International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1720-1726 www.ijprajournal.com ISSN: 2456-4494

A Review on Effervescent Granules

G. S. Sharma, Haripriya Batchan, T. Rama Rao
CMR College of Pharmacy, Kandlakoya, Medchal, Hyderabad

Date of Submission: 10-04-2025 Date of Acceptance: 20-04-2025

ABSTRACT
Effervescent granules are dosage form composed of dry aggregates powder particle. They contain one or more active pharmaceutical ingredient with or without excipients. Due to its low toxicity and onset action will be get fast, so effervescent granules are mostly used. Effervescent granules are uncoated granules containing drug, acid substances, carbonates or hydrogen carbonate which rapidly react with water and liberate CO_2 . In this review, it gives us information regarding basic mechanism of effervescent granules and its fundamentals and excipients used, different formulation development strategies of effervescent granules with suitable pictorial representation and evaluation of effervescent granules.

Key words: Effervescent, Carbonates, Carbondioxide, evaluation, advantages

I. INTRODUCTION TO GRANULES

Granulation is process which involves agglomeration of particles and is a significant unit operations used in the production of tablets and capsules. It transforms fine powders into free-flowing, dust-free granules that are easy to compress. They makes the blend denser so that it takes up less space per unit weight for better transportation and storage, to make volumetric dispensing easier, lessen dust during the granulation process, lessen the risk of toxic exposure and process-related hazards, make the product look better and improves the final product's uniformity. They should have a small and spherical shape, narrow particle size to fill in the spaces between them for better compaction and compression properties. They should have right amount of moisture and hardness to prevent dust formation and breaking. The properties of the particles obtained after granulation are determined by various factors such as the drug and excipients' particle sizes, the type, concentration, and volume of binder and/or solvents, the granulation time, the granulator type, the drying rate (temperature and time), and so on. Granulation is an example of particle design. Solid bridges, sintering, chemical reactions, crystallization, and the deposition of colloidal particles are the main processes that result in the formation of agglomerated granules. Furthermore, binding can also be achieved using high viscosity binders using adhesive and cohesive forces. Granules are generated from the powder particles through a sequence of events that include nucleation and wetting, growth and coalescence, consolidation, and attrition or shattering(1-3)

II. INTRODUCTION TO EFFERVESCENT GRANULES

The term "efferevescence" comes from Latin and refers to a gas escaping from an aqueous or water solution. Effervescent granules are a suitable dose form with excellent solubility, stability, and quick dissolving properties. These granules should be dissolved in a glass of water just before administration, and the resulting mixture or dispersion should be consumed right away As a result of the interaction between acid and base in the presence of water, the granules are rapidly distributed by the development of carbon dioxide in water. (4,5)

THE BASIC COMPONENTS OF EFFERVESCENT

Formulation of efferevescent granules mainly depend on two factors as discussed below

(i) creation of a preparation that dissolves in water viz
a) Acid like Citric acid, Tartaric acid, Malic acid, Adipic acid and Fumaric acid
b) Bases like odium carbonate, Sodium hydrogen carbonate, Potassium bicarbonate, Sodium sesquicarbonate
c) Sweetener like Mannitol,Sucrose, aspartame
d) Binding agent like Starch paste
(ii) requirements for the production process viz.
a) Wet Method
b) Hot Melt Extrusion Technique
c) Hot Melt Extrusion Technique
d) Hot Melt Extrusion Technique

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1720-1726 www.ijprajournal.com ISSN: 2456-4494

The removal of carbon dioxide gas from a fluid as a result of a chemical reaction is known as effervescence. When the preparation comes into touch with the water, which acts as a catalytic agent, this effect begins. The effervescent reaction yields carbon dioxide, which enhances the absorption of active substances by allowing them to penetrate the paracellular route. Since the effervescent formulation avoids direct contact with the gastrointestinal tract, these dosage forms are beneficial for patients in this category. (6,7)

Effervescence is the release of CO_2 gas in response to bicarbonates and acids in the presence of water. Sodium bicarbonate, potassium bicarbonate, sodium carbonate, and potassium are the bicarbonates used in the effervescent reaction. Other frequent acids employed in this reaction are citric, malic, tartaric, adipic, and fumaric acid. The acid-base reaction between citric acid and sodium bicarbonate is the most often occurring medication reaction in pharmaceutical application. H3C6H5O7 (aq) + 3NaHCO3 (aq) + 3H2O + 3CO2 = 3Na3C6H5O7 (aq) Water is present in this reaction, even in minute amounts, acting as a catalytic factor to quicken the process. All moisture-sensitive or effervescent items should be stored in a moisture-free environment since water serves as a catalyst for the reaction (8)

III. BENEFITS OF EFFERVESCENT GRANULES

- They include ease of administration, portability, a quicker start of action, gentler digestion, a superior taste, and greater stability compared to liquid dose forms(9).
- Possibility for formulator to enhance flavor, a kinder effect on the stomach of the patient and marketing elements, higher bioavailability compared to alternative dosage forms, improved patient compliance, and a quick start of action
- Granules have improved wetting, stability, flowability, and uniformity in particle size (9)

IV. THE EFFERVESCENCE ACTION

Na3C6H5O7+ 4H2O + 3CO2 (g) → C6H8O7.H2O+ 3NaHCO3 (aq)

Sodium bicarbonate + Citric acid -> Sodium citrate + Water + Carbon Dioxide

Na2C4H4O6 + 2H2O + 2CO2 (g) → C4H6O6 + 2 NaHCO3

Sodium tartrate + Carbon dioxide + Sodium bicarbonate + tartaric acid (10)

V. USES OF EFFERVESCENT

- It may be more effective to provide a number of active ingredient groups in effervescent preparations:
- For those that cause problems for the stomach or esophagus or are hard to digest
- For those that are sensitive to pH, including antibiotics and amino acids.
- For those who need a high dosage.
- For drugs which can easily affected by moisture, light, or oxygen (11).

VI. ACTIVE INGEDIENTS IN EFFERVESCENT GRANULES FOR ACIDS AND BASES:

A. CITRIC ACID: Citrus fruits, such as lemons, contain mild tricarboxylic acid, or citric acid, ranging from 7 to 9% dry weight. Citric acid monohydrate's three carboxylate groups have varying pKa values: 3.15, 4.78, and 6.40 It serves as a pH regulator as well The most common type of citric acid available for purchase on the commercial market is monohydrate form. It is made by slowly evaporating cold, saturated liquids and crystallizing them. Saturated solutions of hot citric acid are used to create citric acid anhydrous. Citric acid and sodium bicarbonate-based effervescent formulations can produce a pleasing mouth feel experience on the tongue and in the mouth. It has been demonstrated that in effervescent formulations with citric acid, the disagreeable taste of functionalized calcium carbonate and calcium phosphate was covered up. Pharmaceutical formulations intended for oral administration frequently incorporate effervescence. The gas released when an acid and base react with water is referred to as "effervesce." Usually, sodium bicarbonate or sodium carbonate serves as the base and citric acid as the acid Carbonated liquid drinks can be made by mixing effervescent tablets or powders with water or another liquid, such saliva, to release carbon dioxide (CO_2). Pharmaceuticals are administered with effervescence, which helps disperse active substances and facilitates rapid disintegration. This is especially useful for patients who have trouble swallowing tablets or capsules. Citric acid and bicarbonates react effervescingly, releasing CO_2. This reaction is also utilized in the production of stomach-floating tablets. The gel polymers of the tablet capture the CO_2 gas created during the

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1720-1726 www.ijprajournal.com ISSN: 2456-4494

effervescent process, which causes buoyancy. Compared to ordinary tablets, the buoyant tablets float in the stomach's gastric fluid for a longer amount of time, allowing the medication to be absorbed by the stomach over longer periods of time and boosting its bioavailability (12).

B. SODIUM BICARBONATE

Because of its strong reactivity, affordability, and high solubility, **sodium bicarbonate** is one of the most widely utilized carbonates. Therefore, water-soluble lubricants (such PEG 4000, 6000, and sodium benzoate), flavorings, sweeteners, and water-soluble colors are added as excipients.

Compared to bicarbonate, sodium carbonate has a lower CO_2 proportion. The CO_2 content of bicarbonate is higher than that of soda ash. It is less steady and has a faster reaction time. The majority of goods employ a 50/50 ratio of carbonate to bicarbonate. This form's response time and stability are adequate. Magnesium and potassium carbonate are also utilized in effervescent goods (13)

C. TARTARIC ACID

White, crystalline, acidic powder known as tartaric acid (C4H6O6) is found in wine and is present naturally in a variety of plants, including grapes, tamarinds, bananas, and bananas. Medications such as zolpidem tartrate or metoprolol tartrate are examples of tartrates, which are salts of tartaric acid. Potassium tartrate was initially used to isolate tartaric acid. Pharmaceutical manufacture makes extensive use of tartaric acid and its derivatives. For instance, citrate and tartaric acid together can enhance the flavor of oral drugs. Tartaric acid has also been utilized to create effervescent salts (14).

VII. USE OF EFFERVESCENT

- It is easy to take the doses.
- The components, acid and carbonate, act as a pH-optimal buffer for the stomach.
- It offer both the extra liquid intake and the targeted medical benefit. Drinking effervescent table water with diarrhea and during hot summers helps increase daily fluid consumption.
- Benefits for patients with difficulty swallowing: Effervescent pills offer a substitute for these individuals.
- Easy handling and precise dosage measurement: Patients can receive precise dosages as effervescent dissolve fast (15)

In efferevecent granules a carbonate salt is neutralized by acid. Finally, a gas called carbon dioxide is released. Water has a key role in starting the reaction. Acid or carbonate cannot dissociate and the reaction cannot start if there is no water in the media. A greater amount of water is produced once the reaction starts. Effervescent granules need to be manufactured in the best possible conditions and packaged with care. As a result, stability is established. Anhydrous raw materials are used in the manufacture. They ought to be stored in a dry atmosphere. The ratio of relative humidity needs to be lower than 10%. Carbonate is the source of carbon dioxide in effervescent pills. The two most widely utilized carbonate salts are sodium carbonate and bicarbonate (16).

VIII. METHODS FOR PREPARATION OF GRANULES

A. Fluidized bed granulation:

This technique uses a fluid-bed granulator-dryer to granulate all of the ingredients of an effervescent mixture in a single step. By suspending a dry mixture of an acid source and a carbonate source in a heated air stream, this approach produces a fluidized bed. The most popular granulating fluid, water, responds momentarily when injected in small volumes before vaporizing. The process is stopped when the water is no longer sprayed and warm, dry air has finished the drying phase. An alternative method to produce effervescent granules is to utilize a rotor fluid bed spray granulator (17).

B. Wet granulation:

This method is still the most advised one for effervescent granulation. Prior to applying tabletting lubricant, the basic and acidic Using common equipment such as a single pot, high-shear granulator, or fluid bed spray granulator, the components are individually granulated and then thoroughly blended. As an alternative, one of the effervescent sources can be ground up and the other added as a powder when everything is finally mixed together with extra ingredients like lubricants and flavors. This approach eliminates the need for a whole granulation stage, increasing productivity and cutting expenses (18).

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1720-1726 www.ijprajournal.com ISSN: 2456-4494

C. One-step granulation method:

Using a tiny amount of water or organic solvents such as alcohol, isopropanol, or other solvents with a binder, the one-step granulation method combines the granulation of alkaline and acidic components. By controlling the effervescent reaction and causing granule production, this method generates dry effervescent granules instantaneously (19).

D. Dry granulation

There is no need for a heat source or a solvent in dry granulation.This is the least used granulation technique out of all of them. The two main steps involve compressing fibric material to form a compact and then milling the compact to extract granules. There are two techniques for dry granulation. The most used technique is slugging, which involves recompressing the powder and milling the resultant tablets or slug to produce granules (20).

E. Freeze granulation

Spray freezing droplets of a liquid slurry or suspension into liquid nitrogen, followed by freeze-drying of the frozen droplets, is the process known as freeze granulation technology. When a powder suspension is sprayed into liquid nitrogen, the drops instantaneously freeze into granules. The granules are then dried through the sublimation of ice during the freeze-drying process, which prevents any segregation effects. This method produces spherical, freely-flowing granules that can be made with slurries based on water or solvents. Because the structure and homogeneity of the particles in the slurry or suspension are preserved in the granules, this method is significant. This technology can be used to granulate a variety of materials in a dispersed form, but it works best for creating fine powder blends with the right additives for further processing. This technology may prove beneficial in the process of preparing granules from suspensions when it is necessary to maintain uniformity and particle size. Given its capacity to preserve size and homogeneity, this approach may eventually be advantageous for solid self-emulsifying drug delivery systems, nanomaterials, re-dispersible parenteral formulations, etc. The uniformity of the granules is always determined by and reflected in the suspension quality. Low temperatures and gentle freeze drying are crucial advantages in the pharmaceutical business for minimizing damage to organic molecules and enhancing their stability and/or solubility. According to Powder Pro AB, freeze granulation creates protein particles that are clearly lighter and more porous than spray drying, and because of these advantageous aerodynamic qualities, the powders have better aerosol performance. Melt granulation, also known as thermoplastic granulation, is a process that makes it easier for powder particles to clump together by utilizing binders that melt or soften at comparatively moderate temperatures (50–90 °C). Lower melted binders can be added to the granulation process in two different ways: as molten liquid that may or may not contain the dispersed drug (spray-on or pump-on procedure), offering a variety of options to design the final granular properties, or as solid particles that melt during the process (melt-in procedure or in situ melt granulation). More precisely, heating a mixture of medication, binder, and other excipients to a temperature within or above the binder's melting range is part of the melt-in operation of the melt granulation process. In contrast, the spray-on method involves dousing the heated granules with a molten binder that may or may not contain the medicine (21).

F. Steam Granulation

Rather than using conventional liquid water as the granulation liquid, steam granulation is a revolutionary wet granulation process that uses water steam as a binder(47**).** When steam is pure, it is a transparent gas that promotes a better thermal balance throughout the drying process and a faster rate of diffusion into the powder. Water produces a heated, thin coating on the powder particles after the steam condenses, needing less additional energy to remove and evaporating more readily. This method has the advantage of producing spherical granules with a bigger surface area, distributing steam more evenly, diffusing into the powder particles, and requiring less processing time—all while being environmentally benign as it doesn't utilize any organic solvents. For this procedure, a steam generator and a high-shear mixer would be sufficient pieces of equipment. However, the production of steam via this approach necessitates large energy inputs. Additionally, not all binders can be used with this technique, and medications that are thermolabile can cause problems. When compared to traditional wet granulation, the granules produced by this technique have a higher dissolving rate because of their larger surface area (22).

International Journal of Pharmaceutical Research and Applications
Volume 10, Issue 2 Mar–Apr 2025, pp: 1720-1726 www.ijprajournal.com ISSN: 2456-4494

IX. MEDICATIONS IN EFFERVESCENT TABLETS

Drugs that are hard to digest or upset the stomach: When calcium carbonate is consumed in an effervescent formulation, it dissolves in water and becomes rapidly available for the body to absorb. This eliminates the possibility of excessive gas in the stomach and reduces the likelihood of constipation. quantity of acid in the stomach.Drugs that are pH-sensitive, such as antibiotics and amino acids: Effervescent formulations can buffer the water-active solution, causing the stomach's pH to rise and become less acidic. This will stop the active ingredient from degrading or becoming inactive, which is caused by the stomach's low pH. Substances that need an excessive dosage: In a single dosage, a standard effervescent tablet (1 inch in diameter and 5 g in total weight) can contain up to 2 g of water soluble active components. The common method of distribution is the sachet (23,24).

X. EVALUATION OF EFFERVESCENT GRANULES

A. Calculating the medication content

After weighing and properly mixing 100 ml of phosphate buffer solution (pH 6.8) with 100 mg of effervescent granules, the mixture was set aside. The solution was then filtered and examined using a UV-visible spectrophotometer (UV-1800 Shimadzo, Japan) to determine the percentage in the produced granules. Each sample's drug content was calculated using a standard curve that had been previously created (25).

B. Flow properties

Bulk density (BD) and tapped density (TD) are the two categories of density that were identified. A suitable quantity of granules was weighed and added to a 100 ml measuring cylinder. The original volume was then noted. Following that, the measuring cylinder was tapped every two seconds at a height of 2.5 cm until the volume did not change any further. The bulk density and tapped density were computed using the following equation(54. Using the formula, cars index ratio of granules was determined. Good flowing qualities are more evident in Hausner's ratios less than 1.25 than in greater values. Hausner's ratios, ranging from 1.25 to 1.6, indicate somewhat fluid characteristics. A Hausner's ratio greater than 1.6 indicates the presence of more cohesive powders.

To find the flow qualities, one measures the angle of repose. Granules are poured via a funnel that has been fastened. until the funnel's tip is touched by the cone's peak. The following formula is used to calculate the angle of repose.

$\Theta = \tan\text{-}1(h/r)$ Tan ˛ = h/r

where h is the cone's height , r is the con's radius (26)

C. Time of Effervescence

To test the in vitro effervescence period, a portion of the granules were dissolved in 50 milliliters of water in a beaker. From the batch, granules were chosen at random, and the duration of in vitro effervescence was recorded. Measure the effervescent time for each batch and repeat the process for all of the prepared formulas (27).

D. Dissolution

The granules were weighed and dissolved at 37 ± 0.5 0C in a dissolving liquid (0.1 N hydrochloric acid). The dissolving time was recorded, and test samples were taken and examined using ultraviolet-visible spectroscopy at regular intervals (28).

E. CO_2 Content Measurement

After one effervescent granules was dissolved in 100 milliliters of 1N sulfuric acid solution, weight variations were assessed. Amount of CO2 (mg) per tablet was displayed based on the weight differential that was achieved. The reports on CO_2 content are averages based on three calculations (29).

F. Assessment of the Water Content

Granules from every formulation were dried for four hours in a desiccator filled with activated silica gel. A maximum of 0.5% of water content is permitted (30).

G. Content of moisture

One factor that significantly affects a product's quality stability is its water content. Food taste and texture appearance can be influenced by water content (31).

DRAWBACKS

- Slow absorption may be the main drawback in this form
- Greater size, intricate manufacturing procedure
- Need careful packaging (32)

XI. CONCLUSION

A formulation that fizzes out takes effect more quickly. Effervescent granules can be made

using three different methods: wet method, and dry method. The wet method is most frequently used to create effervescent granules.Compared to other medication delivery systems, effervescent granules are a common dosage form that have various advantages. They have a quicker beginning of action and improved bioavailability since theydissolve easily in water and are absorbed by the body. They taste better and are more convenient for people who have trouble swallowing, which improves patient compliance. In addition to having superior stability, effervescent granules are easier to store and transport and can lessen gastrointestinal distress. They can facilitate accurate dosage administration, enhance absorption, and stop first-pass metabolism. A wide range of active substances can be used to make effervescent tablets, such as pharmaceuticals that are difficult to digest or cause stomach problems, medications that are sensitive to pH, medications that call for a high dosage, and medications that are sensitive to oxygen, moisture, stands for light. Effervescent tablets do, however, have many disadvantages, including their bigger size, intricate production process, delicate packaging, and prolonged disintegration time. Notwithstanding these drawbacks, effervescent pills have shown to be a useful and practical dosage form for a range of medical uses.Using citric acid, tartaric acid, sodium bicarbonate, saccharine, croscarmellose, banana powder, effervescent granules were expertly made.

REFERENCES

[1]. Iveson SM, Litster JD, Hapgood K, Ennis BJ. Nucleation, growth and breakage phenomena in agitated wet granulation processes: a review. Powder Technology. 2001;117:3–39.

[2]. Satapathy SR, Patra M, Patnaik M. Process and variation in effervescent formulation: A review. Innovint J Med Pharm Sci 2016;1:1-3.

[3]. Preparation and evaluation of effervescent tablets of paracetamol. Prabhakar C, balakrishna K. A review on effervescent tablets.Int J Pharm Tech 2011;3:704712.

[4]. Parikh, Dilip M. Effervescent granules. Hand book of pharmaceutical granulation technology. Edn 3, informahealthc, 365-384.

[5]. Ansel H. C., Popovich N. G., Allen L. V. Jr., Pharmaceutical Dosage Forms and Drug Delivery Systems, 6, 469-471, B. I. Waverly Pvt. Ltd., New Delhi, 1999.

[6]. Maurya SD, Rawal RK, Jha S, Chauhan PS, Kumar A, Drug Loaded Beads: Current Status, American Journal of Pharm Tech Research, 2013; 3 (1): 331-337.

[7]. Bhavana Dnyandeo Tambe, Formulation and Evaluation of Paracetamol Effervescent Tablet, Research Article, Asian Journal of Pharmaceutical Research and Development. 2021; 9(4): 47-51.

[8]. Apeksha B. Korde*, Suvarna N. Waghmare, Sujata S. Bote, Rohini S. Palekar and Priti B. Ghumre, Formulation And Evaluation of Paracetamol Effervescent Tablet. A Research Article: WJPR, Volume 10, Issue 8, 1062-1072.

[9]. Sangram Biranje, Akshata More, Trusha P. Shangrapawar, Ashok Bhosale, A Review on Formulation and Evaluation of Effervescent Tablet, Review Article, IJPPR, June 2021 Vol.:21, Issue:3

[10]. Kalyani Waghchoure, A Review on: Effervescent Tablet, IJPRA, Volume 8, Issue 1 Jan-Feb 2023, pp: 1246-125

[11]. Shet N, Vaidya I, Banerjee N. Formulation and evaluation of aceclofenac sodium effervescent taste masked granules. Int J Bio Pharm 2014;5:50 8.

[12]. Nagendra kumard,rajusa,shirsandsb,params,Rampur e MV . Fast dissolving Tablets of Fexofenadine hcl by Effervescent Method . Indian J Pharm Sci 2009; 71(22):116-9.

[13]. K.R.Srinath, C. Pooja Chowdary1, Palanisamy.P2, Vamsy Krishna. Formulation and evaluation of effervescent tablets of paracetamol IJPRD, 2011; Vol 3(3): 12; May 2011 (76 - 104)

[14]. Shet N, Vaidya I, Banerjee N. Formulation and evaluation of aceclofenac sodium effervescent taste masked granules. Int J Bio Pharm 2014;5:50 8.

[15]. Vergeire DG, Usefulness of Cost Effectiveness: Evidence versus Applicability. Pharm Anal Acta, 2016; 7:456.

[16]. Awad, Atheer; Trenfield, Sarah J.; Basit, Abdul W. (2021). "Solid oral dosage forms". Remington: The Science and Practice of Pharmacy (23 ed.). Pp. 333–358.

[17]. Eichman, JD; Robinson, JR (June 1998). "Mechanistic studies on effervescent-induced permeability

enhancement". Pharmaceutical Research. 15 (6): 925–30.
[18]. Andersen, MP (1992). "Lack of bioequivalence between disulfiram formulations. Exemplified by a tablet/effervescent tablet study". Acta Psychiatrica Scandinavica. Supplementum. 369: 31–5.
[19]. Sinko P.J. Ionic Equilibria. In: Troy D., editor. Martin's Physical Pharmacy and Pharmaceutical Sciences. Lippincott Williams and Wilkins Philadelphia; New York, NY, USA: 2006. Pp. 161–185.
[20]. Ciriminna R., Meneguzzo F., Delisi R., Pagliaro M. Citric acid: Emerging applications of key biotechnology industrial product. Chem. Cent. J. 2017;11:22..
[21]. Behera B.C., Mishra R., Mohapatra S. Microbial citric acid: Production, properties, application, and future perspectives. Food Front. 2021;2:62–76.
[22]. Wagner-Hattler L., Wyss K., Schoelkopf J., Huwyler J., Puchkov M. In vitro characterization and mouthfeel study of functionalized calcium carbonate in orally disintegrating tablets. Int. J. Pharm. 2017;534:50–59.
[23]. Pagire S.K., Seaton C.C., Paradkar A. Improving Stability of Effervescent Products by Co-Crystal Formation: A Novel Application of Crystal Engineered Citric Acid. Cryst. Growth Des. 2020;20:4839–4844.
[24]. Aslani A., Fattahi F. Formulation, characterization and physicochemical evaluation of potassium citrate effervescent tablets. Adv. Pharm. Bull. 2013;3:217–225.
[25]. Zhai H., Jones D.S., mccoy C.P., Madi A.M., Tian Y., Andrews G.P. Gastroretentive extended-release floating granules prepared using a novel fluidized hot melt granulation (FHMG) technique. Mol. Pharm. 2014;11:3471–3483.
[26]. Blair GT, et al. Hydroxy Dicarboxylic Acids. Kirk Othmer Encyclopedia of Chemical Technology. 2000, pages 1-19.
[27]. Zheng X, Wu F, Hong Y, Shen L, Lin X, Feng Y. Improvements in sticking, hygroscopicity, and compactibility of effervescent systems by fluid-bed coating. RSC Adv. 2019; 9(54):31594-608.
[28]. Zheng X, Wu F, Hong Y, Shen L, Lin X, Feng Y. Improvements in sticking, hygroscopicity, and compactibility of effervescent systems by fluid-bed coating. RSC Adv. 2019; 9(54):31594-608.
[29]. Jean Bru. Process for manufacturing effervescent granules and tablets. Vol. 614. France: United states Patent; 4614648, 1983. P. 01-7
[30]. Jean Bru. Process for manufacturing effervescent granules and tablets. Vol. 614. France: United states Patent; 4614648, 1983. P. 01-7
[31]. Obara T, Prevalence, Determinants, and Reasons for the nonreporting of Adverse Drug Reactions by Pharmacists in the Miyagi and Hokkaido Regions of Japan, Advance Pharmacoepidemiology and Drug Safety, 2015; 4:191.
[32]. Aboud HM, Elbary A, Ali AA, Enhanced dissolution of meloxicam from orodispersible tablets prepared by different methods, Bulletin of Faculty of Pharmacy, Cairo University, 2012;50:89–97.