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BIOPHARMACEUTICAL RESEARCH ON THE SELECTION OF BASE FOR "GLYTACYD" OINTMENT

The article presents results of research on the selection of the optimal base of ointment for the treatment of infectious and allergic skin diseases and wound healing in stage II. It has been found that type of base affects on the release of active substances from ointment. It has been studied that osmotic activity of the ointments' samples depends on the composition of their base. It has been proved that satisfactory osmotic activity has emulsion base, which should be used for further research.

Key words: ointment; anaesthezin; nitazol; bioavailability; kinetics of release of active substances; spectrophotometry

INTRODUCTION

Analysis of the literature of modern biopharmaceutical studies of drugs with local effects showed that maximize efficiency and pronounced pharmacological effect possible under optimal excipients framework that must match the phase of wound healing can control the release of active substances and prevent the development of side effects.

Rationally selected constituent base with a glance their physical, chemical and structural and mechanical properties as well as their right combination of active ingredients will create a drug with the desired pharmacological properties [1, 3, 8].

The aim of the work was to study the release of active substances from samples of ointments.

MATERIALS AND METHODS

To study the release of active substances from foundations were used methods in vivo and in vitro. The most common and convenient method for studying the kinetics of release in vitro equilibrium dialysis is dialysis in the liquid medium through a semipermeable membrane at a temperature of (34 ± 0,1) °C [5, 7].

Spectrophotometric method was used to determinate the quantity of active pharmaceutical ingredients (APIs) in the dialysate.

Semipermeable membrane (brand B-8079) was fixed to the bottom of the bove inner cylinder cell for dialysis on which was applied a investigated sample (5.0 g) equable layer. Then, the inner receptacle together with the stading sample was placed in a chamber for dialysis, which previously had been poured calculated amount of isotonic sodium chloride solution (50 ml ± 0,5). Samples (5 ml) was performed using a pipette every 60 minutes.

The tests were taken out using the thermostat TV-80-1 at a temperature of 34 ± 1,0 °C, which corresponds to a temperature of the skin surface.

The amount of dissolved substances was determined spectrophotometrically by the method of standard (SPU 2.2.25). Optical density of solutions was determined using a spectrophotometer Evolution 60S at a wavelength of 294 nm (for anaesthezin) and 412 nm (for nitazol) in the cell with a thickness of 10 mm layer as deterioration in the quality control solution of ethyl alcohol was used [2].

The concentration of the getting of dialysis solution (g/ml) was calculated using the optical density data obtained in experiments with standard solutions:

$$\frac{A}{A_{st}} = \frac{C}{C_{st}}; \text{ where } C = \frac{A \cdot C_{st} \cdot b}{A_{st}},$$

where: A – optical density of the test solution;
A_{st} – optical density of the standard solution;
C_{st} – concentration of standard solution g/ml;
b – breeding.

RESULTS AND DISCUSSION

Anaesthezin belongs to the primary aromatic amines, as one of the most common methods of its determination of the reaction is colorimetric diazotization with derivatives of phenols in alkaline medium is formed as a result of an orange-yellow color. At the same time, nitazol (2-acetylamino-5-nytrotiazol), available in ointment, is a composition which is characterized by nitro-izonitro tautomerism. In an alkaline medium, it goes in izonitro form that has an intensive yellow color with maximum absorption at 412 nm.

Given the basic biomedical requirements for drugs for topical treatment of wounds in the II-nd phase of wound healing and analysis of published data for research, we have selected ointment bases listed in the Table.

Table

INVESTIGATED OINTMENT BASES

Number of sample	Type of ointment base	Auxiliary	Content of substances, g
1	Hydrophilic	PEO-400 PEO-1500 PG	60.0 30.0 10.0
2	Emulsion type o/w	Corn oil Lanette SX Eumulgin PG PEO-400 Purified Water	20.0 0.5 8.0 10.0 10.0 to 100.0
3	Emulsifier-gel	PG PEO-400 Corn oil Alcohol cetostearyl Carbopol Triethanolamine (TEA)	10.0 10.0 10.0 8.0 1.0 0.5
4	Gel	PG PEO-400 Carbopol TEA Purified Water	10.0 10.0 1.5 1.5 to 100.0
5	Emulsion type w/o	PG PEO-400 Oil vaseline Glycerol Stearic acid Emulsifier № 1 Purified Water	10.0 10.0 20.0 5.0 2.0 5.5 to 100.0

In order to determine the concentration of active substances in dialysate were investigated their adsorption spectra. Concentrations obtained as a result of dialysis solutions was calculated using data of absorbance of standard solutions obtained at construction of calibration graphs.

Analysis of the data obtained during verification of submission of absorbances of nitazol solutions in alkaline to Bouguer-Lambert-Beer law showed that the dependence of absorbance on nitazol concentration is linear in the range of $1.6 \cdot 10^{-5}$ to $9.6 \cdot 10^{-5}$ g/ml (Fig. 1). These borders the specific index of absorption is almost the same and equal to 1031 ± 6.45.

Submission of the optical density of the solution in alkaline medium of anestezin to Bouguer-Lambert-Beer law comes in all the borders of the studied concentrations of $1 \cdot 10^{-4}$ % to $2 \cdot 10^{-3}$ % (Fig. 2). Specific absorption index thus varies within the statistical error and makes up 1186 ± 25.2. Within these quantitative determination, the concentrations of these substances can be performed with acceptable accuracy.

The results of a study to determine the quantity of anaesthezin and nitazol from samples of ointment bases are presented in Fig. 3 and 4.

These results determine the release kinetics suggest that there is a pronounced dependence of the con-

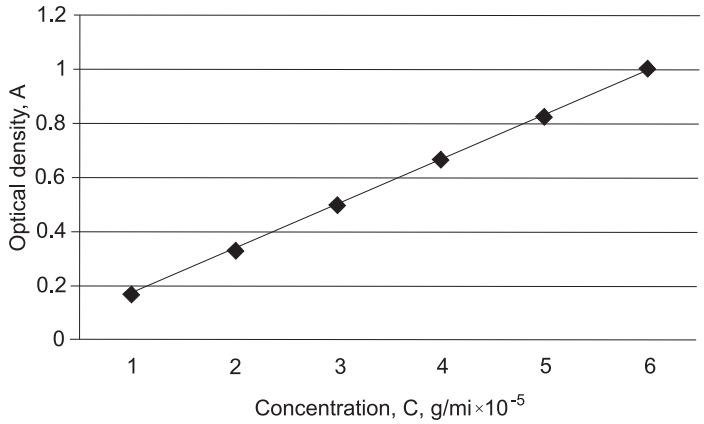

Fig. 1. *Calibration graph of optical density solutions of nitazol depending on concentration.*

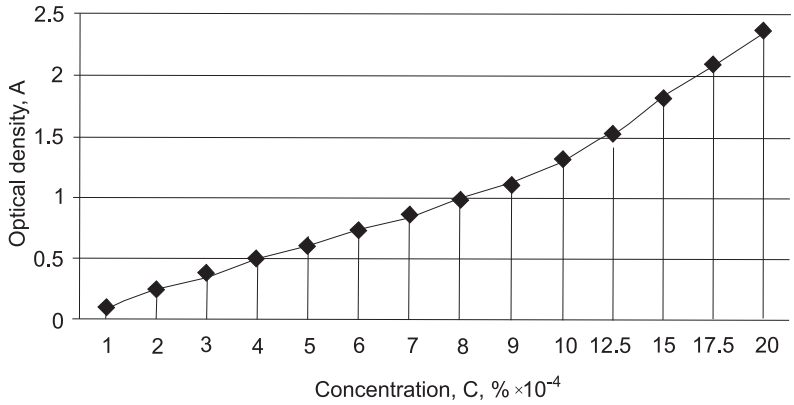

Fig. 2. *Calibration graph of optical density of anaesthezin solution depending on concentration.*

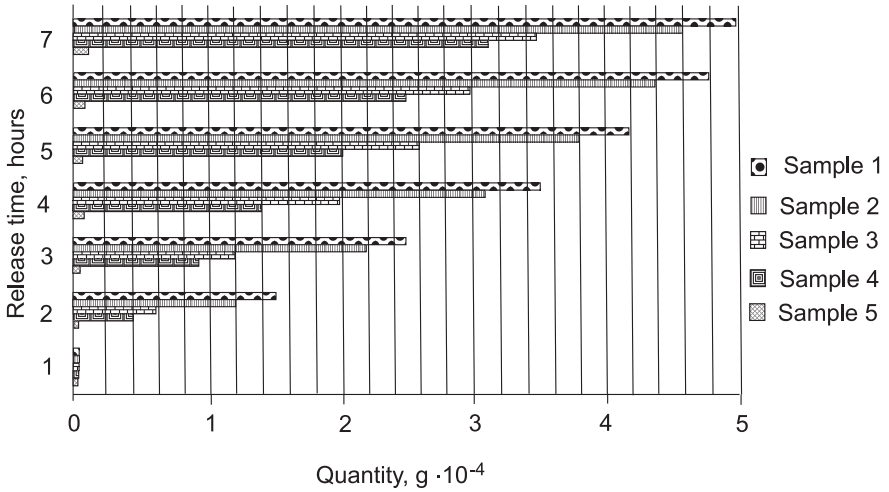

Fig. 3. *Dynamics of anaesthezin release from samples of bases.*

centration of active ingredients in the solution of the duration of the experiment.

Analysis of the data shown in Fig. 1 shows that the total number of dissolved anaesthezin is between $0,01 \cdot 10^{-4}$ g to $5,0 \cdot 10^{-4}$ g. The highest concentration observed in sample number 1, the release in this framework is fast and by sixth hour test in the experiment, the concentration of substances in the dialysate is $5,0 \cdot 10^{-4}$ g. Unleashing the basics № 2, № 3 and number 4 is slower, and at the sixth hour of the experiment, the concentration of the substance is 4,6·10-4 g (sample number 2), $3,5 \cdot 10^{-4}$ g (sample number 3) and $3,1 \cdot 10^{-4}$ g (sample number 4).

Total number nitazol (Fig. 4) that turned into the test solution is within $0,012 \cdot 10^{-4}$ g to $0,5 \cdot 10^{-4}$ g, with a

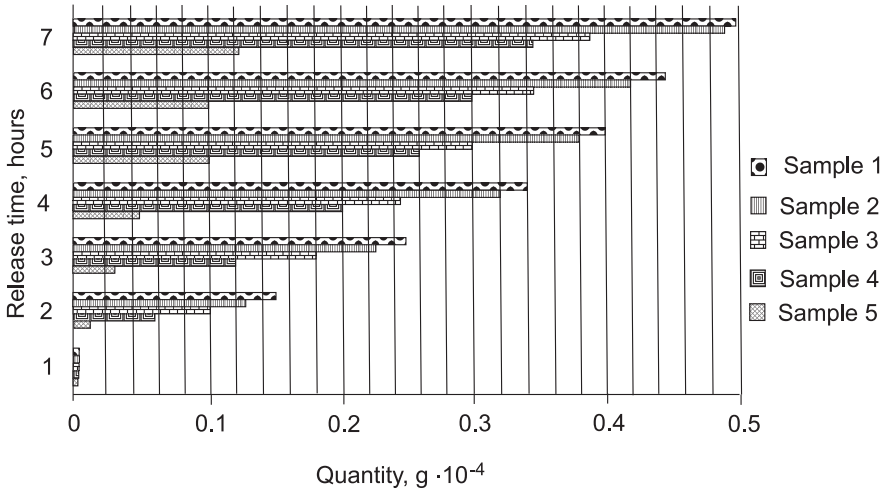

Fig. 4. *Dynamics of nitazol release from samples of bases.*

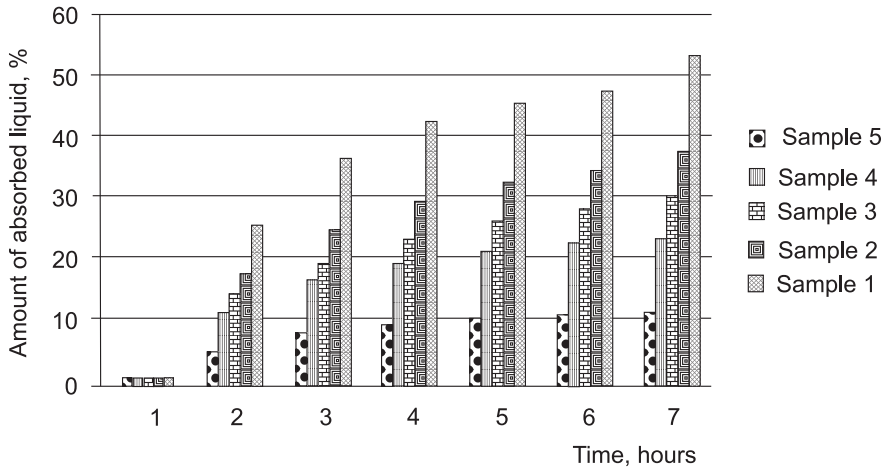

Fig. 5. *The dependence of the amount adsorbed fluid occasionally dialysis.*

maximum content in sample number 1. Emulsion base type w/o (sample number 5) release the active ingredients slowly. At the sixth hour of the experiment the content of active substances in this basis is $0,08 \cdot 10^{-4}$ g (anaesthezin) 10^{-4} and $0,13 \cdot 10^{-4}$ g (nitazol).

The next stage of research was the study of the osmotic activity of ointment base samples. Knowing possibility to display pharmaceuticals osmotic activity allows to use them optimally in medical practice.

Results of the study of osmotic activity of samples indicate that the sample number 1 shows the highest absorption rate of liquid at the sixth hour of experiment is 54 %. The high level of osmotic activity is optimal for treating inflammatory focus of destroyed tissue in the wound and formed by toxic products, which is typical of the first phase of wound healing, but at the stage of regeneration (II phase), it does not contribute to the formation and maturation of granulation tissue and reparative processes will slow down in the wound. Lowest rate of absorption of the sample shows that number 5-12 %, sample number 2, № 3 and № 4 with values of absorbed fluid at a rate of 38 %, 31 % and 24 %, respectively (Fig. 5).

As shown in Figures 3, 4 and 5 like ointments № 2 fully and rapidly releases the active substance (benzocaine and nitazol) from the base and has optimal value of osmotic activity that will promote the growth of granulation tissue in wound healing phase II and prevent secondary infection of the wound [4, 6, 9].

Thus, the data suggests as the optimal carrier base to justify the selection of the sample number 2 – emulsion foundations of in for a new pharmaceutical product "Glytatsyd" for the treatment of dermatological diseases and skin wound healing in phase II.

CONCLUSIONS

1. A biopharmaceutical research of anaesthezin and nitazol release from samples of bases dialysis through a semipermeable membrane, confirmed the influence of the type of base bioavailability of active ingredients. Experimentally proved, the sample number 2 – kind of emulsion base shows dynamic performance the release of active ingredients.
2. Investigated osmotic activity of the samples. Established that the optimal values of osmotic activity has the basics like number 2, to facilitate the growth of granulation tissue in wound healing phase II and prevent secondary infection of the wound
3. Proved the expediency of further study emulsion bases of type I as the basis for a new combination ointment "Glytatsyd" for the treatment of dermatological diseases and skin wound infection at stage II surgery process.

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БИОФАРМАЦЕВТИЧЕСКИЕ ИССЛЕДОВАНИЯ ПО ВЫБОРУ ОСНОВЫ МАЗИ «ГЛИТАЦИД»

Приведены результаты исследований по выбору оптимальной основы мази для лечения инфекционно-аллергических заболеваний кожи и раневого процесса на II стадии. Установлено, что тип основы влияет на высвобождение действующих веществ из мази. Изучена осмотическая активность образцов мазей в зависимости от состава основы. Доказано, что удовлетворительную осмотическую активность имеет эмульсионная основа, которую целесообразно использовать для дальнейших исследований.

Ключевые слова: мазь; анестезин; нитазол; биодоступность; кинетика высвобождения действующих веществ; спектрофотометрия

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БІОФАРМАЦЕВТИЧНІ ДОСЛІДЖЕННЯ З ВИБОРУ ОСНОВИ МАЗІ «ГЛІТАЦИД»

Наведені результати досліджень з вибору оптимальної основи мазі для лікування інфекційно-алергічних захворювань шкіри та ранового процесу на II стадії. Встановлено, що тип основи впливає на вивільнення діючих речовин мазі. Вивчено осмотичну активність зразків мазей залежно від складу основи. Доведено, що задовільну осмотичну активність має емульсійна основа, яку доцільно використовувати для подальших досліджень.

Ключові слова: мазь; анестезин; нітазол; біодоступність; кінетика вивільнення діючих речовин; спектрофотометрія

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