



Formulation optimization of the powder for suspension of flaxweed seeds (*Descurainia sophia* L.), a Persian medicinal drink

Optimizacija formulacije praha za suspenziju od semena biljke *flaxweed* (*Descurainia sophia* L.), persijskog lekovitog napitka

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Abstract

Background/Aim. Flaxweed (*Descurainia sophia* L.) beverage has been used in Persian medicine as an effective remedy for constipation. Allyl isothiocyanate (AITC), the main ingredient of flaxweed essential oil, has been claimed to regulate gastrointestinal contractility. The aim of the study was to stabilize the flaxweed beverage, enhance its flavor, and determine the AITC content in the flaxweed seeds (FS). **Methods.** To prepare a stable formulation of flaxweed with desirable organoleptic properties, the optimal amount of tragacanth as a stabilizer, stevia as a sweetener, and lime and cinnamon powders as flavoring agents were mixed with flaxweed solution. The shelf lives of the suspensions at room temperature (25 °C) and refrigerator temperature (5 °C) were evaluated. The viscosity and pH of the suspensions were also investigated. Finally, flaxweed essential oil was obtained using the Clevenger apparatus. The amount of AITC in FS essential oil was determined by gas chromatog-

raphy coupled with mass spectroscopy (GC-MS). **Results.** Based on our findings, two formulas, including FS (5 g), stevia (3 g), cinnamon (300 mg) or lime (400 mg), and 100 mL of water, had the optimum textural and organoleptic properties. Furthermore, adding 0.5% tragacanth gum as a suspending agent was able to stabilize the FS beverage. From 200 g of FS, 0.14 mL of essential oil was extracted, which corresponded to 0.07% (v/w). GC-MS analysis revealed that each 100 g of FS contained 24.85 mg of AITC, equating to 0.025% w/w AITC. **Conclusion.** Due to the presence of AITC in FS and the favorable characteristics of the FS suspension, this formulation, in the form of a sachet, can be suggested as an herbal supplement product for industrial production.

Key words: beverages; constipation; dietary supplements; herbal medicine; plants, medicinal; plant weeds; seeds; suspensions; tragacanth.

Apstrakt

Uvod/Cilj. Napitak od biljke *flaxweed* (*Descurainia sophia* L.), koristi se u persijskoj medicini kao efikasan lek za konstipaciju. Smatra se da alil izotiocijanat (AITC), glavni sastojak eteričnog ulja biljke *flaxweed*, reguliše gastrointestinalnu kontraktinost. Cilj rada bio je da se uradi stabilizacija i poboljša ukus napitka od biljke *flaxweed*, kao i da se utvrdi sadržaj AITC u semenkama ove biljke. **Metode.** Da bi se pripremila stabilna formulacija biljke *flaxweed* sa poželjnim organoleptičkim svojstvima, optimalna količina tragakanta kao stabilizatora, stevije kao zaslađivača i praha limete i cimeta kao arome, pomešana je sa rastvorom biljke *flaxweed*. Procenjavani su rokovi trajanja suspenzija na sobnoj temperature (25 °C) i temperaturi u frižideru (5 °C). Takođe su ispitivani i viskozitet i pH suspenzija.

Konačno, eterično ulje biljke *flaxweed* dobijeno je pomoću aparata Clevenger. Količina AITC u eteričnom ulju semena biljke *flaxweed* određena je gasnom hromatografijom u kombinaciji sa masenom spektrometrijom (GH-MS). **Rezultati.** Na osnovu naših nalaza, dve formule, koje su uključivale seme biljke *flaxweed* (5 g), steviju (83 g), cimeta (300 mg) ili limetu (400 mg) i 100 mL vode, imale su optimalnu teksturu i organoleptička svojstva. Takođe, dodavanje 0,5% tragakant gume kao sredstva za suspendovanje, omogućilo je da se napitak od semena biljke *flaxweed* stabilizuje. Iz 200 g semena ove biljke, ekstrahovano je 0,14 mL eteričnog ulja, što je odgovaralo 0,07% (v/w). Analizom pomoću GH-MS otkriveno je da svakih 100 g semena biljke *flaxweed* sadrži 24,85 mg AITC, što odgovara 0,025% w/w. **Zaključak.** Zbog prisustva AITC u semenu biljke *flaxweed* i povoljnih karakteristika

suspenzije semena ove biljke, ta formulacija se u obliku kesice može predložiti kao biljni dodatak za industrijsku proizvodnju.

Ključne reči:

napici; opstipacija; ishrana, dopune; fitomedicina; biljke, lekovite; korovi; seme; suspenzije; tragakant.

Introduction

Descurainia sophia (L.) Webb ex Prantl (DS), with the common name of flixweed, belongs to the Brassicaceae family^{1,2}. In Persian medicine (PM), it is named *khobbah*, *khaksheer*, and *khakshee*^{3,4}.

The main ingredients of the fixed oil from the seeds of flixweed are fatty acids, including oleic, erucic, linolenic, linoleic, palmitic, and stearic acid. However, monoterpenes, sesquiterpenes, and their derivatives are the major constituents in aerial parts⁵. In addition, the volatile oils of flixweed seed (FS) contain benzyl, allyl, propenyl isothiocyanate, and allyl disulfide⁶.

Allyl isothiocyanate (AITC) or mustard oil is the most prevalent natural thiocyanate. AITC, with the chemical formula $\text{CH}_2 = \text{CHCH}_2\text{N} = \text{C} = \text{S}$, is a yellowish oily compound insoluble in water with a boiling point of 152 °C. Various techniques, including spectroscopic, silver nitrate titration, and chromatographic approaches, have been reported for determining AITC⁷⁻⁹. However, gas chromatography (GC) is mainly used for measurements of isothiocyanates in samples of plant origin¹⁰⁻¹².

Anticancer¹³, antioxidant¹⁴, analgesic, anti-inflammatory¹⁵, gastric antiulcer¹⁶, and chemopreventive properties¹⁷ are the different beneficial effects of AITC, which various studies have illustrated. Capasso et al.¹⁸ investigated the effects of AITC on gastrointestinal motility in mice. Their *in vitro* experiments demonstrated that AITC decreased contractility in the ileum while promoting contractions in isolated colonic smooth muscle. *In vivo*, AITC was found to reduce upper gastrointestinal transit following intraperitoneal injection but enhance motility when administered intragastrically. Their research indicated that AITC could either stimulate or inhibit motility, depending on the specific area of the gut and the method of administration. Interestingly, these effects were shown to be independent of transient receptor potential ankyrin 1 (TRPA1), a receptor known to regulate gastrointestinal contractions. Additionally, Kojima et al.¹⁹ confirmed AITC may be effective on both types of atonic and spastic constipation induced by clonidine and loperamide, respectively.

According to the reports in the manuscripts of PM, flixweed has several therapeutic advantages. The seeds are aphrodisiacs and digestive tonics, possess appetizing properties, and facilitate childbirth. Not only does PM highlight the therapeutic benefits of medicinal plants, but it also investigates their potential side effects. Furthermore, it proposes suitable interventions to alleviate these adverse effects. In the description of flixweed, headache is introduced as a potential side effect, which can be alleviated by applying tragacanth. Additionally, topical dosage forms of flixweed, whether used alone or in combination with other

medications, have been employed in the treatment of conditions such as uterine wounds, mastitis, gout, eye ulcers, testicular swelling, and cancer^{3,4}. Dr. Ahmadi²⁰, in his book *Raze Darman* (Secret of treatment), has prescribed DS as an effective remedy for the evacuation of black bile (soda) from the body as a main cause of diseases such as palpitation, eczema, low libido in men and women, dyspepsia, varicose veins, hematologic diseases, varicoceles, constipation, and hemorrhoids. Moreover, different pharmacological effects of flixweed have been addressed by several studies, including antiasthmatic^{21,22}, anti-tussive and expectorant²³, antioxidant²⁴, antipyretic and analgesic²⁵, as well as anti-inflammatory properties²³⁻²⁵. Furthermore, its role in the treatment of constipation²⁶⁻²⁸ and its cardioprotective²⁹, anthelmintic³⁰, cytotoxic³¹, anti-hyperthyroid³², and antidiuretic qualities³³, as well as the ability to alleviate thirst, have been stated³⁴.

Constipation is one of the most common gastrointestinal complaints³⁵. Flixweed remedy (made of flixweed, hot water, and sugar) has been introduced in PM as an effective intervention in constipation²⁰. Despite health benefits, instability due to the precipitation of FS is one of the most important challenges for the commercial production of beverages as a supplementary remedy for constipation.

Due to the lack of medicinal products from flixweed in the pharmaceutical market, the aim of this study was to design an oral dosage form of flixweed and examine its physicochemical properties. For the determination of AITC in the extracted essential oils of FSs, GC coupled with mass spectrometry – MS (GC-MS) was used.

Methods

FSs, tragacanth and acacia gums, stevia, red sugar, cinnamon (*Cinnamomum verum* J. Presl) bark, lime [*Citrus aurantifolia* (Christm.) Swingle] fruit, and damask rose (*Rosa damascena* Mill.) flower powder were purchased from an herbal medicine shop in Rasht, Iran. The standard form of AITC was purchased from Titrachem Co. All formulations were prepared with deionized water. A voucher specimen of FS (GUMS-D2) was deposited at the Herbarium of the School of Pharmacy, Guilan University of Medical Sciences, Rasht, Iran. This study was approved by the Ethics Committee of Guilan University of Medical Sciences on May 19, 2021 (No. IR.GUMS.REC.1400.068).

Essential oil extraction

Due to the presence of AITC in flixweed, for this study, we used the Clevenger apparatus and water distillation method to extract the essential oil. Flixweed in the

amount of 200 g was powdered and added to a round-bottom flask, and then distilled water was added. The optimum essential oil amount was obtained after 3 hrs.

Gas chromatography – mass spectroscopy analysis

GC-MS analyses were performed using an Agilent gas chromatograph (Agilent Technologies 7890B) equipped with an HP-5MS fused silica column (5% phenyl methyl polysiloxane 30 m × 0.25 mm i.d., film thickness 0.25 µm), interfaced with an Agilent mass selective detector 5977B (Agilent Technologies, USA) operated by Agilent MassHunter data acquisition software. The oven temperature program initiated at 50 °C rose at 15 °C/min to 180 °C. Other operating conditions were as follows: carrier gas, helium (He) (99.999%), with a flow rate of 1 mL/min; injector temperature 200 °C; split ratio 1 : 20; mass spectra were taken at 70 electronvolts (eV) and solvent delay 1.7 min; the mass range was from 30–200 atomic mass units (AMU).

The extracted essential oil in the amount of 10 µL was mixed with 10 µL of internal standard (anisole) and finally diluted with methanol up to 10 mL. Subsequently, 1 µL of the solution was analyzed by GC-MS. The concentration of AITC in the FSs was assessed using the internal standard calibration curve (300–900 ppm).

Formulation of powder for suspension of flixweed seeds

First, flixweed was formulated as a suspension in order to figure out the appropriate ingredients and their quan-

ties. Then, the optimized ingredients were utilized as a dry homogenous powder dosage form to be packaged as “flixweed powder for suspension”.

Selection and optimization of proper suspending agent

Tragacanth and acacia gums were evaluated as the viscosity modifying and suspending agents in order to stabilize the flixweed suspension and elongate the sedimentation rate for at least 24 hrs. Various concentrations of tragacanth and acacia were hydrated and stirred in distilled water overnight to form a homogenous colloidal dispersion (Table 1). To figure out the minimum required concentration of gums for suspending the FSs, 5% w/v flixweed was added to each medium.

Selection and optimization of proper sweetener and flavoring agent

The selected basic formulation containing gum and flixweed was subjected to stevia and red sugar as natural sweeteners, alone and in combination. After optimization of the sweetening agent, cinnamon, lime, and rose flower powder were utilized as natural flavoring agents (Table 1).

Taste and physicochemical evaluation of flavored formulations

Two optimized final formulations were subjected to a taste panel study: O₂ containing 0.3% w/v cinnamon and O₄ containing 0.4% w/v lime (Table 1). The panel consisted of eight healthy, non-smoking volunteers aged 23–67 years,

Table 1

Formulation optimization of flixweed suspension ingredients (%)

BF	Flixweed seed	Tragacanth	Acacia	Stevia	Red sugar	Cinnamon	Lime	Rose	DW
S ₁	5	0.1	0	0	0	0	0	0	100
S ₂	5	0.5	0	0	0	0	0	0	100
S ₃	5	1	0	0	0	0	0	0	100
S ₄	5	0	1	0	0	0	0	0	100
S ₅	5	0	3	0	0	0	0	0	100
S ₆	5	0	4	0	0	0	0	0	100
K ₁	5	0.5	0	1	0	0	0	0	100
K ₂	5	0.5	0	3	0	0	0	0	100
K ₃	5	0.5	0	5	0	0	0	0	100
K ₄	5	0.5	0	0	1	0	0	0	100
K ₅	5	0.5	0	0	3	0	0	0	100
K ₆	5	0.5	0	0	5	0	0	0	100
K ₇	5	0.5	0	1.5	2.5	0	0	0	100
K ₈	5	0.5	0	2.5	2.5	0	0	0	100
O ₁	5	0.5	0	3	0	0.2	0	0	100
O ₂	5	0.5	0	3	0	0.3	0	0	100
O ₃	5	0.5	0	3	0	0	0.2	0	100
O ₄	5	0.5	0	3	0	0	0.4	0	100
O ₅	5	0.5	0	3	0	0	0	0.2	100
O ₆	5	0.5	0	3	0	0	0	0.3	100

BF – basic formulation; DW – distilled water.

both male and female. Panel members were asked to rate the taste and aftertaste using the following scale: 0 (undesired) to 5 (ideal). All members tasted both formulations with a washing time of 24 hrs.

Suspension viscosity was measured for the finally selected formulation with the 0.5% w/v concentration of tragacanth as the suspending agent 24 hrs after preparation (Brookfield DVI-Prime, USA) at room temperature.

The pH of the final formulation was measured using a pH meter (QIS, Proline B210, Oosterhout, Netherlands) at 25 °C with three replicates.

The stability of organoleptic properties (visual examination, smell, taste) of the formulations was checked at 5 °C and 25 °C at 24 and 48 hrs.

Results

The minimum required concentrations of tragacanth and acacia that stabilized the FSs suspension were 0.5% and 3.5% w/v, respectively. Since a 3.5% acacia solution presented a high viscosity, which is undesirable for a drink, 0.5% tragacanth was considered the optimal suspending agent for this product. Hence, formulation S₂ was selected for sweetener optimization.

Stevia and red sugar produced a desired sweet taste with at least 3% and 5% w/v, respectively. As red sugar was only available in paste form, it could not be used in powder dosage form, therefore, 3% stevia was used as the favorable sweetener (formulation K₂).

Flavoring agents, including cinnamon, lime, and rose flower powder, could successfully create an eligible taste, masking the undesired flavor of flixweed with minimum amounts of 0.3%, 0.4%, and 0.1% w/v, respectively. De-

spite the desirable flavor of rose flowers, the fine particles disfigured the suspension. Consequently, the two final formulations, O₂ and O₄, were subjected to a taste panel study.

The mean scores for taste and aftertaste of formulation O₂ (cinnamon flavor) were 4 ± 0.961 and 3.5 ± 0.534 , and for formulation O₄ (lime flavor), they were 4.5 ± 0.534 and 4 ± 0.462 , respectively (Figure 1). However, the difference was not statistically significant. Due to its higher taste score, O₄ was selected as the final formulation for further evaluation.

The viscosity and pH of O₄ as finally selected formulation were reported to be 974 centipoise (cps) and 5.54 ± 0.012 at room temperature.

Formulations were stable at 24 hrs at 5 °C and 25 °C, and no changes in color, smell, or taste were observed. Moreover, the FSs remained suspended. However, after 48 hrs of storage at both temperatures, an unpleasant bitter smell was detected.

Allyl isothiocyanate content of flixweed seeds

A calibration curve was created using four standard solutions with concentrations of 300 ppm, 500 ppm, 750 ppm, and 900 ppm. The analytical response was determined by the peak area ratio of AITC compared to anisole (at 1,000 ppm). The R-squared (R^2) value for the calibration curve (Equation 1) was 0.994.

The equation is: $y = 0.0007x - 0.1624$; $R^2 = 0.944$ Eq.(1). Figure S1 (in the Supplementary materials) displays the total ion currents (TIC) for the standard solutions, while the calibration curve for AITC is shown in Figure S2. Figure S3 shows the flow of the formulation optimization of powder for suspension of FS.

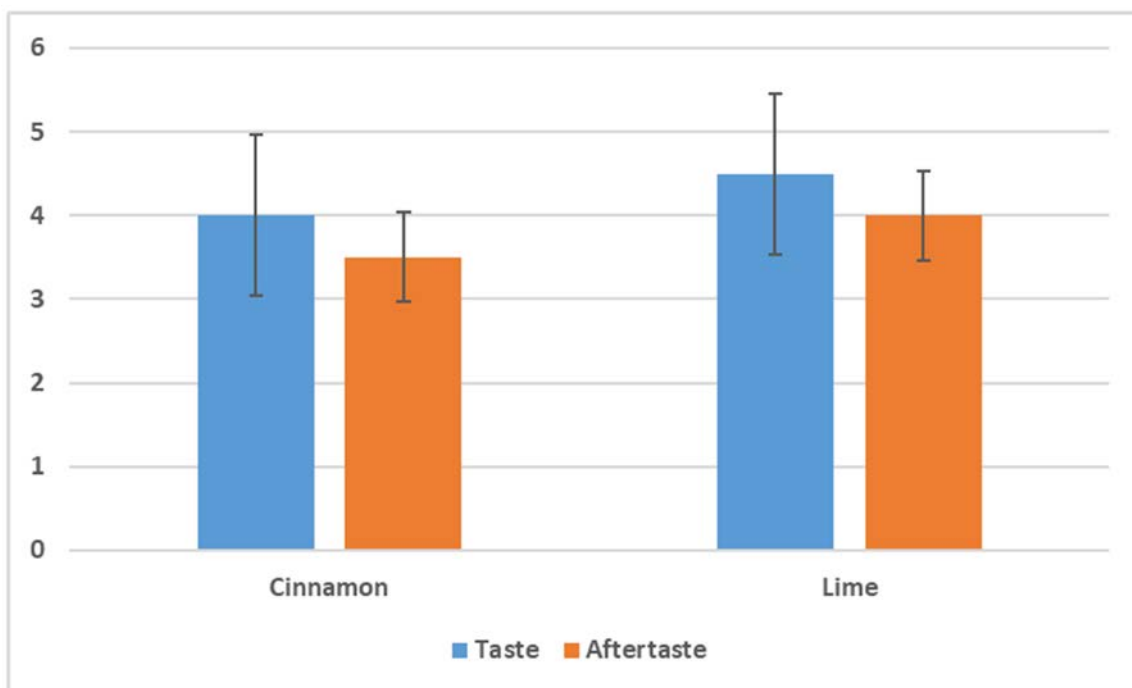


Fig. 1 – Taste panel scores for O₂ (cinnamon) and O₄ (lime) flavors of flixweed seed suspensions. Note: Scale ranges from 0 (undesirable) to 5 (ideal).

Supplementary materials:

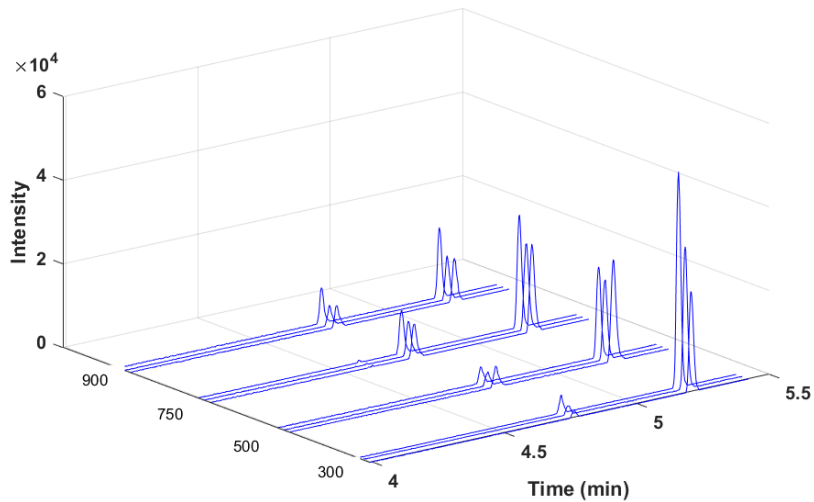


Fig. S1 – Total ion currents of standard AITC solutions at different concentrations (300, 500, 750, and 900 ppm) replicated three times. AITCs came out around 4.76 min while anisole emerged around 5.21 min. AITC – allyl isothiocyanate.

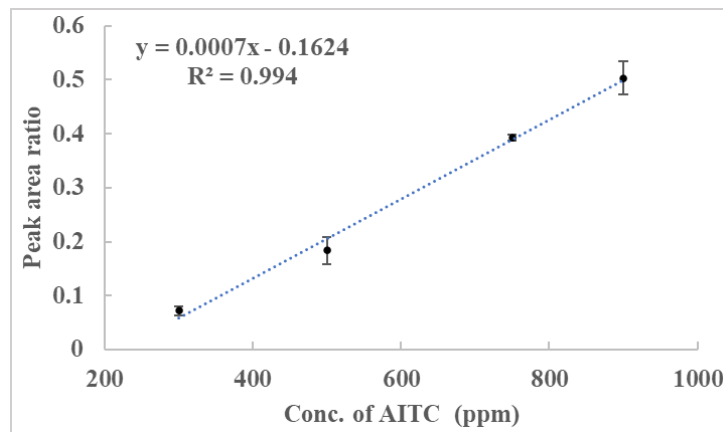


Fig. S2 – Calibration curve of AITC standards. Error bars present standard deviation based on three replicates. Conc. – concentration; AITC – allyl isothiocyanate; ppm – part per million.

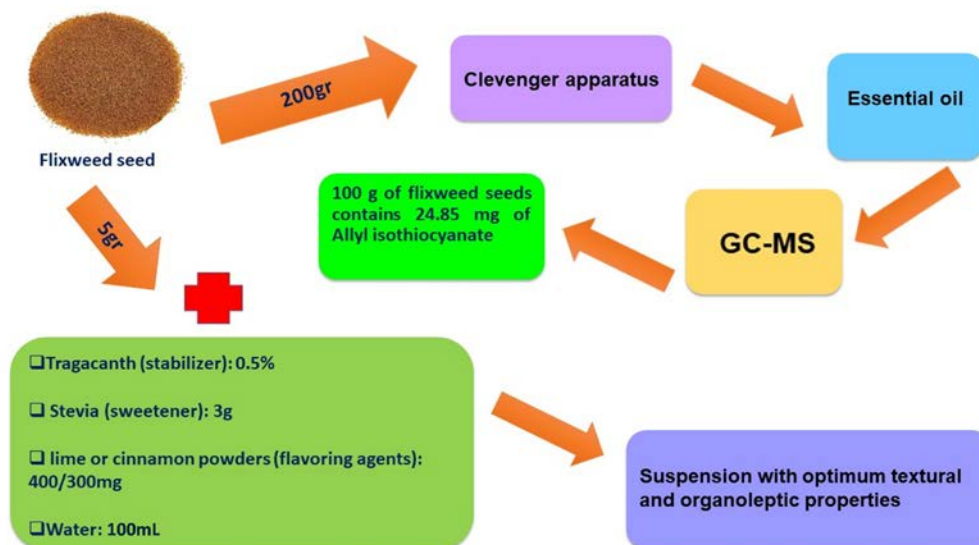


Fig. S3 – The process of formulation optimization of the powder for suspension of flixweed seeds. GC-MS – gas chromatography coupled with mass spectroscopy.

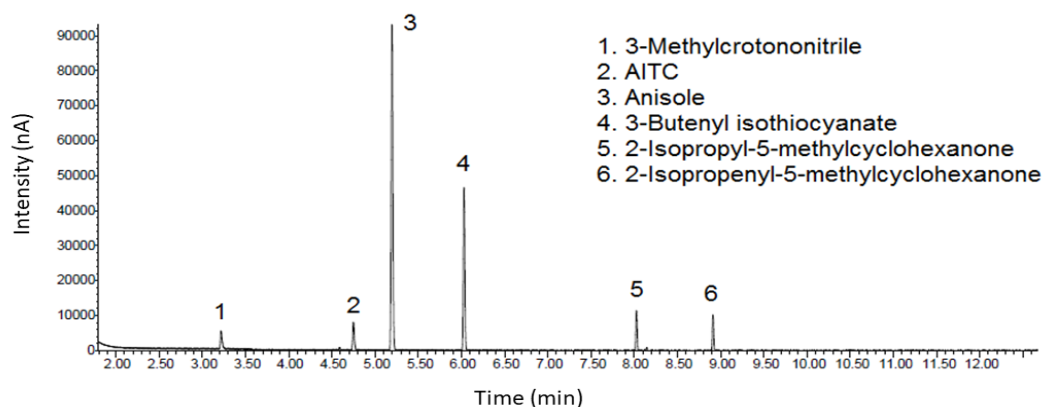


Fig. 2 – Total ion current of flixweed seeds essential oil. The chromatographic peaks represent: 1) 3-methylcrotonitrile; 2) allyl isothiocyanate (AITC); 3) anisole; 4) 3-butenyl isothiocyanate; 5) 2-isopropyl-5-methylcyclohexanone; 6) 2-isopropenyl-5-methylcyclohexanone.

From 200 g of FSs, 0.14 mL of essential oil was extracted, which corresponded to 0.07% v/w. The essential oils of FSs were also analyzed by GC-MS, as shown in Figure 2.

The identity of each peak was assigned using a National Institute of Standards and Technology (NIST) library search. The data revealed that 100 g of FS contained 24.85 mg of AITC, indicating that there was a 0.025% w/w concentration of AITC in the FS.

Discussion

The main objective of this study was to stabilize the flixweed beverage and improve its flavor. Based on our findings, two optimal formulas for the beverage were identified. These formulas included FS (5 g), stevia (3 g), and either cinnamon (300 mg) or lime (400 mg) mixed with 100 mL of water. These formulas exhibited the best textural and organoleptic properties. Additionally, including 0.5% tragacanth gum as a suspending agent stabilized the FS suspension effectively. It has been suggested that tragacanth gum may alleviate the potential side effects associated with FS, as mentioned in the previous studies^{3,4}. However, further research is necessary to provide more evidence for this claim.

Considering the recommended dose of FS in PM texts^{3,4}, a 10 g sachet of flixweed (along with the required ingredients) would be a desirable dosage form, leading to increased stability. In PM, the flixweed drink has been traditionally prescribed as a cold or hot syrup, serving as a cooling or laxative agent, respectively²⁵. Therefore, the designed sachet can be recommended for dual therapeutic goals in line with these traditional practices.

According to the study conducted by Mohamed and Mahrous²⁵ in 2009, FS has been determined to be non-toxic up to a dosage of 2,500 mg/kg of body weight. This finding provides valuable information about the safety of FS when used within the recommended dosage range.

In the field of flixweed formula research, numerous studies have been undertaken to investigate the utilization of different ingredients as flavoring agents or stabilizers.

In their study, Hojjati et al.³⁶ demonstrated that the optimal formulation for a flixweed drink consisted of 5% seed, 6% sugar, and 4% grape syrup. Furthermore, they found that incorporating a concentration of 0.3% xanthan gum effectively prevented the separation of the syrup phase during a thirty-day storage period.

Behbahani and Abbasi³⁷ investigated the impact of different concentrations of two native gums, Persian gum and gum tragacanth, along with their soluble and insoluble fractions, on the stabilization of a Persian refreshing drink containing flixweed or London rocket seeds (5% wt), basil seeds (0.5% wt), and sucrose (10% wt). Additionally, they examined the effect of ferric chloride (FeCl_3) on the rheological and sensory properties of the drink. The results revealed that the insoluble fraction of Persian gum at a concentration of 0.8% wt, the soluble fraction of gum tragacanth at 0.05% wt, and the insoluble fraction of gum tragacanth at 0.14% wt were effective in stabilizing flixweed in the syrup. Additionally, the presence of FeCl_3 at a concentration of 0.0025 mol/L induced the formation of a reversible gel when combined with the soluble fraction of gum tragacanth. In terms of sensory characteristics, the drink stabilized with the soluble fraction of gum tragacanth at a concentration of 0.05% wt, demonstrating the highest similarity to the control sample.

In another study, Hassanpour et al.³⁸ determined that a mixture of xanthan-guar gum and xanthan gum at a concentration of 0.05 g/L had the most favorable effect on stabilizing flixweed particles in a suspension containing 15 g seed, 25 g sugar, and 250 mL of water.

To determine the content of AITC, FS essential oil extraction was done with a yield of 0.07% v/w. In the study by Dekić³⁹, the percentage of extracted essential oil from fresh plants was 0.022% w/w. In a study conducted by Li et al.⁵, the essential oil obtained from the entire aerial parts of the flixweed plant varied from 0.26% to 0.31%. Ara et al.⁴⁰ extracted essential oil from FS with a yield of 0.25% v/w. This difference can be related to the difference in the collection place of the plant, the time passed since the collection time, and the extraction method. Li et al.⁵ proved in their study

that plant growth in different geographical areas significantly affects the amount and content of essential oil. Different ecological environments, weather conditions, and other biological factors can cause the observed difference.

Our research found that AITC constituted 24.85% w/w of the total essential oil extracted from FSs. In a study by Dekić³⁹, it was noted that AITC made up 0.3% of the essential oil derived from the underground parts of flixweed. However, there was no specific information regarding the presence or amount of AITC in the aerial parts or seeds of the plant. It is important to note that in Dekić's³⁹ research, the reported AITC content was based on the peak area of AITC relative to the total peak area of the TIC. On the contrary, we determined the content using a calibration curve, which is a more reliable method. In our study, the peak area percentage of AITC was measured at 3.47%, based on three replicates. One possible reason for the differences in results may stem from the various plant parts used or differences in the geographic locations of the plants studied and extraction methods employed. In addition to AITC, several other compounds were detected in the prepared essential oil, with their peak area percentages relative to the TIC presented in parentheses: 3-methylcrotonitrile (3.05%), 3-butenyl isothiocyanate (18.28%), 2-isopropyl-5-methylcyclohexanone (3.77%), and 2-isopropenyl-5-methylcyclohexanone (3.24%). Among these compounds, 3-butenyl isothiocyanate was found to be the predominant component in the essential oil. This means that it was present in the highest concentration compared to the other detected compounds.

In a study by Brema et al.⁴¹, the essential oil composition of two species, *Brassica cretica* and *Brassica insularis*, from

the Brassicaceae family was analyzed using GC-MS. The results revealed that 3-butenyl isothiocyanate was the second dominant compound in the essential oil of both species.

According to Dekić et al.³⁹, 3-butenyl isothiocyanate was identified in flixweed's underground parts and constituted 27.3% of the total essential oil. However, it was not found in the aerial parts of the plant. This finding suggests that the composition and concentration of compounds can vary between different parts of the flixweed plant.

Conclusion

In the presented study, a flixweed seed suspension with desirable sensory properties and stability was formulated. It was found that a 10 g sachet was a suitable dosage form with stable organoleptic properties. A natural stabilizer was also identified, which could stabilize this supplementary drink and potentially alleviate the adverse effects of flixweed. Additionally, allyl isothiocyanate was quantitatively determined in the formulation. Based on the presence of allyl isothiocyanate in flixweed seeds and the acceptable stability, organoleptic properties, pH, and viscosity of the flixweed seed suspension, it can be suggested that this formulation in the form of a sachet is suitable for industrial production as an herbal supplement product.

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