SUBSTANTIATION OF AUXILIARY SUBSTANCES OF IN THE COMPOSITION OF TABLETS WITH DRY EXTRACT OF ZINGIBER OFFICINALE

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Topicality. Due to its rich chemical composition and pharmacological activity, Zingiber officinale is a promising raw material for creating various drugs, including ones for the treatment of type 2 diabetes.

Aim. To obtain tablets with dry ginger extract by direct pressing using polyfactorial dispersion analysis (taking into account the quality factors).

Materials and methods. The objects of the study were dry ginger extract, filler – Galen IQ 721 and excipients of three technological groups: dry binders, moisture regulators and lubricants. The effect of auxiliary substances on such indicators as bulk density, tapped density and the Carr index of the tablet mass, as well as disintegration, mechanical strength and friability of the obtained tablets have been investigated.

Results and discussion. Using the mathematical planning of the experiment by the $3 \times 3$ Latin square method, the influence of qualitative factors on the pharmacological indicators of tablets with a dry extract of ginger has been studied.

Conclusions. According to the results of analysis of variance, the optimal excipients in the composition of tablets with ginger extract were chosen: from the group of binders – Kollidone k30, as a moisture regulator – Neusilin UFL 2 and lubricant – calcium stearate.

Key words: type II diabetes; dry ginger extract; Excipients; tablets; direct pressing; pharmaceutotechnological indicators of powder masses and tablets; mathematical planning of the experiment; three-factor analysis of variance.
INTRODUCTION

The use of ginger in folk medicine has a centuries-long history, since no other spice has such an amazing combination of taste and healing properties [1].

Ginger rhizomes contain a complex of BAI, the main of which are: essential oil, content of which is 1-4.3 %, linoleic, oleinic, nicotinic acids, sesquiterpene compounds (gingerol, gigerolene, gigeronine A, B, zingerol, zingiberene, p-bisabolone, magnol, curcumene), flavonoids, asparagine, calcium, magnesium, manganese, iron, phosphorus, potassium, sodium, vitamins C, A, B, B., In addition, ginger contains all the essential amino acids (tryptophan, threonine, methionine, phenylalanine, valine, etc.) [2].

Due to the rich chemical composition Zingiber officinale manifests a multifaceted spectrum of pharmacological properties: antipyretic, analgesic, anti-inflammatory, antihypertensive, antimicrobial, sedative, etc. [3, 4].

In the pharmaceutical market of Ukraine there are drugs with different pharmacological activity that contain ginger [5]:
- for the prevention and treatment of metotrophic reactions and autonomic disorders (Antifront, Hungary);
- antitussives (Bronchomed, Doctor Cough, India);
- expectorants (Dr. Mom, Travisil, Cofol, India);
- analgesic and anti-inflammatory (Osteoarthritis, Active, Australia);
- to activate the digestive processes in dyspeptic disorders (Actis, Australia);
- to maintain and improve the functional activity of the body (Vivabon, Pakistan);
- for the correction of overweight (Lipomin, Liponorm, Australia).

In addition, the analysis of literature sources and pharmacological studies have confirmed the presence of hypoglycemic and antioxidant properties in the dry extract of ginger [6, 7]. But medicines based on it for the treatment of diabetes are absent in the pharmaceutical market of Ukraine [11]. For the tablet mass, the following was evaluated: p.2.9.34 – bulk density (у), p.2.9.8 – resistance to crushing (у), p.2.9.7 – friability (у).

The results obtained were subjected to analysis of variance [12-14]. The influence of a factor on each indicator was determined using the Fisher criterion. Based on the data obtained for significant factors, the effect of their levels was evaluated using Duncan’s multiple criterion and, for clarity of such a comparison, histograms were constructed.

### QUALITATIVE FACTORS AND THEIR LEVELS

| Factors          | Factor levels                             |
|------------------|-------------------------------------------|
| A – binding agents | a. – MCC 112.5 %, a. – Polypeplasdone 630.5 %, a. – Kollidone K30 5 % |
| B – moisture regulators | b. – Syloid 244 FP 1 %, b. – Neusilin UFL 2 1 %, b. – Aerosil 1 % |
| C – Lubricants   | c. – Calcium stearate 1 %, c. – Compritol 808 1 %, c. – sodium stearyl fumarate 1 % |

The results of pharmacotechnological studies have shown unsatisfactory flowability and compressibility of the extract, which shows the need to add lubricants and binding excipients in the development of the solid dosage form [8].

Therefore, for our research, 9 excipients have been selected, which were divided into 3 groups: dry binders (factor A), moisture regulators (factor B) and lubricants (factor C). Each factor was considered at three levels, presented in Tab. 1. The levels of factors were chosen based on the literature data [9].

Galen IQ 721, selected on the basis of previous studies [10], was used as a filler. It was added to an average tablet weight of 0.5.

For the experiment, a tablet mass was prepared by mixing 0.3 g of dry ginger extract per tablet with filler and an auxiliary substance from each group (factors A, B, C).

To study the three factors with the same number of levels used 3 × 3 Latin square.

Pharmacotechnological studies were performed according to the methods of the State Pharmacopoeia of Ukraine [11]. For the tablet mass, the following was evaluated: p.2.9.34 – bulk density (у), p.2.9.8 – resistance to crushing (у), p.2.9.7 – friability (у).

In Tab. 2, the matrix of experiment and the results of studies of pharmacotechnological indicators are given. Two series of trials of 9 experiments each were carried out.

The results obtained were subjected to analysis of variance [12-14]. The influence of a factor on each indicator was determined using the Fisher criterion. Based on the data obtained for significant factors, the effect of their levels was evaluated using Duncan’s multiple criterion and, for clarity of such a comparison, histograms were constructed.
RESULTS AND DISCUSSION

The results of analysis of variance showed that factor A (binders) has the most significant effect on such indicators as the bulk density, the Carr index and hardness. Studying the levels of binders allowed ranking them by the degree of influence on the responses. The greatest bulk density \( a_3 > a_2 > a_1 \) and the smallest index of Carr \( a_3 < a_2 < a_1 \) provides Kollidone k30 5%, the highest strength was observed in the presence of Polyplasdone s630 5% \( a_2 > a_3 > a_1 \) (Fig. 1).

Thus, Kollidone k30 has the greatest impact on the bulk density of the powder to the maximum and the Carr index to a minimum compared with other binders: Kollidone k30 > Polyplasdone s630 > MCC 112.

When studying factor B (moisture regulators), it has been revealed that they have the most significant effect on such indicators as tap-density, Carr index, strength and friability of tablets. According to the degree of influence on the responses, they are arranged as follows: tapped density \( b_2 = b_1 < b_3 \), Carr index \( b_2 = b_1 < b_3 \), strength \( b_2 > b_1 > b_3 \), and friability \( b_2 > b_1 < b_3 \) (Fig. 2).

Thus, the use of Neusilin UFL 2 as a moisture regulator has the greatest impact on the tapped density of the powder to the maximum, the Carr index to a minimum, strength to the maximum and friability to a minimum as compared to other moisture regulators:

Neusilin UFL 2 > Aerosil > Syloid 244 FP.

Studies have shown that factor C (lubricants) has a significant impact on all pharmacological parameters, except for the bulk density. According to the degree of

| No | A   | B   | C   | \( y_1' \) | \( y_2' \) | \( y_3' \) | \( y_4' \) | \( y_5' \) | \( y_6' \) |
|----|-----|-----|-----|--------|--------|--------|--------|--------|--------|
| 1  | a_1 | b_1 | c_1 | 0.391  | 0.401  | 0.818  | 0.820  | 52.2   | 51.09  |
| 2  | a_1 | b_2 | c_2 | 0.473  | 0.502  | 0.60   | 0.630  | 21.16  | 20.32  |
| 3  | a_2 | b_1 | c_1 | 0.562  | 0.532  | 0.750  | 0.727  | 25.06  | 26.82  |
| 4  | a_2 | b_2 | c_2 | 0.60   | 0.591  | 0.750  | 0.749  | 20.2   | 21.09  |
| 5  | a_2 | b_1 | c_2 | 0.562  | 0.514  | 0.750  | 0.704  | 25.06  | 26.99  |
| 6  | a_2 | b_2 | c_1 | 0.562  | 0.514  | 0.750  | 0.704  | 25.06  | 26.99  |
| 7  | a_2 | b_3 | c_1 | 0.562  | 0.540  | 0.692  | 0.701  | 23.55  | 22.97  |
| 8  | a_2 | b_3 | c_1 | 0.60   | 0.61   | 0.750  | 0.752  | 20.188 | 20.32  |
| 9  | a_3 | b_3 | c_1 | 0.562  | 0.570  | 0.692  | 0.701  | 18.79  | 18.69  |

Note. \( y_1' \) – bulk density (g/ml); \( y_2' \) – tapped density (g/ml); \( y_3' \) – Carr index; \( y_4' \) – disintegration (sec); \( y_5' \) – tablet strength (N); \( y_6' \) – friability of tablets (%).
influence on the responses, they are arranged as follows:
tapped density – \( c_1 = c_2 = c_3 \), Carr index – \( c_2 < c_3 < c_1 \), disintegration – \( c_1 < c_2 = c_3 \), strength – \( c_2 > c_3 > c_1 \) and friability – \( c_1 = c_2 < c_3 \) (Fig. 3).

Thus, the use of calcium stearate as a lubricant has the greatest effect on powder’s tapped density, disintegration and friability to a minimum compared with other lubricants: calcium stearate < Compritol < sodium stearyl fumarate.

**CONCLUSIONS**

1. Using the method of mathematical planning – a three-factor experiment based on 3 × 3 Latin square the influence of 9 qualitative factors on the pharmacotechnological properties of tablets has been studied.
2. According to the results of analysis of variance, the optimal excipients in the composition of tablets with ginger extract were chosen: from the group of binders, Kollidone k30, as a moisture regulator; Neusilin UFL 2 and lubricant, calcium stearate.
3. The obtained data will be used for further research in order to determine the optimal amount of these excipients in the development of technology of tablets with a dry extract of ginger by direct compression.

**Conflict of interests:** authors have no conflict of interest to declare.
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