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DEVELOPMENT OF RATIONAL TECHNOLOGY AND THE STUDY OF THE STABILITY OF DRUGS PHYTOFILMS WITH THE LIQUID EXTRACT OF NETTLE AND MARIGOLD

To justify optimal technology phytofilms containing liquid extract of nettle leaves and marigold flowers was examined three technological options for getting phytofilms . Defined physical-chemical and technological characteristics of the obtained phytofilms and studied their stability during storage.

Key words: *phytofilms, liquid extract of nettle and calendula, film-forming substance, a plasticizer glycerin, homogenization.*

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ЧАЁНЎТИ ВА ТИРНОҚГУЛ СУЮҚ ЭКСТРАКТИНИ САҚЛОВЧИ ДОРИВОР ФИТОПАРДАЛАРНИНГ МЎЪТАДИЛ ТЕХНОЛОГИЯСИНИ ИШЛАБ ЧИҚИШ ВА УЛАРНИ ТУРҒУНЛИГИНИ ЎРГАНИШ

Чаёнўти ва тирноқгул суюқ экстрактини сақловчи доривор фитопардаларнинг мўътадил технологиясини асослаш мақсадида учта технологик вариантлари ўрганилди. Олинган фитопардаларнинг физик-кимёвий ва технологик кўрсаткичлари аниқланди ва уларни турғунлиги ўрганилди.

Таянч иборалар: *фитопардалар, чаёнўти ва тирноқгул суюқ экстракти, парда хосил қилувчи моддалар пластификатор глицерин, гомогенизация*

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FACTORS INFLUENCING ON THE EXTRACTION OF STAHYDRINE ALKALOID FROM PLANT *CAPPARIS SPINOSA*

We describe results on the study of influence of factors such as degree of raw material grinding, frequency of extraction, and extraction temperature on the yield of alkaloid stahydrine extracted from the aerial part of Capparis spinosa.

Key words: *Capparis spinosa, stahydrine, plant raw materials, extraction, solvent, concentration, temperature, alkaloid, technology*

Capparis spinosa is a perennial herbaceous plant (stahydrine content in the air - dry mass of the raw material was 1.3%), the height reaches up to 2.5 m. Stems branched, and growing inclined. Two kinds of capers grow in Uzbekistan. In some countries, capers are planted as a cultivated plant. Population of the Caucasus and the Mediterranean Sea region use its buds as a spice [1, 2]. In India, capers is used to treat pulmonary tuberculosis, root decoction is used to strengthen the gums.

In the folk medicine, a decoction of roots is used to treat hepatitis. The wort of the flower heals purulent wounds. Decoction of fruits is used to treat hemorrhoids, as an anesthetic for toothache and a medicine to strengthen the gums [3]. From ancient times, the plant *Capparis spinosa* was used to treat various diseases. The Institute of the Chemistry of Plant Substances of the Academy of Sciences of the Republic of Uzbekistan has developed a method for producing stahydrine from the aerial part of Capparis spinosa in laboratory conditions [4].

It is known from the literature that stahydrine isolated from *Capparis spinosa* is of considerable practical interest as a mean having a pronounced positive effect on the process of blood coagulation, and also exhibits hypotensive and sedative effects [5,6]. Capers thorny widespread in all regions of Uzbekistan, and the main alkaloid is stahydrine, which reaches for 50% of the amount of alkaloids [7].

The purpose of the research: to develop a technology for the isolation of biologically active substances from plant materials; the main task is to study the influence of factors on the extraction process. The purpose of our study was to study the influence of such factors as degree of crushing of raw materials, selection of the extractant, extraction process temperature, multiplicity and duration of extraction, which play the main role in the isolation of alkaloids with the highest yield.

To find a selective extractant, the extraction of raw materials by a number of organic solvents and their aqueous mixtures was studied (Table 1). Extraction was carried out under the same conditions by an eight-fold extraction of capers specimens.

0.5 kg air-dried raw material with particle size of 2-6 mm was loaded into 9 extractors with a volume of 5 liters. The first extractor was filled with methanol, 2-6 extractors - ethanol of various concentrations (95, 90, 80, 70, 60 %), 7 - buthanol and 8 - chloroform. All solvents were poured until a mirror formed over the surface of the feed, the extraction was carried out six times at room temperature, and extracts drained every 8 hours. The combined extracts from each extractor were evaporated in a rotary evaporator at a temperature of 40-50° C and a vacuum (- 0.6 ... – 0.4 kgf/cm^2).

Table 1

The effect of the extractant selection on the yield of stahydrine

No.	Extractant	Yield of extractive substances, %	Yield of stahydrine, %	
			relatively to the mass of raw material	relatively to the content of stahydrine in the raw material
1	Methanol	9.4	1.17	90.07
2	Ethanol 95%	5.1	0.99	76.60
3	90%	6.8	1.05	81.31
4	80%	10.5	1.17	90.12
5	70%	11.6	1.08	82.85
6	60%	11.2	0.86	66.50
7	Buthanol	3.4	0.29	22.34
8	Chloroform	4.2	0.13	10.41

To isolate the alkaloid stahydrine from a thick aqueous extract, the latter was loaded into a chromatographic column filled with alumina and washed with a mixture of chloroform: alcohol (80:20).

The obtained stahydrine was recrystallized from acetone, and its content in the obtained substance was quantified by titration method.

As can be seen from the Table 1, methanol (90.07%) and 80% ethyl alcohol (90.12%) extracted approximately the same amounts of stahydrine and exceeded the extracting ability of the other studied extragents.

As ethahol is a more accessible and technological solvent, for extracting stahydrine from the raw material, 80% ethanol was chosen as an extractant.

One of the important factors influencing the extraction process is the degree of crushing of raw materials. To establish the optimum degree of grinding, the raw material was ground and sieved through a sieve with different holes diameter. From each lot, 0.5 kg of raw materials were taken and loaded into extractors as follows: the first extractor - uncrushed raw material, the second - 2-5 mm, the third - 6-9 mm, the fourth - 10-14 mm and the fifth – less 2 mm. Extraction was carried out eight times at room temperature with 80% ethanol, and discharged every 8 hours. Further actions were carried out both in the process of studying the selection of the extractant. The results are provided in the Table 2.

As can be seen from the Table 2, stachydrine was extracted more quickly from the crushed raw material with a particle size of less than 2 mm, but the extract was opaque and difficult to filter. The extraction process of uncrushed raw materials was slow. Thus, for the isolation of stachydrine, we recommend the use of crushed aerial part of *Capparis spinosa* with a particle size of 2-5 mm.

Temperature is one of the key factors in extraction of biologically active substances from plant material. Increasing the temperature accelerates the transition of substances to the solvent from the raw material. A number of experiments were conducted to study the effect of temperature on the process of stahydrine extraction from plant material.

0.5 kg crushed aerial part of Capparis spinosa with particle sizes of 2-5 mm was loaded into four extractors, and filled with 80% ethanol until a

Table 2

Influence of the degree of crushing of raw materials on the yield of stahydrine

No.	Degree of crushing, mm	Yield of extractive substances, %	Yield of stahydrine, %	
			relatively to the mass of raw material	relatively to the content of stahydrine in the raw material
1	Less 2 mm	11.1	1.20	92.36
2	2 – 5	10.6	1.17	90.20
3	6 – 9	10.3	1.08	83.21
4	10 – 14	9.9	1.01	77.54
5	Uncrushed	9.6	0.90	69.52

Table 3

Effect of temperature on the yield of stachydrine

No.	Degree of crushing, mm	Yield of extractive substances, %	Yield of stahydrine, %	
			relatively to the mass of raw material	relatively to the content of stahydrine in the raw material
1	20-30	10.4	1.17	93.8
2	30-40	13.4	1.18	94.1
3	40-50	17.6	1.19	94.7
4	50-60	19.6	1.20	95.1

mirror has formed. Extraction in the first extractor was carried out at room temperature, in the second extractor at 30-40°C, in the third extract at 40-50°C, in the fourth extract at 50-60°C. Extraction at a temperature above 60°C was not carried out, because the yield changes slightly. The temperature regime was regulated in an ITJ-0-03 water thermostat (Russia). The extraction was repeated, the combined extracts were evaporated on a rotary evaporator. Stahydrine was extracted from the condensed extract by the above-mentioned method. The results of the studies are provided in Table 3.

From the data presented in Table 3, it can be seen that the yield of extractive substances increased depending to the rising of temperature. However, the yield of stachydrine changes insignificantly. It may be attributed to the higher yield of concomitant substances. Isolation of stahydrine from this extract was difficult and lead to increasing of the cost of the final product. Therefore, extraction at room temperature is the most optimal and does not require special devices for heating.

The accompanying substances are extracted together with the main compound from the plant raw material. The insufficient extraction time reduces the yield of the product, and the increase in the contact time of the raw material with the extractant leads to an extract with a high content of concomitant substances. Therefore, it is important to study the kinetics of extraction of the target substance.

The experiments were carried out as follows: 0.5 kg of ground raw material was loaded into seven extractors with a capacity of 5 liters, 80% ethanol was used as the solvent. Extraction was carried out at room temperature.

Drains were made sequentially with an interval of 1 hour. In the first extractor the extraction time was 1 hour, in the second extractor - 2 hours, in the third extractor - 3 hours, the fourth - 4 hours, the fifth - 5 hours, the sixth - 6 hours, the seventh - 7 hours.

At the end of the extraction time, the extracts were drained and the yield of stahydrine was determined. Dependence of stahydrine yield from the raw material of the time of infusion during the first contact of the phases is shown in the Table 4, from which it can be seen that the equilibrium between the phases came in 6 hours (51.2%).

To establish the phase equilibrium at the second phase contact, experiments were carried out under the following conditions: 0.5 kg of ground raw material was extracted in six extractors with 80% ethanol for 6 hours (the time required to establish phase equilibrium at the first contact). The extracts were drained and fresh portions of the extractant were poured. Every hour, the extract was removed

Table 4

Dynamics of stahydrine extraction from raw material

Infusion time, h	1-st contact of phases	2-nd contact of phases	3-d contact of phases	4-th contact of phases	5-th contact of phases	6-th contact of phases
1	18.5	8.5	5.4	3.2	0.8	0.1
2	30.2	14.8	9.5	4.6	1.4	0.4
3	38.1	20.4	13.8	5.8	1.4	0.4
4	43.9	23.2	16.4	5.8		
5	48.1	23.2	16.4			
6	51.2	23.2				
7	51.2					

from the appropriate extractor, and the yield of stachydrine determined. Dependence of the yield of stahydrine from the raw material of the extraction time for the second phase contact is shown in the Table 4, in this case the phase equilibrium reached in 4 hours (23.2%).

Results in the Table 4 shown that at the third contact of phases the equilibrium is reached in 4 hours (16.4%), at the fourth - 3 hours (5.8%), the fifth and sixth- in 2 hours (1.4% and 0.4%, respectively). For five drains the recovery rate was 96.6%, which is quite acceptable for the extraction stage. Proceeding from this, we recommend a six-fold extraction, in which the sixth drain is used to enrich the subsequent extractions.

Conclusion: The obtained results of the research show that the extracting of aerial part of capers to obtain stachydrine, it is necessary to use crushed plant raw materials with a particle size of 2-5 mm. 80% ethyl alcohol selected as an extractant. The process should be performed six times at room temperature for 6 hours.

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CAPPARIS SPINOSA ЎСИМЛИГИДАН СТАХИДРИН АЛКАЛОИДИНИ ЭКСТРАКЦИЯ ҚИЛИШ ЖАРАЁНИГА ТАЪСИР ЭТУВЧИ ОМИЛЛАРНИ ЎРГАНИШ

Capparis spinosa ўсимлиги ер устки қисмидан стахидрин алкалоидини экстракция қилиш жараёнига хом ашёнинг майдаланганлик даражаси, эритувчи тури ва концентрацияси, экстракция жараёнидаги ҳарорат каби омилларнинг таъсирини ўрганиш натижалари ёритилган.

Таянч иборалар: *Capparis spinosa, ковул, хом ашё, экстракция, эритувчи, концентрация, ҳарорат, алкалоид, технология.*

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ИЗУЧЕНИЕ ФАКТОРОВ, ВЛИЯЮЩИХ НА ПРОЦЕСС ЭКСТРАКЦИИ АЛКАЛОИДА СТАХИДРИНА ИЗ РАСТЕНИЯ *CAPPARIS SPINOSA*

Приведены результаты по изучению влияния таких факторов, как степень измельчения сырья, кратность экстракции, а также температуры на процесс экстракции алкалоида стахидрина из надземной части каперсов колючих – Capparis spinosa.

Ключевые слова: *Capparis spinosa, стахидрин, растительное сырье, экстракция, растворитель, концентрация, температура, алкалоид, технология.*

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ТЕХНОЛОГИЯ ПОЛУЧЕНИЯ КАПСУЛ «ЭКУСТИМ»

Разработана технология получения капсул «Экустим». Определены основные технологические свойства субстанции и капсулированной массы.

Ключевые слова: *лекарственные растения, сухой экстракт «Экустим», субстанция, капсула, технология.*

Разработка эффективных диуретических лекарственных средств на основе местного растительного сырья является актуальной проблемой фармацевтической науки позволяющая импортозамещению подобного действия синтетических лекарственных средств, таких как фуросемид, верошпирон и др. Используемые в настоящее время в качестве мочегонных средств растения в основном используются в виде настоев, отваров, что затрудняет их применение. Кроме того, сроки хранения настоев и отваров 2-3 дня.

В Государственном реестре РУз за 2012 г о регистрированных и разрешенных к применению в Республике Узбекистан лекарственных средствах, зарегистрирован диуретический лекарственный препарат канеферон (CanephronumN), фирмы BionoricaAG, Германия. Данный препарат является комбинированным лекарством, состоящим из экстрактов растений: *Centauriherbe*, *Levisficiradix*, *Rosmarinifolia*, выпускается в виде раствора по 50, 100 мл и драже №20х5, «20х6» в блистерах [1].

Среди диуретических растительных лекарственных средств хотелось бы отметить использование комбинированных препаратов. Комбинация нескольких активных веществ в одном лекарственном препарате позволяет добиться большой эффективности терапии за счет разнонаправленного действия компонентов, а также повысить ее безопасность в связи с возможностью использования более низких дозировок в комбинированных препаратах благодаря синергизму их воздействия.

На основе сухих экстрактов известных и разрешенных к использованию в медицинской практике отечественных лекарственных растений: травы янтака ложного, травы эрвы шерстистой, травы хвоща полевого, травы якорцев стелющихся, цветки тысячелистника таволголистного, семян огурцов, столбики с рыльцами кукурузы и корни солодки голой нами был создан новый диуретический препарат [2-3], который условно вначале назван «Уростим», потом – «Экустим».

Технология препаратов растительного происхождения имеет свои особенности, связанные с физико-химическими свойствами исходных субстанций, которые необходимо учитывать при выборе вспомогательных веществ.

Начальным этапом при разработки технологии получения лекарственного препарата является изучение структурно – механических и технологических свойств действующих веществ, в зависимости от которых прессуемый материал может вести себя разнообразно. По показателям технологических свойств субстанции можно прогнозировать виды и количества необходимых вспомогательных веществ, а также ход технологического процесса.

Исследуемая нами субстанция «Экустим» является суммарным продуктом растительного происхождения, обладающая разнообразными физико-химическими свойствами. Субстанция «Экустим» гигроскопична. Гигроскопичность играет важную роль в приготовлении твердых дозированных лекарственных форм, содержа-