Acta Scientific Gastrointestinal Disorders (ISSN: 2582-1091)

Volume 8 Issue 4 April 2025

Research Article

The Main Criteria for Choosing the Composition and Technology of a New Combined Anti-Inflammatory Drug in the Form of Tablets

Zufarova ZH* and Yunusova HM

Tashkent Pharmaceutical Institute, Department of Industrial Technology of Medicines Tashkent, Uzbekistan

***Corresponding Author:** Zufarova ZH, Tashkent Pharmaceutical Institute, Department of Industrial Technology of Medicines Tashkent, Uzbekistan.

Received: March 03, 2025

Published: March 27, 2025

Abstract

Nonsteroidal anti-inflammatory drugs (NSAIDs) are one of the most widely used groups of drugs in clinical practice, which are used for the symptomatic treatment of inflammatory processes accompanying many diseases. The most common among them is acetylsalicylic acid (ASA), which is part of the group of acidic NSAIDs.

Keywords: Composition; Combined; Anti-Inflammatory; Drug; Tablets

Introduction

The problem of combating inflammatory diseases in medical practice is becoming increasingly important. In this regard, the creation of highly effective medicines for their prevention and treatment is an important task. Due to the multifaceted analgesic and anti-inflammatory therapeutic activity, the use of acetylsalicylic acid and salicylates has become widespread in medical practice.

Over the past 30 years, the number of NSAIDs has increased significantly and currently this group has a large number of drugs that differ in chemical structure, characteristics of action and application. At the same time, the widespread use of NSAIDs is largely limited by a number of their side effects, primarily ulcerative lesions of the gastrointestinal mucosa with the subsequent development of erosive gastritis and gastric ulcer. In order to improve the tolerability and minimize the ulcerogenic side effects of NSAIDs, the following measures are recommended: changing the tactics of using NSAIDs, involving dose reduction; switching to parenteral, rectal or local administration; taking intestinal-soluble dosage forms; using combined medications.

The purpose of this work was to study the physico-chemical and technological characteristics of active substances and excipients in order to select the composition and develop the technology of a combined anti-inflammatory drug in the form of tablets.

The objects of the study were the medicinal sub-stations GLAS, ascorbic acid and rutin, which are offered in the form of a combined tablet form for the treatment of anti-inflammatory diseases.

GLAS - monoammonium salt of 3-O-(2'-O-β-D-glucopyranosyl)-α-D-glucuronopyranoside - 3β- hydroxy - 11-oxo-12-en-18β-H, 20-olean-30-ovoy acid with ortho - o - acetyl benzenecarboxylic acid.

The substance GLAS is an amorphous powder from light cream to cream color, with a strong sweet taste without odor. It is soluble in water to form a viscous solution, easily soluble in alkali solutions, practically insoluble in 95% alcohol and in other organic solvents such as ether, chloroform, acetone. The melting point is 172 ± 2 ° C, pH = 4.2-4.3.

Preclinical studies have shown that it exhibits anti-inflammatory activity and is superior in its anti-inflammatory effect to such a well-known NSAID as aspirin. At the Institute of Bioorganic Chemistry named after academician A.S. Sadykov Academy of Sciences of the Republic of Uzbekistan synthesized a molecular water-soluble complex of acetylsalicylic acid with a monoammonium salt of glycyrrhizic acid, conventionally named GLAS. The main characteristics of GLAS are low toxicity, absence of ulcerogenic action and breadth of therapeutic action. In terms of anti-inflammatory activity, it is 8-10 times higher than acetylsalicylic acid, although its dose is less than ASA.

Lactose M-80, lactose M-200, microcrystalline cellulose (MCC), potato starch and calcium stearate were used as auxiliary substances.

The study of the shape and particle size of active and auxiliary substances was carried out using an MBI-15 microscope at a magnification of 400 times, which makes it possible to characterize the shape and surface of the particles, as well as the average linear size of the dominant fractions.

The flowability of powders, which is characterized by the rate of their discharge from the funnel, expressed in grams per 1 second, was determined in accordance with the methodology of the State Pharmacopoeia XI.

To determine the compressibility of substances, a weight of 0.3 g was pressed into a tablet with a diameter of 9 mm on a hydraulic press at a pressure of 120 MPa and then the strength of the resulting tablet was determined on an Erweka type device (Germany).

In order to select the optimal method for obtaining tablets, we have studied the physicochemical and technological properties of substances and excipients.

The results of the study of substances in the form of particles of the main fraction, fractional composition, flowability and compressibility are presented in Table 1.

The study of the technological properties of the mixture Glas + ascorbic acid + rutin for the subsequent selection of the optimal composition and technology of tablets "Asrutas".

At this stage of the study, we studied the following technological parameters of the mixture: fractional composition, bulk density, flowability, porosity, angle of natural slope, compaction coefficient, compressibility coefficient, compressibility and residual moisture.

The determination of the above parameters was carried out according to the methods of GF XI and the corresponding NTD. The results of the study of technological properties are shown in table 1.

Studied indicators	Unit of measurement	Indicator values
Appearance		Yellow in color, with a peculiar smell
Fractional composition :	microns, %	
+ 2000		3,12
-2000+1000		16,87
-1000+500		29,55
- 500 + 250		33,44
-250		17,02
Flowability	10^{-3} kg/s	0,812
Angle of natural slope	degree	55
Bulk density	kg/m3	298
Compressibility	H	41
Compressibility factor		1,25
Compaction coefficient		4,2
Residual humidity	%	8,10

Table 1: The results of studying the technological properties of the mixture – Glas + ascorbic acid + rutin In mixtures, some technological properties of the substance - flowability, bulk density have changed slightly.

Also, according to the table, it can be noted that the flowability has decreased, the bulk mass index has increased than separately substances. The research results showed the following values: technological indicators such as bulk density within (298 kg/m3), flowability (0.812.10-3 kg/s), angle of natural slope (55 degrees), compressibility coefficient (1.08), compactness (4.2), etc. had slightly positive values for the mixture than the substance separately. However, these indicators do not fully ensure the quality of the finished product and predict that it is impossible to obtain high-quality tablets without the addition of excipients and granulation technology. The results of the study showed the choice of excipients

for obtaining a high-quality finished product - Asrutas tablets.

The obtained data show that the substance is polydisperse crystalline powders with anisodiametric particles. It was found that all the substances studied are low-flow materials and have different compressibility, i.e. they practically cannot be used in direct pressing technology.

It should be noted that today direct pressing is the most modern technology for tableting medicines and the possibility of its use is provided by the technological properties of medicinal substances, which for most powdery substances require optimization.

There are several techniques in the technology to expand the possibilities of using direct pressing. One of them, the most widespread, is a method that consists in improving the technological properties of a tableted powdery substance or a mixture of substances by selecting and adding excipients. Taking into account the fact that the developed dosage form contains small amounts of active substances, this makes it possible to create tablets by direct pressing. Therefore, the next stage of our research was the study of excipients with the necessary structural, mechanical and technological characteristics. The data obtained are presented in table 2.

The results of the conducted studies (Table.2) show that the shape and size of the particles determine their technological characteristics, each of which must be taken into account when developing the composition and technology of the drug. Thus, the MCC has an elongated particle shape (fiber) with a basic fraction size of 100-250 microns, has medium flowability and good compressibility (181 N). Therefore, MCC was chosen by us as an auxiliary substance that significantly improves the physico-chemical and technological properties of the active substances, namely, resistance to crushing and abrasion of tablets. The technological characteristics of lactose M-80 and lactose M-200 made it possible to include them in the composition of the developed form as an addition to the MCC.

Potato starch was also considered as a filler as an auxiliary substance that improves the wettability and water permeability of the dosage form. In addition, stearic acid and calcium stearate were used as auxiliary antifriction substances. As a result of the conducted studies, calcium stearate (in the amount of 1%) was selected. It should be noted that calcium stearate helps to remove the electric charge from the powder particles, which also improves their flowability.

Name of the substance	Particle shape	Particle size, microns	Flowability, g/s	Compressibility, N
Lactose M-80	Prismatic	10-200	8,3 ± 0,20	41,4 ± 4,8
Lactose M-200	Prismatic	10-100	9,0 ± 0,12	51,2 ± 1,7
MCC	Fibers and conglomerates of them	100-250	5,2 ± 0,07	181,0 ± 1,0
Potato starch	Polyhedra with smoothed corners	10-50	2,5 ± 0,12	121,0 ± 1,0

Table 2: Physico-chemical and technological characteristics of auxiliary substances.

Thus, the conducted research on the study of physico-chemical and technological properties of active substances and excipients make it possible to further work on the development of a tablet form of a combined drug for the treatment of inflammatory diseases.

The technology of obtaining tablets included the following stages: preparation of raw materials, obtaining a mass for tableting by mixing ingredients, moistening them, wet granulation, drying the tablet mass, dry granulation, powdering and tableting on a tablet press. The tablet mass was moistened with 2-5% aqueous starch solution; the dry tablet mass was powdered with a mixture of excipients.

The obtained tablet samples were examined in accordance with the requirements of GF XI. At the same time, the technological characteristics of the tablets (abrasion resistance and diametric crushing) were determined, as well as the characteristics necessary for the development of the draft FSP (pharmacopoeia article of the enterprise) for new drugs (appearance, average weight of tablets, uniformity of dosing, quantitative content of acetylsalicylic acid and dissolution, foreign impurities).

The fracture strength of the tablets was determined on the device RTU -1. In this device, the position of the tablet is fixed and the pressure at the moment of destruction of the tablet is automatically marked on the scale. The average strength for diametric crushing is calculated from the determination of the strength of 10 tablets. The abrasion strength of the tablets was determined by GF XI, issue 2, p.157.

The disintegration of tablets was determined on the device described in Appendix 3 to the article "Tablets" of GF XI, issue 2, dissolution – on the device "Rotating basket" (Appendix 4).

The compositions given in Table 3 ensured the production of high-quality tablets that did not differ in the studied qualitative indicators.

Ingredients	Asrutas tablets						
	A-1	A-2	A-3	A-4	A-5	A-6	A-7
GLAS	0,2	0,2	0,2	0,2	0,2	0,2	0,2
Routine	0,2	0,2	0,2	0,2	0,2	0,2	0,2
Ascorbic acid	0,1	0,1	0,1	0,1	0,1	0,1	0,1
Sucrose		0,0445				0,0225	
Lactose monohydrate	0,020				0,0445		
Glucose							
Potato starch	0,025						
MCC			0,0445		0,0445	0,0220	
PVP							
Calcium Carbonate			0,0445				
Stearic acid		0,0055			0,0055	0,0055	
Calcium Stearate	0,0055		0,0055	0,0055			
Average weight	0,55	0,55	0,55	0,55	0,55	0,55	
Binder	2-5% starch paste						

Table 3: Optimal compositions (in%) of combined tablets containing glas, rutin, ascorbic acid.

The greater the compressibility of the powders, the lower the specific pressing pressure must be in order to achieve satisfactory strength. Since binders are added to increase the adhesion of the particles, the greater the compressibility of the powder, the less binders are required. Table 4 shows the qualitative indicators of model tablets.

Studied indicators	Asrutas Tablets						
	K-1	K-2	K-3	K-4	K-5	K-6	K-7
Appearance	Cream-colored, odorless, cylindrical tablets						
Average mass and deviations from the average mass, g	0,302 ± 4,49	0,301 ± 4,69	0,302 ± 4,55	0,301 ± 4,78	0,302 ± 4,57	0,302 ± 4,63	0,301 ± 4,90
Disintegration, min	10	15	17	19	20	21	20
Abrasion resistance, %	98,88	98,56	99,35	98,99	99,18	99,25	98,58
Fracture strength, %	62	60	59	61	60	59	61
The ratio of the height of the tablets to the diameter, %	37,78	37,98	38,00	37,99	38,90	37,56	38,15

Table 4: Technological properties of combined tablets.

A decrease in the starch content led to an elongation of the disintegration of the tablets, and an increase led to a decrease in the strength of the tablets for diametric crushing and deterioration of the abrasion strength.

Results

the conducted experiments have shown the expediency of introducing potato starch into the tablets as a loosening and binding agent, and antifriction – calcium stearate. Based on the data obtained, the following technology for obtaining tablets is recommended: the substance is sieved through a sieve with a hole diameter of 150 microns, thoroughly mixed and moistened with 5% starch paste until an optimal moist mass is obtained, which is dried at 40-50 ° C, granulated and powdered with a mixture of potato starch and calcium stearate. The finished granules are pressed by 0.500 g on an impact-type tablet machine. The composition does not stick to the mold, the average mass of tablets during the pressing process is stable.

Conclusions

- The shapes and sizes of particles of active and auxiliary substances that will be used to create a combined tablet form for the treatment of inflammatory diseases have been studied.

- Technological characteristics of the powdered system, such as flowability and compressibility, have been experimentally determined in order to further develop tableting technology.
- The main criteria of the approach to the development of the composition and technology of tablets, the choice of which is determined by the characteristics of active substances and excipients, are considered and briefly formulated.
- The optimal composition and quantity of excipients, the method of tableting, ensuring the production of high-quality tablets, have been selected.

Bibliography

1. Astakhova AV. "Nonsteroidal anti-inflammatory drugs (NSAIDs): spectrum of adverse reactions / A.V. Astakhova". *Drug Safety* 4 (2007): 27-30.

2. Alyavi BA. "Topical issues of the safety of the use of non-steroidal anti-inflammatory drugs in clinical practice: scientific publication". *Neurology* (2012): 63-66.

3. Mavlyanov IR. "Non-steroidal anti-inflammatory drugs: mechanism of action, search for new effective and safe drugs". *Medical Science of Uzbekistan* 1 (2002): 94-97.

4. Kaminny AI. "Therapy with antiplatelet and nonsteroidal anti-inflammatory drugs. The ratio of risk and benefit". *The Attending Physician* 7 (2009): 49-54.

5. Walter MB., *et al*. "Step-by-step control in the production of tablets". *Medicine* (1982): 208.

6. State Pharmacopoeia XI, issue 2". *Medicine* (1990): 398.