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Review Article

Emerging Trends in Effervescent Granules: From Conventional Formulation to Novel Drug Delivery System: A Review

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Abstract

Purpose: Widely used pharmaceutical dosages form are effervescent granules designed to improve bioavailability, drug dissolution and improve the patient compliance. This review provide a brief overview of modern formulation approaches and highlights the recent improvement in effervescent granules based delivery.

Effervescent granule a widely used pharmaceutical dosages form designed to improve bioavailability, drug dissolution and improve patient compliance. This review provide a comprehensive overview of conventional formulation approaches and highlights the recent advantages in effervescent granule based delivery system.

Methods: A comprehensive review of published literature, including research articles, review paper, and pharmaceutical text, was conducted. The collected data were analysed with respect of formulation principles, evaluation parameter, and recent technological advancement in effervescent systems.

Results: Effervescent granules work on the function of acid base reaction that generates carbon dioxide when it come in contact with the water result in rapid disintegration and enhanced drug dissolution. This system offers rapid onset of action, enhanced palatability and better patient compliance. Recent innovation include control-release formulation, gastro retentive floating system, nanotechnology-based approaches and 3D printing techniques, have substantially expanded pharmaceutical application and therapeutic prospect.

Conclusion: Effervescent granule portray a versatile and developing drug delivery system that bridges conventional formulation with modern pharmaceutical approach. Continuous advancement are expected to further improve their stability, efficacy and role in patient centric and personalized drug delivery system.

Keywords: Effervescent granules, drug delivery system, bioavailability, formulation, control release, emerging trends

Introduction:

Effervescent granule has emerged as an important pharmaceutical product as having an ability of enhancing drug dissolution, improved bioavailability and rapid onset of action. The formulation is designed to release the carbon dioxide when it comes in contact with the water trough an acid-base reaction, which result in fast disintegration and formulation of homogenous mixture[1]. This mechanism form effervescent granules suitable for paediatric (children) and geriatric (adults) as they have difficulty in swallowing conventional solid dosage forms[2].

Conventional oral dosage form like tablets and capsules, often experienced limitation as slow dissolution, poor bioavailability of poorly soluble drugs, decrease patient compliance. Effervescent system address these challenges by ensuring rapid drug release, improve palatability, therefore enhance therapeutic efficacy[3]. Traditional, effervescent granules are widely use in formulation of antacids, analgesic, and vitamins supplements due to their easy administration and patient compliance characteristics[4].

Recent years, significant advancement in pharmaceutical technology has grown the scope of effervescent granules beyond conventional application. The incorporation of novel drug delivery approaches, such as controlled drug delivery systems and gastro-retentive floating drug delivery systems, has enhanced drug stability, targeting and therapeutic performance[5]. In addition nanotechnology-based formulations and advanced manufacturing techniques such as 3d printing have further enhanced the design and function of effervescent dosages forms[6].

The increasing interest in patient focused drug delivery system and personalized medicine has also delivered increase relevance of effervescent granules in modern pharmaceutical. These dosage forms offer flexibility in

dosing, improved taste, and patient compliance a wide range of active pharmaceutical ingredients, including

herbal ad nutraceutical componds[7].

Therefore, the present review focused on the emerging trends in effervescent granules, highlighting formulation strategies, evaluation parameters, and recent technological advancement emphasizes the transition from conventional formulations to innovative drug delivery system in synchronous pharmaceutical development.

Principle of Effervesce:

Effervescent granules are based on acid-base reaction that occurs with the granules comes in contact with the water, causing rapid release of carbon dioxide gas. The effervescent result in disintegration of the dosage form and formulation of a clear solution, enhance the dissolution and absorption of active pharmaceutical ingredients[1,3].

Organic acids such as citric acid, tartaric acid react with alkaline carbonate (mostly sodium bicarbonate) to produce carbon di oxide, water and the corresponding salts. The release of carbon dioxide form internal pressure, leading to rapid breakdown of granules and increased surface area of the drug, therefore improve dissolution and bioavailability[2,4]

This mechanism help to improving palatability, reduced gastric irritation, and enhanced patient compliance, particularly in pediataric and geriatric popuations[8,9].

Citric acids + $NaHCO3 \Rightarrow$ CO_2 + H2O + Sodium Citrate

Effervescent based systems are widely used in pharmaceutical formulations as provide rapid onset of action and improved dissolution characteristics[10,11]

Composition of Effervesces Granules

Table 1: Composition of Effervescences Granules and their Functions

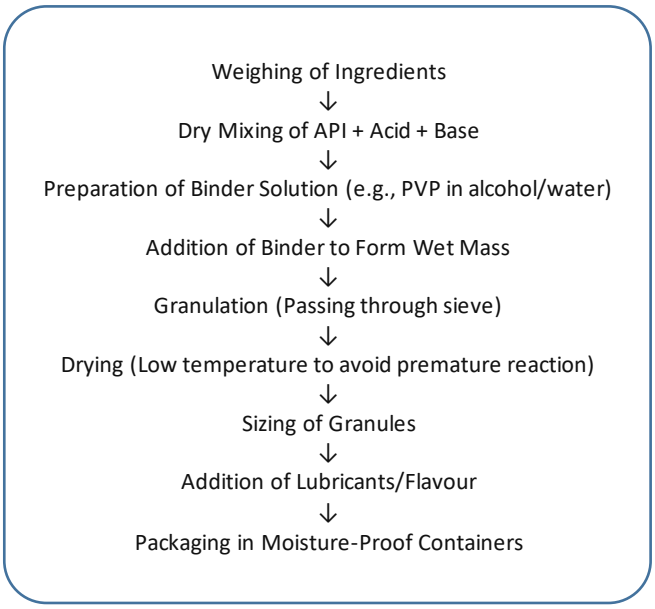
Category	Component	Example	Function	Ref
Acid Source	Organic acids	Citric acids, Tartaric acid, Fumaric acid	React with base to release CO_2, provide effervescence	1,3,8
Alkaline Source	Carbonates/ Bicarbonates	Sodium bicarbonate, Potassium bicarbonate	Generate CO_2 on reaction with acid	3,2,9
Active Pharmaceutical Ingredients (API)	Drug substances	Paracetamol, Ibuprofen, Antacids, Vitamins	Provide therapeutic effect	2,4,10
Sweeteners	Artificial/ Natural	Aspartame, Saccharin sodium, Sorbitol	Improve taste and patient compliance	8,9,11
Flavouring Agent	Natural/ Synthetic	Orange, Lemon, Mint	Mask the unpleasant taste of the drug	8,11
Binders	Polymer binders	PVP ,PEG	Provides granule cohesion and stability	9,10
Lubricants	Flow enhancer	Magnesium stearate, PEG derivatives	Improve flow properties during formulation	9,12
Stabilizers	Moisture protectant	Silica gel, Sodium benzoate	Prevent premature effervescence due to moisture	11,12

Method of Preparation:

Effervescent granules are prepared by various method depending on the nature of the drug and excipients. The most commonly method used are wet granulation, dry granulation, and fusion method. Selection of an appropriate method is very crucial to maintain stability and prevent premature effervescence due to moisture exposure[11,13].

1. Wet Granulation Method:

The wet granulation method, the active pharmaceutical ingredients, acid component, and alkaline component are first blended uniformly. A suitable binder solution like polyvinylpyrrolidine in alcohol or hydroalcoholic medium, then add cohesive wet mass. The wet mass is passed through a sieve to produce granules, and dried at controlled temperatures to prevent premature acid-base reaction. The dried granules are then sized and mixed with lubricants and flavouring agents before packaging[13,14].

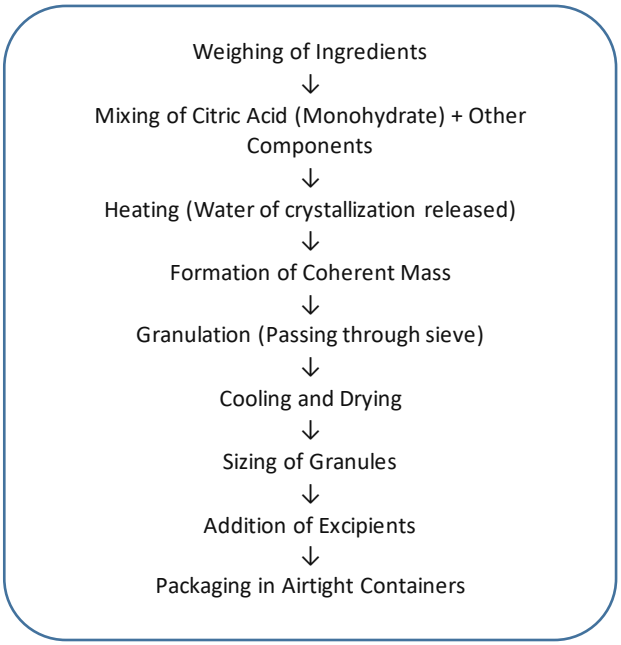


2. Dry Granulation Method:

For moisture-sensitive formulations dry granulation method is preferred. In this method, the powdered mixture of drug, acid, and base is compressed into slugs or compacted using roller compaction. The compacted material is then milled and sieved to obtain granules of desired size. For this method avoids the use of liquid binders, therefore reducing the risk of premature effervescences and improving stability[14,15].

3. Fusion method:

The fusion method employs the water of crystallisation present in certain components, such as citric acid monohydrate. The ingredients are mixed properly and heated gently until the water of crystalline is released, forming a consistent mass. This mass is then granulated, cooled, and dried. The method is simple and effective but requires proper temperature control to prevent degradation of thermolabile drugs[14,16].



Evaluation parameters:

Effervescent granules are evaluated using various physicochemical and performance-based parameters to ensure the quality, safety, and therapeutic efficacy. They are important to get good performance of granules like effervescence behaviour, drug content uniformity, flow property of the granules[11,1]

Table 2: The evaluation parameter of effervescent granules and their significance are summarized in this table.

Parameter	Method/Procedure	Purpose	Acceptance Criteria / Observation	Ref
Colour	Visual and sensory evaluation	Assess appearance and acceptability	Uniform color, pleasant odor and taste	13,17
pH	Measured using pH meter after dissolution in water	Ensure compatibility and stability	Typically between 5.5–7.0	18
Effervescence Time	Time required for complete dissolution in water	Evaluate performance and rapid action	Should be minimal (usually within 1–3 min)	13,15
Bulk Density	Mass/volume of untapped powder	Assess packing ability	Used for further flow calculations	11
Tapped Density	Volume after tapping	Evaluate compressibility	Compared with bulk density	11
Angle of Repose	Funnel method	Determine flow properties	<30° indicates good flow	12
Moisture Content	Loss on drying / Karl Fischer method	Ensure stability against premature reaction	Should be minimal	16
Drug Content Uniformity	UV or HPLC analysis	Ensure uniform distribution of drug	Within pharmacopeial limits (≈95–105%)	17
stability Studies	Accelerated and long-term studies	Assess shelf life and degradation	No significant change in properties	19

Advantages:

1. Rapid onset of action as administered in dissolved form[20].
2. Increased bioavailability due to improved solubility and dissolution[21,29].
3. Enhanced patient adherence, particularly in younger and older patients[22].
4. Precise dosing due to the pre-measured formulation[23].
5. Effective taste masking that increases patient compliance[24].
6. Reduce discomfort in the abdomen as a result of the buffering effect following dissolution[25].
7. Flexibility in combining medications, herbal extracts, and nutraceuticals[26].

Limitations:

1. Instability and rapid responses are caused by high moisture sensitivity[20,22].
2. Need special packaging, which raises the total cost by [23].
3. Chemical instability brought on by acid-base titrations over time[24].
4. This formulation's bulkiness is triggered by a significant excipient[25].
5. Limited compatibility with different medications, especially medicines which are unstable or sensitive to moisture[26].
6. Increased salt concentrations, which could cause hypertension[27].
7. Manufacturing complexity requires a controlled environment[28].

Application:

1. **Analgesic and antipyretic therapy:** effervescent drug compositions, such as paracetamol, possess a quick onset of action since they dissolve before being administered[20,21].
2. **Antacid formulation:** used to neutralise gastric acidity and improve dispersion in the stomach[22].
3. **Herbal and nutraceutical systems:** poly herbal effervesce granules, which improve therapeutic adherence, are a recent innovation[26].
4. **Special population consideration:** adapted according to patient needs, however safety must be put into consideration[27].
5. **Floating drug delivery systems:** effervescent granules are employed in gastro-retentive systems to improve drug absorption and prolong gastrointestinal residence time[28].

Modern Technology in Effervesce Granules:

Lately effervescence drug delivery system has experienced substantial transformation, unfolding rapid-dissolution dosage forms into highly designed and multifunctional delivery platforms. New research focus on overcoming the conventional limitations such as moisture sensitivity, bounded targeting capability, unrestrained drug delivery. At the same time, modern advancement are being consolidated to enhance the precision, stability, and therapeutic ability.

1. Effervescent Systems with Modified and Controlled Release: Effervescent granules have traditionally been developed to disperse rapidly and release medicines. However, new developments have made it possible to create effervescent formulations with controlled and extended release by adding hydrophilic and hydrophobic polymers such ethyl cellulose, HPMC, and Carbopol[1,30]. As dissolved, these polymers create a gel barrier that regulates drug dispersion and extends drug release. For medications that need a longer therapeutic duration and fewer doses, this strategy has particular beneficial. Modified effervescent formulations of cardiovascular and antidiabetic medicines, for instance, have shown controlled drug release profiles that last up to 24 hours, improving therapeutic efficacy and patient adherence[36,37].

2. Floating Effervescent Drug Delivery Systems (FDDS): The development of floating drugs delivery systems is a result of the effective incorporation of effervescent technology with gastro-retentive drug delivery systems. Carbon dioxide generated during effervescence in these formulations decreases the dosage form's density, allowing it to float atop stomach juices [6,32,5].

Several situations benefit significantly from this prolonged GI residence time:

a. Drugs with a restricted window of absorption
b. Drugs with unstable intestinal pH
c. Stomach-specific treatment

Floating effervescent systems significantly enhance drug uptake and therapeutic effectiveness, especially when used with antibiotics and anti-ulcer medications, based on recent studies.

For example, the effectiveness of this approach has been proved by the improved bioavailability and prolonged therapeutic activity of effervescent floating formulations of silymarin[32].

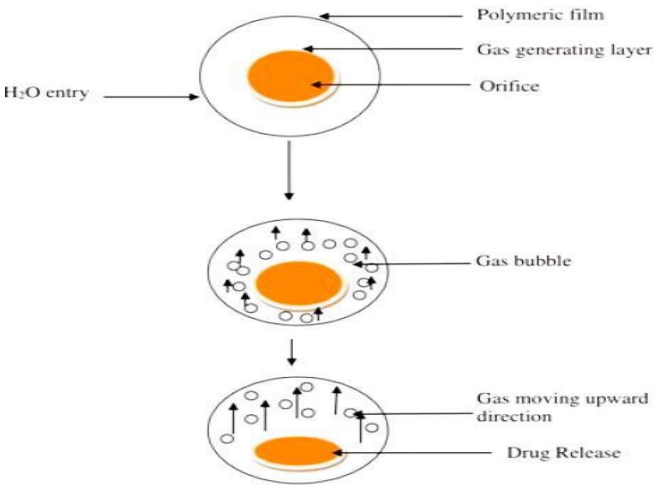


Figure 1: Show mechanism of an effervescent drug delivery system which generates gas.

3. Effervescent Systems Based on Nanotechnology: Innovative possibilities to improve the performance of effervescent formulations are being created possible by nanotechnology. It has been proved that introducing solid dispersions, nanoemulsions and nanoparticles to effervescent granules improves the solubility and rate of dissolution of medications that are poorly soluble in water[31]. Faster absorption and better pharmacokinetic profiles emerge from these nanoscale systems' enhanced surface area and higher wettability of drug particles[31]. Based on recent studies, nano-enabled effervescent formulations work especially effectively for Class II drugs in the Biopharmaceutics Classification System (BCS), which have good permeability but poor solubility[31,32].

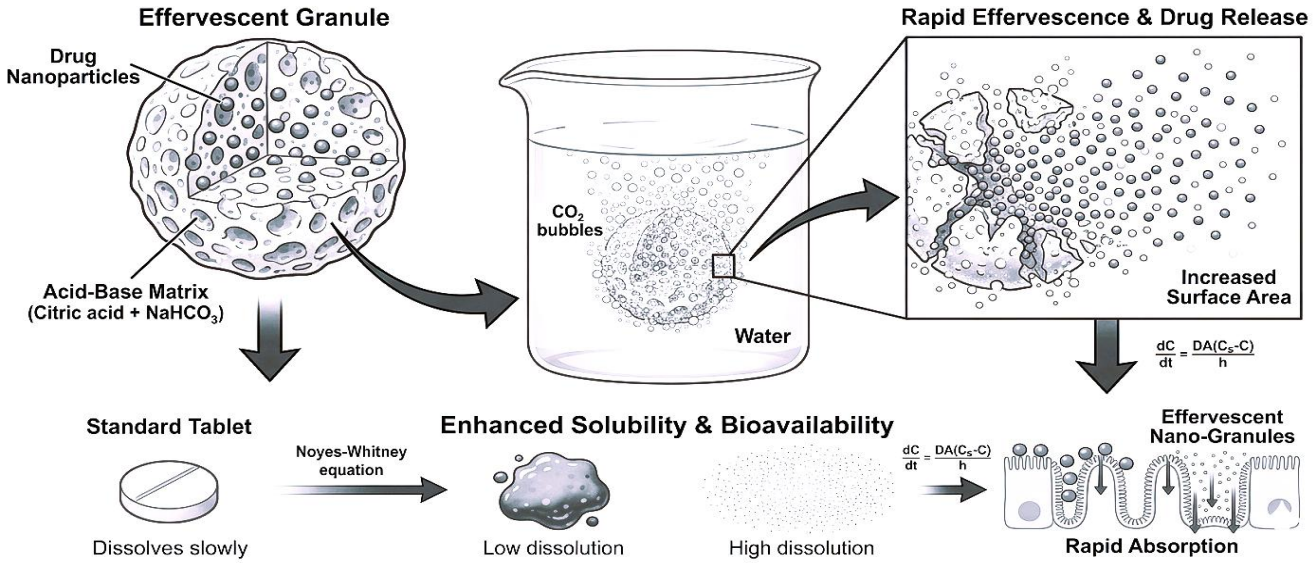


Figure 2: shows how effervescent granules, is compared to conventional tablets, provide a rapid effervescence, better dissolution, and higher medication bioavailability.

4. Integrating 3D Printing Technology: The utilisation of 3D printing technology, particularly semi-solid extrusion and fused deposition modelling techniques, is one of the most innovative advances in effervescent medicine delivery[6].

3D printing makes it possible to:

a. Precise administration of medication dosage and shape

b. Development of intricate interior structures

c. The development of customised healthcare

The homogeneous medication distribution, improved porosity, and controlled disintegration behaviour of 3D-printed effervescent tablets make them ideal for personalised therapy[32]. This approach is an acceptable approach for pharmaceutical production in the future because it minimises manufacturing stages and wasted materials[6].

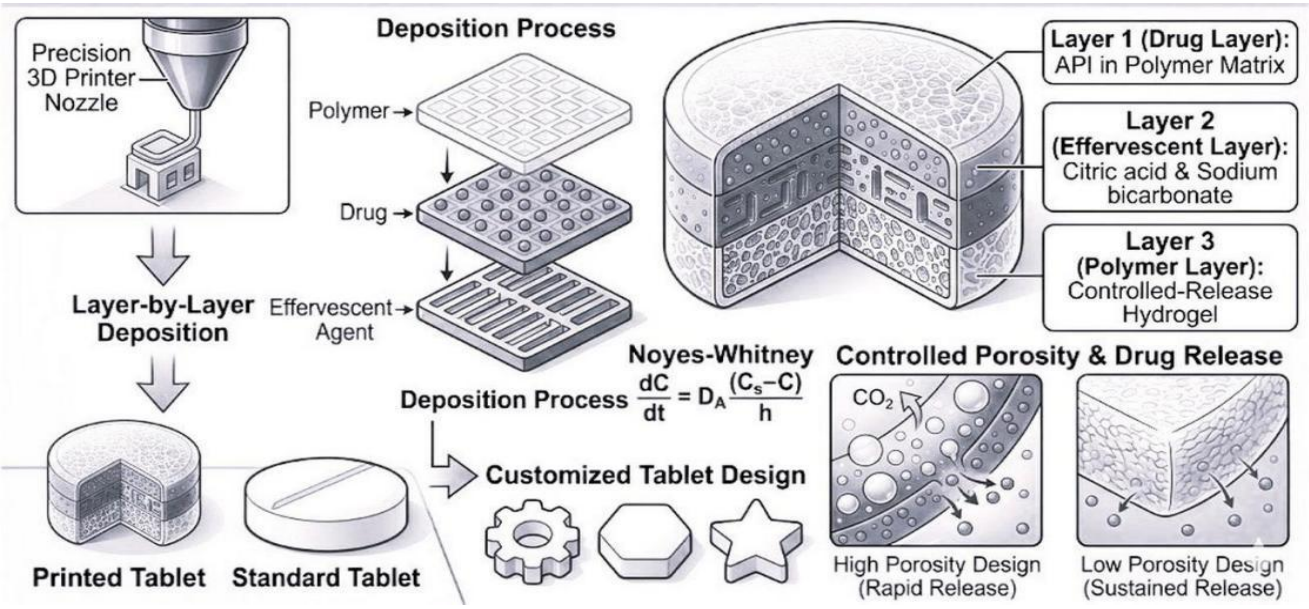


Figure 3: Shows the layer by layer 3D printing technique for manufacturing a controlled release effervescent tablet with various functional layers and how those layers influence drug release and porosity

5.Techniques involving Solid Dispersion and Microencapsulation: Innovative formulation techniques involving solid dispersion and microencapsulation have been widely used to address difficulties with flavour masking and drug stability[31].

Drug particles are enveloped in a protective film during microencapsulation, which:

a. Protects medications from environmental degradation and damp conditions.

b. Modulates the release of drugs

c. Covers up an unpleasant taste

By dispersion drugs in a polymer matrix, solid dispersion techniques further increase drug solubility. In effervescent formulations, these methods demonstrated significant improvements in drug stability, dissolving rate, and acceptance among patients[31,32].

6. Advanced Excipient Development: The growth of co-processed and multifunctional excipients has led to a major evolution in the role of excipients in effervescent formulations[1].

These days, these excipients provide:

a. Flowability and compressibility improvements

b. A decrease in hygroscopicity

c. Strengthened mechanical properties

Furthermore, one of the main issues with effervescent systems—early effervescence caused on by exposure to humidity— has been solved by the emergence of moisture-resistant excipients.

Product stability and manufacturing efficiency are improved by these improvements[1].

7. Nutraceutical and Herbal Effervescent Systems: As consumers have become increasingly interested in natural products, there is a growing trend toward the development of effervescent herbal and nutraceutical formulations[34,39] .

Amongst these formulations are:

a. Mineral and vitamin supplements

b. Herbal extracts (such as antioxidant and anti-inflammatory substances)

c. Effervescent probiotic granules

Antioxidant and anti-inflammatory properties are some of the anticipated therapeutic effects of herbal effervescent tablets made from plant extracts like papaya.

Because it smells good and is simple to administer, effervescent delivery increases the bioavailability of phytoconstituents and increases patient compliance[34] .

Herbal effervescent systems with standardised active ingredients and enhanced therapeutic efficacy have been effectively formulated, as demonstrated by recent studies[34].

8. Combination and Multi-layer Effervescent Systems: For the purpose to incorporate numerous medicines or release profiles into a single dosage form, modern effervescent formulations are increasingly being developed as multi-layer or combination systems[30].

For example: :

Rapid action with a immediate-release outer layer inner layer having sustained release for long-lasting effect.

These systems enhance outcomes of treatment through:

a. lowering the frequency of dose

b. Improving adherence to treatment

c. Giving drugs a synergistic effect[30].

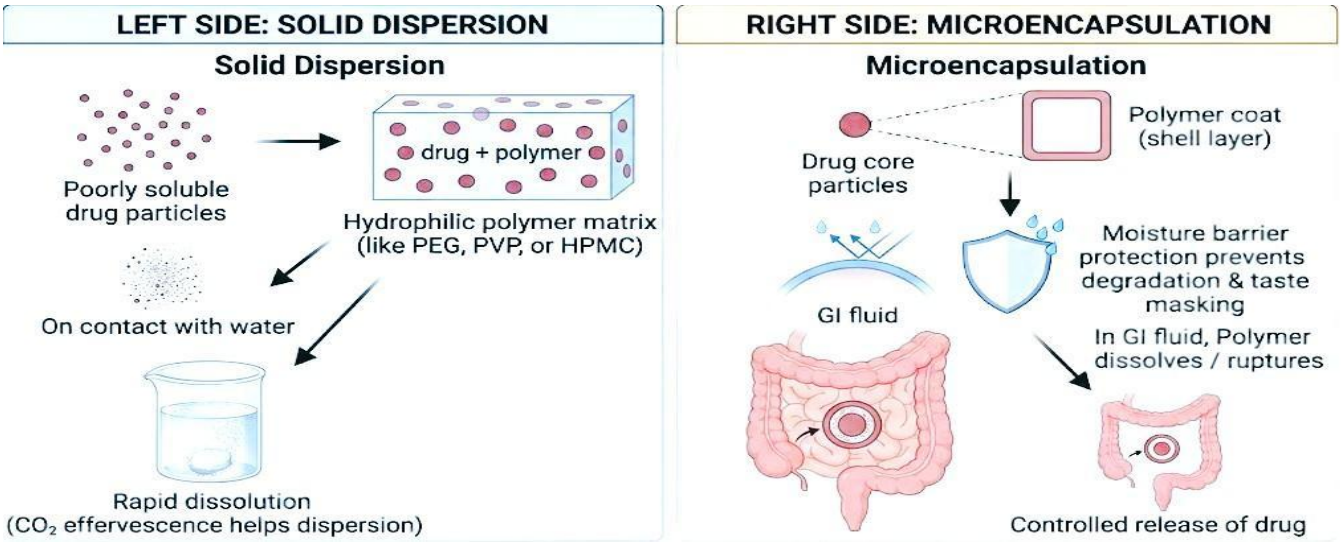


Figure 4: Shows a comparison of standard techniques for increasing drug solubility, stability, and release characteristics using solid dispersion and microencapsulation.

9. Advances in Patient-Centric Design and Taste Masking: A significant factor in oral medication delivery is patient acceptance. Palatability is naturally improved by effervescent systems, but other methods like: Improvement of flavour

Combinations of sweeteners, such as sucralose and aspartame have enhanced these compositions' organoleptic qualities even more[33].

Due to these advancements, effervescent granules are particularly suitable for older and younger individuals, who commonly struggle to swallow traditional tablets[2].

10. Innovations in Packaging and Stability: Moisture sensitivity is one of the primary problems with effervescent formulation. This issue has been addressed by recent developments in packing technology by utilising: Blister packs constructed from aluminium

Containers with desiccant

Laminates with a high barrier

These packaging methods effectively keep moisture out and preserve the stability of the product while it is being stored[1].

Furthermore, the stability and shelf life of effervescent products have been further improved by improved formulation methods and excipient selection[1].

11. Evidence-Based Evaluation and Predictions: The effectiveness of effervescent drug delivery systems in improving bioavailability, patient compliance, and therapeutic outcomes has been confirmed by systematic reviews and clinical studies[39].

Future studies are expected to concentrate on:

a. Integrating smart excipients with nanotechnology

b. The advancement of customised healthcare

c. Cutting-edge production methods including 3D printing Eco-friendly and sustainable formulation procedures

The use of effervescent systems in pharmaceutical and nutraceutical applications will increase as a consequence of these advancements[1,32].

12. Innovations in Clinical and Therapeutic: In a number of therapeutic domains, effervescent formulations showed improved clinical performance. For example, because they are simpler to administer and cause less gastrointestinal distress, effervescent alendronate formulations have shown improved patient compliance in the treatment of osteoporosis[4].In the same way, diclofenac effervescent drugs are useful for managing pain and enhancing patient convenience due to their quick analgesic action. These developments demonstrate the increasing importance of effervescent systems in current clinical practice[35].

Future Perspectives:

Future effervescent granule development is expected to be focused on converting conventional immediate-release methods into advanced, intelligent, and patient-specific drug delivery platforms. Effervescent systems advance toward integration with modern manufacturing techniques, nanotechnology, and personalised medicine because to the rapid developments in pharmaceutical technology.

The emergence of 3D printing technology, allowing for exact control over dose, geometry, and drug release behaviour, is one of the most promising avenues. This makes patient-specific therapy and on-demand manufacturing possible, which is particularly helpful for older and paediatric populations[22]. It is expected that 3D printing will play an important part in dispersed pharmaceutical manufacturing in the years to come.

The application of nanotechnology and microencapsulation techniques, which significantly improve the solubility, stability, and bioavailability of drugs that are poorly soluble in water, is a further important field. Additionally, these methods allow sensitive molecules to be protected from degradation and delivered under controlled circumstances[31,32].

Attention gets paid as well to the development of hybrid and multi-layer effervescent systems. By combining immediate and sustained drug release into a single dosage form, these formulations may improve therapeutic effectiveness and lower the frequency of dosages[1]. These systems are especially important for managing long-term medical conditions.

In addition, it is expected that customer preferences for natural remedies and preventive healthcare will continue to fuel the increasing interest in herbal and nutraceutical effervescent formulations. However, challenges such as standardization and batch-to-batch variability must be addressed to ensure consistent therapeutic outcomes[34].

The stability and shelf life of effervescent formulations will be significantly improved by advances in smart excipients and technology for packaging. It is expected that high-barrier packaging systems and moisture-resistant excipients will prevent degradation and enhance product performance[31].With the goal to create next-generation effervescent systems with improved efficacy and safety, future research will probably focus on integrating artificial intelligence, green chemistry, and customised drug delivery methods[31,39].

Conclusion:

A highly versatile and patient-friendly medication administration method, effervescent granules enable rapid drug release, improved bioavailability, and improved compliance. They are particularly helpful for individuals who have trouble swallowing conventional dosage forms as the their unique carbon dioxide producing method.

Their applications have been greatly extended beyond immediate-release formulations by the most recent advances. Their therapeutic potential and functional versatility have been enhanced by innovations like controlled-release systems, floating drug delivery systems, nanotechnology-based formulations, and 3D-printed dosage forms.

Furthermore, new avenues for natural and preventive healthcare applications have been made available by the use of nutraceuticals and botanical extracts. Clinical research has also shown that effervescent formulations improve patient outcomes in pain management and chronic disease therapy.

Despite these developments, difficulties like packaging limitations, stability problems, and moisture sensitivity still remain. But these challenges are being gradually

addressed by ongoing research in material engineering and formulation science.

To clarify, effervescent granules are evolving into advanced, multifunctional drug delivery systems beyond simple immediate-release dosage forms. They are expected to become more important in modern pharmaceutics and personalised medicine as long as they continue to improve.

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