# CHALLENGES IN EFFERVESCENT TABLET MANUFACTURING

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**Abstract:**

Effervescent technology provides a novel dosage form for nutritional supplements and pharmaceuticals. However, certain undesirable properties of effervescent tablets prevent their commercial applicability. The effervescent technology is based on the chemical incompatibility between its acidic and bicarbonate sources. This article summarizes the challenges or key facts about effervescent dosage forms, their formulation, manufacturing and packaging of final product. The article encompasses what is achievable and what has to be compromised while effervescent products are being developed by the manufacturer.

The most important challenge faced during manufacture of effervescent tablet is the prevention of autocatalytic (Self accelerating) uncontrolled chain reaction of acid and base in the tablet. This phenomenon is termed as Pre-Fizz. Specialized air handling units are necessary which comes with challenges in operating and maintaining them. The most important part of effervescent tablet manufacturing is protecting product from moisture getting inside the hermetically sealed container. Article also covers the challenges involved in selecting the packaging for effervescent product and problems that may occur during primary packing of the product.

Key Words: Effervescent tablets, water activity, Relative humidity, Granulation, Water vapour transmission rate, Pre-Fizz.

**Introduction:**

As two incompatible materials are to be incorporated in one dose, the manufacturing of effervescent tablet becomes very critical. A variety of literature is available on the working principle, designing, manufacturing and processing of effervescent tablets. However, challenges involved in formulation and manufacturing of dosage form is not widely discussed. Some articles do summarize the need for controlled environmental conditions, role of moisture content etc. but here the attempt has been made to understand the problems which a formulator and a manufacturer faces, while working with these many constraints. To prevent the moisture initiated premature effervescent reaction and prepare the most stable effervescent base are the major challenges involved in Effervescent tablet manufacturing. The article also summarizes,

i. What properties the raw and packing materials, which get used in effervescent tablets should possess and the problems a formulator faces due to such constraint,
ii. The requirement of whole manufacturing process which needs to be carried out in controlled environmental conditions of temperatures and humidity.
iii. Hurdles a manufacturer faces in maintaining these stringent controls.

iv. Dilemma the formulator faces, in the amount of moisture to be kept in formulation as there is a very thin line between minimum moisture in blend required for compression and presence of moisture in traces which destabilizes the product.

The article also describes the requirement of higher average weight of effervescent tablets, its effects on hardness, friability, capping and chipping of tablets and an overview of obstacles in masking the taste of bitter drugs which need to be used in effervescent tablets.

## CHALLENGES

### 1. Higher average weight of tablets [1]

Effervescent tablets are required to be dissolved in water before administration. Moreover, Disintegration time as per the pharmacopoeia guideline is 5 minutes. The formulator has to rely on effervescent base only to get the desired disintegration time because, the mechanism by which super disintegrants act to disintegrate tablet, is seen to be non-useful in effervescent tablet process. Since all the super disintegrants available in the market are insoluble in water, this makes them unsuitable for effervescent tablet manufacture usage. As a result, major portion of the tablet comprises of an effervescent base, making them bulkier. Generally, 30% to 40% of average tablet weight is occupied by effervescent base. A number of protein polymers like collagen and polysaccharides like Chondroitin Sulphate, hyaluronic acid are essential elements of bone and skin tissues [2] and required to be supplied in higher quantities as their production declines with age and exposure to factors such as smoking and UV light. Considering their poor stability in aqueous environment and ability of effervescent tablets to handle higher doses, effervescent tablets are one of the best options for administration of these compounds. The Collagen and Hyaluronic acid possesses a peculiar property of swelling in water [3]. When tablet is dropped in water for disintegration, the material gets swollen and forms a coat, which does not allow water to penetrate in the tablet, thereby retarding the disintegration. In such cases elevated amount of effervescent base is required to be used which may go as high as up to 60% of the total weight of tablet. Some surfactants like Sodium lauryl sulfate, Sodium dodecyl sulfate, Sodium lauryl sarcosinate have demonstrated to affect the disintegration time of effervescent tablets[4]. Detergents seems to interact with effervescent base present in the formulation creating a weak inter-particle bond and limiting water uptake responsible for disintegration. Increasing tablet weight resolves the problem to some extent but overall average weight of tablets gets bulged. Some natural extracts like Paullinia cupana, Grape seed extract, Coffee Arabica, rose hip extract are seen to extend the disintegration time thereby forcing the formulator to increase the average weight of tablets.

Due to this size, these tablets are very much prone to chipping. The tablet surface becomes rough during the course of handling from compression to packing. Taking into consideration the size of tablets and to withstand the shock it gets during manufacturing, transportation and distribution, the tablet must have a hardness of not less than 80N. An increase in compression force results in an increased crushing strength and density, thereby the disintegration time increases [5].

**2. Taste [6, 7]**

Effervescent tablets are desired to be dissolved in water before administration. Taste of the resulted solution after dissolution of tablet becomes the prime criteria of acceptance and is required to be palatable and essentially NOT bitter. Masking the taste of bitter drugs is the greatest challenge in an effervescent formulation. Coating the granules with widely available insoluble polymers or binding with ion-exchange resins (to mask the bitter taste of drug) are not useful as these techniques which form an insoluble coat on granules are not useful in case of effervescent tablets as the insoluble particles tend to float on water surface after disintegration of tablet in water, prior to ingestion. High concentration of Cyclodextrin seems to hamper the rate of reaction between acid and base which accounts to increase in disintegration time and also makes the formulation more susceptible to moisture attack [8]. Taste masking by spray congealing with lipids, taste masking by making multiple emulsions and taste masking with gelatin, gelatinized starch, liposomes, lesithins or lesithin like substances surfactants [9] makes the drug immiscible with water which in turn becomes unsuitable for effervescent tablets. Effervescent base itself masks the bitter taste of some drugs like paracetamol but not useful in many cases. However, a formulator has to rely on natural, nature identical or artificial flavors to mask the taste along with artificial sweeteners. Unfortunately, this method of taste masking is not very successful for very bitter and highly water soluble drugs. In many cases flavors and artificial sweeteners do not work alone. They have to be used with other taste masking techniques to improve their efficacy [9]. This is one of the prime reasons why bitter drugs are not widely popular as effervescent tablets. The classic examples are drugs like Ibuprofen and Sildenafil Citrate. The metallic taste of Ferrous compounds can only be masked partially and not fully, in effervescent tablets. Majority of bioactive compounds are bitter, acrid, or astringent and therefore aversive to the consumer [10]. Considering the taste masking limitations of dosage form, it makes it incapable of handling higher doses of most, if not all, these Poly-nutrients.

**3. Water activity and moisture content [11]**

The free water (which is available for reaction) present in the product is called as the water activity in the sample [12]. This free water is the major factor to be monitored during manufacture, packing & storage. Moisture has a significant impact on a wide range of chemical, physical and microbiological properties of the finished pharmaceutical product [13]. In case of effervescent tablets, it specifically impacts the chemical and physical properties of raw material, semi-finished and finished product. Inherent moisture in the dosage form is available via many sources, namely bulk drug, excipients, manufacturing processes and environmental conditions [14].

Moisture in effervescent tablet reacts with effervescent base and produces another water molecule which in turn again reacts with base, the reaction continues until acid or base gets neutralized. The water generated through chain reaction has significant effects on finished product stability, tablet compression, powder flow properties, wet granulation, dry granulation, and microbial growth.

Effervescent dosage form, particularly effervescent tablets containing active pharmaceutical ingredients which are prone to hydrolytic decomposition may easily lead to stability issues. In addition, tablet ageing can affect the chemical stability (of the contained drug) and certain physical parameters like color, hardness, and disintegration time [15]. In such cases disintegration time of the tablet also gets increased. The shelf life of Sodium mono-fluro-phosphate effervescent tablet seems to be reduced drastically to 4.5 months due to higher percentage of moisture present in tablets as compared to conventional tablets which bear a shelf life of minimum 24 months [16]. In Dinepezil HCl effervescent tablet, a water molecule present in donepezil HCl raw material, functions as a catalyst to induce premature effervescence during compounding and accelerated storage [17]. An effervescent blend adsorbs moisture from the environment, thereby increasing their cohesion and decreasing their flow ability [18]. Surface picking and die wall sticking is observed during compression, sticking of powder to turret is also evident in some cases. Weight variation is visible due to poor flow of granules. Hence it becomes essential to keep water activity of finished product as low as possible. In more precise terms, the water activity should not be more than 0.5 $a_w$ so as to avoid an excess & unwanted reaction[19].
The reactive moisture (which is required for compression) remained in granules after drying, leads to bulk powder caking during in-process storage. This results in an unmanageable powder and process downtime, which negatively impacts the production cycle time [20 Following colliding particles adhere to each other at areas which are wetted or plasticized by the impacting liquid droplets [21].

## 4. Requirement of Special Environmental Conditions for manufacturing

In addition to the good manufacturing practices and requirements of premises, plant and equipment for pharmaceutical products manufacturing of oral solid dosage form, effervescent tablet manufacturing requires Low relative humidity and moderate-to cool temperatures in the processing areas. Generally Relative Humidity of not more than 25% and Temperature not exceeding $25^{O}C$ is required to be maintained in the core manufacturing areas [22, 23 and 24]. Humidity control is a critical aspect of treating air used in manufacturing. Relative humidity is preferred over absolute humidity because effect of temperature is taken in to consideration while calculating relative humidity, unlike absolute humidity.
Dehumidification of air is achieved by passing humid air over a chilled coil and cooling it below its dew point to condense out moisture using chilled water or refrigerant. This is then followed by re-heating the air to the required temperature. Other methods used for dehumidification are liquid desiccant systems in which liquid desiccant solution, typically, Lithium Chloride is used for removal of moisture. Solid desiccant system (wherein silica gel is used for dehumidification and compressed air reduces its ability to hold moisture) is also used to dehumidify the air. Whichever method of dehumidification is used, the dehumidification of air is always a costly affair as it takes approximately 3 times more energy to run the AHU with dehumidifier than a normal AHU without the provision of dehumidification.

The system using mechanical dehumidification comes with a big risk of gas leakage in the air conditioning compressor. Ice formation around the coil is another concern while using these type of systems because it results in drastic drop in temperature and inefficient moisture removal from the incoming air. Maintenance cost of this type of systems is also more than those used for conventional tablets.

## 5. Raw Material

*i. Solubility*

Solubility of raw material is one of the most important criterion for effervescent tablet. Selected raw material is required to be highly soluble in water. Insoluble material retards the reaction required for disintegration of the tablet, thereby extending the disintegration time which must not be more than 5 min as per the guidelines. Thus an unpleasant residue either remains at the bottom of the solution or the material floats on the surface of solution after disintegration. This restricts the formulator to use insoluble material.

*ii. Anhydrous form of raw material [25]*

Whether it is excipient or active pharmaceutical ingredient, the material selected for effervescent tablets should be anhydrous in nature. The major ingredient of effervescent tablet is the acid-base duo where, citric acid is the acid of choice and sodium bicarbonate is the alkalizing agent of choice. Anhydrous form of citric acid is preferred over the hydrate one. Citric acid anhydrous itself carries up to 0.5% moisture as surface moisture, which poses a big threat to direct compression, as water remains on the surface while the crystal inside is moisture free. Larger crystals having a smaller surface area will have a higher pool concentration of moisture. The criticality of moisture content is to such an extent that the method of citric acid manufacturing can also affect the stability of effervescent tablets. Citric acid anhydrous is either manufactured by crystallization or by drying of citric acid monohydrate. Dried citric acid monohydrate is more porous and thus more hygroscopic. The particle size of citric acid can also impact the moisture content and moisture absorbing capacity of the material which in turn affects the stability of tablet. Broken crystal tend to be more hygroscopic than the intact crystals [26].

*iii. Binder*

Compared to conventional tablets, the use of binders in effervescent tablet formulation is limited, not because binders are unnecessary but because of the two-way action of the binders themselves. Use of any binder, even the one that is water-soluble, will retard the disintegration of an effervescent tablet. In granulations that require a binder for tableting, a proper balance must be maintained between granule cohesiveness and the desired tablet disintegration. In selecting proper balance one may fail to achieve either of the both [22]. Lamination is more evident due to insufficient binding. As soon as the severity of lamination increases capping is apparent. Binders such as natural and cellulose gums, gelatin, and starch paste are generally not useful due to their slow solubility or high residual water content. Dry binders such as lactose, dextrose, and

mannitol can be used but these are often not very effective in the low concentrations that are permissible in effervescent tablets, due to their disintegration-hindering properties as well as weight/volume restraints. Most effervescent tablets are primarily composed of ingredients that are mandatory to produce effervescence. Usually there is little room for accommodating the excipients, which are needed in large concentrations to be effective. Polyvinylpyrrolidone (PVP) is an effective effervescent tablet binder. This material is usually added to the powders to be granulated either dry, and subsequently wetted with the granulating fluid, or in a solution with aqueous, alcoholic, or hydro alcoholic granulating fluids.

iv. *Lubricants* [27, 28]

Of all the excipients used in the effervescent tablets, lubricant is one of the most important ingredient because, without this material, production of effervescent tablets on high-speed equipment would not be possible. Lubrication of effervescent blend has been one of the most important steps, needed to be taken for an acceptable, marketable product, partly due to the nature of raw materials used and partly due to the rapid tablet disintegration required. Many substances (in certain concentrations) are effective as lubricants but they inhibit tablet disintegration at these certain concentrations. When the concentration is lowered to permit the tablet to properly disintegrate, the lubricating efficiency of the material is lost or greatly diminished to such an extent that it is no longer useful. Commonly used lubricants such as magnesium stearate, stearic acid and talc are of limited use due to their insolubility in water and thus, they tend to float on the surface, creating an unattractive oil stick [29]. Since most of the efficient lubricants are water-insoluble, expectation of a clear solution is marred by the appearance of cloudy nature of the resultant solution.

*v. Sodium content*

Sodium and potassium salts of carbonates are the most commonly used ingredients as a source of alkali in effervescent tablets. Major problem associated with these formulations, is their levels of sodium content which is present in the form of sodium bicarbonate or sodium carbonate. According to various guidelines the ‘per day’ sodium intake is advised to be limited by 2400 mg. This excess sodium will present health problems particularly to cardiac and renal patients [30, 31]. Exposure to sodium containing formulations of effervescent medicines is associated with significantly increased odds of adverse cardiovascular events compared with standard formulations of the same drugs [32, 33]. Thus it makes Sodium as unsuitable for administration to patient with heart failure or cardiac insufficiency.

*vi. Storage of raw materials*

Most of the raw materials used in effervescent tablets are hygroscopic in nature. Hygroscopic materials are generally supplied in sealed bags to reduce moisture absorption but even sealed bags may attract moisture, if stored in a moist and cool area [34]. The process of moisture absorption is very fast in hygroscopic materials and the material can absorb substantial amount of

moisture in 30 minutes or less. However, the remaining portion of material should be protected from moisture either by storing it in humidity controlled area or storing it in a container which protects it from moisture. Moisture content of the remaining material of opened container should be checked prior to use, to ensure that the material has not accumulated moisture during storage.

## 6. Manufacturing process

Manufacturing process for effervescent tablets differs in many ways from the conventional method. High degree of precaution is required to be taken while manufacturing throughout the process as two incompatible materials are to be mixed.

### a. *Granulation* [35, 36, 37]

A variety of granulation techniques are adopted to produce effervescent tablets, namely dry granulation, wet granulation and specialized granulation process. All granulation techniques have their own constraints in manufacturing effervescent tablets.

*i. Dry granulation*

This is theoretically the most advisable method of producing effervescent tablets but it is not really useful due to the fact that the ingredients are compacted without passivation. As there no addition of water or solvent, it is most advisable but not suitable method for effervescent tablets manufacturing because effervescent components are compacted without passivation. This passivation step is important to stabilize the reactive ingredients and maintain product quality during manufacture, transportation and storage. Around 50% of the tablet comprises of effervescent base which includes carbonates and organic acids. Carbonates exhibit good compressibility but acids are not much compressible. It is observed that even after roll compaction there is no substantial improvement in compressibility of acids. Also the dust generated during milling step involved in dry granulation of citric acid, causes respiratory irritation. The granules produced after dry granulation are difficult to get lubricated and thus it creates compressibility issues during compression.

ii. *Wet granulation* [38, 39 ]

Due to the potential onset of effervescent reaction in presence of water, the concentration of moisture at every steps becomes the prime concern. In this technique, the acid and base components can be granulated either separately or as a mixture with water, ethanol, ethanol-water mixture, isopropanol and others.

During aqueous granulation of effervescent tablets, while adding binder solution, a strict control on binder solution quantity, rate of spray, impeller speed and method of addition, helps to play a crucial role. The addition of the binder can take place in three different ways, i.e. by pouring, by spraying, or by melting it. A uniform liquid spray with small droplet size will have the greatest coverage throughout the powder bed and will prevent localized over wetting of the granules [40].

Localized over wetting in effervescent tablets plays a pivotal role in defying the purpose of aqueous wet granulation technique. One of the aims of aqueous wet granulation in effervescent tablets is to stabilize the effervescent base by partial reaction of acid-base which creates a stable salt coat over reactive material. Localized over wetting is more prominent in effervescent tablets as added moisture gives rise to generation of additional water in granules which results in non-uniform coating of material, varied particle size within the granules, hard lumps and ultimately unstable product. Binder addition rate is also critical to avoid over wetting of granules and subsequently over wetting related problems as discussed earlier. As the quantity of added liquid increases, the granule saturation increases, i.e., the ratio between the liquid volume and the interstitial granule volume changes, which results in formation of only a mixture and granules do not get generated [40].

Wet granulation of the effervescent base can be performed by carefully adding 0.1 to 1.0% water [41, 42]. The granulation steps must be precisely timed or reaction may get uncontrolled resulting in hard lumps of granules. Even a 5% excess reaction than stipulated one results in extended disintegration time. Taken in to consideration the criticality of reaction, the granulated blend must be immediately followed by drying. The actual challenge in developmental stage, is to balance the contrasting water preferences of processing and stability and define a moisture range where reasonable tablet hardness, weight uniformity and chemical stability are achieved and this requires herculean efforts. An increased/higher moisture content tends to reduce powder flow and also increases particle to particle adhesion leading to uneven tablet weight uniformity, an increase in sticking issues, which can be particularly challenging with the usage of embossed tooling [43]. Since non-aqueous granulation involves no potential initiation of acid base reaction, wet granulation with non-aqueous ingredients, is preferred.

### *b. Compression*

Considering the pressure that needs to be applied to produce a large tablet, compression machine with a minimum working load of 8 tons is advisable. Water soluble lubricants are also needed to be used in the process, as mentioned before in the choice of lubricants. Sticking of granules to punch surface which may cause loss of surface finish, is possible. Sometimes granules with poor lubrication may adhere to the die wall, which can result in machine overload. This results in uneven movement of lower punches which leads to weight variation of tablets and high ejection force required to eject the tablet from dies, which leads to increased wear on cams. Sticking can frequently occur in the tableting process due to the property of acidic agent to adhere to the punch tip and die wall surfaces during compression. Therefore, it can not only roughen the tablet surface but also the cam can even get damaged as the number of compression run increases. These can severely decrease the tablet quality, yield and productivity [45]. To counter the sticking problem of effervescent material to punch tip, various approaches are deployed. One of them is, upper and lower punches are fitted with rubber inserts but rubber inserts possess their own disadvantages. Firstly, rubber wears out over time and needs replacement. Secondly, the hardness of the rubber must match the operating condition of the press, higher compression force requires a harder

rubber insert, lower compression force require softer rubber or otherwise, the rubber does not move enough between contraction under pressure and expansion after the pressure is released. Lastly, as the rubber is being used and wears out, its surface becomes rough and hence the surface of the tablet may show some roughness too. The organic acids used in effervescent tablets are not compressible and require high force for compression. Citric acid shows elastic deformation when compression force is suddenly removed from the tablet [46, 47]. This phenomena of deformation of material which occupies major part of tablet exaggerates the capping tendency of tablets. Citric acid anhydrous has a very soft crystal structures and deform easily at lower pressure, this early deformation causes filming of small particles of citric acid anhydrous and picking of larger ones on the tablet punch faces. Compression also spreads surface moisture and generates a Pre-Fizz reaction if not neutralized or adsorbed [26]. As a consequence of higher compression force and uneven punch movement, the tooling tends to heat-up. In some cases heat may pass from compression roller to punches and thereby making the turret warm. At elevated temperatures moisture absorbing capacity of granules increases which leads to sticking of granules to the punch surface as well as to the turret.

## 7. Packaging of effervescent tablets

Packaging and transportation are the biggest source of trouble and must be selected with great care in order to avoid any damage to the delicate product. Substantial breakage is inevitable if due attention is NOT given to packaging. The packaging of effervescent tablet must be done in hermetically sealed container irrespective of the type of container [22]. Any tampering of primary packing material will lead to destabilization of product. Material selected should prevent any traces of moisture reaching the product. Glass and metal tubes are best used to try minimizing the damage to the product. However, with the expansion of the global market and increasing distances that medication travels before reaching the end user, these have become both cumbersome and expensive [48]. Moreover, glass is prone to breakage, which may allow exposure of moisture sensitive effervescent tablet to the environment.

### *a. Strip packing*

Each individual tablet is hermetically sealed in a foil. Water vapor transmission rate of foil is very critical while selecting a foil for strip packing of effervescent tablets [49]. Thickness of aluminum layer determines the water vapor transmission of any foil. A typical water vapor transmission rate (WVTR) for 9 µm foil is 0.3 $g/m^2$ per 24 hours at 38 °C and 90% RH. As thickness is reduced, foil becomes more vulnerable to tearing or causes pin holes [26]. Normally a foil with aluminum layer thickness of more than 12 µm is selected for packing of effervescent tablets. Absolute moisture integrity of the foil package is required for product stability [50]. Along with controlled environmental conditions, some additional precautions are required to be taken while packing effervescent tablets [51]. The pocket size of the strip is required to be minimum, to avoid excess air entrapment. Some advanced strip packing machines are provided with vacuum application technology to remove excess air from the pocket immediately before

sealing of pocket. However, speed of the strip packing machine, design of the rollers does not allow complete air removal from the pocket which creates doubt in the mind of formulator whether to rely on the system or not. In some cases non-reactive gas, for instance Nitrogen is purged in the pocket before sealing which displaces air in the pocket. But, the complete displacement of air is not possible with allowed rate of nitrogen flushing as with increasing flow nitrogen flushing may displace the tablet from its desired position in pocket which is not acceptable. As a known fact heavy gauge foil is required to pack effervescent tablets. In some cases, up to 40-micron thick aluminum foil is used, which makes it difficult to handle while strip packing. As the thickness of foil increases, temperature needed for sealing is required to be higher, time required for transfer of heat from rollers to sealing layer through thick aluminum layer also increases. However, longer contact time required for sealing limits the speed. The seal integrity of the strip is of prime importance because without a good seal, moisture will enter the pouch and decompose the tablets prior to its intended use. The common problems observed during strip packing of large tablets are weak seals that peel off easily, wrinkles in sealing area, product getting trapped in sealing, and foil fracture, all of which leads to moisture entering the pocket and deteriorating the product. Effervescent tablets are prone to powder generation by vibration of strip packing machine due to large size of tablets and because of poor binding.

### *b. Tube packing*

The tubes are multi-dose containers and the tablets are packed by piling one on another in a tube having slightly larger diameter than tablets. Metal tubes were commonly in use in effervescent tablets, but are not as cost effective as plastic tubes. The disadvantage of tube packing is that it does not allow easy removal of the tablets which at times get jammed between the inner walls of the container, so that the later has to be turned upside down and shaken vigorously. Another disadvantage is that the entire container of the tablet has to be taken along when it may be necessary to take one tablet away from the place wherein they are normally kept, for example when travelling or at work. One cannot take off the individual tablet according to need from the original container and wrapping it in a sheet of paper or placing it in makeshift receptacle because, the tablet may deteriorate rapidly. In the process, it is no longer in contact with moisture adsorbing agent like silica normally present on the base of the container or in the cap [52]. Although, desiccant material like silica is provided in cap or at the base of tube, the cap of the tube needs to be replaced immediately after removing the tablet or else remaining tablets get deteriorated.

### *c. Blister packaging*

PVC or PVDC blisters are not suitable for Effervescent tablets as they do not offer any protection from moisture. Cold form alu blister packs are used to pack effervescent tablets which are manufactured by sandwiching aluminum foil between polyvinyl chloride (PVC) and nylon (oPA) films using dry bond lamination technology. The key advantage of laminate includes complete barrier for oxygen and water. However, a major problem faced by these manufacturers is, its

slower speed of production as compared to thermoforming which hampers the overall supply and demand chain. Lack of transparency of the package and larger size of blister is also one of the challenges faced by manufacturers [53]. The film laminate is pressed in to a mold by simply stretching a laminate mechanically with the help of pins which reduces the thickness of walls of pocket. Barrier against moisture correlates directly to the thickness of the wall, too thin means that moisture can diffuse easier and quicker inside the cavity, harming the product by reducing its shelf life/efficacy and potentially causing deterioration. Aluminum has a tendency to leech in to other materials and to crack which is corrected by the inclusion of plastic. However, as the thickness of aluminum increases to 30 micron or more, cracking tendency of foil increases.

### *d. Intermediate product handling and storage*

Hold time study of in-process material is extremely essential in case of effervescent tablets. If material left in a machine hopper, then the hopper should be covered with a lid to prevent moisture absorption by the exposed layer [34]. If an in-process material is pneumatically conveyed, it may absorb moisture from the air that is used to convey the material and become very cohesive and have poor flow ability as a result. Although the specific humidity of the air will reduce if it is compressed isothermally beyond the saturation point, its relative humidity will increase. The added material will not only affect material quality but also causes subsequent handling problems. At higher temperatures the air can hold considerable amount of moisture and an increase in pressure or a decrease in temperature can both result in significant quantities of water being precipitated [54].

## 8. Product cost

The overall manufacturing cost of effervescent tablets is way higher than the conventional tablets. Raw materials are the significant part of the production cost involved in manufacturing of effervescent tablets as overall average weight of tablets is higher than the conventional tablets. As the gauge of foil increases, so does the cost, as heavy gauge foil is required to pack effervescent tablets, quantity of foil required per pack also increases. Whichever the method used for dehumidification, whether it is dehumidification by condensation or compressing the air or by using desiccant material, it requires extra energy to do the function. In addition to this reactivation of desiccant material or heating of air to required temperature after performing its function of dehumidification at lower temperature result in consumption of more electricity. Lengthy manufacturing process and constraint of limited machine outputs makes it difficult to be a high yielding product.

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