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## Antifungal Activity of "Antikandid" Gel.

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### ABSTRACT

The optimal composition and rational technology of "Antikandid" gel based on derivatives of 4H-pyrido[4',3':5,6]pyrano[2,3-d]pyrimidine was developed, which has antifungal and antimicrobial activity. The antifungal effect of four samples of the gel was investigated.

**Keywords:** gel, antifungal effect, an optimal composition, a rational technology, derivatives synthesis of 4H-pyrido[4',3':5,6]pyrano[2,3-d]pyrimidine.

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## INTRODUCTION

Currently, the most common skin diseases caused by pathogenic and opportunistic fungi, the risk of infection by fungal diseases is great, because of the way its transmissions.

Fungal diseases - is the widespread pathology having widespread distribution. And besides, and potentially dangerous, because, first, some of the fungal infections are easily transmitted, and secondly, a fungal infection tends to spread rapidly in the human body, when his condition is described as immunodeficiency [1-3].

In recent years, a variety of fungal infections with their localization and clinical manifestations are studied in depth the most doctors of various specialties. Thus, according to the WHO 20% of the world population, ie every fifth inhabitant of the planet, struck by a fungal infection [4, 5].

Widespread fungal in nature, their continued presence in the environment and in the body, and causes the inevitable contact of human infection. Currently, there is an increase in the number of patients with mycotic lesions LOR-bodies and, in particular, the outer and middle ear, including postoperative middle ear cavity.

The growing number of patients due to a significant increase in risk factors for fungal infection, uncontrolled and haphazard use of local antibacterial drugs for the treatment of otitis. In addition, the observed tendency to develop resistance-causing fungus mycosis to specific antifungal drugs. An increased proportion of chronic fungal inflammation with frequent relapses not amenable to drug correction, which - in turn leads to an increase in disability and disability in terms of population [6-8].

Types of fungal diseases.

- Keratomycosis - a group of fungal diseases, affects the stratum corneum (erythrasma, actinomycosis , pityriasis versicolor). One of the most common - pityriasis (multicolored) versicolor . It is characterized by the appearance of pink- brown spots, accompanied defurfuration. Most often found in the neck, back, chest. In connection with the surface lesion is not usually accompanied by inflammation and pruritus.
- Dermatophytosis - group, where in the defeat epidermal layer and hair, has a chronic course. The vast majority of cases (about 80%) suffer from athlete. Most often it is Epidermophyton floccosum and Trichophyton mentagrophytes. This fungal disease affects the skin of feet and inguinal folds and nail plate.
- Trichophytia - disease caused by a antropofilous fungus. The source of infection are people, animals, and various objects which were fungus spores. This group also includes diseases: favus, microsporia. These fungal diseases are caused primarily lesions of hair.
- Candidiasis - Candida affects the skin surface of the mucous membranes. The causative agent - the fungus candida yeast, multiply rapidly, especially with reduced immunity of the person. Most often seen in children, the elderly [ 9-13].

From a marketing point of view, antifungal agents (antimycotics) are very promising pharmacotherapeutic group. Antifungals market is constantly under scrutiny both physicians and large pharmaceutical corporations.

Over the past decade it has been developed and put on the market several new generations of drugs of systemic and local action. Before the advent of medical practice antifungal agents for the treatment of fungal infections used a variety of antiseptics.

Currently available to dermatologists, there are a variety of modern antifungal agents. Selection tool in the treatment of fungal infections depends on the type of pathogen and its sensitivity to prescribers (necessary medication with an appropriate range of actions), generalization of fungal infections and as a result , the characteristics of the pharmacokinetics of the drug , its toxicity , the clinical condition of the patient and

others. All methods of treatment of fungal infections directly or indirectly aimed at the destruction of pathogenic fungi [14-15].

In our country in production and development of new drugs for the treatment and prevention of these diseases is actual. Most of the drugs produced in Kazakhstan, made on a comparable with European equipment, as well as from the same raw material, but the share of domestic producers is very small and the Kazakhstan market of medicines remains a market for imports. In order to proceed with the development of drugs, we need to know the procedure of the treatment of fungus, which is determined by the clinical form and localization of lesions [16].

**Purpose of The Study**

Develop gel composition and technology "Antikandid " based on derivatives of 4H-pyrido[4',3':5,6]pyrano[2,3-d] pyrimidine and study its anti-fungal properties.

**EXPERIMENTAL**

The antifungal activity of the test samples of the gels was studied in vitro in agar diffusion method (method "wells"). This method is based on the ability of active substances diffuse into the solid growth medium - agar inoculated with cultures of microorganisms previously.

Gel - samples of soft dosage form obtained for analysis.

Gel sample	The content of active substance
№1	The basis
№2	1,0 %
№3	3,0 %
№4	5,0 %

The composition of the bases (№1 sample):

**Active substance:**

An active pharmacological substance -

**Excipients:**

Dimexidum 3,0%  
 Propylene glycol ( PG ) 50,0%  
 Carbopol Ultrez 20 1,0%  
 Triethanolamine 1,0%  
 Purified water 45%

Ingredients of 1 % gel (№2 sample):

**Active substance:**

An active pharmacological substance 1,0%

**Excipients:**

Dimexidum 3,0%  
 Propylene glycol 50,0%  
 Carbopol Ultrez 20 1,0%  
 Triethanolamine 1,0%  
 Purified water 44%

Ingredients 3 % gel (№3 sample):

<b>Active substance:</b>	
An active pharmacological substance	3,0%
<b>Excipients:</b>	
Dimexidum	3,0%
Propylene glycol	50,0%
Carbopol Ultrez 20	1,0%
Triethanolamine	1,0%
Purified water	42%

Ingredients 5 % gel (№4 sample):

<b>Active substance:</b>	
An active pharmacological substance	5,0%
<b>Excipients:</b>	
Dimexidum	3,0%
Propylene glycol	50,0%
Carbopol Ultrez 20	1,0%
Triethanolamine	1,0%
Purified water	40%

The test was carried out under aseptic conditions using a laminar box (biological safety cabinet AS2-4E1 "Esco", Indonesia). As the test cultures have used fungal culture from American culture Collections (ATCC): Staphylococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis and yeast-like fungus genus Candida - Candida albicans ATCC 885-653, mold fungi Aspergillus niger ATCC 16404. Also used museum fungal culture Candida tropicalis, Candida krusei. The research was conducted using a two-day suspension cultures of fungi in saline. Microbial load was 107 colony forming units of microorganisms per 1 ml of culture medium (CFU/ml) [17-18].

Antifungal activity index is the size of the zone of delay of growth of test microorganisms that is formed in agar medium on Petri dishes. The diameter of the inhibition growth zones given as wells diameter was measured to within 1 mm, while guided by the complete absence of visible growth.

**RESULTS AND DISCUSSION**

As a result of studies on antifungal properties of the samples of soft medicinal form - gel towards different fungi cultures were obtained. The results shown in Table 1 [19-21].

**Table 1: Antifungal Activity gels experimental samples (n = 5)**

№	Cultures of micro - organisms	Samples of gels in various concentrations, %			
		№ 1 – Basis	№ 2 – 1,0 %	№ 3 – 3,0 %	№ 4 – 5,0 %
The diameters of the zones of microbial growth delay, mm					
1	Staphylococcus aureus	-	29,1±0,5	33,6±0,5	31,6±0,5
2	Pseudomonas aeruginosa	-	27,7±0,4	30,6±0,5	25,6±0,4
3	Bacillus subtilis	-	20,3±0,6	24,1±0,6	29,6±0,5
4	Escherichia coli	-	28,4±0,6	38,2±0,7	39,1±0,4
5	Aspergillus Niger	-	24,6±0,5	30,0±0,7	30,8±0,8
6	Candida albicans	-	41,2±0,4	47,0±0,7	46,8±0,4
7	Candida tropicalis	-	40,2±0,8	44,0±0,7	44,8±0,4
8	Candida Krusei	-	30,0±0,7	38,6±0,5	39,6±0,5

Note: "-" - the delay microorganism growth zone is absent .

The data obtained experimentally and shown in Table 1 demonstrates that the analyzed samples of the soft dosage form - gels has an antifungal activity against all fungi using following culture: Staphylococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis, Escherichia coli, Candida albicans, Aspergillus niger, Candida tropicalis, Candida krusei. Sample № 1 (gel base) does not have antifungal activity.

It should be noted that the gel samples №2, 3, 4 possess a high degree of antifungal activity (diameter zones delay test cultures growing more than 25 mm) with respect to all cultures of fungi.

Samples №3 (active ingredient concentration of 3%) and №4 (active ingredient concentration of 5%) are more active in comparison with the sample № 2 (Table №1).

### CONCLUSIONS

- Present study on samples of the antifungal activity of gels with different concentrations of active ingredients (1.0 % , 3.0 % , 5.0 %) showed high activity against various fungi cultures: yeast-like and musty.
- Samples of gel containing with the active ingredient of 3.0% and 5.0 % are promising for further work on creating formulations with antimicrobial and anti-fungal properties.

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