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Formulation Strategy to Prevent Sticking in Calcium Carbonate–Cholecalciferol Chewable Tablets: The Role of Citric Acid

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Abstract
The sticking phenomenon is a critical issue in the production of calcium carbonate–cholecalciferol (vitamin D3) chewable tablets, primarily driven by the hygroscopicity and reactivity of citric acid, which is used as a flavor-masking agent. This study aims to evaluate and determine the optimal method for mitigating sticking by modifying citric acid excipients using two approaches: granulation with mannitol (F1: 0.5%, F2: 1%) and coating with HPMC (F3: 0.5%, F4: 1%). The evaluation was conducted on the properties of the granule mass and quantitatively measured the percentage of sticking in industrial-scale modifications for 24 hours. The results showed that the control formula (F0), without modification, had the lowest sticking percentage (10.88%) and the highest moisture content (3.36%), as indicated by a "passable" flow property with a compressibility index of 21.47%. The 1% HPMC coating modification method (F4) was successful in eliminating stickiness to 0%, supported by moisture-control data (2.25%) and a significant improvement in powder-flow properties to “fair,” with a compressibility index of 17.06%. Although the 1% mannitol granulation method (F2) is relatively effective in reducing stickiness (0.85%), the 1% HPMC coating (F4) is more effective at physically isolating citric acid. This study concludes that the HPMC coating method is superior to the granulation method for physically isolating citric acid, yielding stable, non-sticking calcium carbonate–cholecalciferol chewable tablets.

Keywords: Chewable Tablets, Citric acid, HPMC, Mannitol, Sticking.

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1. INTRODUCTION

The combination of calcium carbonate and cholecalciferol (vitamin D3) is an essential supplement that is very important in the prevention and treatment of osteoporosis and hypocalcemia (Carugo et al., 2024). The formulation of chewable tablets is widely chosen because it offers ease of consumption and significantly improves patient compliance, especially among children and the elderly (Gawade & Shendge, 2020). To overcome the characteristic chalky taste of calcium carbonate, citric acid is added to the formula as an effective masking agent (Palacios et al., 2020). Functionally, the addition of citric acid is crucial; however, citric acid, particularly the commonly available monohydrate form, has high hygroscopicity and the potential to react with other excipients, making it a critical material in the production process of solid dosage forms (Lambros et al., 2022).

Calcium carbonate–cholecalciferol chewable tablets are generally manufactured in the pharmaceutical industry using a dry mixing method with a minimum batch size of 300 kg (Sharma et. al., 2020). However, in reality, the production process is carried out by dividing these large batches into several lots. This is due to the phenomenon of tablet material sticking during the compression process (Nakamura et. al., 2016). The sticking phenomenon is the most common and critical problem that arises during compression, where tablet material sticks to the surface of the punch and die, which can result in tablet defects, reduced product quality, and low production efficiency (Takeuchi, 2022).

Recent research has identified that the hygroscopicity and inherent stickiness of formula components, including citric acid, are the main triggers of sticking during compression, especially under uncontrolled environmental conditions (Chen et al., 2022; Pagire, Seaton, & Paradkar, 2020). Existing general handling strategies focus on lubricant optimization, such as the addition of magnesium stearate, the addition of anti-adherents, or the adjustment of machine parameters (Abaci et.al., 2021). However, these solutions have not yet completely solved the sticking problem originating from hygroscopic excipients in formulas that require specific compositions (Badawi et al., 2017). The sticking problem is exacerbated by the potential neutralization reaction between citric acid and calcium carbonate, which is an acid-base reaction. This reaction produces water internally within the formulation, which can increase the moisture content of the tablet mass (Nidhu et al., 2021), thereby increasing plasticity and the tendency for sticking during compression (Olowofoyeku et al., 2025). In a dry-mixing process, this neutralization reaction can be initiated by residual moisture in the ingredients and markedly accelerated by the high compression pressure during tableting. The pressure promotes intimate particle contact, creating localized reaction points that release water of crystallization (Chanwetprasat et al., 2025; Koumbogle, Gitzhofer, & Abatzoglou, 2022).

Most previous studies have focused on general strategies involving the control of anti-adherent use or effervescent formulations to address sticking caused by hygroscopic materials (Rosch et al., 2021; Zheng et al., 2019). They have limitations in chewable tablet matrices and have not comprehensively explored and compared methods of direct citric acid processing to suppress specific adhesion in calcium carbonate-cholecalciferol chewable tablet matrices. Therefore, this study was conducted to address this gap by employing two approaches to modify citric acid excipients: granulation with mannitol and HPMC (Hydroxypropyl Methylcellulose) coating. This research provides a novelty in quantitatively comparing the granulation and coating methods at an industrial scale, directly linking moisture control, powder flow properties, and sticking mitigation

In this study, mannitol was selected as the granulation aid due to its lower hygroscopicity than other polyols, such as sorbitol (Poka et al., 2023). The inclusion of mannitol stabilizes citric acid by preventing it from absorbing environmental moisture, which could lead to undesirable reactions with calcium carbonate (Kang et al., 2024). This moisture control reduces

the risk of premature acid-base interactions that could lead to tablet sticking and degradation of the tablet matrix. Mannitol not only enhances moisture control but also improves the overall tabletability due to its unique physical properties. It improves the flowability and compressibility of the powder blend, facilitating uniform tablet formation. Furthermore, mannitol has a pleasant, sweet taste and contributes to a smoother mouthfeel, making it a favorable choice for chewable formulations (Lute, Dhenge, & Salman, 2018). HPMC was chosen as the coating polymer for its excellent film-forming properties, producing a strong yet flexible barrier that is not expected to significantly impede drug dissolution at low concentrations, making it suitable for immediate-release dosage forms (Nyamweya, 2021).

This study aims to evaluate and determine the most optimal method between granulation with mannitol and HPMC coating in preventing sticking by comparing their effects on print mass properties (including moisture content and compressibility index) and measuring the percentage of sticky tablets quantitatively at certain time intervals. This study is expected to make a substantial contribution to formulation and manufacturing operations in the industry, enabling stable production free of sticking problems and greater efficiency.

2. RESEARCH METHOD

This study employed a laboratory experimental, comparative approach to optimize the modification of citric acid excipients, aiming to prevent sticking during the compression of calcium carbonate-cholecalciferol chewable tablets.

Materials used included calcium carbonate (SPI Pharma, USA), mannitol (Roquette, France), citric acid (TTCA Co., Ltd., China), colecalciferol (DSM Nutritional Products, Sisseln, Singapore), sucralose (JK Sweet JK Sucralose Inc., Jiangsu, China), red iron oxide (Univar, USA), 96% pharmagrade ethanol (Merck, Germany), strawberry flavor 052311 (PT Firmenich, Indonesia), magnesium stearate (FACI Asia Pacific Pte. Ltd, Singapore), and hydroxypropyl methylcellulose (Shin-Etsu, Japan).

Approximately 100 g of chewable tablet mass was ground in a mortar with a pestle. Any excessive stickiness to the pestle was visually assessed and recorded. Citric acid was modified using granulation (G1, G2) and coating (C1, C2) methods at two concentration levels each (Table 1). Mannitol (0.5% and 1%) and HPMC (0.5% and 1%) concentrations were selected based on preliminary studies and literature (Vlad et al., 2025; Wang et al., 2022) to evaluate low-level functional effects without significantly altering the core formulation.

Table 1. Treatment of modified citric acid excipients (batch scale 1.00 kg)

Ingredient	Granulation Method		Coating Method	
	G1	G2	C1	C2
Citric Acid (g)	1000	1000	1000	1000
Mannitol (%)	0.5	1	-	-
HPMC (%)	-	-	0.5	1
Total Weight (g)	1005.0	1010.0	1005.0	1010.0

Description: *(G) granulation method and (C) coating method.*

Citric acid and mannitol were sequentially loaded into a supermixer (Jaw Chuan, Taiwan) at low agitator and chopper settings for 300 s. A distilled water–alcohol mixture was then added at low agitator and high chopper settings for 300 s. The wet mass was dried using a fluid bed dryer (Aeromatic) to a target moisture content of 2–3%, then sieved through a 1.00 mm screen using a granulator (Canaan NTFZ200B, China). Each batch was 1.00 kg.

An HPMC solution was prepared at the concentrations listed in Table 1, stirred, and circulated for 45 min in a coating liquid container connected to a coating machine (Sejong SFC100, South Korea). Citric acid was loaded into the coating pan (pan speed 2–5 rpm, peristaltic pump 2–4 rpm, atomization pressure 0.22 MPa, temperature 30–35 °C). Coating

proceeded until a target weight gain of 1% (w/w) was achieved, confirmed by visual inspection for a uniform film without agglomeration. Coated product was sieved through a 14-mesh screen if clumping occurred. Batches were prepared in 1.00 kg quantities.

Chewable tablets were prepared according to Table 2 (5.00 kg batch). Red iron oxide and a portion of mannitol were sieved through 100-mesh and mixed for 30 s (mixture 1). Cholecalciferol was dissolved with 96% ethanol and remaining mannitol, then mixed for 30 s (mixture 2). Both mixtures, sucralose, and strawberry flavor were loaded into a Bin Blender (Canaan, China) with a 30-mesh screen and blended at 10 rpm for 10 min. Calcium carbonate and citric acid (unmodified or modified) were added and mixed at 80–100 rpm for 10 min. Magnesium stearate was then added and blended at 10 rpm for 2 min until homogeneous.

Table 2. Formula for chewable calcium carbonate–cholecalciferol tablets, 5.00 kg batch scale.

Ingredient	**Function**	**F0 (N)**	**F1 (G1)**	**F2 (G2)**	**F3 (C1)**	**F4 (C2)**
Calcium carbonate	Active Ingredient	4.01 kg	4.01 kg	4.01 kg	4.01 kg	4.01 kg
Cholecalciferol	Active Ingredient	0.01 g	0.01 g	0.01 g	0.01 g	0.01 g
Mannitol	Filler	0.15 kg	0.15 kg	0.15 kg	0.15 kg	0.15 kg
Red iron oxide color	Dye	2.94 g	2.94 g	2.94 g	2.94 g	2.94 g
Sucralose	Sweetener	2.94 g	2.94 g	2.94 g	2.94 g	2.94 g
96% ethanol	Solvent	0.30 ml	0.30 ml	0.30 ml	0.30 ml	0.30 ml
Citric acid	Masking agent	0.75 kg	0.75 kg	0.75 kg	0.75 kg	0.75 kg
Strawberry flavor	Flavoring	14.00 g	14.00 g	14.00 g	14.00 g	14.00 g
Magnesium stearate	Lubricant	75.00 g	75.00 g	75.00 g	75.00 g	75.00 g

Description:
N: Untreated citric acid
G1: Treatment of citric acid excipient using the 0.5% mannitol granulation method
G2: Treatment of citric acid excipient using the 1% mannitol granulation method
C1: Treatment of citric acid excipient using the HPMC coating method at 0.5%
C2: Treatment of citric acid excipient using the HPMC 1% coating method

Particle size distribution was determined by sieving 100 g of granules through a six-stage sieve shaker (Retsch AS200, Germany) at 20 rpm for 20 min. The percentage retained on each sieve was calculated as: % Fines = (W_1/W_0) × 100%, where W_1 is the mass retained and W_0 is the initial mass (Atanaskova, Kostovski, & Anevska-Stojanovska, 2020).

Bulk density was determined by pouring 100 g of granules into a 250 mL graduated cylinder and recording the untapped volume (V). Bulk density = W/V (Aultons & Taylor, 2022). Density was measured by tapping the same sample using a tapped density tester (TDTF ZS-2E, China) for 1250 taps (~13 min), then recording the final volume (Vf). Tapped density = W/Vf (Aultons & Taylor, 2022). Compressibility index was calculated as: CI (%) = [(Tapped density − Bulk density)/Tapped density] × 100 (Aultons & Taylor, 2022). Moisture content was measured at 0, 0.25, 0.50, 1, 2, 3, 6, 8, 10, 12, 14, and 24 h under controlled conditions (25 ± 2 °C; 45 ± 5% RH). Five grams of sample were analyzed using a Moisture Content Analyzer (Mettler Toledo HE73, Switzerland) at 80 °C (Al-Hakim et al., 2024).

Evaluation of sticky tablet assessment was performed at the same time intervals and environmental conditions as moisture content testing. One hundred tablets (three machine cycles, 33 punches) were compressed using a tablet press (JCMCO SH-33, China) per interval.

Sticking occurrence was visually observed, and sticky tablets were counted (Nakamura et al., 2016). Sticky tablets (%) = (Number of sticky tablets/Total tablets) × 100%.

Organoleptic testing assessed color, odor, taste, shape, and surface condition of representative samples from each formula. Hardness was tested on 10 tablets per formula using a hardness tester (Erweka TBH 125, Germany) (Chun et al., 2021). Friability was determined on 20 cleaned and pre-weighed tablets (W_1) using a friability tester (CS-2, China) at 25 rpm; tablets were re-weighed (W_2) afterward. Friability (%) = $[(W_1 - W_2)/W_1] \times 100$ (Ismail, El-Biyally, & Sakran, 2023). Weight uniformity was assessed by individually weighing 20 cleaned tablets and calculating the average weight and percentage deviation (Nyarko et al., 2024). Thickness and diameter of 20 tablets were measured using a digital caliper (Stanojević et al., 2020).

All granule and tablet evaluations were performed in triplicate (n=3). Data were analyzed using Minitab version 18. Comparisons between formula groups were conducted using One-Way ANOVA at a 95% confidence level ($p < 0.05$).

3. RESULTS AND DISCUSSION

The results of the particle size distribution test can be seen in Figure 1, which shows that all formulas (F0-F4) are dominated by fine fractions, with particles <90 µm (mesh >170) and 90–150 µm contributing the largest proportion. Specifically, the control formula (F0) contained 34.87% of particles smaller than 90 µm. Interestingly, the granulation modification treatments (F1 and F2) resulted in a significant increase in fines, to 43.53% and 43.13%, respectively. This increase in fines content indicates that the granulation process applied to citric acid, or its subsequent interaction with fine calcium carbonate, failed to form large agglomerates and instead had the potential to worsen the flow properties of the printable mass (Shah et al., 2023). Conversely, the formulas using the modified coating method (F3 and F4) maintained lower fines percentages (35.74% and 34.67%), slightly below the control formula (F0). This implies that the HPMC coating on citric acid particles is more effective in stabilizing particle integrity and preventing excessive fines formation, as an early indicator of better printing process performance (Chen et al., 2022).

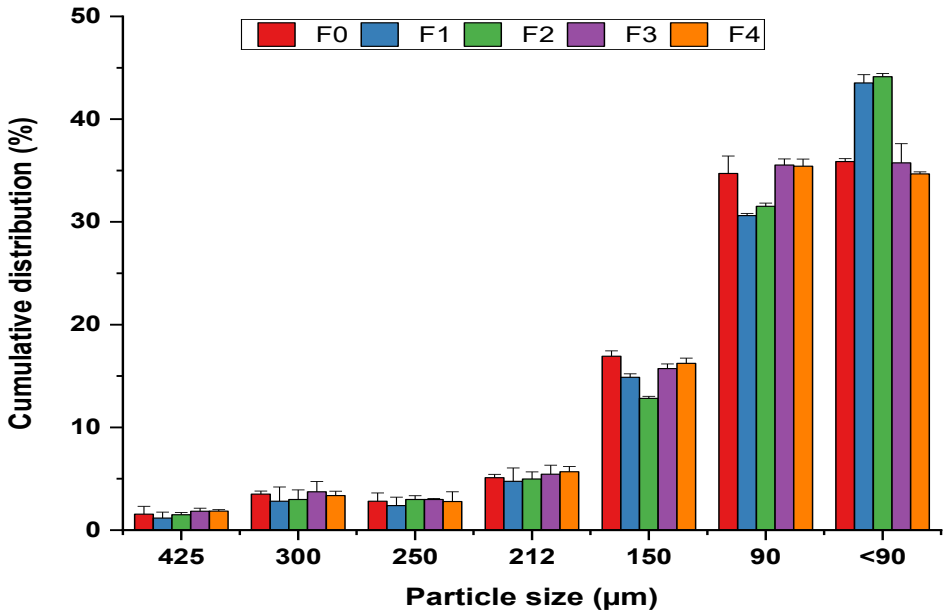

Figure 1. Evaluation of citric acid powder particle size distribution using the granulation method (F1 & F2) and coating method (F3 & F4), while F0 serves as the control formula using the sieving method.

Tests of bulk density, tapped density, and compressibility index on the molded mass showed that bulk density and tapped density were within the normal range for all formulas (F0 -F4), can be seen in Table 3. The bulk density values ranged from 0.62 g/mL to 0.68 g/mL, while the tapped density ranged from 0.77 g/mL to 0.81 g/mL. The main difference was observed in the compressibility index, a direct indicator of powder flow properties (Mititelu et al., 2022). The control formula (F0) showed a compressibility of 21.47%, indicating "fair" flow properties (21–25%) (Al-Hakim, Ratih, & Sabrilla, 2025). Citric acid granulation treatment, with 0.5% mannitol (F1 = 22.32%) and 1% mannitol (F2 = 19.64%), did not yield a significant improvement. In fact, F1 deteriorated slightly, possibly due to an increase in fines as observed in the previous particle-size distribution test. In contrast, modification of citric acid coating with HPMC (F3 and F4) resulted in significant improvement in flow properties. Formula F3 (0.5% HPMC) showed a compressibility value of 14.21%, while F4 (1% HPMC) showed 17.06%. These values place F3 and F4 in the "fairly good to good" flow property category (values of 11-15% are classified as good, and 16-20% as fairly good) (Aultons & Taylor, 2022). Interestingly, the compressibility index of F4 (1% HPMC) was slightly higher than that of F3 (0.5% HPMC), indicating marginally poorer flow. This may be attributed to increased cohesiveness and surface adhesiveness imparted by the higher polymer content, which can enhance inter-particulate forces. This suggests the existence of an optimal HPMC concentration for flow enhancement, likely between 0.5% and 1%. This improvement indicates that the HPMC layer successfully modified the citric acid surface, reducing interparticle friction and adhesion, thereby enhancing powder packing efficiency and movement (Ratih et al., 2022). In this case, the coating method proved superior in improving the flow properties of the printed mass compared to the granulation method.

Table 3. Analysis of bulk density, tapped density, and compressibility index

Evaluation	F0	F1	F2	F3	F4
Bulk density (g/mL)	0.64 ± 0.00	0.62 ± 0.01	0.63 ± 0.00	0.68 ± 0.01	0.64 ± 0.00
Tapped density (g/mL)	0.81 ± 0.01	0.80 ± 0.00	0.78 ± 0.00	0.79 ± 0.00	0.77 ± 0.00
Compressibility index (%)	21.47 ± 0.35	22.32 ± 1.28	19.64 ± 0.40	14.21 ± 0.57	17.06 ± 0.67

Note: *Data represent mean ± SD, n = 3. Significant differences (p<0.05) occurred not only with the control formula but also between the other formulas.*

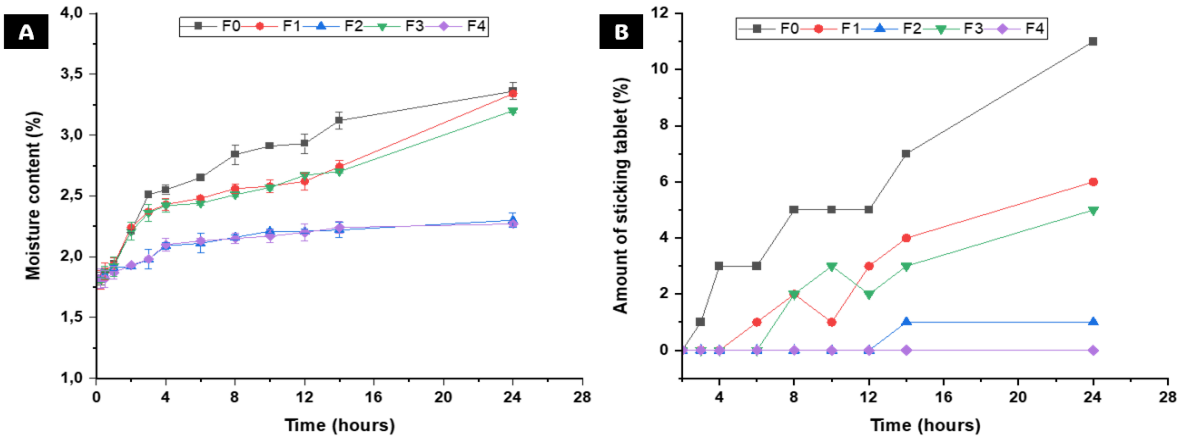

Figure 2. Graphical representation of the evaluation of the compression time of calcium carbonate–cholecalciferol chewable tablets during a 24-hour observation period, (A) moisture content (%), (B) percentage of sticking tablets, and significant difference (p<0.05) compared to the control formula.

Moisture content analysis indicates that the 1% HPMC coating modification (F4) and the 1% mannitol granulation (F2) are most effective in mitigating water absorption relative to the control formula (F0) and other formulas. While F0 and F1 reached more than 3.3% moisture content within 24 hours, F2 (2.27%) and F4 (2.25%) successfully maintained the lowest moisture content. The superiority of F2 and F4 indicates that the excipient modification treatment successfully formed an effective hydrophobic barrier around citric acid by reducing the water absorption rate (Yang et al., 2019). Maintaining powder moisture content below 3% is crucial, as high moisture directly increases plasticity and promotes sticking during compression, according to the pharmaceutical literature.

The analysis of the percentage of sticky tablets showed that excipient modification treatment was highly effective in mitigating sticking. The control formula (F0), which used citric acid without any modification treatment, showed the worst sticking results, reaching (10.88%) during the 24-hour observation period. These results were significantly different for F4 (1% HPMC coating method), which successfully eliminated sticking to 0% during the entire testing period, and F2 (1% mannitol granulation method), which was also very effective with 0.85% sticking at 24 hours. The superiority of F4 indicates that modifying citric acid excipients, particularly by employing a coating method with an adequate HPMC concentration, is the optimal formulation strategy. This elimination of sticking correlates directly with the best moisture content control in F4 (2.25%), as high moisture is a major factor that increases particle plasticity and triggers adhesion in the punch (Fara et al., 2020). These findings are consistent with the literature supporting the use of coating or microencapsulation as the best method to isolate hygroscopic and reactive materials, thereby minimizing contact between citric acid and the punch surface (Kotsur et al. 2024). Thus, the success of F4 in preventing sticking makes it the optimal choice.

Evaluation of Chewable Tablet Formulations. Organoleptic testing of calcium carbonate–cholecalciferol chewable tablets was conducted to assess the physical characteristics of tablets produced from each formula (F0-F4) following compression. In general, all formulas produced tablets with uniform color (pink, derived from the red iron oxide color used in the formula), characteristic odor (strawberry flavor), and identical shape (round tablets with a diameter of ~18 mm).

Evaluation of the hardness of calcium carbonate–cholecalciferol chewable tablets showed that all formulas (F0 to F4) met the ideal chewable tablet hardness requirement of 8–12 kP, indicating that the tablets were strong yet easy to chew (Rodríguez-Pombo et al., 2022). The control formula (F0) had a hardness of 9.63±0.67 kP. All modified formulas showed an increase, with the highest values achieved by F1 (10.80±0.73 kP) and F3 (10.54±0.65 kP). This improvement indicates that modifying citric acid excipients, whether by granulation or coating methods, can enhance compressibility and interparticle bonding (Medarević et al., 2021). These results are consistent with the literature, stating that granulation and coating methods can improve tablet density and bonding during compression (Aleti & Murthy, 2023).

Table 4. Evaluation of calcium carbonate–cholecalciferol chewable tablet formulations.

Evaluation	F0	F1	F2	F3	F4
Hardness (kP)	9.63 ± 0.67	10.80 ± 0.73	10.15 ± 0.49	10.54 ± 0.65	10.52 ± 0.67
Friability (%)	1.70 ± 0.18	1.48 ± 0.16	1.30 ± 0.06	1.65 ± 0.03	1.41 ± 0.08
Weight uniformity (g)	1.71 ± 0.01	1.70 ± 0.00	1.71 ± 0.01	1.71 ± 0.00	1.71 ± 0.01
Thickness (mm)	4.74 ± 0.02	4.76 ± 0.02	4.75 ± 0.02	4.74 ± 0.02	4.76 ± 0.02
Diameter (mm)	18.06 ± 0.02	18.06 ± 0.02	17.98 ± 0.00	18.06 ± 0.02	18.06 ± 0.02

Note: Data represent mean ± SD, n = 3. significant difference ($p<0.05$) compared to the control formula.

The friability test of calcium carbonate-cholecalciferol chewable tablets aims to evaluate the resistance of tablets to friction and pressure during the production, storage, and distribution processes. The results show that all formulas produced friability percentage values above the compendial criteria limit (≤ 1.0%), but other studies have mentioned that for tablet weights of 1-2 grams, the friability value can be less than 2% (Akhtar & Dev, 2017). In this study, the tablet weight was approximately 1.70 – 1.71 g. The F0 friability value reached 1.70%. However, the formula with 1% mannitol granulation (F2) showed the lowest friability at 1.30%. The increase in hardness in F2 accompanied by a decrease in friability confirmed that this modification created a more compact compacted mass structure and stronger interparticle bonds after compression (Adeleye et al., 2022).

The weight uniformity test of calcium carbonate–cholecalciferol chewable tablets showed that all formulas (F0 to F4) met the compendial requirements, with the criterion that the average weight deviation should not exceed 5% (Kementerian Kesehatan Republik Indonesia, 2020). The average weight of all formulations was consistent, ranging from 1.70 to 1.71 g. This excellent weight uniformity indicates stable mass-flow properties during die filling, proving that lubricant optimization and compression parameters are effective in ensuring consistent filling, regardless of adhesion issues (Peddapatla et al., 2021).

Thickness and diameter tests of calcium carbonate–cholecalciferol chewable tablets showed minimal variation between formulas, confirming the consistency of the compression process and the uniformity of the punches used. All formulations met the size uniformity requirement (< 5%). The average diameter of all formulations was 18.06 mm, except for F2 (17.98 mm) (Sharma et al., 2020).

Overall, a comparative analysis of chewable calcium carbonate–cholecalciferol tablet formulations indicates that Formula F4 (1% HPMC coating) is the optimal formulation. The main problem, namely sticking, was found to be very poor in the control formula F0 (10.88%) and was directly correlated with the highest moisture content (3.36%). Formula F4 demonstrates success in addressing the sticking problem, with 0% sticking tablets and a moisture content of 2.25%, compared with other formulas and superior to the sticking results obtained by F2 (0.85%) with a moisture content of 2.27%. This indicates that a 1% HPMC concentration is the critical point required to physically isolate citric acid and prevent neutralization reactions and moisture absorption, in accordance with the microencapsulation principle (Vlad et al., 2025). The effectiveness of the HPMC coating can be further elucidated by its film-forming mechanism. HPMC forms a continuous, flexible film at temperatures above its relatively low glass transition temperature (Tg). This film acts as a robust physical barrier, effectively isolating the hygroscopic and reactive citric acid cores from both environmental moisture and direct contact with calcium carbonate particles during compression, thereby preventing the initiation of the sticky neutralization reaction (Shahrbabaki et al., 2025). In addition to addressing process issues, F4 also demonstrated better physical tablet quality. Although F2 was slightly superior in friability, F4 provided excellent hardness (10.52 kP) and compressibility index (17.06%), indicating good flow properties (Ortiz et al., 2025; Rocha et al., 2019). This study only evaluated sticking for 24 hours and did not cover long-term stability. However, the success of the 5 kg batch indicates initial validation of scalability. HPMC coating adds a step to the process and increases costs, but has the potential to improve production efficiency by reducing cleaning downtime and tablet rejection.

4. CONCLUSION

This study concludes that modifying citric acid excipients is a highly effective strategy for eliminating stickiness during the compression process of calcium carbonate–cholecalciferol chewable tablets. The coating modification method with 1% HPMC (F4) proved to be the most optimal formulation, successfully achieving 0% stickiness and maintaining the lowest water

content (2.25%). This modification has direct practical implications, including increased production efficiency, reduced machine downtime, and lower operating costs. For further research, it is recommended to conduct real-time stability testing to confirm the long-term effectiveness of the HPMC coating and to evaluate its impact on the flavor release profile and calcium dissolution kinetics throughout the product's shelf life.

REFERENCES

Abaci, A., Gedeon, C., Kuna, A., & Guvendiren, M. (2021). Additive manufacturing of oral tablets: Technologies, materials and printed tablets. *Pharmaceutics*, 13(2), 156. https://doi.org/10.3390/pharmaceutics13020156

Adeleye, O., Bamiro, O. A., Albalawi, D. A., Alotaibi, A. S., Iqbal, H., Sanyaolu, S., … Menaa, F. (2022). Characterizations of alpha-cellulose and microcrystalline cellulose isolated from Cocoa Pod Husk as a potential pharmaceutical excipient. *Materials*, *15*(17), 5992. https://doi.org/10.3390/ma15175992

Akhtar, S., & Dev, P. (2017). Formulation and evaluation of chewable multivitamin tablet. *International Journal of Current Pharmaceutical Research*, 9, 61–64. https://doi.org/10.22159/ijcpr.2017v9i4.20958

Al-Hakim, N. A., Fauziyyah, S. A. N., Purnamasari, N., & Faramayuda, F. (2024). Formulation and physical evaluation of Orthosiphon aristatus leaf extract granule preparation as herbal beverage candidate. *Majalah Obat Tradisional*, 29(3), 286–294. https://doi.org/10.22146/mot.91009

Al-Hakim, N. A., Ratih, H., & Sabrilla, N. (2025). Formulation and physical evaluation of Stevia granule preparations as natural sweetener with the incorporation of Polyvinylpyrrolidone (PVP) as binder. *JPS*, 8(2), 827–836. https://doi.org/10.36490/journal-jps.com.v8i2.661

Aleti, R., & Murthy, K. V. R. (2023). Development and characterization of chronotherapeutic tablets of sacubitril-valsartan supramolecular complex using hupu gum and lannea gum by compression coating. *Journal of Applied Pharmaceutical Science*, 13(7), 193-203. https://doi.org/10.7324/JAPS.2023.120714

Atanaskova, E., Kostovski, D., & Anevska-Stojanovska, N. (2020). Investigation of the influence of critical process parameters in roller compaction process on physical properties of granules and tablets using design of experiments. *Arhiv Za Farmaciju*, *70*(1), 34–53. https://doi.org/10.5937/arhfarm2001034A

Aultons, M. E., & Taylor, K. M. G. (2022). *Aulton's pharmaceutics: The design and manufacture of medicines 6th ed.* London, United Kingdom: Churchill Livingstone, Elsevier.

Badawi, A., Hegazy, M. M., Louis, D., & Eldegwy, M. A. (2017). Solving manufacturing problems for L-carnitine-L-tartrate to improve the likelihood of successful product scale-up. *Acta Pharmaceutica*, 67(4), 511–525. https://doi.org/10.1515/acph-2017-0033

Carugo, S., Vescini, F., Giusti, A., Mauro, G. L., Tafaro, L., Festuccia, F., ... & Rossini, M. (2024). The essential role of combined calcium and vitamin D supplementation in the osteoporosis scenario in italy: Expert opinion paper. *Archives of Osteoporosis*, 19(1), 99. https://doi.org/10.1007/s11657-024-01451-x

Chanwetprasat, P., Seangarun, C., Seesanong, S., Boonchom, B., Laohavisuti, N., Boonmee, W., & Rungrojchaipon, P. (2025). Effect of Citric Acid Concentration on the Transformation of Aragonite CaCO3 to Calcium Citrate Using Cockle Shells as a Green Calcium Source. *Materials,* 18(9), 2003. https://doi.org/10.3390/ma18092003

Chen, F. C., Liu, W. J., Zhu, W. F., Yang, L. Y., Zhang, J. W., Feng, Y., ... & Li, Z. (2022). Surface modifiers on composite particles for direct compaction. *Pharmaceutics*, 14(10), 2217. https://doi.org/10.3390/pharmaceutics14102217

Chun, M., Kim, J. Y., Park, E., & Choi, D. (2021). Development of a robust control strategy

for fixed-dose combination bilayer tablets with integrated quality by design, statistical, and process analytical technology approach. *Pharmaceutics*, 13(9), 1443. https://doi.org/10.3390/pharmaceutics13091443

Fara, D. A., Al-Hmoud, L., Rashid, I., Chowdhry, B., & Badwan, A. (2020). Understanding the performance of a novel direct compression excipient comprising roller compacted chitin. *Marine Drugs*, 18(2), 115. https://doi.org/10.3390/md18020115

Gawade, N. L., & Shendge, R. S. (2020). A review on chewable tablet. *Journal of Emerging Technologies and Innovative Research,* 7(3), 342-353. https://doi.org/10.52783/jchr.v14.i6.7573

Ismail, A., El-Biyally, E., & Sakran, W. (2023). An innovative approach for formulation of rutin tablets targeted for colon cancer treatment. *AAPS PharmSciTech*, 24(2), 1–14. https://doi.org/10.1208/s12249-023-02518-7

Kang, C. Y. X., Chow, K., Lui, Y. S., Salome, A., Boit, B., Lefevre, P., … Heng, P. W. S. (2024). Mannitol-coated hydroxypropyl methylcellulose as a directly compressible controlled release excipient for moisture-sensitive drugs: a stability perspective. *Pharmaceuticals*, 17(9), 1167. https://doi.org/10.3390/ph17091167

Kementerian Kesehatan Republik Indonesia. (2020). *Farmakope Indonesia edisi VI.* Jakarta: Kementrian Kesehatan Indonesia.

Kotsur, Y. M., Terenteva, O. A., Flisyuk, E. V, & Narkevich, I. (2024). Application of press-coatings for the development of prolonged release tablets based on hygroscopic substances. *Drug Development and Registration*, 13(4), 113-120. https://doi.org/10.33380/2305-2066-2024-13-4-1952

Koumbogle, K., Gitzhofer, F., & Abatzoglou, N. (2022). Moisture transport coefficients determination on a model pharmaceutical tablet. *Processes,* 10(2), 254. https://doi.org/10.3390/pr10020254

Lambros, M., Tran, T., Fei, Q., & Nicolaou, M. (2022). Citric acid: A multifunctional pharmaceutical excipient. *Pharmaceutics,* 14(5), 972. https://doi.org/10.3390/pharmaceutics14050972

Lute, S. V., Dhenge, R. M., & Salman, A. D. (2018). Twin screw granulation: effects of properties of primary powders. *Pharmaceutics,* 10(2), 68. https://doi.org/10.3390/pharmaceutics10020068

Medarević, D., Djuriš, J., Krkobabić, M., & Ibrić, S. (2021). Improving tableting performance of lactose monohydrate by fluid-bed melt granulation co-processing. *Pharmaceutics,* 13(12), 2165. https://doi.org/10.3390/pharmaceutics13122165

Mititelu, M., Moroșan, E., Nicoară, A. C., Secăreanu, A. A., Musuc, A. M., Atkinson, I., ... & Balaci, T. D. (2022). Development of immediate release tablets containing calcium lactate synthetized from Black Sea mussel shells. *Marine drugs,* 20(1), 45. https://doi.org/10.3390/md20010045

Nakamura, S., Otsuka, N., Yoshino, Y., Sakamoto, T., & Yuasa, H. (2016). Predicting the occurrence of sticking during tablet production by shear testing of a pharmaceutical powder. *Chemical and Pharmaceutical Bulletin*, 64(5), 512–516. https://doi.org/10.1248/cpb.c15-00992

Nidhu, M. S., Sniktha, V. R., Benny, L., Thomas, J., Ajay, A., & Ramaswamy, K. P. (2021). Degradation kinetics of alkali-activated mortar in aggressive citric acid environment. *IOP Conference Series: Materials Science and Engineering*, 989(1), 012007. https://doi.org/10.1088/1757-899X/989/1/012007

Nyamweya, N. N. (2021). Applications of polymer blends in drug delivery. Future *Journal of Pharmaceutical Sciences,* 7(1), 18. https://doi.org/10.1186/s43094-020-00167-2

Nyarko, S., Ofori-Kwakye, K., Johnson, R., Kuntworbe, N., & Yar, D. D. (2024). Investigating the Presence of Falsified and Poor-Quality Fixed-Dose Combination Artemether-

Lumefantrine Pharmaceutical Dosage Forms in Kumasi, Ghana. *Advances in Pharmacological and Pharmaceutical Sciences,* 2024(1), 2650540. https://doi.org/10.1155/2024/2650540

Olowofoyeku, A. E., Aremu, A. K., Olorunnisola, A., Olowofoyeku, A. E., Mendez, J. R. V., & Adekanmi, D. G. (2025). Tunable Hydrophobicity and Photoluminescence in Polystyrene-Calcium Carbonate Composites with Citric Acid-Induced Porosity. *Engineering Innovations*, 14, 1–13. https://doi.org/10.4028/p-V2Z9mr

Ortiz, A. C., Carrasco-Rojas, J., Peñaloza, S., Simirgiotis, M. J., Rubio-Quiroz, L., Ruiz, D., ... & Arriagada, F. (2025). Influence of an Antioxidant Nanomaterial on Oral Tablet Formulation: Flow Properties and Critical Quality Attributes. *Antioxidants,* 14(7), 829. https://doi.org/10.3390/antiox14070829

Pagire, S. K., Seaton, C., & Paradkar, A. (2020). Improving stability of effervescent products by co-crystal formation: a novel application of crystal engineered citric acid. *Crystal Growth & Design*, 20(7), 4839–4844. https://doi.org/10.1021/acs.cgd.0c00616

Palacios, C., Cormick, G., Hofmeyr, G., Garcia-Casal, M., Peña-Rosas, J. P., & Betrán, A. (2020). Calcium-fortified foods in public health programs: considerations for implementation. *Annals of the New York Academy of Sciences*, 1485, 3–21. https://doi.org/10.1111/nyas.14495

Peddapatla, R. V., Sheridan, G., Slevin, C., Swaminathan, S., Browning, I., O'reilly, C., ... & Crean, A. M. (2021). Process model approach to predict tablet weight variability for direct compression formulations at pilot and production scale. *Pharmaceutics,* 13(7), 1033. https://doi.org/10.3390/pharmaceutics13071033

Poka, M., Milne, M., Wessels, A., & Aucamp, M. (2023). Sugars and polyols of natural origin as carriers for solubility and dissolution enhancement. *Pharmaceutics*, 15(11), 2557. https://doi.org/10.3390/pharmaceutics15112557

Ratih, H., Pratiwi, G. K., Alatas, F., Agustin, M., & Saraswati, B. D. (2022). Isoniazid microencapsulation with HPMCP HP-50 and HPMCP HP- 55 (2:3) coating using solvent evaporation method. *Indonesian Journal of Pharmaceutical Science and Technology*, 9(2), 114. https://doi.org/10.24198/ijpst.v9i2.36678

Rocha, H., Augusto, R. S., Prado, L. D., & Carvalho, E. (2019). Characterization of nimesulide and development of immediate release tablets. *Eclética Química Journal*, 44(3), 20–35. https://doi.org/10.26850/1678-4618eqj.v44.3.2019.p20-35

Rodríguez-Pombo, L., Awad, A., Basit, A. W., Alvarez-Lorenzo, C., & Goyanes, A. (2022). Innovations in chewable formulations: the novelty and applications of 3D printing in drug product design. *Pharmaceutics,* 14(8), 1732. https://doi.org/10.3390/pharmaceutics14081732

Rosch, M., Lucas, K., Al-Gousous, J., Pöschl, U., & Langguth, P. (2021). Formulation and characterization of an effervescent hydrogen-generating tablet. *Pharmaceuticals,* 14(12), 1327. https://doi.org/10.3390/ph14121327

Shah, D. S., Moravkar, K., Jha, D., Lonkar, V., Amin, P. D., & Chalikwar, S. (2023). A concise summary of powder processing methodologies for flow enhancement. *Heliyon*, *9*(6). https://doi.org/10.1016/j.heliyon.2023.e16498

Shahrbabaki, M. F., Lavasani, A. S., Zand, N., Nateghi, L., & Eshaghi, M. (2025). Designing an optimized nanocomposite film comprising hydroxypropyl methylcellulose, nanoclay, and dill essential oil to extend the shelf life of eggs. *International Journal of Food Science*, 2025(1), 6633069. https://doi.org/10.1155/ijfo/6633069

Sharma, S. K., Singh, A.-K., Bhandari, A., Singh, S., & Singh, S. (2020). Development and evaluation of chewable tablets of calcium and vitamin D. *Asian Journal of Pharmaceutical Research and Development*, 8(3), 232–234. https://doi.org/10.22270/ajprd.v8i3.704

Stanojević, G., Medarević, D., Adamov, I., Pe\vsić, N., Kovacevic, J., & Ibrić, S. (2020).

Tailoring atomoxetine release rate from DLP 3D-printed tablets using artificial neural networks: Influence of tablet thickness and drug loading. *Molecules*, 26(1), 111. https://doi.org/10.3390/molecules26010111

Takeuchi, H. (2022). Contribution of particle design research to the development of patient-centric dosage forms. *KONA Powder and Particle Journal*, 39, 150–175. https://doi.org/10.14356/kona.2022017

Vlad, R. A., Pintea, A., Pintea, C., Rédai, E. M., Antonoaea, P., Bîrsan, M., & Ciurba, A. (2025). Hydroxypropyl methylcellulose—a key excipient in pharmaceutical drug delivery systems. *Pharmaceutics,* 17(6), 784. https://doi.org/10.3390/pharmaceutics17060784

Wang, Y., Cao, J., Zhao, X., Liang, Z., Qiao, Y., Luo, G., & Xu, B. (2022). Using a material library to understand the change of tabletability by high shear wet granulation. *Pharmaceutics*, 14(12), 2631. https://doi.org/10.3390/pharmaceutics14122631

Yang, Q., Yuan, F., Xu, L., Yan, Q., Yang, Y., Wu, D., ... & Yang, G. (2019). An update of moisture barrier coating for drug delivery. *Pharmaceutics,* 11(9), 436. https://doi.org/10.3390/pharmaceutics11090436

Zheng, X., Wu, F., Hong, Y., Shen, L., Lin, X., & Feng, Y. (2019). Improvements in sticking, hygroscopicity, and compactibility of effervescent systems by fluid-bed coating. *RSC Advances*, 9, 31594–31608. https://doi.org/10.1039/c9ra05884b