

# ЭНТОМИКС®

содержит комплекс антимикробных пептидов FLIP7

designed to create a protective coating and suppress the development of bacterial biofilms on damaged skin areas



a new look at the problem of antibiotic resistance



**World Health  
Organization**

*In the not too distant past,  
antibiotics could be counted on  
to treat a bacterial infection.*

*Those days are almost gone...*

*WHO/CDS/CSR/DRS/2001.10*

The problem of resistance of bacterial infections to antimicrobial drugs is one of the main challenges of modern medicine



Widespread distribution of antibiotic-resistant bacteria under the pressure of natural selection



Formation of biofilms by bacteria-multicellular communicates immersed in a protective matrix

The discovery of antibiotics in the first half of the 20<sup>th</sup> century made it possible to radically improve the methods of treating bacterial infections. However, since then the effectiveness of antibiotics has been steadily declining, and now medicine has entered what is called the “end of the antibiotic era.”



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## Biofilm is :

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The main factor hindering the healing of wounds and promoting their transition to the chronic state

Complex three-dimensional biological structures of the higher organization of microbial life, resembling a multicellular organism

Causes roughly 80% of all bacterial infections

Resistant to most antibiotics and antiseptics

Formed within hours

# COMPOSITION OF ENTOMIX® HYDROGEL COATING

## FLIP7

Natural complex containing antimicrobial peptides of *Calliphora* larvae: defensins, cecrophins, diptericins, proline-rich peptides

## ALLANTOIN

An additional component to maintain the moisture balance of the skin

## CARBOPOL

Gelling agent. When combined with FLIP7, it creates a hydrogel coat that when applied to the skin, forms a film that provides mechanical protection and the necessary moisture level required for wound management.

## EUKSIL

Serves as a preservative that prevents microbial contamination of the product

## COMPLEX OF ANTIMICROBIAL PEPTIDES FLIP7

Inhibits the growth of the most common causative agents of wound and burn infections, including nosocomial multi-drug resistant strains

*Staphylococcus aureus* MRSA

*Klebsiella pneumoniae*

*Escherichia coli*

*Pseudomonas aeruginosa*

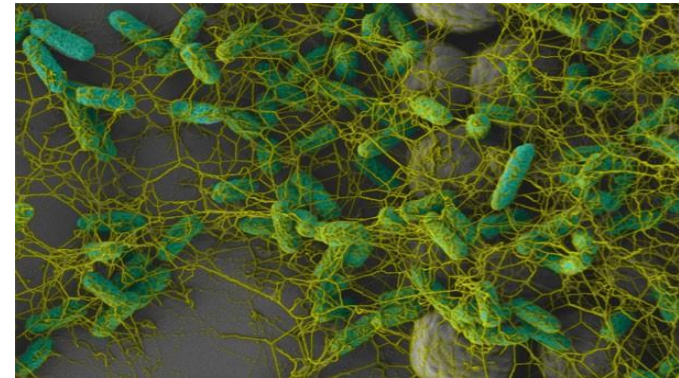
*Staphylococcus epidermidis*

*Streptococcus pyogenes*

*Acinetobacter baumannii*

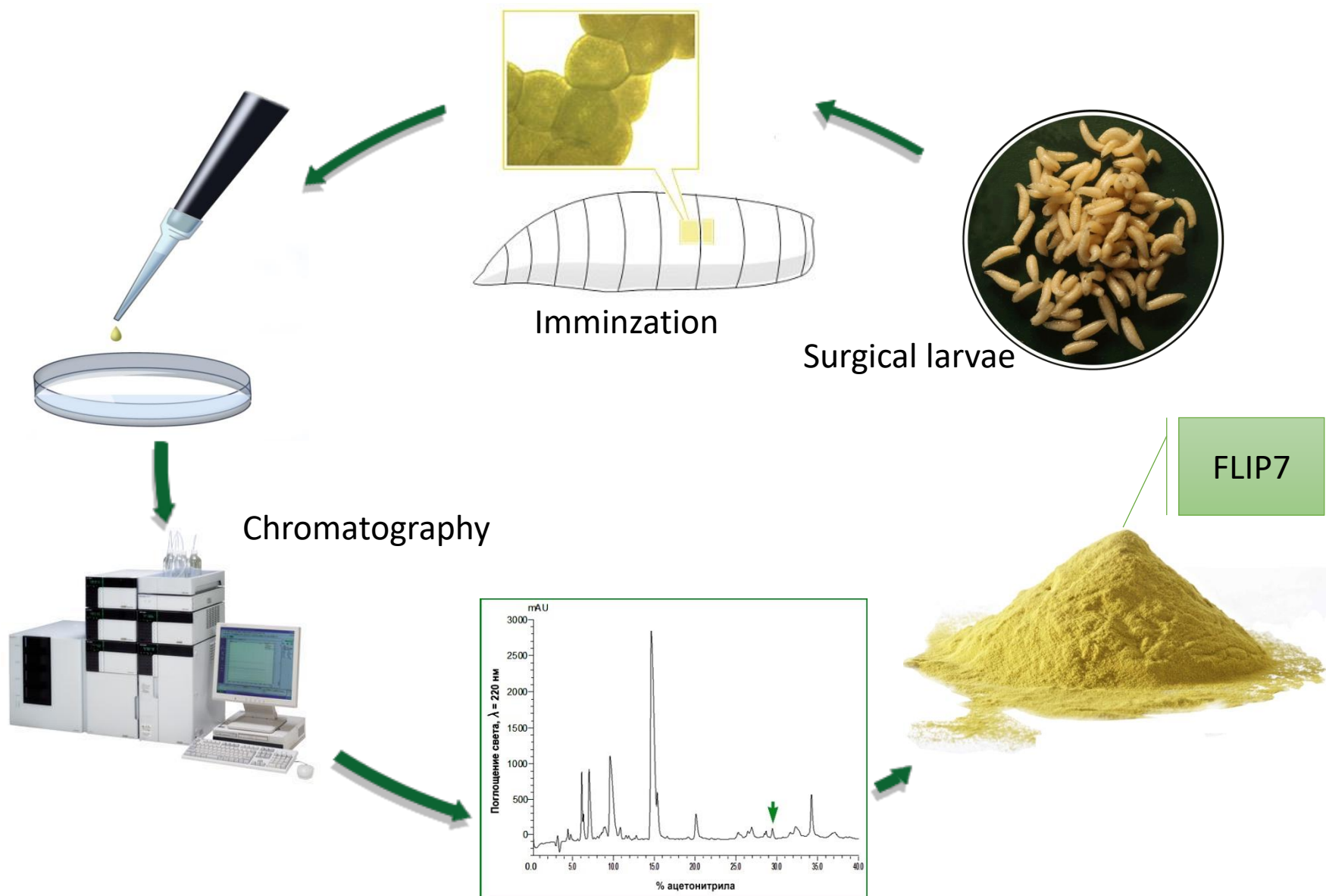
*Enterobacter cloacae*

*Serratia marcescens*



Antimicrobial peptides in FLIP7	The mechanism of action of the peptides included in the FLIP7 complex	Bacteria
Defensins	<b>Cell damage</b> <b>Bacteria walls</b> <b>Destruction of the biofilm matrix</b>	Gram +
Diptericins		Gram -
Cecropins		Gram -
Proline-rich peptides	<b>Blocking synthesis protein and DNA in protein</b>	Gram +/-

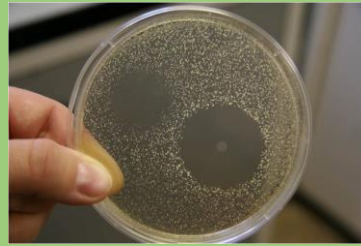
# TECHNOLOGY FOR OBTAINING THE FLIP7 ANTIMICROBIAL PEPTIDES COMPLEX



# ENTOMIX® HYDROGEL COATING



Designed to create a protective coating and suppress the development of bacteria biofilms on damaged skin areas. Indications for use: pyoderma, infected burns, purulent-necrotic skin lesions in diabetes.



Contains peptide complex FLIP7, which prevents the formation of biofilms by pathogenic bacteria in wounds and damaged skin areas. FLIP7 acts on both sensitive and antibiotic-resistant bacteria, does not include the formation of resistance, increases the efficiency of medical procedures aimed at removing bacteria from the wound cavity or inflammation focus, and facilitates access to bacterial cells of phagocytes, antibiotics and other antibacterial drugs.



Due to its gel-like structure, when applied to the damaged skin area, ENTOMIX® creates a film on its surface, which provides not only mechanical protection of the damaged area, but also the level of moisture necessary for wound healing.



“ENTOMIX®” works both independently and in synergy with antibiotics, enhancing the effect of the latter. At the same time, the functional purpose of the hydrogel is not realized through pharmacological, immunological, genetic or metabolic effects on the human body.

## METHOD OF APPLICATION OF ENTOMIX<sup>®</sup> HYDROGEL COATING

The hydrogel coating ENTOMIX<sup>®</sup> effectively prevents the formation of biofilms by microorganisms, which contributes to the uncomplicated course of the wound process. For these purposes, it is best to start applying the ENTOMIX<sup>®</sup> hydrogel coating immediately after injury to the skin. Application of ENTOMIX<sup>®</sup> coating at the later stages of the skin inflammatory process leads to the destruction of already formed biofilms, and further application of ENTOMIX<sup>®</sup> prevents their re-formation.

ENTOMIX<sup>®</sup> should be applied directly to the damaged surface with a thin layer (up to 1 min) in case of :

**Infected burn**  
**Once a day**

**purulent-necrotic skin lesions in diabetes**  
**Once a day**

**pyoderma**  
**1-2 times a day**

### **IMPORTANT:**

Before applying the wound, treat/clean, remove necrotic elements. For effective work of the hydrogel coating ENTOMIX<sup>®</sup>, it is necessary to apply it directly to the surface of the pyoderma, burns, diabetic ulcers. It is necessary to ensure direct contact of the gel components with bacteria in the wound.

The term of application of the ENTOMIX<sup>®</sup> hydrogel coating is during the period necessary for the healing of the wound surface and removal of the symptoms of inflammation of the damaged skin area.

3 minutes after application of the ENTOMIX<sup>®</sup> hydrogel coating, the wound can be closed with a secondary dressing (in case of burns, diabetic ulcers), which does not contain strong oxidants or proteolytic enzymes, as well as cytotoxic antiseptics.

The ENTOMIX<sup>®</sup> hydrogel coating can be used individually or as an adjunct to increase the effectiveness of antibiotic treatment.



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## ADVANTAGES OF ENTOMIX®

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**ENTOMIX®** inhibits the development of biofilms formed by various stages of their life cycle. It is equally effective against bacterial cells, both free-floating and part of the mature biofilm.

**ENTOMIX®** does not cause the development of bacterial resistance, unlike most modern antibiotics.

**ENTOMIX®** can be used in treatment of wounds contaminated with multidrug-resistant hospital strains.

**ENTOMIX®** serves as a powerful synergist of many vital groups of antibiotics (carbapenems, aminoglycosides, cephalosporins, glycopeptides, etc.), making it possible to reduce their effective dose by a factor of tens or hundreds to completely suppress the infection.

**ENTOMIX®** does not contain components toxic to cells that interfere with the process of wound epithelialization.

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## ADVANTAGES OF ENTOMIX®

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**ENTOMIX®** a unique innovative composition that has no analogues. Does not contain hormones and toxic components.

**ENTOMIX®** provides the most necessary moist wound management.

**ENTOMIX®** suitable for use in the treatment of a wide range of infected wounds, including complex configuration.

**ENTOMIX®** does not cause side effects and allergic reactions.

**ENTOMIX®** does not contain components toxic to cells that interfere with the process of wound epithelialization.

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## CLINICAL TRIALS

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Hydrogel coating for suppressing the development of bacterial biofilms **ENTOMIX®** for the purpose of assessing safety and efficacy when used as directed, with human participation in three nosologies: pyoderma, diabetic ulcer, burns, were carried out on the basis of two centers in the city of St Petersburg:

State Budgetary Institution “St Petersburg Institute of Emergency Medicine named after I.I Janelidze”

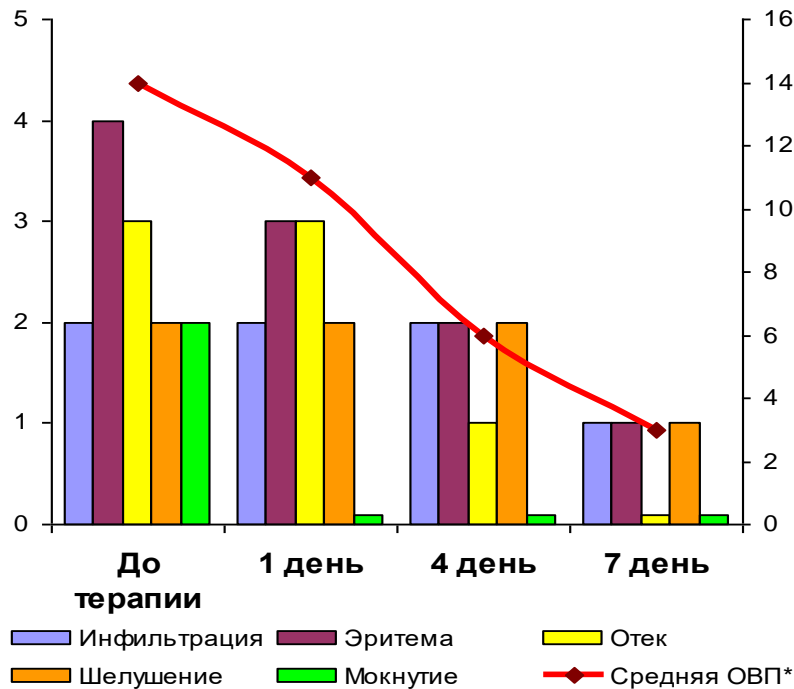


Federal State Healthcare Institution “Clinical Hospital No 122 named after L.G. Sokolov of the Federal Medical and Biological Agency of the Russian Federation”



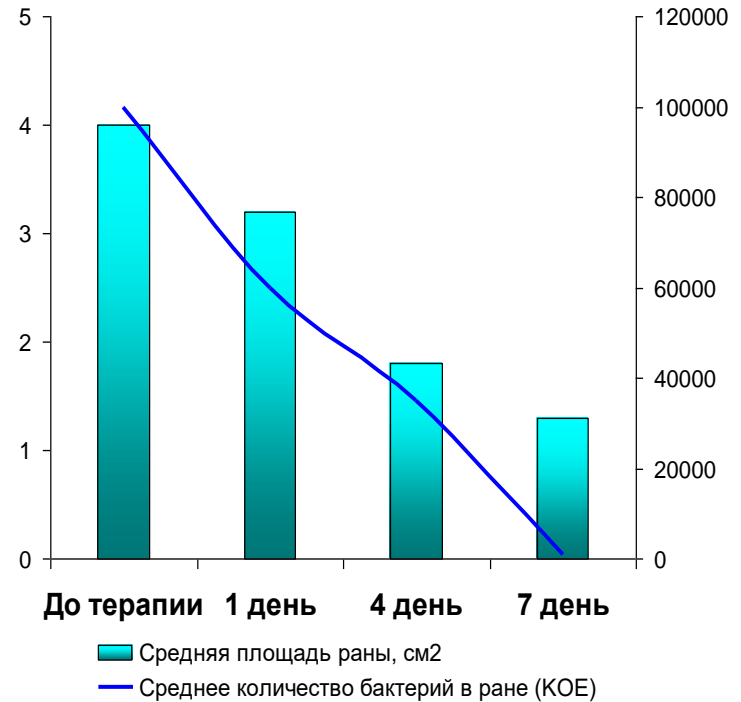
# Results of evaluating the effectiveness and safety of the ENTOMIX® hydrogel coating Nosology - Pyoderma

Dynamics of a decrease in severity of pyoderma symptoms in patients in the course of therapy with ENTOMIX®



\*ORP – General Assessment of the severity of pyoderma

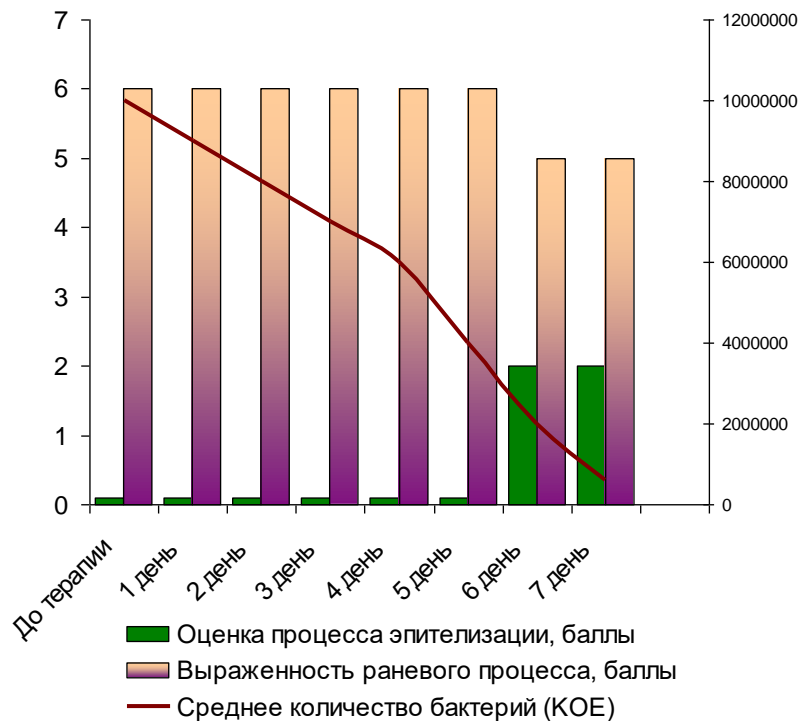
Dynamics of regression of the area on the of the wound infection in patients with pyoderma during therapy with the participation of ENTOMIX®.



The use of ENTOMIX® led to a decrease in the severity of all symptom's of pyoderma, as well as to a decrease in the area of the lesion and microbial contamination of the wound. Moreover, in 100% of patients EENTOMIX® did not cause adverse events and was well tolerated.

# Results of evaluating the effectiveness and safety of the ENTOMIX<sup>®</sup> hydrogel coating Nosology – Diabetic Ultra

Dynamics of the wound process in patients with diabetic ulcers during therapy with ENTOMIX<sup>®</sup>

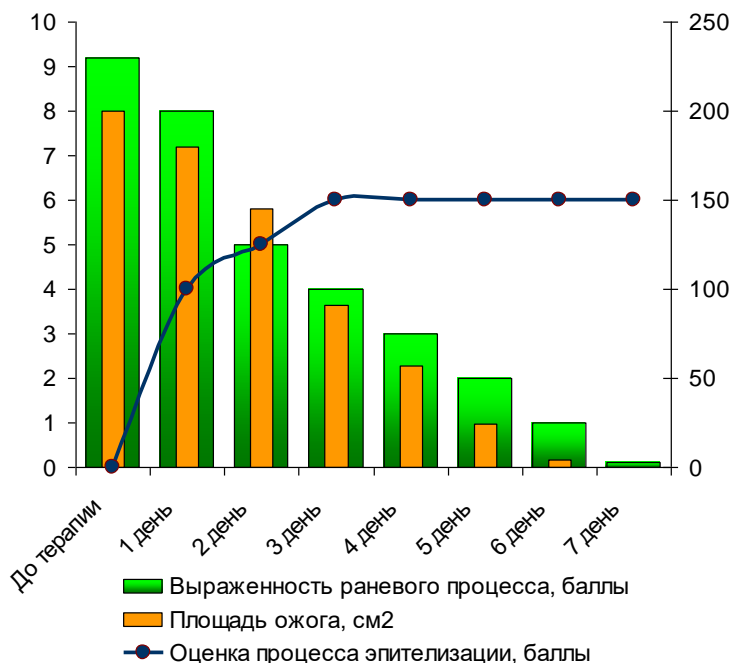


The use of ENTOMIX<sup>®</sup> provided a rapid reduction in the area of the ulcer within 7 days from the start of the treatment and a significant reduction in the microbial load, which is an important condition on the healing of the ulcer. The therapeutic effect, assessed by the sum of indicators of the early stages of treatment, was observed in 100% of patients. ENTOMIX<sup>®</sup> did not cause adverse events and was well tolerated by the patients. Thus, the ENTOMIX<sup>®</sup> hydrogel coating for inhibiting the development of bacterial biofilms is effective and safe for use in diabetic ulcers.

# Results of evaluating the effectiveness and safety of the ENTOMIX® hydrogel coating

## Nosology - Burns

Dynamics of the wound process in patients with burn injuring during therapy with ENTOMIX®



The dynamics of the infectious process in patients with burn injury during therapy with ENTOMIX®

	Before therapy	7 days later
Number of patients with infected burn injury	19 ( 95%)	2* (10%)
Staphylococcus aureus	9 (S) + 6 (R)	2*
Coagulase negative staphylococcus	7 (S)	0
Enterococci	2 (S) + 4 (R)	0
Klebsiella pneumoniae	1 (S) + 1 (R)	0
Corynebacteria	2 (R)	0
Streptococcus pyogenes	1 (R)	0

S - susceptible strains, R-antibiotic-resistant strains \* 2 patients with secondary S. aureus infection on the 7th day from the start of treatment (there was no infection in the period from 0 to 4 days)

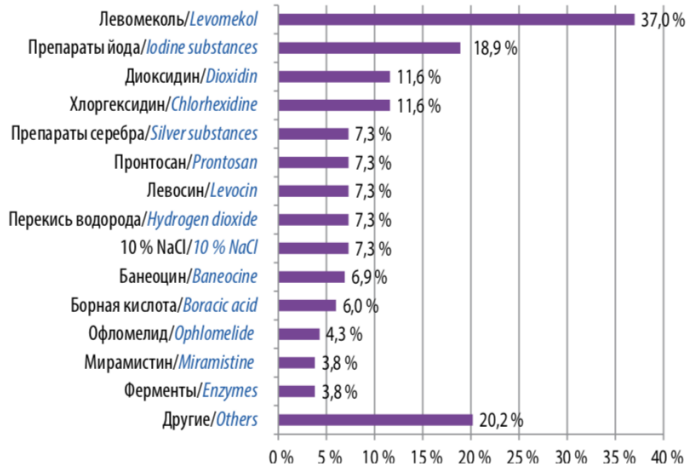
The use of ENTOMIX® in burn patients led to rapid decrease in the area of the burn and the severity of the wound process, rapid elimination of all microbial pathogens including antibiotic resistant ones, and acceleration of wound epithelialization. Moreover, in 100% of patients, ENTOMIX® did not cause any adverse events and was well tolerated.

# MARKETING RESEARCH

## Local preparations used by Russian surgeons

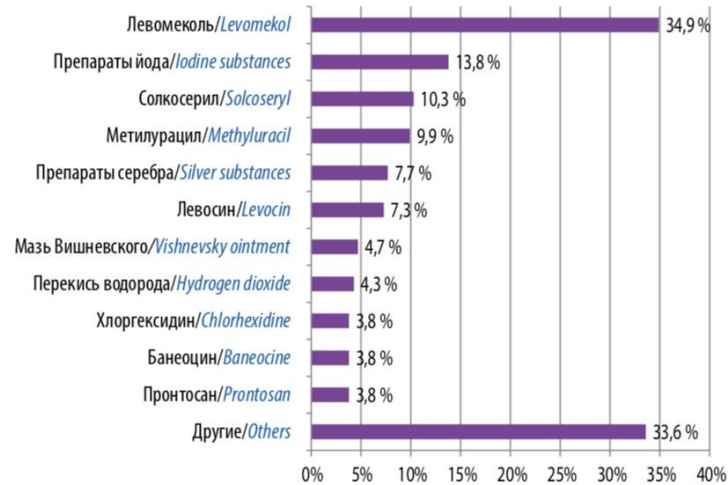
Какое местное средство вы предпочитаете для лечения ран в I фазе раневого процесса?

*Which local medicine do you prefer to treat wounds in the I phase of the wound process?*



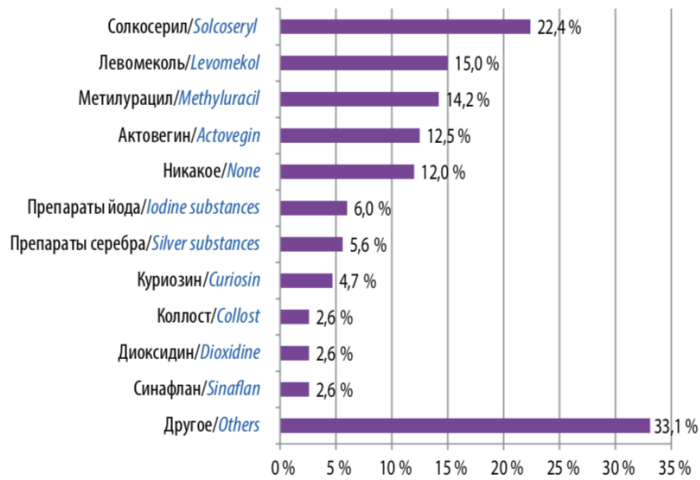
Какое местное средство вы предпочитаете для лечения ран во II фазе раневого процесса?

*Which local medicine do you prefer to treat wounds in the II phase of the wound process?*



Какое местное средство вы предпочитаете для лечения ран в III фазе раневого процесса?

*Which local medicine do you prefer to treat wounds in the III phase of the wound process?*



Какие дополнительные системные препараты вы часто используете при лечении ран?

*Which additional systemic substances do you use for wounds' treatment?*



## MARKING RESEARCH CONCLUSIONS

**В 2015 году было проведено анкетирование 1160 хирургов с целью выяснить, какие местные препараты используют российские хирурги для лечения ран и раневой инфекции в реальной клинической практике.**

In 2015, a survey of 1160 surgeons was conducted in order to find out what local drugs are used by Russian surgeons to treat wounds and wound infections in real clinical practice.

The absence among the drugs used of such forms as a traumatic mesh coatings, alginate, hydrocolloid, hydrogel dressings, indicates either insufficient awareness of specialists, or the lack of the possibility of their real use.

In general, surgeons use 46 topical drugs, many of which have no evidence base and are prescribed "by tradition."

Lack of the desired topical preparation, original effective wound management, or lack of information on wound management, surgeons often supplement treatment with systemic therapy. These agents may play an important role in specific cases, but in general there is a tendency to re-evaluate systemic therapy in the treatment of wounds and wound infections.



# WORLD STANDARDS OF THERAPY FOR THE FOLLOWING NOSOLOGIES:



## PYODERMA

- Surgical debridement
- Wound coating with silver ions Aquacel Ag
- Wounds covering with iodine ions Iodoform
- Provoidine (povidone iodine), antiseptic for external use
- Trimethoprim-sulfamethoxazole (co-trimoxazole), an antibacterial drug



## DIABETIC ULCER

- Santyl ointment - collagenase ointment for cleaning wounds and ulcers
- The analogue of Santyl ointment with collagenase, registered in Russia - atraumatic dressing on a textile basis with Iruksol ointment "Voskopran-II"
- Wound coating with silver ions Wound covering Aquacel Ag
- Wound covering Urgotul Silver
- Urgotul wound covering
- Gauze bandage + surgical debridement



## BURNS

- Dermazin® drug (Registration certificate PN013945 / 01 dated December 29, 2016) - 1% cream for external use, the active substance is silver sulfadiazine (SSD).

# EFFICIENCY OF ENTOMIX® hydrogel coating



## CHRONIC PYODERMA

ENTOMIX® surpasses the characteristics of coatings, dressings, surgical debridement methods and agents used in clinical practice, used to reduce the severity of manifestations of chronic recurrent pyoderma, in terms of their clinical characteristics: area of skin rashes, severity of erythema, edema, purulent discharge. Comparison of ENTOMIX® with such well-known methods of treatment such as surgical dressings with silver and iodine ions reveals the maximum advantages.



## DIABETIC FOOT ULCER:

ENTOMIX® surpasses the characteristics of wound dressings, dressings and methods of surgical debridement used in clinical practice (data are presented in the literature based on the results of 13 clinical trials) in terms of the rate of decrease in the area of diabetic ulcer.



## BURNS

ENTOMIX® indirectly caused a significant and statistically highly significant ( $P < 0.001$ ) reduction in the epithelialization time in infected burns compared to the reference object SSD. Treatment of the wound surface with a hydrogel ENTOMIX® coating against the background of doxycycline application provided fast (within 3 days) and complete clearance of the wound from pathogenic bacteria, including *Staphylococcus aureus*, coagulase-negative staphylococcus, *Enterococcus* spp., *Klebsiella pneumoniae*, *Corynebacterium* spp.

# INTELLECTUAL PROPERTY

РОССИЙСКАЯ ФЕДЕРАЦИЯ



**ПАТЕНТ**  
НА ИЗОБРЕТЕНИЕ  
№ 2447896

**АНТИМИКРОБНОЕ ВЕЩЕСТВО**

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РОССИЙСКАЯ ФЕДЕРАЦИЯ



**ПАТЕНТ**  
НА ИЗОБРЕТЕНИЕ  
№ 2664708

**Способ разрушения и предотвращения образования бактериальных биопленок комплексом антимикробных пептидов насекомых**

Патентообладатель: *Черныш Сергей Иванович (RU)*  
Авторы: *Черныш Сергей Иванович (RU), Гордя Наталья Александровна (RU), Яковлев Андрей Юрьевич (RU)*

Заявка № 2017120258  
Приоритет изобретения **08 июня 2017 г.**  
Дата государственной регистрации в Государственном реестре изобретений Российской Федерации **21 августа 2018 г.**  
Срок действия исключительного права на изобретение истекает **08 июня 2037 г.**

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РОССИЙСКАЯ ФЕДЕРАЦИЯ



**СВИДЕТЕЛЬСТВО**  
на товарный знак (знак обслуживания)  
№ 460058

**ЭНТОМИКС**

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Заявка № 2011710958  
Приоритет товарного знака **11 ноября 2011 г.**  
Зарегистрировано в Государственном реестре товарных знаков и знаков обслуживания Российской Федерации **20 апреля 2012 г.**  
Срок действия регистрации истек

Руководитель Федеральной службы по интеллектуальной собственности  
*Г. П. Иванов*



РОССИЙСКАЯ ФЕДЕРАЦИЯ



**СВИДЕТЕЛЬСТВО**  
на товарный знак (знак обслуживания)  
№ 710906

**FLIP**

Правообладатель: *Общество с ограниченной ответственностью "Аллофарм", 199178, Санкт-Петербург, 7-я линия В.О., 76, литера А, П.62-Н, комн. 18 (RU)*

Заявка № 2017745819  
Приоритет товарного знака **01 ноября 2017 г.**  
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**Thank you for your attention!**

Store in a dry place at temperatures between + 2 ° C and + 8 ° C. Expiration date 24 months. TP TC  
009/2011 TU 9158-006-72500079-2011 (rev. 1-4)