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Original Article

Spondias pinnata Leaf Extract Tablets: Impact of Primojel® and Maltodextrin Variations on Physical Properties, Stability, and Antioxidant Activity

Tablet Ekstrak Daun *Spondias pinnata*: Pengaruh Variasi Primojel® dan Maltodekstrin terhadap Karakteristik dan Stabilitas Fisik serta Aktivitas Antioksidan

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Kata Kunci: antioksidan, *don cemcem*, maltodekstrin, mutu fisik tablet, Primojel®.

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Abstract

Cemcem leaves (*Spondias pinnata*) are rich in phenolic and flavonoid compounds with antioxidant potential. However, their traditional beverage form lacks stability, necessitating tablet formulation to improve stability and dosing convenience. This study evaluated the effect of varying concentrations of maltodextrin (binder) and Primojel® (disintegrant) on the physical quality and antioxidant activity of *cemcem* leaf extract tablets. Prior to formulation, extraction temperature optimization was performed using ultrasonic-assisted maceration at 30 °C and 45 °C, each for 3 minutes per cycle over three cycles. Three tablet formulations were prepared using optimized extract with different maltodextrin–Primojel® ratios: F1 (3%-8%), F2 (6.5%-5%), and F3 (10%-2%). Granule evaluation included moisture content, flow rate, angle of repose, and compressibility index. Tablets were assessed on days 1, 14, and 28 under room temperature storage for organoleptic properties, weight and size uniformity, hardness, friability, and disintegration time. Data were analyzed using Repeated Measures ANOVA and Friedman test at a 95% confidence level. Extraction at 30 °C yielded superior antioxidant activity, with lower IC_{50} values and higher total flavonoid content, and was therefore selected for formulation. All granules met physical quality standards; however, among tablet parameters, only disintegration time complied with pharmacopeial requirements. Formula F3, containing the highest maltodextrin concentration (10%) and lowest Primojel® concentration (2%), demonstrated the best physical stability from day 1 to day 28 ($p > 0.05$) and the strongest antioxidant activity, with the lowest IC_{50} value (23.88 µg/mL; AAI 1.68). These findings confirm a causal relationship between excipient concentration and tablet performance, supporting F3 as a promising prototype for antioxidant supplement development.

Abstrak

Daun *cemcem* (*Spondias pinnata*) kaya akan senyawa fenolik dan flavonoid yang berpotensi sebagai antioksidan. Namun, bentuk minuman tradisionalnya kurang stabil sehingga diperlukan formulasi tablet untuk meningkatkan stabilitas dan kemudahan pemberian dosis. Penelitian ini bertujuan mengevaluasi pengaruh variasi maltodekstrin (pengikat) dan Primojel® (disintegran) terhadap mutu fisik dan aktivitas antioksidan tablet ekstrak daun *cemcem*. Sebelum formulasi, dilakukan optimasi suhu ekstraksi menggunakan metode maserasi berbantu ultrasonik pada suhu 30°C dan 45°C, masing-masing selama 3 menit per siklus sebanyak tiga siklus. Tiga formula tablet disiapkan menggunakan ekstrak hasil optimasi dengan variasi maltodekstrin–Primojel®, yaitu F1 (3%-8%), F2 (6,5%-5%), dan F3 (10%-2%). Evaluasi granul meliputi kadar air, kecepatan alir, sudut istirahat, dan indeks kompresibilitas. Tablet diuji pada hari ke-1, 14, dan 28 yang disimpan pada suhu kamar terhadap parameter organoleptik, keseragaman bobot dan ukuran, kekerasan, friabilitas, serta waktu hancur. Data dianalisis menggunakan *Repeated Measures* ANOVA dan uji Friedman pada taraf kepercayaan 95%. Hasil optimasi menunjukkan ekstrak pada suhu 30 °C memiliki aktivitas antioksidan lebih baik dengan nilai IC_{50} lebih rendah dan kandungan total flavonoid lebih tinggi, sehingga digunakan untuk formulasi. Seluruh granul memenuhi kriteria mutu fisik, namun dari parameter tablet hanya waktu hancur yang sesuai standar. Formula F3 dengan konsentrasi

maltodekstrin tertinggi (10%) dan Primojel® terendah (2%) menunjukkan stabilitas fisik terbaik dari hari ke-1 hingga ke-28 ($p > 0,05$) serta aktivitas antioksidan tertinggi dengan nilai IC_{50} terendah (23,88 µg/ml; AAI 1,68). Temuan ini menegaskan hubungan kausal antara konsentrasi eksipien dan kinerja tablet, mendukung F3 sebagai prototipe yang menjanjikan untuk pengembangan suplemen antioksidan.

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INTRODUCTION

Loloh don cemcem is a traditional Balinese herbal drink empirically consumed for general health maintenance;[1–5] however, standardized pharmacological evidence for many claimed benefits remains limited. The plant source, *cemcem* or forest hog plum (*Spondias pinnata* (L.f.) Kurz), contains secondary metabolites—including phenolics, flavonoids, terpenoids, and alkaloids—reported to exhibit antimicrobial and antioxidant activities.[6]

Previous studies found that *cemcem* in liquid "*loloh*" form shows relatively weak DPPH radical-scavenging activity, namely the loloh 1 sample of 471.9440 µg/mL and the loloh 2 sample of 322.2943 µg/mL,[7] whereas its ethanolic extract displays much stronger antioxidant capacity (IC_{50} value of 49.97 µg/mL).[8] Moreover, the beverage form is physically unstable, with a room-temperature shelf life of only about half a day,[9] limiting practical use and distribution. Converting *cemcem* into a tablet dosage form could improve stability, dose accuracy, portability, and patient acceptance.[10,11]

Successful tableting of botanical extracts depends on excipient selection and optimization to achieve acceptable weight uniformity, hardness, friability, and disintegration without compromising active release. Maltodextrin is a widely used binder with film-forming and compressible properties; typical use levels in wet granulation are about 3–10% w/w[12] and may also help protect labile phytochemicals during drying.[13,14] Primojel® (sodium starch glycolate) is a superdisintegrant that rapidly absorbs water and swells, promoting tablet breakup and potentially enhancing dissolution of herbal actives; its concentration can influence mechanical strength and performance. Literature further indicates that excipients are not always pharmacologically inert—variations in type or level can affect release, stability, and even biopharmaceutical behavior of actives.[15]

A previous study formulated cemcem extract tablets using maltodextrin as a binder and varied only the concentration of Primojel®; however, the resulting tablets exhibited poor antioxidant activity and suboptimal physical properties.[15] This suggests that optimizing both binder and superdisintegrant levels may be critical for achieving desirable mechanical integrity and functional performance.

To date, no published work has systematically evaluated the combined effect of binder and superdisintegrant levels on cemcem tablet quality and antioxidant activity. This represents a key gap in transforming a traditional herbal drink into a standardized, stable solid dosage form.

Therefore, the objective of this study is to formulate cemcem leaf extract into a tablet dosage form and to investigate how varying concentrations of maltodextrin (binder) and Primojel® (superdisintegrant) influence (1) precompression granule properties, (2) physical quality and short-term stability of the tablets, and (3) antioxidant activity (DPPH assay). The findings are expected to provide a scientific basis for developing a stable, user-friendly herbal tablet derived from *cemcem* leaves, contributing to the modernization and standardization of traditional Balinese medicine.

RESEARCH METHODS

A laboratory-based experimental design was employed to assess the effect of varying maltodextrin and Primojel® concentrations on the physical quality and antioxidant activity of cemcem leaf extract tablets. Independent variables were maltodextrin and Primojel® concentrations, while dependent variables included tablet physical quality, physical stability, and antioxidant activity. Three formulations were prepared with different maltodextrin–Primojel® ratios: F1 (3%, 8%), F2 (6.5%, 5%), and F3 (10%, 2%). Specific composition details are withheld due to intellectual property considerations.

Materials

Cemcem leaves (*Spondias pinnata* (L.f) Kurz) were collected from Penglipuran Village, Bangli Regency. The leaves were approximately 2–3 months old at harvest, mature but not yet yellowing, and hand-picked individually. Other materials used include ethanol 96% (Sabha Kimia, Indonesia), polyvinylpyrrolidone (PVP; Fadjar Kimia, Bogor), maltodextrin (Subur Kimia Jaya, Indonesia), lactose monohydrate (30320-Lactose-Edible-200M-25 KG FB, Grade A, Dairy Road & Hwy 49, USA), Primojel® (sodium starch glycolate USP, maize-based, Type A; Sigachi Industries LTD, India), magnesium stearate (Fadjar Kimia, Bogor), talc (PT. Karunia Sejahtera Abadi, Denpasar), Dragendorff and Liebermann-Burchard reagents, distilled water (aquadest), magnesium, hydrochloric acid, amyl alcohol, gelatin, ferric chloride ($FeCl_3$), ammonia 25%, chloroform, and ether.

Research Procedure

Plant Identification and Preparation of Simplicia

The botanical identification of *Spondias pinnata* (*cemcem* leaves) was conducted at the Characterization Laboratory of Eka Karya Botanical Garden – BRIN, Bali. *Cemcem* leaves were collected from Penglipuran Village, Bangli Regency. The leaves were sorted, washed thoroughly under running water, cut into small pieces, and air-dried at room temperature. The dried material was then oven-dried at 60°C for 6 hours. The dried simplicia was powdered using a blender and sieved through a mesh No. 20.[16]

Extraction of Cemcem Leaf

The powdered simplicia was extracted using ultrasonic-assisted maceration with 96% ethanol (1:8 ratio) in an ultrasonic bath (Elmasonic® S40H, Germany). Prior to tablet formulation, an initial optimization study was conducted to determine the most suitable extraction temperature. Among the tested conditions (30 °C and 45 °C), 30 °C yielded better extraction efficiency and was therefore selected for the current study. Ultrasonic waves at 20 kHz were applied for 3 minutes per cycle at 30 °C, repeated three times. The resulting extract was filtered using a Buchner funnel (PT. Mitra Sarana Instrumentasi, Indonesia) and concentrated under reduced pressure using a rotary evaporator (Buchi Rotavapor R-300 EL, Switzerland) at 50 °C to obtain a thick extract.[17]

Phytochemical Screening of Cemcem Leaf Extract

A test solution was prepared by dissolving 1 gram of the thick extract in 100 mL of hot water and filtering it to obtain filtrate A.[18]

1. Flavonoid Test
   Five milliliters of filtrate A were mixed with 0.1 g of magnesium powder, 1 mL of hydrochloric acid, and 2 mL of amyl alcohol. The mixture was shaken until layers separated. The presence of flavonoids was indicated by an orange color in the amyl alcohol layer.
2. Tannin Test
   Five milliliters of filtrate A were mixed with gelatin. The formation of a white precipitate indicated the presence of tannins.
3. Phenol Test
   Five milliliters of filtrate A were mixed with 1% ferric chloride solution. A dark blue coloration indicated the presence of phenolic compounds.
4. Alkaloid Test
   Two grams of thick extract were triturated with 5 mL of 25% ammonia and 20 mL of chloroform. The mixture was filtered, and the filtrate was spotted onto filter paper and treated with Dragendorff's reagent. An orange coloration indicated the presence of alkaloids.
5. Steroid or Triterpenoid Test
   One gram of thick extract was macerated in 20 mL of ether for 2 hours, then filtered. Five milliliters of the filtrate were evaporated in a porcelain dish and treated with Liebermann-Burchard reagent. A green-blue or purplish-red color indicated the presence of steroids or triterpenoids.

Tablet Formulation of Cemcem Leaf Extract

Three tablet formulations were prepared, each with a tablet weight of 650 mg, totaling 250 tablets per formula, with variations in the concentrations of maltodextrin and Primojel® [F1 (3%, 8%), F2 (6.5%, 5%), and F3 (10%, 2%)]. All equipment was prepared and materials weighed, following the wet granulation method adapted from Suena et al.[19] PVP and *cemcem* leaf extract (7%) were each dissolved in 15 mL of 96% ethanol, then combined and mixed until homogeneous. The lactose–maltodextrin mixture was gradually added to the PVP–extract solution until a kneadable wet mass formed. The wet granules were passed through a mesh No. 14 sieve (ASTM E-11, Indonesia) and spread on a parchment-lined tray. They were dried in an oven (Memmert UN110, Germany) at 50–60°C for 10–15 minutes, then re-sieved using mesh No. 20 (ASTM E-11, Indonesia). The granules were further dried to a moisture content of 2–4%. The dry granules were weighed, and Primojel®, magnesium stearate, and talc were added based on the percentage of dry granule weight. The mixture was homogenized in a plastic bag.

Granule Physical Quality Evaluation

1. Moisture Content
   Three grams of granules were placed on the pan of a moisture analyzer (MB90, Ohaus Corporation, USA). The instrument was tared and started. The test ended when the moisture percentage was displayed.[20]
2. Compressibility Test
   Ten grams of granules were placed in a 25 mL graduated cylinder, and the initial volume was recorded. The cylinder was placed in a tap density tester (LYCB220S, Linix) set to 300 taps. The final volume was recorded after the test.[15]
3. Flow Properties
   One hundred grams of granules were placed in a flow tester with the bottom outlet closed. The outlet was opened while simultaneously starting a stopwatch. The time taken for all granules to flow through was recorded. Flow rate was calculated. The diameter and height of the granule pile were measured to calculate the angle of repose.

Tablet Physical Quality Evaluation

Physical quality tests were performed on Days 1, 14, and 28 after tablet formulation. During the 28-day study period, tablets were stored in glass jars with silica gel desiccant to control moisture, kept at room temperature, and protected from direct sunlight.

1. Organoleptic Evaluation
   The tablets were observed for appearance, including aroma, color, taste, and shape.[21]
2. Weight Uniformity
   Twenty tablets were weighed individually and their average weight calculated. The deviation of each tablet from the average was assessed. For tablets >300 mg, no more than two tablets may deviate from the average weight by an amount greater than the limit specified in Column A (5%), and no single tablet may deviate from the average weight by more than the limit specified in Column B (10%).[22]
3. Size Uniformity
   Twenty tablets were randomly selected, and their diameter and thickness were measured using a caliper.[23]
4. Hardness Test
   Twenty tablets were tested using a hardness tester (Graigar YD-1, Mitra Medika Solo, China). Each tablet was placed horizontally, and the dial turned counterclockwise until the tablet broke. The breaking force (kg) was recorded.[15]
5. Friability Test
   Twenty dust-free tablets were weighed, placed in a friabilator (CS-0, UniLab, California), and rotated at 25 rpm for 4 minutes (100 rotations). Afterward, tablets were dusted and reweighed. The percentage weight loss was calculated.[21]

6. Disintegration Time

   One tablet was placed in each tube of a disintegration tester (BJ-3, Flight Pharmaceutical Machinery CO., LIMITED, China) filled with warm water at 37°C and covered with a disc. The timer was set for 15 minutes. All tablets should disintegrate completely within this time. If 1–2 tablets fail, the test is repeated with 12 additional tablets.[22,24]

Antioxidant activity assay

Antioxidant activity was assessed using the DPPH (2,2-diphenyl-1-picrylhydrazyl) radical scavenging method. A 40 µg/mL DPPH working solution was prepared by dissolving 4 mg of DPPH in 100 mL of 96% ethanol and homogenizing. The maximum absorption wavelength of the DPPH solution was determined by incubating it for 30 minutes and measuring absorbance across 400–800 nm. A 100 µg/mL vitamin C stock solution was prepared by dissolving 10 mg in 100 mL of ethanol, followed by serial dilutions to obtain concentrations of 2, 4, 6, 8, and 10 µg/mL. *Cemcem* leaf extract tablets (100 mg per formulation) were powdered, dissolved in 100 mL of ethanol, homogenized, and sonicated for 5 minutes. Serial dilutions of the sample solutions were prepared similarly to match the same concentration range. For each concentration, 2 mL of sample or vitamin C solution was mixed with 2 mL of DPPH solution, incubated for 30 minutes, and absorbance was measured using UV-Vis spectrophotometry at the determined maximum wavelength (typically 517–518 nm). A control was prepared by mixing 2 mL of DPPH with 2 mL of ethanol. Antioxidant activity was expressed as % inhibition, calculated using the formula (1).

$$\% \text{ Inhibition} = \frac{Control\ absorbance - Sample\ absorbance}{Control\ absorbance} \times 100\% \quad \text{.....(1)}$$

Notes:

The control absorbance refers to the DPPH solution mixed with solvent (96% ethanol), while the sample absorbance refers to the DPPH solution mixed with *cemcem* leaf extract tablets.

A regression curve was plotted using % inhibition versus concentration. The IC_{50} value (concentration required to inhibit 50% of DPPH radicals) was calculated by substituting y = 50 into the regression equation (y = bx + a), where y is % inhibition and x is the sample concentration. The Antioxidant Activity Index (AAI) was calculated using the formula: AAI = DPPH concentration (µg/mL) / IC_{50} (µg/mL).

Data Analysis

Data distribution was assessed using the Shapiro–Wilk test. All results are presented as mean ± standard deviation (SD) for consistency. For variables with normal distribution, between-group differences were analyzed using one-way ANOVA, with homogeneity of variances tested by Levene's test. For variables not normally distributed, differences were analyzed using the Kruskal–Wallis test, followed by Mann–Whitney U tests for post-hoc comparisons. Statistical significance was set at $p < 0.05$.

RESULT AND DISCUSSION

Plant Identification

Botanical identification of the *cemcem* plant was conducted at the Characterization Laboratory of Eka Karya Botanical Garden – BRIN, Bali. The results confirmed that the plant used in this study is *Spondias pinnata* (L.f) Kurz (ID: 71783), belonging to the genus *Spondias* L. and the family *Anacardiaceae* R.Br. The identification test was conducted to confirm the botanical authenticity of the plant material, ensuring it corresponds precisely to the intended species selected for the study. This step is essential to minimize the risk of misidentification, which could compromise the validity of subsequent experimental procedures.[15,25]

Extraction Yield of *Cemcem* Leaf Simplicia

Fresh *cemcem* leaves (9 kg) were dried to obtain 1.7063 kg of dry simplicia. The extraction process yielded 148 g of thick extract, corresponding to an extraction yield of 8.7%. Ultrasonic-assisted maceration was employed to enhance extract yield, reduce extraction time, and minimize solvent usage compared to conventional maceration.[15,26] However, this method may also lead to degradation of phenolic compounds due to hydrolysis, ionization, and oxidation reactions.[27,28]

Phytochemical Screening Results

Qualitative phytochemical screening of *cemcem* leaf extract was performed to identify the presence of secondary metabolites. The phytochemical screening of the *cemcem* leaf extract in this study revealed the presence of flavonoids, phenols, alkaloids, and steroids/triterpenoids, while tannins were not detected. These findings are partially consistent with previous reports, which identified flavonoids, alkaloids, tannins, saponins, glycosides, and steroids in ethanol extracts of *S. pinnata* leaves.[29,30] The absence of tannins in the present extract may be attributed to several factors. Previous studies have shown that extraction conditions, including solvent polarity and temperature, strongly influence tannin recovery.[31] Additionally, leaf maturity plays a critical role, as younger leaves typically contain higher tannin concentrations compared to mature leaves.[32] Furthermore, environmental factors such as climate and soil conditions can significantly affect tannin biosynthesis and composition.[33,34] Phytochemical screening is essential for identifying bioactive compounds in plant extracts, ensuring quality control, validating traditional medicinal uses, and supporting the discovery and development of novel therapeutic agents.[35–37]

Physical Quality of *Cemcem* Leaf Extract Granules

Granule quality was evaluated on Day 0 for three formulations varying maltodextrin–Primojel® ratios: F1 (3%–8%), F2 (6.5%–5%), and F3 (10%–2%), with results detailed in **Table 1**. Moisture content across all formulations showed no significant differences (F1 vs. F2: $p = 0.943$; F1 vs. F3: $p = 0.437$; F2 vs. F3: $p = 0.299$), indicating that variations in maltodextrin and Primojel® concentrations had minimal influence. All formulations met the pharmacopeial moisture standard (2–4%)[38] with values ranging from 2.78% to 3.27%, supporting optimal flowability for tablet compression. The relatively small SD values (≤0.5) indicate low variability within each formulation, suggesting consistent granule moisture distribution. Statistical analysis was performed using one-way ANOVA, as the data were normally distributed.

Previous literature has noted that maltodextrin, owing to its hygroscopic nature, tends to retain moderate moisture levels,[39,40] whereas Primojel® (sodium starch glycolate) demonstrates a higher water uptake capacity due to its pronounced swelling and hydration behavior.[41,42] In contrast, the relatively low and controlled moisture content observed in this study underscores the effectiveness of the formulation strategy, promoting granule stability and reducing the likelihood of moisture-induced processing complications. Excessive moisture can lead to particle agglomeration, adversely affecting flowability and uniformity during downstream processing.[43]

The average compressibility index values for formulations F1 and F3 were 20.33% and 16.63%, respectively, both falling within the "fair" category. Formulation F2 exhibited a slightly higher value of 21.21%, classified as "passable".[44] Statistically, F1 and F2 did not differ significantly ($p = 0.268$). However, F3, which showed the lowest compressibility index—indicating superior flowability—differed significantly from F2 ($p = 0.046$), and marginally from F1 ($p = 0.050$). The SD values (≤1.5) suggest moderate variability, with F2 showing slightly higher dispersion, consistent with its less favorable flowability. Because the data for F2 were not normally distributed, Kruskal–Wallis was applied, followed by Mann–Whitney for post-hoc comparisons.

The improved flow characteristics observed in F3 are attributed to its higher maltodextrin concentration, which likely enhanced granule cohesion during wet granulation. A lower compressibility index generally reflects better flowability, reducing the risk of processing issues such as poor die filling or weight variation during tablet compression.[45] Previous studies indicate that maltodextrin, due to its binding and particle-coating properties, can enhance granule flow and reduce compressibility index,[46,47] whereas formulations containing Primojel® (sodium starch glycolate) often exhibit slightly higher compressibility values because of its high water uptake and swelling capacity, which can increase interparticle friction.[42] Compared to these trends, the present study demonstrates that increasing maltodextrin concentration effectively improved flowability without compromising granule integrity, aligning with its reported role as a flow-enhancing binder.

Flow rate testing using 100 g of granules revealed that all three formulations exhibited free-flowing properties, with flow rates ranging from 13.22 to 14.22 g/s.[45] A good flow rate is typically greater than 10

g/second, while an acceptable angle of repose falls between 25° and 45°.[44,48] The SD values for flow rate (≤0.45) indicate high uniformity within each formulation, supporting consistent granule performance. Statistical analysis for flow rate and angle of repose was conducted using ANOVA, as both datasets were normally distributed. Previous studies have shown that increasing maltodextrin concentration generally improves flow rate and reduces the angle of repose, while combining maltodextrin with a higher concentration of Primojel® can further enhance flowability.[48] In the present study, F3 exhibited the highest flow rate, which was statistically significantly different from F1 ($p = 0.014$), whereas no significant difference was observed between F1 and F2 ($p = 0.489$) or between F3 and F2 ($p = 0.058$). This finding supports the reported positive effect of higher maltodextrin levels on granule flow.

Interestingly, F2 achieved the best angle of repose, although the differences were not statistically significant when compared with F1 ($p = 0.105$) or F3 ($p = 0.869$), and no significant difference was observed between F1 and F3 ($p = 0.202$). The SD values for angle of repose (≤0.6°) indicate minimal variability, with F3 showing slightly higher dispersion, suggesting consistent particle packing behavior within each formulation. These results suggest that a balanced ratio of maltodextrin and Primojel® may optimize particle packing and surface interaction.

Table 1. Physical Quality Test Results of *Cemcem* Leaf Extract Granules

Formula	Replication	Moisture content (%)	Compressibility index (%)	Flow rate (g/s)	Angle of Repose (°)
F1	1	3.11	19.05	13.14	32.97
	2	2.97	21.95	13.12	33.49
	3	2.56	20.00	13.39	33.36
Average±SD		**2.88±0.29^{a}**	**20.33±1.48^{ab}**	**13.22±0.15^{a}**	**33.27±0.27^{a}**
F2	1	3.09	20.45	13.85	30.96
	2	2.72	22.73	13.68	31.97
	3	2.54	20.45	13.00	31.61
Average±SD		**2.78±0.28^{a}**	**21.21±1.32^{a}**	**13.51±0.45^{ab}**	**31.51±0.51^{a}**
F3	1	3.67	16.67	14.43	32.97
	2	3.39	18.60	14.04	32.35
	3	2.74	14.63	14.20	30.31
Average±SD		**3.27±0.48^{a}**	**16.63±1.99^{b}**	**14.22±0.20^{b}**	**31.88±1.39^{a}**

Notes:
F1, F2, and F3 refer to granule formulations of cemcem leaf extract tablets with varying Maltodextrin–Primojel® concentrations: 3%–8%, 6.5%–5%, and 10%–2%, respectively.
Identical superscript letters indicate no statistically significant difference; differing letters denote a significant difference.

The angle of repose measurements for all three formulations fell within the "good" category, ranging from 31.51° to 33.27°.[44] Particle size, interparticle attraction, and frictional forces are key factors influencing the angle of repose.[49] There is an inverse relationship between flow rate and angle of repose—higher flow rates typically correspond to lower angles of repose, indicating better flowability into the hopper.[50]

Overall, these findings align with previous reports and highlight that the interplay between binder and disintegrant concentrations can influence different aspects of flowability. Granule flowability is influenced by factors such as particle size, surface characteristics, and moisture content.[49] Larger granule particles tend to have lower cohesive forces, which facilitates smoother flow.[50] Flowability is directly related to weight uniformity during tablet production; poor flow can lead to inconsistent filling of the die cavity, resulting in variable tablet weights.[51]

Tablet Physical Quality and Stability

Physical quality testing of cemcem leaf extract tablets was conducted on Days 1, 14, and 28 post-formulations. Throughout the 28-day study period, tablets were stored in glass jars containing silica gel desiccant, maintained at room temperature, and shielded from direct sunlight to control moisture exposure. The organoleptic assessment of the formulated herbal tablets revealed consistent characteristics across all formulations, including a distinct herbal aroma, greenish-brown coloration with a speckled appearance, a slightly sour and astringent taste, and a round tablet shape. Representative visual characteristics of the tablets are shown in **Figure 1**. The speckled appearance was likely associated with incomplete homogenization of the

extract during the formulation process rather than variations in binder composition. A similar observation was reported by Pradhan et al., where polyherbal tablets formulated using *Carica papaya*, *Emblica officinalis*, and *Foeniculum vulgare* and polyvinylpyrrolidone as the binder exhibited a speckled surface, attributed to non-uniform distribution of herbal powders during granulation.[52] In contrast, Ratrinia et al.[53] reported that binder type significantly influenced sensory attributes in *Sonneratia caseolaris* effervescent tablets. They compare the binders polyvinylpyrrolidone, gelatin, pulvis gummi arabic, and maltodextrin, with gelatin producing the most preferred aroma, color, and taste due to its ability to enhance homogeneity and maintain flavor stability under acidic conditions. Similar findings have been observed in other herbal tablet studies, where formulation factors such as binder choice and granulation technique affected sensory acceptability and physical uniformity. For example, Jatinkumar et al.[54] noted that polyherbal digestive tablets exhibited satisfactory taste and odor when wet granulation was optimized for uniformity. Likewise, Kushwah et al.[55] demonstrated that polyherbal chewable tablets achieved improved taste and overall acceptability through factorial optimization of excipients. Dhage et al.[56] also emphasized that nutraceutical herbal tablets formulated with multiple botanicals required careful process control to maintain consistent color and sensory properties. These comparisons suggest that while binder selection plays a critical role in effervescent systems, conventional herbal tablets rely more on process optimization to prevent visual inconsistencies and ensure desirable organoleptic characteristics.

Figure 1. Physical Appearance of *Cemcem* Leaf Extract Tablets

The results of the weight uniformity test are presented in **Table 2**. Formula F1 exhibited deviations beyond the specified limits on days 1, 14, and 28, with more than two tablets deviating by over 5%, thus failing Column A requirements, and at least one tablet exceeding 10%, thereby failing Column B.[22] Formula F2 met the requirements on days 1 and 14; however, on day 28, weight uniformity was not achieved due to more than two tablets deviating by over 5% (Column A). For F3, similar deviations to F1 were observed on days 1 and 14, but compliance was achieved on day 28, as no more than two tablets deviated by over 5% and none exceeded 10%. These findings indicate that none of the three formulations consistently met the uniformity criteria. Nevertheless, statistical analysis revealed no significant differences ($p > 0.05$) across observation days (1, 14, and 28) for all formulations (Table 4), suggesting overall weight stability. The actual tablet weights ranged from 409.2 mg to 597.8 mg, which is notably lower than the intended target of 650 mg per tablet. Weight uniformity is influenced by granule flow properties and bulk density, as represented by the compressibility index.[44] All three formulations demonstrated good flowability (free-flowing category), but compressibility indices were suboptimal: F1 and F3 were classified as fair, while F2 was passable. Variations in tablet weight can result in inconsistent active ingredient content, which may compromise dosage accuracy. Therefore, ensuring weight uniformity is essential, as it directly supports content uniformity—both being critical quality attributes that guarantee accurate dosing, consistent therapeutic performance, product safety, and regulatory compliance.[57,58]

In contrast, Ratrinia et al.[53] reported that all effervescent tablet formulations of *Sonneratia caseolaris* met the weight uniformity requirements, with deviations remaining within the 5% and 10% limits prescribed by the Indonesian Pharmacopoeia and USP standards. Their study emphasized that binder type did not affect weight uniformity, which was primarily influenced by tablet press consistency, die filling uniformity, and accurate granule weighing. Similar observations have been reported in other herbal tablet studies. Dhage et al.[56] found that nutraceutical herbal tablets prepared by wet granulation exhibited acceptable weight variation when granule flow and compression parameters were optimized. Kushwah et al.[55] demonstrated that polyherbal chewable tablets maintained weight uniformity across batches when factorial design was applied to optimize excipient ratios and compression force.

Table 2. Results of Weight Uniformity Test of *Cemcem* Leaf Extract Tablets

Formula	Day	Average Tablet Weight (g)	Average Weight Deviation		Conclusion
			A (5%)	B (10%)	
F1	1	0.515±0.027	5 tablets	1 tablet	Non-Compliant
	14	0.533±0.024	5 tablets	0 tablet	Non-Compliant
	28	0.527±0.037	5 tablets	3 tablets	Non-Compliant
F2	1	0.484±0.017	1 tablet	0 tablet	Compliant
	14	0.482±0.012	0 tablet	0 tablet	Compliant
	28	0.487±0.022	4 tablets	0 tablet	Non-Compliant
F3	1	0.525±0.027	5 tablets	1 tablet	Non-Compliant
	14	0.514±0.030	4 tablets	1 tablet	Non-Compliant
	28	0.526±0.014	1 tablet	0 tablet	Compliant

Notes:
F1, F2, and F3 refer to formulations of cemcem leaf extract tablets with varying Maltodextrin–Primojel® concentrations: 3%–8%, 6.5%–5%, and 10%–2%, respectively.

The dimensional uniformity test results for the three *cemcem* leaf extract tablet formulations (**Table 3**) indicate that none of the formulations complied, as the diameter-to-thickness ratio fell outside the specified range, i.e., D/T > 3 or D/T < 1⅓.[23] In comparison, Imtihani et al.[59] in their study, reported that the dimensional uniformity test results showed that the diameters of tablets F1 and F2 were identical at 1.004 cm. Consequently, both F1 and F2 did not meet the requirements because the tablet diameter was more than three times the tablet thickness. These findings from both studies highlight similar challenges in achieving dimensional compliance, which may be attributed to inadequate control of compression force and granule distribution during the tableting process. Based on statistical analysis (**Table 4**), F1 and F3 were stable with respect to dimensional uniformity from Day 1 through Days 14 and 28 ($p > 0.05$). In contrast, F2 was unstable from Day 1 to Day 28 ($p < 0.05$). Insufficient fill volume and compression force during tableting can lead to dimensional non-uniformity.[60] Non-uniform diameter and thickness (in addition to weight non-uniformity) may affect dosage accuracy and complicate packaging operations.[61]

Hardness testing (**Table 3**) revealed that none of the formulations met the requirement of ≥4 kgF.[62] However, F3 exhibited the highest hardness compared to F1 and F2. An increase in maltodextrin concentration as a binder and a decrease in Primojel® (disintegrant) were associated with improved hardness. Tablet hardness is influenced by several factors, including granulation method, compression force, granule strength, and the type and amount of binder used.[50] Low hardness values may result from insufficient compaction pressure, as lower pressure tends to produce friable tablets.[63] The combination of maltodextrin and polyvinylpyrrolidone (PVP) in cemcem extract tablets likely contributed to the relatively higher hardness observed in F3, which maintained the best hardness from Day 1 to Day 28. These binders can occupy inter-particulate voids in heterogeneous blends, producing more compact tablets.[64] Statistical analysis using repeated measures ANOVA (**Table 4**) indicated that all three formulations exhibited significant changes in hardness over time ($p < 0.05$).

Herlinawati[65] reported that varying maltodextrin concentrations (10%, 15%, and 20%) in tablet formulations resulted in hardness values within the acceptable range of 4–8 kgF,[66] with higher maltodextrin levels correlating with increased hardness. Manan et al.[67] also reported that an increase in maltodextrin concentration enhances tablet hardness. The present study reflects a similar trend, as F3—the formulation with the highest maltodextrin content—showed the greatest hardness, although all formulations failed to meet the pharmacopeial requirement of ≥4 kgF, likely due to the use of lower maltodextrin concentrations (3%, 6.5%, and 10%). Similarly, Syukri et al.[68] observed that tablet hardness decreased as Primojel® concentration increased. Their study evaluated five formulations containing Primojel® at 2%, 3.5%, 5%, 6.5%, and 8%, with the lowest concentration yielding an average hardness of 4.88 kgF. In the present study, hardness was also highest in F3, which contained the lowest Primojel® concentration, although all formulations exhibited hardness values below the acceptable range. This discrepancy may be attributed to the hydrophilic nature of cemcem leaf thick crude extract, which influences the physical characteristics of granules and tablets. While Herlinawati utilized dry extracts and Syukri did not employ natural extracts as active ingredients, the inclusion of hydrophilic cemcem extract in this study likely affected granule integrity and tablet hardness. Hydrophilic molecules can weaken interparticle bonding by increasing wettability and moisture uptake, leading to less compact granules during compression and consequently lower tablet hardness.[69]

Friability testing results (**Table 3**) indicated that all formulations complied with pharmacopeial limits for uncoated tablets (friability < 1%)[38,70] on Days 1 and 28, with values ranging from 0.20% to 0.93%. In contrast, none of the formulations met the requirement on Day 14, exhibiting friability between 2.88% and 10.12%. Consequently, overall compliance was not maintained throughout the study period. The highest friability was observed in F3, which contained the lowest Primojel® and highest maltodextrin concentrations, whereas F1 exhibited the lowest friability among F1–F3. This suggests that reducing maltodextrin (binder) while increasing Primojel® (disintegrant) enhances mechanical strength. These findings are consistent with previous reports. Imtihani et al.[59] noted that tablet friability increases at lower Primojel® concentrations, while Syukri et al.[68] demonstrated that increasing Primojel® from F1 to F4 reduced friability; however, at the highest concentration (F5, 8%), friability increased again, exceeding that of F1. Similarly, Kaewnoi et al.[71] reported that reducing maltodextrin concentration also decreases friability. Despite these trends, all formulations complied with pharmacopeial friability limits on Days 1 and 28. The pronounced increase on Day 14 may be attributed to storage-related changes and suboptimal granule compressibility, as inadequate compressibility typically results in friable tablets.[72]

Disintegration testing results (**Table 3**) showed that all formulations met the pharmacopeial criterion for uncoated tablets (<15 minutes)[38] and complied with safety and quality requirements for traditional medicines,[22] with mean disintegration times ranging from 3.52 to 10.88 minutes. Among the formulations, F1 disintegrated the fastest, whereas F3 was the slowest, consistent with its higher hardness and greater maltodextrin content. These observations align with Rijal et al.,[51] who reported that higher tablet hardness generally prolongs disintegration time because greater binder content strengthens granule bonding and increases hardness, thereby increasing resistance to water penetration. Similarly, the other previous studies[15,68] demonstrated that increasing Primojel® concentration reduced disintegration time, promoting faster breakdown. Primojel® acts by rapidly absorbing water and swelling upon contact, generating internal stress that facilitates tablet rupture and accelerates disintegration. Kaewnoi et al.[71] further noted that reducing maltodextrin concentration also shortened disintegration time, as lower binder levels weaken interparticulate bonding, enabling quicker dispersion. Overall, higher Primojel® (disintegrant) and lower maltodextrin (binder) concentrations were associated with shorter disintegration times.[51] Statistical analysis (Table 4) revealed that F1 and F2 exhibited significant variability in disintegration time from Day 1 through Days 14 and 28 ($p < 0.05$), whereas F3 remained stable across the study period ($p > 0.05$).

Table 3. Mean Data of Dimensional Uniformity, Hardness, Friability, and Disintegration Time on Days 1, 14, and 28

Formula	Day	Dimensional Uniformity (cm)		Hardness (kg)	Friability (%)	Disintegration time (minutes)
		Diameter	Thickness			
F1	1	1.115±0.016	0.340±0.019	1.67±0.20	0.20	6.15±0.39
	14	1.118±0.004	0.348±0.031	1.36±0.21	10.12	4.42±0.60
	28	1.119±0.003	0.356±0.012	1.41±0.18	0.47	3.52±0.53
F2	1	1.123±0.023	0.346±0.031	2.20±0.52	0.67	7.90±0.58
	14	1.123±0.023	0.348±0.031	1.66±0.14	7.13	6.80±1.27
	28	1.119±0.003	0.322±0.006	1.93±0.12	0.49	6.04±1.80
F3	1	1.118±0.003	0.350±0.024	1.75±0.45	0.93	10.02±1.01
	14	1.118±0.003	0.350±0.024	2.28±0.51	2.88	10.68±1.99
	28	1.115±0.005	0.354±0.008	2.52±0.20	0.61	10.88±3.45

Notes:
F1, F2, and F3 refer to formulations of cemcem leaf extract tablets with varying Maltodextrin–Primojel® concentrations: 3%–8%, 6.5%–5%, and 10%–2%, respectively.

Based on the evaluation results, the cemcem leaf extract tablet formulations exhibited suboptimal overall quality, as none of the three formulations consistently met all requirements throughout the 28-day observation period. All formulations complied with the disintegration time criterion; however, only F3 remained stable throughout the entire study. F1 failed to meet weight uniformity requirements at all time points, while F2 complied on Days 1 and 14 but not on Day 28. F3 initially did not meet weight uniformity requirements but achieved compliance by Day 28. Despite these variations, all formulations maintained relatively stable weight over the 28-day period. None of the formulations met dimensional uniformity requirements during the study, and all exhibited instability in hardness, failing to meet the specified limits. Friability requirements were met only on Days 1 and 28, but not on Day 14. Statistical analysis (**Table 4**) indicated that F3 demonstrated the best physical stability from Day 1 to Day 28.

According to Fiana et al.,[43] a higher concentration of maltodextrin increases total solids, thereby reducing granule moisture content. Consequently, the addition of 10% maltodextrin in F3 contributed to lower moisture content, improved granule flowability, and enhanced tablet properties. Furthermore, the presence of 2% Primojel® was sufficient as a disintegrant in the formulation.[73] Therefore, the combination of 10% maltodextrin and 2% Primojel® in F3 resulted in superior physical quality and stability compared with the other formulations.

Table 4. Results of Physical Stability Analysis of Cemcem Leaf Extract Tablets Using Repeated Measures ANOVA

Parameter	Formula	*p*-value	Interpretation
Weight uniformity	F1	0.165**	Stable
	F2	0.687*	Stable
	F3	0.235*	Stable
Dimensional uniformity	F1	0.071**	Stable
	F2	0.005**	Unstable
	F3	0.965**	Stable
Hardness	F1	0.000**	Unstable
	F2	0.000**	Unstable
	F3	0.000**	Unstable
Disintegration time	F1	0.002**	Unstable
	F2	0.004*	Unstable
	F3	0.607**	Stable

Notes:
p-value > 0,05: not significantly different
p-value < 0,05: significantly different
(*): tested using *repeated measures ANOVA*
(**): tested using *friedman*

Antioxidant Activity Test

The antioxidant activity of three *cemcem* leaf extract tablet formulations (F1, F2, and F3) and vitamin C were evaluated using the DPPH method. Five concentration levels (2, 4, 6, 8, and 10 µg/mL) were prepared, followed by the addition of DPPH solution and incubation for 30 minutes. The 30-minute incubation period was necessary because the reaction proceeds slowly, allowing sufficient time for the sample to interact with free radicals. The progress of the reaction was indicated by a color change in the sample—from purple to yellow—signifying the ability of the *cemcem* leaf extract tablets to act as antioxidants.[74]

For the DPPH assay, the absorbance of the control solution was measured, yielding a value of 0.746. Based on the absorbance values obtained for the five concentrations, the percentage inhibition (**Table 5**) for the DPPH solution combined with *cemcem* leaf extract tablets (F1, F2, and F3) at a concentration of 2 µg/mL, with a sample absorbance of 0.686 and a control absorbance of 0.746, is calculated as using Formula (1).

Based on the calculated percentage inhibition values for *cemcem* leaf extract tablets and vitamin C, a relationship between concentration and percentage inhibition was established, from which the following linear regression curve was obtained.

Table 5. Percentage Inhibition of Cemcem Leaf Extract Tablet Formulations and Vitamin C Against DPPH

Sample	Concentration (µg/mL)	Sample absorbance	Control absorbance	% Inhibition
F1	2	0.686	0.746	8.043
	4	0.681	0.746	8.713
	6	0.674	0.746	9.651
	8	0.671	0.746	10.054
	10	0.661	0.746	11.394
F2	2	0.671	0.746	10.054
	4	0.666	0.746	10.724
	6	0.655	0.746	12.198
	8	0.648	0.746	13.137
	10	0.641	0.746	14.075
F3	2	0.722	0.746	3.217
	4	0.680	0.746	8.847
	6	0.654	0.746	12.332
	8	0.625	0.746	16.219
	10	0.592	0.746	20.643

Sample	Concentration (µg/mL)	Sample absorbance	Control absorbance	% Inhibition
Vitamin C	2	0.566	0.592	4.392
	4	0.437	0.592	26.182
	6	0.337	0.592	43.074
	8	0.243	0.592	58.953
	10	0.148	0.592	75.000

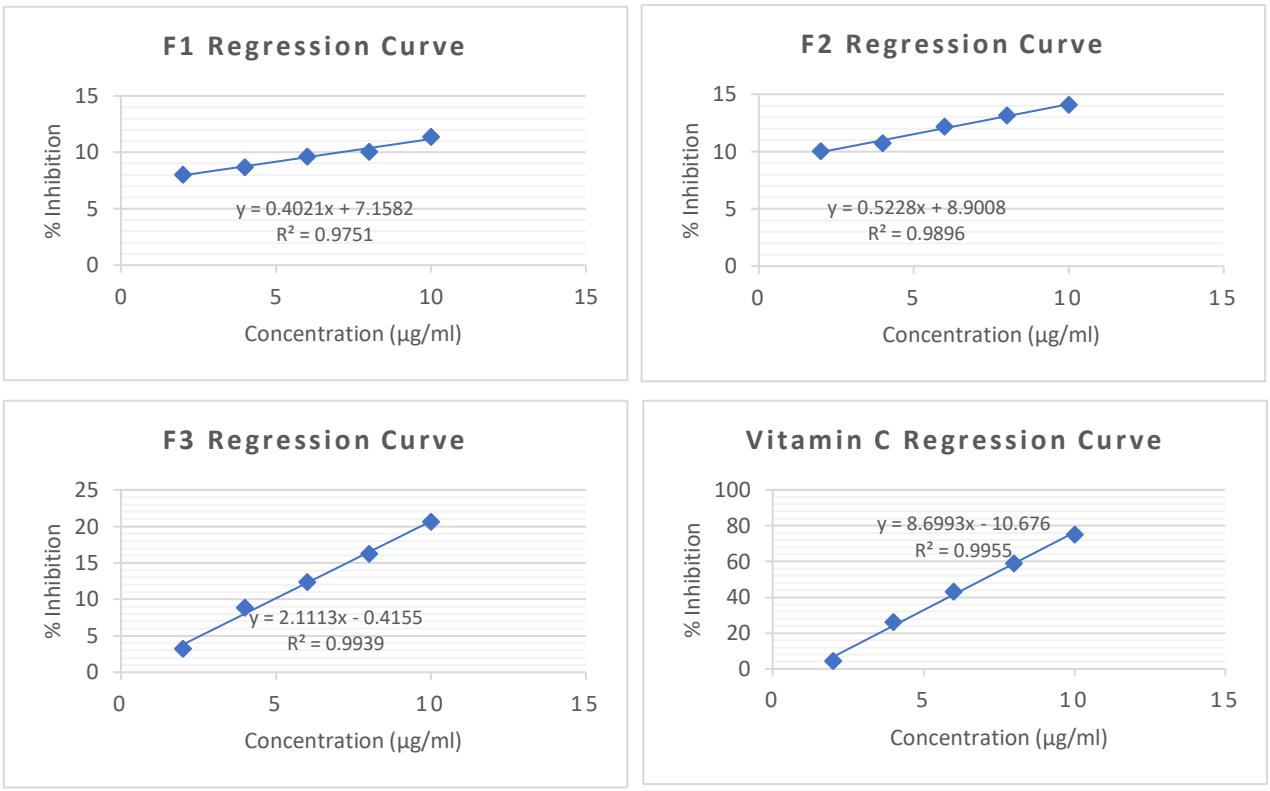

Figure 2. Linear Regression Curves of F1, F2, F3, and Vitamin C

Linear regression analysis was performed to establish the relationship between concentration and percentage inhibition for F1, F2, F3, and vitamin C. The regression equations and R^2 values were as follows: F1 ($y = 0.4021x + 7.1582$, $R^2 = 0.9751$), F2 ($y = 0.5228x + 8.9008$, $R^2 = 0.9896$), and F3 ($y = 2.1113x – 0.4155$, $R^2 = 0.9939$). IC_{50} values were determined by substituting $y = 50$ into the respective regression equations, where y represents % inhibition and x represents sample concentration (**Table 6**). The R^2 values obtained from the linear regression analysis—F1 (0.9751), F2 (0.9896), and F3 (0.9939)—indicate a strong linear relationship between concentration and percentage inhibition for all formulations. These high coefficients of determination reflect the reliability of the regression models in predicting antioxidant activity based on concentration. Notably, F3 exhibited the highest R^2 value, suggesting the most consistent and predictable antioxidant response.

Table 6. IC_{50} and AAI Values

Sample	IC_{50} (µg/mL)	IC_{50} Category	AAI	AAI Category
F1	106.545	Moderate	0.375	Mild
F2	78.614	Strong	0.509	Moderate
F3	23.879	Very strong	1.675	Strong
Vitamin C	6.975	Very strong	5.735	Very strong

Based on the above findings, the highest antioxidant activity was observed in Formula F3, which contained 2% Primojel® and 10% maltodextrin. In this study, increasing the concentration of maltodextrin correlated with stronger antioxidant activity in the *cemcem* leaf extract tablets. Maltodextrin protects key compounds, such as antioxidants, from extreme temperatures due to its ability to form a matrix and bind

strongly to encapsulate active substances.[75] Therefore, F3, which had the highest maltodextrin concentration (10%), exhibited the most potent antioxidant activity, as maltodextrin preserved the antioxidant components from thermal degradation during the wet granulation drying process in tablet formulation. Although heat exposure during processing can lead to oxidation and degradation of antioxidant compounds, maltodextrin helps retain these components, preventing complete loss of activity.[76] According to Aditya et al.,[77] maltodextrin concentrations between 6–12% show a positive parabolic trend in enhancing antioxidant activity, with 10% being the optimal concentration. Similarly, Purwati, Yuwanti, and Sari reported that effervescent tablets made from ant nest–roselle extracts using 10% maltodextrin as a binder exhibited higher antioxidant activity compared to those using dextrin, due to maltodextrin's protective effect on nutrient release.[78] Nurzarah et al. (2017) also found that tablets formulated with 5% maltodextrin had higher antioxidant activity than those with 5% dextrin.[64] Furthermore, maltodextrin concentrations up to 15% have demonstrated the ability to effectively protect encapsulated compounds.[79]

The antioxidant activity test on these three tablet formulations containing 7% cemcem leaf extract demonstrated significantly superior results compared to previous studies that used 2% and 5% extract concentrations along with 5% maltodextrin and 6% Primojel®.[15] The earlier research reported relatively low antioxidant capacities of 83.537 mg AEAC/100 g and 170.782 mg AEAC/100 g, respectively. These findings clearly indicate that increasing the cemcem leaf extract concentration to 7%, combined with optimized levels of maltodextrin and Primojel®, substantially enhances antioxidant activity in tablet formulations. Compared to formulations with lower extract concentrations, this approach achieved markedly higher antioxidant capacity, underscoring the critical role of extract loading and excipient synergy in improving functional properties. These results provide a strong foundation for developing antioxidant-rich herbal tablets with enhanced efficacy and suggest that formulation strategies focusing on extract concentration and excipient optimization can significantly influence therapeutic potential.

This study was limited to evaluating the short-term physical stability and antioxidant activity of cemcem leaf extract tablets over a 28-day period under controlled storage conditions. The formulations focused solely on varying concentrations of maltodextrin and Primojel®, without exploring other excipients or formulation techniques that may further enhance tablet performance. Additionally, the antioxidant activity was assessed using a single in vitro method (DPPH assay), which may not fully represent biological efficacy. Future studies should consider long-term stability testing under accelerated conditions, inclusion of alternative binders and disintegrants, and broader antioxidant assays—such as ABTS, FRAP, or cellular models—to validate and expand upon the observed bioactivity. Investigating the pharmacokinetics and in vivo antioxidant potential of the optimized formulation (F3) would also be valuable in supporting its development as a functional nutraceutical product.

CONCLUSION

This study demonstrated that varying concentrations of maltodextrin and Primojel® significantly influence the physical quality, short-term stability, and antioxidant activity of *cemcem* leaf extract (*Spondias pinnata* (L.f.) Kurz) tablets. Among the formulations, F3—containing the highest binder (10% maltodextrin) and the lowest disintegrant (2% Primojel®)—exhibited the most favorable tablet properties, including superior physical stability over 28 days and the strongest antioxidant activity (IC_{50} = 23.879 µg/mL). These results establish a clear causal relationship between excipient concentration and tablet performance, supporting F3 as a promising prototype for antioxidant supplement development.

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest regarding the authorship or publication of this manuscript.

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