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AQUA FOENICULI: DIFFERENT APPROACHES TO THE COMPOUNDED TECHNOLOGY

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Abstract

The modern Ukrainian pharmaceutical market is characterized by a constant growth in the range of finished drugs, both of domestic and foreign production. At the same time, a significant arsenal of drugs due to the high cost, significant amount of excipients, difficulty in adjusting the dosage, etc., does not allow to optimize therapy fully. At the same time, the use of more personalized and affordable extemporaneous medicines is reduced. According to the International Pharmaceutical Federation, the practice of compounding drugs in pharmacies is widespread in the United States, Germany, Poland, the Czech Republic and other European countries, which allows to find an individual approach to each patient patient and rationally combine drugs. Increasingly popular phytopreparations, having a milder effect and not inferior to synthetic, they provide a wide range of pharmacological action, without causing unwanted side effects and can be produced in pharmacies in various dosage forms. Medicinal plants are the oldest source of pharmacotherapy used by mankind. A significant number of traditional systems of medicine (folk medicine) have developed over the past millennia under different cultural conditions. Even today, most people in less developed countries have to rely on herbal remedies as their primary care.

The aim of the work was to study dill water of extemporaneous production with the use of various technological methods to determine possible ways to optimize and improve it.

We used the historical, structural and system analysis, scientific synthesis and logical generalization of research results, physicochemical, chemical and pharmacotechnological research methods in our research.

The technology of preparation and application of fennel fruits (Foeniculum vulgare L.) by folk medicine, as well as the use and features of extemporaneous formulation of dill water for more than 100 years are analyzed. As a result of experimental studies, dill water was obtained using a number of techniques (infusion of fennel fruit in a water bath; shaking fennel essential oil with warm water; grinding fennel essential oil with talc, then shaking with warm water). Microscopic and organoleptic analysis of the obtained model samples of dill water was carried out, the quantitative content of essential oil in them was determined. According to the results of research, when ground with talc, there is a more even distribution of fennel oil inclusions and its drops are much smaller, compared to model samples where dill water was obtained without the addition of talc. Model samples of dill water were stored at a temperature of 15-25 °C, every 5 days they were analyzed: for 15 days (observation period), samples No. 2-7 and 9 remained stable. Prospects for further research are to improve the technology of dill water to extend its shelf life. Prospects for further research are to improve the technology of dill water and methods for determining its quality.

Key words: composition, technology, dill water, extemporaneous prescription, historical analysis, logical generalization, quantitative analysis.

Introduction

According to the World Health Organization, the rational use of medicines is their use when patients receive drugs as clinically necessary, in doses that meet individual needs, for an adequate period of time and at the lowest cost for themselves and society [1, 2]. At the same time, the use of more personalized and affordable extemporaneous medicines is reduced [2-4]. Increasingly popular phytopreparations, having a milder effect and not inferior to synthetic, they provide a wide range of pharmacological action, without causing unwanted side effects and can be produced in pharmacies in various dosage forms [1, 5]. Medicinal plants are the oldest source of pharmacotherapy used by mankind. A significant number of traditional systems of medicine (folk medicine) have developed over the past millennia under different cultural conditions. Even today, most people in less developed countries have to rely on herbal remedies as their primary care. Based on scientific and technological progress, options for the production of high-quality herbal medicines have improved significantly in recent decades. The adoption of herbal medicine as a "natural and easy alternative" to synthetic drugs is highly developed among the general public of developed countries, and, from a global point of view, sales of herbal medicines are constantly growing. However, there are still many problems in this area. In addition to dogmatic barriers, a critical look at herbal remedies is often based on the lack of clinical trials that would demonstrate their effectiveness and safety. It is because of the lack of scientific evidence that there is a misunderstanding of the principles of rational herbal medicine [6, 7].

We were interested in fennel (Foeniculum vulgare L.) ("dill", "walnut dill"), health and healing properties of which are described by the founders of modern medicine Hippocrates and Avicenna. For therapeutic purposes, fennel fruits, which contain essential oil, flavonoids, glycosides, vitamins A, B_1, B_2, B_6, B_{12}, C, PP, tocopherol (vitamin E), minerals - potassium, magnesium, zinc, chromium, phosphorus, calcium, sodium, manganese, copper, aluminum, iron, nutrients – proteins, fats, carbohydrates, fatty oils, etc., are used [9]. Due to the wide range of action of biologically active substances, fennel products have antispasmodic, carminative and disinfectant effects, increase the secretory activity of the digestive glands, promoting digestion; act as a weak diuretic and expectorant, they are prescribed for diseases of the gastrointestinal tract, accompanied by spasms, flatulence, pain in the intestine (spastic colitis and intestinal colic). Dill water is especially effective for children [9].

Fennel has virtually no contraindications for medicinal purposes, so it is part of many herbal soothing species, laxative teas, including children's, traditional medicines and Ayurvedic medicines. Despite the high content of essential oil, fennel is hypoallergenic. The only contraindication is individual intolerance. Pregnant women should not eat a lot of fennel, because it can increase uterine tone. In Indian medicine, the fruit is used as a stimulant, and the roots – a laxative [10, 11].

Methods

The objects of the study were the current regulatory framework, international and domestic regulations, questionnaires, model samples of dill water, obtained on the basis of fruit, essential oil and extract of dried fennel common in various technologies [13-19]. Studies of the dry residue were performed according to the methods of SPU [12], quantitative determination of essential oil by direct alkalimetric titration with 0.01 mol / l NaOH solution in the presence of methylene blue and phenolphthalein indicators according to the Guidelines of the Ministry of Health of Ukraine [19].

To 10 ml of the drug add 4 ml of 0.002 N iodine chloride solution, 1 ml of 1% potassium iodide solution, 1 ml of starch solution and titrate with 0.002 N sodium thiosulfate solution until the blue color disappears (V1). To 10 ml of a standard solution of fennel essential oil add 4 ml of 0.002 n iodine monochloride solution, 1 ml of 1 % potassium iodide solution, 1 ml of starch solution and titrate 0.002 n sodium thiosulfate solution until the blue color disappears (V2). To 10 ml of purified water add 4 ml of 0.002 n iodine monochloride solution, 1 ml of 1% potassium iodide solution, 1 ml of starch solution and titrate with 0.002 n sodium thiosulfate solution until the blue color disappears (V3). The content of fennel essential oil in percent (X) was calculated by the standard method according to the formula:

$$X, \% = \frac{(V_3 - V_1) \cdot 0.005}{V_3 - V_2}$$

where V_1 – volume of 0.002 M sodium thiosulfate solution, which was used for titration of a model sample of dill water;

V_2 – volume of 0.002 M of sodium thiosulfate solution used for titration of standard essential oil solution;

V_3 – volume of 0.002 M sodium thiosulfate solution used for titration in the control experiment (control – purified water);

0,005 – the percentage of essential oil in the standard solution.

The concentration of essential oil in dill water should be 0.004-0.006 %.

Notes.

1. Making a standard solution of fennel essential oil. Pipette 10 ml of 96% ethanol with a pipette to 0.1000 g (exact portion) of fennel essential oil and stir until dissolved. Place 1 ml of the resulting solution in a 200 ml volumetric flask, make up to volume with water and mix. The concentration of essential oil in the standard solution is 0.005%.

2. Production of 0.002 n iodine monochloride solution. Place 2 ml of 0,1 N iodine monochloride solution in a 100 ml volumetric flask and make up to volume with water. The solution is used freshly made. The drug is poured into vials of 100 ml, sealed with plastic plugs and screwed plastic lids. Store at a temperature not exceeding 25 ° C in a dark place. Shelf life - 30 days.

Results

Analysis of the technology of preparation and application of fennel fruits in folk medicine **[11]** is given in table 1.

As can be seen from the table 1, folk medicine recommends receiving only water extracts of various concentrations from the fruits of fennel, however, in a number of diseases.

We also conducted a retrospective analysis of the use of dill water in pharmacy for almost a century. Pharmacopoeias of II, V, VI, VII, VIII, IX, X editions (SP) were analyzed [13-18]. The results of studies of bibliosemantic analysis of pharmacopoeias of different publications on the composition and ratio of ingredients of dill water, features of technology and analysis are given in table 2.

As can be seen from the table 2, in SP VIII dill water is described for the last time as it is not included in the SP IX, X, XI and SP of Ukraine.

We obtained model samples of dill water based on fruits, essential oil and dried fennel extract (sweet) using different technologies and analyzed them. The composition, technology and organoleptic characteristics of model samples of dill water are given in table 3.

Freshly obtained model samples of dill water were analyzed for physicochemical parameters and quantitative determination of the essential oil content. In order to determine (homogeneity) the most uniform distribution of oil droplets in the model samples, we made their microphotographs (Fig. 1).

As can be seen from Fig. 1, samples No. 4-7 have a more uniform distribution of fennel oil inclusions and its drops are much smaller, compared to sample No. 2, where dill water was obtained without the addition of talc. On microphotographs No. 1 and 2 (dill water obtained by infusing fennel fruit with purified water in a water bath) there are some accumulations of insoluble substances.

Thus, it can be concluded that talc usage in dill water technology is expedient.

Next, we quantified the essential oil content in the obtained model dill water samples by direct alkalimetric titration with 0.01 mol/l NaOH solution in the presence of methylene blue and phenolphthalein indicators [19], for 30 days (in 5 days). Model samples of dill water were stored at a temperature of 15-25 ℃.

The results of the analysis of the indicators of quantitative determination of the essential oil content are given in table 4.

As can be seen from the table, for 15 days (study period), samples No. 2-7 and 9 remained stable. Observations continue.

Discussion

The obtained data allowed to draw a conclusion about the relevance and prospects of expanding the range and more active use of extemporaneous drugs based on herbal raw materials in order to implement the concept of personalized medicines. Given the instability of dill water during storage, the

problem of extending its shelf life remains unrealized, which is of interest for further work. Prospects for further research are to improve the technology of dill water and methods for determining its quality.

There is no conflict of interest.

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Table 1. Technology of preparation and application of fennel fruits in folk medicine

Recipe	Technology	Signature	Application
1 tsp. fennel fruits	Pour 150 ml of boiling water, leave to infuse, strain	Drink as tea or on an empty stomach three times a day for 100 ml	Use for flatulence, abdominal pain, cough, insomnia, to improve milk production in nursing mothers
1/2 tsp. ground fruits	In the morning, afternoon and evening brew in 200 ml of boiling water, sweeten	Take with food	When flatulence and to facilitate digestion
2 tsp. ground fruits	Add to 400 ml of water and infuse on low heat for 10 minutes. Cool, strain	**Rinsing**	Gargle for colds, hoarseness
2 tsp. ground fruits	Pour 300 ml of boiling water, leave to infuse, strain	Infusion for rinsing	Rinse eyes for conjunctivitis, skin for purulent diseases
Fennel fruits	–	Every time after a meal	Chew fennel fruit for stomach pain
40.0 g of fennel fruits	Pour 500 ml of boiling water and keep in a thermos for 50 minutes	Drink 80 ml of infusion before each meal	When flatulence
15.0 g of fennel, mullein and mallow fruits	Pour boiling water and let the fennel seeds stand, separately - the flowers of small-flowered mallow and mullein. Mix in equal amounts	Take 150 ml before each meal	When tracheitis
60.0 g of fennel fruit	Pour 1200 ml of boiling water	Breastfeeding mother in 40 minutes after a meal to drink 400 ml	During lactation
1 tsp. fennel fruits	Pour 230 ml of boiling water and infuse in a water bath for 2 minutes	Cool and consume into 5 parts	When cystitis
30.0 g of fennel fruits	Pour 400 ml of water and infuse for 30 minutes	Strain and drink 120 ml 15 minutes before meal	When constipation

Table 2. Composition and ratio of dill water ingredients (Aqua Foeniculi)

Composition		Technology	Description	Test
SP II (1871)				
R.	Olei Feniculi *scrupulous duos*, Aquae destillate tepidae *libras decem.*	Fennel* oil is strongly shaken with warm, distilled water, after cooling the dill water is filtered through the pass paper	–	–
SP V (1902)				
Fructuum Feniculi contusorum 1 p. Aquae communis sufficientem quantitatem		No more than thirty parts of dill water should be obtained from one part of fennel fruit	Muddy, dill smell and taste	–
SP VI (1924.)				
Dill oil 1 p. Pure talc 10 p. Water 60-70 °C 1500 p.		Dill oil, previously thoroughly ground with pure talc, shake vigorously with warm water. After cooling, filter	Transparent, peculiar fragrant smell, first sweet, then bitter taste. Has a neutral reaction	Should not react with heavy metal salts. At 10 cm^3 of dill water and calcination there should be no significant residue
SP VII (1937)				
Dill oil 1 p. Pure talc 10 p. Water 60-70 °C 1500 p.		Dill oil, previously thoroughly ground with pure talc, shake vigorously with warm water. After cooling, filter	Transparent, peculiar fragrant smell, first sweet, then bitter taste. Has a neutral reaction	Should not react with heavy metal salts. At 10 cm^3 of dill water and calcination there should be no significant residue
SP VIII (1952)				
Dill oil 1 p. Pure talc 10 p. Water 50-60 °C 1000 p.		Fennel oil is ground with talc, the mixture is transferred into a glass of warm water and shaken for 15 minutes. After cooling, the liquid is filtered	Clear or slightly cloudy liquid, colorless, peculiar fragrant odor, sweet and then bitter taste, neutral reaction	10 ml of the drug should not react to heavy metals. 20 ml of the drug is evaporated and the residue is calcined. The residue should not exceed 0.005 %
Storage. Dill water is prepared for a short time and stored in a cool place in well-sealed glasses				

Note. * – the table retains the originality of the text

Table 3. Composition, technology and research results of model samples dill water

No.	Prescription	Technology	Organoleptic indicators
1.	Fructuum Foeniculi 1 p. Aquae purificatae 10 p. (Guidelines "Requirements for the preparation of non-sterile drugs in pharmacies")	1 p. of fennel fruit pour with 10 p. of purified water, infuse on a water bath for 15 minutes, strain after complete cooling	Light brown liquid, with slight opalescence, anethole odor, tasteless
2.	Fructuum Foeniculi 1 p. Aquae purificatae 30 p. *(SP V)*	1 p. of fennel fruit pour with 30 p. of purified water, infuse on a water bath for 15 minutes, strain after complete cooling	
3.	Olei Foeniculi 1 p. Aquae purificatae 1500 p. *(SP II)*	Fennel oil is thoroughly shaken with warm (60-70 °C) water to cool, filtered through a paper filter	Liquid with light opalescence, with a pronounced smell of anethole, colorless, tasteless
4.	Olei Foeniculi 1 p. Talci 10 p. Aquae purificatae 1500 p. *(SP V)*	Fennel oil is thoroughly ground with pure talc, shaken vigorously with warm (60-70 °C) water to cool, filtered through a paper filter	
5.	Olei Foeniculi 1 p. Talci 10 p. Aquae purificatae 1500 p. *(SP VI)*	Fennel oil is thoroughly ground with pure talc, shaken vigorously with warm (60-70 °C) water for 1 minute. After cooling, filter through a paper filter	
6.	Olei Foeniculi 1 p. Talci 10 p. Aquae purificatae 1500 p. *(SP VII)*	Fennel oil is thoroughly ground with pure talc, shaken vigorously with warm (60-70 °C) water for 5 minutes. After cooling, filter through a paper filter	
7.	Olei Foeniculi 1 p. Talci 10 чр. Aquae purificatae 1500 p. *(SP VIII)*	Fennel oil is thoroughly ground with pure talc, shaken vigorously with warm (60-70 °C) water for 15 minutes. After cooling, filter through a paper filter	
8.	Fennel essential oil	Fennel essential oil is distillated by water vapor	Clear, yellowish color with anethole odor

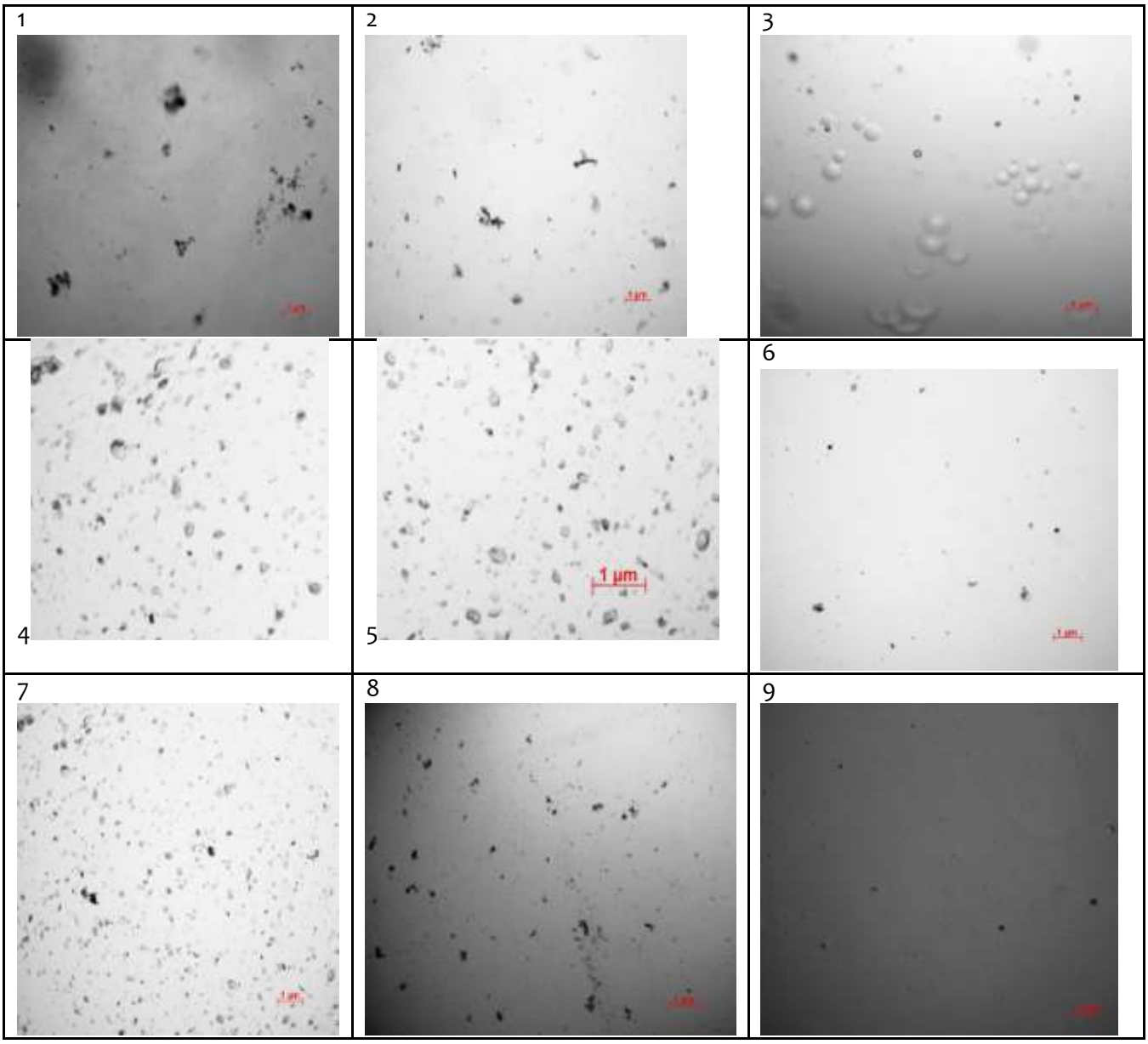

Fig. 1. Microphotographs of model samples of dill will obtained by different technology

Table 4. The results of quantitative determination of essential oil in model samples of dill water

Model sample	Quantitative determination of essential oil, %			
	Freshly made	5 days	10 days	15 days
1.	The dark color of the solution prevents the indicator fixation of the titration endpoint	No studies performed		
2.	0.017 (solution diluted 10 times)	0,017 ± 0,0002	0,016 ± 0,0002	0,016 ± 0,0001
3.	0.006	0,006 ± 0,0001	0,006 ± 0,0001	0,006 ± 0,0002
4.	0.014	0,014 ± 0,0002	0,014 ± 0,0002	0,014 ± 0,0003
5.	0.017	0,017 ± 0,0002	0,017 ± 0,0002	0,017 ± 0,0002
6.	0.016	0,016 ± 0,0001	0,016 ± 0,0001	0,016 ± 0,0002
7.	0.014	0,014 ± 0,0001	0,014 ± 0,0002	0,014 ± 0,0002
8.	The dark color of the solution prevents the indicator fixation of the titration endpoint	No studies performed		
9.	0.005	0,005 ± 0,00007	0,005 ± 0,00006	0,005 ± 0,00007