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Study of the Physical Properties of Lemongrass and Lemon Balm Plants for Tablet Production

Ali Hashemi[1*], Mohammad Hossein Kianmehr[2] and Jafar Massah[2]

[1] *Faculty of Agriculture and Natural Resources, Persian Gulf University, Bushehr, Iran*
[2] *Department of Agrotechnology, College of Aburaihan, University of Tehran, Tehran, Iran*

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***Corresponding author**
Ali Hashemi,
Faculty of Agriculture and Natural Resources,
Persian Gulf University
Bushehr, Bushehr, Iran
Hashemi@pgu.ac.ir

ABSTRACT

The main objective of this study is to investigate some physical properties of lemongrass and lemon balm medicinal plants for tablet production. In this research, the bulk and tapped densities are the most important physical properties of lemongrass (*Cymbopogon citratus*) and lemon balm *(Melissa officinalis)* powders. Powders prepared with a size of less than 0.3 mm had good flowability. The moisture content was determined to be 0.0681% and 0.0792% for lemongrass and lemon balm, respectively. The design of experiments using the response surface methodology (RSM) of the Box-Behnken Design (BBD) was used by the Minitab-19 software to determine the optimal conditions of the tableting process, including tablet formulation, force, and granule size. The ambient humidity and temperature were constant; the binders at three formulation levels and three force and granule levels were examined in an ANOVA statistical analysis system to study the tableting process. The results showed that by decreasing the amount of polyvinyl pyrrolidone by 3 mg, the force increased and the granule size decreased by 5 N and 10 mm, respectively, which led to an increase in disintegration time, hardness, and a decrease in tablet friability. The physical and mechanical parameters of lemongrass and lemon balm tablets showed that the disintegration time, hardness and friability of lemongrass and lemon balm tablets are 285 *S*, 30.8 *SC*, 0.250% and 300 *S*, 31.3 *SC* (Strong Cobb units), and 0.245 %, respectively. At the highest force of 5 N in a mold with a diameter of 19×6×10 mm, the highest unit density for lemongrass and lemon balm samples was1.15g/cm^3 and 1.28 g/cm^3, respectively, and for particle sizes less than 0.3 mm, the changes in the compression percentage were in the range of 54.76% and 56.18%.

Keywords: Tablet press, Lemongrass, Lemon balm, Hardness, Friability, Disintegration time

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INTRODUCTION

Medicinal plants are plants that contain compounds with therapeutic properties, and they are utilized in the pharmaceutical industry for their health benefits for both humans and animals [1]. Over millions of years of evolution, natural products have developed remarkable structural diversity, which underpins their wide range of biological activities and highlights their importance as a valuable resource for drug discovery and development. [2]. Until approximately half a century ago, plants constituted one of the principal sources for the production of pharmaceuticals. However, following advancements in organic chemistry and endeavors to synthesize complex drug molecules, the majority of pharmaceuticals came to be produced synthetically. Nevertheless, over the past few decades, the observation of adverse effects associated with synthetic drugs has led to a renewed inclination toward the utilization of medicinal plants [3]. Currently, about one-third of the drugs used in human societies are of natural and herbal origin. Each medicinal plant contains one or more active ingredients, and according to the active ingredient of the plant the use is defined. The value of medicinal plants has been preserved after several centuries, and this is due to the adverse effects of chemical drugs. Herbal medicines contain active ingredients, many of which are still unknown. Some pharmaceutical drugs are based on an active ingredient obtained from a plant source. Lemongrass has anti-cancer and antibacterial properties, and lemon balm has antioxidant properties, which are used to make oral tablets [4, 5]. In addition to medicinal uses, lemongrass is an important economic crop in the food and cosmetic industries. The essential oil extracted from the leaves is commonly used in perfumes, soaps, beverages, and flavoring agents. Recent scientific studies also suggest that lemongrass extracts may have anticancer potential due to their antioxidant compounds [6]. Despite their relatively low yields per unit area, medicinal plants provide high economic returns due to their greater value added, making them a profitable crop for

farmers [7]. The excessive use of chemical fertilizers and synthetic pesticides has raised environmental and health concerns due to their adverse effects on soil quality, water resources, and human health [8].

Medicinal plants are less expensive than chemical drugs, and are more accessible than chemical drugs. Medicinal plants are very different from chemical drugs in terms of effectiveness and how they are used [9]. Medicinal plants have been used for thousands of years as important sources of therapeutic agents. According to the World Health Organization (WHO), more than 80% of the world's population relies on medicinal plants in traditional or modern healthcare, and many pharmaceutical drugs are derived from plant-based compounds [10,11]. In the 21st century, with the increasing effectiveness of the therapeutic effects of medicinal plants, herbal medicines have become a suitable alternative for the treatment of diseases [12, 13]. Pharmaceutical forms produced under optimal processing conditions of medicinal plants include decoctions, syrups, ointments or creams, granules, tablets, capsules, oral solutions, etc [14]. Common steps in the preparation of plant powder tablets include reversible elastic or irreversible plastic deformation [15]. Three stages are considered for the compression of raw materials: In the first stage, the particles are closely packed together and form a single mass, in the second stage, the particles exert forces on each other and elastic and plastic deformations occur in them, and in the third stage, due to a significant reduction in the volume of the material at a constant mass, the actual density of the material increases. [16, 17]. Using herbal pills and capsules is considered a simple and effective method due to their therapeutic and health benefits for the body. The main purpose of this study is to investigate the physical properties of lemongrass and lemon balm medicinal plants for tablet production, which has not been reported in similar literature. Therefore, in the formulation of tablets, according to the type and characteristics of the materials, various types of binders and some other additives such as lubricants and disintegrating agents, are used to increase the strength of the final product. Sajjadi *et al.* [18] studied the preparation of a type of sedative coated tablet from extracts of lemon balm and valerian. The results of their research showed that the prepared tablets with suitable physical properties could be used as cores in the preparation of coated tablets. Regarding the role of phenolic compounds in Diabetes, DBC & DMV could be an appropriate candidate for reducing the blood sugar level with respect to its traditional use in Ayurveda [19]. Bikash *et al.* [20] investigated the formulation of antidiabetic nutritional tablets based on edible plants from Tripura. The results indicated that the newly formulated herbal tablet may be recommended as an antidiabetic nutritional drug. Gallo *et al.* [21] investigated the physical properties of compressed tablets of dried extract of Valeriana officials. The results showed that the produced tablets have good compressibility, friability, hardness, and disintegration time. Morus alba has properties to treat fever, protect against liver damage, improve eyesight, strengthen joints, facilitate discharge of urine, and prevent high blood pressure. Extracts from herbal plants have hygroscopic and low flowability characteristics [22]. They investigated the formulation and statistical analysis of herbal medicinal tablets containing Morus alba leaf extract. The goal of this project was to prepare tablets based on lemon balm and lemongrass plants.

MATERIALS AND METHODS

Fresh specimens of *Cymbopogon citratus* (lemongrass) and *Melissa officinalis* (lemon balm) were procured from a local market in Tehran. Polyvinylpyrrolidone with the chemical formula and structure $(C_6H_9NO)_n$ (Fig. 1-a), was used as a binder in the pharmaceutical formulation, Avicel 101 and Avicel 102 with the chemical structure (Fig. 1-b) were used as a compacting and densifying agent, purchased from Sigma-Aldrich company.

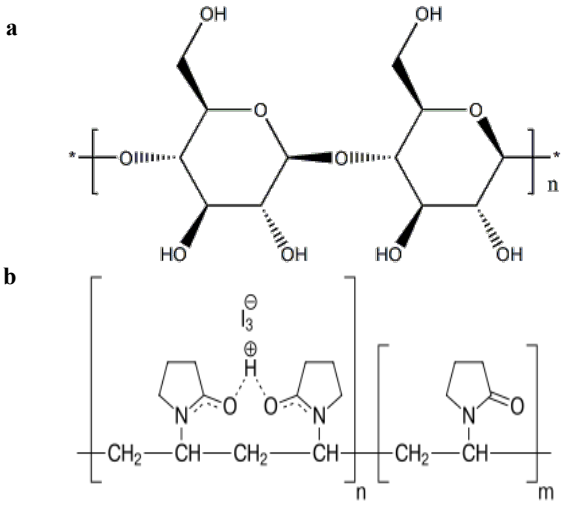

Fig. 1 Chemical structures of (a) polyvinylpyrrolidone and (b) microcrystalline cellulose Avicel (Extragranular)

Colloidal silicon dioxide with a chemical structure (Fig. 2), chemical formula SiO_2, and molecular weight 60.08 g/mol purchased from Sigma-Aldrich was used to prevent clumping.

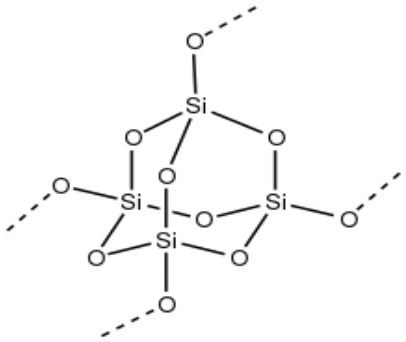

Fig. 2 Chemical structure of colloidal silicon dioxide.

Croscarmellose sodium with the chemical structure (Fig. 3- a) was used as a disintegrating agent in the pharmaceutical formulation, and magnesium stearate with the chemical structure (Fig. 3-b), chemical formula Mg $(C_{18}H_{35}O_2)_2$ and molecular weight 591.27 g/mol, was used as an anti-adhesion agent in the manufacture of tablets purchased from Sigma-Aldrich company.

Preparation of Lemon Balm and Lemongrass Powder

To prepare lemon balm and lemongrass powder, the desired plants were first ground for 12 hours by a mill (Retsch of Germany) with conditions of 220V-AC, 2000W, and 28000 rpm. To understand the effect of particle distribution, the prepared powder was classified by laboratory sieves into three categories (particles smaller than 0.3 mm, particles between 0.3-0.4 mm and particles between 0.4-0.7 mm). During the sieving process, 100 g of the samples were sieved by laboratory sieves with 8-inch form and mesh numbers of 50, 100, and 150 for 10 minutes [23].

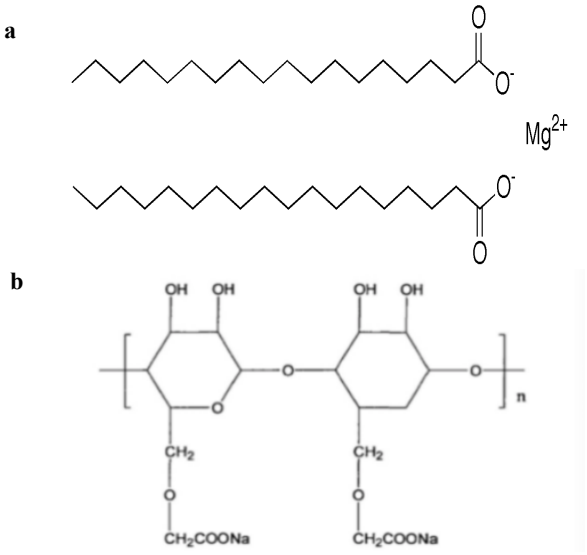

Fig. 3 Structural formulas of (a) croscarmellose sodium and (b) magnesium stearate.

Determination of the Moisture Content of Lemon Balm and Lemongrass Powder

In order to determine the initial moisture content of lemon balm and lemongrass powder, two grams of the sample was placed in an oven (Memert, Germany) at 120 °C for 24 hours until constant weight was reached. After reaching constant weight, the samples were weighed using a digital balance (Mettler Toledo, Switzerland) with a resolution of 0.0001 g. Their initial moisture content was calculated using equation (1) [24].

$$\mathrm{LOD} = \frac{W_1 - W_2}{W_1} \quad (1)$$

Where W_1 and W_2 represent the initial and secondary weights of lemon balm and lemongrass powder.

Determination of Bulk Density of Lemon Balm and Lemongrass Powder

Bulk density is a measure for examining the compaction properties of particulate solids. To determine bulk density, two grams of lemon balm and lemongrass powder were poured freely into a glass cylinder graduated to 10 mm (resolution 0.5 ml) and then the volume occupied was recorded. Bulk density was determined using equation (2) [16].

$$\rho_b = \frac{m}{V_b} \quad (2)$$

Where ρ_b is the bulk density (g ml^{-3}), m is the mass of the powder (g) and V_b is the volume of the powder (ml).

Determination of the Tap Density of Lemon Balm and Lemongrass Powder

In order to determine the tapped density, 2 grams of lemon balm and lemongrass powder were poured freely into a glass cylinder graduated to 10 mm (resolution 0.5 ml) and the occupied volume was recorded using an impact device for 5 minutes. The tap density was determined using equation (3) [16].

$$\rho_t = \frac{m}{V_t} \quad (3)$$

Where ρ_t is the bulk density (g cm^{-3}), m is the mass of the powder (g), and V_t is the volume of the powder (ml).

Carr's Index and Hausner Ratio

The Carr's index and Hausner ratio measure the flowability of the powder and are both measured based on the bulk and tapped densities. The Carr's index and Hausner ratio were calculated using equations 4 and 5, respectively [16].

$$\mathrm{CI} = \frac{(\rho_t - \rho_b)}{\rho_t} \times 100 \quad (4)$$

$$\mathrm{HI} = \frac{\rho_t}{\rho_b} = \frac{V_0}{V_n} \quad (5)$$

Where *CI* is the Carr's index (%), *HI* is the Hausner ratio (dimensionless), V_0 and V_n are the bulk and tapped volumes, respectively.

Static Angle of Repose and Slide Angle

To calculate the static angle of repose, 10 g of lemon balm and lemongrass powder was weighed and passed through a funnel with a fixed height and a 12 mm outlet diameter to be poured onto a flat horizontal surface to form a mass. The angle of repose was calculated from the angle formed by the inclination of the mass of the product with respect to the reference surface, according to Equation (6) [25].

$$\theta = \tan^{-1}\frac{h}{r} \quad (6)$$

Where, r is the heap radius (m), h is the heap height (m), and θ is the angle of repose (degrees).

In order to calculate the slide angle, 5 g of lemon balm and lemongrass powder was weighed and poured onto a rectangular glass plate with a length of 130 mm. Then, the glass plate was gradually lifted until the surface of the lemon balm and lemongrass powder started to move and cuts were made on its surface. The slide angle was calculated according to Equation (7) [25].

$$\alpha = \sin^{-1}\frac{H}{L} \quad (7)$$

Where, L is the length of the glass (130 mm), H is the vertical distance (m) from the top of the glass plate to the reference surface, and α is the slide angle (degrees).

Granule Preparation

In order to prepare the granules, the formulation in Table 1 was used. After determining the amount of the components, granules of 10, 13 and 16 were made using 50, 100 and 150 meshes, respectively.

Table 1 Tablet Ingredients

Ingredients (mg)	Formulation %		
	(1)	(2)	(3)
Lemongrass/lemon balm powder	55.5	55.5	55.5
Polyvinyl pyro lidone	5	4	3
Avicel 101	15	16	17
Avicel 102	17.5	17.5	17.5
Croscarmellose sodium	5	5	5
Colloidal silicon dioxide	1	1	1
Magnesium stearate	1	1	1

Optimization of the Tableting Process

According to previous studies, variables such as force, granule size, and formulation have a significant effect on tablet manufacturing. Force, granule size, and formulation were selected as variables (Table 2). The size of the matrix (tablet mold) was fixed and determined to be 19×6×10 mm. Therefore, the experimental design was used to investigate the effects of the aforementioned independent variable using the response surface methodology as the main application of the experimental design in the tablet manufacturing process. In the course of the experiments, an attempt was made to optimize each of the aforementioned items and examine its effective parameters.

Table 2 Tableting process experimental design

	Factors level		
	Down (-1)	Center (0)	Up (+1)
Formulation	1	2	3
Force (N)	3	4	5
Granules(mm)	10	13	16

In order to investigate the effect of parameters, experiments were designed using Minitab software version 19, response surface methodology (RSM) and Box-Behnken design (BBD). Comparisons between different parameters were performed using statistical analysis (ANOVA), and a significance level of p-value < 0.05 was considered.

Table 3 Effect of particle distribution on powder density

Medicinal plants	Particle size (mm)	Bulk density (kg/m^3)	Impact density (kg/m^3)
	Ps<0.3	178	204
Lemon balm	0.3<Ps<0.4	173	198
	0.4<Ps<0.7	163	179
	Ps<0.3	188	210
Lemongrass	0.3<Ps<0.4	181	206
	0.4<Ps<0.7	172	195

Tableting Process

Figure 4 shows a schematic representation of the closed-end mold used to manufacture cylindrical tablets. As can be seen, this image consists of five main parts, including the upper jaw, lower jaw, cylindrical tablet forming die, piston, and punch. A chamber die is located in the center of the lower jaw. By moving the jack downward and applying pressure to the piston material by the hydraulic jack piston of the press machine, the material passes through the middle chamber of the upper jaw and punch and enters the end matrix of the die and is compressed inside it to form a tablet. By moving the piston upward, the pressure is removed from the material. After the tablet is formed, the lower jaw of the die opens and the compressed tablet is removed from the die [16].

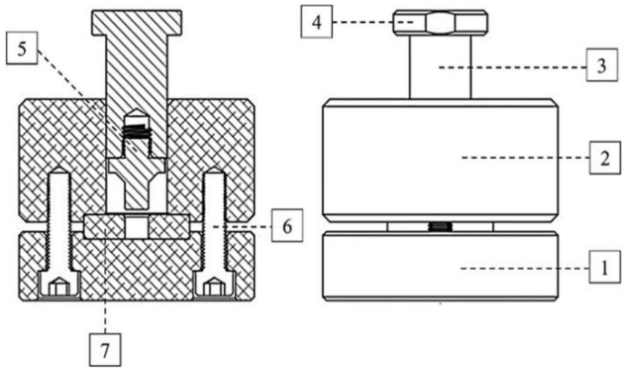

Fig. 4 Schematic view of a tablet forming machine: 1. Lower jaw, 2. Upper jaw, 3. Piston, 4. The location of force application on the piston, 5. Mandrel, 6. Guide screws, and 7. Matrix [16].

In this study, during the tableting process, the jack compressed the materials into a mold measuring 19×6×10 mm at a constant speed of 6 m/s. When the jack force reached three levels of 3, 4, and 5N, the pressure on the materials was maintained for 15 seconds to perform the stress relaxation process, and then the pressure was removed from the materials by moving the piston upward.

Determination of the Unit Density of Tablets

The unit density of each tablet was determined by measuring its mass and volume. The volume of each cylindrical tablet was obtained by measuring the diameter and length of the tablets using a caliper. The mass of each tablet was also measured using a digital balance with an accuracy of 0.0001 g. The unit volume and density were calculated using Equations 8 and 9, respectively [16].

$$V = \pi r^2 h \quad (8)$$

$$\rho = \frac{m}{V} \quad (9)$$

Where h is the tablet length (mm), r is the diameter (mm), V is the tablet volume (m^3), m is the tablet mass (g), and ρ is the tablet density (kg/m^3).

Tablet Compression Percentage

The compression percentage was calculated according to equation (10) [15].

$$\text{Compressoin}\ (\%) = \frac{V_c}{V_b} \times 100 \quad (10)$$

Where V_c is the volume of the compressed tablet and V_b is the volume of the powder inside the mold before compression.

Determination of Tablet Hardness

The compressive strength of tablets was measured using a hardness tester. During the test, a force was applied to the tablets in the direction of their diameter. For this purpose, a tablet was placed between two parallel plates and compressed at a constant loading rate of 1 mm.s-1 until the sample cracked and broke. The average hardness of 10 tablets was taken as the hardness (N) of the tablets [26].

Determination of Tablet Friability

In order to determine the friability of the prepared tablets, 10 tablets were weighed and transferred to the friability tester. Duration of 10 minutes and a speed of 25 rpm were considered as the friability test conditions. Then, the tablets were removed from the device and after cleaning them, they were weighed again. The friability percentage was calculated according to equation 11 [26].

$$\text{friability}\ (\%) = \frac{W_1 - W_2}{W_1} \times 100 \quad (11)$$

Where, W_1 and W_2 represent the initial and final weights of the tablets.

Determination of Tablet Disintegration Time

To determine the disintegration time of the tablets, 6 tablets were selected and placed in a special basket of the disintegration time device. Then, the time required for the tablets to disintegrate in a one-liter beaker containing water at a temperature of ± 2 °C (with an up-down movement) was recorded [26].

Physical Properties of Lemongrass and Lemon Balm Powders

Bulk and Tapped Density

Bulk density is one of the important characteristics for transporting granular materials. The values of bulk and tapped bulk density were measured in three replicates and finally their values were obtained according to table 3. From the results of this table, the bulk and tapped density increased with decreasing particle size, which is likely due to the decrease in empty spaces between the particles [16].

Hausner Ratio and Carr's index

Flowability and stickiness are two important properties of dried particles. The former is expressed as Carr's index and the latter as Hausner ratio. The Carr's index is also used to indicate the compressibility of the powder, while higher values of Carr's index indicate poor flowability and high compressibility. Hausner ratio is defined as the ratio of tapped density to bulk density. The lowest Hausner ratio indicates the highest flowability of a powder [19]. Hausner ratio, Carr's index and flowability of lemongrass and lemon balm powder were determined according to Table 4. The results showed that powders prepared with a size less than 0.3 had good flowability.

Table 4 Carr's index and Hausner ratio of lemon balm and lemongrass powder

Medicinal plants	Particle size (mm)	Work Index (%)	Hassner ratio	Flowability
Lemon balm	Ps<0.3	1.12	11	Good
	0.3<Ps<0.4	1.19	16	Relatively good
	0.4<Ps<0.7	1.23	18	Relatively good
Lemongrass	Ps<0.3	1.14	12	Good
	0.3<Ps<0.4	1.19	16	Relatively good
	0.4<Ps<0.7	1.21	17	Relatively good

The bulk and flow properties of powders are generally influenced by the interactions between particles. The relative measure of these interactions is practically determined by comparing the bulk and tapped densities. This comparison is often used as an index of powder flowability [15]. The interactions are very low for a free-flowing powder, with both densities showing close values, while powders with poor flowability have a significant difference between the bulk and tapped densities due to the interactions between particles [25,27].

Angle of Repose and Slide

Repose is an empirical measure of the fluidity of granular materials. This property depends on factors such as moisture content, particle size, and storage time. Powders with a higher repose angle are less likely to break apart after being poured onto a liquid surface due to their inherent adhesion [25,27]. The results of the repose angle and slide angle are presented in table 5.

Table 5 Repose and slide angle values for lemon balm and lemongrass powders

Medicinal plants	Particle size (mm)	Repose angle (D)	Slide angle (D)
	Ps<0.3	30.19	42.15
Lemon balm	0.3<Ps<0.4	29	30
	0.4<Ps<0.7	32.78	38
	Ps<0.3	30.95	43
Lemongrass	0.3<Ps<0.4	32.56	36.91
	0.4<Ps<0.7	33.75	48.16

Moisture of Lemongrass and Lemon Balm Powders

The final moisture content of the processed powder affects its physical properties such as bulk and tapped bulk density, Carr's and Hausner ratio, flowability (static angle of repose and slide), compressibility index and solubility. Moisture content determines powder flowability, adhesion and storage stability (due to its effect on glass transition temperature and crystallinity behavior) [29]. This is also very important for tablets, as it is positively related to bulk density and compaction to a certain extent, but negatively related to flowability. The moisture content of the powder should be less than 5% for the powder to be considered microbiologically safe. The moisture content of lemongrass and lemon balm powders was determined to be 0.0681% and 0.0792%, respectively.

Analysis of Variance

To achieve optimal conditions for tablet preparation, an experimental design was carried out as a function of the main parameters. Analysis of Variance (ANOVA) was performed to check the model's validity, significance, and accuracy table 6.

The results presented in tables 6 and 7 show that the p-value for the effective parameters is less than 0.05, which indicates significant confirmation of the proposed model. The Lack-of-Fit value for the proposed model for lemongrass and lemon balm is greater than 0.05, which is not significant. High and close values of the coefficient of determination and adjusted coefficient indicate compliance with the experimental results. The residual plot for evaluating the normal distribution of residuals is shown in figure 5. For lemon balm tablets, the plots for disintegration time (a), friability (b), and hardness (c) showed only slight deviations from linearity, suggesting the absence of significant outliers or systematic errors. This indicates that the selected formulation variables adequately explained the observed responses and that the assumptions of normality for regression analysis were satisfied. Similarly, for lemongrass tablets, the residual plots for disintegration time (d), friability (e), and hardness (f) also exhibited a close alignment of the residual points with the normal probability line.

Table 6 Results of Analysis of Variance (ANOVA) for Lemon Balm.

Powder	Factor	Confidence level	optimal	Lack-of-fit	R^2 (%)	R^2_{adj} (%)	R^2_{pred} (%)
Opening Time	formulation	0.000	3	0.729	98.92	96.98	91.36
	Force(N)	0.000	5				
	Granule size(mm)	0.001	10				
	Formulation	0.000	3	0.134	99.68	99.10	95.24
Hardness	Force(N)	0.000	5				
	Granule size(mm)	0.000	10				
	Formulation	0.000	3	0.187	98.59	96.04	79.89
Erosion	Force(N)	0.003	5				
	Granule size(mm)	0.000	10				

Table 7 Results of Analysis of Variance (ANOVA) for Lemongrass.

Powder	Factor	Confidence level	optimal	Lack-of-fit	R^2 (%)	R^2_{adj} (%)	R^2_{pred} (%)
Opening Time	Formulation	0.000	3	0.67	98.50	95.80	86.76
	Force(N)	0.000	5				
	Granule size(mm)	0.002	10				
	Formulation	0.000	3	0.064	99.37	99.25	95.85
Hardness	Force(N)	0.000	5				
	Granule size(mm)	0.000	10				
	Formulation	0.000	3	0.235	98.30	95.24	76.62
Erosion	Force(N)	0.006	5				
	Granule size(mm)	0.000	10				

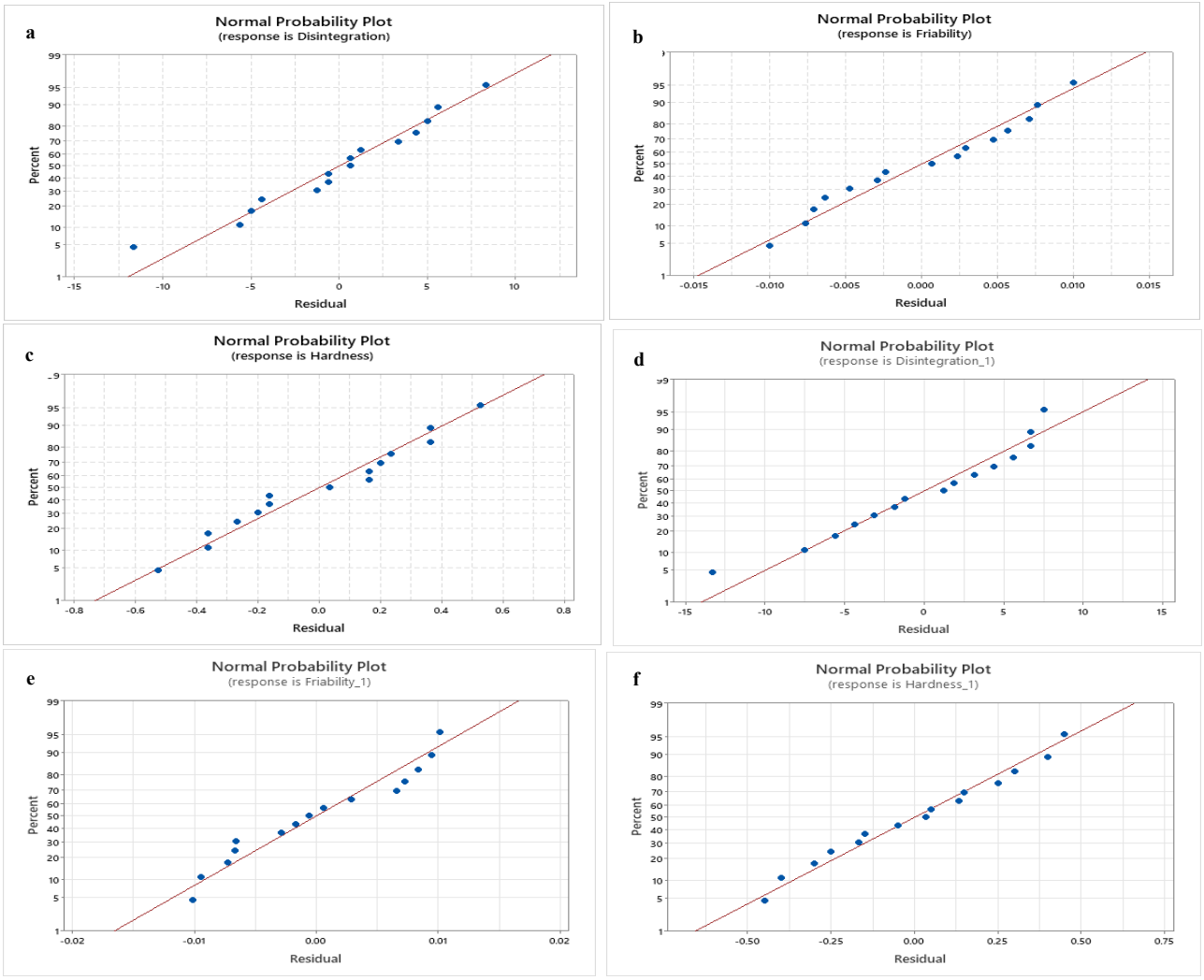

Fig. 5 Normal probability plots of residuals for the responses of lemon balm and lemongrass tablets: (a) Lemon balm tablet disintegration time, (b) Lemon balm tablet friability, (c) Lemon balm tablet hardness, (d) Lemongrass tablet disintegration time, (e) Lemongrass tablet friability, and (f) Lemongrass tablet hardness.

Although minor dispersion was observed at the extreme residual values, the deviations were not substantial, confirming the reliability and predictive capability of the developed models. Overall, the points in the normal residual plot are linear and normally distributed. The normal probability plots presented in figure 5 demonstrate that the residuals for all evaluated responses were distributed approximately along the straight reference line, indicating that the experimental data followed a normal distribution and that the developed models were statistically adequate.

As can be seen in figure 6, decreasing the amount of polyvinylpyrrolidone, increasing the force, and decreasing the granule size to 3 mg, 5 N, and 10 mm, respectively, leads to an increase in the disintegration time and hardness and a reduction in tablet friability. The regression results showed that increasing the formulation level from 1 to 3 increased the disintegration time of lemon balm tablets from approximately 135 s to 245 s and lemongrass tablets from about 120 s to 228 s. Similarly, tablet hardness increased from nearly 16 SC to 26 SC for lemon balm tablets and from 15 SC to 25 SC for lemongrass tablets. In contrast, friability decreased with increasing formulation level, from approximately 0.39% to 0.29% in lemon balm tablets and from 0.38% to 0.28% in lemongrass tablets. An increase in compression force from 3 to 5 also increased disintegration time and hardness while reducing friability in both formulations. However, increasing granule concentration from 10% to 16% decreased disintegration time and hardness but increased friability.

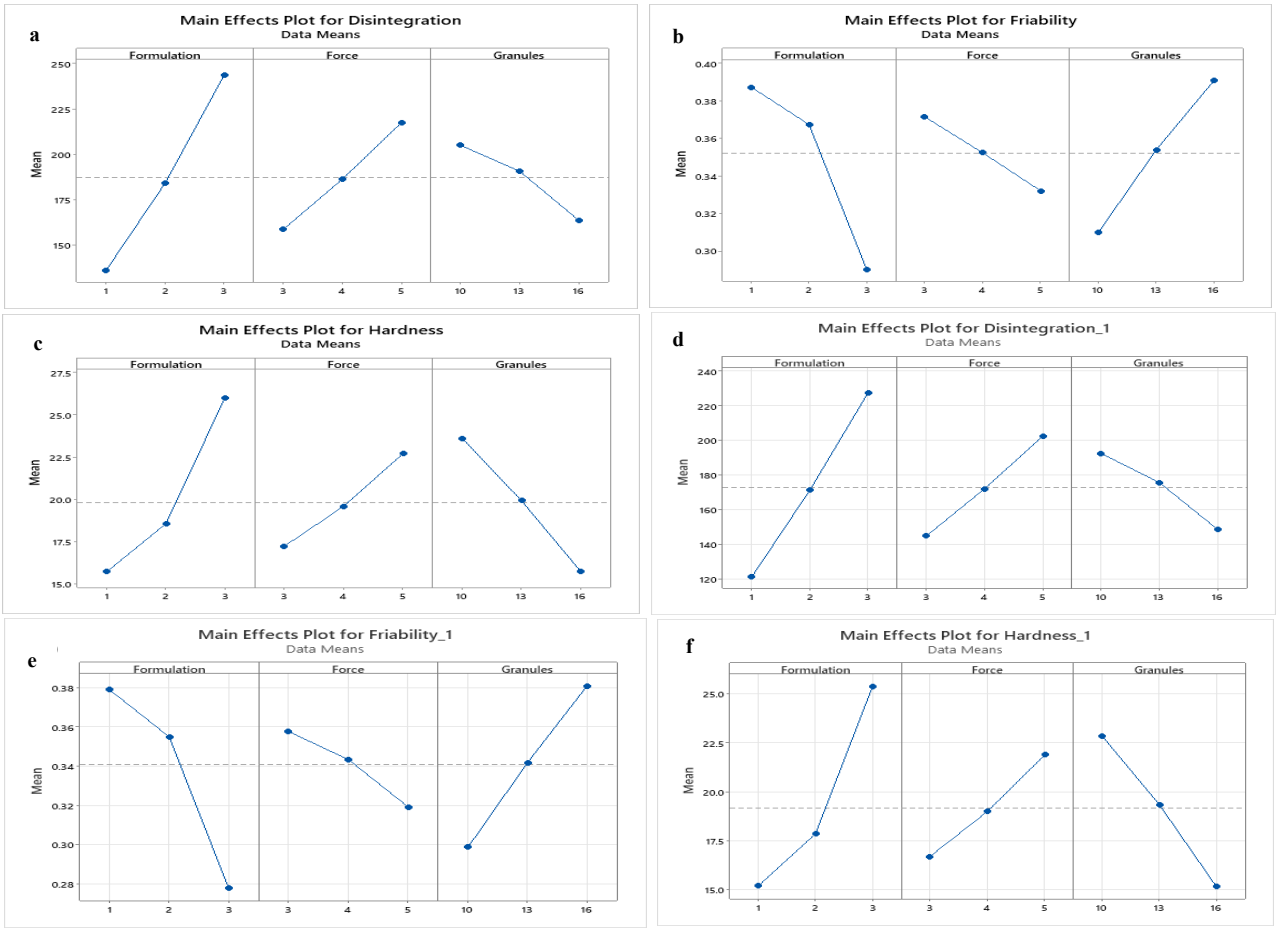

Fig. 6 Influence diagrams illustrating the effects of the main formulation parameters on tablet characteristics: (a) Opening time of lemon balm tablets, (b) Friability of lemon balm tablets, (c) Hardness of lemon balm tablets, (d) Disintegration time of lemongrass tablets, (e) Erosion of lemongrass tablets, and (f) Hardness of lemongrass tablets.

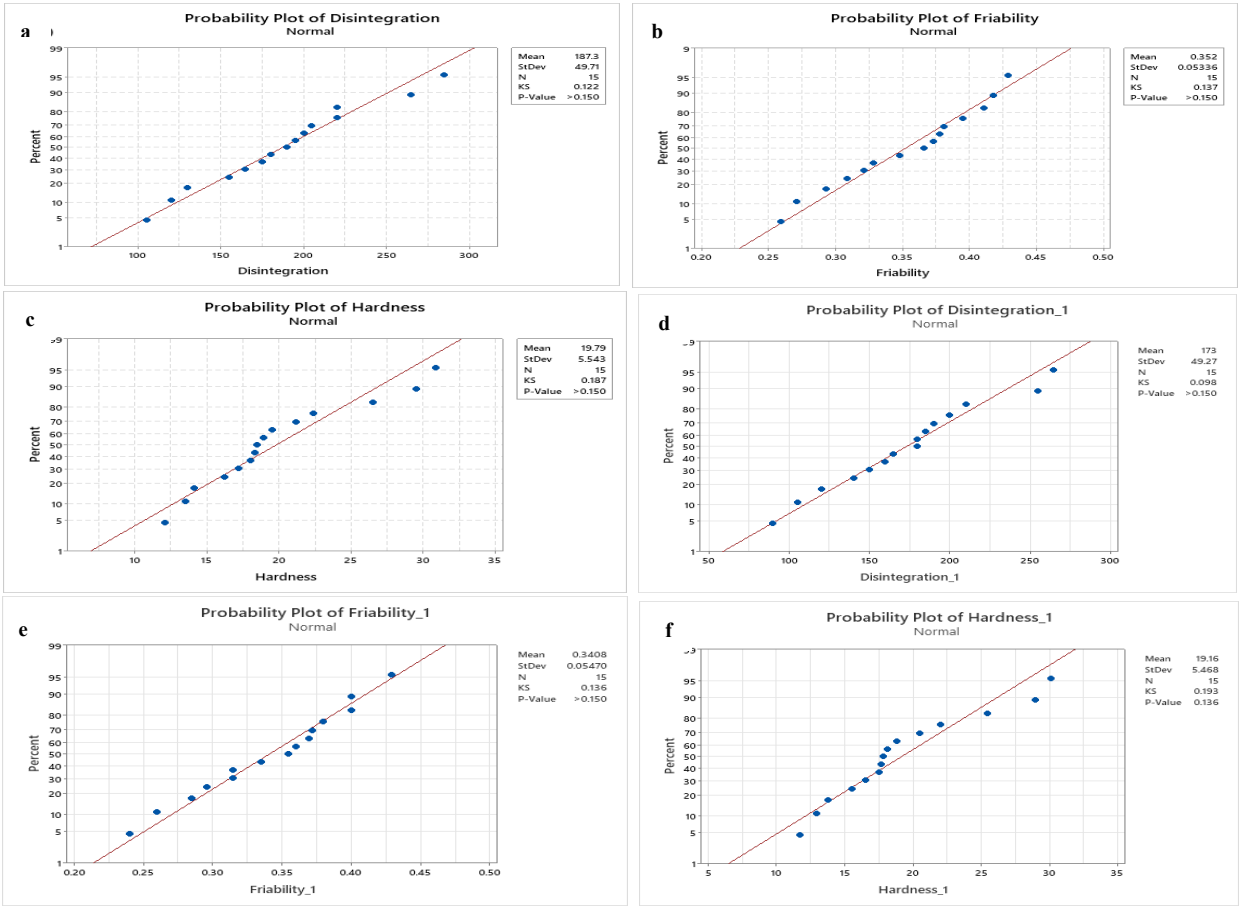

Fig. 7 Normality of data using the Kolmogorov-Smirnov method. (a) Lemongrass tablet disintegration time, (b) Lemongrass tablet friability, (c) Lemongrass tablet hardness, (d) Lemon balm tablet disintegration time, (e) Lemon balm tablet friability, (f) Lemon balm tablet hardness.

These regression trends confirm that formulation concentration and compression force positively affected tablet strength, whereas higher granule levels negatively influenced the mechanical properties of the tablets.Figure 7 presents the normality assessment of tablet responses using the Kolmogorov–Smirnov (K–S) test (7). The probability plots for disintegration time, friability, and hardness of both lemongrass and lemon balm tablets showed that the data points were closely distributed along the reference line, indicating an approximately normal distribution. The K–S test results revealed p-values greater than 0.150 for most responses, while lemon balm tablet hardness showed a p-value of 0.136, which also remained above the significance level of 0.05.

The mean values for lemongrass tablets were 187.3 s for disintegration time, 0.352% for friability, and 19.79 SC for hardness. Similarly, lemon balm tablets showed mean values of 173 s for disintegration time, 0.3408% for friability, and 19.16 SC for hardness. The standard deviation values ranged from 0.05336 to 49.71, indicating acceptable variability among the measurements. Overall, the probability plots and K–S test results confirmed that all datasets followed a normal distribution and were suitable for regression and statistical analysis.

Normality is an essential assumption for the application of parametric statistical tests. Parametric analyses are primarily based on the estimation of the mean and standard deviation of the dataset. Therefore, deviations from normal distribution may affect the accuracy and validity of the statistical inferences. Consequently, assessment of data normality is necessary to ensure the reliability and appropriateness of the applied statistical models.

Investigation of Parameters Affecting the Tableting Process

Flowability and compressibility are vital properties required for powders or granules. The uniformity of particle size, hardness, disintegration and compressibility of granules depend on the type and amount of binder used in the formulation. The binder in tablet production can cause intergranular bonding between granules, which causes bridging between adjacent granules. Using a stronger binder or a very concentrated binder solution produces hard granules that require more force to produce tablets [15]. The formulation considered for tablet preparation was investigated. By varying the amount of polyvinylpyrrolidone binder, the results showed that reducing the amount of polyvinylpyrrolidone (formulation 3) leads to an increase in disintegration time, hardness and reduced tablet friability. The adhesive property of povidone has made it widely used in tableting (in powder form). This product can be used as a solubility enhancer in polar solvents for topical and oral applications. In addition, polyvinylpyrrolidone plays a significant role in emulsion stabilization and anti-fouling performance. Owing to its chemical structure, particularly the presence of a lactam ring, polyvinylpyrrolidone is capable of forming complexes with a wide range of molecules containing functional groups such as hydroxyl, carboxyl, and amine groups. The present findings are in agreement with those reported by Aziz *et al.* [16].

Force and Granulation

The granulation process is one of the most important and main processes in tablet production after tablet formulation. Granulation is the most important and well-known method for achieving a flowable and compressible powder for tablet production. The main feature of granulated powder is homogeneity and high compaction of the powder. Figures a–l presents the response surface analysis showing the effects of formulation composition, granule size, and compression force on the disintegration time, friability, and hardness of lemon balm and lemongrass tablets. In figures a, c, and e for lemon balm tablets, and Figures g, i, and k for lemongrass tablets, granule size was kept constant at 13 while formulation level and compression force were varied. Under these conditions, disintegration time increased with increasing formulation level and compression force, with values ranging approximately from 100 to 280 (Fig. a and g). Friability decreased with increasing formulation level and compression force, with values ranging from approximately 0.25 to 0.40 (Fig. c and i). Hardness also increased markedly with increasing formulation level and compression force, with values ranging approximately from 15 to 32 (Fig. e and k).

In Figures b, d, and f for lemon balm tablets, and figures h, j, and l for lemongrass tablets, formulation level was maintained constant at 2 while granule size and compression force were varied. Figures b and h showed that disintegration time increased with increasing granule size and compression force, with values ranging approximately from 150 to 220. Figures d and j demonstrated that friability slightly increased with increasing granule size but decreased with increasing compression force, with values ranging from approximately 0.30 to 0.43. Figures f and l indicated that hardness increased with increasing compression force but slightly decreased with increasing granule size, with hardness values ranging approximately from 15 to 25.

The non-linear and curved response surfaces observed in several figures suggested possible interaction effects among formulation composition, granule size, and compression force on tablet disintegration, friability, and hardness. Overall, the response surface analysis confirmed that these independent variables significantly influenced the physicochemical properties of both lemon balm and lemongrass tablets

According to figure 8, with an increase in the loading force from 3 to 5 N, the compressive strength value increased. The reason for this is the increase in van der Waals forces due to the increase in pressure. Also, with a decrease in the size of the granule particles, the compressive strength value increased, which is due to the increase in van der Waals forces due to the increase in the contact surface area with the decrease in particle size [28, 29].

Study of Physical and Mechanical Parameters of Lemongrass and lemon Balm Tablets

The physical and mechanical parameters of the prepared tablets, including unit density, compression percentage, disintegration time, hardness and friability, were investigated. The results are given in Table 8. The disintegration time, hardness, and friability of lemongrass and lemon balm tablets were determined to be 285 s, 30.8 SC (Strong Cobb units), and 0.250%, and 300 s, 31.3 SC and 0.245%, respectively. The highest unit density at the highest compression process force (5N), particle size less than 0.3 and mold diameter 19×6×10 mm for lemongrass and lemon balm samples was 115 g/cm^3 and 1.28 g/cm^{-3}, respectively. According to the results obtained, the variable of applied loading pressure had a positive effect on unit density. With increasing loading pressure, the unit density value increased. The possible reason for this increase in unit density with increasing force can be considered as the volume reduction due to the reduction of pores between particles, the increase in contact surface area in order to form bridges between particles, which leads to higher material density [22, 24].

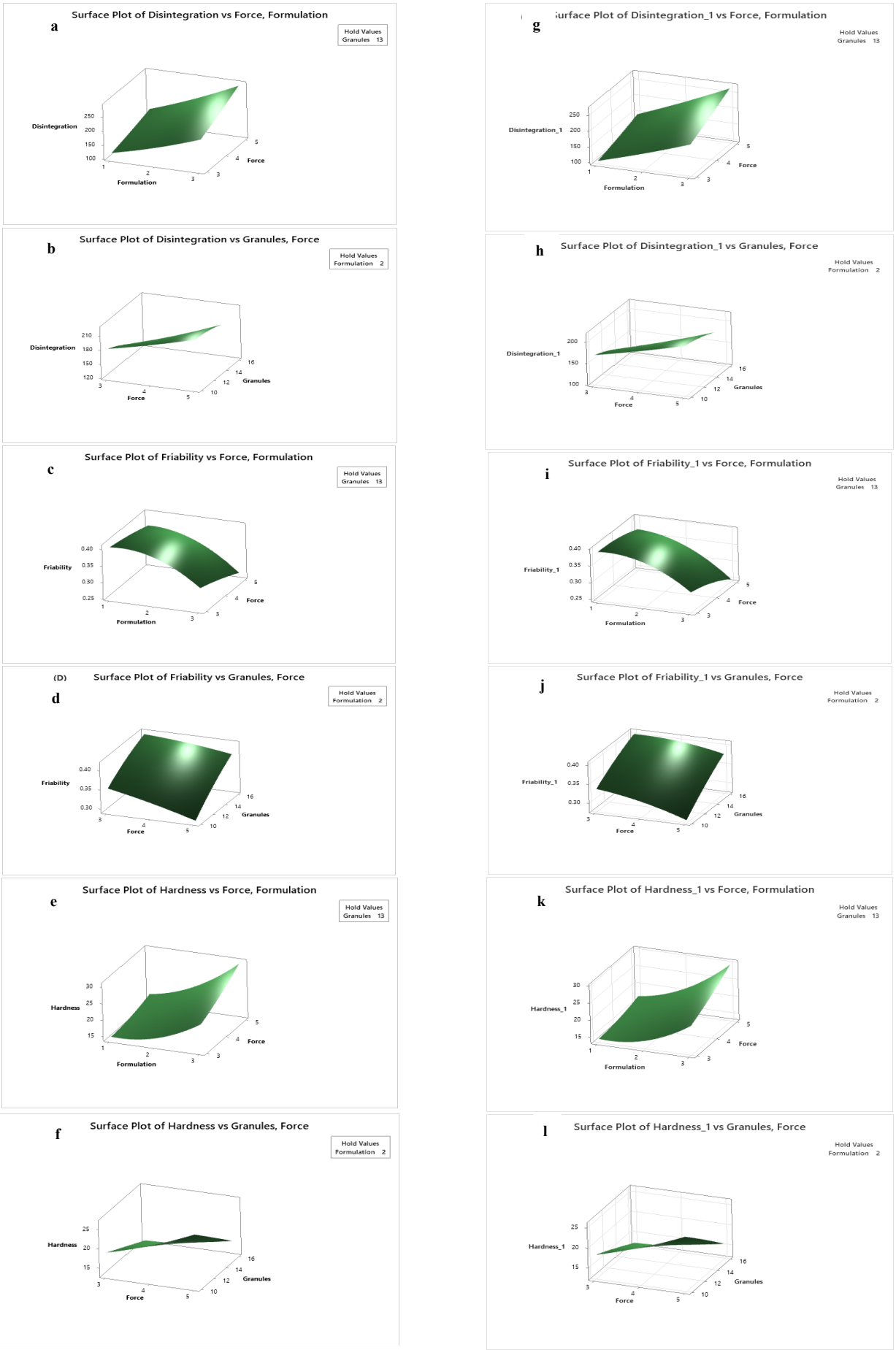

Fig. 8 Response surface plots showing the effects of formulation composition, granule size, and compression force on tablet disintegration time, hardness, and friability of lemon balm (a–f) and lemongrass (g–l) formulations.

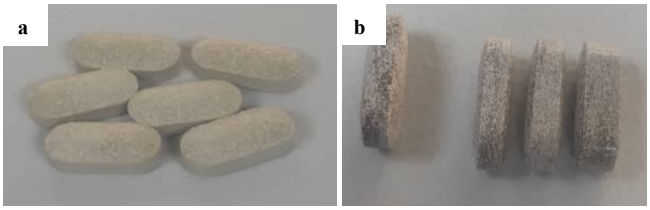

Fig. 9 Representative images of herbal tablets formulated with (a) lemongrass extract and (b) lemon balm extract.

The amount of change in the percentage of compaction for lemongrass and lemon balm was in the range of 56.18% and 54.76% with a force of 5 N and a particle size smaller than 0.3, respectively. With increasing loading pressure, the percentage of compaction of the prepared tablets increased. The reason for this is that high pressure causes greater proximity and the elimination of empty space between the powder particles; therefore, loading force has a positive effect on the percentage of compaction. Our findings are consistent with those reported by Ghasemi (26) and Lerma-Arce *et al.,* [28], who reported that tablets prepared with smaller particle sizes exhibited a larger interparticle contact surface area, thereby promoting stronger van der Waals interactions between particles. Consequently, tablets with higher density and enhanced mechanical strength were produced. These observations suggest an inverse relationship between particle size and the percentage of compaction.

Table 8 Physical and mechanical parameters of lemongrass and lemon balm tablets with optimal conditions

Parameters	lemongrass	lemon balm
Tablet Density (g/m^3)	1.15	1.28
Tablet Compression (%)	56.18	54.76
Tablet Opening Time (s)	285	300
Hardness (SC)	30.8	31.3
Erosion (%)	0.25	0.245

CONCLUSION

The highest values of bulk and tapped density were 178, 204, 188, and 210 for lemongrass and lemon balm with particle sizes less than 0.3, respectively. The results showed that bulk and tapped densities increased with decreasing particle size due to the decrease in the void space between the particles. The Carr's index is used to indicate the compressibility of the powder, while higher values of the Carr's index indicate poor flowability and high compressibility. The results showed that powders prepared with a size less than 0.3 have good flowability. Repose is an experimental measure to determine the fluidity of granulated materials. This property depends on factors such as moisture content, particle size, and storage time. The highest degree of repose angle and slide angle were 30.19, 42.15, 30.95, and 43 for lemongrass and lemon balm with particle size less than 0.3, respectively. The final moisture content of the processed powder affects its physical properties such as bulk and compact bulk density, Carr's and Hausner ratio, flowability, compressibility index and solubility. The moisture content of lemongrass and lemon balm powders was determined to be 0.0681% and 0.0792%, respectively. Analysis of variance showed that reducing the amount of polyvinylpyrrolidone, increasing the force, and reducing the granule size to 3 mg, 5 N, and 10 mm, respectively, led to an increase in disintegration time, hardness, and a decrease in tablet friability. The results showed that decreasing the amount of polyvinylpyrrolidone (Formulation 3) led to an increase in disintegration time, and hardness, and reduced tablet friability. By increasing the loading pressure from 3 to 5 N, the compressive strength value increased. The reason for this is the increase in Van Der Waals forces due to the increase in pressure. By decreasing the size of the granule particles, the compressive strength value increased, which is due to the increase in Van Der Waals forces due to the increase in the contact surface area with the smaller particle size. The disintegration time, hardness, and friability of lemongrass and lemon balm tablets were determined to be 285 S, 30.8 SC, 0.250 SCU, 300 S, 31.3 SC, and 0.245 SCU, respectively. The highest unit density at the highest compression process pressure (5 N), particle size less than 0.3, and mold diameter 19×6×10 mm for lemongrass and lemon balm samples was 1.15 g/cm$^{/3}$ and 1.28 g/cm^3, respectively. The amount of change in the percentage of compaction for lemongrass and lemon balm was in the range of 56.18% and 54.76% with a force of 5N and a particle size smaller than 0.3.

Consent for Publication

Not Applicable.

Data Availability

Not Applicable.

Conflict of Interests

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