**Orodispersible Dosage Forms**

Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy and ease of administration lead to high levels of patient compliance.

Besides delivering drug to the body, a drug delivery system aim to improve patient compliance and convenience, and fast dissolving delivery systems are no exception.

Fast dissolving drug delivery systems (FDDs) disintegrate and/or dissolve rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate.

**Advantages of Fast Dissolving Drug Delivery System**

1. Ease of administration for patients who are mentally ill, disabled and uncooperative.

For patients who may have difficulty swallowing tablets or liquids. Traditional tablets and capsules administered with an 8-oz. glass of water may be inconvenient or impractical for some patients. However, some patients, particularly pediatric and geriatric patients, have difficulty swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take these solid preparations due to fear of choking2. For example, a very elderly patient may not be able to swallow a daily dose of antidepressant. An eight-year-old with allergies could use a more convenient dosage form than an antihistamine syrup. A schizophrenic patient in the institutional setting can hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic. A middle-aged woman undergoing radiation therapy for breast cancer may be too nauseous to swallow her H2-blocker. Fast-dissolving/disintegrating tablets (FDDTs) are a perfect fit for all of these patients.

1. Requires no water and so it is convenient outside home.
2. Self administration
3. Overcomes unacceptable taste of the drugs and could provide a pleasant mouth feel.

As most drugs are unpalatable, mouth dissolving delivery systems usually contain the medicament in taste masked form. Delivery systems dissolve or disintegrate in patient’s mouth, thus releasing the active ingredients which come in contact with the taste buds and hence, taste masking of the drugs becomes critical to patient compliance.

Mouth feel is critical, and patients should receive a product that feels pleasant. Any large particles from the disintegrating tablet that are insoluble or slowly soluble in saliva would lead to an unpleasant gritty feeling. This can be overcome by keeping the majority of the particles below the detectable size limit. In some cases, certain flavors can imbibe an improved mouth feel perception, resulting in a product that is perceived as being less gritty, even if the only change is the flavor. Effervescence can be added to aid disintegration and improve mouth feel by reducing the “dryness” of a product.

1. Allows high drug loading.
2. Ability to provide advantages of liquid medication in the form of solid preparation.
3. Adaptable to existing processing and packaging machinery.
4. A major claim is increased bioavailability compared to traditional tablets.Because of dispersion in saliva while still in the oral cavity, there can be pre-gastric absorption from some formulations in those cases where the drug dissolves quickly. Buccal, pharyngeal and gastric regions are all areas of absorption of the many formulations. However, other formulations show nearly identical plasma-concentration profiles. Any pre-gastric absorption avoids first pass metabolism and can be a great advantage in drugs that undergo a great deal of hepatic metabolism. However, if the amount of swallowed drug varies, there is the potential for inconsistent bioavailability.

**While the claimed increase in bioavailability is disputable, it is clear that the major advantage of these formulations is convenience.**

The advantages of Fast Dissolving Dosage Forms are increasingly being recognized in both industry and academia. Their growing importance was underlined recently when [**European Pharmacopoeia**](http://www.pheur.org/)adopted the term “Orodispersible Tablet” as a tablet that to be placed in oral cavity where it disperses rapidly before swallowing.

There are multiple fast-dissolving OTC and Rx products on the market worldwide, most of which have been launched in the past 3 to 4 years. There have also been significant increases in the number of new chemical entities under development using a fast-dissolving drug delivery technology.

### ****Approaches for Fast Dissolving Tablets****

The fast-dissolving property of the tablet is attributable to a quick ingress of water into the tablet matrix resulting in its rapid disintegration. Hence, the basic approaches to developing fast dissolving tablets are:

* Maximizing the porous structure of the tablet matrix
* Incorporating the appropriate disintegrating agent
* Using highly water-soluble excipients in the formulation.

**Conventional Techniques Used in the Preparation of Fast Dissolving Drug Delivery Systems**

Various technologies used in the manufacture of Fast dissolving tablets include

#### a.Freeze drying or Lyophilization

A process in which water is sublimated from the product after freezing. Lyophilization is a pharmaceutical technology which allows drying of heat sensitive drugs and biologicals at low temperature under conditions that allow removal of water by sublimation. Lyophilization results in preparations, which are highly porous, with a very high specific surface area, which dissolve rapidly and show improved absorption and bioavailability. Jaccard and Leyder used lyophilization to create an oral pharmaceutical preparation that not only dissolve rapidly but also improved the bioavailability of several drugs such as spironolactone and trolendomycin. Corveleyn and Remon studied various formulation and process parameters by using hydrochlorthiazide as a model drugon the basis of which US Patent 6,010,719 was granted. Tablets prepared by lyophilization, are fragile and possess low mechanical strength, which make them difficult to handle and they also exhibit poor stability on storage under stressed conditions.

#### b.Molding

Tablet produced by moulding are solid dispersion. Moulded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is in general made from water soluble sugars. The active ingredients in most cases is absorbed through the mucosal lining of the mouth.

The manufacturing process of molding tablets involves moistening the powder blend with a hydroalcoholic solvent followed by pressing into mold plates to form a wetted mass (compressing molding). The solvent is then removed by air drying. Thus the process is similar to what is used in the manufacture of tablet triturates. Such tablets are less compact than compressed tablets and possess a porous structure that hastens dissolution.

Molded forms are also prepared using a heat-molding process that involves setting the molten mass that contains a dispersed drug. The heat-molding process uses an agar solution as a binder and a blister packaging well as a mold to manufacture a tablet. The process involves preparing a suspension that contains a drug, agar, and sugar (e.g., mannitol or lactose), pouring the suspension into the blister packaging well, solidifying the agar solution at room temperature to form a jelly, and drying at -300C under vacuum.

Another process used is calledno-vacuum lyophilization*,* which involves the evaporation of a solvent from a drug solution or suspension at standard pressure. Pebley et al., evaporated a frozen mixture containing a gum (e.g., acacia, carageenan, guar, tragacanth, or xanthan), a carbohydrate (e.g., dextrose, lactose, maltose, mannitol, or maltodextrin), and a solvent in a tablet shaped mould. Moulded tablets typically do not possess great mechanical strength. Erosion and breakage of the moulded tablet often occur during handling and opening of blister packs.

#### c. Spray drying

Spray drying is a process by which highly porous, fine powders can be produced. Spray-dryers are invariably used in the pharmaceutical industry to produce highly porous powders. Allen et al. have reported applying this process to the production of fast dissolving tablets. The formulations that were produced contained hydrolyzed and unhydrolyzed gelatin as a support agent for the matrix, mannitol as a bulking agent, and sodium starch glycolate or crosscarmellose as a disintegrant. Disintegration and dissolution was further enhanced by adding an acid (e.g., citric acid) or an alkali (e.g., sodium bicarbonate). The formulation was spray dried to yield a porous powder. Tablets manufactured from this powder disintegrated in less than 20 s in an aqueous medium.

#### d.Sublimation

The key to rapid disintegration for mouth dissolving tablets is the presence of a porous structure in the tablet matrix. Conventional compressed tablets that contain highly water-soluble ingredients often fall to dissolve rapidly because of low porosity of the matrix. Hence. To generate porous matrix, volatile ingredients are used that are later subjected to a process of sublimation. In studies conducted by Heinemann and Rothe, Knitsch et al., and Roser and Blair, inert solid ingredients that displayed high volatility (e.g., ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethonium tetramine, naphthalene, phthalic anhydride, urea, and urethane were compressed along with other excipients into a table. The volatile material was then removed by sublimation, leaving behind a porous matrix. Solvents such as cyclohexane and benzene were also suggested for the generation of porosity in the matrix.

Koizumi et al. applied sublimation technology to manufacture tablets that rapidly dissolve in saliva. Mannitol is used as a matrix former, and camphor was used as a sublimating agent. The tablets dissolved in 10-20 s and displayed satisfactory handling properties. Makino et al. reported a method using water as pore-forming material. A mixture of drug and a carbohydrate (e.g., erythritol, glucose, maltitol, sucrose, xylitol). The water was then removed, yielding highly porous tablets with satisfactory mechanical strength and a high dissolution rate.

#### e. Direct compression

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods. This technique can now be applied to fast dissolving tablets because of the availability of improved tablet excipients, especially tablet disintegrants and sugar-based excipients.

***Addition of disintegrants:***Addition of disintegrants in fast dissolving tablets, leads to quick disintegration of tablets and hence improves dissolution. In many fast dissolving tablet technologies based on direct compression, the disintegrants principally affect the rate of disintegration and hence the dissolution. The introduction so-called superdisintegrants and a better understanding of their properties have increased the popularity of this technology. Tablet disintegration time can be optimized by concentrating the disintegrants. Below critical concentration, tablet disintegration time is inversely proportional to disintegrants concentration. Above the critical concentration level, however, disintegration time remains approximately constant or even increases.

Microcrystalline cellulose, cross linked carboxymethyl cellulose sodium, cross linked polyvinyl pyrrolidone and partially substituted hydroxypropyl cellulose, though water insoluble, absorb water and swell due to capillary action and are considered as effective disintegrants in the preparation of first dissolving tablets.

Bi et al. and Watanbe et al.,used microcrystalline cellulose (MCC) and low substituted hydroxypropyl cellulose (HPC) to manufacture rapidly disintegrating tablets. The ratios of MCC to HPC varied from 8:2 to 9:1. Ito and Sugihan investigated applying agar powder as a disintegrants because the powder absorbs water and swells considerably without forming a gel at physiological temperatures.

Fast disintegration of tablets can also be achieved by incorporating effervescent disintegrating agents, which generates carbon dioxide. This phenomenon also resulted in partial taste masking of unacceptable taste of the drug. The major drawback of effervescent excipients is their hygroscopicity (i.e., the ability to absorb atmospheric moisture). Hence, their manufacture requires control of humidity conditions and protection of the final product. This is reflected by the overall cost of the product.

***Sugar-based excipients:***another approach to fast dissolving tablets by direct compression is the use of sugar-based excipients (e.g., dextrose, fructose, isomalt, maltitok, maltose, mannitol, sorbitol, starch hydrolyse, polydextrose, and xylitol), which display high aqueous solubility and sweetness, and hence, impart taste masking and a pleasing mouthfeel.

#### f.Taste masking

Taste masking is an essential requirement for fast dissolving tablets for commercial success. Taste masking of the active ingredients can be achieved by various techniques.  Drugs with unacceptable bitter taste can be microencapsulated into pH sensitive acrylic polymers42.  Cefuroxime axetil is microencapsulated in various types of acrylic polymers (e.g., Eudragit E, Eudragit L-55 and Eudragit RL) by solvent evaporation and solvent extraction techniques. These polymer microspheres showed efficient taste masking and complete dissolution in a short period. Fine granules of drug and disintegrant (e.g. low substituted hydroxypropyl cellulose) when coated with a water insoluble polymer (e.g. ethylcellulose) masked the bitter taste of sparfloxacin43. The addition of low substituted hydroxypropyl cellulose as disintegrant to the drug in cores, resulted in increased dissolution rate and bioavailability of sparfloxacin compared to its conventional tablets 44.

Ozer and Hincal45 reported a simple coacervation method using gelatin, and anhydrous sodium sulphate as coacervating agent for taste making of beclamide. Beclamide is an anti-epileptic drug with unpleasant taste. It is microencapsulated into gelatin, with sodium sulphate as coacervating agent, and glutaraldehyde as hardening agent. The microcapsules after formation are dehydrated using alcohol. The core: wall substance ratio was 1:1, and the taste could be successfully masked.

A novel technique for taste masking of macrolides (e.g. erythromycin and clarithromycin) is reported by Yajima et al, 46. Monoglycerides having a low melting point which can form good elaborate film, and easily soluble in intestine, and polymers which are insoluble in the mouth (pH 5-8), but are freely soluble in stomach (pH 1-4), are selected for taste masking of drugs with unpleasant taste. The polymer is dissolved or dispersed in monoglyceride, and the drug is granulated with above mixture and the resultant granules are cooled.

#### g.Mass extrusion

This technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby masking their bitter taste.

### Drawbacks of Fast Dissolving tablets prepared by conventional:

#### Hygroscopicity

Several fast dissolving dosage forms are hygroscopic and cannot maintain physical integrity under normal condition from humidity which calls for specialized product packaging.

#### Friability

In order to allow fast dissolving tablets to dissolve in the mouth, they aremade of either very porous and soft- moulded matrices or compressed into tablets with very low compression force, which makes the tablets friable and/or brittle which are difficult to handle, often requiring specialized peel-off blister packaging.

To overcome this problem, some companies introduced more robust forms of fast dissolving tablets.

### Patented Technologies for Fast Dissolving Tablets

Some patented technologies are available. Each technology has a different mechanism, and each fast-dissolving/disintegrating dosage form varies regarding the following:

-Mechanical strength of final product;
-Drug and dosage form stability;
-Mouth feel;
-Taste;
-Rate of dissolution of drug formulation in saliva;
-Swallowability;
-Rate of absorption from the saliva solution; and
-Overall bioavailability.

#### ****a.Zydis Technology****

Using concept of Gregory et al.51 Scherer has patented the Zydis technology. Zydis, the best known of the fast-dissolving/disintegrating tablet preparations, was the first marketed new technology tablet. The tablet dissolves in the mouth within seconds after placement on the tongue. A Zydis tablet is produced by lyophilizing or freeze-drying the drug in a matrix usually consisting of gelatin. The product is very lightweight and fragile, and must be dispensed in a special blister pack. Patients should be advised not to push the tablets through the foil film, but instead peel the film back to release the tablet. The Zydis product is made to dissolve on the tongue in 2 to 3 seconds.The Zydis formulation is also self-preserving because the final water concentration in the freeze-dried product is too low to allow for microbial growth. A major claim of the Zydis product is increased bioavailability compared to traditional tablets. Because of its dispersion and dissolution in saliva while still in the oral cavity, there can be a substantial amount of pregastric absorption from this formulation. Buccal, pharyngeal and gastric regions are all areas of absorption of the Zydis formulation.Any pre-gastric absorption avoids first-pass metabolism and can be an advantage in drugs that undergo a great deal of hepatic metabolism. However, if the amount of swallowed drug varies, there is the potential for inconsistent bioavailability. While the claimed increase in bioavailability is debatable, it is clear that the major advantage of the Zydis formulation is convenience. The amount of drug that could be incorporated should generally be less than 60 mg for soluble drugs. The partical size of the insoluble drugs should be less than 50mm and not more than 200mm to prevent sedimentation during processing52. There are some disadvantages to the Zydis technology. The process of freeze-drying is a relatively expensive manufacturing process. As mentioned earlier, the Zydis formulation is very lightweight and fragile, and therefore should not be stored in backpacks or the bottom of purses. Finally, the Zydis formulation has poor stability at higher temperatures and humidities. It readily absorbs water, and is very sensitive to degradation at humidities greater than 65%.

#### b.Orasolv Technology

OraSolv was Cima's first fast-dissolving/disintegrating dosage form. The OraSolv technology, unlike Zydis, disperses in the saliva with the aid of almost imperceptible effervescence. The OraSolv technology is best described as a fast-disintegrating tablet; the tablet matrix dissolves in less than one minute, leaving coated drug powder. The taste masking associated with the OraSolv formulation is two-fold. The unpleasant flavor of a drug is not merely counteracted by sweeteners or flavors; both coating the drug powder and effervescence are means of taste masking in OraSolv. This technology is frequently used to develop over-the-counter formulations. The major disadvantage of the OraSolv formulations is its mechanical strength. The OraSolv tablet has the appearance of a traditional compressed tablet. However, the OraSolv tablets are only lightly compressed, yielding a weaker and more brittle tablet in comparison with conventional tablets. For that reason, Cima developed a special handling and packaging system for OraSolv. An advantage that goes along with the low degree of compaction of OraSolv is that the particle coating used for taste masking is not compromised by fracture during processing. Lyophilization and high degrees of compression, as utilized in OraSolv's primary competitors, may disrupt such a taste masking approach. The OraSolv technology is utilized in six marketed products. These formulations can accommodate single or multiple active ingredients, and tablets containing more that 1.0 g of drug have been developed. Their disintegration time is less than 30s.The OraSolv formulations are not very hygroscopic.

#### c. Durasolv Technology

DuraSolv is Cima's second-generation fast-dissolving/disintegrating tablet formulation. Produced in a fashion similar to OraSolv, DuraSolv has much higher mechanical strength than its predecessor due to the use of higher compaction pressures during tableting. DuraSolv tablets are prepared by using conventional tabletting equipment and have good rigidity(friability less than that 2%). The DuraSolv product is thus produced in a faster and more cost-effective manner. DuraSolv is so durable that it can be packaged in either traditional blister packaging, pouches or vials.

One disadvantage of DuraSolv is that the technology is not compatible with larger doses of active ingredients, because the formulation is subjected to such high pressures on compaction. Unlike OraSolv, the structural integrity of any taste masking may be compromised with high drug doses. The drug powder coating in DuraSolv may become fractured during compaction, exposing the bitter-tasting drug to a patient's taste buds. Therefore, the DuraSolv technology is best suited for formulations including relatively small doses of active compound54.

#### d.Flash Dose Technology

Fuisz Technologies has three oral drug delivery systems that are related to fast dissolution. The first two generations of quick-dissolving tablets, Soft Chew and EZ Chew, require some chewing. However, these paved the way for Fuisz's most recent development, FlashDose. The FlashDose technology utilizes a unique spinning mechanism to produce a floss-like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the active drug and be compressed into a tablet. This procedure has been patented by Fuisz and is known as Shearform. The final product has a very high surface area for dissolution. It disperses and dissolves quickly once placed onto the tongue.

Flash dose tablets consists of self–binding shearform matrix termed as “floss”. Shearform matrices are prepared by flash heat processing and are of two types.

ØSingle floss or Unifloss, consisting of a carrier, and two or more sugar alcohols, of which one is xylitol.

ØDual floss consists of a first shearform carrier material (termed “base floss”, contains a carrier and at least one sugar alcohol generally sorbitol), and a second shearform binder matrix (“binder floss”, contains a carrier and xylitol).

Interestingly, by changing the temperature and other conditions during production, the characteristics of the product can be altered greatly. Instead of a floss-like material, small spheres of saccharides can be produced to carry the drug. The process of making microspheres has been patented by Fuisz, and is known as CEFORM and serves as an alternative method of taste masking.

#### e.Wowtab Technology

The Wowtab fast-dissolving/disintegrating tablet formulation has been on the Japanese market for a number of years.  Wowtab technology is patented by Yamanouchi Pharmaceutical Co. The WOW in Wowtab signifies the tablet is to be given “With Out Water”. It has just recently been introduced into the U.S. The Wowtab technology utilizes sugar and sugar-like (e.g., mannitol) excipients. This process uses a combination of low mouldability saccharides (rapid dissolutio) and high mouldability saccharide(good binding property).The two different types of saccharides are combined to obtain a tablet formulation with adequate hardness and fast dissolution rate.Due to its significant hardness, the Wowtab formulation is a bit more stable to the environment than the Zydis or OraSolv. It is suitable for both conventional bottle and blister packaging. The taste masking technology utilized in the Wowtab is proprietary, but claims to offer superior mouthfeel due to the patented SMOOTHMELT action. The Wowtab product dissolves quickly in 15 seconds or less55.

#### f. Flashtab Technology

Prographarm laboratories has patented the Flashtab technology56. This technology involves the preparation of rapidly disintegrating tablet which consists of an active ingredient in the form of microcystals. Drug microgranules may be prepared by using the conventional techniques like coacervation, extrusion-spheronization, simple pan coating methods and microencapsulation. The microcrystals of microgranules of the active ingredient are added to the granulated mixture of excipients prepared by wet or dry granulation, and compressed into tablets. All the processing utilized the conventional tabletting technology, and the tablets produced are reported to have good mechanical strength and disintegration time less than one minute.

#### g.Oraquick Technology

The OraQuick fast-dissolving/disintegrating tablet formulation utilizes a patented taste masking technology. KV Pharmaceutical claims its microsphere technology, known as MicroMask, has superior mouthfeel over taste-masking alternatives57. The taste masking process does not utilize solvents of any kind, and therefore leads to faster and more efficient production. Also, lower heat of production than alternative fast-dissolving/disinte-grating technologies makes OraQuick appropriate for heat-sensitive drugs. KV Pharmaceutical also claims that the matrix that surrounds and protects the drug powder in microencapsulated particles is more pliable, meaning tablets can be compressed to achieve significant mechanical strength without disrupting taste masking. OraQuick claims quick dissolution in a matter of seconds, with good taste-masking. There are no products using the OraQuick technology currently on the market, but KV Pharmaceutical has products in development such as analgesics, scheduled drugs, cough and cold, psychotropics, and anti-infectives.

#### h. Quick –Dis Technology

Lavipharm Laboratories Inc. (Lavipharm) has invented an ideal intraoral fast-dissolving drug delivery system, which satisfies the unmet needs of the market(Table 3). The novel intraoral drug delivery system, trademarked Quick-Dis™, is Lavipharm’s proprietary patented technology and is a thin, flexible, and quick-dissolving film. The film is placed on the top or the floor of the tongue. It is retained at the site of application and rapidly releases the active agent for local and/or systemic absorption. The Quick-Dis™ drug delivery system can be provided in various packaging configurations, ranging from unit-dose pouches to multiple-dose blister packages.

The typical disintegration time, which is defined as the time at which the film begins to break when brought into contact with water, is only 5 to 10 seconds for the Quick-Dis™ film with a thickness of 2 mm. The dissolving time, which is defined as the time at which not less than 80% of the tested film is dissolved in aqueous media, is around 30 seconds for Quick Dis™ film with a thickness of 2 mm. The typical release profile of an active ingredient exhibited by a Quick-Dis™ drug delivery system is 50% released within 30 seconds and 95% within 1 minute.

#### i.Nanocrystal Technology

For fast dissolving tablets, Elan's proprietary NanoCrystal technology can enable formulation and improve compound activity and final product characteristics. Decreasing particle size increases the surface area, which leads to an increase in dissolution rate. This can be accomplished predictably and efficiently using NanoCrystal technology. NanoCrystal particles are small particles of drug substance, typically less than 1000 nanometers (nm) in diameter, which are produced by milling the drug substance using a proprietary wet milling technique. NanoCrystal™ Fast dissolving technology provides for:

·Pharmacokinetic benefits of orally administered nanoparticles (<2 microns) in the form of a rapidly disintegrating tablet matrix

·Product differentiation based upon a combination of proprietary and patent-protected technology elements

·Cost-effective manufacturing processes that utilize conventional, scalable unit operations

·Exceptional durability, enabling use of conventional packaging equipment and formats (i.e., bottles and/or blisters)

·Wide range of doses (up to 200mg of API per unit)

·Use of conventional, compendial inactive components

·Employment of non-moisture sensitive inactives

NanoCrystal colloidal dispersions of drug substance are combined with water-soluble GRAS (Generally Regarded As Safe) ingredients, filled into blisters, and lyophilized. The resultant wafers are remarkably robust, yet dissolve in very small quantities of water in seconds. This approach is especially attractive when working with highly potent or hazardous materials because it avoids manufacturing operations (e.g., granulation, blending, and tableting) that generate large quantities of aerosolized powder and present much higher risk of exposure. The freeze-drying approach also enables small quantities of drug to be converted into ODT dosage forms because manufacturing losses are negligible.

### Fast dissolving films

### Mouth dissolving film is a thin film with an area of 5-20 cm2 containing an active ingredient. The immediate dissolution, in water or saliva respectively, is reached through a special matrix from water-soluble polymers. Drugs can be incorporated up to a single dose of 15 mg formulation. Considerations (plasticizers, etc.) have been reported as important factors affecting mechanical properties of the films, such as shifting the glass transition temperature to lower temperature.

**Plasticizers-**

### Formulation considerations (plasticizer, etc.) have been reported as important factors affecting mechanical properties of films. The mechanical properties such as tensile strength and elongation to the films have also been improved by the addition of plasticizers. Variation in their concentration may affect these properties. The commonly used plasticizers are glycerol, dibutylpthallate and polyethylene glycols.

**Manufacturing Methods**

One or a combination of the following processes can be used to manufacture the mouth dissolving films**.**

**1) Solvent casting method:**

In solvent casting method water soluble polymers are dissolved in water and the drug along with other additives is dissolved in suitable solvent then both the solutions are mixed, stirred and finally casted in to the Petri plate, and dried.

**2) Semisolid casting:**

In semisolid casting method firstly a solution of water-soluble film forming polymer is prepared. The resulting solution is added to a solution of acid insoluble polymer (e.g. cellulose acetate phthalate, cellulose acetate butyrate), which was prepared in ammonium or sodium hydroxide. Then appropriate amount of plasticizer is added so that a gel mass is obtained. Finally the gel mass is casted in to the films or ribbons using heat controlled drums. The thickness of the film is about 0.015-0.05 inches. The ratio of the acid insoluble polymer to film forming polymer should be 1:4.

**3) Hot melt extrusion:**

In hot melt extrusion method firstly the drug is mixed with carriers in solid form. Then the extruder, having heaters, melts the mixture. Finally the melt is shaped in to films by the dies. There are certain benefits of hot melt extrusion e.g.:

Fewer operation units, better content uniformity and an anhydrous process.

**4) Solid dispersion extrusion:**

In this method immiscible components are extrude with drug and then solid dispersions are prepared. Finally the solid dispersions are shaped in to films by means of dies.

**5) Rolling Method:**

In rolling method a solution or suspension containing drug is rolled on a carrier. The solvent is mainly water and mixture of water and alcohol. The film is dried on the rollers and cut into desired shapes and sizes**.**

**TECHNOLOGIES**

**1) SOLULEAVES™**technology is used to produce a range of oral delivery films that can incorporate active ingredients, colors and flavors. SOLULEAVES™ films can be designed to dissolve rapidly on contact with saliva, quickly releasing the active ingredients and flavors. This quality makes edible films an excellent delivery method for a large range of products requiring fast release in the mouth. For pharmaceutical uses this method of administration is especially useful for pediatrics or elderly patients who may have difficulty swallowing traditional tablets or capsules.

The delivery system can be used for the cough/cold, gastrointestinal and pain therapeutic areas as well as delivering nutritional products. SOLULEAVES™ films can also be designed to adhere to mucous membranes and to release the active ingredient slowly over 15 minutes.

**2) WAFERTAB™**is a drug delivery system that incorporates pharmaceutical actives into an ingestible filmstrip. The system provides rapid dissolution and release of actives when the strip comes into contact with saliva in the mouth. The WAFERTAB™ filmstrip can be flavored for additionally improved taste masking. The active ingredient is precisely dosed and integrated into the body of a pre-manufactured XGEL™ film, thus preventing exposure to unnecessary heat and moisture and potentially enhancing product stability. The WAFERTAB™ system lends itself to many possibilities for innovative product design, enabling multiple films with different actives to be bonded together. WAFERTAB™ can be prepared in a variety of shapes and sizes and is an ideal method for delivery of medicines, which require fast release or for use by patients who have difficulty in swallowing.

**3) FOAMBURST™**is a special variant of the SOLULEAVES™ technology where an inert gas is passed into the film during production. This results in a film with a honeycombed structure, which dissolves rapidly giving a novel mouth sensation. FOAMBURST™ has attracted interest from food and confectionary manufacturers as a means of carrying and releasing flavors.

**4) XGEL™**film is at the heart of Meldex International's intellectual property, used in all its film systems and its ingestible dosage delivery technologies. XGEL™ film provides unique product benefits for healthcare and pharmaceutical products: it is non-animal-derived, approved on religious grounds and is suitable for vegetarians; the film is GMO free and continuous production processing provides an economic and competitive manufacturing platform. XGEL™ film can be taste masked, colored, layered, and capable of being enteric properties whilst also having the ability to incorporate active pharmaceutical ingredients. The XGEL™ film systems can be made to encapsulate any oral dosage form, and can be soluble in either cold or hot water. XGEL™ film is comprised of a range of different water-soluble polymers, specifically optimized for the intended use.