# EXPERIMENTAL STUDY OF ANTIMICROBIAL ACTIVITY OINTMENT ON THE BASIS OF DYPEROKSYM AZELAIC ACID

Blazheyevskiy M. Ye., Strelnikov L. S., Prysiazhniuk O. V.
*National University of Pharmacy, Kharkiv, Ukraine*
*e-mail: blazejowski@ukr.net*

One of the urgent tasks of modern dermatology is acne treatment. The condition is considered to be one of the most common skin diseases. Among the large number of proposed in the present drugs for the treatment of acne stipulates the dosage form surface action based on azelaic acid and benzoyl peroxide. Azelaic acid ($HOOC(CH_2)_7COOH$) – the active pharmaceutical ingredient known Skynoren® cream 20% (Schering, Germany) is an antibiotic drug which is produced by the yeast *Pityrosporum acne*, inhibits the growth of propionic bacteria and the generation of LCD, contributing to the emergence acne.

In turn, active pharmaceutical ingredient drugs Uhresol 10% (Farmasayns, INC., Canada), and others. Benzoyl peroxide ($C_6H_5C(O)OO(O)CC_6H_5$) effectively regulate keratinization process in the sebaceous follicles, improves oxygenation of tissues, reduces free LCD lipids in tissue has an antimicrobial effect, especially with regard to *Propionibacterium acne* and *Staphylococcus epidermidis*.

Research of interest clarify the applicability as an active pharmaceutical ingredient in preparations of surface action regarding acne basis dypiroksym azelaic acid, which, unlike benzoyl peroxide, not capable of radical decomposition, and therefore will not have the ability to enhance carcinogenesis by UV radiation.

The aim of the study was a comparative study of antimicrobial activity of the ointment on the basis of our proposed new substance – dypiroksym azelaic acid and two European branded drugs – AkneStop 20% (Corporation "Arterium", Kyiv) and Uhresol Lotion 10% (Brie 30 EDTA, Carbomer 940) (Farmasayns, Canada).

Ointment containing hydrophilic polyethylene oxide basis (PEO 400, PEO-1500 in a ratio of 8:2), 1% dypiroksym azelaic acid (DPAK), sodium edeteat. DPAK synthesized by known methods:

$$HO(O)C(CH_2)_7C(O)OH+H_2O_2.= HOO(O)C(CH_2)_7C(O)OOH + H_2O.$$

Determination of antimicrobial activity of the objects carried by agar diffusion, based on the ability of active substances to diffuse in the culture medium, previously inoculated microorganisms. According to WHO recommendations for evaluation of antibacterial and antifungal activity of drugs as a test culture was used museum strains (gram-negative bacillus *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, Gram-positive cocci *Staphylococcus aureus* ATCC 25923 and spore-forming bacillus *Bacillus subtilis* ATCC 6633, yeast fungi *Candida albicans* ATCC 653/885) and clinical isolates (*Candida tropicalis*, *Candida krusei*, *Candida glabrata*).

In the experiment used daily suspension of microorganisms in saline. Microbial load was $1 \cdot 10^7$ colony forming units in 1 ml of nutrient medium. Antimicrobial effect of 1% ointment dyperoksizelayinovoyi acid studied in 1 day after preparation, after 2 weeks, 1 month deposit.

The results determine the antimicrobial activity of 1% ointment DPAK and preparations comparison presented in Table 1 show that 1% ointment DPAK detect antimicrobial action with respect to *Candida albicans* and *Candida tropicalis* level comparator AkneStop 20%.

While antibiotic ointment investigated the effect DPAK against Gram-negative (*Escherichia coli*, *Pseudomonas aeruginosa*) and gram-positive bacteria (*Staphylococcus aureus*, *Bacillus subtilis*) far exceeds the effect of other investigational drugs. As seen from the data in Table 1, ointment based DPAK revealed high antimicrobial activity to the *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Candida albicans*, less pronounced – as *Bacillus subtilis*, *Candida tropicalis*, *Candida krusei*, *Candida glabrata*.

*Table 1*

**The results determine the antimicrobial activity**

| Test culture | Zones of growth inhibition test cultures mm (n = 3) |
|---|---|
| **Ointment based DPPK 1%** | |
| *St. aureus* | 45.4±1.3 |
| *Escherichia coli* | 45.0±0.4 |
| *Pseudomonas aeruginosa* | 38.8±2.6 |
| *Bacillus subtilis* | 22.7±2.8 |
| *Candida tropscalis* | 23.7±1.4 |
| *Candida albicans* | 31.3±3.7 |
| *Candida krusei* | 21.5±1.5 |
| *Candida glabrata* | 14.8±1.7 |
| **Aknestop 20%** | |
| *St. aureus* | 35.1±0.4 |
| *Escherichia coli* | 21.3±0.7 |
| *Pseudomonas aeruginosa* | 29.0±1.2 |
| *Bacillus subtilis* | 15.0±0.7 |
| *Candida tropscalis* | 22.3±0.3 |
| *Candida albicans* | 27.1±1.1 |
| *Candida krusei* | 22.4±0.6 |
| *Candida glabrata* | 9.0±0.5 |
| **Uhresol 10%** | |
| *St. aureus* | 15.1±1.2 |
| *Escherichia coli* | 12.8±1.3 |
| *Pseudomonas aeruginosa* | - |
| *Bacillus subtilis* | 16.1±1.2 |
| *Candida tropscalis* | 17.7±0.5 |
| *Candida albicans* | 24.5±0.5 |
| *Candida krusei* | - |
| *Candida glabrata* | - |

Note. "-" - A zone of stunted growth of microorganisms available.

In addition, studies of antimicrobial activity of the ointment on the basis DPAK day after making, 2 weeks and 1 month of storage showed that the cream does not lose its properties throughout the observation time. Consequently, studies have shown that the new dyperoksiazelayinovoyi acid ointment on hydrophilic high inherent antimicrobial activity, which makes it promising for further in-depth research.

**Conclusions.** The synthesis dypiroksym azelaic acid. Made antimicrobial hydrophilic ointment on the basis of which contained 1% dypiroksym azelaic acid. In comparative perspective explored antimicrobial activity of the ointment and branded drugs AkneStop and Uhresol. Clarified the expiration date for application of the ointment as it extemporal drug form (for one month).