RESEARCH ARTICLE

Microencapsulation of Furacilin as a Method of Creating New Medicinal Forms, Possessing with Increased Biological Accessibility and Prolongable Effect

Elena V. Grekhnyova, Tatyana N. Kudryavtseva, Ilona B. Kometiani, Yuriy O. Velyaev

Head of Research Laboratory of Organic Synthesis, Kursk State University, 33, Radischeva str., Kursk, 305000, Russia

Abstract

Aim: Furacilin (nitrofural) is an antibiotic widely used in the form of ointment for the initial treatment of wounds on both skin and mucous membranes. The present study was aimed to develop and formulate create long-acting furacilin-based formulations. **Materials and Methods:** Double coat microcapsules were prepared using "Eudragit®" as a water-insoluble biocompatible polymer(inner coat) and sodium alginate, guar gum, polyvinyl alcohol, or polyvinylpyrrolidone as water-soluble polymer (second coat). Quantitative analysis of the microcapsules was confirmed using a ultraviolet (UV)-1800 UV spectrometer (Shimadzu). **Results and Discussion:** The microcapsules were prepared by solvent extraction method microcapsules and double coated using water insoluble and soluble polymers. Prepared microcapsules were evaluated for morphological characteristics; particle size, distribution, and release kinetics of microcapsules were studied. Furacilin microcapsule images obtained using a Quanta 650 FEG microscope with an autoemission cathode. *In vitro* release kinetics show prolonged drug release of furacilin from microcapsules. **Conclusion:** Furacilin microcapsules seemed to be appropriate for prolonged release and easily applied to a bandage intended, for purulent wound treatment.

Key words: Furacilin, increasing the bioavailability, insoluble polymers, microencapsulation, water-soluble

INTRODUCTION

Short stay of many medicinal compounds in the body is one of the main problems of modern pharmacology. It causes the impossibility of creation in blood and tissues of a long-lasting uniform and constant therapeutic concentration of the active substance. Thus, one of the main ways to improve the effectiveness of modern medicines is creating compositions with a slowed release of the active substance using microencapsulation methods.[1,2]

The wide application of medicinal substances' microencapsulation is caused by the need to instill them with new properties. Continuous release of the active substance from the microcapsule, the ability to mask the bitter and nauseating taste of substances, to increase the pharmaceutical preparation's resistance to environmental factors and targeted delivery of medicinal preparations are the properties with which the drug compound can be instilled through microencapsulation methods.[2,3]

Furacilin (nitrofural) is widely used in medical practice for the initial treatment of wounds on both skin and mucous membranes. However, the issue of furacilin-based prolonged dosage forms remains unresolved. At the same time, the creation of furacilin-based prolonged dosage forms is important for the treatment of extensive purulent wounds on the skin and will allow to avoid problems associated with additional traumas during bandaging and treatment.

Address for correspondence:
Tatyana N. Kudryavtseva, Candidate of Sciences, Head of Research Laboratory of Organic Synthesis, Kursk State University, 33, Radischeva str., Kursk, 305000, Russia. E-mail: labOS.kgu@mail.ru

Received: 22-11-2017
Revised: 10-12-2017
Accepted: 15-12-2017

Therefore, to create long-acting furacilin-based formulations, we decided to microencapsulate it in a double coat. The use of a water-insoluble biocompatible polymer as the inner coat of the microcapsule will determine the prolonged release of the substance. The second coat of a water-soluble polymer will simplify the use of the product and increase its bioavailability.

For a water-insoluble biocompatible polymer, we have chosen the methacrylic acid derivatives under the trade name "Eudragit®." Such polymers are insoluble in water and are intended to provide sustained release of the drug at certain physiological pH values.

Water-soluble polymers such as sodium alginate, guar gum, polyvinyl alcohol (PVA), or polyvinylpyrrolidone (PVP) were chosen for the second coating of microcapsules. It can be expected that the use of these polymers will make it possible to obtain new forms basing on water-insoluble drugs, which are stable aqueous fine-dispersed systems. This assumption is based, in particular, on the ability of sodium alginate and guar gum to gelatinize. The choice of the above-mentioned polymers is determined by the fact that they are widely used in medicine as auxiliary compounds in the manufacture of ready-made drug dosage forms.[4]

MATERIALS AND METHODS

Microencapsulation into the water-soluble polymer coating was carried out with the physicochemical method consisting of polymer reprecipitation on the surface of the encapsulated substance by replacing the solvent.[5,6] There were revealed the factors affecting the size and quality of the resulting microcapsules, such as dispersing method, precipitant, and pH of the reaction mixture. As a result of analysis and processing of a large amount of experimental data, the optimal conditions of microencapsulation process were chosen. We have shown that the use of mechanical dispersion (more preferable than ultrasonic) with the help of a magnetic or other stirrer and the use of acetone or ethyl alcohol as a precipitant allowed to increase the yield of the target product, to shorten the process time, and to reduce the size of the obtained capsules.

Experimental

The use of non-ionic surfactant agents ensures the maintenance of a stable dispersion prevents the aggregation of individual capsules, thereby increasing the yield of the product.[5] Microencapsulation into double coating was carried out sequentially. Initially, furacilin microcapsules were obtained in a coating of water-insoluble polymer Eudragit® L100, and then, they were encased in water-soluble polymer coating: PVP, PVA, sodium alginate, or guar gum. During the encapsulation of furacilin in Eudragit® L100 at the ratio of the substance and polymer by mass equal to 1:1, we also used the physicochemical method.[2] The process was carried out with the help of a magnetic stirrer at room temperature. Polymer solution in acetone was added by drops to the aqueous dispersion of furacilin. To apply a second layer of polymer, an aqueous solution of the second polymer (PVP, PVA, sodium alginate, or guar gum) is added to the obtained dispersion of the furacilin microcapsules into Eudragit® L100 in a water-acetone medium, and then, acetone or ethanol is added slowly by drops to achieve the full precipitation of the water-soluble polymer on the surface of the capsules. The obtained product is extracted by filtration or centrifugation and air dried.

The structure of the obtained microcapsules was confirmed by infrared (IR) spectroscopy using the FSM-1201 Fourier spectrometer in the range of 400–4000 cm^{-1} with a resolution of 4 cm^{-1} (20-fold scanning). IR spectra of the encapsulated substances were obtained in a KBr tablet, and the spectra of the obtained microcapsules were measured by the attenuation total reflection method. Quantitative analysis of the microcapsules was carried out by a calibration curve using a ultraviolet (UV)-1800 UV spectrometer (Shimadzu).

RESULTS AND DISCUSSION

The process of encapsulation into water-soluble polymers of almost any biologically active substance (BAS) requires both an individual approach to each of the BAS and compliance with some general patterns. As a rule, reducing the temperature of the reaction mixture to 3–5°C leads to increase in the yield of the target product by 10–20%. To prevent coagulation of the system during the precipitation, it is mandatory to use surfactants. In addition, the higher the mixing intensity is, the finer dispersed is the suspension of microcapsules and the less id probability of this suspension coagulation. The optimum speed of addition of the polymer's precipitator is from 0.5 to 1.0 ml/min.

The microencapsulation of furacilin in water-soluble polymers makes it possible to convert it into a form capable of forming stable aqueous dispersions with an active substance concentration of up to 1%. This, in turn, significantly increases the biological activity of furacilin preparations. This is particularly noticeable in the case of microcapsules of furacilin in natural polymers (guar gum and sodium alginate). We have previously shown that the activity of aqueous dispersions of these microcapsules exceeds not only the activity of the aqueous solution of furacilin but also solutions of furacilin in dimethyl sulfoxide with similar concentrations [5] Moreover, since furacilin is widely used as an antiseptic for local administration, the way to increase its solubility in water can significantly expand its field of application. As mentioned above, there is a need for furacilin drugs with a sustained release. Therefore, microcapsules of furacilin in a double coating were obtained. Furacilin

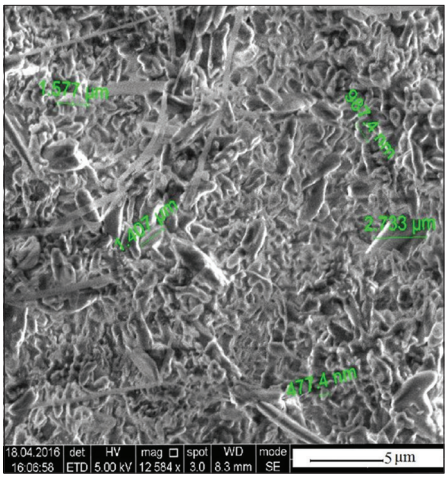

Figure 1: Furacilin microcapsules cased with EUDRAGIT® L100

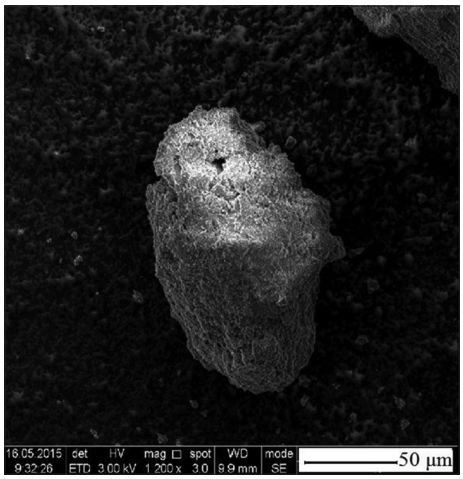

Figure 2: Furacilin microcapsule in a double coating consisting of EUDRAGIT® L100 and polyvinylpyrrolidone

microcapsule images obtained using a Quanta 650 FEG microscope with an autoemission cathode are shown in Figures 1 and 2.

The inner coating made of Eudragit® L100 polymer causes a prolonged delivery of the active substance to the lesion focus. The kinetics of the transition of furacilin from microcapsules to an aqueous solution is shown in Figure 3.

For convenience in the use of a long-acting furacilin form, another outer coating of a water-soluble polymer (PVP, PVA, sodium alginate, or guar gum) was used. The use of the second coating facilitates the dispersion of the microcapsules in water forming more or less stable dispersions. The kinetics of precipitation of an aqueous dispersion of furacilin microcapsules in a double coating is shown in Figure 4.

Thus, furacilin from the obtained microcapsules is gradually releasing within a few days. Moreover, with the help of an aqueous dispersion of furacilin microcapsules, this drug can be easily applied to a bandage intended, for example, for purulent wounds treatment.

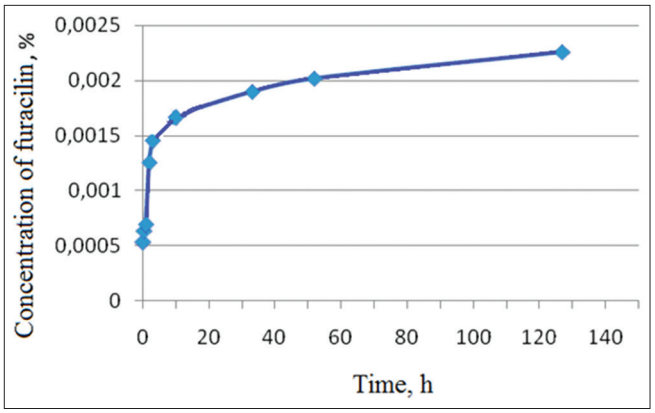

Figure 3: Speed of furacilin release from its microcapsules in Eudragit® L100

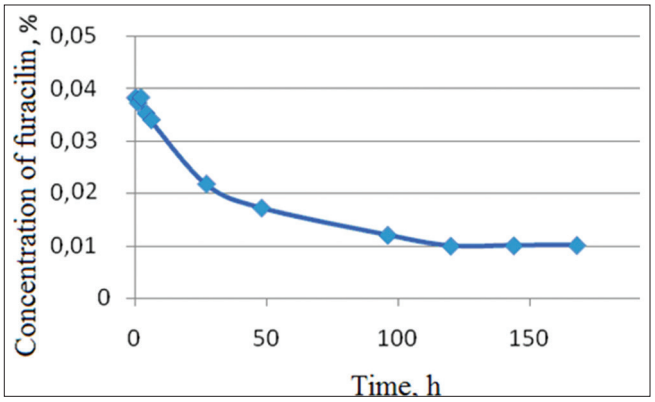

Figure 4: Kinetics of precipitation of an aqueous dispersion of furacilin microcapsules in a double coating (Eudragit® L100 and polyvinylpyrrolidone)

To program the rate of release of the active compound from the microcapsules obtained by this method, the thickness of the polymer coating may be varied using different ratios of the encapsulated substance: Polymer.

CONCLUSION

Thus, using the method of microencapsulation, it is possible not only to increase the biological activity of furacilin but also to show the possibility of creating furacilin-based preparations with prolonged action. The introduction of such drugs will reduce the frequency of taking medications, prevent multiple traumatizations of tissues, optimize the concentration of active substance in the place of insertion, thereby preventing side effects of the drug.

ACKNOWLEDGMENTS

The work was performed with the financial support of the Ministry of Education and Science of the Russian Federation (project No. 4.9516.2017/БЧ).

REFERENCES

1. Dai C, Wang B, Zhao H, Li B, Wang J. Preparation and characterization of liposomes-in-alginate (LIA) for protein delivery system. Colloids Surf B Biointerfaces 2006;47:205-10.
2. Valuev LI, Valueva TA, Valuev IL, Plate NA. Polymer systems for controlled isolation of biologically active compounds. Adv Biochem 2003;3:307-28.
3. Grekhnyova EV, Yu DO. Preparation and analysis of furacilin microcapsules in water-soluble polymers. Russ J Sci Publ 2013;5:5-6.
4. Grekhnyova EV, Kudryavtseva TN. Patent No. 2582274, RF, IPC (2016): A61K 31/65. 2016.
5. Grekhnyova EV, Kudryavtseva TN, Klimova LG. Properties of furacilineincapulated in water-soluble polymers. Aud Electron Sci J Kursk State Univ 2017;1. Available from: http://www.auditorium.kursksu.ru/pdf/013-004.pdf. [Last accessed on 2017 Oct 19].
6. Grekhnyova EV, Efanov SA, Kometiani IB. Soluble Forms of Some Drugs Based on Sodium Alginate. XV International Scientific Conference – High-Tech in Chemical Engineering. Moscow: MITHT Publisher; 2014. p. 149.

Source of Support: Nil. **Conflict of Interest:** None declared.