian Federation).

The economic impact on the industry is especially noticeable against the background of US and European sanctions. Trade wars and weaknesses in national currencies will slow down the development of national industries in every possible way. Do not discount the fact that Russia makes up 85% of the population and economy of the EAEU. The creation of a single market and the ousting of foreign suppliers will be beneficial first of all to Russia; it is quite expected that Russian companies will seize national markets in the near future. It is not excluded that the market in five to seven years will have a similar structure as now, but 75-90% of the products will be imported not from India or Europe, but from Russia.

Difficulties with the protection of intellectual property, the weak efficiency of the courts of the EAEU countries calls into question the development of original drugs. Pharmaceutical companies prefer to develop the generics niche. Unfortunately, this is a dead-end branch of development, which may contribute to the achievement of financial goals of manufacturers in the short term, but will not contribute to improving public health in the long term.

Given the described situation, it is assumed that the current economic situation and the policies undertaken by the EAEU member states in the long term will contribute to the development of national industries and the displacement of imported products.

According to BMI Research forecasts, the pharmaceutical market will grow and reach a volume of USD 1.55 billion in 2018. Going forward, growth will continue with an average (CAGR) of 14%, doubling by 2022.

In 2017, as a whole in the Eurasian Economic Union, there was a positive trend in industrial production, agricultural production, freight turnover, passenger turnover, retail trade, volumes of foreign and mutual trade.

There was an increase in industrial production in all the EAEU member states, agricultural production - in Belarus (by 4.1%), Kazakhstan (by 2.9%), Kyrgyzstan (by 2.2%) and Russia (by 2.4%). %, the volume of construction work performed - in Armenia (by 37.7%), Kazakhstan (by 1.9%), cargo turnover, passenger turnover, retail trade turnover - in all EAEU member states.

The index of the physical volume of the gross domestic product in the EAEU in January - September 2017 compared to January - September 2016 amounted to 101.9% (in January - September 2016 compared to January - September - 2015 - 99.6%).

With a population of 6.1 million, the market is one of the smallest in the region - Tajikistan (8.9 million), Azerbaijan (9.8 million) and Kazakhstan (18.2 million). In addition, the rural population predominates; only 36.1% live in urban areas, which is one of the lowest rates in the entire region. Market size is only 246 million USD and 41 USD per capita. Kyrgyzstan is one of the smallest and least developed pharmaceutical markets in the Central Asia region. Pharmaceutical sales in 2017 amounted to 3.3% of GDP and 54.0% of total healthcare spending. While data on the size of market sectors are not currently available, limited purchasing power of the population, combined with a high dependence on cash payments, leads to the fact that the demand for drugs is almost exclusively for generic drugs (mainly non-brand) and OTC drugs.

The Porter's Five Forces methodology was used to analyze the dental market. Breakdown of the competitive environment into five components allows you to visually examine the market.

Competitors, international conglomerates with powerful sales and marketing divisions that hold the overwhelming market share have the greatest influence on the market. Despite the large potential audience, population growth is limited. Supplier influence and entry of new players is seen as limited.

Direct drug competitors are plant-based products.

We managed to obtain reliable sales data on "Kamistad-gel", manufactured by "Stada".

According to the "MedElement" company, as of January 30, 2018, 3,970 pharmacies function in large cities of Kazakhstan (excluding pharmacy points in state medical institutions).

The largest number of pharmacies is in Almaty - 870. Also, in the top three in terms of the number of pharmacies are in Nur-Sultan and Shymkent - 442 pharmacies. Among the three outsiders are Taraz, Kokshetau, Temirtau - 69, 59, 57 pharmacies, respectively.

According to news-bulletin of World Health Organization №318 dated May 2012, severe paradontosis (gum disease), which can lead to tooth loss, is found in 15-20% of middle-aged people (35-44 years), while worldwide 60-90% of school-age children and almost 100% of adults have dental caries or other oral diseases.

According to BMI Research data, Kazakhstan's population was 17.7 million in 2018, with an average growth of 1.3% through 2025.

For a more accurate calculation of the target audience, the urban population of the Republic of Kazakhstan was taken into account.

Given the prevalence of diseases, it can be concluded that the risk group (35-44 years) will be 156 thousand people in 2020 and will double to 323 thousand by 2025. School-age children currently (according to 2015 data) are 1.5 million children, and will increase to 2.2 million in 2025.

The target audience is estimated at 1.4 million in 2020 and 2.5 million in 2025. The maximum possible target audience will be 5.9 million people in 2020 and 8.4 million people in 2025.

The analysis of Sell-in, Sell-out and calculations allow us to conclude that the vast majority of retail chains have a stock of 6% in their own warehouses. It can be assumed that "Metrogyl" almost never stays on the shelves, and is almost entirely sold by pharmacy chains. The only exceptions are some regions of the country. Perhaps this is due to the fact that pharmacy chains sold drugs from their stocks and did not purchase new ones.

The target audience of the drug is divided into two large groups, B2B sector and patients.

B2B sector - health-promoting institutions, dental clinics and dental rooms, as well as pharmacy chains.

Patients - risk groups (35-44 years old), school-age children.

To calculate marketing costs and tools, the experience of the Russian market was taken as an example.

Pharmaceutical companies increased their TV advertising expenses in 2016, increasing the share of expenses to 90%. Some companies have sharply increased their expenses in the regions. According to the assessment of Media Direction Group (part of the BBDO group), which also monitors the pharmaceutical segment of the advertising market, STADA CIS increased its advertising costs on regional television more than 20 times in 2016.

Based on the experience of Russian colleagues described above, it seems rational to focus on television advertising. Comparing the volume of advertising budgets of the largest companies in Russia and their range of drugs, the following conclusions can be drawn using the example of PJSC "OTCPharm". In 2016, the company spent 3.359 million rubles on advertising to advertise 145 names of drugs 23.17 million rubles or 115 million tenge were spent on advertising one drug in year.

The sales plan is based on the following assumptions:

- Proven annual market volume of 470 thousand tubes per year.
- The minimum required market capture of 16% (181 thousand tubes per year) is needed from the requirements to maintain a break-even point of 174 thousand tubes.
- This section presents the minimum required production volume, in the sensitivity analysis section, financial indicators are indicated taking into account different productivity.

It should be especially noted that the original drug "Matripin-Dent" requires regular use, which will help to maintain demand. Market size of 470 thousand tubes per year is proven and only reflects a known part of the market.

Treatment of the disease with the use of gels is temporary; complete cure of parodontosis without medical intervention is unlikely. Regular use of soft dosage forms is essential to prevent the development and spread of the disease. In this regard, the patient will need to regularly purchase the drug "Matripin-Dent".

In the first years of production, the level will be 180 thousand tubes per year, occupying 16% of the market. In 2027, the market capture will reach 20% and will amount to 234 thousand tubes. Starting from 2029, the occupied share will be 30% and will be equivalent to 358 thousand tubes. It is assumed that the market size will grow by 1% annually, which corresponds to natural population growth. By 2048, the volume will reach 432 thousand per year.

These assumptions are based on the fact that the real market size can be 1,070 thousand tubes per year, given that there are 8 competitor drugs on the market.

### **Conclusions.**

The results of clinical studies and pharmacological indicators of a new drug indicate the correctness of the chosen path to create a comparatively competitive drug. The drug "Matripin-Dent" with a high



degree of probability by the end of all stages of testing will confirm its characteristics and will be able to surpass the currently available competing drugs.

Understanding the environment and business activities of competitors, one can conclude that the original drug is promising and has every chance of achieving commercial success. At the same time, the success of the domestic drug "Matripin-Dent" will largely be determined by the chosen development strategy. The optimal strategy for its promotion will allow you to realize the full potential of the market and minimize risks.

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### **ПАРОДОНТОЗҒА ҚАРСЫ ПРЕПАРАТТАРДЫ ФАРМАКОЭКОНОМИКАЛЫҚ ТАЛДАУ**

**Аннотация.** Жұмыста бірегей «Матрипин-Дент» препаратын фармацевтикалық нарыққа шығару үшін «аурудың құны» (тікелей шығын), «шығын-тиімділік» фармакоэкономикалық талдау әдістерін қолдана отырып, пародонтозға қарсы дәрілік құралдарға ретроспективті талдау жүргізілді.

С.Ж. Асфендияров атындағы ҚазҰМУ-дың стоматология институты клиникасында (Алматы қ.) жаңа отандық «Матрипин-Дент (Matripin-Dent) стоматологиялық гелі» фитопрепаратына клиникалық сынақ жүргізілді. Гельдік препарат қабыну және қабыну-деструктивті сипаттағы пародонт ауруларының кешенді терапиясында қолданылды. Жүргізілген эксперименттік зерттеу нәтижесінде «Матрипин-Дент» гельдік композицияның бірегей құрамының арқасында шырышты беттерге жоғары адгезияны және дәрілік құралдың қызыл иекке сенімді бекітілуін қамтамасыз ететіні, бұған қоса жақпамай композициясының жақсы сіңуінің арқасында әсер етуші компоненттердің жақсы таралуына ықпал ететіні анықталды.

Бальзамды терек бүршігі мен дәрілік түймедақ гүлі, жапырағы, гүлшанақтарының фармакологиялық белсенді қосылыстары негізінде жасалған «Матрипин-Дент» дәрілік түрі стоматологиялық тәжірибеде қолданылатын фармацевтикалық нарықтағы дәрі-дәрмектермен салыстырғанда бірқатар артықшылығы бар екендігі дәлелденді.

**Түйін сөздер:** пародонтоз, Матрипин-Дент, «Камистад», фармакоэкономика.

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### **ФАРМАКОЭКОНОМИЧЕСКИЙ АНАЛИЗ ПРОТИВОПАРОДОНТОЗНЫХ ПРЕПАРАТОВ**

**Аннотация.** В данной работе проведен ретроспективный анализ противопародонтозных лекарственных средств с использованием методов фармакоэкономического анализа: анализ «стоимость болезни» (прямые затраты), «затраты-эффективность» для продвижения на фармацевтический рынок оригинального препарата «Матрипин-Дент».

В клинике стоматологического института КазНМУ им. С.Д. Асфендиярова (г. Алматы) проводились клинические испытания нового отечественного фитопрепарата «Стоматологический гель Матрипин-Дент (Matripin-Dent)». Гелевый препарат использовали в комплексной терапии заболеваний пародонта воспалительно-деструктивного характера. В результате проведенных экспериментальных исследований, было установлено, что «Матрипин-Дент», благодаря оригинальному составу гелевой композиции, обеспечивает высокую адгезию к слизистым поверхностям, обеспечивает надежную фиксацию лекарственного средства на деснах,

способствует лучшему распределению действующих компонентов благодаря хорошей всасываемости основы мазевой композиции.

Доказано, что разработанная лекарственная форма «Матрипин-Дент» на основе фармакологически активных соединений почек тополя бальзамического и цветов, листьев, бутонов ромашки аптечной имеет ряд преимуществ в сравнении с существующими на фармацевтическом рынке средствами, применяемыми в стоматологической практике.

**Ключевые слова:** пародонтоз, Матрипин-Дент, «Камистад», фармакоэкономика.

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**ISSN 2518-1483 (Online), ISSN 2224-5227 (Print)**

<http://reports-science.kz/index.php/en/archive>

Редакторы: *М. С. Ахметова, Д. С. Аленов, А. Ахметова*

Верстка на компьютере *А. М. Кульгинбаевой*

Подписано в печать 12.10.2020.

Формат 60x881/8. Бумага офсетная. Печать – ризограф.

8,5 п.л. Тираж 500. Заказ 5.