WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.421
Volume 8, Issue 1, 260-266 Research Article ISSN 2278 – 4357

THE SUBSTANTION OF THE TABLET MASS "AMBROL" COMPOSITION CHOICE FOR TABLETIZING

Z. Kh. Abdijalilova[1]* and Kh. M. Yunusova[2]

Department of Industrial Medicine Technology, Tashkent Pharmaceuticals Institute, Tashkent, Uzbekistan.

Article Received on
08 Nov. 2018,

Revised on 28 Nov. 2018,
Accepted on 18 Dec. 2018

DOI: 10.20959/wjpps20191-12902

***Corresponding Author**
Z. Kh. Abdijalilova
Department of Industrial Medicine Technology, Tashkent Pharmaceuticals Institute, Tashkent, Uzbekistan.

ABSTRACT

Non-narcotic drugs are divided into two main groups. First group includes drugs of central action for instance, butamiratome, glaucine, ledin, pentoxiverin, okseladin and folkodinom; second group includes drugs that have peripheral effects, such as benpropyrin, butiodine, levodropropizin and other remedies. We aimed to study substantiate choice of optimal composition and technology of Ambrol tablets. More than 25 tablet formulations, differing in nature and amount of excipients, were studied. Compositions No.1 and No.2 contained microcrystalline cellulose in an amount from 5% to 10%. Composition No.3 contained 0.08% of aerosil. Compositions No. 4-6 differed in the ratio of lactose and starch, respectively). The remaining mixtures had the same composition, but differed in preparation technology. We found that from solutions of binders (potato starch, methylcellulose, polyvinyl pyrrolidone, sodium carboxymethyl cellulose), the most suitable for a tablet mass is a 5% starch solution in an amount of 8% by weight. It is shown that the tablets have satisfactory performance: disintegration (10.1 ± 0.32) min., Abrasion (99.22%) and compressive strength (75.9 ± 3.45) N.

KEYWORDS: Ambrol; non-narcotic drugs; ambroxol; tablet mass; flowability; microcrystalline cellulose.

INTRODUCTION

Cough is a protective reaction of the body, manifested at the reflex level. This condition frees the airway from excess sputum and foreign particles. Non-narcotic antitussive drugs combines drugs in which there are no side effects inherent in alkaloids. These medicines are used to treat acute cough, during preparation for surgery with surgery and in the

postoperative period. They are effective antitussives for bronchitis, whooping cough, bronchial asthma and other respiratory diseases.[1]

Non-narcotic drugs are divided into two groups: the first group includes drugs of central action: butamiratome, glaucine, ledin, pentoxiverin, oxeladine and folkodinom. Their action is aimed at partial suppression of the cough center. However, they do not seek to oppress the respiratory center. In terms of their impact, they are not inferior to codeine, but the use of non-narcotic drugs is not addictive and does not lead to side effects. The second group includes drugs that have peripheral effects. This includes benpropyrin, butiodine, levodropropizin and other drugs that directly affect the lesions that cause coughing. As a result, the mucosa is anesthetized. Under the influence of drugs, there is a decrease in cough reflex stimulation. At the same time, these drugs have an anti-inflammatory effect, relaxing the smooth muscles of the bronchi. Some types of drugs have a combined effect. He calms down coughing by blocking peripheral reflex links.[2]

One of the promising areas of pharmacy development is the expansion of the range of highly effective generic drugs. In order to achieve these goals, peripheral cough preparations are also promising objects.

The purpose of this study is to substantiate the choice of the optimal composition and technology of Ambrol tablets.

MATERIAL AND METHODS

We used a number of excipients that are used in the pharmaceutical industry as filling, binding, disintegrating agents.

More than 25 tablet formulations, differing in nature and amount of excipients, were studied. Compositions No.1 and No.2 contained microcrystalline cellulose (MCC) in an amount from 5% to 10%. Composition No.3 contained 0.08% of aerosil. Compositions No. 4-6 differed in the ratio of lactose and starch, respectively). The remaining mixtures had the same composition, but differed in preparation technology. To obtain a granulate under laboratory conditions, the powder mixture was moistened with a solution of a binder, and then rubbed through a sieve with a 3 mm hole diameter. Dried oven at temperature not exceeding 50°C to a residual moisture content of 3.5–4.5%, then rubbed through a sieve with a hole diameter of 1.5 mm. Powdered in a mortar with a plastic scoop. In industrial conditions, the tablet mass

was prepared as follows: excipients and pharmaceutical substances were loaded into a granulator mixer; a solution of a binder was added and granulated for 15 minutes. The granulate was dried at a temperature of 40-50°C for 30 minutes, rubbed through a sieve with a hole diameter of 1.5 mm. The dusting was performed on a two conical mixer at a rotation speed of 22 revolutions per minute. The composition of the active substance was made in four ways: a) the substance was completely introduced into the tablet mass at the stage of granulate production. The mixture was stirred for 30 minutes; b) the substance was introduced at the stage of granulate production, keeping the mixing ratio of 1:1 while mixing. To do this, a weighed amount of the substance was placed in the container and the same amount of auxiliary mixture was added, stirred for 1 minute (composition No. 8) and 3 minutes (composition No. 9). The process was repeated until all ingredients were fully mixed; c) the substance was introduced in the composition of the powder mixture at a constant ratio of 1:1. To do this, a weighed amount of substance was placed in a container and the same amount of granulate was added, stirred for 1-3 minutes. The process was repeated until all ingredients were fully mixed; g) the substance was dissolved in the granulating liquid, which was used to prepare granulates.

Technological characteristics of the tablet mass (flowability, bulk density with compaction and without compaction) were determined by the methods of GF XII. It has been established that tablet blends with microcrystalline cellulose have the best tableting properties.

Direct pressing is a modern technology of tableting drugs, which has several advantages over other tableting methods: reducing the number of technological operations, high labor productivity, eliminating the effect of moisture on unstable medicinal substances, less microbial contamination, saving production space, equipment costs.[3,5]

However, this method can be used only if the tableted material has certain properties: good flowability, compressibility, good adhesive interaction of drugs and excipients.

RESULTS AND DISCUSSION

It is established that the substance of ambroxol has unsatisfactory flowability, has a low bulk density. Therefore, it is impossible to produce tablets by direct compression.[4]

Currently, in the domestic pharmaceutical market there are a number of modified fillers with precisely defined necessary properties of flowability, disintegration and compressibility.

Tablets with a diameter of 9 mm in the production conditions were obtained on a tablet press. To assess the compressibility, a portion of a powder with a mass of 0.3 g was pressed on a manual hydraulic press into a pellet with a diameter of 9 mm at a pressure of 120 MPa. The crushing load was determined on a spring dynamometer. The technological properties of tablet blends and granules were determined in accordance with the XI State Pharmacopoeia: flowability was studied using a fixed funnel, disintegration of tablets was investigated on a laboratory disintegration identifier in a rotating basket; in the device with a basket, and the height and diameter of the tablets were studied using calipers.

At the first stage of work, 6 series of tablets were manufactured using wet granulation according to technology No.1 (series No.1-6). It was established that the difference between the test results for compressive strength of mixtures 1 and 6 is not statistically significant ($p>0.05=0.99$). It was shown that for all other mixtures, the nature and amount of auxiliary substances statistically significantly influenced the disintegration and compressive strength of tablets ($p<0.05$) (Table 1).

Table 1: Influence of the nature and amount of excipients on the quality indicators of Ambrol tablets (laboratory samples).

Number series	Disintegration, min (n=6)	Abrasion, %	Compressive strength, H (n=10)
1	12,0±0,87	97	68,9±2,87
2	10,0±0,56	92	76,1±3,22
3	10,9±0,65	95	75,1±2,97
4	9,8±0,77	91	68,5±2,99
5	11,9±0,49	94	68,1±4,11
6	10,4±0,35	98	63,7±3,32

The next stage of the experiment was the study of the technological characteristics of the obtained tablet masses in order to determine the compositions most suitable for subsequent tableting by the wet granulation method. Evaluation of technological characteristics was carried out according to generally accepted methods. The moisture content of the model mixtures was also monitored, the measurement was carried out on a Kett moisture meter (Japan). Experiments were carried out in at least 5nb repetitions, and statistical processing of the results was performed using the standard Microsoft Excel package. The results of the experiments are presented in table 2.

Table 2: Technological characteristics of tablet mass of model compositions with Ambroxol.

Composition, №	Flowability, g/s	Bulk density, kg/m^3		Humidity, %
		Without seal	With seal	
1	2,5+0,57	0,42±0,01	0,52±0,03	3,1±0,02
2	4,4+1,15	0,40±0,04	0,61±0,04	2,9±0,05
3	6,1+1,15	0,39±0,05	0,60±0,05	2,5±0,09
4	0,6±0,57	0,51±0,04	0,49±0,03	4,3±0,06
5	13,53±0,05	0,45±0,03	0,57±0,01	3,1 ±0,01
6	13,5±0,01	0,52±0,05	0,63±0,04	2,9 ± 0,03

Flowability is one of the main factors imposed on the quality of tablet weights and determining the performance of tablet machines. As follows from the data presented in Table 2, composition No.4, containing the highest percentage of aerosil (1.5%), is the worst flowability. It is also worth noting that with increasing content of aerosil, there is a significant decrease in flowability, as well as an increase in the clumping of the mixture (an example of compositions No.1 - No.4).[2,7]

Most manufacturers pay great attention to this indicator and contribute to the acceptable limits of the moisture content in the regulatory documentation for pharmaceuticals. According to literature data, compositions with a fairly low water content of less than 4.0%, preferably less than 3.0%, are reliably stable, if determined by the method of "weight loss during drying", or less than 5.5% (preferably less than 4.5%), if defined in kett.[6]

In the examples of compositions No. 2-No. 5, the following dependence was revealed: with increasing content of aerosil, the amount of moisture in the mixture decreases. It is believed that the protective effect of aerosil is due to the mechanical obstacle to the interaction of the reacting particles and the absorption of moisture by the aerosil resulting from the interaction of the components of the mixture; however, an increase in the proportion of aerosil in the mixture by a factor of 2 or more does not give a proportional decrease in the moisture content. Tablet mixes with MCC have optimal properties in this respect.

CONCLUSION

We found that from solutions of binders (potato starch, methylcellulose, polyvinyl pyrrolidone, sodium carboxymethyl cellulose), the most suitable for a tablet mass is a 5%

starch solution in an amount of 8% by weight. In order to test the technology at the plant equipment, the composition No. 5 of the recommended tablets was manufactured using the No. 1 technology.

It is shown that the tablets have satisfactory performance: disintegration (10.1 ± 0.32) min., Abrasion (99.22%) and compressive strength (75.9±3.45) H.

Thus, it was shown that the No.5 composition developed using wet granulation and prepared according to the No.1 method ensures the production of tablets that meet the requirements of the XI State Pharmacopoeia.

Consent

It is not applicable.

Conflict of Interest

Authors declare that there is no determined any conflict of interest.

REFERENCES

1. Ivaschenko, A. A., Kravchenko D. V., The concept of innovative development of the domestic pharmaceutical industry / A. A. Ivaschenko, D.V. Kravchenko // Remedium, 2008; 5: 14-18.
2. Alekseev, K.V. Technological aspects of the production of modern solid dosage forms. / K.V. Alekseev // Manufacture of drugs by GMP. -Moscow: "Medical Business", 2005; 165-176.
3. Dmitrieva E.V. The influence of Aerosil on the technological characteristics of the tablets obtained by direct compression / EV. Dmitrieva, S.N. Egorova // Actual issues of improving the quality of postgraduate training of pharmaceutical personnel: materials rep. scientific-practical conf. Kazan, 2011; 57-59.
4. Studies of various samples of microcrystalline cellulose in the preparation of tablets by direct compression / L. I. Kucherenko, A. V. Trigubchak, M. B. Demchuk [and others] // scientific and technical progress and optimization of technological processes for the creation of drugs: mater. 3rd scientific and practical. Conf., October 1-2, 2009, Ternopil. - M.: Ukrmedkniga, 2009; 59.
5. Sizyakov S.A. Modern auxiliary substances in the technology of direct compression / S.A. Sizyakov, A.S. Suldin, C.K. Alekseeva // Pharmacy, 2008; 4: 52-56.

6. Dmitrieva E.V., Egorova S.N. Justification of the choice of the composition of the tablet mass of ramipril for tabletting // Modern medicine: topical issues: Coll. st. on mater. XXXII Intern. Scientific-practical conf. No. 6 (32). - Novosibirsk: SibAK, 2014.
7. Rjeussky, S.E. Study of the technological properties of calcium glycinate and calcium prolinate / S.E. Rjeussky, V.V. Kugach // Proceedings of the IX International Scientific and Practical Conference. ñ Vitebsk: VSMU, 2009; 493.