

**RESEARCHES ON PHARMACEUTICAL
DEVELOPMENT OF SOLID GELATINE
CAPSULES WITH DRIED MULTIPLE
COMPONENT EXTRACT OF
ANTIPHLOGOGENIC, DIURETIC AND
CHOLERETIC ACTION**

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Pharmaceutical drug development is based on the selection and study of the drug-comparison, safety and efficacy, taking into account the route of administration, the dosage form, the substantiation of the composition and concentration of the active pharmaceutical ingredient (API) and the excipients, bioavailability, strength and stability; identifying potential critical quality indicators; the choice and proposals of optimal technological scheme for obtaining this drug, the definition of critical operations and parameters of the technological process; definition of strategy of control, development of specifications and methods of control of raw materials, intermediate, non-prepackaged and finished products; the choice of packaging; validation or verification of methods of quality control of a medicinal product; carrying out studies on the stability of the medicinal product during the predicted shelf life [1].

One of the components of the delivery of the API to the site of the pathology is the dosage form of the drug, which significantly influences the preservation of its effectiveness, determining the degree of absorption and concentration in biological fluids [2, 3]. Recently, the attention of developers attracts a dosage form of capsule, which among the dosage forms of industrial production occupies the third place after tablets and solutions in ampoules [2, 4, 5]. They have more advantages (accuracy of dosing, high bioavailability, stability and productivity of obtaining, corrective ability, minimization of production errors, aesthetics, the ability to provide medicinal products with planned properties: the ability to dissolve in certain parts of the gastrointestinal tract, possess prolonged release of the API), sparing technological mode, etc.) than disadvantages, therefore the assortment of capsular preparations is varied [6, 7, 8, 9].

The aim of our work was to develop the technology of medicinal product in the form of capsules with an active pharmaceutical ingredient - a dry extract of urocholum, possessing anti-inflammatory, diuretic and choleric properties, as well as to determine the critical parameters in their production.

In our experimental research we have developed the optimal composition of the capsule mass recipe, the API of which is a multi-component dry extract obtained by condensation and drying in a vacuum-drying cabinet of a liquid urochlorum extract (1: 1) (extragent- 40% ethanol

and a mixture of wild carrots fruits, orthosiphon leaves, knotgrass grass, corn columns with pots, black elder flowers, horsetail grass, hop cones, birch buds, St. John's Wort grass, mint leaves). Lactose monohydrate and magnesium stearate were selected as auxiliary substances, as well as a number of characteristics of the model samples (fluidity, bulk density, bulk density after shrinkage, mass loss during drying, etc.) that were used in further technological studies [10].

The technological process of production of capsules with a multi-component dry extract consists of the following stages: sifting of raw materials, preparation of mass for encapsulation (mixing of components, rubbing); encapsulation; packing of capsules into blisters; packing blister packs; packing bundles in boxes.

The raw material is weighed in the amount indicated in the formulation, sifted.

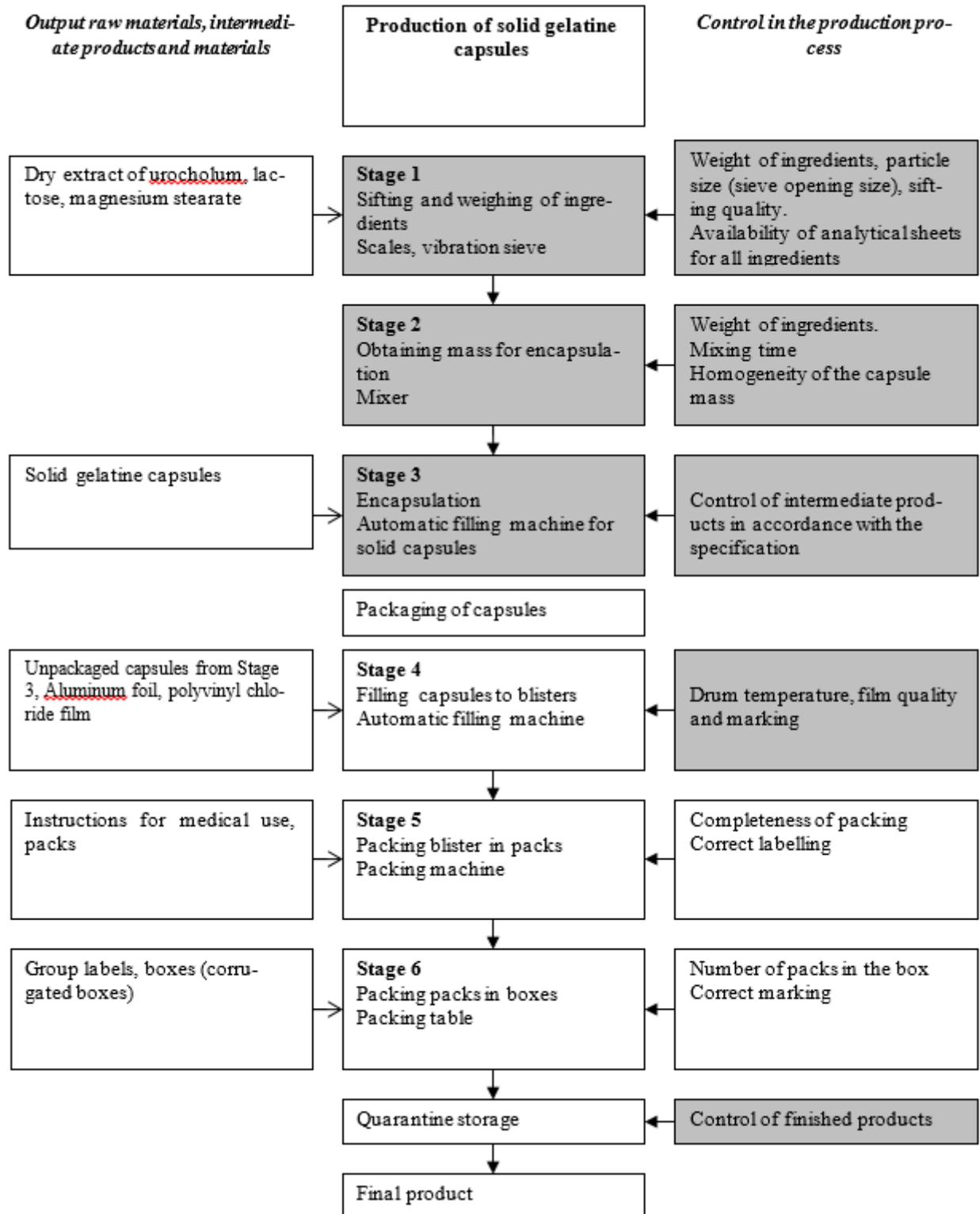
Dispensing of lactose monohydrate, a multi-component dry extract are placed in a prepared mixer and mix for 5-10 minutes, until homogeneous component distribution (visual control). The resulting mixture is calibrated through a sieve with a diameter of 0.25 mm holes. To the calibrated mix of components loaded with magnesium stearate and spend rubbing for 3-5 minutes.

The resulting mass for encapsulation is placed in a collection of a capsule machine and is carried out by a process of encapsulation. Absorption of filled capsules is carried out with the help of a duster. According to the technological instruction, during the adjustment of the capsule machine, the first 20 capsules are taken to check the correctness of the process.

Before pre-packaging and packaging, they carry out visual checking of the graphic design of the text and the quality of labelling on the packaging materials in accordance with the approved original layout.

The capsules are not pre-packaged in blister packs, according to the technological production scheme. Blisters with capsules are automatically delivered to the packaging machine by conveyor.

The packagings of capsules in the blisters, together with the instructions for medical use, are done on the packaging machine in packets. Packages are packed in bulk packaging on the machine packing in boxes. The package and the label of the group container indicate the name of the preparation in Ukrainian and Latin, the content of the active substance in mg, the number of capsules in the package, "Use according to the prescription", storage conditions, "Keep out of the reach of children", registration number, serial number, expiration date, bar code. In addition, the conditions for the release and "Do not use after expiration" apply to the package. The group packaging label further specifies the number of packages. The technological scheme for the production of capsules with urocholum with a dry multi-component extract is given in Fig. 1



Note: Gray colour indicate the critical stages and points of control in the manufacture of the drug

Fig. 1. Technological scheme of manufacture of urocholum capsule with multi-component dry extract

In order to obtain a documentary confirmation that as a result of a clear implementation of all stages of the technological process reproduction of the production of capsules of urocholum, which would correspond to the specification developed on them, was validated on 3 experimental series (0040319,0050319, 0060319).

The most significant aspects affecting the techno-

logical process, which are to be controlled during the routine production of capsules with a multi-component dry extract, are shown in the Ishikawa diagram [11] (Fig. 2).

In fig. 2 the risks are identified and an assessment of the probability of their occurrence regarding the impact on the quality of the intermediate product / product / process, as well as the degree of their significance.

On the basis of the conducted researches, the design of a technological regulation for the production of gelatinous capsules with a multi-component dry extract possessing anti-inflammatory, choleric and diuretic properties was developed and tested in industrial conditions by LLC DKP "Pharmaceutical Factory", Zhytomyr.

Experimentally established parameters of the technological process are basic for the development of pilot-industrial series of the drug in the conditions of the enterprise and the development of a scheme for the validation of the technological process.

Consequently, in the process of work, the technology of a medicinal preparation in the form of hard gelatine capsule with an active pharmaceutical ingredient, a multi-component extract dry, possessing anti-inflammatory, choleric and diuretic activity was developed.

Developed gelatine capsules with multi-component dry extract are stored in order to investigate their stability.

Conclusions

1. Based on the complex of scientific and experimental researches, the optimum technological mode of production of hard gelatinous capsules with a multi-component dry extract with anti-inflammatory, choleric and diuretic activity was established.
2. The critical stages of the process of gelatinous capsules being developed and the parameters of their control and the criteria of acceptability according to the requirements of the SPHU were determined.
3. Technology has been tested in the conditions of industrial production of LLC DKP "Pharmaceutical Factory", Zhytomyr, in accordance with the project of the technological regulations for the production of gelatin capsules with a multi-component dry extract.

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Introduction. Pharmaceutical drug development is based on the selection and study of the drug-comparison, safety and efficacy, taking into account the route of administration, the dosage form, the substantiation of the composition and concentration of the active pharmaceutical ingredient (API) and the excipients, bioavailability, strength and stability; identifying potential critical quality indicators; the choice and proposals of optimal technological scheme for obtaining this drug, the definition of critical operations and parameters of the technological process; definition of strategy of control, development of specifications and methods of control of raw materials, intermediate, non-prepackaged and finished products; the choice of packaging; validation or verification of methods of quality control of a medicinal product; carrying out studies on the stability of the medicinal product during the predicted shelf life. One of the components of the delivery of the API to the site of the pathology is the dosage form of the drug, which significantly influences the preservation of its effectiveness, determining the degree of absorption and concentration in biological fluids. Recently, the attention of developers attracts a dosage form of capsule, which among the dosage forms of industrial production occupies the third place after tablets and solutions in ampoules. They have more advantages (accuracy of dosing, high bioavailability, stability and productivity of obtaining, corrective ability, minimization of production errors, aesthetics, the ability to provide medicinal products with planned properties: the ability to dissolve in certain parts of the gastrointestinal tract, possess prolonged release of the API, sparing technological mode, etc.). The aim of our work was to develop the technology of medicinal product in the form of capsules with an active pharmaceutical ingredient - a dry extract of urocholum, possessing anti-inflammatory, diuretic and choleric properties, as well as to determine the critical parameters in their production. **Material&methods.** Pharmaco-technological research methods were applied. **Results&discussion.** The

technological process of production of capsules with a multi-component dry extract consists of the following stages: sifting of raw materials, preparation of mass for encapsulation (mixing of components, rubbing); encapsulation; packing of capsules into blisters; packing blister packs; packing bundles in boxes. On 3 experimental industrial series (0040319, 0050319, 0060319), it was validated by the technological process of producing urocholum capsules and proved its reproduction in industrial conditions. With the help of the Ishikawa diagram, the most significant aspects that influence the technological process and which need to be controlled at the routine production of capsules of urocholum were identified. The design of a technological regulation for the production of gelatinous capsules with a multi-component dry extract possessing anti-inflammatory, bile and diuretic properties was developed and tested in industrial conditions of the LLC DKP "Pharmaceutical Factory", Zhytomyr. **Conclusion.** 1. Based on the complex of scientific and experimental researches, the optimum technological mode of production of hard gelatinous capsules with a multi-component dry extract with anti-inflammatory, choleric and diuretic activity was established. 2. The critical stages of the process of gelatinous capsules being developed and the parameters of their control and the criteria of acceptability according to the requirements of the SPHU were determined. 3. Technology has been tested in the conditions of industrial production of LLC DKP "Pharmaceutical Factory", Zhytomyr, in accordance with the project of the technological regulations for the production of gelatin capsules with a multi-component dry extract.

Keywords: pharmaceutical development, solid gelatine capsules, multi-component extract.

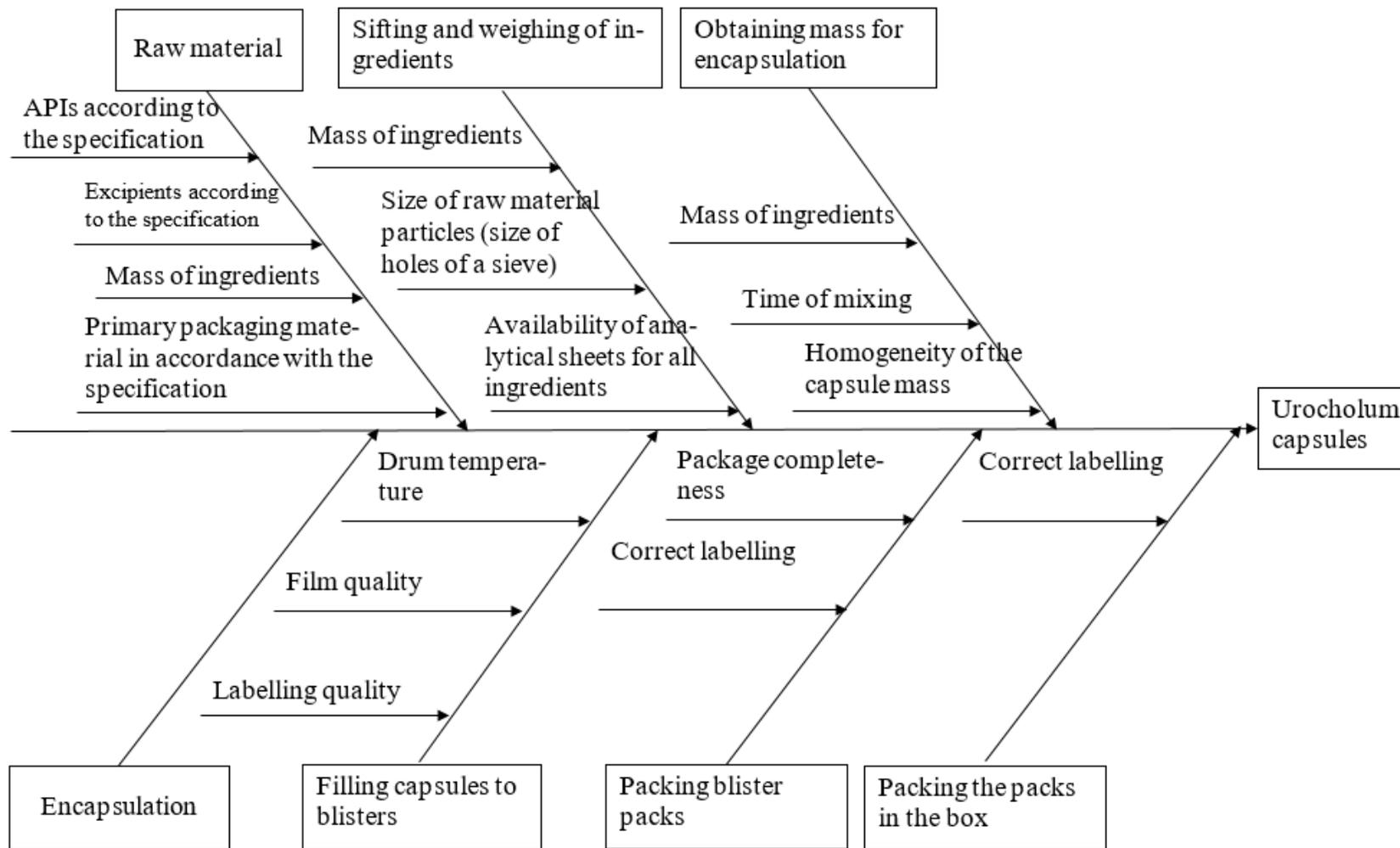


Fig. 2. Ishikawa Diagram with indication of possible risks in the urocholum capsules manufacturing