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DEPENDENCE OF THE ANTIMICROBIAL ACTIVITY AND STRUCTURAL AND MECHANICAL PROPERTIES OF THE OINTMENT ON THE MANUFACTURING TECHNOLOGY

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The results of the experimental studies of the antimicrobial activity and rheological properties of model samples are given depending on the technology of preparation. It has been found that the antimicrobial activity of the drug depends on the technology of preparation, in particular the way of introduction of active substances into the base. It has been determined experimentally that into the ointment's composition such components as nimesulide, clotrimazole and ceftriaxone must be introduced as a suspension with vaseline oil, and benzocaine – as a solution in ethanol, which is added to the finished product. Structural and mechanical properties of the drug are also dependent on the way of introduction of active substances into the base. It has been proven that the model sample rheogram is included in the rheological optimum in the following way of introduction of active substances into the base: nimesulide, clotrimazole and ceftriaxone in the form of suspension with vaseline oil, and benzocaine in the form of solution in ethanol.

The problem of treatment of wounds despite the wide variety of the methods and drugs proposed remains relevant to modern medicine of injuries [1, 7, 8]. Pathogenesis of the wound process described as the interaction of local and systemic reactions is not fully understood at present. Duration of individual phases of the wound process is determined by a number of factors, among which the nature of the damage, the state of the body reactivity and treatment of the wound process are fundamental [2, 9]. Terms of the course of each phase – exudation, wound cleansing and its reparation are almost impossible to determine in advance. Only the sequence of these phases change is stable, each of which is characterized by certain functional and morphological changes that occur in the wound and surrounding tissues [1, 2, 5].

Separation of particular phases and stages of the inflammatory process is conditional; it is impossible to draw a clear line between the end of one and beginning of another. Scientists differently define the beginning and end of each phase, describing them from the point of the profile of their research [5, 6].

Based on the biomedical requirements for development of soft drugs [3, 4, 10] according to the phases of the wound process the ointment containing antimicrobial, anti-inflammatory and anesthetic active pharmaceutical ingredients (APIs) has been worked out to treat wounds in the first phase of the wound process.

As antimicrobial and antifungal components we have selected clotrimazole and ceftriaxone, respectively, as an anti-inflammatory agent nimesulide has been used, and benzocaine has been chosen as an anesthetic.

The aim of our study was to study the way of introduction of APIs – ceftriaxone, and nimesulide and clotrimazole to the composition of the ointment for treating wound processes.

Materials and Methods

The microbiological studies have been conducted at the Department of Clinical Immunology and Microbiology of Kharkiv Medical Academy of Postgraduate Education under the supervision of prof. S.V.Birokova.

The antimicrobial activity of model samples has been studied by the agar diffusion method according to the requirements of SPU on solid culture media; the method is based on the ability of a drug sample to inhibit the growth of microorganisms. In this experiment the effect of nimesulide on the antimicrobial activity of clotrimazole and ceftriaxone have been also studied.

Structural and mechanical properties of model samples have been studied according to SPU using a rotational viscosimeter «Reotest 2» (Germany) with coaxial cylinders.

Results and Discussion

Experimental studies have shown that the best way to introduce an API to the ointment base is suspension with auxiliary substances – glycerine, PEO-400, vaseline oil and water. Therefore, at the first phase of our research the dependence of the antimicrobial activity of a model sample on the way of APIs introduction to the base composition has been studied.

The research results of the antimicrobial activity of APIs depending on the suspending liquid used are shown in Table.

A comparative analysis of the experimental results (Table) shows that all model samples possess a high antimicrobial activity in the range from 25.3 to 41.7 mm for *E. coli*, from 24.9 to 41.1 mm for *K. pneumoniae*, from 25.6 to 39.6 mm for *B. subtilis*, from 12.2 to 13.7 mm for *C. albicans* (ATCC 885-653) and from 8.3 to 9.5 mm for *St. epidermidis* (ATCC 12228). The antimicrobial activity of model samples varies depending on the liquid used for suspending APIs. When comparing the antimicrobial activity of samples 1-3 and 4-7 the conclusion

Table

The effect of the way of introduction of APIs on the antimicrobial activity of model samples

Ceftriaxone	Nimesulide	Clotrimazole	Microorganisms				
Way of introduction			E. coli	K. pneumoniae	B. subtilis	C. albicans ATCC 885-653	*St. epidermidis* ATCC 12228
Suspension			Diameter of the growth inhibition zone of test cultures (mm)				
Glycerine	PEO-400	Glycerine	25.3±0.1	24.9±0.2	25.6±0.2	12.9±0.1	8.6±0.2
PEO-400	Vaseline	PEO-400	29.6±0.1	31.8±0.2	34.6±0.2	12.8±0.2	8.4±0.2
Water	Glycerine	Vaseline oil	33.6±0.2	32.3±0.1	32.3±0.1	12.3±0.1	8.3±0.1
PEO-400			35.4±0.1	36.8±0.1	36.7±0.1	12.8±0.1	8.8±0.1
Vaseline oil			*41.7±0.1*	*41.1±0.1*	*39.6±0.1*	*13.7±0.1*	*9.5±0.1*
Propylene glycol			34.6±0.2	33.2±0.2	31.9±0.2	12.2±0.1	9.2±0.2
Glycerine			29.7±0.2	30.9±0.2	27.8±0.2	12.8±0.1	8.8±0.1

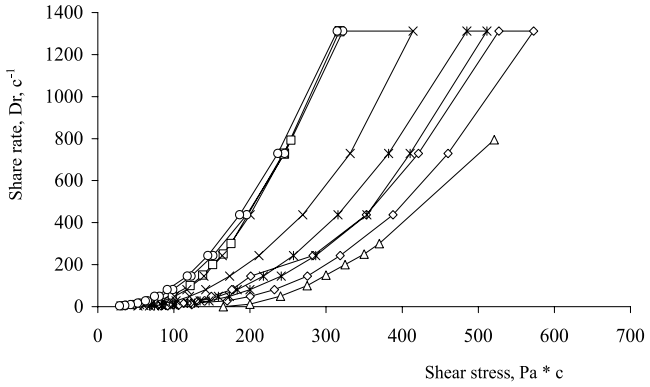

Fig. 1. Rheograms of the model samples flow of the ointment depending on the way of introduction of API: 1 – with propylene glycol, 2 – with PEO-400, 3 – with vaseline oil, 4 – with glycerine.

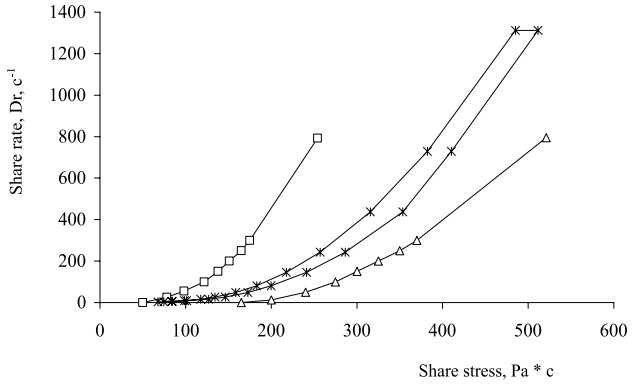

Fig. 2. The rheogram of the model samples flow of the ointment with benzocaine.

can be made that the antimicrobial activity of model samples 4-7 exceeds the activity of samples 1-3. Therefore, based on microbiological tests it is advisable to use vaseline oil or a hydrophilic nonaqueous solvent (PEO-400, glycerene or propylene glycol) for suspension of APIs. Model samples 4-7 depending on the suspending liquid used can be arranged in the following sequence: glycerene > propylene glycol > PEO-400 > vaseline oil. That is sample 5 shows the highest antimicrobial activity. The zones of the growth inhibition of test cultures for *E. coli*, *K. pneumoniae*, *B. subtilis*, *C. albicans* and *St. epidermidis* are 41.7±0.1 mm, 41.1±0.1 mm and 40.8±0.1 mm, 13.7±0.1 mm and 9.5±0.1 mm, respectively. Therefore, it is expedient to introduce ceftriaxone, clotrimazole and nimesulide to the composition of the ointment as a suspension with vaseline oil.

One of the important indicators of the technological quality of a soft drug is to study its structural and mechanical (rheological) properties. Rheograms of the model samples depending on the way of introducton of APIs into the base are given in Fig. 1.

The results of rheological studies have shown that the model samples 2-4 are included in the boundaries of the rheological optimum. The rheogram of sample 1 exceeds the limits of the optimum. The study of structural and mechanical properties of the ointment has shown that the best way to introduce ceftriaxone, clotrimazole and nimesulide into the ointment base is a suspension with vaseline oil.

The next stage of our research was to study the way of benzocaine introduction to the ointment. Benzocaine was introduced into the ointment as a solution in ethanol (Fig. 2).

CONCLUSION

Thus, as a result of the experimental studies it has been found that it is expedient to introduce nimesulide, clotrimazole and ceftriaxone as a suspension with vaseline oil into the ointment's composition, and benzocaine – as a solution in ethanol, which is added to the finished product.

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ЗАВИСИМОСТЬ АНТИМИКРОБНОЙ АКТИВНОСТИ И СТРУКТУРНО-МЕХАНИЧЕСКИХ СВОЙСТВ МАЗИ ОТ ТЕХНОЛОГИИ ПРИГОТОВЛЕНИЯ

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Приведены результаты экспериментальных исследований антимикробной активности и реологических свойств модельных образцов в зависимости от технологии приготовления. Установлено, что антимикробная активность препарата зависит от технологии приготовления, в частности от способа введения действующих веществ в основу. Экспериментально установлено, что в состав мази такие компоненты, как нимесулид, клотримазол и цефтриаксон необходимо вводить в виде суспензии с вазелиновым маслом, а анестезин – в виде раствора в этаноле, который добавляется к готовому продукту. Структурно-механические свойства препарата также зависят от технологического способа введения действующих веществ в основу. Доказано, что реограмма модельного образца входит в реологический оптимум при следующем способе введения действующих веществ в основу: нимесулид, клотримазол и цефтриаксон в виде суспензии с вазелиновым маслом, анестезин – в виде раствора в этаноле.

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ЗАЛЕЖНІСТЬ АНТИМІКРОБНОЇ АКТИВНОСТІ ТА СТРУКТУРНО-МЕХАНІЧНИХ ВЛАСТИВОСТЕЙ МАЗІ ВІД ТЕХНОЛОГІЇ ВИГОТОВЛЕННЯ

В.В.Руденко

Наведені результати експериментальних досліджень антимікробної активності та реологічних властивостей модельних зразків у залежності від технології виготовлення. Встановлено, що антимікробна активність препарату залежить від технології виготовлення, зокрема від способу введення діючих речовин до складу основи. Експериментально встановлено, що до складу мазі німесулід, клотримазол та цефтриаксон доцільно вводити у вигляді суспензії з олією вазеліновою. а анестезин – у вигляді розчину з етанолом, який додається до готового продукту. Структурно-механічні властивості препарату також залежать від способу введення діючих речовин. Доведено, що реограма модельного зразка входить в реологічний оптимум при наступному способі введення діючих речовин: німесулід, клотримазол і цефтриаксон – у вигляді суспензії з олією вазеліновою, а анестезин – розчину в етанолі.