Chapter-12

ORAL DISINTEGRATING TABLET

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A solid dosage form that dissolves or disintegrates rapidly in oral cavity, resulting in solution or suspension without the need of water is known as fast dissolving tablet or oral dispersing dosage form. Oral disintegrating tablets are also known as mouth dissolving, fast dissolving, rapid- dissolve, rapimelt, fast melts, porous tablets, EFVDAS or Effervescent drug absorption system (Elan corporation), Orosolv (cima labs inc., USA), Zydis (R. P. Scherer, UK) etc. The concept of Fast dissolving drug delivery system (FDDS) emerged from the desire to provide patient with moreconventional means of taking their medication. It is difficult for many patients to swallow tablets and hard gelatin capsules and do not take their medicines as prescribed. The difficulty experienced in particular by pediatrics and geriatrics patients, but this also applies to the patients who are ill in bed or travelling. Other groups that may experience problems using conventional oral dosage form include the mentally sick, developmentally disable and patients who are non-cooperative. Such problems can be resolved by means of oral disintegrating tablets (ODTs). For the above reasons, tablets that can dissolve or disintegrate in oral cavity, have attracted a great deal of attention. Indeed, ODTs are an important and attractive alternative to liquid dosage form. ODTs are not only indicated for people having difficulty in swallowing but also ideal for unfavorable conditions of administrations where water is not available. Syrups are best for pediatrics but they are bulky and drugs are not as stable in liquid form as in solid form like tablets.

To increase the tablet disintegration, super-disintegrants are added in it, which are very helpful toincrease the bioavailability of tablet and to increase the disintegration properties of tablet in saliva. Disintegrants are mainly added in the tablets by three methods. These methods are extra- granular,intra- granular and partially extra-granular and intra-granular method.

To ensure the tablet's fast dissolving attribute, saliva must quickly egress into the tablet matrix tocause rapid disintegration and instantaneous dissolution of the tablet. Maximizing the porous structure of the tablet matrix and incorporating an appropriate disintegrating agents or highly water soluble excipients in the tablet formulation are the basic approaches used in current fast dissolving tablet technologies. Basically, the disintegrant major function is to oppose the efficacy of the tablet binder and the physical forces that act under compression to form the tablet. The mechanism by which tablet is broken down into smaller particles and then produces a homogeneous suspension or solution is based on: (i) Capillary action (ii) High swellability of disintegrants (iii) Capillary action and high swellability (iv) Chemical reaction (Release of Gases).

Bioavailability of a drug depends on absorption of the drug, which is affected by solubility of the drug in gastrointestinal fluid and permeability of the drug across

gastrointestinal membrane. The solubility of drug mainly depends on physio-chemical properties of the drug. However, the rate of drug dissolution is greatly influenced by disintegration of the tablet. The drug will dissolve at a slower rate from a non-disintegrating tablet due to exposure of limited surface are to the fluid.

When we put ODTs on tongue, this tablets disintegrates instantly, releasing the drug, which dissolves or disperses in the saliva. Some drugs are absorbed from the mouth, Pharynx and oesophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form.

USP approved these dosage form as ODTs. EP has used the term orodispersible tablet for tablets that disperse rapidly and within 3 min in mouth before swallowing. United States Food and Drug Administration defined ODTs as " A solid dosage form containing medicinal substances or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon a tongue." The disintegration time for ODTs generally ranges from several seconds to about a min.

Significance

- Improved patient compliance
- Rapid disintegration of tablet result in quick dissolution and rapid absorption, whichprovide rapid onset of action.
- Useful for pediatric, geriatric and psychiatric patients having difficulty in swallowingtablet.
- Pre-gastric absorption of drugs avoids hepatic metabolism, which reduces the dose andincrease the bioavailability.
- Suitable during travelling where water may not be available.

Medications as "Bitter pill" has changed by excellent mouth feel property produced byflavours and sweeteners in ODTs.

Characteristics of ODTs

- A ODT should be dissolve or disintegrate in the mouth (in saliva) within seconds.
- It should not require any liquid or water to show its action.
- Be compatible with taste masking and have a pleasing mouth feel.
- Be portable without fragility concern.
- The excipients should have high wettability, and the tablet structure should also have ahighly porous network.

- It should not leave minimal or no residue in the mouth after oral administration of thetablet.
- It should be less effective by environmental conditions like humidity, temperature etc.
- More rapid drug absorption from the pre-gastric area i.e. mouth, pharynx, and esophaguswhich may produce rapid onset of action.
- Be adaptable and amenable to existing processing and packaging machinery.
- Allow the manufacture of tablets using conventional processing and packagingequipment's at low cost.
- Allow high drug loading.
- Have sufficient strength to withstand the rigors of the manufacturing process and postmanufacturing handling.

Limitations of ODTs

- The tablets usually have insufficient mechanical strength. So, careful handling is required.
- The tablets may leave unpleasant taste and/or grittiness in mouth if not formulatedproperly.
- Drugs with relatively larger doses are difficult to formulate into MDT e.g. antibiotics like ciprofloxacin, amoxicillin with adult dose tablet containing about 500 mg of the drug.
- Patients with Sjorgen's syndrome or dryness of the mouth due to decreased salivaproduction may not be good candidates for these tablet formulations.

Salient feature of Fast Dissolving Drug Delivery System

- Ease of administration to the patient who can't swallow.
- No need of water to swallow the dosage form.
- Rapid dissolution and absorption of the drug, which will produce quick onset of action.
- Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach (pregastric absorption). In such cases bioavailability of drug is increased and improves clinical performance through a reduction of unwanted effects.
- Good mouth feel property.

- The risk of chocking or suffocation during oral administration of conventional formulationdue to physical obstruction is avoided.
- Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing,where an ultra-rapid onset of action required.
- An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, dueto rapid disintegration and dissolution of these tablets.
- Benefit of liquid medication in the form of solid preparation.
- Pregastric absorption can result in improved bioavailability, reduced dose and improvedclinical performance by reducing side effects.
- Pregastric drug absorption avoids the first-pass metabolism; the drug dose can be reducedif a significant amount of the drug is lost through the hepatic metabolism.
- Rapid drug therapy intervention.
- New business opportunities: product differentiation, line extension and life-cyclemanagement, exclusivity of product promotion and patent-life extension.

Criteria for drug selection

- It should not have bitter taste, hence taste masking is required.
- The dose should be less than 20 mg.
- Molecular weight should be small to moderate.
- Should be of good solubility in water and saliva.
- It should have partially non ionized at the oral cavities pH.
- It should have ability to diffuse and partition into the epithelium of the upper GIT (logp >1, or preferably >2).
- Should have extensive first pass metabolism.
- Should have oral tissue permeability.

Challenges in the formulation of ODT

- Mechanical strength and disintegration time: Disintegration time will be delayed if the mechanical strength is strong. So a good compromise between these two parameters is always essential.
- Taste masking: Effective taste masking of the bitter drugs must be done so that the taste ofthe drug is not felt in the oral cavity.
- Mouth feel: The particles generated after disintegration of the ODT should be as small as possible. ODT should leave minimal or no residue in mouth after oral

administration. Moreover, addition of flavors and cooling agents like menthol improves the mouth feel.

- Sensitivity to environmental conditions: ODT generally should exhibit low sensitivity to environment conditions such as humidity and temperature.

Additives Used in ODT formulation

Superdisintegrants: Croscarmellose sodium, crospovidone, carmellose calcium, sodium starch glycolate etc.

Sweetners: Sorbital, mannitol, maltitol solution, maltitol, xylitol, erythritol, sucrose, fructose,maltose, aspartame, glycerin, sugar derivatives etc..

Binders: Binders commonly used are cellulosic polymers such as ethylcellulose, hydroxypropylcellulose (HPC), and hydroxypropylmethylcellulose (HPMC), alone or in admixtures povidones, polyvinyl alcohols, and acrylic polymers. Acrylic polymers used are the ammoniomethacrylate copolymer, polyacrylate, and polymethacrylate.

Antistatic agent: Colloidal silica (Aerosil), precipitated silica (Sylod.FP244), micronized or non-micronized talc, maltodextrins, beta-cyclodextrins, etc.

Lubricants: Magnesium stearate, stearic acid, leucine, sodium benzoate, talc, magnesium lauryl sulphate etc.

Flavours: Peppermint flavour, clove oil, anise oil, eucalyptus oil, vanilla, citrus oils, fruit essences etc.

Fillers: Directly compressible spray dried mannitol, Sorbitol, xylitol, calcium carbonate, magnesium carbonate, calcium phosphate, pregelatininized starch, magnesium trisilicate, aluminium hydroxide etc.

Surface active agents: Sodiumdoecylsulfate, SLS, Tweens, Spans, polyoxyethylene stearate etc.

Technologies for manufacturing MDTs: The technologies used to manufacture mouth dissolving tablets can be classified as below varioustechnologies used to manufacture of FDTs include (**Table 12.1**).

Table 12.1: Technologies used for manufacturing MDTs

Technologies	
Conventional technologies	**Patented technologies**
Freeze drying	Zydus technology
Sublimation	Orasolv technology
Spray drying	Durasolv technology
Moulding	Wowtab technology
Mass extrusion	Flashdose technology
Direct Compression	Flashtab technology
Cotton-candy process	Oraquick technology
Nanotization	Pharmabust technology
Fast dissolving Films	Nanocrystal technology
Melt granulation	Frosta technology
Phase transition Process	Despersible technology

Conventional manufacturing techniques for MDTsLyophilization or freeze-drying

Freeze-drying, also known as lyophilization, or cryodesiccation, in this method water is sublimatedfrom the product after freezing. This technique creates an amorphous porous structure that can dissolve rapidly. The active drug is dissolved in an aqueous solution of a carrier. Then the mixtureis dosed by weight and poured into the wells of the preformed blister packs. The trays holding theblister packs are passed through a liquid nitrogen freezing tunnel to freeze the drug solution or dispersion. Then the frozen blister packs are placed in refrigerated cabinets to continue the freeze- drying. After freeze-drying, the aluminum foil backing is applied on a blister-sealing machine. Finally, the blisters are packaged.

The major disadvantage of lyophilization technique is high cost of equipment and processing. Other disadvantages include lack of resistance necessary for standard blister packs of the final dosage forms.

Moulding

Moulded tablets are designed to facilitate the absorption of active ingredients through mucosal linings of mouth. In this method, tablet disintegrates and dissolves rapidly due to the presence of water-soluble ingredients. Moistened powder blend is molded in to tablet using compression pressure lower than used in conventional tablet`s compression. Then the solvent is removed by air-drying. Moulded tablets have a porous

structure that enhances dissolution. The two major problems with molding are less mechanical strength and poor taste masking.

Sublimation

In this technique, highly volatile ingredients like ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, naphthalene, urea, etc., are added that volatilize readily, to other tablet excipients and the mixture is then compressed in to tablets. Volatile material is then removed via sublimation, leaving behind a highly porous matrix. These compressed tablets which have high porosity (approximately 30%) rapidly dissolved within 15 seconds in saliva.

Direct compression

It is the easiest and most popular method to manufacture tablets by using conventional equipments. In this method, tablets are compressed directly from the mixture of the drug and excipients. This technique can now be applied to fast dissolving tablets because of the availability of improved tablet excipients (superdisintegrants) and sugar based excipients. This technology is cost-effective and easy to implement at the industrial level.

Spray drying

In this technique, processing solvent is evaporated rapidly and can produce highly porous and fine powder, which was compressed into tablets. Hydrolyzed and non-hydrolyzed gelatin used as a supporting agent for the matrix, mannitol as a bulking agent and sodium starch glycolate or crosscarmellose as a disintegrant. Tablets manufactured by this method shows disintegration time < 20 sec in an aqueous medium.

Mass extrusion

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

Nanonization

Nanomelt technology has been recently developed method, which involves the reduction in the particle size of drug to nano size by wet-milling technique. Surface adsorption of the nano crystals of the drug is done on selected stabilizers for stabilizing them against agglomeration, which are then incorporated into MDTs. This technique is

mainly advantageous for poor water soluble drugs and Other advantages of this technology include fast disintegration/dissolution of nanoparticles leading to increased absorption and hence higher bioavailability and reduction in dose, cost effective manufacturing process, conventional packaging due to exceptional durability and wide range of doses.

Melt granulation

In this process, MDTs can be prepared by incorporating a hydrophilic waxy binder (super polystate) PEG-6-stearate. Super polystate is a waxy material with a melting point of 33-37 °C and a hydrophilic- lipophilic balance of 9. It not only acts as a binder and increases the physical resistance of tablets, but also helps in the disintegration of tablets as it melts in the mouth and solubilizes rapidly leaving no residue. Super polystate was incorporated into the formulation of MDTs by melt granulation method where granules are formed by the molten form of this material.

Patented technologies for preparation of MDTsZydis technology

Zydis formulation was first marketed and fast disintegrating tablet preparation`s technique in which the tablet dissolves in the mouth within seconds after placement of the tongue. It is a unique freeze dried tablet in which drug is physically entrapped or dissolved within the matrix of fast dissolving carrier material. When Zydis units are put to the mouth, the freeze-dried structure disintegrates instantaneously. To provide strength and resilience to tablet`s polymers such as gelatin, dextran or alginates are incorporated with it which also from glossy amorphous structure. Saccharides such as Mannitol or sorbitol are incorporated to obtain crystallinity, elegance and hardness. Water is used for the manufacturing process to ensure production of porous units to achieve rapid disintegration while various gums are used to prevent sedimentation of dispersed drug particles during the manufacturing process.

The major advantage of Zydis formulation is that 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. Zydis products are packed in blister packs to protect the formulation from moisture to the environment.

Limitation of Zydis formulation is that the particle size of the insoluble drugs should not be less than 50 µm and not more than 200 µm to prevent sedimentation during processing, and the amount of drugs could be incorporated should generally be less than 400 mg for insoluble drugs and less than 60 mg for soluble drugs. There are some disadvantages of Zydis technology. The process of freeze drying is a relatively

expensive manufacturing process. The Zydis formulation has poor stability at higher temperatures and humidity. It readily absorbs water, and is very sensitive to degradation at humidity greater than 65%.

Orasolv Technology

Orasolv formulation has been developed by CIMA labs. In this system, active medicament is taste masked in two-fold. It also contains effervescent disintegrating agent. Tablets are made by direct compression technique, low compression force in order to minimize oral dissolution time. Soft and friable tablets produced by Conventional blenders and tablet machine, and the tablet matrix dissolve in less than one minute.

The advantage of Orasolv Technology is that the formulations are not very hygroscopic, and it also provides a distinct, pleasant sensation of effervescence in the mouth. The major disadvantage of the Orasolv formulations is its Poor mechanical strength and Manufacturing require a controlledenvironment at low relative humidity.

Durasolv technology

Durasolv is the patented technology of CIMA labs. The tablets made by this technology consist ofa drug, fillers and a lubricant. In this system, active medicament is taste masked. It also contains effervescent disintegrating agent. 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 tableting equipment and have good rigidity (friability less than that 2%). The DuraSolv product is thus produced in a faster and more cost-effective manner. 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.

Wowtab technology

Wowtab Technology is patented by Yamanouchi Pharmaceutical Co. WOW means "Without Water ". In this process, combination of low mouldable and high mouldable saccharides is used to obtain a rapidly melting, strong tablet. The active ingredient is mixed with a low mouldability saccharide (e.g. lactose, glucose, and mannitol) and granulated with a high mouldability saccharide (e.g. Maltose, oligosaccharides) and compressed into the table.

Tablets formulated by Wowtab technology offers the superior mouth feel due to the smooth melt action and suitable for both conventional bottle and blister packaging.

Flash dose technology

Flash does technology has been patented by Fuisz. This technology is based upon the preparation of sugar based matrix known as floss, which is made from a combination of excipients either alone or in combination of drugs by flash heat processing. Tablets are made by direct compression technique. The final product has a very high surface area for dissolution. It disperses and dissolves quickly once placed on the tongue. Interestingly, by changing the temperature and other conditions during production, the characteristics to the product can be altered greatly.

Flashtab technology

Ethypharm, Saint Cloud, France has patented the Flashtab technology. Tablets formulated by this technology consist of an active ingredient in the form of micro crystals. Drug micro granules maybe prepared by using the conventional techniques like coacervation, micro encapsulation, and extrusion spheronisation. Reticulated polyvinyl pyrrolidine or carboxy methylcellulose is used as disintegrating agents and carboxy methylcellulose, starch, modified starch, microcrystalline cellulose, carboxy methylated starches, etc are used as Swelling agents. All the processing utilized the conventional tableting technology, and the tablets produced have good mechanical strength and disintegration time less than one minute. All the processing utilized conventional tableting technology.

Oraquick technology

The OraQuick fast dissolving/disintegrating tablet formulation is patented by K.V Pharmaceuticals. It utilizes taste masking microsphere technology called as micro masking which does not utilize solvents of any kind, which provides superior mouth feel, significant mechanical strength, and quick disintegration/dissolution of product, therefore, leads to faster and more efficient production. Lower heat of production than alternative fast dissolving/disintegrating technologies make OraQuick appropriate for heat sensitive drugs.

Ziplets/Advatab technology

This technology is patented by passano con Barnago, Italy. It utilizes water-insoluble ingredient combined with one or more effective disintegrants. AdvaTab tablets disintegrate rapidly in less than 30 seconds. These tablets are prepared using polymer-coated drug particles that are uniformly dispersed in an ultra-fine, low-water content, rapidly disintegrating matrix with superior organoleptic properties. AdvaTab tablets are compressed using a proprietary, patented, external lubrication system in which the

lubricant is applied only to the tablet surface, resulting in robust tablets that are hard and less friable and can be packaged in bottles or blister.

Lyoc technology

Lyoc technology is patented by pharmalyoc. Oil in water emulsion is prepared and placed directly into blister cavities followed by freeze-drying. Non-homogeneity during freeze drying is avoided by incorporating inert filler to increase the viscosity finally the sedimentation. High proportion of filler reduces porosity of tablets due to which disintegration is lowered.

Pharmaburst technology

Pharmaburst technology is patents by SPI Pharma, New Castle. It utilizes the coprocessed excipients to develop MDTs, which dissolves within 30-40 s. This technology involves dry blending of drug, flavour, and lubricant followed by compression into tablets. Tablets obtained have the sufficient strength, so they can be packed in blister packs and bottles.

Nanocrystal technology

Nanocrystal technology is patented by Elan, King of Prussia. Nanocrystal Technology which includes lyophilization of colloidal dispersions of drug substance and water soluble ingredients filled into blister pockets. This method avoids the manufacturing process such as granulation, blending and tableting which is more advantages for highly potent and hazardous drugs.

TASTE MASKING

Taste of a pharmaceutical product is important parameter governing compliance. Bitter tasting drugs, drugs with an objectionable odour, or drugs that are sensitive to oxygen or atmospheric moisture may require encapsulation or entrapment prior to compression. Hence taste masking of oral pharmaceuticals has become important tool to improve patient compliance and the quality of treatment especially in pediatrics. Hence formulation of taste masked products is a challenge to the pharmacist.

As more than 50% of pharmaceutical products are administered orally, undesirable taste is one of the important formulation problems that can be encountered with certain drugs. Oral administration of bitter drugs with acceptable level of palatability is a key issue for health care providers especially with paediatrics and geriatric patient. Thus elimination or reduction of bitterness is an important issue during design of oral pharmaceutical formulations.

An ideal taste masking process and formulation should have the following properties:

- ✓ Rapid and easy to manufacture.
- ✓ Involves least number of equipment.
- ✓ Require minimum number of excipient for an optimum formulation.
- ✓ Has no adverse effect on drug bioavailability.
- ✓ Requires excipient that is economical and easily available.
- ✓ Least manufacturing cost.

A major component of success in orally disintegrating tablets (ODT) is good taste. If the product does not taste good, ODT formulations are emerging and gaining popularity in the industry and have a significant impact on patients of all ages. ODT dissolve or disintegrates in the oral cavity in a relatively short time and do not need to be swallowed with water. This has made taking medication easier, especially for children and the elderly who have traditionally had difficulties in swallowing more conventional dosage forms. The single most significant issue with ODT is the bitterness of the drug that can be exposed and combining this with the right flavours/sweetness levels will result in a superior product.

Taste masking is defined as perceived reduction of an undesirable taste that would exist. The ideal solution to reduce or inhibit bitterness is the discovery of a universal inhibitor of all bitter tasting substances that does not affect the other taste modalities such as sweetness or saltiness. Informal taste tests with different flavours have shown that age is also significant in taste preference. Younger people likes flavour like tutti- fruity and chocolate. Older generations typically prefer more traditional flavours, such as orange or mint. The indication can also play a part in flavour.

Mouth feel

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 flavours 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 flavour.

Methods of Taste Masking

- ✓ Various techniques available for masking bitter taste of drug include:
- ✓ Taste masking with ingredients such as flavours, sweeteners and amino acids

- ✓ Taste masking by polymer coating
- ✓ Inclusion Complexes with β-Cyclodextrin Derivative
- ✓ Taste masking by ion exchange resins
- ✓ Miscellaneous taste masking technologies
- ✓ Taste masking with ingredients such as flavours, sweeteners and amino acids.

Addition of flavours and sweeteners is the simplest approach for taste masking especially in paediatric formulation. However, this approach is not very successful for highly bitter and highlywater soluble drugs.

Discovery of the flavouring agent best suited to mask an unpleasant taste is often a very empirical matter. Experience and experimentation have produced some general guidelines regarding the type of flavour best suited to mask a given taste. Number of Pharmaceuticals like dentifrices and mouthwashes applied to oral cavity elicits co-pleasant taste perception. Menthol reduces the bitter taste and gives a low calorie formulation with beneficial anti- caries effect. Clove oil has been found to be a good taste and anaesthetic effect. To support the taste masking capabilities of clove, vanilla, flavouring agents.

Sweeteners: Aspartame is a prominent sweetener for bitterness reduction. A concentration of as small as 0.8% was effective in reducing the bitterness of a 25% formulation of acetaminophen. Artificial sweeteners like neohesperidine dihydrochalone which is a bitterness suppressor and flavour modifier, elicits a very intense sweet taste. Vitamins containing oral solutions are rendered bitterness free by adding sugars, amino acids and apple flavours.

Taste masking by polymer coating

Coating is an extremely useful technique for a number of applications, but its major application is in masking the unpleasant taste. Various inert coating agents can be used to coat bitter drugs. They include starches; polyvinyl pyrrolidones (povidone) of various molecular weights, gelatin, methylcellulose, hydroxymethylcellulose, microcrystalline cellulose and ethyl cellulose. One of the most efficient methods of drug particle coating is the fluidized bed coating. Increasing the length of coating cycle can increase coating thickness.

Inclusion Complexes with β- Cyclodextrin Derivative

In inclusion complex formation, the drug molecule fits into the cavity of a complexing agent, i.e., the host molecule, forming a stable complex. The complexing agent is capable of masking the bitter taste of drug either by decreasing its oral solubility

on ingestion or decreasing the amount of drug particles exposed directly to taste buds, thereby reducing the perception of bitter taste. This method is most suitable only for low dose drugs. Vander-walls forces are mainly involved in inclusion complexes. β-Cyclodextrin is the most widely used complexing agent for inclusion typecomplexes. It is a sweet, nontoxic, cyclic oligosaccharide obtained from starch. The strong bitter taste of carbetapentane citrate was reduced to approximately 50% by preparing a 1:1 complex with β-Cyclodextrin. Palatable ibuprofen solutions are prepared by forming inclusion complexes with Hydroxy Propyl β-Cyclodextrin respectively. The complex masked the bitter component but created a sore taste that was masked by sweeteners.

Taste masking by Ion- Exchange Resins

Ion exchange resins are solid and suitably insolubilized high molecular weight polyelectrolytes that can exchange their mobile ions of equal charge with the surrounding medium reversibly and stiochiometrically. They are available in desired size ranges. Bitter cationic drugs can get adsorbed on to the weak cation exchange resins of carboxylic acid functionally to form the complex whichis not bitter. Further resinates can be formulated as lozenges, chewing gum, suspension, or dispersible tablet and mask the taste.

Drug can be bound to the resin by either repeated exposure of the resin to the drug in prolonged contact of resin with the drug solution. Drugs are attached to the oppostively charged resin substrates or resinates through weak ionic bonding so that dissociation of the drug- resin complex does not occur under salivary pH conditions. This suitably masks the unpleasant taste and odoursof the drugs.

Chemical means: Chemical modifications such as use of insoluble pro-drug have been reported for masking or reducing the bitterness of compounds. Salt preparation is one of the classical approaches to mask the taste of the bitter drugs by either decreasing solubility or by increasing hydrophobicity and thereby reducing contact of bitter drugs with the tastebuds. Aspirin tablets are rendered tasteless by making magnesium salt of aspirin D- chlorpheniramine maleate was also taste masked salt of chlorpheniramine. The alkyloxyallyl carbonates of clarithromycin have remarkably altered bitterness when administered orally.

Microencapsulation: Microencapsulation as a process has been defined by Bokan as a means of applying relatively thin coating to small particles of solid, droplets of liquid and dispersion. This process can be used for masking the bitter tasting drugs, microencapsulating drug particles with various coating agents. Coating agents employed includes gelatin, povidone, hydroxyl propyl methyl cellulose, ethyl cellulose,

bees wax, carnauba wax, acrylics and shellac. Bitter tasting drugs can first be encapsulated to produce free flowing microcapsules, which can then be blended with other excipient and compressed into tablets. Microencapsulation can be accomplished by variety of methods including air suspension, coacervation phase separation, spray drying, congealing, pan coating, solvent evaporation and multi orifice centrifugation techniques.

Multiple Emulsion: A novel technique for taste masking of drugs employing multiple emulsions have been prepared by dissolving drug in the inner aqueous phase of w/o/w emulsion under conditions of good shelf stability. The formulation is designed to release the drug through the oil phase in the presence of gastrointestinal fluid.

Using Liposomes: Another way of masking the unpleasant taste of therapeutic agent is to entrap them into liposomes. For example, incorporating into liposomal formulation prepared with phosphatidyl choline masked the bitter taste of chloroquine phosphate.

Spray drying: Spray dryig process mainly involves five steps

Concentration: Feedstock is normally concentrated prior to introduction into the spray dryer.

Atomization: The atomization stage creates the optimum condition for evaporation to a dried product having the desired characteristics.

Droplet-air contact: In the chamber, atomized liquid is brought into contact with hot gas, resulting in the evaporation of 95% + of the water contained in the droplets in a matter of a few seconds.

Droplet drying: Moisture evaporation takes place in two stages-

During the first stage, there is sufficient moisture in the drop to replace the liquid evaporated at the surface and evaporation takes place at a relatively constant rate.

The second stage begins when there is no longer enough moisture to maintain saturated conditions at the droplet surface, causing a dried shell to form at the surface. Evaporation then depends on the diffusion of moisture through the shell, which is increasing in thickness.

Separation: Cyclones, bag filters, and electrostatic precipitators may be used for the final separation stage. Wet scrubbers are often used to purify and cool the air so that it can be released to atmosphere.

Figure 12.1: Image of Spray dryer at our research lab.

Design and critical elements of spray drying

Atomizers

The important component of any spray dryer is the atomizer, small in size, installing the right atomizer is essential to spray drying success (**Figure 12.1**). The atomizer must fulfill several important functions which are summarized below:

It must disperse the feed material into small droplets, which should be well distributed within the dryer and mixed thoroughly with the hot gas.The droplets produced must not be so large that they are incompletely dried, nor sosmall that product recovery is difficult. Small particles may also overheat and become scorched.

The atomizer must also act as a metering device, controlling the rate at which the material is fed into the dryer:

- ✓ Air atomization or two fluid nozzles
- ✓ Airless atomization nozzles
- ✓ Pressure nozzles
- ✓ Rotary or disk nozzles
- ✓ Ultrasonic nozzles
- ✓ Air flow

Co-current flow: in a co- current dryer, the spray is directed into the hot air enteringthe dryer and both pass through the chamber in the same direction.

Counter-current flow: in this dryer design, the spray ant the air are introduced at opposite ends of the dryer, with the atomizer positioned at the top and the air entering at the bottom.

Mixed flow: dryers of this type combine both concurrent and counter current flow.In a mixed flow dryer, the air enters at the top and the atomizer is located at the bottom.

Spray drying chamber: Air within the chamber maintains a flow pattern, preventing deposition of partially dried product on the wall or atomizer. Air movement and temperature of inlet air influence the typeof final product.

Critical parameters of spray drying

Inlet temperature of air: Higher the temperature of inlet air, faster is the moisture evaporation but the powder is subjected to higher temperature, which may distort the chemical/physical properties of heat sensitive product.

Outlet temperature of air: It governs the sizing of powder recovery equipments`, higher is the outlet air temperature, larger will be the size of powder recovery equipment and conveying ducts and plenums. Outletair temperatures control final moisture content of powder.

Viscosity: High viscosity hinders correct drop formation. As the viscosity is lowered, less energy or pressure is required to form a particular spray pattern.

Solid content: Care must be taken with high solid loading (above 30%) to maintain proper atomization to ensure correct droplet formation.