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DEVELOPMENT AND RESEARCH OF THE PHYTODRUGS RECEIVED BY VARIOUS METHODS OF EXTRACTION

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Abstract

Extraction of medicinal raw materials is widely used in technology of various drugs of natural compounds. The completeness of extraction of natural compounds from medicinal vegetable raw materials significantly is affected by the choice of extragent which is defined by the properties of the extracted substances and also a type of the prepared drug. It can be liquid or dry extract, or individual substance.

Impose a number of serious requirements to extragents, basic of which are:

• ability to extract a certain group of active ingredients;

• chemical and pharmacological indifference;

• possibility of regeneration.

1. Introduction

The choice of extragent is defined by degree of hydrophily of the extracted substances: for extraction of polar substances with high value of a dielectric constant use polar extragents: water, glycerine, methanol; for unipolar – acetic acid, chloroform, ethyl oxide, acetone, vegetable oils.

It is necessary to take the requirements for ready drug into account: so, if extragent remained in already ready medicine, as the dispersive environment, it is extracted liquid, tinctures, then it is necessary to pay special attention to the pharmacological indifference of extragents. For medicines in which technology removal of extragent from a ready-made product is provided (dry extracts, neogalenical drugs, individual substances) widest choice of extragent, and not so categorical requirements are possible.

Nowerdays, perspective extragents should be considered liquefied gases: carbon dioxide, propane, butane, liquid ammonia. The dioxide liquefied carbon, which is chemically indifferent to a large number of active ingredients is most often used, he well extracts, essential, fat oils, etc. Extraction process of liquefied gases is carried out under pressure at which removal extragent disappears, and extractive substances remain in pure form.

2. Justification of the choice of extragent and conditions of extraction of flavonoids from complex medicinal vegetable raw materials

Receiving complex extract from 13 medicinal vegetable objects for further use in soft dosage forms was a problem of our researches. It was necessary to choose extragent and conditions of extraction. In table 1, the structure of the considered plants is brought.

Table 1 – Composition of complex

№	Component composition	Amount
1.	Celandine grass	0,02
2.	Wormwood grass	0,40
3.	Calendula flowers	0,05
4.	Pine buds	0,50
5.	Chamomile flowers	0,04
6.	Dog-rose fruit	0,06
7.	Caraway Fruits	0,03
8.	Fennel fruits	0,30
9.	Thyme herb	0,15
10.	Yarrow Grass	0,05
11.	Licorice roots	0,25
12.	Mint leaves	0,10

13.	Hypericum grass	0,05

We carried out the extragent choice, based on relevant requirements for the last and based on the analysis of data of literature on the optimum concentration of alcohol for the extraction of biological active substances of various groups. We investigated 3 extragents with concentration of ethanol 40, 70, 90 percent of ethanol in addition of 10% of methylene chloride [2].

The maximum extraction of flavonoids from medicinal vegetable raw materials is reached when using an alcohol-water mixture with concentration of ethanol by 70% in addition of 10% of methylene chloride.

Methylene chloride (CH_2Cl_2). Extragent with a high relative density – 1.33 and with the temperature of boiling of 40-41 °C. It is applied to the extraction of hydrophobic substances (glycosides, alkaloids, etc.). Methylene dichloride addition, significantly increased an exit of flavonoids that confirmed the quantitative definition [2].

3. Method

3.1. Remaceration method in the ratio 1:8.

Placed the crushed raw materials in a matseratsionny tank and filled in with 5-fold amount of extragent (70% alcohol of ethyl 10% of methylene chloride). Methylene chloride addition, significantly increased an exit of flavonoids that is proved by quantitative definition of flavonoids at extraction by pure ethanol and mix with it.

Extraction was carried out in the room temperature within 24 hours. Then raw materials were wrung out, the extract was filtered, and the meal was repeatedly filled in with 3-fold amount of extragent, and extracted within 12 hours at the room temperature. Then the meal was wrung out, and the received extract was filtered. Periodic change of extragent allowed, at a smaller expense of time for extraction, to exhaust raw materials more stoutly, to reduce losses at diffusion as the difference of concentration is supported and as a result of it is the speed of diffusion increases. After completion of extraction, the received extracts united.

3.2. Extraction by the dioxide liquefied carbon.

Now one of perspective methods of extraction is CO_2 extraction. Therefore, for receiving the extract of a Rhodiola pink we used CO_2 extraction. Extraction by the dioxide liquefied carbon is carried out in installations (fig. 1) having an extractor, the evaporator and chambers for pretreatment of raw materials and removal of residues of solvent from the meal. Installation is supplied with the conveyor The plant material loaded into the container representing mesh capacity comes at first to the camera for soaking by liquefied gas under pressure of 5.8 — 6.0 N/m2 which moves from the collections located in the top part of the installation. The stage of impregnation passes at a temperature of 18 — 25 °C within several minutes. Then it is transferred to the crushing camera with the lowered pressure. As a result of the difference of pressure in a solid material and on a surface there is an explosion, which is broken off it in small pieces. It is promoted also by

the formation of crystalline of ice in a timely and cracks of the extracted raw materials from vapors of water and carbon dioxide. Further raw materials come to an extractor, and on it from above by means of the pump the dioxide liquefied carbon moves. Extraction goes by the principle of a countercurrent. The received extraction goes to filters and further into the heat exchange where there is a collecting the cleaned extraction and removal of vapors of carbon of dioxide which come to the condenser on liquefaction [1]. Meal rises in the following camera warmed by steam through a steam shirt for removal of vapors of carbon of dioxide from the fulfilled raw materials which also get to the condenser for liquefaction. With it couples from the evaporator are taken away. The dioxide liquefied carbon comes to production again. After an exit from the camera containers with the fulfilled raw materials unload [5].

Principle of work of installation: 1 load the crushed raw materials via the loading union by means of a vacuum into extractors. From extractors and the evaporator air is deleted with pumping out and filled with gaseous CO_2 from cylinder 2. After achievement of balance of pressure 1 gives the liquefied CO_2 from pressure head capacities to extractors 3. Solvent passes through a raw materials layer, takes soluble components and via filter 5 merges in evaporator 6. In the evaporator extract is warmed up, vapors of solvent separate and at the expense of the difference of pressure come to condenser 7 cooled by refrigerating unit 8 where are condensed, and solvent is returned to pressure head capacities 3 [5].

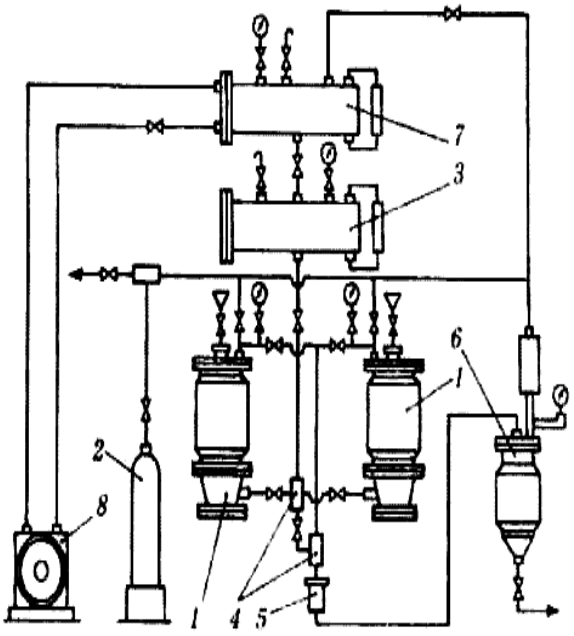

Figure 1. The schematic diagram of installation for extraction of vegetable raw materials the liquefied carbon dioxide

4. Results & discussion

Despite all advantages of the chosen extragent from ethanol and methylene chloride, it was necessary to make sure of full removal of the last. For this purpose subjected the received complex extract to pumping out.

Studying of existence of residual amounts of methylene chloride was carried out proceeding from the requirements of GF-XIII by Residual organic solvents (OFS.1.1.0008.15) [3].

Determination of content of residual organic solvents can be carried out by various validated techniques [4]. Most often for these purposes the method of gas chromatography is used.

Table 2 - the Maximum permissible content in medicines of residual organic solvent 2 classes of toxicity – methylene chloride.

Solvent	Marginal content, mg/day	Marginal content, ppm
Methylene chloride	6,0	600

Definition of concentration of methylene chloride was carried out over complex extract by method of gas chromatography after pumping out, for the purpose of removal of residual amounts of methylene chloride. That is reflected in table 3.

Concentration unit: per thousand

Test: phytoextract

Column: HP-B ALC of 7.5 m * 0.32mm*20tkt

Comments: Qualitatively

Table 3 – Content of solvents over complex extract

Component name	Group Time	Window, %	Type of	Detectors
methanol	0:00:48	5	Usual	Flame ionization detector-1
ethanol	0:01:20	5	Usual	Flame ionization detector-1
methylene chloride	0:01:42	5	Usual	Flame ionization detector-1
acetone	0:01:50	5	Usual	Flame ionization detector-1
isopropanol	0:02:17	5	Usual	Flame ionization detector-1
propanol	0:03:09	5	Usual	Flame ionization detector-1
ethyl acetate	0:04:39	5	Usual	Flame ionization detector-1

benzene	0:05:36	5	Usual	Flame ionization detector-1
butanol	0:08:41	5	Usual	Flame ionization detector-1
toluene	0:16:25	5	Usual	Flame ionization detector-1

Primary test of a phytoextract, showed presence of methylene dichloride in number of 6.9 mg/ml. Test over phytoextract after additional pumping out, for the purpose of removal of excess content of methylene chloride made – 0.0006 mg/ml. S=0. 996 (the area under a curve). What confirms optimally conditions of removal of excess content of methylene chloride in a system as the keeping of the last does not exceed admissible concentration according to SF-XIII – no more than 6.0 mg/dose (600 ppm) [3].

Figure 2 - Chromatogram

The received an extract with the use of the liquefied dioxide, carbon, differs in a higher content of biologically active agents, stability in storage, resistance to microbe contamination. Especially it belongs to the raw materials containing polyphenol connections, alkaloids and glycosides. And in roots and rhizomes of a rhodiola dominant glycosides the Main active ingredients in a rhizome of a rhodiola rosea — phenolic connections are pink: phenolic alcohols and their glycosides, flavonoids and tannins of a group of pyrogallol (up to 20%). Phenolic alcohol p-oksifeniletanol (тирозол) in raw

materials is contained in the basic in the form of a glycoside — a salidrozid. The maintenance of a salidrozid varies from 0.5 to 1%, depending on conditions of a habitat and a phase of development of a plant. Underground bodies contain still carbohydrates, organic acids, terpenoids (rosiridin, rosiridol), essential oil, sterols, aromatic connections (rosavin, rosin, rosarin), fenolkarbonovy acids and their derivatives (Gallic, etc.), anthraquinones, lipids (fats, wax).

5. Conclusions

Thus, in this article, we considered the possibilities of extraction of biological active substances from medicinal vegetable raw materials extragents, such as ethanol, methylene chloride, CO_2 and methods various methods of extraction. It is obvious that, medicinal vegetable raw materials demand various approaches as to the extragent choice, and an extraction method depending on the forthcoming basic purpose of a target product. Expected purpose of extract of roots of a Rhodiola pink – cosmetics, therefore CO_2-extraction use positively and in this regard.

6. References

1. Bobilev R.V. (1991) Technology of medicinal forms: / R.V. Bobilev, G.P. Gryadunova, L.A. Ivanova// - Moscow: Medicine, 1991. - 544 c.

2. Chueshov V.I. (2014) Technology of industrial drugs / V.I. Chueshov, E.V. Gladuh, I.V. Saiko // - Vinnitsa: NovaBook, 2014. – 696 c.

3. State Pharmacopoeia of the Russian Federation. XIII edition. (2015). Federal Electronic Medical Library, 2015. – 1465 c.

4. Koga K., Ohmachi K., Kawashima S., Takada K., Murakami M. Determination of 18a-glycyrrhizin and 18P-glycyrrhizin in dog plasma by high-performance liquid chromatography // J. Chromatography B. 2000. – 738 c.

5. Kurkin V.A. (2015) Rhodiola rosea (golden root). Standardization and creation of drugs / V.A. Kurkin // – Samara: Ofort; SamGMU, 2015. – 240 c.