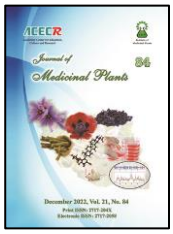
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Research Article

Post-marketing control of *Matricaria chamomilla* L. and *Thymus vulgaris* L. products by reference and developed methods

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ABSTRACT

Background: Post-market surveillance (PMS) is an integral part of ongoing safety evaluation, for natural health products. *Matricaria chamomilla* (chamomile) and *Thymus vulgaris* (thyme) are the most widely used plants in herbal medicinal products. *Thymus* species contain phenolic compounds such as thymol, carvacrol and terpenoids, flavonoids, and saponins. *T. vulgaris* is an antiseptic and antitussive, so it is very effective in treating dry coughs, colds, and inflammation of the upper respiratory tract. *Matricaria chamomilla* (chamomile) products containing apigenin-7-glycoside, some flavonoids and chamazulene in its essential oil that have anti-inflammatory, anti-fungal and anti-bacterial therapeutic properties. **Objective:** In this study, various dosage forms containing thyme (8 products) and chamomile (9 products) separately, (which are available in the form of drops, syrups, ointments, and creams) were provided. Then, physicochemical controls were performed based on the reference methods of herbal pharmacopeias and in-house validated methods to ensure quality and stability of these products. **Methods:** Since many of these products have no special monograph in pharmacopeias, so validated extraction and analysis methods were developed to quantify the apigenin-7-glycoside by high performance liquid chromatography, and chamazulene by gas chromatography in the chamomile products and thymol and carvacrol by gas chromatography in thyme products in different complex dosage forms. **Results:** In some products that formulated by thyme and chamomile products, the amount reported for standardization does not match the values obtained. **Conclusion:** It's recommended more control of herbal medicines for appropriate and effective consumption of them.

Abbreviations: DLLME, Dispersive Liquid-Liquid Microextraction; GC/MS, Gas Chromatography/Mass Spectroscopy; HPLC, High Performance Liquid Chromatography; LOD, Loss on Drying; PMS, Post-Market Surveillance; TLC, Thin-Layer Chromatography

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1. Introduction

Herbal medicinal products are usually used for preventing, treating, and chronic disease management [1, 2]. Herbal products are not necessarily completely safe, as long as having problems such as batch variations, dosage and concentration inconsistencies of the active ingredients [3]. In one study, 28.8 % of herbal preparations investigated were found to be contaminated with heavy metals and 7 % of the herbal products were consciously adulterated with conventional drugs to improve efficacy [4]. Herbal medicines though are perceived to be generally safe but they can pose a health risks to consumers [5-8]. The department of Natural Products of the Food and Drug Administration of Iran was established with the mission of promoting, controlling and regulating the natural and alternative medicine in Iran. Despite the creation of Food and Drug Administration of Iran, many herbal medicines still get to the market under inadequate control [9]. There has not also been regular field postmarketing surveillance (PMS) on both registered and unregistered herbal medicines in the market thereby creating a major public health concern, especially for high-consumption products.

Matricaria chamomilla L. (*M. chamomilla*, chamomile) is one of the most frequently herbal products and, in addition, is applied in pharmaceutical and cosmetic industries [10-13]. Many of its properties such as antimicrobial, antispasmodic, and anti-inflammatory effects have been reported [14-16]. About chemical components, more than 120 secondary metabolites have been identified in chamomile, including phenolic compounds like flavonoids, sesquiterpenes (α-bisabolol, bisabolol oxides A and B, chamazulene, and farnesene), coumarins, and several others [15]. In this context, characterizing a high-quality and effective chamomile product possesses great importance in the industrial field.

Thymus vulgaris L. (*T. vulgaris*, thyme) is an aromatic and medicinal plant of increased commercial interest. *T. vulgaris* is widely used to treat different respiratory problems such as bronchitis, allergy, cold, flu and cough [17]. Carvacrol and thymol are the most frequent in thyme. Recently, several studies have reported that the carvacrol and thymol isomers exhibit antioxidant, antifungal, and antibacterial effects [18]. Thymol is safe with negligible toxicity [19] and carvacrol has been permitted by the EU Commission as a flavoring substance in food products [20].

The primary aim of this postmarketing surveillance (PMS) was to obtain concerns regarding the efficacy and safety of thyme and chamomile products available in the Iranian pharmaceutical market from the consumers perspectives. So various dosage forms were controlled and controlled with precise and validated methods, especially for the amount of effective ingredients and physicochemical and microbial properties.

2. Materials and Methods

2.1. Chemicals

Analytical grade standards of chamazulene, eugenol, carvacrol and rutin (Quercetin 3-rutinoside) (> 98 %) were purchased from Sigma- Aldrich (Sigma-Aldrich, Zwijndrecht, Netherlands). Dichloromethane, chloroform, HPLC-grade methanol, ethanol, ethyl acetate and hexane, were purchased from Merck (Merck, Darmstadt, Germany). Individual stock solutions of chamazulene, eugenol, carvacrol and rutin (Quercetin 3-rutinoside) at 1 mg/ml were

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prepared in methanol. All stock solutions were kept at 2 °C.

2.2. Herbal Products

The examined medicinal products that contain the extract or essential oil of the thyme and chamomile as the single or main ingredient, were purchased from pharmacies in Tehran province. The characteristics of the nine products of the chamomile and the eight products of the thyme are shown in Table 1.

Table 1. The characteristics of the chamomile and *T. vulgaris* products

	Product code	Dosage form	Active ingredients	Standardization
Matricaria chamomilla	**C1**	Buccal drop (30 ml)	*Matricaria chamomilla* extract	0.09-0.17 mg of chamazulene per 1 ml
	C2	Topical solution (250 ml)	*Matricaria chamomilla* extract	0.14 mg of flavonoid per 1 ml
	C3	Topical solution (250 ml)	*Matricaria chamomilla* extract	52 mg of apigenin per 100 ml
	C4	Ointment (30 g)	*Matricaria chamomilla* extract	-
	C5	Syrup (120 ml)	*Matricaria chamomilla* extract (principle)- *Pimpinella anisum* extract	20.9 mg of apigenin per 10% total weight
	C6	Ointment (20 g)	*Matricaria chamomilla* extract& *calendula officinalis* L. extract	0.15 mg of α-bisabolol per 17% total weight
	C7	Cream (30 g)	*Matricaria chamomilla* & *Quercus infectoria extract*	9.85-30.22 mg of phenol & 77-104 mg of apigenin per 1 g
	C8	Cream (30 g)	*Matricaria chamomilla* & *Myrtus communis* extract	3 g chamomile extract & 1.8 g essential oil of myrtus per 30 g
	C9	Ointment (15 g)	*Matricaria chamomilla* essential oil	0.07mg of essential oil per 100 g
Thymus vulgaris	**T1**	Syrup (120 ml)	*Thymus vulgaris* extract	50 mg thymus extract per 5 ml
	T2	Syrup (60 ml)	*Thymus vulgaris* extract	50 mg thymus extract per 5 ml
	T3	Syrup (120 ml)	*Thymus vulgaris* extract (principle)- *Origanum majorana* extract	1 mg total phenol as thymol per 5 ml
	T4	Syrup (120 ml)	*Thymus vulgaris* extract	1-1.5 mg total phenol as thymol per 5 ml
	T5	Syrup (120 ml)	*Thymus vulgaris* extract	17.5-26.5 mg total phenol as thymol per 100 ml
	T6	Syrup (120 ml)	*Thymus vulgaris* extract (principle)- honey	150 mg thymus extract as 0.6 mg thymol
	T7	Syrup (120 ml)	*Thymus vulgaris, Convolvulus arvensis, Malva, Zingiber officinale*	85 mg total phenol as thymol per 5 ml

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T8	Syrup (120 ml)	*Thymus vulgaris* (principle), *Eucalyptus, Satureja, Foeniculum vulgare*	8-12 mg total phenol as thymol per 100 ml

2.3. Quality Control Tests

Three types of tests based on the dosage forms were performed on the products. Physicochemical, ingredient assay and microbial characteristics were investigated in the two time periods (0 and 6 months) for each product.

2.3.1. Physiochemical controls

The organoleptic properties (color, odor and taste), pH, density and thin layer chromatography (TLC) were tested for all products. In addition, the moisture and uniformity of semisolid products and loss on drying (LOD) of liquid products were investigated. TLC analysis was done to identify of the active ingredients of the plants in the products.

TLC analysis of the chamomile products was done on the 254 GF silica gel as the stationary phase. To prepare standard solution, 10 mg of borneol, 10 mg of borneol acetate and, 5 mg of bisabolol oxide were dissolved in 10 ml of toluene: chloroform solvent (3:1 ratio). Also, the mixture of toluene and chloroform solution ratio of 3:1 was used as the mobile phase [21]. To better separate and identify chamazulene (because chamazulene is formed by the heating of matricin (precursor of chamazulene)), all products were refluxed at 80 °C for 135 min. After cooling to ambient temperature and centrifuging for 5 min at 3000 rpm, 5 ml of the upper phase was used for sampling on a chromatographic plate. Also, 2.5 g of each ointment and cream sample were refluxed with 10 ml of hexane (for degreasing) for 135 min at 80 °C, then after cooling to the ambient temperature, were centrifuged at 3000 rpm for 10 minutes. After phase separation, the upper phase was sampled on the plate of TLC.

For the TLC of *T. vulgaris* products, 5 ml of each sample with 2.5 ml of the mixture of 93 % toluene and 7 % ethyl acetate was mixed thoroughly and sampled on the TLC plate. 13 mg of thymol and 10 mg of carvacrol were dissolved in 2.5 ml of 93 % toluene and 7 % ethyl acetate solution and used as a standard solution. For the mobile phase, a mixture of 93 % toluene and 7 % ethyl acetate was used. After drying, the TLC plate was sprayed with a benzaldehyde reagent and then placed in a furnace at 100 °C for 5 min. The standard solution pattern and samples were compared [21].

2.3.2. Quantification of active ingredients

Since all products don't have their special monograph in the pharmacopeias, the methods of pharmacopeias for measuring active ingredients of thyme and chamomile are more limited to their raw materials such as extracts or essential oils. Therefore, clean-up methods are needed to determine accurate active ingredients in the products with complex matrix. In this study dispersive liquid-liquid extraction (DLLME) based internal standard method was used to clean the samples [22].

2.3.3. DLLME method

In this study the micro-extraction method include three basic steps:

a) To the all 5 ml of thyme and pretreatment chamomile products (based on the mentioned method in section 2.3.1), were added 20 µl of eugenol and thymol with concentration of 100

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mg/L as internal standards, respectively and reached to 15 ml with water in the falcon tube.

b) 300 µl of the mixtures of toluene and ethyl acetate (93:7) and toluene and chloroform (1:3) as extraction solvents and 1 ml of acetone as the dispersive solvent were injected into the aqueous solutions of the chamomile and thyme products, respectively.

c) The cloudy solutions were centrifuged 10 min at 1000 rpm and settled the heavier organic phase in the bottom of the falcon tube. The separated organic phase was introduced to the instrumental analysis [22].

The extraction and analysis process was performed focusing on the compound which is the claimed standardization base. Therefore, the compounds of chamazulene, thymol and carvacrol were analyzed with GC/MS, apigenin analyzed with HPLC-DAD and total flavonoids and phenols analyzes with UV-vis.

2.3.4. Gas chromatography/Mass spectroscopy (GC/MS)

After extraction, GC/MS analysis of thymol, carvacrol and chamazulene components was performed on Agilent 6890 system (Agilent, Littleton, Colorado, USA) coupled with Agilent 5973 N mass selective detector equipped with a BPX5 fused silica column (30 m × 0.25 mm i.d., film thickness 0.25 µm). Following injection, 5 min after injection, the oven temperature was increased from 50 to 240 °C at a the rate of 3 °C/min and then reached to 300 °C at rate of 15 °C/min and hold 3 min in this temperature. Other operating conditions were as follows: carrier gas, He (99.999 %), with a flow rate of 0.5 ml/min; injector temperature, 250 °C; and split ratio, 1:35. Mass spectra were taken at 70 eV a scan time of 1 s and a mass range of 40-500 amu [23].

2.3.5. HPLC condition

After extraction, apigenin was quantified with the HPLC system (Knauer, Germany) equipped with a Knauer- UV K2501 detector, an Eclipse – XBD-C_{18} column (25 cm × 4.6 mm × 5 µm) and a Knauer-K1001 pump. An isocratic mobile phase consisted mobile phase A (phosphoric acid R, water R (0.5:99.5 V/V)), and mobile phase B (phosphoric acid R, acetonitrile R (0.5:99.5 V/V)); and its flow rate was 1.0 ml/min. The UV detection wavelength was 340 nm, injection volume was 20 µl [24].

2.3.6. Total phenol analysis

5 ml of distilled water and 1 g of the previously prepared chamomile products were added to the 10 ml volumetric flask. Then 0.5 ml of Folin-Ciocalteu reagent was added to the flask and after 3 min, 1 ml of the 20 % sodium carbonate solution was added to it. The mixture reaches 10 ml with distillated water. When the Folin-Ciocalteu reagent is added, the solution turned green and after adding sodium carbonate, the solution turned blue [25]. Finally, after one hour, the absorption of the solution at 725 nm is measured by the UV-vis device. This procedure was repeated three times. For the preparation of the calibration curve, all the above procedure was performed with gallic acid in five concentration (10, 50, 100, 250, 500 mg/ml). This procedure was repeated three times. For the preparation of the blank solution, all the above procedure was performed without the extract [25].

2.3.7. Total flavonoid analysis

1 g of the samples, was added into a 10 ml flask containing 4 ml of distilled water. Then 0.3 ml of sodium nitrite 5 % was added to it and mixed well. After 5 min, add 0.3 ml of 10 % aluminum chloride, which we have already prepared, and mix well. After 6 minutes, 2 ml of

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NaOH solution 1 M was added to it and shacked. Then, for making 10 ml solution, distilled water was added to it. Then, after 15 minutes, the absorption of the pink solution was measured at 510 nm. For preparation of the calibration curve, all the above procedure was performed on the rutin in five concentration (10, 50, 100, 250, 500 mg/ml). This procedure was repeated three times. For preparation of the blank solution, all the above procedure was performed without the extract [26].

3. Results

3.1. Thin layer chromatography

The R_f results of the thin-layer chromatographic identification test for the all products are given in the table 2 and 3. Based on the R_f values, the presence of chamomile compounds in the products C2, C5 and C6 is not confirmed. While, it is claimed that the product C6 is standardized as α-bisabolol.

According to the R_f values, the presence of thymol was confirmed in all thyme products except T3 and T8. Also, Carvacrol was detected in all samples except T6.

3.2. Optimization of DLLME method for assay determination

To quantify the amount of active ingredients by GC/MS, first, the samples were prepared based on the pretreatment method was mentioned in section 2-3-2. But the first, the pretreatment DLLME method should be optimized. To select the optimal conditions, various parameters such as extraction and dispersive solvents and the effect of electrolyte on the extraction efficiency of total thymol and carvacrol and also chamazulene as the quantitative indexes of thyme and chamomile products, respectively were investigated. It is noteworthy that to remove the matrix effects all samples were prepared and analyzed by internal standard methods.

To determine the best extraction solvent, the mixture of toluene: ethyl acetate (97:3), chloroform and dichloromethane for the thymol and carvacrol and the mixture of toluene: chloroform (1:3), chloroform and dichloromethane for chamazulene were investigated and the recovery of extraction procedure was investigated. Based on the obtained results (Fig. 1), the mixture of toluene and ethyl acetate and chloroform and dichloromethane were choosen as the best extraction solvents for thymol, carvacrol and chamazulene respectively.

The volume of extraction solvents (0.1, 0.2, 0.3, 0.5, 1.0 ml) were investigated for achieving the best extraction recovery. Toluene:ethyl acetate (97:3) with 0.2 ml and toluene:chloroform (1:3) with 0.3 ml were showed maximum extraction recovery.

Acetone, methanol, and acetonitrile were tested as the dispersive solvents. The mixture of 0.2 ml of toluene:chloroform (1:3) and toluene:ethyl acetate (97:3) with 1 ml of dispersive solvents were dispersed in 5 ml of the sample solutions of chamazulene and thymol and carvacrol, respectively. Then, after centrifugation 1 µl of the collected organic phase was injected into the GC/MS device. In both cases, acetone as a dispersive solvent showed the best extraction efficiency than other solvents (Fig. 2). Finally, acetone was selected as the dispersive solvent.

To investigate the salting-out effect on the extraction efficiency, NaCl salt with different concentrations was added to the sample solutions

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of thymol and carvacrol and also chamazulene and was not observed any effect on the extraction efficiencies.

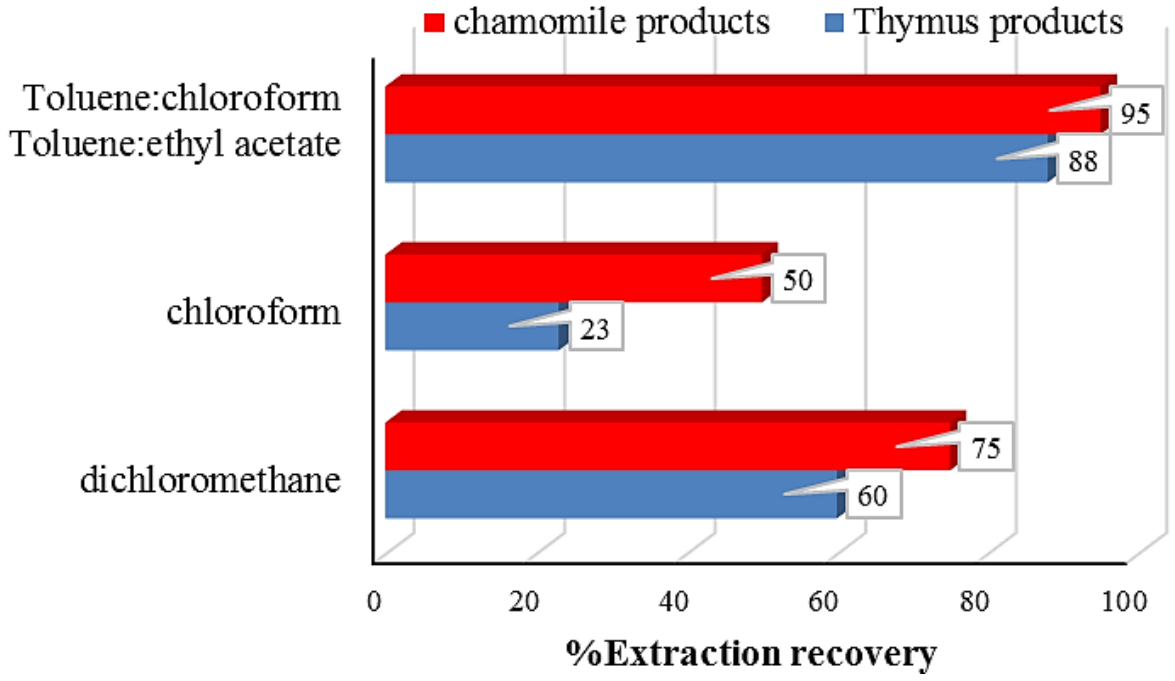
Optimal conditions according to the obtained results were 0.3 ml of extraction solvent, 1 ml of acetone as a dispersant solvent and no addition of salt.

Table 2. R_f values related to thin layer chromatographic tests of chamomile products

Standard components	R_f values of standards	Product codes								
		C1	C2	C3	C4	C5	C6	C7	C8	C9
Borneol	0.087	–	–	–	0.086	–	–	0.090	0.087	–
Bisabolol	0.175	–	–	0.167	0.172	–	–	–	–	0.172
Borneol acetate	0.38	–	–	–	0.34	–	–	0.37	0.38	–
Chamazulene	0.84	0.85	–	0.87	0.86	–	–	0.88	–	0.81

Table 3. R_f values related to thin layer chromatographic tests of T. *Vulgaris* products

Standard components	R_f values of standards	Product codes							
		T1	T2	T3	T4	T5	T6	T7	T8
Thymol	0.642	0.660	0.642	–	0.642	0.628	0.640	0.629	-
Carvacrol	0.607	0.612	0.602	0.603	0.603	0.581	–	0.601	0.584



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Fig. 1. Effect of different extraction solvents on the recovery of chamazulene (red diagram) and sum of thymol and carvacrol (blue diagram).

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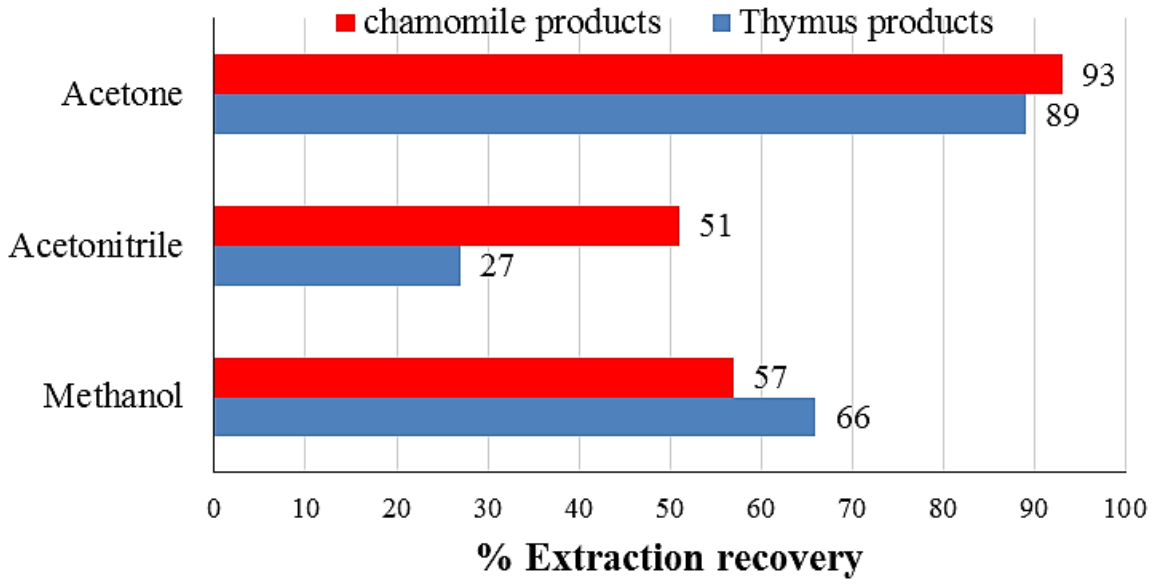


Fig. 2. Effect of different dispersive solvents on the recovery of chamazulene (red diagram) and sum of thymol and carvacrol (blue diagram).

4. Discussion

In one study, the quality assessment of marketed chamomile tea products were studied by HPTLC method and were founded, the chamomile tea bags sold on the market not only prepare with crude flowers but also to be adulterated with other plant materials [27]. In another study, a RP-HPLC-DAD method were validated for assessment of apigenin-7-glucoside in *Matricaria chamomilla* preparations [28].

In this study, all products were examined for microbial contamination and other, physicochemical properties, in two time periods the beginning of the preparation of the products and 6 months after preparation and storage at accelerated stability conditions (temperature of 40 °C under humidity 75 %). All results are listed in Table 4 and 5 for all products of chamomile and thyme, respectively.

In the case of chamomile products, according to the obtained results related to the identification test by TLC, only in C4 product, all the active ingredients of chamomile were detected. Regarding the C1, C7 and C8 brochures; chamazulene is mentioned as the main active ingredient but inconsistency with brochure information is evident in C8. In the C1, the amount of obtained chamazulene is less than the reported amount. According to the factory information, three solutions of C3, C5 and C7 have been standardized based on the apigenin. In the case of C5, the amount of obtained apigenin according to the results is about three times the reported amount and does not comply with the standardized amount on the brochure. The obtained amount of apigenin in C7 product doesn't confirm with the brochure information. Therefore, the amount of apigenin mentioned in the C3, C5 and C7 product brochure does not match to the obtained contents. In C2 product, standardization was performed based on the 0.14 mg of total flavonoids per ml of product, which obtained results was much higher than expected. In the stability study, C5 was sugared and sediment was observed at it.

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Table 4. All quality control results of chamomile products (0 month)

Product code	Physical properties			Appearance		Assay of active ingredients				
	Density (g/ml)	pH	Moisture (% w/w)	Odor & taste	color	Bisabolol oxide B	α-bisabolol	Chamazulene	Bisabolol oxide A	Apigenin
C1	1.009	5.68	94.0	chamomile - bitter	Dark brown	0.019 %	ND[a]	0.005%	0.152 %	-
C2	1.014	6.30	96.5	chamomile - bitter	Dark brown	ND	ND	ND	0.084 %	-
C3	1.077	6.43	97.8	chamomile - bitter	brown	0.0268 %	0.045 %	0.009 %	0.298 %	0.6 mg/100 ml
C4	1.596	7.00	7.00	chamomile	white	ND	ND	ND	ND	-
C5	1.253	4.41	85.0	sweet - chamomile	Light green	ND	ND	ND	0.0428	0.57 mg/ml
C6	0.535	7.20	8.20	chamomile	milky	ND	ND	ND	ND	-
C7	1.620	6.40	57.12	chamomile	Greenish milky	0.005 %	ND	0.003%	0.003 %	0.003 mg/g
C8	0.652	7.33	8.20	chamomile	Light yellow	ND	ND	ND	ND	-
C9	0.862	7.44	2.98	chamomile	Colorless	ND	0.002 %	0.003 %	0.019 %	-

[a] Not detected.

Table 4. All quality control results of chamomile products (0 month) (Continued)

Product code	Microbial tests					
	Total Plate Count	Yeast & Mold	*Escherichia coli*	Salmonella spp.	*Staphylococcus aureus*	*Pseudomonas aeruginosa*
C1	< 10	< 10	Negative	Negative	Negative	Negative
C2	170	< 10	Negative	Negative	Negative	Negative
C3	81	< 10	Negative	Negative	Negative	Negative
C4	< 10	< 10	Negative	Negative	Negative	Negative
C5	< 10	< 10	Negative	Negative	Negative	Negative
C6	< 10	< 10	Negative	Negative	Negative	Negative
C7	< 10	< 10	Negative	Negative	Negative	Negative
C8	< 10	< 10	Negative	Negative	Negative	Negative
C9	< 10	< 10	Negative	Negative	Negative	Negative

Table 5. All quality control results of *T. vulgaris* products (0 month)

Product code	Physical properties		Appearance		Assay of active ingredients	
	Density (g/ml)	pH	Odor &taste	Color	Thymol (mg/L)	Carvacrol (mg/L)
T1	1.33	4.84	Sweet & bitter	Light brown	168.2	24.5
T2	1.33	4.43	sweet and sour	Light brown	184.6	10.2
T3	1.32	5.84	Sweet & bitter	Light yellow	14.8	56.8
T4	1.36	4.44	Sweet & bitter	Light brown	58.3	35.4
T5	1.35	5.90	Sweet & bitter	Dark brown	51.6	55.4
T6	1.27	4.8	sweet and sour	Light yellow	34.5	4.95
T7	1.23	5.67	sweet and sour	Light yellow	44.7	32.8
T8	1.34	4.67	Sweet & bitter	Light brown	7.7	18.8

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Table 5. All quality control results of *T. vulgaris* products (0 month) (Continued)

Product code	Microbial tests					
	Total Plate Count	Yeast & Mold	*Escherichia coli*	Salmonella spp.	*Staphylococcus aureus*	*Pseudomonas aeruginosa*
T1	54	< 10	Negative	Negative	Negative	Negative
T2	100	< 10	Negative	Negative	Negative	Negative
T3	< 10	< 10	Negative	Negative	Negative	Negative
T4	< 10	< 10	Negative	Negative	Negative	Negative
T5	< 10	< 10	Negative	Negative	Negative	Negative
T6	< 10	< 10	Negative	Negative	Negative	Negative
T7	< 10	< 10	Negative	Negative	Negative	Negative
T8	< 10	< 10	Negative	Negative	Negative	Negative

Accelerated stability condition, which indicates the instability of the product. Topical C2, C3 and C1 were precipitated at low temperature.

During the accelerated stability period, the amount of their active ingredients of T1, T2 and T5 products, was stable. Also during the stability time, no significant changes were observed in the density values of any of the products. All samples were clear and free of turbidity, and their taste, odor and color were evaluated, which did not change during the accelerated stability test. However, it should be noted that products with codes of T1, T3 and T5 in very small amounts, T4 in moderate amounts and T8 with high were observed sugar intensity. This makes it difficult to open the bottle cap and can lead to rejection by the consumer. Low-temperature deposition, indicates the instability of the product formulation in changes in ambient temperature, which was not observed in any of the products, even during the stability period.

5. Conclusion

In the case of chamomile products, liquid products showed less chemical and physical stability compared to other investigated ointments and creams. C9 ointment had the highest stability among all products containing essential oil or extract of the chamomile. In some thymus products, the reported amount of the standardized compound did not match the obtained values. Not mentioning the amount of active ingredients on the label of some products is a weakness in providing information and labeling. Also, based on the matrix and dosage form of the products, special validated methods for pretreatment and analysis of the active ingredients are needed. More care in PMS control of the herbal medicines for better and more appropriate quality and effective consumption of herbal medicines is recommended. In addition to using high-quality initial materials with the proper amounts of active ingredients, manufacturers must also use appropriate other ingredients that protect the main ingredients, such as antioxidants, in the dosage forms. Therefore, according to the obtained results, it is suggested that the PMS investigation be taken seriously, especially for high-consumption products.

Author contributions

F. T. & Sh. R.: Investigation, Data curation, Supervision, F. T: Scientific adviser, M. SV. Gh.: HPLC operator, M. A. & M. S.: Data analysis,

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M. P., A. J. & D. Y.: Review & Editing the original draft.

Conflict of interests

The authors declare that they have no known competing financial interests or personal relationships that could appear to influence the work reported in this paper. The authors alone are responsible for the content of the paper.

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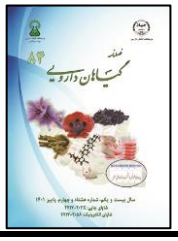
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کنترل پس از ورود به بازار محصولات بابونه و آویشن با روش‌های مرجع و توسعه یافته

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اطلاعات مقاله

گل‌واژگان:
آویشن
بابونه
ارزیابی پس از فروش
میکرو استخراج
محصولات طبیعی
آزمایشات کنترل کیفی

چکیده

مقدمه: نظارت پس از فروش، بخشی جدایی‌ناپذیر از ارزیابی ایمنی مداوم برای محصولات بهداشتی و فرآورده‌های دارویی طبیعی است. بابونه و آویشن پرمصرف‌ترین گیاهان در فرآورده‌های دارویی گیاهی هستند. گونه‌های آویشن حاوی ترکیبات فنلی مانند تیمول، کارواکرول و ترپنوئیدها، فلاونوئیدها و ساپونین‌ها هستند. آویشن ضد عفونی‌کننده و ضد سرفه است، بنابراین در درمان سرفه‌های خشک، سرماخوردگی و التهاب مجاری تنفسی فوقانی بسیار موثر است. فرآورده‌های بابونه حاوی آپیژنین-۷-گلیکوزید، مقداری فلاونوئید و کامازولن در اسانس آن است که خواص درمانی ضد التهابی، ضد قارچی و ضد باکتریایی دارد. **هدف:** در این مطالعه، اشکال دارویی مختلف حاوی آویشن (۸ فرآورده) و بابونه (۹ فرآورده) به صورت جداگانه (که به صورت قطره، شربت، پماد و کرم موجود است) خریداری شد. سپس کنترل‌های فیزیکوشیمیایی بر اساس روش‌های مرجع داروسازی‌های گیاهی و روش‌های معتبر داخلی برای اطمینان از کیفیت و پایداری این محصولات انجام شد. **روش بررسی:** از آنجایی که بسیاری از این فرآورده‌ها مونوگراف خاصی در داروسازی ندارند، روش‌های استخراج و آنالیز معتبر برای تعیین کمیت آپیژنین-۷-گلیکوزید با کروماتوگرافی مایع با کارایی بالا و کامازولن به وسیله کروماتوگرافی گازی در فرآورده‌های بابونه و تیمول و کارواکرول به وسیله کروماتوگرافی گازی در محصولات آویشن در اشکال مختلف دوزاژ پیچیده، توسعه داده شد. **نتایج:** در برخی از محصولات آویشن و بابونه، مقدار گزارش شده برای استانداردسازی با مقادیر به دست آمده مطابقت نداشت. **نتیجه‌گیری:** توصیه می‌شود برای مصرف مناسب و مؤثر داروهای گیاهی کنترل بیشتری انجام شود.

مخففها: DLLME، میکرو استخراج مایع- مایع پخشی؛ GC/MS، کروماتوگرافی گازی متصل به طیف‌سنج جرمی؛ HPLC، کروماتوگرافی مایع با کارایی بالا؛ LOD، باقیمانده خشک؛ PMS، کنترل پس از ورود به بازار؛ TLC، کروماتوگرافی لایه نازک

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