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CONTENT

AGRICULTURAL SCIENCES

BIOLOGICAL SCIENCES

CHEMICAL SCIENCES

MEDICAL SCIENCES

PHARMACEUTICS

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ANALYSIS OF TECHNOLOGY FOR PLANT EXTRACT PRODUCTION USING THE MATHEMATICAL MODELING METHOD

Kukhtenko O.
Candidate of Pharmaceutical Sciences, Associate Professor, Vice-Rector for Scientific and Pedagogical (Educational) Work of the National University of Pharmacy, Kharkiv, Ukraine
ORCID: 0000-0003-4908-6717
Gladukh Ie.
Doctor of Pharmacy, Professor,
Head of the Industrial Pharmacy Department of the National University of Pharmacy, Kharkiv, Ukraine
ORCID: 0000-0002-5739-9257
Kharkiv, 53, Pushkinska str, 61002

Abstract

Upon receipt of a sedative action liquid extract based on valerian root, motherwort herb, hop seedballs and peony roots by percolation the influence of a number of factors extractant (ethanol) concentration , extraction ratio and infusion time before the extraction process on the yield of extractive substances and active components (hydroxycinnamic acids in terms of chlorogenic acid) has been studied. The studies have been carried out using mathematical planning by a three-phase fractional experiment plan based on a 4x4 Latin square. According to the data obtained, the optimal conditions for the extraction are the use of 70% ethanol, the extraction multiplicity 4, the process of infusion 24 hours before actually percolation.

Keywords: Mathematical planning of the experiment, extract, hydroxycinnamic acids, the yield of extractive substances, factors.

To date, worldwide trends are increasing towards the use of medicinal products based on medicinal plant materials (MPM). These drugs have several advantages over synthetic ones, the main of which can be called the minimal side effects on the patient's body with possible high therapeutic activity. However, the therapeutic activity of a medicinal product based on plant raw materials depends not only on the raw material itself, but also on the technology for obtaining and isolation of active components for their further use in the preparation of finished dosage forms. Particularly important the technology for the production of active substances (complexes of substances) is in the development of preparations of complex compositions, comprising several types of MPM [1,2].

We have carried out a study of the pharmaceutical market of Ukraine, on the basis of which it was proposed to develop a line of ready-made dosage forms of sedative action with the content of the extract obtained from valerian roots, motherwort herb, hop seedballs and peony roots [2].

Extracting is a complex pharmaco-technological process, in which a significant number of factors affect the yield of the finished product .The main factors are: method of extraction (percolation, maceration, ultrasonic extraction, etc.), type and nature of the raw materials used (humidity, degree of grinding, initial content of active substances in the raw material), nature of the extractant (its polarity, concentration), extraction conditions (temperature, pressure, process intensification), etc.

Taking into account the preliminary research and analysis of the instrumentation of pharmaceutical enterprises in Ukraine, we have chosen percolation method with presoaking and infusion of raw materials. Using as unchanged factors the moisture content of the raw materials, the degree of grinding and standard percolation conditions (temperature 25 ^{0} C, pressure 740 mm Hg) of the total mixture of components for obtaining the liquid extract, we have been tasked to determine the effect of the extractant, the extraction multiplicity and the time of raw material infusion on the yield of extractives and active components of the extract (the presence of hydroxycinnamic acids in terms of chlorogenic acid).

Variation of variable factors in the analysis of extract production can lead to a significant amount of research, which will affect the development time of the drug and its cost. It is advisable to use mathematical planning of the experiment when conducting this study.

For the study 12 factors were selected, in 3 groups: the concentration of the extractant, the multiplicity of raw materials extraction, the time of infusion before the process of actually extraction (Table 1). To study the influence of 3 factors, each of which was taken at 4 levels, a three- phase fractional design of the experiment was used based on the 4x4 Latin square (Table 2) [3,4,5].

Table 1

Factors and their levels, which were studied in the process of the extract production technology optimization

Factors	Factor levels
A - concentration of the extractant	a_1 - ethyl alcohol 40% a_2 - ethyl alcohol 50% a_3 - ethyl alcohol 60% a_4 - ethyl alcohol 70%
B - the multiplicity of raw materials extraction	b_1 - the multiplicity of extraction = 2 b_2 - the multiplicity of extraction = 3 b_3 - the multiplicity of extraction = 4 b_4 - the multiplicity of extraction = 5
C - time of infusion before the extraction process	c_1 - 12 hours c_2 - 24 hours c_3 - 36 hours c_4 - 48 hours

Table 2 shows the research data obtained from the extraction of raw materials using various combinations of factors and their levels.

Table 2

Three-phase fractional experiment plan based on the Latin 4 * 4 square and the results of the of active components presence

No.	A	B	C	y^1	y^2
1	a_1	b_1	c_1	0.025	2,150
2	a_1	b_2	c_2	0,033	8,220
3	a_1	b_3	c_4	0.092	12,140
4	a_1	b_4	c_3	0,100	10,130
5	a_2	b_1	c_2	0.050	6.110
6	a_2	b_2	c_1	0.056	2,240
7	a_2	b_3	c_3	0.085	11,750
8	a_2	b_4	c_4	0,120	10,150
9	a_3	b_1	c_3	0.075	9,800
10	a_3	b_2	c_4	0.108	12,280
11	a_3	b_3	c_1	0.114	13,080
12	a_3	b_4	c_2	0.130	14,750
13	a_4	b_1	c_4	0,102	13,600
14	a_4	b_2	c_3	0.118	13,200
15	a_4	b_3	c_2	0.148	21,240
16	a_4	b_4	c_1	0.135	13,800

Note.

y^1 - hydroxycinnamic acids content in terms of chlorogenic acid, %;

y^2 - the content of extractives, %;

The dispersion analysis of experimental data with regard to comparison using the Duncan multiple criterion showed the dependence of both extractive and active substances yield on the extraction factors [3].

As can be seen from table 2, the content of hydroxycinnamic acids in the resulting extract varies in the range of 0.025-0.148%. According to the statistical data processing, the acids content significantly depends on the concentration of the extractant and the multiplicity of the raw material extraction (factors A and B).The effect of factor A (the concentration of the extractant) can be described by the inequality $a_4 = a_3 > a_2 = a_1$, according to which the use of ethyl alcohol 70% and 60% is optimal. In this concentration range, there is almost equal content of hydroxycinnamic acids. The smallest amount of active ingredients is observed in the extract when using alcohol with a concentration of 50-40%.

The dependence of changes in the raw materials extraction multiplicity on the yield of hydroxycinnamic acids corresponds to the following inequality: $b_4 = b_3 > b_2 = b_1$. The most optimal is the use of the extraction multiplicity 4-5. The content of the active components in the extract at extraction multiplicity of 4-5 significantly exceeds the parameters of the extract at 2-3 times extraction.

The results of analysis of variance to determine the presence of hydroxycinnamic acids when changing such a factor as the time of infusion (C) showed statistical insignificance, since $F_{exp.} < F_{0.05}$.

The content of extractives in the obtained extracts ranged from 2.150% to 21.240%. In the study of this parameter, it was determined that all factors affect the yield of extractive substances.

The maximum yield of extractives, as in the example with hydroxycinnamic acids, is observed when using ethyl alcohol 70% as an extractant ($a_4 > a_3 > a_2 = a_1$). The lowest yield of extractives is at alcohol concentration of 40-50%.

Unlike the presence of hydroxycinnamic acids, where the maximum yield was in the experiment with the extraction multiplicity 4 and 5, the yield of extractive substances is maximum at the extraction multiplicity of 4.A decrease or increase in the extraction multiplicity does not lead to an increase in the yield of extractive substances ($b_3 > b_4 > b_2 = b_1$).

A slight difference in the yield of extractive substances depending on the infusion time of 48, 36 and 24 hours ($c_4 = c_3 = c_2 > c_1$) and the minimum yield at the infusion time of 12 hours allows us to conclude that the effective infusion time is 24 hours. It is at this time, as the experiment showed, the yield of extractive substances will be optimal and will not lead to a delay in the process of extract production.

Conclusion. The influence of technological factors on the extraction of medicinal plant materials in the obtaining of a liquid extract of sedative action has been studied. According to the data obtained, the optimal conditions for the extraction are the use of 70% ethyl alcohol, with extraction multiplicity as 4 and the process of infusion before actual percolation for 24 hours.

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