

OPTIMISATION AND TECHNOLOGIES OF «VISPULIN» TABLETS

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Summary: the article shows the investigation results of two quantitative factors of pharmaceutical and technological indicators of «Vispulin» tablets and characteristics of mass for tablets. The appropriate set of excipients in tablets and optimal formula were suggested due to the experiment.

Key words: tablets, aspen bark extract, bismuth subcitrate, optimal formula, pressing.

Introduction. The most important aims during the treatment of peptic ulcer disease is to eliminate the symptoms of acute peptic ulcer, reaching healing of peptic ulcer and prevent recurrence of the disease as soon as possible [1, 2].

The possibility of pharmacological enhancement and reduction of side effects were the results for the development of combination remedies period. Thus, the combined remedy therapy, confirmed with incontroverted evidence, has become the standard treatment of cancer, human immunodeficiency virus, hypertension, peptic ulcer [3].

In recent years, combination treatment regimens at the combination therapy of peptic ulcer disease are used quite widely. They include medicine like synthetic and plant origin, which can significantly increase the effectiveness of treatment by the influence on different pathogenetic areas of this disease.

The possibility to get more intense pharmacological effect as a result of combination of medicinal substance compared to each component has become the aim to create tablets containing aspen bark extract and bismuth subcitrate with codename «Vispulin». While combining these substances, it is predicted the potentiation of gastro-protective features and speeding the process of reparative regeneration in erosive ulcerative lesions of the gastrointestinal tract, better healing of gastric mucosal damage and reduce the frequency and degree of expression of the destructive action of ulcerogenic factors.

Methods of the research. Vispulin tablets obtained by direct compression have been chosen as the object of research. Studying the optimal formula of tablets containing extract of the bark of aspen and bismuth subcitrate we studied the effect Ludipress and magnesium carbonate basic, and also their percentage rate in tablets in a narrow range as the most important quantitative factors. Level of factors and their intervals have been selected on previous studies [4, 5, 6] and are mentioned in Table. 1.

Results and discussion. At the final stage of our research we have studied the two most important quantitative factors such as the substance of Ludipress and magnesium carbonate basic. To find the optimal formula of Vispulin tablets, it has been used rotation symmetric composite uniform of the second order design[7]. Preparing Vispulin tablet formula due to the experiment plan when the factors have been studied at low levels or low «star» points, the average weight of tablets is provided to MCC 102 in appropriate quantity. As lubricate substance it has been used magnesium stearate in an amount of 1% of the average weight of tablets.

The tablets obtained were investigated by the following factors: y_1 – pressing process quality of tablets, point; y_2 – mass uniformity of tablets, $\pm\%$; y_3 – average weight of tablets, g; y_4 – resistance to crushing tablets, H; y_5 – abrasion of tablets, $\%$; y_6 – disintegration, min.

According to the results of the experiment we have received the regression equation of which we can analyze the influence of the excipients amount

Table 1. Factors and levels studied during the process of formula optimization and technologies of Vispulin tablets

Factor	Factor level				
	Low «star point» «- α »	Low «-»	Main «0»	High «+»	High «star point» «+ α »
x_1 – substance Ludipress, g	0,068	0,077	0,098	0,119	0,128
x_2 – substance of magnesium carbonate basic, g	0,011	0,014	0,021	0,028	0,031

to the pharmaco-technical features of tablets obtained and get the optimal solution concerning the composition and technology of Vispulin tablets. Relation between quantitative factors and researched opinions were described by the second order regression equations that show the mutual influence of the studied factors, while the features of factors are determined by measures and signs of the regression coefficients.

Experimentally it was found that examined excipients substance at the formula of Vispulin tablets within the studied periods do not affect to the free bulk density, density after compaction and fluidity of powder mixture and general appearance of tablets obtained, so the regression equation for this data was not analyzed.

The dependence of the pressing process of Vispulin tablets and quantitative factors are described by the following second order regression equations:

$$y_1 = 4,502 + 0,228x_1 - 0,478x_2 - 0,25x_1x_2 - 0,314x_1^2 - 0,314x_2^2$$

The analysis of this equation shows that the most significant impact on the process of Vispulin tablets pressing affects the content of basic magnesium carbonate basic at their composition. Especially, the coefficient of linear factor x_2 is at 2,09 times higher than the factor x_1 . Thus, while increasing Ludipress and decreasing substance of magnesium carbonate basic at the tablet formula, the pressing process runs without any problems.

Change of the deviation from the average weight of obtained Vispulin tablets and substance at examined factors are described by the following mathematical model:

$$y_2 = 1,035 - 0,066x_1 + 0,278x_2 - 0,067x_1x_2 + 0,164x_1^2 + 0,102x_2^2$$

The quantitative number of magnesium carbonate basic as the substance of tablets impacts to the results of this qualitative indicator. Sign «+» before the regression coefficient shows while changing the meaning of factor levels at the range of «-б» to «+ б» tablet weight uniformity becomes worse. Low impact on the results of uniformity has Ludipress substance, also it is observed negligible interaction among the studied factors.

The relation among the studied quantitative factors and average weight of Vispulin tablets are described by the second order regression equation:

$$y_3 = 0,82 + 0,013x_1 - 0,003x_2 + 0,004x_1^2 + 0,005x_2^2$$

The substance of Ludipress at Vispulin tablets mostly affects to the results of y_3 . In particular, while the quantity of Ludipress within the studied periods increases, then the average weight of the tablet increases too.

Relation among quantitative factors and resistance to crushing Vispulin tablets is described by the second order regression equation:

$$y_4 = 83,049 + 11,461x_1 - 10,259x_2 + 5x_1x_2 + 1,656x_1^2 - 0,592x_2^2$$

The analysis of the equation shows that during the increasing of Ludipress quantity and decreasing of magnesium carbonate basic at the formula of Vispulin tablets, their resistance to crushing increases too. Also received significant meaning of coefficient of doubled interactions x_1x_2 , shows the mutual influence of studied factors. The meaning of this interaction is that one factor on which level is studied depends on the meaning of the other one. We can check this interaction by using the single factor of graphic relations.

The relation among resistance to crushing obtained tablets and substance of Ludipress in their formula is shown by straight lines on Fig. 1.

Adding more Ludipress in mass for tableting leads to increasing mechanical resistance of obtained tablets regardless of the level at which factor x_2 examines. The highest values of the studied parameters (110?H) are received by adding Ludipress in quantity of 0,128?g for 1 tablet and at the same time to stabilize the factor x_2 at the level «-б» or «-1» (lines 2, 3).

Influence of studied factors to the abrasion of Vispulin tablet weight is described by the following regression equation:

$$y_5 = 0,415 - 0,144x_1 + 0,068x_2 + 0,007x_1x_2 + 0,024x_1^2 - 0,007x_2^2$$

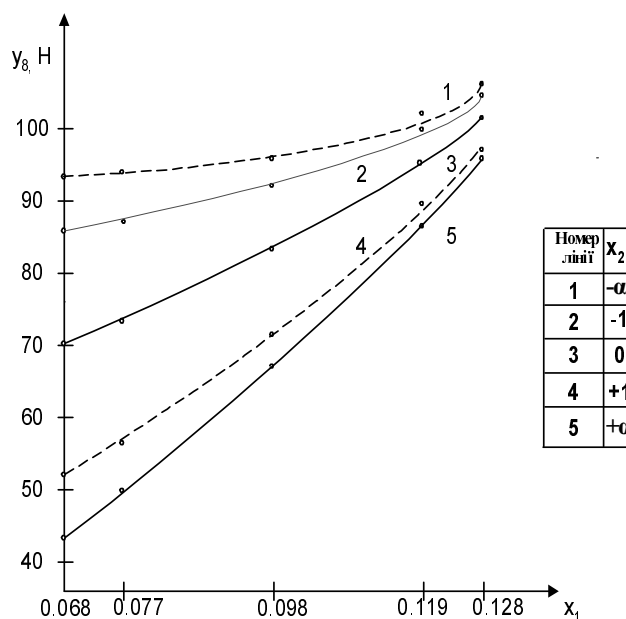


Fig. 1. Influence of Ludipress substance to resistance to crushing of Vispulin tablets

The abrasion of obtained tablets mostly depends on the substance of Ludipress (x_1) in their formula, linear coefficient for x_1 is 2,11 times higher than x_2 . The sign «-» before the regression coefficient indicates that while changing the factor levels x_1 in the range of «-6» to «+6» the meaning of tablet abrasion decreases.

The second order regression equation, which describes the process of disintegration of obtained Vispulin tablets by direct compression, is the following one:

$$y_6 = 5,753 + 0,515x_1 - 0,301x_2 - 0,25x_1x_2 + 0,216x_1^2 + 0,091x_2^2$$

Analyzing this equation, we can conclude that the studied parameter is equally dependent on both quantitative Ludipress substance, and of magnesium carbonate basic in the formula of Vispulin tablets. Also it is observed the interaction of quantitative factors x_1, x_2 , leading to a shorter time of disintegration for obtained tablets.

The next step of the regression equation analysis is to build lines of equal access in the plane of two factors intersection. This helps to identify visually a compromise solution of optimization problem. That's why regression equations were given the so-called canonical form. On the basis of the transformed equations we built lines of equal access at the coordinate system x_1, x_2 (Fig. 2).

The analysis of this figure shows that in any combination of quantitative factors x_1 and x_2 all meanings of studied reviews meet pharmacopoeial requirements to the quality of this dosage form.

Optimal results of studied pharmaceutical and technological indicators of quality of Vispulin tablets can be achieved when $x_1 = «+6»$, and $x_2 = «0»$.

After analyzing the data due to all reviews, it was set the optimal quantity of excipients for tablet formula, so the quantity of Ludipress is 0,128 g, magnesium carbonate basic – 0,021 g, MCC 102 – 0,16975 g, magnesium stearate – 0,007 g in one unit of dosage medicine.

The obtained Vispulin tablets with the specified formula have the required pharmaceutical and technological indicators, that meet the requirements of the State Pharmacopoeia of Ukraine (SPU): resistance to crushing – 100 H, abrasion – 0,3% weight uniformity of tablets – $\pm 1,25\%$, disintegration – 7 minutes.

Conclusions. 1. It has been studied the quantitative influence of significant excipients on pharmaceutical and technological indicators of Vispulin tablets using the mathematical planning.

2. It has been determined the quantitative substance of excipients for Vispulin tablets formula, which provides to receive tablets with indicators that meet the requirements of SPU, using the regression analysis.

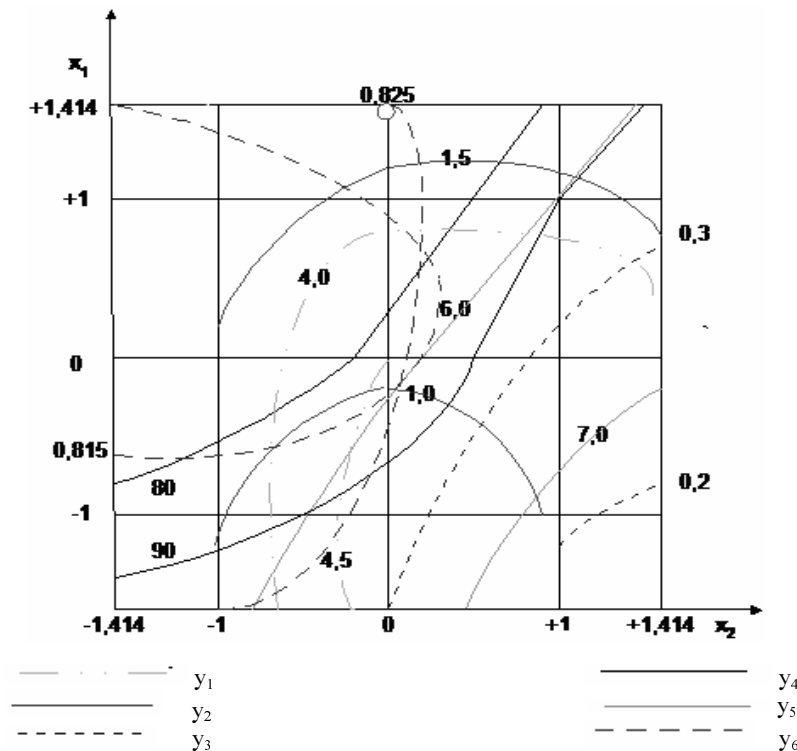


Fig. 2. Lines of equal access at the coordinate system x_1, x_2

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ОПТИМІЗАЦІЯ СКЛАДУ ТА ТЕХНОЛОГІЇ ТАБЛЕТОК «ВІСПУЛІН»

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Резюме: у статті наведено результати дослідження впливу двох кількісних факторів на фармако-технологічні показники таблеток «Віспулін» та властивості мас для таблетування. На основі проведеного експерименту були визначені оптимальні кількості допоміжних речовин у складі таблеток та запропоновано оптимальний склад.

Ключові слова: таблетки, екстракт кори осики, вісмут субцитрат, оптимальний склад, пресування.

ОПТИМИЗАЦИЯ СОСТАВА И ТЕХНОЛОГИИ ТАБЛЕТОК «ВИСПУЛИН»

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Резюме: в статье приводятся результаты исследования влияния двух количественных факторов на показатели качества таблеток «Виспулин» и свойства масс для таблетирования. На основе проведенного эксперимента были определены оптимальные количества вспомогательных веществ в составе таблеток и получен оптимальный состав.

Ключевые слова: таблетки, экстракт коры осины, висмут субцитрат, оптимальный состав, прессование.

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