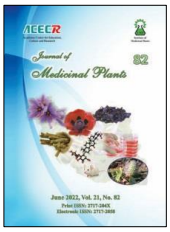
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Research Article

Development and evaluation of taste-masked pellets loaded with *Matricaria chamomilla* L. extract

Noushin Bolourchian[1,*], Sahel Shirvani[1], Faraz Mojab[2]

[1] *Department of Pharmaceutics and Pharmaceutical Nanotechnology, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

[2] *Department of Pharmacognosy, School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran*

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ABSTRACT

Background: Remarkable properties of *Matricaria chamomilla* L. (Mch) have caused it to be considered widely in the treatment of different ailments including gastrointestinal disorders. **Objective:** In the present study, the Mch extract-loaded coated pellets were developed with the aim to mask its bitter taste and to improve its dosing flexibility and patient compliance, especially in children. **Methods:** The plant extract was obtained by maceration with ethanol 70 % and dried using rotary evaporating and freeze drying methods. Then it was used for pellet preparation along with different proportions of various additives such as Avicel, starch and lactose by extrusion-spheronization technique. The pellets were analyzed for their size, sphericity, aspect ratio and friability. The optimized formulation, subjected for coating by Eudragit E, was evaluated for taste-masking efficiency, dissolution and morphology. **Results:** The optimized pellets were produced with particle size, sphericity and aspect ratio equal to 1.13 mm, 0.924 and 1.172, respectively. Low friability, suitable flow properties (carr's index = 3.01 %) as well as dissolution led this sample to be considered for taste-masking coating. Based on *in vitro* dissolution studies, although the coating layer significantly decreased the release of the components at higher pH compared to the uncoated particles, acceptable dissolution was observed at pH 1.2. Appropriate taste-masking of the product was also confirmed by *in vivo* analysis. **Conclusion:** The taste-masked Mch-loaded pellets with suitable characteristics could be an appropriate delivery system with improved patient compliance.

Abbreviations: Mch, *Matricaria chamomilla* L.; SLS, Sodium Lauryl Sulfate; MS, Magnesium Stearate; PVP, Polyvinyl Pyrrolidone; SSG, Sodium Starch Glycolate; DEx, Dry Extract; TPC, Total Phenol Content; TFC, Total Flavonoid Content; AR, Aspect Ratio; CI, Carr's Index; HR, Hausner Ratio; DE, Dissolution Efficiency; RDR, Relative Dissolution Rate

*Corresponding author: bolourchian@sbmu.ac.ir

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1. Introduction

Herbal extracts are widely used in the treatment of various diseases in traditional-based medicine in different countries. *Matricaria chamomilla* L. (German chamomile) is an important plant belong to the family Asteraceae, used in the traditional medicine of different regions [1]. It is a plant that grows in many parts of the world including Asia, Africa and Europe. German chamomile is also distributed and widely used in Iran [2]. This plant contains many compounds for the treatment of variety of diseases [3]. The main constituents of German chamomile are sesquiterpenes (chamazulene, α-bisabolol, bisabolol oxide) [4], flavonoids (apigenin, quercetin, luteolin, patuletin, rutin and isorhamnetin) and coumarins (umbelliferone and herniarin) [5]. Flavonoids such as apigenin and their glucosides are among the components that cause the biological activity after oral administration [6].

According to the researches, chamomile extract has antioxidant properties, with a protective effect on brain tissue oxidative damage [2]. Also it has strong anti-inflammatory effect associated with the existence of terpenoids and flavonoids in this plant [1]. Besides to its anti-diabetic and anti-cancer properties [7], antidiarrheal and antispasmodic activities of chamomile has also been shown in pharmacological investigations [3, 8]. While the plant flowers are used as antipyretic and carminative, its essential oil has been used in flatulence and colic [3] which are more common in children. In fact, chamomile is widely used in the treatment of gastrointestinal disorders in children, with few adverse effects [9].

Various preparations such as aqueous extracts and tinctures have been developed in order to use chamomile alone or in combination with other herbal materials [6]. As an oral preparation, dry forms of herbal extract such as tablets and capsules are more stable compared to the aqueous form. Due to the poor physical properties of dry extracts, using several additives and additional operations in preparation process is necessary [10]. Application of pellets as multi-particulate delivery systems, while having several advantages, could facilitate the preparation process. Lower gastric transit time, less irritation of gastro-intestinal tract, reduced intra- and inter-subject variability and food effect are some of the benefits of pellets following oral administration [11]. Besides, high patient compliance due to easy swallowing as well as flexible dose fractionation are other important features of the pellets [12], especially in pediatrics. During the recent years, attention has also been paid to the production of pellets containing plant extracts alone or in combination [11, 13]. Due to the ideal surface properties, taste masking of extract-loaded pellets as well as various release profiles could be achieved by polymeric film coatings.

Considering the various advantages of pellets, the purpose of the present study was to develop and physicochemical characterization of *M. chamomilla* extract-loaded pellets as multiparticulate dosage form by extrusion-spheronization technique. At the same time, taste masking of the product through coating process was one of the stages of this research. To the best of our knowledge, no study has so far been published regarding to the pellet formulation of *M. chamomilla* extract.

2. Materials and Methods

2.1. Chemicals

Avicel PH101, maize starch, sodium lauryl sulfate (SLS), magnesium stearate (MS), polyvinyl pyrrolidone (PVP), sodium starch glycolate (SSG), lactose, sodium carbonate,

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aluminum chloride, Folin-Ciocalteu reagent, isopropanol and ethanol were all purchased from Merck (Germany). Eudragit E100 (Evonik Industries AG, Germany) was used as coating material. Gallic acid and rutin (Sigma-Aldrich, Germany) were also used in this study.

2.3. Preparation of the plant extract

Matricaria chamomilla L. (Mch) was obtained from Zardband Co. (Iran) as dried form and identified as the plant of interest (code: SBMU-8060). Then the herb (aerial parts) was grounded (500 g) and subjected to extraction by maceration method. It was soaked in ethanol 70 % (1000 ml) for 24 h at ambient temperature with intermittent shaking. The extraction was performed for three times and the obtained extract was separated from the plant material by filtration. The extract was then concentrated in a rotary evaporator (Heidolph, Germany) with a temperature below 40 ^{o}C under the reduced pressure. Due to the adhesive nature of the above sample and to prepare the extract dry powder, the material obtained from the previous stage was freeze-dried. Samples were frozen in a laboratory freezer at -80 ^{o}C for 24 h before the freeze-drying process. Then, frozen samples were freeze-dried using a laboratory scale freeze-dryer (Christ, Alpha 1-2, Germany), set at -55 ^{o}C for 48 h. The dried solid mass was then powdered using a laboratory mill. The obtained dry extract (DEx) was passed through a 40-mesh screen and kept in closed containers away from moisture until used. DEx was also tested for total phenol and flavonoid contents by the following methods.

2.4. Total phenol content (TPC)

The Folin-Ciocalteu method was used to estimate TPC [14]. One milliliter of the extract (400 µg/ml) was stirred with Folin-Ciocalteu's reagent (5 ml) at room temperature. After 10 min, 4 ml of sodium carbonate solution (75 mg/ml) was added, mixed thoroughly and incubated at ambient temperature for 120 min. Quantification of the sample was done on the basis of gallic acid standard curve, over the concentration range of 25-150 µg/ml, by a UV-Vis spectrophotometer (Shimadzu, UV-1800, Japan) at 765 nm. All tests were performed in triplicate. TPC was expressed as mg gallic acid equivalent per gram of dry basis (mg GAE/g).

2.5. Total flavonoid content (TFC)

A 2.5 ml solution of the extract (400 µg/ml) was mixed with ethanolic solution (2.5 ml) of aluminum chloride with the concentration of 20 mg/ml. After 120 min, the absorbance of each sample was measured using a UV-Vis spectrophotometer at 415 nm [14]. Standard curve of rutin, over the concentration range of 25-150 µg/ml, was used for quantification (expressed as mg rutin equivalent per gram of dry basis (mg RUE/g)).

2.6. Pellets preparation

Pellets were prepared by extrusion spheronization technique. Specific amount of DEx was blended with the additives. PVP and SSG were added to the formulations to improve the quality of the pellets, reduce their friability and provide a suitable disintegration and dissolution behavior, respectively. The granulation liquid consisted of SLS aqueous solution was gradually added to the powder mixture and mix thoroughly for 15 min. The dough mass was transferred to the screen axial extruder (Dorsa Tech, Iran) and extruded immediately through a perforated die screen of 1.2 mm diameter. Then, the obtained extrudates were immediately transferred to the spheronizer with a cross-hatched friction plate rotating at 400 rpm for 10 min, where the extrudates were

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broken into smaller cylindrical rods and rounded into pellets. Pellets were left to dry at room temperature for 24 h. The composition of pellet formulations was presented in Table 1.

Table 1. Composition (%) of different pellet formulations loaded with *M. chamomilla* extract

Formulation	DEx[a]	Avicel	Starch	PVP[b]	Lactose	SSG[c]	MS[d]	SLS[e]
F1	10	89	-	-	-	-	1	0.1
F2	10	89	-	-	-	-	1	1
F3	10	80	10	-	-	-	-	0.1
F4	10	80	10	-	-	-	-	1
F5	10	78	10	2	-	-	-	1
F6	10	88	-	2	-	-	-	1
F7	10	86	-	4	-	-	-	1
F8	10	76	10	4	-	-	-	1
F9	10	78	-	2	10	-	-	1
F10	10	76	-	4	10	-	-	1
F11	10	56	30	4	-	-	-	1
F12	10	56	32	2	-	-	-	1
F13	10	54	30	6	-	-	-	1
F14	10	50	30	6	-	4	-	1
F15	10	54	20	6	10	-	-	1
F16	10	50	20	6	10	4	-	1
F17	20	40	30	6	-	4	-	1
F18	30	30	30	6	-	4	-	1
F19	20	40	30	4	-	6	-	1
F20	20	30	30	4	10	6	-	1
F21	20	30	30	6	10	4	-	1

[a] DEx: Dry extract, [b] PVP: Polyvinyl pyrrolidone, [c] SSG: Sodium starch glycolate, [d] MS: Magnesium stearate, [e]:The percentage of sodium lauryl sulfate in wetting liquid

2.7. Coating of pellets

Due to the unpleasant taste of Mch, coating of pellets is required for better patient compliance, particularly in the children. Eudragit E as a cationic copolymer, can prevent the drug release at higher pH of saliva (6.8), but dissolves at lower pH of gastric fluid [15]. A solution of Eudragit E100 (10 %) was prepared in isopropyl alcohol using mechanical stirrer. Pellets were coated by pan coating process using a conventional laboratory-scale coating pan with a diameter of 17 cm and the rotation speed of 10 rpm. The coating solution was sprayed on the rotating pellets using a spray gun with the rate of 0.3 ml/min. Inlet air at the temperature of 50-60 ^{o}C was used to evaporate the solvent. The coating process was continued until the required coating percentage (5 %) was obtained [16].

2.8. Pellets characterizations

2.8.1. Yield

The percentage of a mass of pellets retained between sieve numbers 14 and 20 was reported as yield value. Further experiments on pellets were also performed on this size range.

2.8.2. Friability test

The friability (F) of the pellets was determined using a friability tester (Erweka). A sample of pellets (W1 = 3 g) along with 50 glass beads with

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4 mm diameter was placed in the abrasion wheel of friabilator. The instrument was operated for 100 revolutions (4 min) at the rotation speed of 25 rpm and pellets were subjected to falling shocks [17]. Then, fine particles were removed from the pellets by sieving through a 350 µm mesh for 3 min, and the particles above the sieve were weighed accurately (W2) and used to calculate the friability of pellets by the following equation [18]:

$$F\ (\%) = ((W1-W2)/W1) \times 100$$

2.8.3. Size and shape of pellets

The particle size, shape and sphericity of pellets were determined by an image analysis system. Pellets (50-100) were selected randomly and images were taken by a stereo-microscope (Optika, B810, Italy) equipped with a camera, under 40-fold magnification. A light source was used on a black surface to reduce the shadow. The images were analyzed by image analysis software (Image J). Each individual pellet was characterized by maximum and minimum Feret diameters and the surface area of pellet image (A). In this study, the maximum Feret diameter was expressed as the size of pellets. Aspect ratio (AR), the ratio of the maximum to minimum Feret diameter of each pellet, was also reported [19]. Perfect spherical pellets have an AR value equal to 1, while deviation of AR from unity indicates elongated particles [20].

Projection sphericity was calculated according to the following equation in which P is the actual perimeter of the pellet [17]:

$$\text{Projection sphericity} = 4\pi A/P^2$$

2.8.4. Flow properties

The bulk and tapped densities of the optimized pellets were determined using a graduated cylinder. Twenty g of pellets was introduced into a 100 ml cylinder and the initial volume (Vb = bulk volume) and volume after 1250 taps (Vt = tapped volume) were recorded (tapping until no further change in the volume). Mass of the pellets divided by Vb and Vt resulted in bulk and tapped densities, respectively. The carr's index (CI) and hausner ratio (HR) were calculated using the following equations [21]:

$$CI\ (\%) = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

$$HR = \frac{\text{Tapped density}}{\text{Bulk density}}$$

2.8.5. Assay

In order to measure the TPC and TFC in Mch extract-containing pellets, 500 mg particles were triturated in a mortar and pestle and transferred to 100 ml water. After stirring for 3 hrs, 1 ml of sample was filtered and tested using the similar methods as described above in TPC and TFC.

2.8.6. Fourier transform infrared spectroscopy (FTIR)

FTIR analysis was performed on DEx and optimized formulation. Samples were well mixed with potassium bromide in a mortar and the FTIR spectrum was recorded using an Agilent Technologies (CARY 630, USA) spectrophotometer.

2.8.7. Scanning Electron Microscope (SEM)

Optimized pellets were examined for their shape using scanning electron microscope (Hitachi High-Technologies, SU3500, Japan) operated at 15 kV. A sputter coater was applied to coat a layer of gold (10 nm) on the surface of pellets prior to observation.

2.8.8. Dissolution test

The dissolution behavior of coated and uncoated pellets (500 mg) was carried out in 300 ml simulated gastric fluid (0.1 N hydrochloric

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acid (pH = 1.2)) at 37 ± 0.5 °C, using a USP type I (basket) dissolution test apparatus (Erweka DT6R, Germany) at the rotation speed of 100 rpm. At predetermined time intervals, samples were withdrawn and replaced with the same amount of fresh medium for volume adjustment. Samples were analyzed for phenol contents with Folin-Ciocalteu method as already described for TPC. All experiments were performed in triplicate for each formulation.

2.8.9. Dissolution parameters

Q_{10} as the cumulative mean percentage of dissolved polyphenols during the first 10 min of the dissolution test was used to compare the dissolution profiles. Also, dissolution efficiency (DE), the area under the dissolution curve at time t, was calculated according to trapezoidal rule, expressed as a percentage of the area at 100 % dissolution [22]. RDR (relative dissolution rate) which is the ratio between the amount of drug dissolved from uncoated and coated pellets at 30 min was also calculated.

2.8.10. Moisture content

The moisture content of selected optimum pellets was analyzed by thermo-gravimetric method using a moisture analyzer (Ohaus, MB45, US). A sample of pellets (M1 = 0.8 g) was placed on the sample pan and heated at 50 °C until the change in the weight was no longer observed (M2) which lasted 2 h. The moisture content of the pellets was calculated by ((M1-M2)/M2) × 100.

2.9. Taste-masking evaluation

In order to ensure that the taste-masking has been achieved following coating of pellets, this experiment was carried out on both optimized uncoated and coated pellets by the following methods.

2.9.1. In vitro analysis

Since the coating method was used to cover the taste of prepared pellets, the dissolution study could provide useful information to evaluate taste-masking efficiency. A sample of pellets (about 100 mg) was placed in a volumetric flask containing 30 ml phosphate buffer solution (pH = 6.8, similar to the pH of saliva) and stirred for 5 min [23]. The mixture was filtered and analyzed for the content released from pellets.

2.9.2. In vivo analysis

For evaluation of taste-masking efficiency of both coated and uncoated pellets, a single-blind study was performed by 10 healthy volunteers in the age group of 20-36 years (5 males and 5 females), which was approved by ethics committee of Shahid Beheshti University of Medical Sciences (approval no. IR.SBMU. PHARMACY.REC.1397.194). Pellets equal to 100 mg were placed on the tongue of each volunteer and held for 60 sec. Afterwards, the volunteers rinsed their oral cavity with 200 ml water. The bitterness level of the pellets was scored by the volunteers (1 = tasteless, 2 = slightly bitter, 3 = moderately bitter and 4 = strongly bitter) [24]. The bitterness scores of each sample were compared by Wilcoxon, with a significance level of $P < 0.05$.

3. Results

3.1. TPC and TFC evaluation of DEx

Total phenol and flavonoid contents in Mch extract were measured based on gallic acid and rutin standards, respectively. According to the results, TPC was obtained 8.09 ± 0.50 mg GAE/g. Also, the amount of flavonoids was found 4.35 ± 0.81 mg RUE/g. Depending on different conditions, such as the type of solvent and extraction method, as well as the type of plant sample, collection area and storage

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conditions, various amounts have been reported for TPC and TFC. The value of TPC was equal to 2689.2 ± 15 mg GAE/100 g or less for different chamomile samples, reported in the literature [25]. However, in another research [26], this value was obtained 3.5 ± 1.7 mg GAE/g for chamomile flowers ethanolic extract.

3.2. Formulation of pellets containing Mch extract

Table 2 shows the physical characteristics of different pellet formulations prepared using DEx and various additives. All formulations resulted in pellet formation with the particle size in the range of 1.01-1.29 mm with different properties. The friability of the formulations F1-F10 was found to be higher than 1 %, which was not acceptable. Changing the composition of the pellets resulted in reduced friability.

Except the formulation F18, the yield of all pellets was in the range of 52.2-80.4 %. The low yield of F18 was due to the presence of 30 % DEx, that made the wet formulation more adhesive and to stick more to the walls of the extruder. The highest yield was related to F21, containing 20 % DEx. As it is obvious, the sphericity of the particles was affected by the formulation parameters which was improved for F13-F21. Different AR values in the range of 1.749-1.056 were obtained for the pellets (Table 2).

Table 2. Physical characteristics of different pellet formulations containing *M. chamomilla* extract

Formulation	Yield (%)	F[a] (%)	Size (mm)	Sphericity	AR[b]
F1	54.8	5.02	1.13 ± 0.19	0.72 ± 0.12	1.34 ± 0.14
F2	60.2	1.55	1.12 ± 0.27	0.81 ± 0.17	1.14 ± 0.15
F3	52.2	7.32	1.14 ± 0.19	0.75 ± 0.14	1.21 ± 0.10
F4	60.4	1.10	1.21 ± 0.14	0.83 ± 0.02	1.06 ± 0.17
F5	72.2	1.39	1.23 ± 0.18	0.79 ± 0.10	1.07 ± 0.12
F6	58.6	1.30	1.02 ± 0.18	0.79 ± 0.07	1.20 ± 0.16
F7	78.8	1.20	1.18 ± 0.17	0.85 ± 0.07	1.31 ± 0.15
F8	56.0	1.09	1.27 ± 0.11	0.83 ± 0.07	1.59 ± 0.17
F9	64.2	1.34	1.29 ± 0.09	0.80 ± 0.05	1.75 ± 0.32
F10	60.2	1.09	1.21 ± 0.18	0.81 ± 0.06	1.24 ± 0.13
F11	63.0	0.95	1.06 ± 0.16	0.80 ± 0.06	1.18 ± 0.21
F12	53.8	0.75	1.06 ± 0.27	0.75 ± 0.04	1.17 ± 0.22
F13	78.4	0.30	1.02 ± 0.16	0.88 ± 0.07	1.22 ± 0.21
F14	76.2	0.21	1.02 ± 0.19	0.90 ± 0.07	1.23 ± 0.12
F15	75.0	0.19	1.01 ± 0.16	0.92 ± 0.08	1.11 ± 0.13
F16	75.8	0.15	1.05 ± 0.14	0.92 ± 0.08	1.15 ± 0.12
F17	75.4	0.50	1.11 ± 0.17	0.90 ± 0.01	1.19 ± 0.19
F18	24.2	0.49	1.03 ± 0.13	0.90 ± 0.01	1.19 ± 0.38
F19	74.2	0.97	1.09 ± 0.25	0.91 ± 0.01	1.16 ± 0.14
F20	68.0	0.61	1.12 ± 0.18	0.91 ± 0.01	1.15 ± 0.17
F21	80.4	0.34	1.13 ± 0.26	0.92 ± 0.03	1.17 ± 0.17

[a] F: Friability, [b] AR: Aspect ratio

3.3. Selection of optimum pellet formulation

Based on Table 2, formulations F15, F16 and F21, had less friability as well as better sphericity compared to the other formulations. Sphericity and AR of all these pellets were about 0.92 and less than 1.2, respectively. Among these formulations, F21 was selected for further experiments, due to the higher load of the extract. Low friability of this formulation was also another advantage that could show its positive effect during coating process.

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3.4. Optimum pellet characterization

The amount of TPC and TFC in the optimum pellets were measured based on gallic acid and rutin standard curves, respectively. The obtained results were 1.36 ± 0.21 mg GAE/g and 0.69 ± 0.14 mg RUE/g, respectively, which indicated acceptable values for these components in the pellets. The moisture content of selected pellets (F21) was equal to 0.2 ± 0.1 %, representing their proper drying after preparation.

Bulk and tapped densities of optimum pellets were obtained 0.740 and 0.763 g/ml, respectively. CI and HR are two indicators of particles flowability which were calculated for F21 (CI = 3.01 % and HR = 1.031). The shape and sphericity of the pellets could be also observed by SEM micrograph (Fig. 1).

FTIR spectra of DEx and the optimum formulation are illustrated in Fig. 2. Characteristic peaks at 3425 cm^{-1}, 2933 cm^{-1}, 1614 cm^{-1} and 1070 cm^{-1} could be observed for DEx spectrum, which were in accordance with the literature [27]. All above peaks were also appeared at the same position for the optimum formulation, indicating no serious incompatibilities between the ingredients.

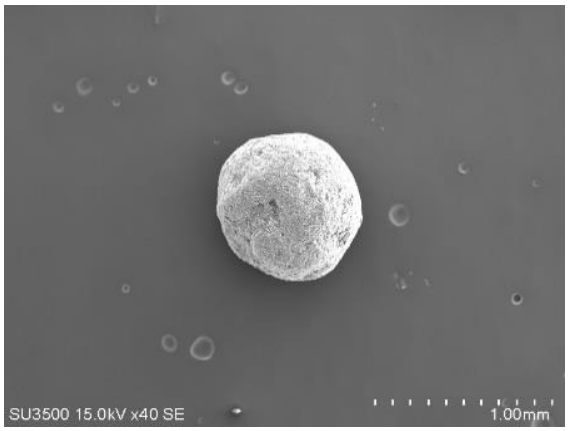


Fig. 1. SEM micrograph of the optimized pellet (× 40)

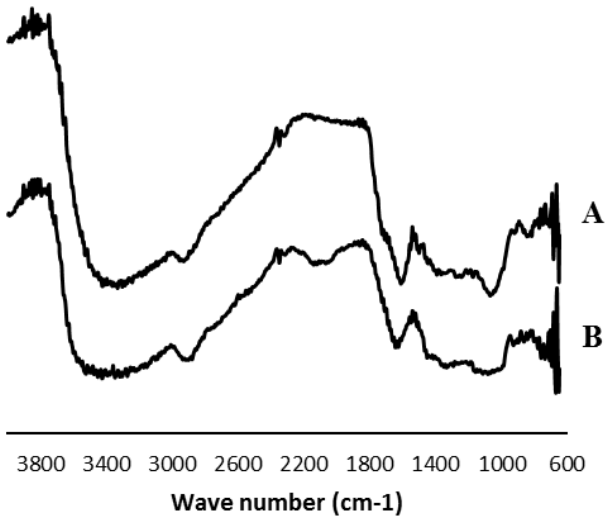


Fig. 2. FTIR spectra of A) DEx and B) optimum formulation

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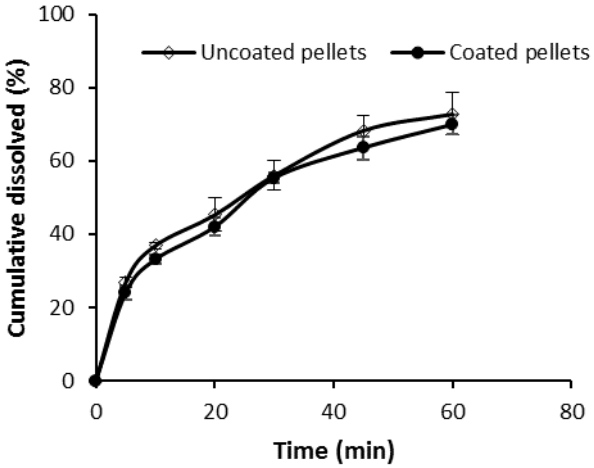


Fig. 3. Dissolution profiles of polyphenols from uncoated and coated pellets at pH= 1.2 (n = 3)

Since the results of the optimum pellets confirmed their suitability for further studies, in the next step, the pan coating process was performed on the pellets using Eudragit E100. It must be mentioned that the measured TPC of the coated pellets was equal to 1.22 ± 0.27 mg GAE/g.

3.5. Dissolution studies

The dissolution profiles of the uncoated and coated pellets in hydrochloric acid solution (pH = 1.2) are shown in Fig. 3.

3.6. Taste-masking evaluation

3.6.1. In vitro analysis

The amount of polyphenols released from two groups of uncoated and coated pellets in phosphate buffer solution (pH = 6.8) over 5 minutes were equal to 3.50 ± 0.18 and 0.08 ± 0.01 %, respectively. The relative quantity of solubilized phenolics was decreased significantly ($P < 0.001$) by using the polymeric coating layer.

3.6.2. In-vivo analysis

Based on the experiments, uncoated pellets have relative bitterness (2.2 ± 0.42), while the coated pellets were tasteless (1.0 ± 0.00) to the volunteers. According to the Wilcoxon analysis, the bitterness of the coated pellets was significantly ($P = 0.003$) lower compared to that of the uncoated particles.

4. Discussion

Taste-masked *M. chamomilla* extract-loaded pellets were developed with the aim to improve its dosing flexibility, ease of swallowing, taste-masking as well as patient compliance, especially in children. Extrusion–spheronization, the most popular technique to produce pellets, was used in this study. Easy operation, high drug loading ability, preparation of uniform particles with low friability, and high throughput process are some of the advantages of this method [28].

Additive selection is an important step in formulation development, due to their influence on physicochemical properties of pellets. In the two first pellet formulations (F1 and F2), MS was used to reduce the friction between the material and the die-wall of the extruder, but it did not result in particles with proper appearance and surface properties (Table 2).

The use of SLS in the wetting liquid could act as a pore forming agent in final product. Also, the presence of SLS results in more appropriate

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particles due to the improved wetting of the powder mixture and uniform moisture in dough mass [29]. In fact, by reducing the surface tension and contact angle, wetting liquid can move more easily in the powder mass [30]. Based on Table 2, the friability of the formulations F1 and F3, prepared using lower SLS concentration (0.1 %) in the wetting liquid, was very high compared to F2 and F4, respectively, made in the presence of 1 % SLS solution. In addition, better sphericity was obtained for pellets prepared using higher SLS concentration. It has been shown that the presence of SLS, could reduce the friction at the die wall during extrusion process and decrease the surface defects [31].

Formulations F4-F10 showed high friability (≥ 1 %) indicating improper pellets hardness [32], while the friability of F13-F18 and F21 was equal or less than 0.5 %. The use of binder is recommended in pellet formulations specially in the presence of lower Avicel concentration. Application of higher amount of PVP (6 %) as a binder in the formulations seems necessary in order to obtain pellets with low friability. Higher friability of F19 might to be due to the use of less binder. This was partially compensated by using 10 % lactose in F20; because after wetting, lactose shows adhesive properties and causes better particles bonding. Obviously, to achieve more desirable pellets, it was necessary to use the appropriate amounts of each component. Comparison of F14 and F16 and also F18 and F21 showed that the use of lactose along with Avicel resulted in a relative improvement in the quality of particles which was in accordance with the literature [33].

The optimum formulation, F21, had appropriate properties, including flowability. Suitable values for CI and HR of pellets are considered ≤ 10 % and 1.00-1.11, respectively [34]. The obtained results indicated excellent flow properties for the prepared pellets.

Based on the dissolution tests, the amount of content dissolved from the optimized coated pellets (F21) during the first 10 minutes (Q_{10} = 33.16 ± 1.13 %) were significantly different from those of the base formulation without coating (Q_{10} = 36.94 ± 0.85 %) ($P< 0.01$). In fact, the presence of polymeric layer around the particles, reduced the dissolution rate at the initial stage of the dissolution test. On the other hand, the DE calculated for coated pellets (49.30 ± 0.42 %) was not significantly different from that of uncoated particles (52.26 ± 1.93 %), and an acceptable dissolution was occurred for the active components. The RDR obtained for the dissolution at 30 min was equal to 0.99. RDR value close to 1 indicated the almost similar dissolved compounds from both type of pellets at that time. Based on the above findings, it seems that the coating layer, while covering the core pellet particles, did not prevent the dissolution of the material in the gastric simulated environment (pH = 1.2).

Various ingredients in Mch extract may be responsible for the bitter taste. In the present study, phenolic compounds were considered as one of these materials and their release at higher pH from both coated and uncoated pellets was investigated. Due to the insolubility of Eudragit E at high pH of 6.8 (the pH of the oral cavity), no rapid dissolving of coated pellets in that medium was observed, which was in accordance with the *in vivo* analysis in which no bitter taste was reported for the coated pellets by the volunteers. This is attributed to the strong effect of polymeric barrier on taste-masking and a significant suppression of the bitter taste for the coated pellets.

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5. Conclusion

M. chamomilla extract-loaded pellets were successfully prepared using extrusion-spheronization technique and coated by Eudragit E. The taste-masking efficiency of the pellets was one of the desirable features of the prepared formulation. Rapid dissolving of Eudragit E in acidic medium resulted in suitable dissolution rate, confirmed by the DE and RDR values.

Author contributions

NB: Supervision, conceptualization, methodology, writing-review and editing; SS: Investigation, data collection; FM: Methodology, conceptualization.

Conflict of interest

The authors declare that there is no conflict of interest.

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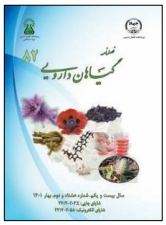
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مقاله تحقیقاتی

تهیه و ارزیابی پلت‌های حاوی عصاره گیاه بابونه دارویی با طعم پوشانده شده

نوشین بلورچیان[1,*]، ساحل شیروانی[1]، فراز مجاب[2]

[1] گروه فارماسیوتیکس و نانوتکنولوژی دارویی، دانشکده داروسازی، دانشگاه علوم پزشکی شهید بهشتی، تهران، ایران

[2] گروه فارماکوگنوزی، دانشکده داروسازی، دانشگاه علوم پزشکی شهید بهشتی، تهران، ایران

اطلاعات مقاله

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پلت

عصاره گیاهی

اکستروژن– اسفرونایزیشن

پوشش طعم

روکش‌دهی

چکیده

مقدمه: خواص قابل توجه گیاه بابونه دارویی (بابونه شیرازی) موجب شده است که به طور گسترده‌ای در درمان بیماری‌های مختلف از جمله اختلالات گوارشی مورد توجه قرار گیرد. **هدف:** در مطالعه حاضر، پلت‌های روکش داده شده حاوی عصاره بابونه با هدف پوشاندن طعم تلخ آن، بهبود دوزینگ و نیز پذیرش بیمار به ویژه در کودکان، ساخته شد. **روش بررسی:** عصاره گیاه به روش خیساندن در اتانول ٪ ۷۰ استخراج و به روش تبخیر دوار و خشک کردن انجمادی خشک گردید. سپس به همراه نسبت‌های مختلف مواد افزودنی گوناگون مانند آویسل، نشاسته و لاکتوز برای تهیه پلت به روش اکستروژن – اسفرونایزیشن مورد استفاده قرار گرفت. پلت‌ها از نظر اندازه، کرویت، نسبت ابعاد و فرسایش‌پذیری بررسی شدند. فرمولاسیون بهینه، پس از انجام فرایند روکش‌دهی با استفاده از اودراژیت E، از نظر کارایی پوشاندن طعم، انحلال و مورفولوژی ارزیابی گردید. **نتایج:** پلت‌های بهینه با اندازه ذره‌ای، کرویت و نسبت ابعاد به ترتیب برابر با ۱/۱۳ میلی‌متر، ۰/۹۲۴ و ۱/۱۷۲ ساخته شدند. فرسایش پذیری کم، جریان‌پذیری (شاخص کار = ۳/۰۱ ٪) و همچنین انحلال مناسب موجب گردید که این نمونه برای پوشاندن طعم به روش روکش‌دهی مورد استفاده قرار گیرد. بر اساس مطالعات انحلال برون‌تن، گرچه لایه روکش به طور قابل توجهی آزادسازی اجزا را در pH بالاتر نسبت به ذرات فاقد روکش کاهش داد، ولی انحلال قابل قبولی در pH برابر با ۱/۲ مشاهده شد. پوشش مناسب طعم این فرآورده با آنالیز درون‌تن نیز تایید گردید. **نتیجه‌گیری:** پلت‌های حاوی عصاره گیاه بابونه دارویی با طعم پوشانده شده و ویژگی‌های مناسب می تواند سامانه مطلوبی همراه با پذیرش بالاتر بیمار باشد.

مخففها: Mch، بابونه شیرازی؛ SLS، سدیم لوریل سولفات؛ MS، استئارات منیزیم؛ PVP ، پلی وینیل پیرولیدون؛ SSG، سدیم استارچ گلیکولات؛ DEx، عصاره خشک؛ TPC، محتوای تام فنلی؛ TFC، محتوای تام فلاونوئیدی؛ AR، نسبت ابعاد؛ CI، شاخص کار؛ HR، نسبت هاسنر؛ DE، کارایی انحلال؛ RDR، سرعت انحلال نسبی

* نویسنده مسؤول: bolourchian@sbmu.ac.ir

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