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RESEARCH ARTICLE

Prospects for the Use of the Herb Chamomile in the Manufacture of Dietary Supplements

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Abstract

Objective: Chamomile flowers is a widely studied pharmaceutical raw material, however, pharmaceutical herb chamomile herbal raw material practically has not been studied, but in practice is an interesting and promising item for further study. The objective of the study was carrying out of the analysis of the herb chamomile raw material (two types-fresh and dried). Method: In accordance with the Russian SP (State Pharmacopoeia) procedures, there were produced etheroleum and alcohol extract. Moisture content was determined as for dried raw material: 14.00±0.74%, for fresh raw material: 71.40±2.23%. Quantitative and qualitative composition was assessed by GLC (gas-liquid chromatography, mass detector) and HPLC (high-performance liquid chromatography) methods. Results: As of comparative analysis of etheroleum and alcoholic extract from herb chamomile, it should be pointed out that azulene derivatives were present in etheroleum and in alcoholic extract; however, chamazulene as such was identified just in etheroleum. In alcoholic extract there was no chamazulene. In alcohol extract there were identified vitamins, flavonoids (kaempferol is the important one), phenol compounds, coumarins, organic acids-ferulic acid and its derivatives, peptides and sugars. Conclusion: The herb chamomile is both a promising dietary food supplement, and a pharmaceutical preparation. There are a lot of studies concerning the determination of herbal`s bioactive components. This process is important for quality control of herbs and its products.

Keywords: *Herb chamomile, Chamazulene, Matricin, Kaemferol, Ferulic acid.*

Introduction

Background

Herb chamomile- Chamomilla recutita (L.) Rauschert (Matricaria recutita L., M. chamomilla L.), sunflower family-Asteraceae- is a well-known pharmaceutical plant which flowers as a pharmaceutical herbal raw material are in widespread use in form of pharmaceutical agents and dietary food supplement. Herb chamomile is a pharmaceutical plant included in many drug codices.

The pharmaceutical herbal raw material has a certified pharmacopeial description of external features of the pharmaceutical herbal raw material and main performance indices (etheroleum content, moisture content, total ash, ash insoluble in hydrochloric acid, organic and mineral related substances) [1].

Herb chamomile flowers are suggested for using as an antispasmodic and anti-inflammatory pharmaceutical agent [2, 3, 4, 5].Chamomile etheroleum also "seems to be a promising candidate for topical therapeutic application as virucidal agents"[6]. However, the folk medicine holds out vast opportunities of using herb chamomile raw material.

Literature Review

Chamomile in Ancient Times

The author of “Natural History”-the Roman philosopher of nature Pliny the Elder in his description of herb chamomile gave its Latin name matrix - womb, because in days of old this plant was used for gynaecological diseases, hence a popular synonym for a plant-matricular herb.

The recent study has shown that "Chamomile presents a safe, well-tolerated and effective treatment for women with moderate mastalgia" [7]. The highest-profile physicians of ancient Greece-Hippocrates (469-377 BC), Dioscorides (I century AD)-made in their medical practice use of pharmaceutical properties of herb chamomile [8]. Hippocrates put emphasis on using herb chamomile as a cosmetic product for eye treatment and a dental illness preventive remedy [8], apparently keeping in mind the anti-inflammatory activity, that is widely used and is studied nowadays [4, 5].

Chamomile in the Middle Ages

The Arabian physician Abu Ali Ibn Sina (Avicenna (980-1037)) described this healing plant in his works and generally proposed to use is as a sedative and analgesic [8]. This property of herb chamomile is also confirmed in current studies [2, 9, 10].Tibetan monks gave attention to herb chamomile as one of the most important components of anti-aging drugs, in the modern beauty therapy this effect is also widely used in good reason [3, 11].

In the Renaissance era, Florentine medical men had in their arsenal some three hundred hair-, skin- and décolleté area-care products which compulsorily included the herb chamomile extract [8]. The Scythian medicine keeping abreast of that of East and Europe proposed a great number of drinks, honeys and other recipes with the use of herb chamomile as a pharmaceutical herbal raw material [8]. Those recipes were collected in herbals, books of home cures and gardens-medical literature which appeared in Russia several centuries ago.

Chamomile Nowadays

Today, French nutrition specialists consider the infusion of herb chamomile flowers to be one of six pharmaceutical herbal extracts which have to be taken both for pleasure (that is as tea or other nutritional beverage) and for medical treatment. At the moment, there exist and are widely used such complex preparation as Romazulan and Rotocanum [12]. All modern sources, regulatory documents, monographs consider as a pharmaceutical herbal raw material only chamomile flowers Flores Chamomillae. For another type of raw material-herb chamomile there is no regulatory documents at all.

Material and Methods

The Objective of this Work

The investigation of chemical composition of the pharmaceutical herb chamomile herbal raw material. There are a lot of studies concerning the determination of herbal`s bioactive components [13, 14]. This process is important for quality control of herbs and its products.

The Subject of Research

A fresh herb chamomile Herba Chamomillae recutitaerecens; herb chamomile (dried raw material) Herba Chamomillae. The raw material was grown within the territory of the botanic garden of the I.M. Sechenov First Moscow State Medical University. Production of etheroleum, alcoholic extract (matrix homeopathic tincture), investigation of the raw material moisture content was conducted according to the State Pharmacopoeia methods [1].

Component analysis of alcoholic extract and etheroleum samples was made by gas chromatography-mass spectrometry using the Agilent Technologies instrument consisting of:

- Gas chromatograph 7890 (column HP-5, 50 m x 320 µm x 1.05 µm);
- Mass selective detector 5975°C with quadrupole mass analyzer.
- The temperature program is at 40°C-isotherm 2 min;
- Further programmable heating up to 250°C at a rate of 5°C/min;
- At 250°C-isotherm 15 min;
- further programmable heating up to 320°C at a rate of 25°C/min;
- At 320°C-isotherm 5 min.
- Split injector: 1:50.
- Injector temperature: 250°C.
- Interface temperature: 280°C.
- Carrier gas: helium;
- Flow rate: 1 ml/min.
- Sample chromatogram: total ion current.

- Mass spectrometric analysis: ionizing energy 70 eV;
- Mass spectrum registration in positive ions within the range (m/z) from 20 to 450 at a rate of 2.5 scan/s.
- Software: ChemStation E 02.00.
- Component (qualitative) analysis was made using the library of full mass spectra NIST-05 and corresponding values of chromatographic linear retention indices.
- Relative content (%) of mixture components (quantitative analysis) was calculated from the chromatographic peak composition (by simple normalization) [15].

Mass Spectrometric analysis is an expensive method. Nevertheless, it provides good sensitivity and selectivity and important structural information [16].

The flavonoid composition of alcoholic extract was investigated by the ultra-performance liquid chromatography/MS [17, 18] method using the Waters Acquility chromatograph with tandem quadrupole MS detector TQD (Waters):

- Movable phase A: (MP A).
- Mixture: water-acetonitrile (95:5) with formic acid.
- Movable phase: B (MP B). Acetonitrile with formic acid.

Chromatography of solution under study and standard solutions is carried out in the following conditions:

- Sample volume 5 µl;
- Column 0.21 x 15.0 cm Acuility UPLC BEH C18 (1.7 µm);
- Column temperature 35 °C;
- Flow rate 0.3 ml/min;
- Gradient elution mode is formed by mixing of movable phases A and B UV detection: 220-500 nm.
- MS conditions: MS detection in positive ion mode;
- Detector parameters: capillary voltage +3 kV;
- Cone voltage 50 V;
- Capillary temperature 450°C;
- Source temperature 120°C;
- Drying gas flow rate 800 l/h, gas flow rate in cone 50 l/h and scanning within mass range from 100 to 1500 units;
- MS detection MC in negative ion mode;
- Detector parameters: capillary voltage 3 kV;
- Cone voltage - 30 V;
- Capillary temperature 350°C;
- Source temperature 120°C;
- Drying gas flow rate 500 l/h, gas flow rate in cone 50 l/h and scanning within mass range from 100 to 1500 units.

Results and Discussion

The air-dry raw material usually comprises 10-14 % of hygroscopic water. The elevated moisture content in raw material results in degradation: color is changed, abnormal smell appears, active ingredients are destroyed. Such material cannot be employed. Moisture content of raw material means a loss in weight in drying due to hygroscopic water and other volatile components [15]. Within our study, moisture content was determined both in fresh and dried raw material. Sample weight: 3.00 g. Accuracy: ± 0.01 Moisture content of fresh raw material was 71.40±2.23 (Table 1). Moisture content of dried raw material was 8.74±0.08 (Table 2).

Table 1: Statistical data processing for determination of moisture content of fresh herb chamomile

№	X	$\bar{x}$	S	$\Delta\bar{x}$	$\bar{x}\pm\Delta\bar{x}$	E
1	72					
2	77.67					
3	67.67	71.40	1.74	2.23	71.40±2.23	3.12%

4	68.67					
5	71					

Table 2: Statistical data processing for determination of moisture content of dried herb chamomile

№	X	$\bar{x}$	S	$\Delta\bar{x}$	$\bar{x}\pm\Delta\bar{x}$	E
1	8.7%					
2	9.0%				8.74±0.08	
3	8.7%	8.74				1.5%
4	8.7%		0.15	0.08		
5	8.6%					

In five samples the quantitative etheroleum content was determined and was expressed as the weight of raw material 0.03 ±0.002%. The derived etheroleum presented a transparent aromatic oily blue liquid.

In a sample of etheroleum derived from herb chamomile there were identified 30 compounds. Among them from terpenoid groups:

- **Monoterpenoids and sesquiterpenoids**-menthone 0.051%, carvone 0.147%; 1-methyl-8-(1-methylethyl)-tricyclo[4.4.0.0(2,7)]dec-3-en-3-methanol 0.129%, cis-lanseol 0.475%; trans-chrysanthemol 0.152% (Figure 2); farnesene 1.501%, isoaromadendrene epoxide (bicyclic) 57.488%, spathulenol 2.708% (bicyclic terpene)
- **Bicyclic terpenoids**: 10,10-dimethyl-2,6-dimethylenbicyclo[7.2.0]undecane-5-ol 0.150%, trans-2-isopropylbicyclo[4.3.0]nan-3-en-8-on 7.730%, 2-(2,4-hexa divinylidene)-1,6-dioxa[4.4]non-3-en 10.539% (Figure 3).
- **Sesquiterpene oxides**: bisabolol oxide B 11.399%, bisabolol oxide A 0.187%, eudesmol 0.231%;
- **Sesquiterpene alcohols**: cadinol (bicyclic) 1.106%, santalol 1.045%, alpha-bisabolol 1.851% (monocyclic) (Figure 4).
- **Azulene derivatives**: chamazulene 0.139%.

The sesquiterpenoid compounds such as chamazulene and alpha-bisabolol with its oxide-derivates may act as antibiotics. These effects are provided "by damaging the normal barrier function of the bacterial cell membrane, allowing the permeation into the cell of exogenous solutes" [19]. Alpha-bisabolol also provides antioxidant and anti-apoptotic activities [20]. We consider these two compounds (chamazulene and bisabolol) to be the markers for etheroleum derived from herb chamomile.

Unsaturated alcohols and other compounds: 1,11-dodecandiene-4,5,9-triol 0.194%, (Z)6-pentadecene-1-ol 0.294%.: hexahydrofarnesylacetone 0.238%, 1-methyl 3 - ethyladamantane - 0.043% -(saturated tricyclic bridging hydrocarbon), trilaurin, laurel acid 0.640% (Figure 1).

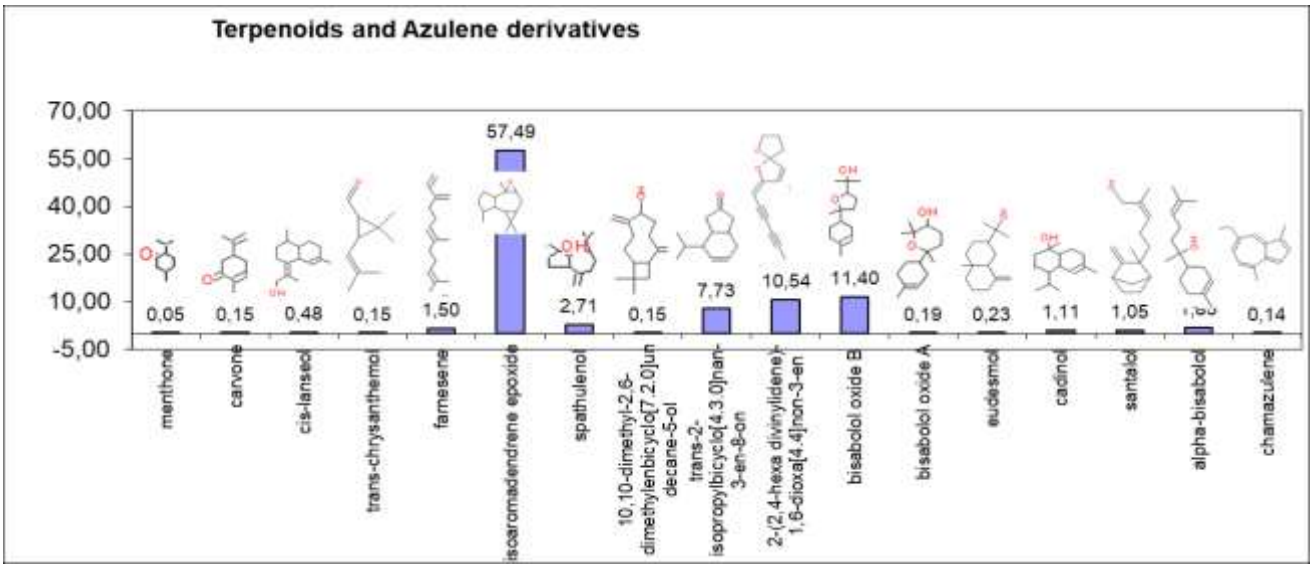

Fig.1: Sample of etheroleum derived from herb chamomile

Using chromatography-mass-spectrometry in alcohol extract from dried herb camomile raw material there were identified 52 compounds such as:

Classified with different terpene derivatives: limonene diepoxide-0.11%, umbellulol-0.09%, verbenol -0.29%, ethyl linalool -0.16%, eucarvone -3.21%, caryophyllene-3.36%, 4-hydroxy-6,10-dimethyl-3-methylene -2-oxo-2, 3, 3a, 4, 5, 8, 9,11a-octahydrocyclo[b]furfurane-9-il acetate-1.07%, isoaromadendrene epoxide-1.18%, 4,9-dihydrocyclo-6-methyl-3,10- dimethylene-3a, 4, 7, 8, 9, 10, 11, 11a-octahydro-3H-cyclodeca [b] furfurane-2-on-0.15%, arteannuin-0.59%, korimbolon-0.75 %, spathulenol-2.46 %, a-octahydro- 5, 9- etheno-1, 4-methanobenzocycloheptene- 6- on- 7.60%, longifolene-2.44%, veridiflorol- 1.38 %, aromadendrene-22.93% (Figure 2).

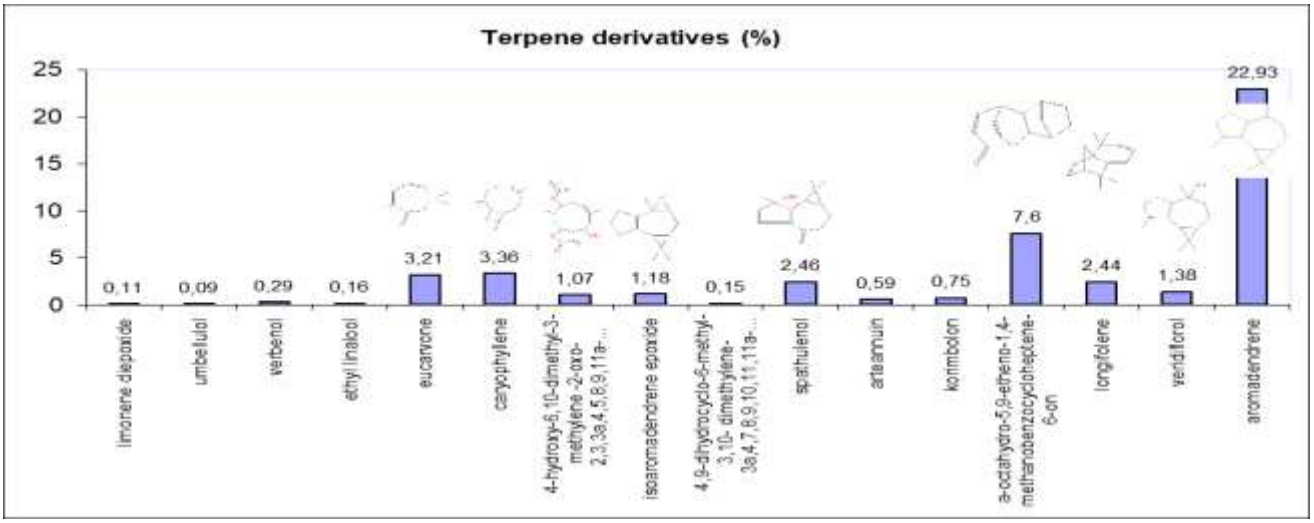

Fig. 2: Classified with different terpene derivatives

Azulene derivatives: 8-propoxycedrane-0.16%, xanthumine-0.05%, 7-hydroxy-6,9a-dimethyl-3-methylene-decahydro-azuleno[4, 5-b] furfurane-0.05%, ambrosial-0.48%, 5H-cyclo [3,4] benzo[1,2-e]azulene-5-on- 1.27%, xanthinine-0.14%, azuleno [4,5-b] furfurane - 2(3H)-on, - 039%, benzo[e]azulene-3(3aH)-on – 0.16% (Figure 3).

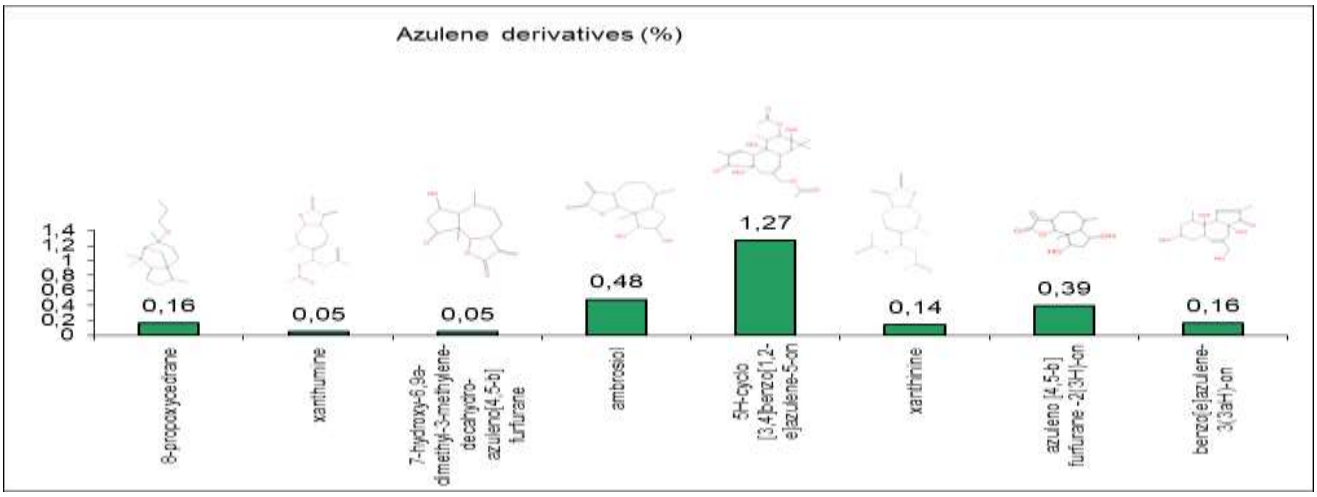

Fig. 3: Classified with different Azulene derivatives

Sugars: 3-deoxyglucose 0.10%, L-glucose 0.15%, 1,4-anhydro-d-mannitol 0.06%, 6-acetyl-á-mannose 0.08%, d-glyceropo-l-gluco-heptose 0.03%, arabinose-0.92%, hexopyranose-6.40%, L-mannose-0.83%

Vitamins: vitamin C-0.20%, retinol-0.06%, phytol-5.47%, á carotene-0.30%, 24.25-dihydroxy vitamin D-0.16%, fenretinide-0.21%

Amino Acids: arginine-0.22%, cystathionine-0.05%, citrulline-0.31%

Other Compounds: sorbitol-4.28%, cyclohexane-1,4,5-triol-3-on-1-carboxylic acid-0.02%, guanosine-0.04%, cytosine-0.10%,

glycocyamine-0.42%, galactonolactone-0.17%, santonin-0.10%, estragole-16.34%, methyl 1-ethylycloindecancarboxylate-0.85%, ethyl palmitat - 0.82%, oleic acid-0.77%.In comparison of etheroleum and alcoholic extract from herb chamomile it is worth noting that azulene derivatives are present in both etheroleum and alcohol extract, but no chamazulene in alcohol extract was identified. Alcohol extract of herb chamomile contains a richer composition of bioactive substances (compounds of terpenoid nature, vitamins, amino acids, sugars, organic acids and other).Using HPLC in the herb chamomile there were identified flavonoids and derivatives of ferulic acid. Two peaks with retention time 4.37 and 6.66 min contain a fragment with mass 194 (M+H=195, M+H-H2O=177, M-H=193) corresponding to ferulic acid, and practically identical UV and mass spectra (M+Na=379, M-H=355) shown in Figure 4.

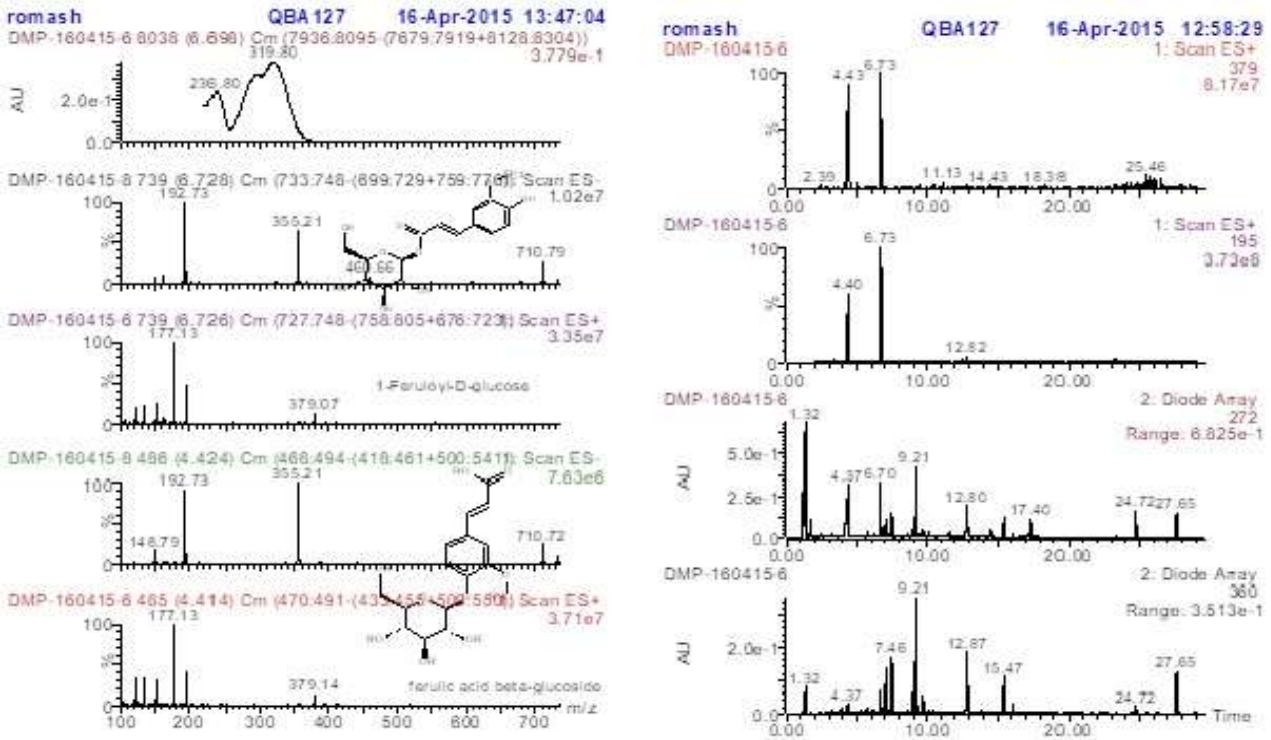

Fig. 4: Correlation between the antioxidant activity of herbal extracts and the high amount of phenolic acids and flavonoids that present in chamomile products

Several studies have reported the remarkable correlation between the antioxidant activity of herbal extracts and the high amount of phenolic acids and flavonoids that present in chamomile products [21, 3, 22].

Based on the difference in retention time it is fair to assume that the peak with retention time 4.37 min has a structure shown in Figure 5 (1) while the peak with retention time 6.66 min has a structure shown in Figure 5 (2).

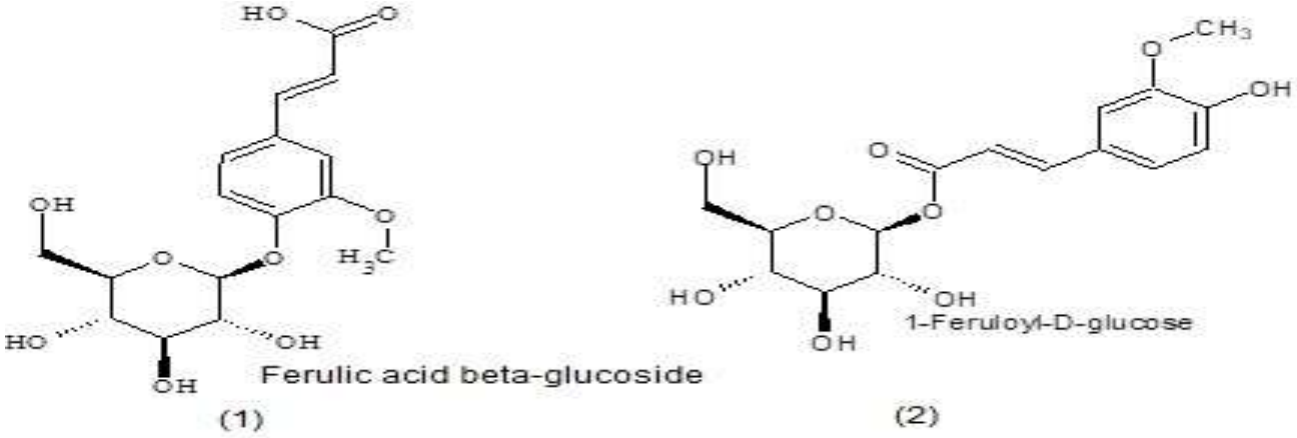

Fig. 5: Difference in retention time of ferulic acid (1)-4.37min, (2)-6.66 min

Chromatogram at 360 nm shows 4 sufficiently intensive peaks with molecular ion masses in positive ion registration mode comprising 517, 517, 287 and 593, in negative ion registration mode-515,515, 285 и 591 and with retention time 9.2, 10.3, 13.5 and 13.9 min. Peaks with retention time 9.2 and 10.3 min apparently are isomers, in positive ion registration mode they have a fragment with ion weight 163, typical for flavanoids, but do not have fragmentation typical for ordinary glycosides.

Among common flavanoids and their glycosides, no compounds with molecular weight 516 were detected. The peak with retention time 13.5 min presumably has the kaempferole structure (Figure 6). Several studies have reported kaempferole`s beneficial effects on human health [17, 23, 24]. We consider this compound to be the marker one for herb chamomile alcoholic extract. The peak with retention time 13.9 has a molecular weight 592. In negative mode apart from molecular ion 591 of small intensity we may see the intensive peak with weight 637, which is adduct with formate ion (592+45=637).

In positive ion registration mode fragmentation is noted up to ion 447 with loss of weight 146, typical for a number of glycosides-derivatives of rutinoside (for example, rutin). However, any further fragmentation to aglucone is hardly in evidence. For this reason, one may assume, for instance, the structure of Isoswertisin 2"-rhamnoside (Figure 6).

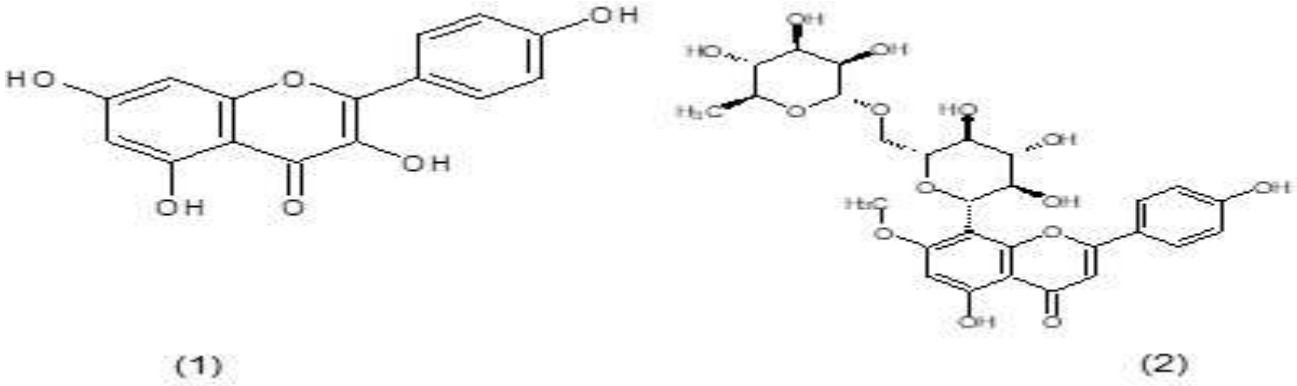

Fig. 6: structure of kaempferole and Isoswertisin 2"-rhamnoside

Conclusion

Chamomile flowers is a widely studied pharmaceutical raw material, however, pharmaceutical herb chamomile herbal raw material practically has not been studied, but in practice is an interesting and promising item for further study. Flowers chamomile is described in certified pharmacopeial descriptions in many world Pharmacopoeias, yet herb chamomile certified pharmacopeial description is missing from the State Pharmacopoeia of Russia.

Analysis was made of the content of bioactive substances in alcohol extract and etheroleum derived from herb chamomile raw material. Studies concerning the determination of herbal`s bioactive components are important for quality control of herbs and its products. As of comparative analysis of etheroleum and alcoholic extract from herb camomile, it should be pointed out that azulene derivatives were present in etheroleums and in alcoholic extract; however chamazulene as such was identified just in etheroleum. In alcoholic extract there was one of the active compounds-kaempferole and its derivatives. There were identified vitamins, flavonoids, phenol compounds, organic acids-ferulic acid and its derivatives, peptides and sugars in alcohol extract.

The sesquiterpenoid compounds of etheroleum such as chamazulene and alpha-bisabolol and its oxide-derivates are considered to be active herbal components that provide beneficial effects on human health and therefore must be identified in herbal products of chamomile. The herb chamomile is a promising pharmaceutical herbal raw material which should be used both as a bioactive dietary food supplement and as a drug product [25, 26].

Acknowledgement

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