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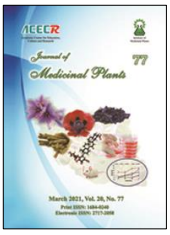

Research Article

Polyherbal tablet based on Iranian traditional medicine

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ABSTRACT

Background: Medicinal plants have important role for prevention and treatment of diseases regarding their traditional uses. In Iranian traditional medicine (ITM), herbal medicines have been considered as the key agents in the treatment of wide ranges of disorders. Traditional preparations can be reformulated to achieve pharmacopoeia standards as modern medicines. **Objective:** In this research, a polyherbal tablet namely "Monzej-e-balgham", which is widely used for treating different diseases, has been formulated and quality control assessments have been done to present a proper formulation. **Methods:** *Glycyrrhiza glabra* L., *Rosa x damascena* Herrm., *Adiantum capillus-veneris* L., *Onopordum acanthium* L., *Vitis vinifera* L., *Ficus carica* L. and *Foeniculum vulgare* Mill. were extracted with water, filtered, concentrated and dried with spray drying method. Thirteen tablets formulations by direct compression and pre- and post- formulation analyses were prepared. Finally, the most proper formulation was selected and evaluated physicochemically and microbiologically according to standard protocols. The total phenol content as marker of the tablets was determined and accelerated stability tests were conducted (40 °C/75 % RH) as per ICH guidelines for six months. **Results:** For the selected formulation (F2), the hardness, weight variation, friability, disintegration time and drug release were determined as 6.78 ± 0.28 kg/cm^2, 714.36 ± 1.71 mg, 0.79 ± 0.05 %, 10.18 ± 0.39 min and 97.67 ± 0.16 % in one hour, respectively. The amount of total phenol was found to be 25.15 ± 0.13 mg/tablet. Microbial levels were in agreement with requirements. In the accelerated stability tests, no significant changes were observed. Total phenol content decreased 1.03 % during 6 months. **Conclusion:** After completing complementary tests such as *in vivo* and clinical trials, the formulated tablet (F2) could be presented for mass production.

Abbreviations: ITM: Iranian traditional medicine; ICH: The International Council for Harmonisation of Technical Requirements

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1. Introduction

Herbal medicines have been used to treat various disorders since ancient times [1, 2]. Despite the significant progress in modern medicine in recent decades, plants still play a considerable role in health care and interest in drugs derived from plants has increased dramatically [3]. At present, the major pharmaceutical companies are interested in researching medicinal plants as sources for new lead structures, as well as for the development of standardized phytotherapeutic agents with proved efficacy, safety and quality [1]. Usually, herbal medicinal products are very popular in developing countries with a long tradition in the use of medicinal plants. However, modern scientific methods should be used to confirm the claims related to the therapeutic effects of the plants in the traditional medical system [1, 4].

Among various kinds of traditional and complementary systems of medicine, Iranian traditional medicine (ITM), is one important traditional approach to medicine that has promoted healthy life [4, 5]. In ITM, medicinal plants have been used to treat different diseases [6]. The present study tried to formulate one traditional drug form, namely "Monzej-e-balgham". The medications that maturate phlegm (balgham) are widely used in ITM for the treatment of different diseases such as stroke [7, 8], hemiplegia due to ischaemic stroke [9], cardiovascular disease risk factors such as metabolic abnormalities like abdominal obesity, high cholesterol, high blood pressure and high blood glucose [10], overweight [11], atherosclerosis [12], premature ovarian failure (POF) [13], impotence [14], bronchitis [15] and vitiligo [16, 17] according to modern studies. Various formulations of "Monzej-e-balgham" could be found in important traditional pharmacopeia and the types of plants have been proposed in different medical prescriptions. Among them, a manuscript [18] in the form of "Matbookh*"* (decoction), containing the roots of *Glycyrrhiza glabra* L., fruits of *Foeniculum vulgare* Mill., aerial parts of *Adiantum capillus-veneris* L., fruits of *Vitis vinifera* L., fruits of *Ficus carica* L., flowers of *Rosa x damascena* Herrm. and seeds of *Onopordum acanthium* L. was selected. The prescription was decided to be converted into new dosage form for better acceptance and easier usage by patients compared to the traditional formulation [4]. Solid dosage forms like tablet is more desirable in comparison with the liquid dosage forms because of more stability, uniformity and correct potency, less microbial problems, better flavor masking and easier transportation [2]. In this study, tablets of "Monzej-e-balgham" have been prepared according to prescriptions in ITM and standard pharmaceutical controls of the tablets have been performed to present a qualified formulation for usage.

2. Materials and Methods

2.1. Chemicals

All chemicals were of analytical grade. Sodium carbonate was provided from Sigma, Germany and other chemicals and solvents were prepared from Merck, Germany.

2.2. Equipment

The friability of tablets was determined using Pharma-test friabilator (Model TAR, Erweka, Germany). Hardness of the tablets was evaluated by hardness tester (Model TBH28, Erweka, Germany). Disintegration time was measured using disintegration testers (Model ZT3, Erweka, Germany) and dissolution behavior was determined with dissolution testers (Kavosh Co., Iran). The tablets were pressed with Excentric Tabletting Machine (EKO) (Model single-punch tablet machine, Erweka, Germany).

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2.3. Plant material

Required plants for preparation of the tablets were purchased from Tehran local market in 2017. The samples were identified by botanists at the Herbarium of Traditional Medicine and Materia Medica Research Center, Shahid Beheshti University of Medical Sciences, Tehran, Iran. Herbal Market Samples (HMS) of the fruits of *F. carica* (No. 490), roots of *G. glabra* (No. 494), fruits of *F. vulgare* (No. 492), flowers of *R. damascena* (No. 488), aerial parts of *A. capillus-veneris* (No. 491), fruits of *V. venifera* (No. 489), and seeds of *O. acanthium* (No. 493) have been deposited at the Herbarium of TMRC.

2.4. Physicochemical parameters analysis of plant materials

Quality control assessments of plants such as loss on drying, foreign matters, total ash, acid insoluble ash, water soluble extractive and alcohol soluble extractives were carried out according to the Pharmacopeia [19-21].

2.5. Formulation of polyherbal tablets

According to the selected prescription [18] *Ficus carica* (6 parts), *Adiantum capillus-veneris* (3 parts), *Rosa x damascena* and *Glycyrrhiza glabra* (2 parts), *Foeniculum vulgare* and *Onopordum acanthium* (1.3 parts) and *Vitis vinifera* (1 part) were crushed and coarse powdered and then mixed and extracted with distilled water (plant: water 1:10 w/v) using infusion method at 90 ºC for two hours. After extraction, the mixture was filtered, concentrated and dried with spray drying method to produce a dry powder from the extract.

Amount of dry extracts used in tablets was 500 mg based on daily dosages of traditional usages. Thirteen formulations were prepared with various ingredients containing microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, colloidal silicon dioxide and maltodextrin (F1-F13) (Table 1). The ingredients were mixed in various ratios according to formulation design and they were prepared using direct compression method. Pre- and post- formulation tests were used for controlling of polyherbal tablets. According to the results of the tests, the most suitable formulation (F2) was selected.

2.6. Quality control tests

The ideal properties of a tablet are compactness, rapid production capability, physical and chemical stability and efficacy. Therefore, various physiochemical tests and pharmaceutical parameters have been developed to monitor suitability of tablets such as powders angle of repose, Carr's index and Hausner ratio, also tablets appearance, diameter, thickness, weight variation, hardness, friability, disintegration times, dissolution behavior studies and drug assay according to standard methods [22].

2.7. Preformulation studies of powder mixture

The flowability of formulations was calculated on the basis of Carr's index, Hausner ratio and angle of repose [23, 24].

2.7.1. Angle of repose

Angle of repose was determined by fixed funnel method and calculated regarding the following formula. In this formula "H" is height and "R" is radius of granules:

$$\tan \alpha = H/R$$

Alpha: angle of repose

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Table 1. Ratio of different constituents in the experimental formulations

Formulations	Ingredients						
	Herbal powder (mg)	Maltodextrin (mg)	Colloidal silicon dioxide (mg)	Microcrystalline cellulose (Avicel 102) (mg)	Croscarmellose sodium (mg)	Lactose monohydrate (mg)	Total (mg)
F1	500	180	20	-	-	-	700
F2	500	180	20	-	14	-	714
F3	500	180	20	-	35	-	735
F4	500	180	20	-	70	-	770
F5	500	180	20	126	14	-	840
F6	500	180	20	105	35	-	840
F7	500	180	20	70	70	-	840
F8	500	180	20	140	-	-	840
F9	500	180	20	70	-	70	840
F10	500	180	20	-	-	140	840
F11	500	180	20	-	14	126	840
F12	500	180	20	-	35	105	840
F13	500	180	20	-	70	70	840
Function	Active ingredient	Binder	Glidant, disintegrant	Binder, Direct compression excipient	Disintegrant	Bind, Direct compression excipient	-

2.7.2. Compressibility index (Carr's index)

It was measured by using Bulk Density (BD) and Tapped Density (TD).

Sufficient quantity of powder blend was introduced to a measuring cylinder of 100 ml. The cylinder was tapped 100 times and the tapped volume of packing was noted. BD and TB were calculated by [25]:

BD = Weight of powdered blend/Untapped volume of the powder

TD = Weight of powdered blend/Tapped volume of the powder

Carr's Index = (Tapped Density – Bulk Density ×100)/ tapped Density

2.7.3. Hausner ratio

It is an index of ease of powder flow and was measured using the following formula:

Hausner ratio = Tapped Density/ Bulk Density

2.8. Formulation studies of tablets

2.8.1. Hardness

Using a hardness tester, crushing strength of tablets was evaluated. Six tablets of each formulation were selected randomly and the average force to the tablet to cause fracture was recorded.

2.8.2. Friability

Friability test determines the ability of tablets to withstand abrasion during packaging, handling, and shipping processes. Ten pre-weighed tablets were placed in the friability tester and rotated at 25 rpm for 4 min (100 revolutions). Then, the tablets were taken out from the tester and reweighed. The weight loss due to abrasion was expressed as percentage. A maximum weight loss of not more than 1 % is acceptable [26].

The friability was determined by the following formula:

% Friability = (Initial weight–Weight after friability testing × 100)/ Initial weight

2.8.3. Weight variation

For weight variation analysis, ten tablets were chosen randomly and weighed individually; the average weight and standard deviation (SD) were then calculated.

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2.8.4. Disintegration time

Six tablets were selected for the test and were placed in distilled water at temperature of 37 ± 1.0 ºC using a disintegration tester; time of complete disintegration was noted.

2.8.5. Dissolution rate

Dissolution test of polyherbal tablets was performed on six tablets using the paddle method according to the United States Pharmacopoeia (USP) guidelines [27]. Dissolution apparatus type II at a speed of 75 rpm, with 900 ml distilled water as the dissolution medium was used and the temperature was maintained at 37 ± 0.5 ºC. Fifteen ml of the sample was withdrawn, replenished with fresh and equivalent medium at predetermined time intervals (15, 30, 45, 60 min) and the amount of dissolved total phenol of each withdrawn sample was calculated using UV spectroscopy by comparing the measured absorbance with the calibration curve prepared for that purpose. Quantity (Q) more than 75 % was considered acceptable for dissolution test [27].

2.8.6. Total phenol content assay

Ten tablets were weighed and powdered. An accurately weighed portion of the powder, equivalent to one tablet, was dissolved and diluted to 100 ml distilled water. The solution was allowed to shake for 1 h and was then filtered. Total phenolic contents of samples were determined by Folin-Ciocalteu reagent. Two ml of diluted sample, 1 ml Folin-Ciocalteu reagent and 10 ml distilled water were mixed and afterwards aqueous solution of sodium carbonate (29 %, w/v) was added to the mixture up to 25 ml and allowed to stand at room temperature for 30 min. Absorbance was measured by UV spectrophotometry at 760 nm. Total phenol content was calculated on the basis of the standard calibration curve of pyrogallol. All measurements were carried out at room temperature in triplicate.

2.9. Stability evaluation of polyherbal tablets

The evaluation of drug accelerated stability was performed as per ICH guidelines. The tablets were stored at 40 ºC/75 % RH ± 2 ºC/5 % RH up to 6 months. Physicochemical specifications of the tablets were evaluated afterwards [28].

2.10. Statistical analysis

The data were analyzed using ANOVA (one-way analysis of variance) followed by Tukey's post hoc test. $P < 0.05$ was considered as statistically significant.

3. Results

In this research, several of tablets were formulated based on Iranian traditional medicine. Polyherbal tablets with different ratios of excipients have been shown in Table 1 and precompression studies results of powder mixture of all formulations have been presented in Table 2.

Polyherbal tablets were prepared and physicochemical properties were reported in Table 3. In order to prepare the experimental formulations, maltodextrin as binder and silicon dioxide as glidant and disintegrant were added to the extract of the plants.

The results of acceleration test of selected formulation have been shown in Table 4.

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Table 2. Results of precompression test of powder blend of F1-F13

Formulations	Parameters		
	Angle of repose (º)	Carr's index (%)	Hausner ratio
F1	27.33 ± 0.65	10.29 ± 0.17	1.11 ± 0.02
F2	27.56 ± 0.09	11.37 ± 0.32	1.12 ± 0.01
F3	28.03 ± 0.62	11.45 ± 0.41	1.12 ± 0.01
F4	28.54 ± 0.40	11.76 ± 0.26	1.13 ± 0.02
F5	32.84 ± 1.02	14.57 ± 0.29	1.16 ± 0.02
F6	32.55 ± 0.02	13.43 ± 0.35	1.15 ± 0.01
F7	30.67 ± 0.23	12.05 ± 0.09	1.13 ± 0.02
F8	33.41 ± 0.43	15.41 ± 0.18	1.17 ± 0.02
F9	33.89 ± 0.66	16.82 ± 0.07	1.19 ± 0.02
F10	34.85 ± 1.13	16.36 ± 0.38	1.18 ± 0.01
F11	33.60 ± 1.42	15.75 ± 0.14	1.18 ± 0.04
F12	32.66 ± 0.83	15.34 ± 0.52	1.17 ± 0.02
F13	30.34 ± 1.01	14.45 ± 0.16	1.16 ± 0.03

Table 3. Physicochemical properties of the experimental formulations

Tests	Formulations				
	F1	F2	F5	F6	F8
Appearance	Oval, Cream color, smooth and biconvex	Oval, Cream color, smooth and biconvex	Oval, Cream color with white spots, smooth and biconvex	Oval, Cream color with white spots, smooth and biconvex	Oval, Cream color with white spots, smooth and biconvex
Length (mm)	19.44 ± 0.03	19.45 ± 0.02	19.44 ± 0.01	19.46 ± 0.03	19.44 ± 0.01
width (mm)	8.31 ± 0.02	8.31 ± 0.01	8.32 ± 0.01	8.30 ± 0.01	8.32 ± 0.02
Thickness (mm)	6.15 ± 0.05	6.16 ± 0.03	6.64 ± 0.02	6.63 ± 0.03	6.64 ± 0.01
Weight variation (mg)	701.40 ± 1.25	714.36 ±.71	841.11 ± 2.54	839.48 ± 1.14	840.37 ± 0.95
Friability (%)	0.71 ± 0.04	0.79 ± 0.05	0.69 ± 0.05	0.83 ± 0.06	0.63 ± 0.02
Hardness (Kg/Cm^2)	7.11 ± 0.27	6.78 ± 0.18	7.34 ± 0.24	6.62 ± 0.32	7.96 ± 0.21
Disintegration Time (min)	12.43 ± 0.17	10.18 ± 0.39	13.53 ± 0.48	12.29 ± 0.22	14.50 ± 0.34
Dissolution (%) after 60 min	95.88 ± 0.62	97.67 ± 0.16	94.69 ± 0.57	96.21 ± 0.71	93.46 ± 0.69
Assay of total phenol (mg/cap)	25.09 ± 0.18	25.15 ± 0.13	24.94 ± 0.19	25.08 ± 0.24	24.90 ± 0.21

Table 4. Results of accelerated stability test of polyherbal tablets

Tests	Results*		
	Start	3 Month	6 Months
Appearance	Cream color, smooth and biconvex	Cream color, smooth and biconvex	Cream color, smooth and biconvex
Length (mm)	19.45 ± 0.02	19.45 ± 0.02	19.45 ± 0.01
width (mm)	8.31 ± 0.01	8.31 ± 0.01	8.31 ± 0.02
Thickness (mm)	6.16 ± 0.03	6.15 ± 0.05	6.15 ± 0.04
Weight variation (mg)	714.36 ± 1.71	714.41 ± 1.18	714.49 ± 1.63
Friability (%)	0.79 ± 0.05	0.77 ± 0.06	0.77 ± 0.04
Hardness (Kg/Cm^2)	6.78 ± 0.18	6.81 ± 0.12	6.82 ± 0.15
Disintegration Time (min)	10.18 ± 0.39	10.22 ± 0.45	10.24 ± 0.26
Dissolution (Total phenol content) (%)	97.67 ± 0.16	97.59 ± 0.32	97.55 ± 0.23
Assay of total phenol (mg/tab)	25.15 ± 0.13	25.03 ± 0.21	24.89 ± 0.28

* Data are expressed as means ± SD; the stability results showed no significant differences after 6 month

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Dissolution profile analysis is an essential tool to evaluate formulation development for quality control and establishing similarity between multisource and reference formulations. A graphical representation of the percentage in drug releases of polyherbal tablets in distilled water has been shown in Fig. 1.

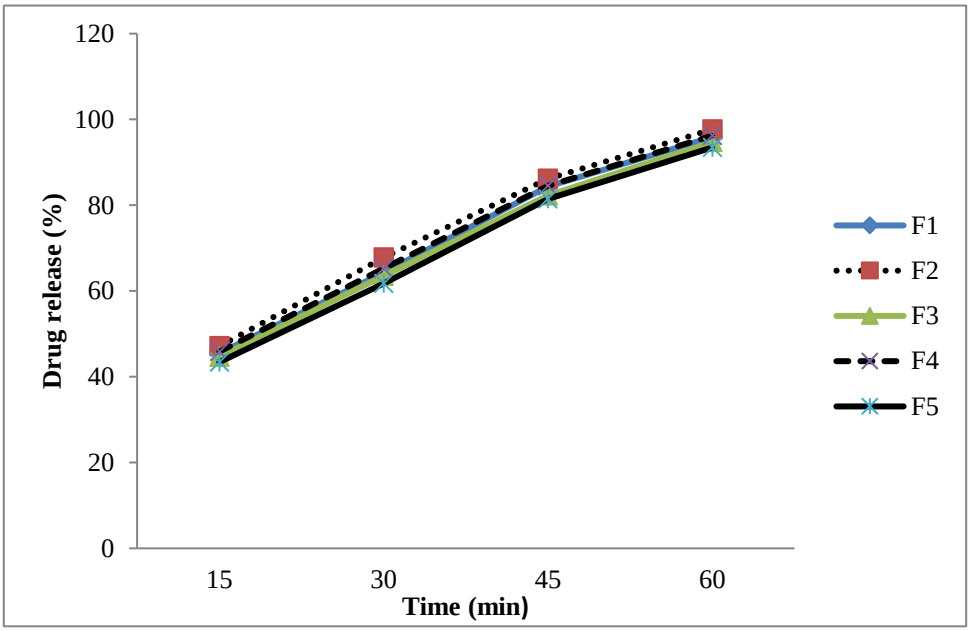

Fig. 1. Release profile of five different formulated polyherbal tablets (n = 6, mean ± S.D).

4. Discussion

There is a strong potential in the traditional and ethnomedical knowledge of different countries for developing new and efficacious drugs for the treatment of diseases as modern formulations [5, 29]. Although traditional medicines can be used as new therapeutic agents, they need to be reformulated to achieve pharmaceutical standards for modern medicine. Evaluation of the quality control parameters of the final formula will have a major role in the effectiveness and safety of the drug.

In preformulation studies of tablet formulation, angle of repose shows flowability of powders and in this search, it was between 27º to 34º indicating good flow characteristics of the powders. The Carr's index and Hausner ratio are indirect methods for predicting the powder flow properties. The value of Carr's index was in the range of 10-16 indicating good flow and compressibility. Hausner ratio amount was obtained below 1.19 which is in the acceptable limit of good flow indicating low interparticle friction [22]. Poor flow characteristics of formula may cause problems such as nonuniformity and weight variation problems in formulations [23]. From the above mentioned precompression results, it was found that the flowability of the powders was acceptable, so all were pressed to determine the appropriate formula according to the quality control tests.

Polyherbal tablets (F1-F13) were prepared but F3, F4 and F7 formulations did not show suitable strength and their friability exceeded the acceptable level (due to the high percentage of croscarmellose sodium), so they were discarded.

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The color of lactose-containing tablets changed over time and turned into dark brown color, indicating that lactose was incompatible with other constituents. Regarding these results, F9- F13 were not considered suitable because the drug and excipients compatibility requires an aforementioned acquaintance of physicochemical properties for the development of pharmaceutical formulation [30].

The physicochemical properties of other tablets (F1, F2, F5, F6 and F8) were evaluated and compared.

As shown in Table 3, length and width of tablets were not significantly different in formulations. The assessment of thickness and weight values demonstrated that formulations of each group showed a narrow variation range and there was a significant difference between the groups. Minimum and maximum friability of the formulations were obtained as 0.63 % and 0.83 %, respectively. The percent of friability was less than 1 % in all formulations ensuring that the tablets were mechanically stable. Another measurement of the mechanical integrity of tablets is their breaking force, which is the force required to cause them to fail (i.e., break) in a specific plane, called hardness in the pharmaceutics. The hardness of tablets was measured in the range of 6.62 to 7.96 kg/cm^2 that showed appropriate hardness.

Disintegration time is one of the most important factors in quality control of drugs, especially in the formulation of natural products, since lots of these compounds become sticky when they are used as powders or extracts which makes usage of disintegrants inevitable. There was a significant difference between disintegration times of formulations. The shortest disintegration time belonged to F2 with 10.18 minutes. Croscarmellose sodium as disintegrant led to faster disintegration; on the contrary, when microcrystalline cellulose was used, disintegration time increased in tablets.

Various factors such as the disintegration rate and the nature of the excipients may influence dissolution results. Sample F2 could be considered as the fastest in disintegration rate though the difference was not significant compared to other formulations. The dissolution profile indicated that at least 75 % of the active ingredient was released within 45 min and was higher than 97 % of labeled amount dissolved in 60 minutes for F2.

Croscarmellose sodium 2 % (F1) showed more appropriate disintegration time and dissolution tests for tablets. In general, by reducing microcrystalline cellulose and increasing croscarmellose sodium, tablets hardness and disintegration time decreased and friability and dissolution increased.

Among all formulations, F2 showed more acceptable physicochemical properties. The final formulation included 500 mg of herbal extracts mixture, 180 mg of maltodextrin, 20 mg silicon dioxide and 14 mg of croscarmellose sodium per tablet (only three expedients). Less use of excipients results in the lower costs and fewer problems during formulation and production in industrial scale.

The tablets were subjected to short time accelerated stability study (40 ºC /75 % RH) as per ICH guidelines [28]. Establishment of the drug stability plays an important role in the safety and efficacy. The final formulated tablets were cream color, biconvex with an acceptable appearance. The tablets had narrow weight variation which ensured tablet contained proper amount of medicine which maintained the good quality and effectiveness. The tablets displayed suitable hardness and friability which means they would not erode during transportation. Disintegration time was approximately

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10 minutes and the percentage of released total phenol was more than 97 % (Q) after 60 min that is suitable for herbal tablets [22]. Total phenol content as the stability indicating assay of polyherbal tablets was monitored throughout the study and was found to be stable (total phenol: 25.15 to 24.89 mg/tab). After six months, the amount of total phenolic content decreased by 1.03 %, which is in accordance with acceptable limits [28]. Similarly, the results of the microbiological limit tests were in accordance with WHO guidelines [31].

As the results show, no significant changes ($P > 0.05$) were found in physicochemical characteristics of polyherbal tablets after 6 months at 40 ºC and 75 % humidity.

5. Conclusion

The purpose of this research was to formulate tablets of "Monzej-e-balgham" and evaluate its quality control. Various formulations were prepared and their pre-and post-formulation parameters were assessed. Among formulations, F2 was selected with its acceptable physicochemical characteristics and stability results and this formulation can be used after further optimization processes to mass production.

Author contributions

M. R. was involved in the experimental parts; SA. M. supervised the formulation section; Sh. F. and R. Ch. were involved in traditional data collection; MA. Sh. conducted the pharmacological experiments; M. HM. designed and supervised the research.

Conflict of interest

The authors declare that there is no conflict of interest.

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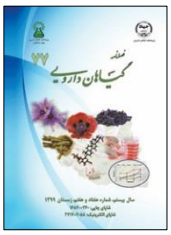

مقاله تحقیقاتی

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اطلاعات مقاله

گل‌واژگان:

منضج بلغم

کنترل کیفیت

قرص

محتوای ترکیبات فنلی تام

طب سنتی ایرانی

چکیده

مقدمه: گیاهان دارویی مورد استفاده در طب سنتی نقش مهمی در پیشگیری و درمان بیماری‌ها دارند. در طب سنتی ایرانی، گیاهان دارویی عوامل کلیدی در درمان طیف وسیعی از بیماری‌ها می‌باشند. بسیاری از این داروهای سنتی قابلیت تبدیل به فرمولاسیون‌های استاندارد مدرن را دارا می‌باشند. **هدف:** در این مطالعه قرص گیاهی منضج بلغم که به فرم سنتی در درمان بسیاری از بیماری‌ها کاربرد دارد فرموله شده و آزمون‌های کنترل کیفیت آن به جهت دستیابی به فرمولاسیون بهینه انجام شده است. **روش بررسی:** شیرین بیان، گل محمدی، پرسیاوشان، شکاعی، مویز، انجیر و رازیانه توسط آب عصاره‌گیری شدند و عصاره حاصل پس از صاف کردن به کمک خشک‌کن پاششی، خشک شد. ۱۳ فرمولاسیون قرص به روش پرس مستقیم تهیه شدند؛ مطالعات پیش و پس فرمولاسیون انجام شد. در نهایت مناسبترین فرمولاسیون انتخاب شد و از لحاظ فیزیکوشیمیایی و میکروبی مورد بررسی قرار گرفت. میزان ترکیبات فنلی تام فرآورده به عنوان شاخص فرمولاسیون، اندازه‌گیری شد و آزمون‌های پایداری تسریع شده در دمای ۴۰ درجه سانتی‌گراد و رطوبت ۷۵ درصد به مدت شش ماه انجام شد. **نتایج:** در فرمولاسیون انتخابی (F2)، سختی، یکنواختی وزن، فرسایش، زمان باز شدن و میزان آزادسازی به ترتیب ۶/۷۸ ± ۰/۲۸ kg/cm^2، ۷۱۴/۳۶ ± ۱/۷۱ mg، ۰/۰۵ ± ۰/۷۹ درصد، ۱۰/۱۸ ± ۰/۳۹ دقیقه و ۹۷/۶۷ ± ۰/۱۶ درصد در یک ساعت محاسبه شدند. میزان ترکیبات فنلی تام ۲۵/۱۵ ± ۰/۱۳ میلی‌گرم در هر قرص به دست آمد و نتایج آزمون میکروبی در محدوده قابل قبول بود. در آزمون‌های پایداری تسریع شده تغییر معنی‌داری مشاهده نشد و میزان ترکیبات فنلی تام طی ۶ ماه ۱/۰۳ درصد کاهش یافت. **نتیجه‌گیری:** فرمولاسیون قرص تهیه شده در مطالعه فعلی (F2)، پس از گذراندن آزمون‌های تکمیلی شامل مطالعات درون‌تنی و بالینی قابلیت تولید انبوه را دارد.

مخففها: ITM، طب سنتی ایرانی؛ ICH، شورای بین المللی هماهنگی الزامات فنی

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