Tablet: Manufacturing Methods / Granulation

Introduction
Granulation may be defined as a size enlargement process which converts small particles into physically stronger & larger agglomerates.
Granulation method can be broadly classified into two types: Wet granulation and Dry granulation

Ideal characteristics of granules
The ideal characteristics of granules include spherical shape, smaller particle size distribution with sufficient fines to fill void spaces between granules, adequate moisture (between 1-2%), good flow, good compressibility and sufficient hardness.
The effectiveness of granulation depends on the following properties
i) Particle size of the drug and excipients
ii) Type of binder (strong or weak)
iii) Volume of binder (less or more)
iv) Wet massing time (less or more)
v) Amount of shear applied
vi) Drying rate (Hydrate formation and polymorphism).

Wet granulation

Introduction
The most widely used process of agglomeration in pharmaceutical industry is wet granulation.
Wet granulation process simply involves wet massing of the powder blend with a granulating liquid, wet sizing and drying.

Important steps involved in the wet granulation
i) Mixing of the drug(s) and excipients
ii) Preparation of binder solution
iii) Mixing of binder solution with powder mixture to form wet mass.
   (screens)
iv) Coarse screening of wet mass using a suitable sieve (6-12
screen).
v) Drying of moist granules.
   (screen).
vi) Screening of dry granules through a suitable sieve (14-20
vii) Mixing of screened granules with disintegrant, glidant, and lubricant.

Limitation of wet granulation
i) The greatest disadvantage of wet granulation is its cost. It is an expensive process because of labor, time, equipment, energy and space requirements.
i) Loss of material during various stages of processing
iii) Stability may be major concern for moisture sensitive or thermo labile drugs
iv) Multiple processing steps add complexity and make validation and control difficult
v) An inherent limitation of wet granulation is that any incompatibility between formulation components is aggravated.

Special wet granulation techniques
i) High shear mixture granulation
ii) Fluid bed granulation
iii) Extrusion-spheronization
iv) Spray drying

i) High shear mixture granulation
High shear mixture has been widely used in Pharmaceutical industries for blending and granulation. Blending and wet massing is accompanied by high mechanical agitation by an impeller and a chopper. Mixing, densification and agglomeration are achieved through shear and compaction force exerted by the impeller.
Advantages:
- Short processing time
- Less amount of liquid binders required compared with fluid bed.
- Highly cohesive material can be granulated.

ii) Fluid bed granulation
Fluidization is the operation by which fine solids are transformed into a fluid like state through contact with a gas. At certain gas velocity the fluid will support the particles giving them free mobility without entrapment.
Fluid bed granulation is a process by which granules are produced in a single equipment by spraying a binder solution onto a fluidized powder bed. The material processed by fluid bed granulation are finer, free flowing and homogeneous.

iii) Extrusion and Spheronization
It is a multiple step process capable of making uniform sized spherical particles. It is primarily used as a method to produce multi-particulates for controlled release application.
Advantages:
- Ability to incorporate higher levels of active components without producing excessively larger particles.
- Applicable to both immediate and controlled release dosage form.

iv) Spray drying granulation
It is a unique granulation technique that directly converts liquids into dry powder in a single step. This method removes moisture instantly and converts pumpable liquids into a dry powder.
Advantages:
- Rapid process
- Ability to be operated continuously
- Suitable for heat sensitive product

Lists of equipments for wet granulation

High Shear granulation:
- Little ford Lodgie granulator
- Little ford MGT granulator
- Diosna granulator
- Gral mixer

Granulator with drying facility:
- Fluidized bed granulator
- Day nauta mixer processor
- Double cone or twin shell processor
- Topo granulator

Special granulator:
- Roto granulator
- Marumerizer
Current topics related to wet granulation

I. Hydrate formation
For example, theophylline anhydrous during high shear wet granulation transfers to theophylline monohydrate. The midpoint conversion occurs in three minutes after the binder solution is added.
For online monitoring of the transformation from one form to another, Raman spectroscopy is most widely used.

II. Polymorphic transformation
The drying phase of wet granulation plays a vital role for conversion of one form to another. For example, glycine which exist in three polymorphs that is α, β, γ. γ is the most stable form and α is the metastable form. The stable Glycine polymorph (γ) converts to metastable form (α) when wet granulated with microcrystalline cellulose.

Dry granulation

Introduction
In dry granulation process the powder mixture is compressed without the use of heat and solvent. It is the least desirable of all methods of granulation. The two basic procedures are to form a compact of material by compression and then to mill the compact to obtain a granules. Two methods are used for dry granulation. The more widely used method is slugging, where the powder is precompressed and the resulting tablet or slug are milled to yield the granules. The other method is to precompress the powder with pressure rolls using a machine such as Chilosonator.

Advantages
The main advantages of dry granulation or slugging are that it uses less equipments and space. It eliminates the need for binder solution, heavy mixing equipment and the costly and time consuming drying step required for wet granulation. Slugging can be used for advantages in the following situations:
   i) For moisture sensitive material
   ii) For heat sensitive material
   iii) For improved disintegration since powder particles are not bonded together by a binder

Disadvantages
   i) It requires a specialized heavy duty tablet press to form slug
   ii) It does not permit uniform colour distribution as can be
   iii) Achieved with wet granulation where the dye can be incorporated into binder liquid.
   iv) The process tends to create more dust than wet granulation, increasing the potential contamination.

Steps in dry granulation
   i) Milling of drugs and excipients
   ii) Mixing of milled powders
   iii) Compression into large, hard tablets to make slug
   iv) Screening of slugs
   v) Mixing with lubricant and disintegrating agent
   vi) Tablet compression

Two main dry granulation processes
i) Slugging process
Granulation by slugging is the process of compressing dry powder of tablet formulation with tablet press having die cavity large enough in diameter to fill quickly. The accuracy or condition of slug is not too important. Only sufficient pressure to compact the powder into uniform slugs should be used. Once slugs are produced they are reduced to appropriate granule size for final compression by screening and milling.
Factors which determine how well a material may slug
i) Compressibility or cohesiveness of the material
ii) Compression ratio of powder
iii) Density of the powder
iv) Machine type
v) Punch and die size
vi) Slug thickness
vii) Speed of compression
viii) Pressure used to produce slug

ii) Roller compaction
The compaction of powder by means of pressure roll can also be accomplished by a machine called chilsonator. Unlike tablet machine, the chilsonator turns out a compacted mass in a steady continuous flow. The powder is fed down between the rollers from the hopper which contains a spiral auger to feed the powder into the compaction zone. Like slugs, the aggregates are screened or milled for production into granules.

Formulation for dry granulation
The excipients used for dry granulation are basically same as that of wet granulation or that of direct compression. With dry granulation it is often possible to compact the active ingredient with a minor addition of lubricant and disintegrating agent. Fillers that are used in dry granulation include the following examples: Lactose, dextrose, sucrose, MCC, calcium sulphate, Sta-Rx® etc.

Advancement in Granulations

Steam Granulation
It is modification of wet granulation. Here steam is used as a binder instead of water. Its several benefits includes higher distribution uniformity, higher diffusion rate into powders, more favourable thermal balance during drying step, steam granules are more spherical, have large surface area hence increased dissolution rate of the drug from granules, processing time is shorter therefore more number of tablets are produced per batch, compared to the use of organic solvent water vapour is environmentally friendly, no health hazards to operators, no restriction by ICH on traces left in the granules, freshly distilled steam is sterile and therefore the total count can be kept under control, lowers dissolution rate so can be used for preparation of taste masked granules without modifying availability of the drug. But the limitation is that it is unsuitable for thermolabile drugs. Moreover special equipments are required and are unsuitable for binders that cannot be later activated by contact with water vapour.

Melt Granulation / Thermoplastic Granulation
Here granulation is achieved by the addition of meltable binder. That is binder is in solid state at room temperature but melts in the temperature range of 50 – 80°C. Melted binder then acts like a binding liquid. There is no need of drying phase since dried granules are obtained by cooling it to room temperature. Moreover, amount of liquid binder can be controlled precisely and the production and equipment costs are reduced. It is useful for granulating water sensitive material and producing SR granulation or solid dispersion. But this method is not suitable for thermolabile substances. When water soluble binders are needed, Polyethylene Glycol (PEG) is used as melting binders. When water insoluble binders are needed, Stearic acid, cetyl or stearyl alcohol, various waxes and mono-, di-, & triglycerides are used as melting binders.
Moisture Activated Dry Granulation (MADG)
It involves moisture distribution and agglomeration. Tablets prepared using MADG method has better content uniformity. This method utilizes very little granulating fluid. It decreases drying time and produces granules with excellent flowability.

Moist Granulation Technique (MGT)
A small amount granulating fluid is added to activate dry binder and to facilitate agglomeration. Then a moisture absorbing material like Microcrystalline Cellulose (MCC) is added to absorb any excess moisture. By adding MCC in this way drying step is not necessary. It is applicable for developing a controlled release formulation.

Thermal Adhesion Granulation Process (TAGP)
It is applicable for preparing direct tableting formulations. TAGP is performed under low moisture content or low content of pharmaceutically acceptable solvent by subjecting a mixture containing excipients to heating at a temperature in the range from about 30ºC to about 130ºC in a closed system under mixing by tumble rotation until the formation of granules. This method utilizes less water or solvent than traditional wet granulation method. It provides granules with good flow properties and binding capacity to form tablets of low friability, adequate hardness and have a high uptake capacity for active substances whose tableting is poor.

Foam Granulation
Here liquid binders are added as aqueous foam. It has several benefits over spray(wet) granulation such as it requires less binder than Spray Granulation, requires less water to wet granulate, rate of addition of foam is greater than rate of addition of sprayed liquids, no detrimental effects on granulate, tablet, or invitro drug dissolution properties, no plugging problems since use of spray nozzles is eliminated, no overwetting, useful for granulating water sensitive formulations, reduces drying time, uniform distribution of binder throughout the powder bed, reduce manufacturing time, less binder required for Immediate Release (IR) and Controlled Release (CR) formulations.

Key Phrases:
• In wet granulation process a granulating liquid is used to facilitate the agglomeration process. Wet granulation has been and continues to be the most widely used agglomeration process. Typically wet massing of pharmaceutical powder is carried out in the high shear mixture before wet screening and dried in fluidized bed equipment.
• In the dry granulation process granulation takes place without utilizing liquid. In this process dry powder particles may be brought together mechanically by compression into slug or by rolled compaction.
• Steam Granulation , Melt Granulation, MADG, MGT, TAGP, Foam Granulation are some of the new advancements in granulation and show better quality granule formation as compared to conventional granulation methods.
After making a good tablet, you must often coat it. The coating can have several functions. It can strengthen the tablet, control its release, improve its taste, color it, make it easier to handle and package, and protect it from moisture. This article reviews the basics of tablet coating and describes common tablet coating defects.

There are many ways to coat tablets. Sugar coating was one of the earliest methods, and the process is still widely used in the confectionery industry. Wurster coating is another means. It employs a cylindrical chamber in which tablets are suspended by air and a coating solution is introduced into the air stream. Fluid-bed coating is a similar process. Dry coating is the technique of making a tablet within a tablet. But the principle means of applying a coating to pharmaceutical and nutraceutical tablets is called film coating, and it is the focus of this article.

**Coating solutions:**

Film coatings are a mixture of solids and liquids. For many years, the liquid component of coatings was a volatile solvent, such as alcohol or other quick-drying substances like methylene chloride. While solvent-based coatings performed well in many respects, they presented problems in handling, operator safety, recovery, and odor. They could even make the finished tablets smell like solvent, which is not a desirable side effect. Solvent-based coatings are still used in some applications, but water-based, or aqueous, coatings have largely replaced them.

As a result, coating has become much more challenging, because water-based coatings are much less forgiving. You must apply the coating and remove the water before it can jeopardize the integrity of the tablet. The liquid component. It might be helpful for you to think of film-coating tablets as spray-painting a bunch of golf balls. You can envision that it’s best to spray them lightly and evenly so that successive light coatings lock together. That’s how tablet coating works.

Once the base coating is applied, you can increase the rate of solution addition and the pan speed proportionately. Typically, it takes about 20 minutes before you can increase the spray rate and pan speed significantly. Soft tablets and tablets that are very porous may require an initial spray rate that is slower than the average of 100 milliliters per minute per gun. Be sure to monitor spraying to see whether the spray pattern changes. If it does, there is likely a buildup of solids on the gun tips. You can correct this only by cleaning the tips, which means stopping the spray and the pan. The images on page 20 show tablet coating spray nozzles being cleaned.

The film coating solution dries on the tablet surface because there is a constant supply of hot air entering the drum and passing through the drum’s perforations into the bed of tablets. Over time, the film builds layer after layer of solids. How long it takes to form the final film varies from dozens of minutes to a few hours. It depends on tablet quality, the coating solution type (solvent-based coatings dry faster), the percentage of solids in the coating, and the rate of coating addition. Other important factors include the air volume, air temperature, and the air pressure within the coating cabinet. After you’ve finished applying the solution and drying it, the tablets must cool.

For coatings to adhere properly, the tablets must remain at a specific temperature, the solution must be applied at a consistent rate, and the motion of the tablets must be active yet tranquil. Disrupt any of these conditions, and you will often produce a defective tablet. For reproducible results, you have to eliminate or minimize every possible variable. That begins with tablet quality.
Tablet quality

My description of tablet coating presumes you are coating high-quality tablets that are tough enough to tumble as they’re coated and dried. If tablet quality is consistent, the coating process is much easier. Consistency is typically not a problem for pharmaceutical manufacturers. It’s more of an issue for makers of vitamins, herbals, and other dietary supplements, because they use many natural ingredients that vary in moisture content, bulk density, granule structure, flow characteristics, and compressibility. So naturally—pardon the pun—the quality of their tablets tends to vary. You can’t coat a bad or marginal tablet and expect a good tablet when you’re done.

First, the tablets must be consistent in porosity and hardness. They must also be free of dust. Furthermore, they must not break apart during the preheat cycle at the start of the coating process or during the first few minutes of exposure to the atomized solution.

Coating equipment:

A modern tablet coating system combines several components: a coating pan, a spraying system, an air handling unit, a dust collector, and the controls. The coating pan is actually a perforated drum that rotates within a cabinet. See Figure 1. The cabinet enables you to control airflow, air temperature, air pressure, and the coating application. The spraying system consists of several spray guns mounted on a manifold, a solution pump, a supply tank and mixer, and an air supply. The pump delivers the coating solution to the guns, where it combines with atomizing air to create a fine mist that is directed at the bed of tablets in the coating pan. The air handling unit heats and filters the air used to dry the coating on the tablets. Depending on your circumstances, it may include a humidifier or dehumidifier. The dust collector extracts air from the coating pan and keeps a slightly negative pressure within the cabinet. The controls enable you to orchestrate the operation of all the components to achieve the desired results.

Coating in action:

Once you load a batch of tablets into the coating pan, you need to preheat the tablets and allow time for dust and tablet flash to exit the pan. Once the temperature of the outlet air reaches 42° to 46°C, usually within 15 minutes, spraying can begin.

The spray guns create a fine mist of coating solution that dries just after it contacts the tablet. As the water evaporates, it leaves the solids behind to form a thin film on the tablet. The key to tablet coating is to get the surface slightly wet and immediately dry. Your objective is to apply the coating in many short, fast exposures, not in long, slow exposures.

I was taught the three D’s of tablet coating: dose, distribute, and dry. Dose is the exposure to the solution.

Distribute is the fast motion of the tablets rubbing against one another to transfer the solution. Dry is the removal

Tablet coating checklist:

Since spraying, coating distribution, and drying take place at the same time, tablet coating is a dynamic, complex process that is affected by many variables. In no particular order, here are some of the parameters that you should check when evaluating your coating operation to determine the source of defective coated tablets Control. Many problems occur in coating when you can’t control every important parameter, such as temperature, pan pressure, spray rates, and atomization pressure.

Consistent hardness of the tablet surface enables the coating to “lock” into the surface. If the surface is too soft, the impingement of the solution can erode the tablet.

Too hard a surface will not allow the solution to impinge and adhere, and the coating will peel away. Both of these coating defects can also occur by over- or under-applying the coating solution or by applying the coating with too much or too little force. A combination of these factors
could also be at work. See the sidebar on defects on page 22 and the accompanying photos.

Here is a list of common defects associated with coated tablets and some likely causes.

**Picking and sticking**: This is when the coating removes a piece of the tablet from the core. It is caused by over-wetting the tablets, by under-drying, or by poor tablet quality.

**Bridging**: This occurs when the coating fills in the lettering or logo on the tablet and is typically caused by improper application of the solution, poor design of the tablet embossing, high coating viscosity, high percentage of solids in the solution, or improper atomization pressure.

**Capping**: This is when the tablet separates in laminar fashion. The problem stems from improper tablet compression, but it may not reveal itself until you start coating. How you operate the coating system, however, can exacerbate the problem. Be careful not to over-dry the tablets in the preheating stage. That can make the tablets brittle and promote capping.

**Erosion**: This can be the result of soft tablets, an over-wetted tablet surface, inadequate drying, or lack of tablet surface strength.

**Twinning**: This is the term for two tablets that stick together, and it’s a common problem with capsule shaped tablets. Assuming you don’t wish to change the tablet shape, you can solve this problem by balancing the pan speed and spray rate. Try reducing the spray rate or increasing the pan speed. In some cases, it is necessary to modify the design of the tooling by very slightly changing the radius. The change is almost impossible to see, but it prevents the twinning problem.

**Peeling and frosting**: This is a defect where the coating peels away from the tablet surface in a sheet. Peeling indicates that the coating solution did not lock into the tablet surface. This could be due to a defect in the coating solution, over-wetting, or high moisture content in the tablet core.

**Chipping**: This is the result of high pan speed, a friable tablet core, or a coating solution that lacks a good plasticizer.

**Mottled color**: This can happen when the coating solution is improperly prepared, the actual spray rate differs from the target rate, the tablet cores are cold, or the drying rate is out of spec.

**Orange peel**: This refers to a coating texture that resembles the surface of an orange. It is usually the result of high atomization pressure in combination with spray rates that are too high.

**T&C**: This photo shows multiple defects. The initial problem was erosion of the tablet edge due to a soft or friable tablet or because the pan was turning too fast or both. Peeling and breakage also appear here.

I attribute the peeling in this photo to excessive moisture within the tablet, which prevented the coating from adhering. However, the tablet coating also pulled the granulation out of the tablet, a picking defect. That is usually caused by over-wetting the tablet or by a tablet that is too soft.

Just one broken tablet can distribute particles to all the other tablets and mar their appearance. These tablets likely broke because they had poor hardness. It shows a very porous tablet that prevented the coating from adhering to the surface. These tablets should have been coated longer, and the atomization pressure should have been reduced to decrease the slight orange peel, or textured, surface.

**Coating defects:**

**Tablet quality**: As discussed earlier, the tablets must have the proper porosity, surface, hardness, and moisture content. You can’t have consistent coating without consistent tablet quality.

**Waiting period**: Most tablets cannot be coated immediately after they’ve been compressed. The energy within the tablets is still fairly high. In fact, they are still warm. In addition, tablet hardness changes over 24 to 48 hours. Let the tablets rest at least that long before you coat them.

**Batch size**: Variation in batch size changes the required pan speed, gun geometry, spray rates, and temperature. The more your batch sizes vary, the more quality issues that will arise in the coating process.
Solution preparation: Again, consistency is the name of the game. Does your company prepare coating solutions the same way, regardless of the batch, the shift, or the operator? Track the solution temperature, mixer speed, and storage time. All are important. Oh, and is the mixing blade correctly installed? Be sure by marking it “top” and “bottom.”

Spray gun calibration: You should calibrate or check the calibration of the guns every time you change products. This means checking the gun’s overall condition and its filter, nozzle alignment, and needle condition.

Gun geometry: Geometry refers to the gun-to-gun alignment, gun-to-tablet bed alignment, and distance from the gun to the end of the pan. Use a ruler to be sure the distances are consistent. Furthermore, make sure all the guns are pointed in exactly the same direction and are maintaining the same spray pattern. Make certain that the tubing and connections are tight and do not interfere with alignment, which is a common problem.

Gun nozzles: The spray gun nozzles must be kept clean and free of product buildup. Use a flashlight during coating to look into the cabinet and check the nozzles.

Pan loading: While loading the tablets, look for tablets that are broken, capped, chipped, or covered with black specks. Doing so will help you pinpoint the source of any defects that occur. Do the defects appear during loading, during initial pan rotation, or after preheating? A visual inspection is critical when coating tablets that are friable or that chip or break easily.

Cleaning: Make sure you’ve cleaned and dried each component of the spraying system before re-installing it after a product changeover. In tablet coating, small changes in almost any parameter can lead to big differences in results. The more consistent you make operations, and the tablet, the less you must rely on the skill of the operator. Coating may be something of an art, but you’ll get better results when you apply a little science to it.

AQUEOUS FILM COATING: CRITICAL ASPECTS

One of the major steps in formulation development activity is the development of film coating formulation and process. Different dosage forms may need different kind of coating formulation, technique and process. Therefore a formulation development scientist has to understand the critical aspects associated with each case. Different dosage forms which can be coated are: tablets, capsules, pellets, granules, particles and powder.

All the above mentioned dosage forms may need coating for different reasons such as:
1. Change in appearance - to impart colour for easy identification and brand image building.
2. To eliminate dust generation – to reduce handling problems and to reduce dust induced toxicity.
3. Taste masking – mask the bitter or unpleasant taste.
4. Odour masking – mask the unpleasant odour of active ingredients like vitamins, antibiotics etc.
5. Isolation of incompatible materials – some of the ingredients may be incompatible to each other, and these can be separated by putting a barrier coating inbetween them.
6. Protection from environmental conditions – Some of the ingredients may not be stable in the presence of moisture, light, oxygen etc. The product stability can be improved by coating.
7. Change in release characteristics – drug release profile from the dosage form can be tailored by coating techniques for example – delayed release (by enteric coating), extended release (by semi permeable membrane coating or mixing of pellets which are coated to various degree or with different coating materials).

The application of coating, which is an additional step in the manufacturing process increases the overall processing time and cost of production. Therefore, the decision regarding the coating technology has to be based on:
1. Available facility.
2. Overall productivity desired (film coating process is always much faster than sugar coating)
3. Environmental and regulatory considerations (all organic solvents are toxic and inflammable)
4. Overall cost of the product.
**Aqueous film coating technology**

As the sugar coating process is very time consuming and is dependant on the skills of coating operator, this technique has been replaced by film coating technology. This technique was started with the use of organic solvents but now has been replaced with aqueous film coating due to environmental and regulatory considerations. Moreover the cost of any organic solvent is far more than the cost of purified water. Therefore, the conversion from organic solvent based coating to aqueous based coating makes the coating process more economical, though initially it may need a little investment to upgrade the coating facility. The need of this upgradation arises due to the need of higher drying capacity (the latent heat of water is 2200 kJ as compared to 550 kJ for methylene chloride which implies that to evaporate water one will need 4 times more energy as compared to organic solvent).

The problems associated with organic solvent-based film coating and the advantages of aqueous based systems have long been recognized. Film coating technology has now advanced to the level where aqueous coating has become a matter of routine rather than the exception. The successful introduction of a wide variety of aqueous based film coating products under the brand name DRUGCOAT has resulted in easy conversion from organic solvent based coatings to aqueous film coating for several companies; many of them still use the conventional coating equipment.

**Development of film coating formulation**

The optimization of film coating formulation may be necessary to improve adhesion of the coating to the core, to decrease bridging of intagiations, to increase coating hardness or to improve any other property that the formulator deems deficient. The development scientist has to consider three major factors which affect the film quality - tensile strength of the film coating formulation (mainly dependant on polymer properties), elasticity of the resultant film (mainly dependant on properties and quantity of plasticizer used) and the film-tablet surface interaction (each and every ingredient used in the coating formulation can affect this interaction and can change the adhesion properties of the film on the tablet surface).

Due to these considerations, it becomes very important to use the most optimized coating formulations in order to get the best results.

**Problems in film coating**

It is very common to see that though one may have a decent coating equipment, the final product is still not very satisfactory. One may find various defects in the final products. The basic source of these defects could be any three listed below:

1. Defects arising due to defective core formulation or the tablet shape (like high friability, capping, logo or embossing, cratering, high contact surface area causing twinning.
2. Non-optimised coating formulation (problems like logo bridging, poor colour dispersion, film cracking and peeling)
3. Non-optimised coating conditions (like pricking & sticking, surface roughness, colour variation, spray drying, orange peel, poor coating efficiency)

The development scientist, therefore has to critically evaluate the problem and find out the basic reason for the problem, then only the most optimized solution to the problem can be ascertained.

**Equipment requirement for film coating**

Tablet coating has undergone numerous developments during the last few decades. These changes have resulted in increased interest in equipment designed for film coating from conventional set-up to side-vented pan to fluid-bed coater for different applications. However the process is complex and requires careful monitoring and control to ensure satisfactory results. The film coating process as such is a combination of four processes going on simultaneously:

1. Distribution of coating material on large number of tablets.
2. Mixing of large batch for homogeneous result.
3. Drying or evaporation of solvent.

In order to achieve best results, one has to optimize each process in relation to each other. The major difference between sugar coating and film coating is that generally film coating is a continuous process and is run in almost dry conditions, which implies that the rate of drying has to match the rate of spray. This being the most important aspect in film coating process, ensures good/poor finish of the final product. Coating equipment set-up, therefore, has to have provisions to meet these criteria. With careful designing such conditions can be achieved in different set-ups – be it conventional pan/side-vented pan or fluid-bed coater.

**Solvent to Aqueous Film Coating**

These tablets/ pills have to be coated for various reasons using a wide variety of materials and processes. The majority of tablets are coated for cosmetic reasons and for identification of specific brand in market place, however, a number of products are now coated to provide some functional benefits like enteric coating, moisture protective coating, coatings for control release, flavour coating, taste mask coating etc.

Until about 1950, sugar was the first choice as coating agent for pharmaceutical preparations and much time and efforts were spent in perfecting the sugar coating techniques. Nobody ever was concerned about the problems like material cost, toxic effects due to coating or pollution etc. because the solvent used was always water. However, sugar coating technique was time consuming, affecting the productivity and the quality of finished product was dependent on the skills of operator. Many a times the companies had to reschedule their production plans due to the non-availability of skillful coating operator. These problems led to the development of film coating technique which was mainly based on solutions of different polymers in various organic solvents. All these solvents are toxic in nature. As the level of understanding regarding the toxic effects of these solvents is increasing, industrial hygiene rules and FDA regulations are being tightened world over, limiting the use of these solvents and exposure of workers to these solvents. Another area of concern is the cost of these solvents, which can only be expected to increase in coming times. In today's competitive business environment any cost saved will improve the market viability and success of any product. We are, therefore, left with no other choice but to eliminate the use of organic solvents and start using water as the solvent system for tablet coating. Like any other system, aqueous film coating has some disadvantages. The main reason for using organic solvents was to avoid possible decomposition of active ingredients and many other process related problems such as over wetting, picking and sticking etc. which may occur with aqueous coating systems. However, research and experience of industry has indicated that the decomposition of active ingredients and possible coating difficulties are not so serious issues in actual applications and all such problems can be sorted out by scientific evaluation of the reasons for these problems. Most of these problems could be categorized as :

1) Material related problems
2) Coating instrument related problems
3) Coating process related problems

In this article we will discuss various issues related to Materials used for Aqueous Film Coating.

A large number of problems observed during conversion from organic solvent based coating to aqueous film coating are related to material selected for coating formulation. Some of these problems could be :

a) Poor film adhesion
b) Poor tablet finish due to high viscosity of coating solution
c) Uneven surface of finish product
d) Non-uniform colour of finished product
e) Longer coating cycle time
To understand these coating problems, we will have to understand the properties and role of various materials used in film coating formulations.

**Polymers**

As the tablet coating technique was changed from sugar coating to film coating, polymers like methyl cellulose, hydroxypropyl methylcellulose, ethyl cellulose etc. became the main coating materials in place of sugar. The higher viscosity grades of HPMC though provided film with good tensile strength but produces films having poor adhesion with the core surface and very often one can easily peel-off the film from the tablet surface. The same HPMC when dissolved in water give rise to many other problems like -

* high solution viscosity
* water is a poor solvent for HPMC as compared to organic solvents, therefore, solution preparation is difficult
* water has much higher surface tension than organic solvents, material wetting is difficult resulting in poor film adhesion
* films produced using water as solvent has poor mechanical properties like low tensile strength, higher modulus of elasticity and low film adhesion.

Therefore, the selection of correct polymer system is very critical for the success of aqueous coating formulation. By selecting the lower viscosity polymers, the solid content in the coating formulation can be increased which will result in lesser amount of water required which in turn can increase the coating speed. However, the lower viscosity HPMC produces the films with lower tensile strength. As described earlier the film produced by HPMC using water as solvent system may have poor film adhesion resulting in easy peel-off from the tablet surface. To overcome this problem some formulators have used the combination of HPMC and HPC. HPC provides better film adhesion to the substrate than HPMC, however, other mechanical properties of HPC are not comparable to HPMC, moreover, the cost of HPC is much higher then HPMC and thus makes the formulation economically non-viable. Various other polymers are also used in developing aqueous film coating formulations like Sod. CMC, PVA, PVP, Soy. Alginate, PEG etc. either alone or in combination.

**Plastisizers**

The next most important component of the coating formulation is plasticizer. A wide range of plasticizers are available to the formulator such as phthalate esters, phos-phate esters, other esters like citrates, stearates, sebacate, oleate, adipate etc. oils, glycerol, glycols etc. The important factors to be considered here are :

- Water solubility of the plasticizer : Hydrophobic plasticizers will create problems in solution preparation and can affect the D.T. and dissolution profile of the finished product.
- Water vapour transmission rate through the film : Higher concentration of plasticizer in the film generally tends to increase the water vapour permeability.

**Concentration in the coating formulation**

Higher concentration of plasticizer reduces the modulus of elasticity (a desired effect) and thus reduces the possibility of logo bridging but also reduces the tensile strength of the film (undesired effect).

- Film adhesion generally tends to increase with increased concentration of plasticizer.
- Higher concentration of plasticizer can lead to its bleeding (making the tablet surface feel oily).
- in most of the cases presence of plasticizer improves the gloss level in the finished product (depending on the quality and concentration of the plasticizer).
- Volatility of the plasticizer : Aqueous coating generally need higher drying capacity during the coating cycle due to less volatility of water, if the plasticizer is more volatile e.g. propylene glycol, much of the plasticizer may get lost during the coating process.

Therefore, one needs to strike a balance between the desired and undesired effects of the plasticizer and optimize its concentration in the coating formulation. Many a times use of combination of plasticizer becomes necessary to achieve the most optimum results.
Additives
The properties and composition of other components of the film coating formulation also need to be considered and optimized to get the most desired effects without affecting the quality of the film. Various other components which could be used in coating formulation are -
- Pigments
- Opacifier
- Anti-tacking agent
- Film adhesion enhancer
- Sweetners
- Flavours
- Anti foaming agent

The concentration and the properties of each of these excipients can affect the quality of the resulting film, e.g.
- The commonly used colourants in sugar coating are water soluble dyes. However, the overall colour effect of these dyes depend on the dye concentration at a particular point, thickness of film at that point and the residual moisture content in the film at that point. As these parameters can differ from tablet to tablet, the colour difference among various tablets within the same batch may become very visible.
- The opacity of the film depends on the difference between the refractive index of the polymer and other components of the coating formulation. The lake colours used in film coating has refractive index similar to that of various polymers, thus the opacity of lake colours is very poor.
- The most commonly used anti- tacking agent is Talc, which if used in higher concentration tends to settle down from the coating suspension, thus affecting the composition of suspension during the coating process. Further, it is poor opacifier and tends to produce translucent films.
- As the aqueous film coating need higher drying capacity, the volatile matter in the flavours used may get lost, changing the nature of the flavour. These volatile matters may also interact with other components of the coating formulation and can affect their properties. One, therefore, need to use specific flavours and incorporate them in the coating formulation in such a manner so that it does not affect the film quality.

It, therefore, once again becomes a lot of balancing act while developing the optimized coating formulation.

Effect of Residual Moisture
One should keep in mind that water is less volatile than organic solvents, and will require much better drying capacity resulting in higher energy cost to the coating process. However, exceptions do exist in optimized film coating formulations which have a very low affinity for water, and therefore, can be run at lower temperatures, higher spray rates. Ideal Cures Pvt. Ltd. has developed few such products (under DRUGCOAT range of products) which dries faster and the whole coating process can be completed in the same or sometimes little less time as compared to organic solvent based coatings.

The use of organic solvents raises the possibility of residual solvent in the finish product which is increasingly becoming a concern to the regulatory agencies due to their adverse effects on the consumer health.