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Research Article

DEKSKETOPROFEN TRAMETAMOL CAPSULE DRUG FORM COMPOSITION SELECTION AND TECHNOLOGY DEVELOPMENT

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ABSTRACT

Previous research has investigated the technological properties of the dexketoprofen trametamol substance and has been shown to be negative. For this reason, the article covers research on the selection, technology development of a complex of various auxiliary substances for the development of a capsule drug form based on the substance dexketoprofen trametamol. In it, the size of the capsule was determined on scientific basis, based on the scattering density of the substance, and encapsulated masses were prepared using various excipients. As a result of determining the technological properties of these compositions as well as the quality indicators of the capsules obtained, the optimal composition was selected and the capsule technology was developed, in which the dexketoprofen trametamol substance was stored.

KEYWORDS

Deksketoprofen trometamol, substance, capsule, technology, excipients, composition, technological properties.

INTRODUCTION

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Adaptation of highly effective, stable and high-quality medicines produced in foreign countries to the practice of domestic production without affecting their quality and, thus, partial provision of the domestic market of the Republic of Uzbekistan with high-quality, affordable and necessary medicines is one of the most important and urgent tasks facing pharmaceutical technologists. [1,2].

Today, capsules occupy a special place among ready-made medicines and occupy the third place in pharmaceutical production after tablets and ampoules. [8].

Capsule types of medicines are the leaders among ready-made medicines produced on an industrial scale. The main reason for this is a number of advantages of the capsule type of medicine: accurate dosage, rapid action on the body, the fact that the medicinal substance is protected from exposure to light, moisture, air, its stability is ensured, the unpleasant smell and taste of the medicinal substance are disguised, dyes and easily pollinated substances can be used when air moves, as well as high bioefficiency, as well as the ability to prolong the action of the active substance and use it for what has control capabilities [4,7].

Many synthetic drugs have the property of tickling the mucous membrane of the gastrointestinal tract, and when taken for a long time, the wound can become a dressing. Also, some active substations lose their effect from the action of acid in gastric juice. Even in such cases, it is advisable to apply gelatin capsules. Such capsules will be intended for dissolution in the intestine, that is, they will not decompose under the action of acid from gastric juice[8].

Based on the results of research carried out by many scientists in recent years, the absence of a pressing process in the development of the capsule drug form ensures that they decompose faster than tablets and dragees and are absorbed into the body faster, and pharmacotherapeutic activity Ham manifests much faster [3].

The purpose of the study. Taking into account the above, the goal was set to develop a capsule drug form of dexketoprofen trometamol substance.

Experience part

Research methods and tasks. In our scientific research, we used the substance deksketoprofen trametamol (NN 42 Uz-8979-2018). This substance is a white crystalline powder, freely soluble in methanol and water, slightly soluble in chloroform and slightly soluble in ethanol.

Deksketoprofen trametamol is a non-selective nonsteroidal anti-inflammatory drug of the arylpropionic acid group containing the active c-enantiomer of racemic ketoprofen, an analgesic characterized by a rapid onset of action and a relatively short half-life. Trometamol salt ensures rapid dissolution and absorption, which is especially important in severe pain. The duration of pain relief is 4-6 hours, the mechanism of dual action from the

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central and peripheral side is of particular interest to him, as a result of which dexketoprofen prevents the increase of pain, as well as the formation of "Pain memory" does. [2,6,7].

According to the regulatory document (NN 42 Uz-8979-2018) and with the recommendation of pharmacologists, the therapeutic dose of deksketoprofen-trametamol substance was determined to be equal to 36.9 mg.

Size 8 empty capsules were used for scientific justification of capsule size.

For determination of encapsulable masses and technological properties and quality indicators of capsules, such as dispersion, fraction of fractions 0.2-0.5 mm in size, dispersion density, angle of natural deviation, disintegration and residual moisture Uz DF Volume 1 and DF was performed according to the methods defined in Edition XIV (RF). Tests were performed five times and average values were calculated. [5,9,10].

Research results and their discussion. First of all, it was necessary to scientifically justify the size of the capsule. For this, the volume occupied by deksketoprofen trametamol substance based on the dispersion density indicator is calculated.

The obtained results are presented in Table 1.

Table 1.

Results of choosing the size of the capsule that stored deksketoprofen trametamol

Capsule size	5	4	3	2	1	0	00	000
The average volume of the capsule, sm3	0,13	0,21	0,30	0,37	0,5	0,68	0,95	1,37
The volume occupied by the therapeutic dose of deksketoprofen trametamol substance, %	95%	45%	32%	26%	19%	14%	10%	7%
Empty volume, %	5%	55%	68%	74%	81%	86%	90%	93%

The results presented in Table 1 showed that the therapeutic dose of deksketoprofen trametamol substance is small, so the occupied volume is also small. For this reason, it was determined that it is appropriate to use 3-dimensional capsules in the development of the capsule drug form.

When choosing the composition of the capsule containing deksketoprofen trametamol, from auxiliary substances that are widely used in the pharmaceutical industry today: corn starch as a filler, microcrystalline cellulose, NaKMS, maltose, isomalt, dextrose, maltodextrin, silicon dioxide, potato starch,

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magnesium stearate from antifriction agents, stearate, talc, calcium stearate, purified water as a wetting agent, alcohols of various concentrations were used, and capsule masses were prepared by wet granulation method.

When creating a capsule drug form on the basis of deksketoprofen trametamol, methods presented in the literature were used to study its technological properties of compositions in volatility, volatility density, natural deviation angle, fragmentation, fraction content from 0.2 to 0.5 mm in size and residual moisture.

In total, about 15 compositions were prepared, and from them the bulk compositions with good mass dressing and positive technological bearings are presented in Table 2.

Table 2.

Components of recommendations and technological views for a capsule containing the substance deksketoprofen trametamol

Compositions	Technological properties of encapsulated masses					
	scattering, 10^{-3} kg/s	scattering density, kg/m^3	natural deviation angle, degree	size Percentage of fractions 0.2-0.5 mm , %	residual moisture, %	moment of Decay
compound-1	4.43±0,78	0,442±20,62	31,09±1,05	80,32±1,65	2,03±0,22	7,75±1,13
compound-2	5,79±1,09	0,578±16,47	32,04±1,66	92,14±1,38	2,05±0,33	6,55±1,45
compound-3	3,78±0,68	0,622±17,83	35,22±1,70	92,32±1,91	2,02±0,20	6,07±0,58
compound-4	5,93 ±0,92	0,785±20,19	32,5±1,52	97,41±1,02	1,92±0,42	5,10±0.21
compound-5	4,08±1,29	0,698±18,20	30,02±1,28	88,8±0,78	1,8±0,21	5.07±0,54

According to the data presented in the literature, the volatility and scattering density of the encapsulated mass depends on the percentage of fractions from 0.2 to 0.5 mm relative to the total amount, and it is recommended that this figure is not 85% less. 1 in the mixture obtained by composition, the amount of this fraction was less than 85%, which was 80.32±1.65%. At the same time 2, 3, 4 and 5 mixtures according to the composition the fraction amount given above 92,14±1,38%, 92,32±1,91%, 97,41±1,02 and 88.8±0.78%. The proof of the cited opinion was demonstrated in the results of the determination of volatility: with the

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proportion of fractions of 0.2-0.5 mm greater than 85%, the volatility was also higher, for example 4.43±0,78 10-3 kg/s (1-composition), 5,93 ±0,92 10-3 kg/s (4-composition), 4,08±1,29 10-3 kg/s (5-composition).

It was the scattering density of compositions 3, 4 and 5 that also showed high performance and, respectively 0,622±17,83 kg/m3, 0,785±20,19 kg/m3 va 0,698±18,20 kg/m3 was equal.

The angle of natural deviation was positive in all analyzed compositions and this indicator was from 30.02±1.28 degrees to 32.5±1.52 degrees.

According to UzR DF and DF XIV edition (RF), the disintegration of granules should not exceed 15 minutes. All tested compositions met the requirement for this indicator and their disintegration time ranged from 5.10±0.21 minutes to 7.75±1.13 minutes, i.e. did not exceed the specified 15 minutes. At the same time, residual moisture should not exceed 5%. All the analyzed contents met the requirement and the moisture content in them was 2,03±0,22%, 2,05±0,33%, 2,02±0,20%, It was 1.92±0.42% and 1.8±0.21%.

Taking into account the above, the most optimal mass for the capsule was 2 and 4 compositions. But since the scattering indicator is of great importance at the time of filling the capsule, 4 ingredients with a high level of this indicator were selected.

The obtained mass according to this composition was prepared according to the following technology: Taking into account the physico-chemical and technological properties of the substances, it was considered preferable to prepare the encapsulated mass by wet granulation method. For this, dexketoprofen, trometamol and maltose substances were passed through a sieve with a hole diameter of 150 µm.Half the amount of cornstarch was added and mixed until a uniform mass was formed. Purified water was added by spraying until a moderately wet mass was formed. The wet mass was passed through a sieve with a diameter of 3000 µm and dried on a drying rack at a temperature of 40-500C until moderate moisture remained.The dried mass was passed through a sieve with a hole diameter of 1000 µm and mixed with the rest of corn starch and a mixture of calcium stearate.The resulting mass was placed in 3-dimensional capsules of 100 mg.

A drawing of the technological process of obtaining the capsule drug form of the deksketoprofen trametamol substance is shown in Figure 1.

The quality indicators of finished capsules depend on the technological indicators of the mass. At the same time, the technological properties of the mass are affected by the added auxiliary substances and the technology of mass preparation. For this reason, the technological properties of the encapsulable mass were studied in the next research and compared and studied with these properties of the substance. The results obtained were presented in Table 3.

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Table 3.

Comparative study of Deksketoprofen trametamol substance and technical properties of capsular mass

Identified indicator	Unit of measure	Deksketoprofen substance	encapsulated mass
Fractional composition: +1000mkm -1000mkm +500mkm -500mkm +250mkm -250mkm +160 mkm -160 mkm	%	 2,04 19,97 50,42 20,25 7,32	 1.6 20,82 51,49 21,31 4,78
scattering	10^{-3} kg/s	0,511	5,93
scattering density	g/sm^3	0,39	0,785
Natural deviation angle	grade	62	32,5
Residual moisture	%	2,07	1,92

Based on the given results, the technological properties of the encapsulable mass were more positive than those indicators of the deksketoprofen trametamol substance. In it, the smallest amount of the substance (2.04%) corresponded to particles larger than +1000 mkm and to the encapsulated mass (1.6%). The main part of the substance -1000 mkm +500 mkm (19,97%) composed of particles, it has a mass to be encapsulated (20.82), particles -500 mkm +250 mkm (50.42%) of the mass to be encapsulated (51,49) and -250 mkm +160 mkm (20,25%) from (21.31%), substation (7,32%) from (4.78%) to -160 mkm consisted of small particles. This, in turn, shifted the dispersibility of the encapsulated mass in a positive direction. This index 0,511*10-3 kg/s from increased to 5.93*10-3 kg/s. Similarly the scattering density of ham increased (0.39g/sm3 from up to 0,785 g/sm3). Deksketoprofen trametamol substance had a negative result of the angle of natural deviation (62,0 grade) and the encapsulated mass showed a positive result (32.5 degrees). At the same time, it was proved that it has residual moisture (2.07%) to (1.97%).

Scheme 1.

Technological process

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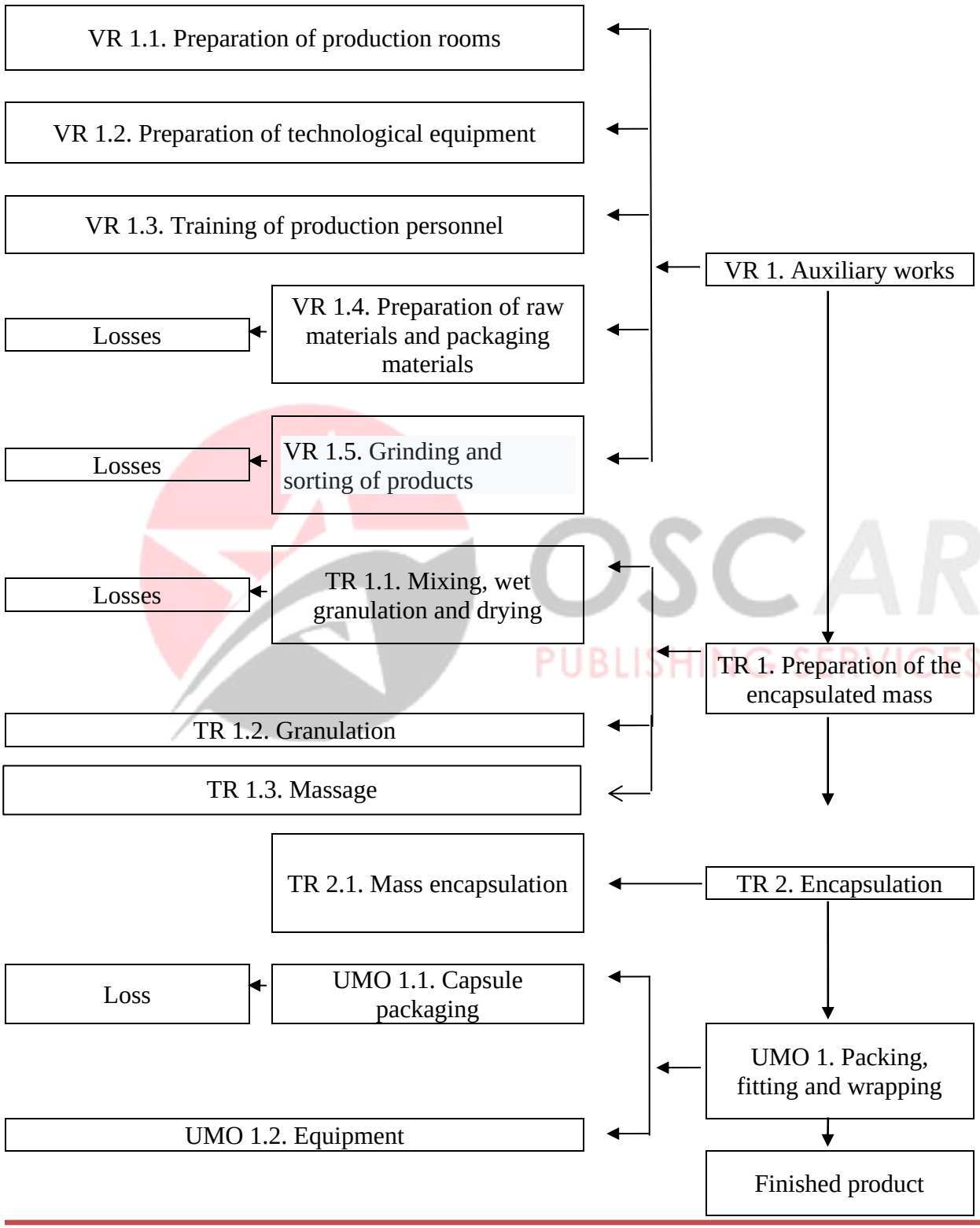

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Scheme 1. The technological process of obtaining a capsule

CONCLUSION

The composition of the capsule drug type was selected and the technology was developed using the method of auxiliary substances and wet granulation, which were used in order to improve the negative technological properties of the capsule in the creation of the drug form on the basis of deksketoprofen trametamol substance. The technological properties of the substance and the encapsulated mass were studied in a comparative way, and the selected content was proven to be purposeful. This ensures that the quality and shelf life of the removable capsules is on demand.

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