Mini Review
Sciences of Pharmacy

Recent Advances in Herbal Effervescent Formulations: Challenges and Opportunities

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[The author informations are in the declarations section. This article is published by ETFLIN in Sciences of Pharmacy, Volume 4, Issue 1, 2025, Page 40-50. https://doi.org/10.58920/sciphar0401311]

Received: 09 March 2025
Revised: 21 March 2025
Accepted: 24 March 2025
Published: 28 March 2025

Editor: Adeleye Ademola Olutayo

Keywords: Nutraceutical effervescent, Increasing herbal solubility, Effervescent moisture problem, Tablet palatability.

Abstract: The growing demand for convenient and palatable delivery systems for herbal medicines has significantly increased the interest in herbal effervescent formulations as an alternative to conventional dosage forms. Effervescent dosage forms offer rapid dissolution and the potential for enhanced absorption while masking unpleasant tastes often associated with herbal extracts. However, the successful formulation of herbal effervescent tablets presents unique challenges, including managing the complex physicochemical properties of herbal extracts, ensuring their stability and antioxidant activity within the effervescent matrix, and optimizing taste without compromising efficacy. Various studies have explored the formulation of effervescent tablets from diverse herbal sources like Kelakai root, *Kaempferia galanga*, and red ginger, employing different formulation methods, excipients like binders, lubricants, and sweeteners, and optimization techniques to achieve desired physical attributes and dissolution profiles. Given the expanding research in this area and the inherent complexities of herbal effervescent formulation, a comprehensive review is crucial to synthesize current knowledge, address existing challenges, and provide a roadmap for future research aimed at designing more effective and patient-friendly herbal effervescent products with improved stability, palatability, and bioavailability.

Introduction

The increasing interest in health and well-being has led to a greater focus on nutraceuticals and herbal medicines (1). However, incorporating herbal extracts into conventional oral dosage forms often presents challenges such as unpleasant taste, odor, and potential for incomplete absorption (2, 3). To overcome these limitations and enhance patient compliance, the effervescent tablet has emerged as a promising alternative (4-6). Effervescent tablets offer several advantages, including rapid dissolution, the formation of a palatable and refreshing solution, and potentially improved drug absorption due to the release of carbon dioxide (7). These tablets are formulated with a mixture of acids (such as citric acid and tartaric acid) and bases (like sodium bicarbonate) that react in the presence of water to produce carbon dioxide gas, leading to rapid disintegration and dissolution of the active ingredients (8).

Effervescent formulations offer a convenient and appealing method for delivering herbal extracts. However, several formulation challenges must be addressed. The complex chemical composition, hygroscopic nature, and interactions of herbal extracts with excipients can create difficulties (9, 10). Many extracts, such as *Moringa oleifera* and Kelakai root, contain bioactive compounds that require taste masking and stability improvements (2, 4). Current solutions involve sweeteners and flavorings, but achieving full taste masking without compromising stability or efficacy demands precise excipient selection (4, 5). Additionally, maintaining optimal tablet properties, including hardness, friability, and effervescence time, while preserving the stability and antioxidant activity of herbal components requires understanding interactions between extracts, gas-generating agents, and excipients (4-6).

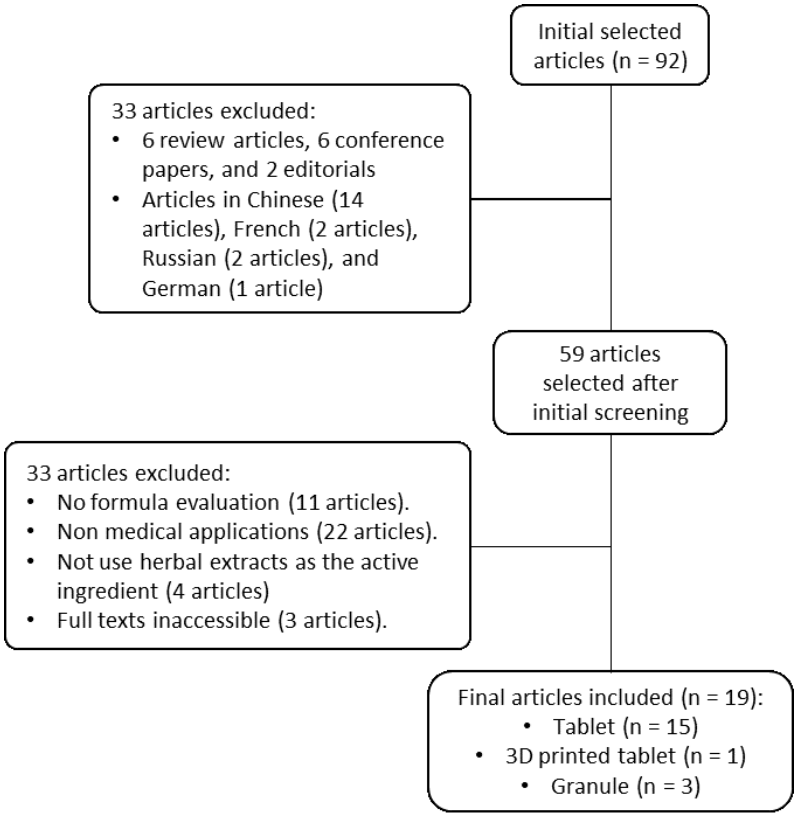

Figure 1. Flowchart of the methodology.

Despite the growing body of research on herbal effervescent formulations, a comprehensive review consolidating the key formulation considerations, challenges, and optimization strategies is currently lacking. Understanding the impact of different gas-generating agents, binders, sweeteners, and other excipients on various herbal effervescent tablets' physicochemical properties, stability, and efficacy is crucial for developing robust and patient-friendly products (9, 11). Therefore, a review article synthesizes existing knowledge and highlights the critical factors in herbal effervescent formulation design, which is essential to guide future research and facilitate the development of improved herbal effervescent products with enhanced stability, palatability, and bioavailability. This review would serve as a valuable resource for researchers and formulators seeking to harness the benefits of the effervescent dosage form for delivering the therapeutic potential of herbal medicines.

Methodology

This review paper was conducted through a systematic literature search using the Scopus database. The search strategy employed the following keywords: TITLE-ABS-KEY ("effervescent" OR "effervescence") AND TITLE-ABS-KEY (tablet) AND TITLE-ABS-KEY ("extract"). This search yielded a total of 92 articles. Only research articles were considered to ensure relevance to the topic, excluding 6 review articles, 6 conference papers, and 2 editorials. Additionally, articles in Chinese (14 articles), French (2 articles), Russian (2 articles), and German (1 article) were excluded due to language constraints, leaving a total of 59 research articles for further evaluation. Articles that lacked analysis or did not focus on the characteristics of effervescent formulations were excluded (11 articles). Those not intended for medical applications were also removed (22 articles). Furthermore, 3 articles were excluded as they did not use herbal extracts as the active ingredient, and 2 more were eliminated as their full texts were inaccessible. Following the selection process, the remaining research articles were thoroughly analyzed to assess their contribution to the field of effervescent formulations incorporating herbal extracts. The review focuses on the formulation, characteristics, stability, and potential applications of herbal effervescent products in medical and pharmaceutical contexts. The flowchart of the methodology can be seen in **Figure 1**.

What is Herbal?

Herbal medicine, also known as phytotherapy or herbalism, uses plants for medicinal purposes (12). This practice dates back to the Paleolithic age, with written evidence from the Sumerians over 5,000 years ago (13). Herbals are collections of plant descriptions for medical use, primarily serving as descriptive drug lists or pharmacopeias. Unlike scientific botanical treatises, herbals focus on practical applications rather

than theoretical foundations (14). Herbal medicines are distinct from plant-derived pharmaceutical drugs as they use chemically complex plant extracts or dried herbs rather than isolated compounds. These remedies can be administered in various forms, including tablets, capsules, powders, extracts, and fresh or dried plants (15).

Effervescent and Its Benefits in Herbal Formulation

Effervescent is a pharmaceutical or supplement formulation that undergoes a chemical reaction when dissolved in water, producing carbon dioxide (CO_2), enhancing the active ingredient's solubility and bioavailability (16). This formulation comes in several main forms.

Effervescent tablets are the most common type, developed by compressing a mixture of active ingredients with a weak acid and a carbonate or bicarbonate salt, which react upon contact with water. Effervescent granules have similar characteristics but come in coarse or fine granule form, often packaged in sachets for easier use and better moisture stability than tablets. Effervescent powders, with smaller particle sizes than granules, serve as an alternative to tablets, allowing for faster dispersion in water, and are often used in herbal-based nutritional supplements. Though less common, effervescent capsules contain reactive powder that must be removed from the capsule before dissolving and are typically used for active ingredients that are unstable in tablet or granule form. Lastly, effervescent liquids contain active components in a solution that produces a fizzy effect when mixed with water, primarily used in specialized liquid pharmaceutical formulations. These different formulation types provide flexibility in drug design, optimizing the stability and efficacy of active ingredients according to their pharmacokinetic and pharmacodynamic needs.

Effervescent formulations are becoming increasingly popular due to their ease of formulation. Effervescents can be produced in powder, granule, and tablet forms. Their manufacturing process is similar to regular tablets, using dry granulation, wet granulation, or direct compression. Compared to other dosage forms like coated tablets or suspensions, they do not require coating equipment, dispersion systems, or expensive emulsification processes.

One of the primary benefits of effervescent formulations is their ability to enhance the bioavailability of herbal compounds (17). The effervescent reaction significantly improves the solubility of active ingredients in water, facilitating their absorption in the gastrointestinal tract (18). This is particularly advantageous for compounds with low water solubility, such as flavonoids and certain polyphenols, which may exhibit limited bioavailability in tablet or capsule form. By dissolving these compounds into a liquid solution, the body can absorb them more efficiently, improving therapeutic effects.

Effervescent formulations offer a practical and user-friendly alternative for individuals who experience difficulty swallowing solid dosage forms (19). The liquid nature of effervescent solutions provides an easier method of administration, particularly for elderly individuals, children, or patients with dysphagia (20). Additionally, natural sweeteners and flavoring agents can mask herbal extracts' often bitter or astringent taste, further enhancing patient compliance and acceptability (21).

Critical Aspects in Herbal Effervescent Formulation

There are several crucial aspects to consider when formulating herbal ingredients into effervescent preparations. This section does not discuss common factors, such as the effect of acid-to-base ratio on disintegration time, as these are well established. Instead, this section reviews research reports on formulation aspects that may influence the physicochemical properties of effervescent products and their acceptability by patients, particularly in specific cases. Refer to **Table 1** for a summary of herbal effervescent formulations.

Table 1. Various herbal formulations in effervescent dosage forms.

Active ingredient	Dosage form	Application	Acid	Alkaline	Binder	Granulation	Ref
Josapine pineapple powder	Tablet	Vitamin	Citric acid	Sodium bicarbonate	-	Direct compression	(22)
Hibiscus sabdariffa L. water extract	Tablet	Anti-dental-microbe	Citric acid	Sodium bicarbonate	-	Direct compression	(7)
Red ginger crude extract	Granule	Antioxidant	Citric acid and tartaric acid	Sodium bicarbonate	Povidone	Wet granulation	(5)

Phyllanthus niruri, *Strobilanthes crispus*, and *Orthosiphon aristatus* water extract	Tablet	Antioxidant	Citric acid and malic acid	Sodium bicarbonate and sodium carbonate	-	Direct compression	(6)
Elderberry extract powder and vine tea powder	Tablet	Antioxidant	Citric acid	Sodium bicarbonate	Povidone	Wet granulation	(9)
Aloe vera gel powder	Tablet	Cytoprotective in peptic ulcer	Citric acid	Sodium bicarbonate	Avicel PH 102	Direct compression	(23)
Grape seed extract	Tablet	Antioxidant	Citric acid and tartaric acid	Sodium bicarbonate	Povidone	Wet granulation	(1)
Robusta coffee ethanol extract	Granules	Psychostimulant	Citric acid and tartaric acid	Sodium bicarbonate	Avicel PH 102	Wet granulation	(24)
Moringa oleifera ethanol extract	Tablet	Antianemia	Citric acid and tartaric acid	Sodium bicarbonate	PEG 600	Wet granulation	(2)
Stenochlaena palustri root extract	Tablet	Antioxidant	Citric acid and tartaric acid	Sodium bicarbonate	Povidone	Wet granulation	(4)
Bryophyllum pinnatum leaves extract	Tablet	Antiurolithiatic	Citric acid and tartaric acid	Sodium bicarbonate	Povidone	Wet granulation	(11)
Azadirachta indica and Curcumin powder	Tablet	Anti-dental-microbe	Citric acid and tartaric acid	Sodium bicarbonate	-	-	(25)
Freeze-dried *Chromolaena odorata* and *Glochidion arborescens* leaves juice	Granules	Antioxidant	Citric acid	Sodium bicarbonate	Povidone	Wet granulation	(26)
Monoammonium glycyrrhizin and aloe vera gel powder	Tablet	Cytoprotective in peptic ulcer	Citric acid	Sodium bicarbonate	Avicel PH 102	Wet granulation	(3)
Brassica spp. (seeds), *Blumea balsamifera* (L.) DC. (leaves), *Terminalia chebula* Retz. (fruit pulp), *Piper nigrum* L. (fruits), *Citrus hystrix* DC. (fruit peels), and *Coriandrum sativum* L. (fruits) powder	Tablet	Expectorant	Anhydrous citric acid and tartaric acid	Sodium bicarbonate	Microcrystalline cellulose	Direct compression	(27)
Pedalium murex and *Tribulus terrestris* fruit extracts	Tablet	Demulcent and diuretic	-	Sodium bicarbonate	Microcrystalline cellulose	Direct compression	(28)

Phyllanthus emblica and licorice extract powder	3D-printed tablet	Cryoprotectant	Tartaric acid	Sodium bicarbonate	Povidone	3D-printing	(10)
Roselle petals extract nanocapsule	Tablet	Antioxidant	Citric acid and malic acid	Sodium bicarbonate	PEG	-	(29)
Kaempferia galanga	Tablet	Antioxidant	Citric acid and tartaric acid	Sodium bicarbonate	Povidone	Dry granulation	(8)

Palatability and Taste Masking

Herbal extracts often contain bitter, astringent, or unpleasant taste (2). If the effervescent solution doesn't taste acceptable, patients are less likely to use it, impacting compliance and the effectiveness of the treatment (29). The effervescent action can contribute to a more palatable experience by releasing flavors and creating a fizzy sensation, but it's often not enough to completely mask strong undesirable tastes (1).

The type and concentration of sweeteners and flavoring agents must be carefully selected and optimized. Forestryana D. et al. (2021) found that at a concentration of 15.5% used in all three formulations, aspartame could not completely mask the bitter taste of Kelakai root extract in the resulting effervescent tablets (4). However, another study reported that 3% aspartame was sufficient to mask the unpleasant taste of *Coffea canephora* ethanolic extract (24), highlighting the need for optimization in determining the appropriate sweetener concentration. Additionally, another study found that lemon and strawberry flavors were insufficient to mask the bitterness of *Moringa oleifera* extract, suggesting the necessity of more potent masking agents (2). On the other hand, using stevia, a natural sweetener, significantly influences the sweetness and, consequently, the overall acceptability of the effervescent tablet (9, 22). For active ingredients with a more tolerable taste, such as ginger, sucrose is sufficient to improve the taste of the effervescent formulation and can also serve as a filler (5).

Effervescent inducers (acid and base components) can also influence taste. For example, one study reported that basic ingredients derived from sodium bicarbonate were used to mask the astringent flavor of *Kaempferia galanga* extract (8). However, it is important to note that these components also affect the pH of the formulation and generate gas, which, if used excessively, may cause nausea (9, 11). In addition to acid and base components, incorporating other extracts that enhance the taste of the effervescent formulation is highly recommended, such as fruit juices or tea aromas (9). Furthermore, the choice of flavoring agents should be aligned with the color of the extract solution (1). For instance, purple-colored extracts are best paired with grape flavoring, while yellow or orange extracts can be complemented with citrus or pineapple flavors.

Stability of Herbal Extract

Herbal extracts contain complex bioactive compounds susceptible to degradation over time due to factors like moisture, heat, light, and interactions with other excipients (29). Loss of active compounds reduces the therapeutic efficacy of the product. Formulating herbal extracts into a dry, effervescent tablet form can help improve their stability compared to liquid extracts or other solid dosage forms by reducing water activity. However, some components, like acids used in the effervescent base, can be hygroscopic and attract moisture, potentially leading to the degradation of moisture-sensitive herbal constituents (4, 8, 10, 27). Techniques like using cryoprotectants during freeze-drying of the extract, as mentioned in the Xianganfang study, can help make the powder less hygroscopic and protect the drug (10).

Adding maltodextrin, Arabic gum, or other matrix-forming polymers during extract drying can protect active compounds from degradation (22, 29). In some cases, nanoencapsulation of the herbal extract may be necessary to safeguard the active compounds (29). However, it is important to consider the solubility of the major compounds concerning the polymer base used, as this can affect adsorption efficiency in the system. For instance, maltodextrin is more water-soluble than Arabic gum. However, Arabic gum has been reported to bind more phenolic compounds, such as anthocyanins, thereby enhancing antioxidant effects (29).

Aerosil can act as a filler and adsorbent. Aerosil's role as an adsorbent is significant as it can absorb moisture, especially from the Kelakai root extract. However, the study also suggests that aerosil might have affected the tablet dissolution time by absorbing moisture (4).

Regarding the emerging method of 3D printing effervescent tablets, the type and concentration of cryoprotectants used during freeze-drying of an extract influence the properties of the resulting powder, including formability, rehydration time, hygroscopicity, and viscosity of the printing paste. A study reported

that using 50% (w/w) mannitol was optimal, providing good formability, appearance, rehydration, hygroscopicity, and viscosity for the paste. However, higher concentrations, such as 150%, produced excessively viscous pastes (10).

Gas Generating Agents

The reaction between an acid source (like citric acid, tartaric acid, or malic acid) and an alkaline source (like sodium bicarbonate or sodium carbonate) is what produces carbon dioxide gas, resulting in the effervescence (4, 8, 27). The choice and ratio of these agents directly influence the speed and intensity of the effervescent reaction (22), the taste of the resulting solution (1), and its pH (8).

Using a combination of acids, such as citric and tartaric acid, is often preferred over using a single acid to achieve a balanced reaction and avoid issues like excessive stickiness (with only citric acid) or weak granules (with only tartaric acid) (1, 24). The ratio of acid to base needs to be carefully optimized to ensure complete effervescence without leaving excessive unreacted acid or base, which could affect taste and pH. The Kelakai root study highlights the varying ratios of citric acid, tartaric acid, and sodium bicarbonate in different formulations. It was found that higher amounts of citric and tartaric acid increased moisture content in the granules and enhanced cohesive forces, thereby increasing the angle of repose of the granules (4). These interparticle cohesive forces were also reported to improve tablet hardness and resistance to shock and friction (8).

Beyond influencing the effervescent properties, the type and amount of acidic agents significantly impacted the phytochemical content (total phenolic and total flavonoid content) and antioxidant activities (DPPH radical scavenging activity and ferric-reducing antioxidant power). A high content of acidic agents generally resulted in increased phytochemical content and antioxidant activity (6). The increase in phytochemical content and antioxidant activity with higher amounts of acidic agents can be attributed to several factors. Acidic conditions enhance the solubility and extraction efficiency of phenolic compounds and flavonoids by breaking down cell walls and releasing bound phytochemicals into the solution (30). Additionally, many phenolic compounds are more stable in acidic environments, which helps prevent their degradation and preserves their antioxidant properties (31). Acidic conditions also improve the redox potential of phenolic compounds, enhancing their ability to donate electrons and scavenge free radicals, thereby increasing antioxidant activity in assays such as DPPH radical scavenging and ferric-reducing antioxidant power (FRAP) (32). Moreover, some polyphenols exist in bound or glycosylated forms, which are less bioavailable or active, and acid hydrolysis can break these bonds (33), releasing more potent antioxidant compounds. Furthermore, certain acidic agents, such as citric acid and ascorbic acid, have intrinsic antioxidant properties that contribute to the overall antioxidant capacity.

On the other hand, combining floating tablet technology with the effervescent effect to prolong drug contact time in the stomach can be achieved solely using alkaline agents (sodium bicarbonate) without the need for acidic components. The generation of CO_2 gas from the reaction between sodium bicarbonate and the acidic dissolution medium (0.1 N HCl, gastric fluid) reduces the tablet's density, allowing it to float (28). This suggests gastric acid can induce effervescence as the acidic phase, thereby avoiding the potential negative effects of incorporating acidic agents during formulation.

Binder

As an effervescent dosage form, selecting a binder is crucial, as effervescent tablets are highly soluble, fragile, and prone to moisture absorption due to their hygroscopic nature. The binder must enhance compressibility and maintain tablet integrity without causing excessive stickiness or reducing granule flowability.

A study mentions that PVP as a binder can increase the solubility of drugs that are difficult to dissolve from solid dosage forms. Furthermore, the results indicated that the concentration of PVP contributed to the larger size and more homogeneous shape of the granules, which led to uniform tablet weight across the different formulations. The concentration of the binder can also affect the hardness of the tablet, with a greater concentration potentially leading to harder tablets (4). It is important to note that gummy-textured extracts may also affect tablet hardness, requiring careful consideration of binder selection (11).

As previously discussed, applying the effervescent effect to floating tablets is highly beneficial for prolonging drug contact time in the stomach. In this case, the binder's matrix capacity and swelling ability play a critical role, as they must effectively trap the gas generated by the effervescent reaction to optimize the tablet's buoyancy. For example, Ranade A. N. et al. (2014) reported that the grade and amount of HPMC significantly impact the gelling properties of the tablet upon contact with gastric fluids (3). Higher viscosity grades (K-series) led to more extensive gelling and longer floating times but also slower drug release. Conversely, a lower viscosity grade like HPMC E5, when used in an optimized formulation (OF2), provided a balance between floating properties and drug release. The polymer matrix is crucial for trapping the carbon dioxide generated by the effervescent reaction, thus

enabling and sustaining the floating of the tablet. Insufficient polymer concentration or an inappropriate type can lead to rapid gas escape or tablet disintegration (3, 23). A source also suggests that rapid erosion occurs instead of floating if the sodium bicarbonate concentration is too high relative to the polymer concentration (23).

Formulation Methods

The method used to prepare the effervescent granules or tablets (e.g., wet granulation, dry granulation, direct compression, 3D printing) can significantly impact the stability, flowability, compressibility, and ultimately the quality of the final product. The method should be chosen based on the properties of the herbal extract and other excipients, and it should aim to minimize any premature reaction between the acid and base components during manufacturing.

Wet granulation involves using a liquid binder, potentially triggering the effervescent reaction if the acid and base components are not kept separate during the initial stages. Additionally, thoroughly mixing all ingredients before granulation is crucial, affecting drug dose distribution (11).

Dry granulation eliminates the need for liquids but requires good flowability and compressibility of the dry powder mix. Direct compression is the simplest method but may not be suitable for all formulations, especially when herbal extracts or other ingredients have poor flow properties or compressibility. The quality of tablets produced via dry granulation and direct compression depends on the sieving stage. Particle size uniformity achieved through sieving influences the homogeneity of the tablet blend, drug content uniformity, and dissolution rate (1, 7, 28).

Emerging techniques such as 3D printing offer new possibilities but require specific considerations for the printing paste and drying process. Improper selection of acidic components has been reported to lead to poor viscosity and excessive moisture absorption during printing (10). Additionally, the distance between printing filaments (infill distance) significantly affects printed tablets' disintegration time and hardness. Smaller infill distances result in longer disintegration times and higher tablet hardness. An infill distance of 1.0 mm has been found to provide an optimal balance between disintegration speed and mechanical strength.

Pharmacokinetic Advantages of Effervescent Formulations

Effervescent drug delivery systems offer several potential benefits that can improve pharmacokinetics compared to conventional solid oral dosage forms. One key advantage lies in the efficient and easy setup of a solution containing an accurate dose, which is then more easily absorbed by the body (4). This is because the active substance is already in solution form, bypassing the initial disintegration and dissolution steps required for solid tablets or capsules.

The effervescent action itself plays a crucial role in enhancing dissolution. When an effervescent tablet comes into contact with water, a chemical reaction between the acidic and alkaline components (typically citric and/or tartaric acid and sodium bicarbonate) generates carbon dioxide gas. This effervescence dissolves the tablets and rapidly forms a clear solution (1, 8). The bubbling action can also contribute to mechanical cleaning and better active ingredient dispersion (7).

Furthermore, the resulting solution from effervescent tablets is distributed in the gastrointestinal tract in a large area, leading to quicker drug absorption into the blood and rapid onset of action (10). This is particularly advantageous when a fast therapeutic effect is desired. The enhanced solubility and dispersion can be especially beneficial for poorly soluble drugs in their conventional solid form. Wet granulation, a common method used to prepare effervescent tablets, can further increase the solubility of difficult drugs to dissolve (4). The hydrophilic nature of binders like polyvinylpyrrolidone (PVP) used in wet granulation facilitates water entrance into the tablet pores, accelerating the dissolving process and the effervescent reaction (8).

In some cases, effervescent technology is combined with other drug delivery principles to achieve specific pharmacokinetic profiles. For instance, the development of floating effervescent tablets aims to prolong the gastric retention time of the dosage form (3, 23, 28). This approach can be particularly useful for drugs primarily absorbed in the stomach, as it allows for a more sustained release and potentially increased bioavailability.

Beyond direct effects on dissolution and absorption, effervescent formulations can also indirectly improve pharmacokinetics by enhancing patient compliance (2). The fresh taste and ease of administration of effervescent solutions can make them more palatable and acceptable to consumers, encouraging adherence to the prescribed dosage regimen.

Critical Effervescent Characterizations

Effervescence Performance

Effervescence performance is a critical aspect of drug formulations influencing patient compliance and therapeutic efficacy. The reaction time and onset of effervescence determine how quickly the tablet or

granule begins dissolving upon contact with water. A well-optimized formulation ensures a prompt but controlled reaction, preventing premature CO_2 loss while ensuring a pleasant user experience. The dissolution rate is equally important, as it dictates how fast the active pharmaceutical ingredient (API) becomes bioavailable. Slow dissolution may lead to inconsistent dosing, while overly rapid dissolution can cause excessive foaming. Additionally, the CO_2 release profile must be monitored to ensure uniform gas evolution without excessive bubbling or incomplete reaction, as inefficient gas release can affect dissolution consistency and drug absorption.

pH Stability and Buffering Capacity

Effervescent formulations require precise pH control to maintain drug stability and optimize absorption. The final pH of the solution must be suitable for the API to prevent degradation and ensure bioavailability. Some drugs require an acidic environment for dissolution, while others need neutral or alkaline conditions to remain stable. Additionally, the buffering capacity of the formulation ensures that the pH does not fluctuate significantly upon dissolution. Maintaining a stable pH is particularly critical for acid-labile or ionizable drugs, as excessive changes may lead to precipitation, reduced solubility, or irritation upon ingestion. Proper formulation of buffering agents, such as citric acid and sodium bicarbonate, is essential to achieving this balance.

Wettability and Dispersion

The ability of an effervescent formulation to wet, disintegrate, and disperse in water is fundamental to its performance. Wettability influences how quickly the formulation interacts with water, affecting the speed of CO_2 generation and dissolution. Poor wettability may lead to floating tablets or granules, delaying dissolution. The disintegration mechanism must be optimized to ensure rapid and uniform formulation breakdown before complete dissolution occurs. This is especially crucial in formulations containing poorly water-soluble drugs, where incomplete dispersion may result in dose inconsistency. Uniformity of dispersion ensures that all active and excipient components dissolve homogeneously, preventing sedimentation or layering that could lead to improper dosing and patient dissatisfaction.

Carbonation Level and Sensory Properties

Carbonation plays a significant role in patient acceptability of effervescent formulations. The level of CO_2 generated directly influences mouthfeel, taste masking, and overall palatability. An optimal balance is needed, as excessive carbonation can lead to an overpowering sensation, while insufficient CO_2 release may result in a flat, unappealing taste. Taste and mouthfeel considerations include bitterness masking, using sweeteners, and the prevention of grittiness, which can negatively impact compliance. The foaming characteristics must also be controlled, as excessive foaming can cause difficulties in swallowing and lead to spillage or loss of dosage. Effervescent formulations should provide a refreshing and pleasant sensory experience while maintaining their intended therapeutic function.

Stability and Moisture Sensitivity

Effervescent formulations are highly sensitive to moisture, requiring robust stability considerations during production and packaging. Hygroscopicity is a major concern, as exposure to humidity can prematurely trigger the effervescent reaction, rendering the formulation ineffective. The use of moisture-resistant excipients and protective coatings can enhance stability. Packaging integrity is crucial, often necessitating airtight containers, foil blisters, or desiccants to prevent degradation. Furthermore, chemical stability post-dissolution must be evaluated, ensuring the drug remains effective for a reasonable duration after dissolving. Certain APIs may degrade rapidly in solution, necessitating immediate consumption after preparation to maintain therapeutic potency.

Gas Pressure Considerations

Effervescent formulations must account for gas pressure dynamics in packaging and upon dissolution. Internal pressure within sealed containers should be monitored to prevent unintended CO_2 buildup, which can lead to bursting or compromised product integrity. This is particularly relevant in high-humidity environments where residual moisture can initiate slow effervescence within sealed packaging. After dissolution, controlled CO_2 release in solution is necessary to avoid excessive gas buildup that may cause patients bloating, discomfort, or irritation. Managing gas pressure ensures patient safety while preserving the efficacy of the effervescent formulation.

Conclusion and Future Perspective

In conclusion, the development of herbal effervescent formulations holds significant promise for enhancing the delivery and patient acceptance of herbal medicines. The inherent advantages of effervescent tablets, such as rapid dissolution, potential for improved bioavailability, and palatable administration due to taste masking, make them particularly suitable for overcoming the limitations of traditional herbal dosage forms. Studies across the sources demonstrate the successful formulation of effervescent tablets and granules from a diverse range of herbal extracts, including Kelakai root, *Kaempferia galanga*, red ginger, green coffee bean, and elderberry vine, with

evaluations confirming acceptable physical properties and, in some cases, antioxidant activity.

However, the formulation of these products is not without challenges. Issues such as the complex physicochemical properties of herbal extracts, the difficulty in achieving effective taste and odor masking, potential interactions with excipients, and maintaining stability during manufacturing and storage require careful consideration. For instance, the bitter taste of tannins and phenolic compounds in plant extracts and the peculiar odor of some extracts can affect the final product's acceptability. Furthermore, ensuring that the required biological properties remain available after the effervescence reaction is crucial.

Looking towards the future, several key areas warrant further research and development. Advanced taste masking technologies tailored to herbal extracts' specific and often complex flavor profiles are crucial for enhancing patient compliance. Further investigation is needed into novel excipients that can improve the stability and bioavailability of herbal compounds within the effervescent matrix. The application of advanced manufacturing techniques, such as 3D printing, to create tablets with spatially separated acid and alkali components holds the potential for overcoming premature reactions and enabling more complex formulations. Additionally, more comprehensive in vivo and clinical studies are required to definitively evaluate the impact of effervescent formulations on the absorption and bioavailability of herbal constituents.

Optimization strategies employing Design of Experiments (DOE), as seen in studies optimizing formulations for *Kaempferia galanga* and Semha–Pinas extract, will continue to be essential for achieving desired product characteristics such as disintegration time, hardness and sensory attributes and for ensuring overall quality. These methods allow for systematically investigating formulation and process variables to identify optimal conditions.

Ultimately, continued innovation in formulation science and technology will further unlock the potential of herbal effervescent products as a valuable tool for delivering the therapeutic benefits of medicinal plants in a user-friendly and effective manner. Addressing the existing challenges and pursuing the identified future directions will contribute to developing high-quality, stable, and efficacious herbal effervescent products that meet consumer needs and preferences.

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Conflict of Interest

The authors declare no conflicting interest

Data Availability

The data is available upon request to the corresponding author.

Ethics Statement

Not applicable.

Funding Information

Not applicable.

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How to cite: Butar-Butar, M.E., Roni, A., Pahlevi, M.R., Zaelani, D., Sagita, N.D., Pratama, R.. Recent Advances in Herbal Effervescent Formulations: Challenges and Opportunities. Sciences of Pharmacy. 2025; 4(1):40-50