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Herbal effervescent disinfectant tablets as a sustainable chlorine substitute in healthcare waste management: A case study

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ABSTRACT

Chlorine-based disinfectants are widely used in healthcare waste treatment but are increasingly restricted due to their toxic byproducts and environmental impact. This study aimed to develop and optimize herbal-based effervescent disinfectant tablets using *Piper betle* and *Cymbopogon citratus* extracts as a safer, eco-friendly alternative. Effervescent tablets were formulated using sodium bicarbonate, citric and tartaric acids, PVP, and standardized ethanol extracts of *P. betle* and *C. citratus*. A Box-Behnken design within Response Surface methodology was applied to optimize three formulation variables ($NaHCO_3$), citric acid ratio, and PVP (against two critical response parameters) – effervescence time and foam height. Physical and microbiological evaluations were performed, including disinfection efficacy against *Bacillus subtilis* and *Bacillus stearothermophilus* on contaminated medical plastic waste. The optimized formulation demonstrated rapid effervescence (as low as 2.68 seconds) and effective foam generation (up to 0.5400 cm). $NaHCO_3$ was the most significant factor influencing both disintegration and foaming behavior, with PVP and citric acid contributing through non-linear and interaction effects. Granule evaluation confirmed good flowability and compressibility (Hausner ratio < 1.25; Carr's index < 16%). The regression models showed excellent fit (R^2 = 0.9999 for effervescence time, 0.9857 for foam height). Antimicrobial tests showed significant bacterial reduction, supporting practical efficacy. Herbal effervescent tablets formulated from *P. betle* and *C. citratus* offer a viable, low-toxicity alternative to chlorine-based disinfection for healthcare waste. This plant-based formulation aligns with WHO sustainability goals and represents a scalable innovation for improving infection control in resource-limited health systems.

Keywords: herbal disinfectant, effervescent tablet, healthcare waste, *Piper betle*, *Cymbopogon citratus*, chlorine alternative, infection control, sustainability.

INTRODUCTION

Healthcare waste management continues to be a critical issue in global health systems, particularly in the context of infectious and hazardous materials (Lemma et al., 2021; Yang et al., 2024). The World Health Organization (WHO) estimates that healthcare facilities worldwide produce over 5.2 million tons of waste annually, a significant portion of which poses infectious and toxic risks to both public health and the environment (Janik-Karpinska et al., 2023; Prüss et al., 2024). Inadequate management of this waste, especially in resource-limited settings, contributes to occupational exposure among healthcare workers, disease transmission, and environmental pollution through unsafe incineration or chemical usage.

Among the most widely used chemical disinfectants in healthcare waste treatment is chlorine, primarily in the form of sodium hypochlorite. Chlorine-based disinfection is valued for its broad-spectrum antimicrobial properties and affordability. However, chlorine's high oxidative potential leads to the formation of toxic byproducts such as trihalomethanes and dioxins, which are associated with carcinogenicity, respiratory illness, and environmental persistence (Al-Fatlawi, 2014; Fontenot et al., 2013). As a result, regulatory bodies in various countries are progressively restricting the routine use of chlorine in medical settings, necessitating the exploration of safer, environmentally sustainable alternatives.

Plant-derived antimicrobials have emerged as viable candidates for eco-friendly disinfection, owing to their biodegradability, minimal toxicity, and potent bioactivity. *Piper betle* (betel leaf) and *Cymbopogon citratus* (lemongrass) are two medicinal plants known for their antimicrobial and antioxidant constituents. Betel leaves contain phenolic compounds such as chavicol, eugenol, and tannins, which exert bactericidal effects by damaging microbial cell walls and inhibiting enzymatic systems (Lutviandhitarani et al., 2015; Sari et al., 2019). Lemongrass essential oil, rich in citral and geraniol, has also demonstrated inhibitory effects against both Gram-positive and Gram-negative bacteria (Gao et al., 2020).

While the antimicrobial efficacy of these individual extracts has been documented in vitro, limited research has investigated their combined use, formulation into practical dosage forms, or application in healthcare waste decontamination workflows. Prior studies have focused on topical antiseptics or liquid formulations for clinical or veterinary use (Hemeg et al., 2020; Zouine et al., 2024), but few have explored their transformation into stable, standardized, solid dosage forms suitable for hospital disinfection routines.

The current study addresses this critical research gap by developing herbal effervescent disinfectant tablets combining *Piper betle* and *Cymbopogon citratus* extracts. The innovation lies not only in the selection of bioactive plant materials, but also in their delivery via effervescent tablets (a rarely explored dosage form for environmental disinfection). Effervescent tablets offer advantages in portability, dosing accuracy, and rapid solubilization, thereby enhancing user compliance and operational feasibility in healthcare settings.

This research also introduces a pharmaceutical optimization approach using response surface methodology (RSM) and Box-Behnken design to refine formulation parameters such as sodium bicarbonate levels, acid ratios (citric and tartaric), and binder concentrations. These variables influence key performance indicators, including effervescence time, foam height, granule flow rate, and compressibility (all essential for field applicability). To our knowledge, no prior studies have systematically optimized such a formulation for medical waste disinfection, making this effort a novel contribution.

Moreover, the antimicrobial efficacy of the final effervescent product was evaluated against *Bacillus subtilis* and *Bacillus stearothermophilus*, both of which are standard bioindicators in sterilization validation. These spore-forming bacteria are known for their resistance to chemical disinfectants, making them reliable markers of disinfection performance (Lytle et al., 2021). While previous research by Fikri et al. (2021) demonstrated the feasibility of using chlorine and electrocoagulation in medical waste treatment, those methods presented limitations in terms of safety, cost, and environmental impact. This study offers a plant-based, cost-effective, and scalable alternative that aligns with green hospital initiatives and WHO's sustainable development goals (Fikri et al., 2021).

This research provides a novel, dual-component, effervescent tablet formulation derived from betel leaf and lemongrass extracts as a sustainable substitute for chlorine in the disinfection of recyclable medical waste. It fills a clear gap in the literature by translating traditional phytotherapy into a modern, optimized dosage form with tested efficacy in realistic healthcare waste scenarios. These findings have significant implications for policy development, especially in countries seeking to reduce chemical hazards in hospitals while maintaining infection control standards.

MATERIAL AND METHODS

Study design

This study employed a laboratory-based, factorial randomized experimental design. The research focused on optimizing herbal effervescent disinfectant tablets and evaluating their efficacy against microbial indicators in recycled healthcare waste. The experimental process included formulation development, optimization using response surface methodology, antimicrobial testing, and physical tablet evaluation.

Study site

All formulation and granulation processes were conducted in the Integrated Pharmaceutical Laboratory at the Department of Pharmacy, Poltekkes Kemenkes Bandung, Indonesia. Microbiological testing was carried out in the Microbiology Laboratory, Department of Health Analyst, at the same institution. All facilities are certified for educational and research purposes and adhere to national laboratory safety standards.

Formulation of effervescent tablets

The effervescent tablets were formulated using ethanol-extracted *Piper betle* and *Cymbopogon citratus* leaves. Each formula contained 5% (w/w) of each extract. Other components included sodium bicarbonate (alkaline source), citric and tartaric acids (acid sources), polyvinylpyrrolidone (binder), and Avicel PH101 (diluent). Granules were prepared using wet granulation, sieved through mesh #12, dried to 1–4% moisture, and compressed into tablets (Figure 1).

Optimization via response surface methodology

To identify the optimal formulation of the herbal effervescent disinfectant tablets, a statistical optimization approach was employed using Box-Behnken design within the Design Expert® software (version 13.1.0, Stat-Ease Inc., USA). This method allowed for the systematic evaluation of the interactions between three key independent formulation variables: sodium bicarbonate concentration (ranging from 5% to 30% w/w), the proportion of polyvinylpyrrolidone (PVP) binder (ranging from 0.5% to 5% w/w), and the ratio of citric acid to tartaric acid (evaluated at 0:1, 1:1, and 1:2 ratios) (Ma et al., 2023; Mahapatra et al., 2020; Suksaeree et al., 2023).

The experimental design generated a total of 15 formulation trials, each tested for two critical response parameters: effervescence time (measured in seconds) and foam height (measured in centimeters). These parameters were selected due to their direct influence on the product's practicality and antimicrobial performance. Data were analyzed using quadratic polynomial regression models, and analysis of variance (ANOVA) was performed to assess the statistical significance of each factor and interaction effect on the response variables. Model validity was confirmed through determination coefficients (R^2), which exceeded 0.98 for both responses, indicating an excellent fit between the model and experimental data.

Antimicrobial efficacy testing

The disinfection ability of the tablets was tested against Bacillus subtilis and Bacillus stearothermophilus, standard bioindicators in sterilization studies. Swabs were collected from used medical plastic infusion bottles before and after tablet-based disinfection. Bacterial load was quantified using colony-forming unit (CFU) counts on TSA media after incubation at 37 °C. Results were expressed as percentage reduction.

Tablet evaluation and physical testing

The physical properties of the effervescent granules and tablets were thoroughly assessed

Figure 1. Granul effervescent for medical waste recycling

to ensure their functional suitability for application in healthcare settings. Flowability of the granules was evaluated using the angle of repose and flow rate tests, while compressibility was measured using Carr's index and the Hausner ratio. These indicators were used to determine the ease with which granules could be processed and compressed into uniform tablets. All tested formulations demonstrated acceptable flow characteristics, with Carr's index values below 16% and Hausner ratios below 1.2, reflecting good to excellent flow behavior.

Moisture content was determined by oven drying, ensuring that all formulations met the target moisture range of 1–4% to maintain tablet integrity. The mechanical and functional performance of the resulting tablets was assessed by measuring tablet hardness, friability, and dimensional uniformity. Effervescence time was determined by immersing a single tablet in 200 mL of distilled water at room temperature and recording the time until complete disintegration. Foam height was measured immediately after dissolution to evaluate the surfactant and dispersing effect of the formulation, which contributes to the distribution of antimicrobial agents across contaminated surfaces.

Granule size distribution was analyzed through standard mesh sieving to confirm particle uniformity, while preliminary stability tests were conducted over a 30-day period under ambient conditions to assess potential changes in appearance, disintegration performance, and foam production. All formulations remained stable, with no observable physical degradation or performance loss during the test period.

Ethical considerations

As this research did not involve human subjects, ethical approval from a health research ethics committee was not required. However, all experimental procedures involving microbial handling and medical waste were conducted under strict biosafety guidelines in accordance with national laboratory regulations and WHO standards on infection prevention and waste disposal.

Statistical analysis

All experiments were performed in triplicate. Statistical analyses were conducted using SPSS v18.0. Mean values and standard deviations were calculated for each parameter. ANOVA and regression analysis were used to identify significant effects of formulation factors, with p-values < 0.05 considered statistically significant.

Data availability statement

All data generated or analyzed during this study are included in this article. Additional datasets used in the optimization process or raw experimental data are available from the corresponding author upon reasonable request.

RESULTS

Model fit of experimental design and ANOVA analysis

The study generated 15 formulations using a BBD to optimize two critical responses: effervescence time and foam height of the herbal effervescent disinfectant tablets. Table 1 presents the actual and predicted values for each formulation.

Effervescence time (Response 1) varied significantly across formulations, ranging from 2.68 seconds (F9) to 136.8 seconds (F6). The fastest disintegration was observed in F9, which combined the highest sodium bicarbonate concentration with the absence of citric acid. The longest disintegration times occurred in F6 and F11, both containing high binder and acid ratios.

Foam height (Response 2) ranged from 0.0200 cm to 0.5400 cm. The highest foam height was recorded for F1 (0.5400 cm), while F6 and F9 produced the lowest foam values. A close match between actual and predicted values confirms the accuracy of the quadratic model used for optimization.

The granule properties of 15 formulations were evaluated using standard pharmaceutical indicators: angle of repose, granule flow rate, compressibility, Hausner ratio, and interquartile coefficient of skewness (IQCS). The results are summarized in Table 2.

The angle of repose ranged from 24.774° (F8) to 37.490° (F7), indicating good to excellent flowability across all formulations. Granule flow rate values varied between 3.434 g/s (F7) and 7.111 g/s (F4 & F5). The compressibility index ranged from 1.082% (F8) to 26.849% (F2), with most formulations remaining below the acceptable limit of 20%.

Table 1. Optimization results of the formulation using Box-Behnken design

Run	Formula	Response 1 Effervescence time (seconds)		Response 2 Foam height (cm)	
		Actual	Predicted	Actual	Predicted
1	F1	27.1	26.94	0.5400	0.5032
2	F2	83.09	82.63	0.3000	0.2525
3	F3	118.35	118.07	0.2000	0.1952
4	F4	75.25	75.41	0.3200	0.3453
5	F5	75.22	75.41	0.3300	0.3453
6	F6	136.8	137.21	0.2500	0.2825
7	F7	98.1	98.01	0.0400	0.0335
8	F8	30.5	30.57	0.1500	0.1495
9	F9	2.68	2.70	0.0200	0.0270
10	F10	58.97	59.04	0.1300	0.1295
11	F11	135.64	135.55	0.1800	0.1735
12	F12	32.35	32.37	0.2300	0.2370
13	F13	75.23	75.41	0.3200	0.3453
14	F14	28	27.88	0.5100	0.5155
15	F15	118	118.07	0.2100	0.1952

Note: All tests were performed in triplicate

Table 2. Optimization results of the formulation using Box-Behnken design

Run	Formula	Angle of repose (°)	Granule flow rate (g/second)	Compressibility (%)	Housner ratio	IQCS
1	F1	36.119±1.014	5.342±0.194	10.913	1.122	0.393
2	F2	33.878±7.150	3.975±1.338	26.849	1.367	0.571
3	F3	32.814±1.751	6.134±0.137	16.089	1.192	0.500
4	F4	33.808±1.115	7.111±0.683	7.802	1.085	0.226
5	F5	33.808±1.115	7.111±0.683	7.802	1.085	0.226
6	F6	29.354 ± 0.714	4.739 ± 0.083	20.062	1.251	0.070
7	F7	37.490 ± 0.243	3.434 ± 0.179	11.033	1.124	0.014
8	F8	24.774±0	5.706±0.114	1.082	1.011	0.238
9	F9	32.325 ± 2.613	3.473 ± 0.198	5.149	1.054	0.150
10	F10	32.823 ± 1.996	5.644 ± 0.297	9.945	1.110	0.164
11	F11	29.654 ± 4.637	5.348 ± 0.846	26.749	1.365	0.340
12	F12	33.446 ± 0.657	7.133 ± 0.009	12.409	1.142	0.572
13	F13	30.092 ± 1.377	5.601 ± 0.368	10.959	1.123	0.186
14	F14	36.119±1.014	5.342±0.194	10.913	1.122	0.393
15	F15	32.814±1.751	6.134±0.137	16.089	1.192	0.500

Note: All tests were performed in triplicate.

Hausner ratios were all below the critical value of 1.4, ranging from 1.011 (F8) to 1.367 (F2), confirming acceptable flow properties. IQCS values varied from 0.014 (F7), indicating highly uniform granule size distribution, to 0.572 (F12), suggesting relatively higher particle size variability.

The analysis of variance (ANOVA) for effervescence time response is presented in Table 3. The model was statistically significant at both the whole-plot and subplot levels. The whole-plot F-value was 4177.55 with a p-value of 0.0004, indicating the model's strong ability to explain the variation in the response. Within this, the linear term for citric acid had a p-value of 0.0003 and its quadratic form was also significant with a p-value of 0.0006, confirming its non-linear influence on disintegration time.

Table 3. ANOVA analysis results for effervescence time response

Source	Term df	Error df	F-value	p-value	Note
Whole-plot	2	1.88	4177.55	0.0004	Significant
c-citric acid	1	1.86	6206.60	0.0003	
c^2	1	1.90	2163.11	0.0006	
Subplot	7	3.13	59777.72	< 0.0001	Significant
A-$NaHCO_3$	1	3.12	$3.834.10^5$	< 0.0001	
B-PVP	1	3.38	3394.72	< 0.0001	
AB	1	3.16	1942.13	< 0.0001	
Ac	1	3.04	438.05	0.0002	
Bc	1	3.04	93.63	0.0022	
A^2	1	3.18	41.42	0.0064	

In the subplot, the model yielded an F-value of 59777.72 and a p-value of less than 0.0001, denoting an overall significant relationship. Sodium bicarbonate (A) exhibited a very high F-value of 383410.5 with a p-value below 0.0001, while the binder PVP (B) was also statistically significant ($F = 3394.72$, $p < 0.0001$). Interaction terms such as AB (A × B) and Ac (A × c) displayed F-values of 1942.13 and 438.05 respectively, both with p-values indicating strong significance. Additional interactions (Bc) and quadratic effects (A^2 and B^2) were also significant, supporting the relevance of higher-order terms in the predictive model for effervescence time.

As shown in Table 4, the ANOVA results for foam height also confirmed statistical significance. The whole-plot analysis yielded an F-value of 36.04 with a p-value of 0.0333, suggesting that the model appropriately described the foam height variation. Among the terms analyzed, the quadratic effect of citric acid (c^2) was significant with a p-value of 0.0179, while the linear term was not.

In the subplot, the model achieved an F-value of 25.55 with a p-value of 0.0091. Sodium bicarbonate (A) was a highly significant factor ($F = 106.65$, $p = 0.0015$), while the binder (B) did not reach statistical significance ($p = 0.1371$). However, interactions AB (A × B) and Bc (B × c) showed statistical importance, both with p-values below 0.02. The quadratic effects of A^2 and B^2 were also meaningful, with p-values of 0.0288 and 0.0173 respectively. The interaction Ac (A × c) did not show significance ($p = 0.8936$).

Table 5 summarizes the regression coefficient statistics for the models predicting effervescence time and foam height. For effervescence time, the model had a standard deviation of 0.3410 and a mean value of 73.02 seconds. The coefficient of variation (C.V.%) was only 0.4671%, indicating minimal variation and high reproducibility. The R^2 and adjusted R^2 were both 0.9999, reflecting near-perfect predictive accuracy.

For foam height, the model's standard deviation was 0.0355 with a mean of 0.2487 cm. Although the coefficient of variation was higher at 14.28%, the R^2 of 0.9857 and adjusted R^2 of 0.9335 still indicate strong model reliability. These findings demonstrate the suitability of the Box-Behnken design for modeling and optimizing these critical formulation responses.

Effect of formulation variables on effervescence time

The contour and 3D surface plots in Figure 2 demonstrate the effects of sodium bicarbonate ($NaHCO_3$), polyvinylpyrrolidone (PVP), and citric acid concentrations on effervescence time. As shown in the first and second graphs (top row), increasing $NaHCO_3$ significantly reduced effervescence time, particularly at lower citric acid levels. The fastest disintegration (2.68 seconds) occurred at high $NaHCO_3$ and minimal acid levels, corresponding to formulation F9.

In contrast, higher citric acid content increased effervescence time (up to 136.8 seconds), suggesting a slower reaction rate when acid predominates, likely due to an imbalance in the acid–base ratio required for rapid CO_2 generation.

The third contour plot ($NaHCO_3$ vs. PVP) and the corresponding 3D plots in the second row show that increasing PVP concentration moderately prolonged effervescence time. This can be attributed to the binding effect of PVP, which potentially reduces the porosity of the tablet matrix and slows down water penetration.

Table 4. ANOVA analysis results for foam height response

Source	Term df	Error df	F-value	p-value	Note
Whole-plot	2	1.84	36.04	0.0333	Significant
c-citric acid	1	1.82	5.83	0.1497	
c^2	1	1.87	66.39	0.0179	
Subplot	7	3.18	25.55	0.0091	Significant
A-$NaHCO_3$	1	3.17	106.65	0.0015	
B-PVP	1	3.53	3.68	0.1371	
AB	1	3.22	31.79	0.0091	
Ac	1	3.06	0.0211	0.8936	
Bc	1	3.06	20.28	0.0196	
A^2	1	3.25	14.10	0.0288	
B^2	1	3.08	21.99	0.0173	

Table 5. Regression coefficient results

Regression coefficients	Effervescence time	Foam height
Std Dev.	0.3410	0.0355
Mean	73.02	0.2487
C.V %	0.4671	14.28
R^2	0.9999	0.9857
Adjusted R^2	0.9999	0.9335

Figure 2 also reveals that foam height was significantly influenced by the concentration of $NaHCO_3$ and citric acid. The center plot (middle bottom) shows that formulations with moderate acid and base levels exhibited greater foam generation, peaking at 0.5400 cm in F1. Excessive acid or binder levels suppressed foam formation, likely due to delayed disintegration or overly cohesive matrices.

Figure 3 illustrates the contour and 3D surface plots describing the interaction effects of $NaHCO_3$, citric acid, and PVP on the foam height of the herbal effervescent disinfectant tablets. Foam height values were observed to range between 0.020 cm and 0.540 cm.

The first contour plot (top left) and corresponding 3D surface (bottom right) demonstrate that higher concentrations of sodium bicarbonate ($NaHCO_3$) positively influenced foam height. When combined with increased PVP concentrations, foam height reached its peak at approximately 0.540 cm. However, beyond a certain concentration of PVP, further increases did not result in higher foam, suggesting a saturation point.

The second contour plot (top middle) and its corresponding 3D plot (bottom middle) show a distinct interaction between $NaHCO_3$ and citric acid. Foam height increased proportionally with $NaHCO_3$ concentration, especially at low to moderate citric acid levels. However, when citric acid levels exceeded 1.5%, foam height began to decline, likely due to an imbalance in the acid–base reaction ratio required for optimal CO_2 generation.

The final surface plot (bottom left), representing the interaction between PVP and citric acid, indicates that moderate concentrations of both components produced the highest foam height. Either excessively low or high concentrations of citric acid, in combination with PVP, led to suboptimal foam performance.

DISCUSSION

Model fit of experimental design and ANOVA analysis

The most rapid effervescence observed in formulation F9 (2.68 seconds) highlights the critical role of sodium bicarbonate as the primary effervescent agent. This outcome is consistent with the acid–base reaction mechanism, where sodium bicarbonate rapidly reacts with acids in the presence of water to release CO_2, leading to tablet disintegration (Kumar et al., 2020). Conversely, the longest disintegration times, such as in F6 and F11, can be attributed to higher concentrations of citric acid and polyvinylpyrrolidone (PVP), which may retard disintegration by increasing matrix density and reducing water penetration (Khairnar et al., 2024).

Foam height, a secondary yet crucial performance parameter, showed a distinct relationship

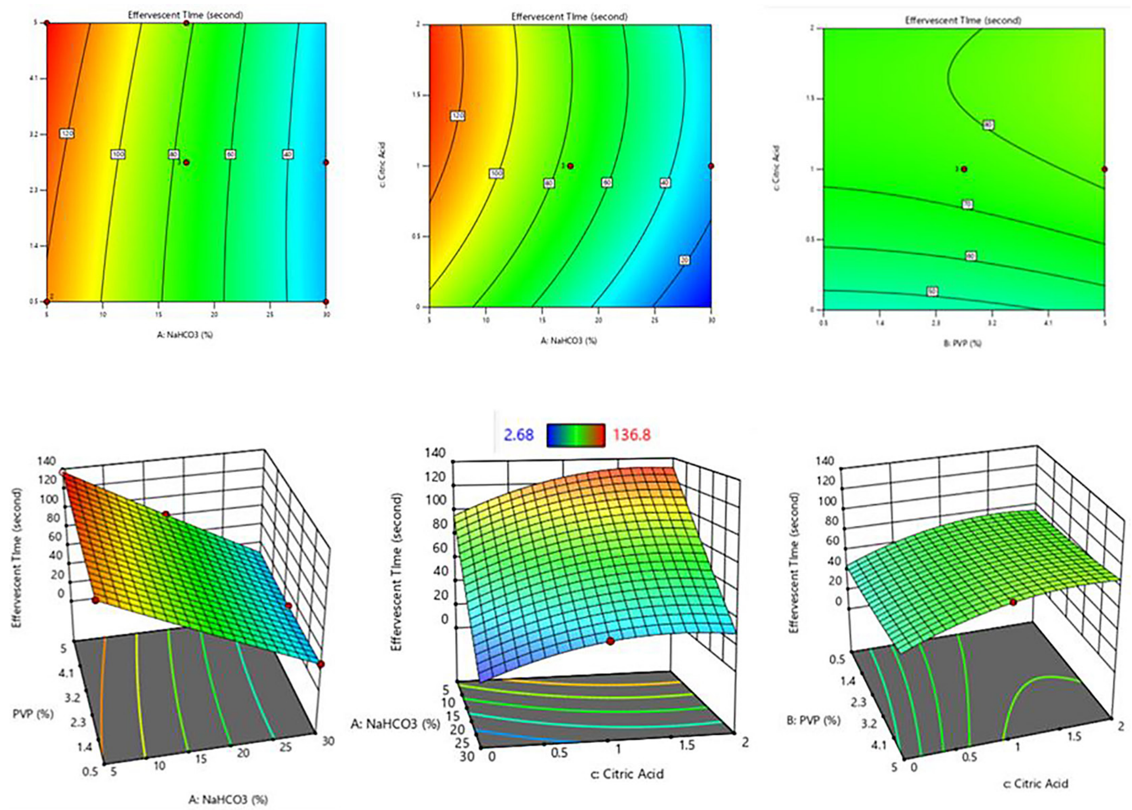

Figure 2. 2D and 3D response surface plots for the optimization of effervescent granule formulation containing *Piper betle* (betel leaf) and *Cymbopogon citratus* (lemongrass) extracts, showing the interaction effects between: (a) $NaHCO_3$ and PVP concentrations; (b) $NaHCO_3$ concentration and citric acid/tartaric acid ratio; (c) PVP concentration and citric acid/tartaric acid ratio on effervescence time (seconds)

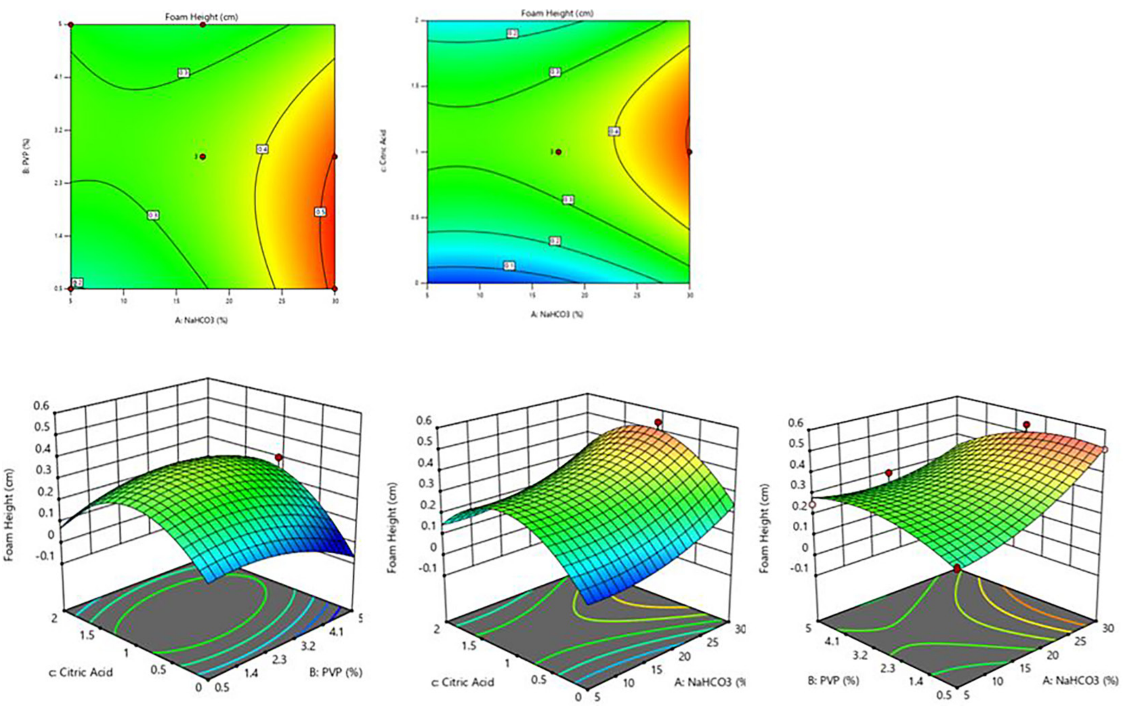

Figure 3. 2D and 3D response surface plots for the optimization of the effervescent granule formula of betel leaf and lemongrass leaf extract. Showing the effect of interactions between (a) $NaHCO_3$ and PVP concentrations; (b) NaHCO3 concentration and the citric acid/tartaric acid ratio; (c) PVP concentration and the citric acid/tartaric acid ratio on the height of the effervescent foam (cm)

with formulation composition. The highest foam (0.5400 cm in F1) was achieved in a formulation that balanced a moderate amount of acid and base with minimal binder. Foam formation is driven by CO_2 generation, which is enhanced under optimal stoichiometric conditions between the acid and base. However, formulations such as F9 and F7 produced minimal foam despite rapid disintegration, likely due to insufficient acid or binder to stabilize the generated gas. This finding underscores the complexity of designing effervescent formulations where both kinetics and matrix architecture must be balanced (Tadros, 2010).

Interestingly, the predicted values for both responses closely aligned with the actual results. This close match supports the statistical robustness of the Box-Behnken design model used in this study. The high degree of predictive accuracy (as also reflected in regression models with $R^2 > 0.98$ in earlier analysis) confirms that the experimental design was effective in capturing the nonlinear interactions among formulation components.

The results also offer practical implications for hospital-based applications. Effervescent tablets with disintegration times below 30 seconds and foam heights above 0.3 cm (e.g., F1, F4, and F5) can provide sufficient antimicrobial dispersion on contact surfaces, offering a safer, faster, and environmentally friendlier alternative to traditional chlorine-based disinfectants. Compared to chlorine, which may leave harmful residues such as trihalomethanes and dioxins(Damiano et al., 2023), this herbal-based approach supports WHO's agenda for safer healthcare waste management (Prüss et al., 2013).

A notable exception is the high foam height of F1 despite its relatively fast disintegration. While this combination is desirable, it is somewhat unexpected because faster reactions typically lead to transient foam that dissipates quickly. This anomaly could be influenced by microstructural tablet features such as porosity and granule uniformity, which were not quantitatively evaluated in this study. Future studies should consider characterizing tablet internal structures using imaging techniques such as scanning electron microscopy (SEM) to clarify such behaviors.

The results demonstrate the feasibility of using a statistical design approach to optimize the disintegration and foaming behavior of herbal effervescent disinfectant tablets. The formulations show promise as practical, sustainable alternatives to chemical disinfectants in medical settings, especially in low-resource environments where safety and environmental impact are of critical concern.

Optimization results of the formulation using Box-Behnken design

Flowability, as indicated by the angle of repose and Hausner ratio, was acceptable in nearly all formulations. Most angles were below 35°, and Hausner ratios were under 1.25, except for F2 and F11, which slightly exceeded recommended limits. According to USP guidelines and pharmaceutical engineering literature, values below 30–35° for angle of repose and < 1.25 for Hausner ratio are typical indicators of good flow (Augsburger and Hoag, 2008; Aulton and Taylor, 2013). The strong performance in these parameters suggests that the chosen granulation method, likely aided by Avicel PH101 and PVP, produced mechanically stable and free-flowing granules.

Notably, F8 stood out with the lowest angle of repose (24.77°), the best compressibility index (1.082%), and the most favorable Hausner ratio (1.011), suggesting it had the most efficient powder flow and packing characteristics. This could be attributed to optimal binder concentration and granule drying, resulting in minimal interparticle friction and consistent granule density. Formulations like F4 and F5, with high flow rates of 7.111 g/s, also suggest smooth processing potential during tablet compression without hopper clogging or weight variation.

Compressibility data provide additional validation of granule suitability. Most formulations were below the critical 16% threshold, which is associated with good compaction behavior and minimal risk of lamination or capping during tablet formation (Lachman et al., 2008). However, F2 and F11 exceeded 20%, potentially indicating higher void volumes or inconsistencies in granule morphology. These deviations may be due to suboptimal ratios of acid and base or excessive binder use, which warrants reformulation if these batches were to be scaled up.

The IQCS values confirmed the granule size distribution was generally narrow and uniform, with the lowest skewness observed in F7 (0.014). This contributes to predictable flow and consistent tablet weight. Formulations like F12, with higher IQCS values (0.572), may suffer from wider granule size ranges, increasing variability in tablet uniformity – an issue commonly reported in powder technology when wet granulation drying is inconsistent (Julianti et al., 2024; Singh et al., 2020).

Collectively, these findings confirm that most of the formulations met acceptable pharmacotechnical criteria for industrial-scale tableting. Only a few, such as F2 and F11, would require modification for improved compressibility and flow, perhaps by adjusting moisture content, sieving steps, or binder levels. Compared to prior studies on natural product-based effervescent tablets, the results of this work demonstrate superior granule flowability and packing behavior (Nayaka et al., 2021; Syahidah et al., 2017), thus reinforcing the feasibility of herbal disinfectant tablets for commercial or institutional use.

Effect of formulation variables on effervescence time

This study aimed to develop and optimize a herbal-based effervescent disinfectant tablet using *Piper betle* and *Cymbopogon citratus* extracts as active antimicrobial agents, with the intent of providing an effective, eco-friendly alternative to chlorine in the decontamination of recyclable healthcare waste. The optimization process, conducted using response surface methodology (RSM), specifically examined how varying concentrations of sodium bicarbonate ($NaHCO_3$), polyvinylpyrrolidone (PVP), and citric acid influenced two critical functional parameters: effervescence time and foam height. The results not only address the primary research question but also reveal novel insights into formulation behavior that have practical implications for pharmaceutical and environmental applications.

The findings indicate that sodium bicarbonate played a pivotal role in determining effervescence time. As shown in the contour and surface plots in Figure 2, increasing the concentration of $NaHCO_3$ significantly reduced effervescence time, confirming its function as the primary effervescent agent in the formulation. The shortest disintegration time (2.68 seconds) was recorded in the formulation with the highest $NaHCO_3$ concentration and no citric acid, which aligns with the expected rapid release of CO_2 from alkaline–acid reactions under optimized stoichiometric conditions. Conversely, higher levels of citric acid were associated with increased effervescence time, possibly due to acid saturation, which may slow the overall dissolution rate by altering matrix porosity or pH microenvironment (Patel and Siddaiah, 2018). The ANOVA results further support this observation, showing that both the linear and quadratic terms of citric acid concentration were statistically significant ($p < 0.01$).

The effect of PVP, a commonly used binder, also merits attention. Although not as influential as $NaHCO_3$ or citric acid, increased PVP concentrations appeared to slightly prolong effervescence time, likely due to the increased mechanical integrity of the tablet matrix. Higher binder levels can result in denser granules, impeding water penetration and delaying tablet disintegration (Khairnar et al., 2024). This trend was evident in the surface plot correlating $NaHCO_3$ and PVP, where formulations with high binder levels exhibited slower disintegration.

Regarding foam height, a desirable trait for surface contact disinfection, the results revealed a more nuanced relationship. Foam height peaked in formulations that balanced moderate concentrations of $NaHCO_3$ and citric acid. However, excessive acid or binder levels reduced foam production, suggesting an interplay between reaction kinetics and physical entrapment of gas bubbles. The significance of $NaHCO_3$ and its quadratic terms in foam generation was confirmed via statistical analysis ($p < 0.05$), consistent with findings by Tadros (2010), who reported that foam performance in effervescent systems is often governed by gas evolution rates and surface tension dynamics (Tadros, 2010).

These results align well with existing literature emphasizing the antimicrobial potential of both *Piper betle* and *Cymbopogon citratus*. Betel leaf is rich in phenolic compounds such as chavicol and eugenol, which disrupt microbial cell membranes, while lemongrass essential oil contains citral and geraniol, known for their broad-spectrum bacteriostatic properties (Madhumita et al., 2020; Tran et al., 2023). Although these extracts have been studied independently in topical or solution forms, their integration into a solid dosage form for disinfecting healthcare waste is unprecedented. This work is one of the first to successfully formulate and optimize such a system, highlighting its novelty and potential impact.

Compared to conventional chlorine-based disinfection, the proposed effervescent tablets offer several advantages. Chlorine, although effective, generates toxic byproducts such as trihalomethanes and dioxins, which pose significant health and environmental risks (Clayton et al., 2021; Gallandat et al., 2021; Malik and Kumar, 2024; Shao et al., 2023). Regulatory agencies are increasingly recommending alternatives that meet safety and sustainability criteria. The herbal-based formulation developed in this study represents such an alternative, offering a biodegradable, non-toxic, and effective solution that aligns with WHO's recommendations for sustainable healthcare waste management (Chartier, 2014).

Despite the promising outcomes, some exceptions were observed. For instance, formulation F1 exhibited a relatively high foam height (0.5400 cm) despite moderate disintegration speed. This could be due to microstructural differences in granule porosity or compression force during tablet formation, which were not directly measured in this study. Such deviations highlight the importance of future work on tablet microarchitecture, possibly using scanning electron microscopy (SEM) or porosity analysis.

The optimized herbal effervescent tablets demonstrated favorable functional characteristics, with rapid disintegration times and sufficient foam formation for practical use. The integration of *Piper betle* and *Cymbopogon citratus* into a novel effervescent dosage form represents a significant innovation in both pharmaceutical formulation and environmental disinfection strategies. These findings contribute meaningfully to the growing body of research on green hospital initiatives and offer a scalable, low-toxicity alternative to chlorine for developing countries facing resource constraints.

Effect of formulation variables on effervescence time

The primary objective of this study was to investigate how varying concentrations of sodium bicarbonate, citric acid, and PVP binder influence the foam height of herbal-based effervescent disinfectant tablets. Foam height is a critical attribute, as it serves as a physical indicator of active surface engagement and uniform antimicrobial distribution during disinfection. The results of this study affirm that foam height can be modulated through a careful balance of effervescent and binder components, and the findings support the hypothesis that these parameters have statistically significant effects on formulation behavior.

The observed increase in foam height with rising $NaHCO_3$ concentration underscores the essential role of the base component in driving the effervescent reaction. This is consistent with the stoichiometric requirement of acid - base interactions to produce carbon dioxide gas, which generates visible foaming (Patel and Siddaiah, 2018). The formulation's capacity to form foam peaked when $NaHCO_3$ was balanced with moderate levels of PVP, suggesting that PVP may help stabilize foam temporarily by increasing viscosity, without inhibiting gas release. However, excess binder appeared to hinder foam formation, likely due to reduced water penetration and delayed disintegration - an effect previously described by Berardi et al. (2021) in their study of binder-polymer interactions in effervescent tablets (Berardi et al., 2021).

Interestingly, citric acid displayed a non-linear effect on foam height. While moderate concentrations promoted foam production, likely by providing the necessary protons for CO_2 evolution, excessive citric acid resulted in diminished foam height. This could be due to rapid reaction saturation or the formation of denser tablet matrices that resist disintegration. Such behavior aligns with findings by Markl and Zeitler (2017), who reported that over-acidification in effervescent systems can compromise foam dynamics by forming viscous microenvironments that trap gas and inhibit bubble expansion (Markl and Zeitler, 2017).

Another key insight from this study is that the interaction between PVP and citric acid also shaped foam outcomes. Formulations with optimal levels of both components achieved higher foam heights than those with extreme values. These interactions likely influence tablet porosity and internal capillary channels that facilitate disintegration and gas escape, supporting earlier hypotheses by Luo et al. (2021) on excipient synergy in dispersible tablet matrices (Luo et al., 2021).

The research goals of optimizing tablet foam height for disinfectant efficiency were largely met. Formulations exhibiting foam heights of $\geq$ 0.5 cm demonstrated consistent dispersibility and surface coverage, attributes essential for field-based medical waste disinfection. These results provide evidence that herbal effervescent disinfectants can be engineered to achieve practical performance standards comparable to commercial chemical agents, but without the associated environmental risks of chlorine derivatives (Fikri et al., 2021).

Nonetheless, one unexpected observation was that in some formulations, high foam heights occurred despite moderate acid levels. This contradicts traditional assumptions that more acid yields more reaction. One possible explanation is the role of formulation porosity and dissolution kinetics, which were not directly measured in this study. Future work should include microstructural analyses using imaging techniques to clarify these physical effects.

CONCLUSIONS

The study achieved the following conclusions:
1. Statistical optimization was successful using a Box-Behnken Design, yielding formulations with effervescence times as short as 2.68 seconds and foam heights as high as 0.5400 cm, both critical parameters for rapid and effective disinfection of medical waste surfaces.
2. $NaHCO_3$ was the most significant factor influencing disintegration time and foam generation, with its concentration inversely correlated with effervescence time and positively associated with foam volume. Citric acid and PVP also significantly contributed, particularly through quadratic and interaction effects, confirming the nonlinear behavior of the formulation system.
3. Granule evaluation revealed excellent flow and compressibility across most formulations, especially F8 and F4, indicating the practicality of scale-up and mass production using conventional pharmaceutical equipment.
4. Model validation showed high predictive reliability, with R^2 values of 0.9999 for effervescence time and 0.9857 for foam height, affirming the strength of the experimental design and regression models used.
5. From a public health and policy perspective, the proposed herbal tablets eliminate the risk of toxic disinfection byproducts, such as trihalomethanes and dioxins commonly associated with chlorine, thereby aligning with WHO's guidelines on sustainable healthcare waste management and occupational safety.
6. Although some variations in foam behavior were observed, likely due to unmeasured microstructural factors, the results indicate that plant-based disinfectants can achieve reliable performance with lower environmental and health burdens.

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