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Review Article

**REVIEW OF FAST DISSOLVING TABLETS CONTAINING
SOLID DISPERSION OF CYCLOSPORINE****Prof. Tanvir .Y. Shaikh, Mr. Bhavesh .R. Nhayade, Dr. Bharat .V. Jain,
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Chopda - 425107**Abstract:**

The concept of solid dispersion was proposed by Sekiguchi and Obi in the early 1960's, who investigated the generation and dissolution performance of eutectic, melts of a sulfonamide drug and water soluble carrier. Solid dispersion represents a useful pharmaceutical method for increasing the dissolution, absorption and therapeutic efficacy of the drug in the dosage forms. In present study was an attempt was made to develop fast dissolving tablets containing solid dispersion of Cyclosporine by using PVP K30 as a carrier and croscarmellose sodium as a perdisintegrants. From data obtained from formulation and evaluation of dissolving tablet, following conclusions were made:.

Keywords: Solid Dispersion, Cyclosporine, Fusion method

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1. INTRODUCTION:

The effectiveness of drug is depending upon the ability of the dosage form to deliver the medicament to its site of action at a rate and amount sufficient to elicit the desired pharmacological response. This property of dosage form is referred to as physiologic availability, biologic availability or simply bioavailability. Thus the term bioavailability is defined as the rate and extent of unchanged drug from its dosage forms.[1] The In-vivo performance of orally administered drugs depends upon their solubility and tissue permeability characteristics. BCS is a scientific framework for classifying drugs substances according to their aqueous solubility and permeability. BCS guidelines are provided by U.S. Food and Drug Administration (USFDA), world Health Organization (WHO), European Medicines Agencies (EMA). According to BCS classification, drug substances are grouped into four major classes

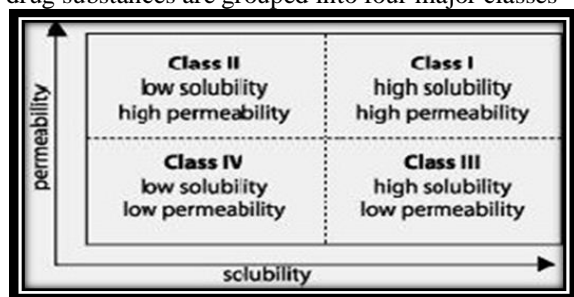


Fig. No. 1: The Bio pharmaceuticals Classification System

a. Class I: (High Solubility, High Permeability)

Drugs under this class are well absorbed and their absorption rate is higher than excretion. The rate limiting step is dissolution and if drug dissolution is very rapid then gastric emptying time is rate limiting step

Example: verapamil, Metoprolol, Diltiazem

b. Class II: (Low solubility, High Permeability)

The bioavailabilities of these drugs are depending upon solvation rate. Absorption rate of class II drug is slower than class I drugs.

Example: Ketocanazole, Mefenamic acid, Itraconazole

c. Class III: (High solubility, low permeability)

The absorption is limited by the permeation rate but the drug is solvated very fast. The drug exhibits high variation in rate and extent of drug absorption.

Example: Cimetidine, Captopril

d. Class IV: (Low solubility, low permeability)

These compounds have poor bioavailability and not good to be absorbed to entire gastrointestinal tract
Example: Hydrochlorothiazide, taxol[2]

The rate limiting step for bioavailability and absorption of active pharmaceutical ingredients are release of medicament from its dosage forms or drug permeation through the biological membrane. Drugs having high solubility and high permeability (class I), release from dosage forms occur very rapidly then gastric emptying time will be a rate limiting step for drug absorption. Whereas drugs having low solubility and high permeability (class II), release from dosage forms occur slowly. In-vivo drug dissolution is rate limiting step for absorption of class II drugs. Class II drugs exhibited variable bioavailability and need enhancement of dissolution so as to increase drug bioavailability. There are various methods of enhancement of bioavailability.

1.1 Methods of enhancing dissolution:

- Use of surfactant
- Complexation
- By making the pro drug
- Use of selected polymeric forms
- Use of solvates and hydrates
- Use of salt of weak acids and weak bases

1.1.1 Methods of enhancing dissolution by increasing surface area

- Micronisation
- Solid dispersion
- Solid disposition

For class III drugs permeation through intestinal membrane is rate limiting step for drug absorption. Drugs under these class showed low bioavailability and need enhancement in permeability.

Class IV drugs exhibit variable and poor bioavailability. Different factors such as dissolution rate, permeability, and gastric emptying time forms rate limiting steps for the drug absorption. [3]

1.2 BCS class boundaries:

Class boundary parameters i.e. permeability, solubility, and dissolution, are for easy identification of BCS class

1) Solubility: A drug substance is considered highly soluble when the highest dose strength is soluble in 250ml or less of water over pH range of 1-7.5 at 37°C.

2) Permeability: A drug substance considered highly permeable when the extent of absorption in human is greater than 90% of administered dose

depend upon massbalance or compared with intra venous reference dose.

3) Dissolution: A drug substances is considered fast dissolving when 85% or more of the labeled amount of drug substance dissolved within 30 min using USP apparatus 1 or 2 in a volume of 900 ml or less of buffer solution. [4]

Oral route is the most common route of drug administration because of ease of ingestion and convenience in self-administration as compared to other route of administration .The oral bioavailability is depend upon various factors including aqueous solubility , permeability of drug, dissolution rate , first pass metabolism, pre -systemic metabolism . The most frequent cases of low oral bioavailability are due to poor solubility and low permeability. When an active agent is administered by oral route, initially it dissolve in gastric or intestinal fluid further there is partitioning of drug particles between fluid and membrane of GI tract and finally it enter into systemic circulation. Therefore for poorly soluble drugs (class II) dissolution is rate limiting step of drug absorption. Approximately 60 % of new drug chemical molecules and several existing drug molecules are lipophilic in nature and low aqueous solubility. [1, 5].

There are various conventional methods that have commonly used to overcome drawback related to poor solubility and enhance their bioavailability. Salt formation, use of surfactant, complexation, particle size reduction etc are commonly used methods to increase dissolution rate and thereby oral absorption and bioavailability of poorly water soluble drugs; however there are substantial limitations with each of these techniques. In above techniques like salt formation is not suitable for neutral compounds. Solubilization of drug in organic solvents or in aqueous media leads to a formation of liquid formulation which is undesirable from the view of commercialization and patient's convenience. In case of particle size reduction by grinding or by controlled crystallization may create a problem. The use of very fine powders is a dosage form may also be problematic because of poor wettability and poor handling. [6] Solid dispersion method has come to existence to eliminate many of the limitations.

Formulation of drug as solid dispersions offers a variety of processing and excipients options that allow for flexibility when formulating oral delivery system for poorly water soluble drugs. When solid dispersion exposed to aqueous media and the carrier dissolved, the drug was released as very fine, colloidal particles. Due to enhanced surface area in this way, the dissolution rate and bioavailability of

poorly water soluble drugs were expected to be high. [7]

1.3 Solid Dispersion:

The concept of solid dispersion was proposed by Sekiguchi and Obi in the early 1960's, who investigated the generation and dissolution performance of eutectic, melts of a sulfonamide drug and water soluble carrier. Solid dispersion represents a useful pharmaceutical method for increasing the dissolution, absorption and therapeutic efficacy of the drug in the dosage forms.

The concept of solid dispersion refers to a group of solid products consisting of at least two different components, generally a hydrophilic matrix and a hydrophobic drug.

1.3.1 Classification of solid dispersion:

- a. Simple eutectic mixture
- b. Solid solution
- c. Glass solution
- d. Amorphous precipitation in crystalline carrier
- e. Complex formation

a. Simple eutectic mixture:

A simple eutectic mixture is an intimately blended physical mixture of two crystalline components, which are miscible in the liquid state, but immiscible in solid state. A mixture of components A and B with composition E is cooled then A and B crystallize out simultaneously. Whereas when other composition is cooled, one of the components starts to crystallize out before the other.

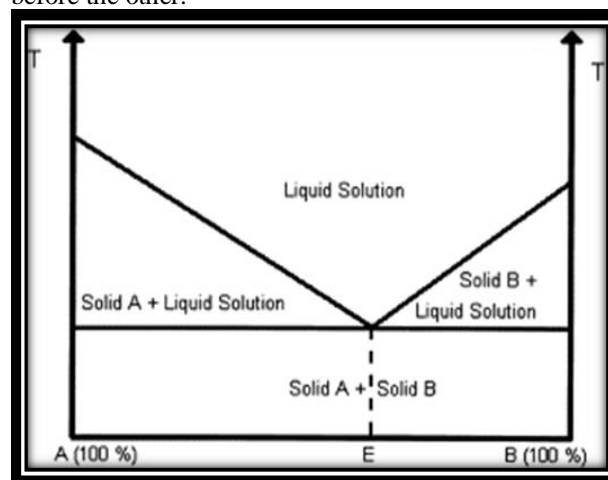


Fig. No. 2: Phase diagram for simple eutectic mixture

b. Solid solution:

Solid solution consists of a solid solute particles dissolved in a solid solvent. The particle size is reduced up to molecular level. When the drug is

dispersed in the carrier matrix, its effective surface area is significantly higher and hence the dissolution rate is enhanced.

Solid solution has improved physical stability of amorphous drug by inhibiting drug crystallization by reducing molecular mobility. Solid solution is classified into sub types are as follow: Depending upon their miscibility characteristics –

- i. Continuous solid solution
- ii. Discontinuous solid solution

Depending upon by the in which solute/solvent molecules are distributed in the lattice

- i. Interstitial solid solution
- ii. Substitutional or amorphous solid solution

i. Continuous solid solution:

In a continuous solid solution, the components are miscible with another in all proportion in both liquid and solid state. The lattice energy of the continuous solid solution at all compositions is higher than that of the respective pure components in the solid state, because the heteromolecular bonding strength is higher than the homomolecular one in order to form a continuous solid solution.

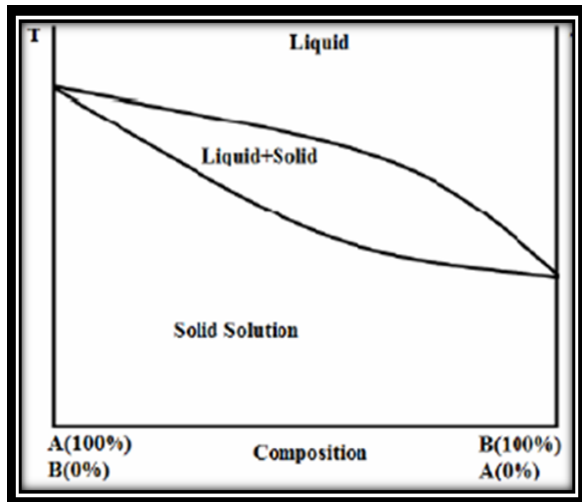


Fig. No. 3: Phase diagram for Continuous solid solution

ii. Discontinuous solid solution:

In this class, the miscibility or solubility of one component in the other is limited. α and β shows the regions of true solid solutions. The region α is a solid solution of B in A that is component A as the solvent and B as the solute. Similarly the region β is a solid solution of A in B. Below a certain temperature, the mutual solubility of the two components start to decrease

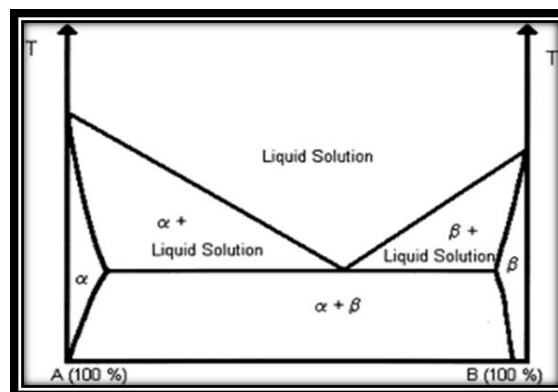


Fig. No. 4: Phase diagram for discontinuous solid solution

iii. Interstitial solid solution:

In interstitial solid solutions the dissolved drug molecules occupy the interstitial spaces between the solvent molecules in the solvent crystal lattice.

iv. Substitutional solid solution:

In the substitutional solid solution the solute molecule are dispersed molecularly but irregularly within an amorphous solvent lattice

c. Glass solution:

Glass solution is an amorphous, homogeneous solution system in which a glassy or a vitreous form of the carrier solubilises drug molecules. The glassy or vitreous state characterizes by transparency and brittleness below the glass transition temperature (T_g). The advantage of glass solution over the solid solution is that they do not possess a strong lattice like a solid solution so that they do not present this barrier to rapid dissolution. The main disadvantages of glass solution is that the glassy state is metastable as compared to crystalline state, and depending upon its physicochemical properties and storage conditions a glass can convert into a crystalline solid

d. Amorphous precipitation in a crystalline carrier:

Instead of simultaneous crystallization of the drug and the carrier, the drug may also precipitate in an amorphous form in the crystalline forms of the drug.

e. Complex formation:

In the complex formation, a drug forms a complex with water soluble carrier in the solid state. The availability of drug is depend on the stability constant of the complex, solubility and the absorption rate of the drug. Due to formation of water soluble complex, dissolution rate and oral absorption of drug is enhanced. Example – cyclodextrin [8]

1.4. Carriers used in the solid dispersion:

Carriers are the substances which are soluble and dissolve in water at a fast rate, are widely used in pharmaceutical formulations to enhance dissolution of drugs.

a. Polyethylene Glycol:

Range of 200 – 300000. Their water solubility is good but generally decreases with increasing molecular weight. They have good solubility in organic solvents. The melting point of PEGs are lies under 650c. These relatively low melting points are advantageous for the preparation of solid dispersion by melting method.

b. Poly vinyl pyrrolidone:

Polymerization of vinyl pyrrolidone forms poly vinyl pyrrolidone (PVP) of molecular weight ranging 2500 – 3000000. They can be classified according to the K value. They have good water solubility and in organic solvents. Therefore, They are particularly suitable for preparation of solid dispersion by solvent evaporation method. The chainlength of PVP greatly influence on dissolution rate of drug dispersed in a solid dispersion. The water solubility and viscosity of PVP becomes lower with increasing chain length.

c. Urea

Urea is the end product of human protein metabolism, has diuretic effect and non toxic. Its solubility in water is greater than 1 in 1 and it also exhibit good solubility in many organic solvents. Urea is not often used as carrier now days.

d. Sugars:

Sugars and related compounds are highly water soluble. The melting point of many sugars is high, so that making solid dispersions by melting method is problematic. Solubility of sugars in organic solvents is poor. Due to these drawbacks they are less suitable carrier than other carriers for the manufacturing of solid dispersion. Despite these limitations several attempts to prepare solid dispersion by using sugars like lactose, mannitol, chitosan, sorbitol etc.

e. Cellulose derivatives:

Cellulose is naturally occurring polysaccharides. They consists of high molecular weight unbranched chains, in which the saccharides units are linked together by β -1, 4-glycoside bonds. The cellulose can be derivatized to form methyl cellulose, hydroxypropyl cellulose, and other semi synthetic cellulose by appropriate alkylation.

f. Eudragits (Polyacrylates and polymethacrylates):

Polyacrylates and polymethacrylates are glassy substances that are produced by the polymerization of acrylic and methacrylic acid and derivatives of these polymers such as esters amides and nitriles. Commonly they are referred by trade name Eudragit. Among all the Eudragits, Eudragit E is used to improve release rate of poorly soluble drugs

g. Emulsifiers:

By improving wetting characteristics and solubilisation of drug, emulsifying agents can be used as carriers. Due to potential toxicity problems emulsifying agents are used in combination with another carrier. Examples – tween 20, polysorbate 80, Myrj 52, pluronic F 98, Gelucire® 44/14

1.5. Method of preparation of solid dispersion:

Various preparation methods of solid dispersions are as follows

a. Fusion method:

The fusion method also called as the melt method. In this method, the melting phase consists of suspended active drug in a previously melted carrier mass, instead of using both drug and carrier in the melted state, therefore reducing the process time and temperature. After cooling, the obtained mixture must be pulverized regarding further use. This method is less difficult technically. However, the use of high temperature, several drugs can be degraded during melting process can be a limitation of this method.

Another limitation of method is incomplete miscibility of drug and carrier. To avoid this limitation several modification were introduced to the original method like hot stage extrusion method, melt agglomeration method.

b. Solvent method:

This method consists of two main steps; first step consists of preparation of solution containing carrier material and drug. Another step involves the removal of solvents resulting in formation of a solid dispersion. Due to mixing at molecular level, dissolution properties of poorly soluble drugs are increases. Common advantages of this method are – 1) Preparation of solid dispersion of thermo labile substances is possible with this solvent method. 2) Also polymers that could not be used for melting method due to their high melting points could be now considered as carrier possibilities. Identification of common solvents for both carrier and drug can be problematic. Complete removal of solvent from the prepared product can be lengthy process. Also large

volume of solvent are required which can leads to toxicological problems.

c. Hot melt extrusion:

This method consists of the extrusion, at high rotational speed, of the carrier and drug, previously mixed, at melting temperature for little period of time. The obtained product is collected after cooling and then milled.

Hot melt extrusion method offers several advantages over a traditional techniques including the absence of solvents, limited processing steps, continuous operation and improved bioavailability.

d. Supercritical Fluid (SCF)process:

Supercritical fluid (SCF) is novel nanosizing and solubilisation technology. Supercritical fluid are fluids whose pressure and temperature are greater than its critical pressure (TP) and critical temperature (TC), allowing it to assume the properties of gas and liquid. Once the drug particles are solubilised within SCF, they may be recrystallised at greatly reduced particle sizes. This method is eco-friendly, safe and economical.

e. Lyophilization method:

In this lyophilization technique, drug and carrier are dissolved in a common solvents, frozen and sublimed to obtain a lyophilized molecular dispersion. This method was proposed as an alternative method to solvent evaporation.

f. Spray drying:

In this method, suspensions or solutions is atomizing into fine droplets followed by a drying process which gives fine dust free powder as well as agglomerated one to precise specifications. Spray drying is simple and cost effective method. Now days, spray drying finds great application in pharmaceutical industry because of fast drying and specific characteristics like particle size and shape of the final product. [9]

1.6. Advantages of solid dispersions:

There are several reasons for the improvement of solubility of poorly water soluble drug by using solid dispersion methods. The advantages of solid dispersion or the reasons for solid dispersions are as follows:

1.6.1 Particles with reduced particle size:

In the solid dispersions, drug is dissolved in dissolution medium or inert matrix. A high surface area is formed which gives increased dissolution rate and further enhance the bioavailability of poorly water soluble drug

1.6.2 Particle with improved wettability:

Solid dispersions improved the wettability of poorly water soluble drug due to this improved in bioavailability of drug.

1.6.3 Particle with higher porosity:

Particles in solid dispersion have found to have high porosity. Porous nature of particle results higher dissolution rate. Increase in porosity of particles is depend upon properties of carrier .when the polymer having linear structure are utilized it formed larger and porous particles compared with solid dispersion that prepared with reticular polymer.

1.6.4 Drug in amorphous state:

Drug substances in amorphous state shows higher drug release because no energy is required to break up the crystal lattice during dissolution. Therefore, poorly water soluble drug in amorphous state gives high degree of solubility.

1.7 Disadvantages of solid dispersion:

Instability is the major disadvantage of solid dispersion. Many solid dispersion systems have shown changes in crystallinity on ageing, phase separation, by moisture absorption, crystal growth which leads to decrease in dissolution rate and reduct ion of drug solubility. Presence of moisture and temperature enhance the deteriorating effect on solid dispersion. Many times it is difficult to handle because of tackiness.

1.8 Limitations of solid dispersions:

Although a great interest in solid dispersion in the past few decades, the commercial application is very limited .problems or limitations of solid dispersion involve-
The chemical and physical stability of drugs and vehicles

- Method of preparation of solid dispersion
- Reproducibility of its various physicochemical characteristics
- Formulation of solid dispersion into various dosage forms
- Scale up of manufacturing processes[10]

1.9. Pharmaceutical applications of solid dispersions:

Apart from solubility enhancement, the solid dispersion method may have number of pharmaceutical applications, which should be further explored.

- To obtain a homogeneous distribution of very small amount of drug substances in solid state

- To dispense various liquid or gaseous compounds in solid dosage forms
- To stabilize various unstable drugs
- To formulate immediate release primary dose in sustained release dosage forms
- To formulate sustained release regimen of soluble drug by using various insoluble or poorly soluble polymers or carriers.
- To reduce first pass metabolism or pre systemic inactivation of various drugs like morphine , progesterone.[11]

1.10. Fast Dissolving Tablet:

1.10.1. Definition

United States Food and Drug Administration (USFDA) defined fast dissolving tablet as “A solid dosage forms containing active ingredient or medical substances which disintegrates rapidly within a matter of seconds when placed upon the tongue.” The disintegration time for fast dissolving tablets ranges from few seconds to about a minute.

Also, United state Pharmacopeia approved this dosage form as orally disintegrating tablet. European pharmacopeia defines a similar terms, Or dispersible tablets, that disperses rapidly within 3 minutes in mouth before swallowing. Over a decade, the demand for development of fast dissolving tablets has tremendously increased as it has impact on the patient's compliance. Fast dissolving tablets are beneficial for various groups of populations particularly who have difficulty in swallowing. Fast dissolving tablet are also appreciated by pediatric, geriatric patients, institutional patients along with mentally disabled patients who enable to take self-medication, and patients who suffering from nausea, vomiting and motion sickness complications. Fast dissolving tablets are also called as orodispersible tablets, orally disintegrating tablets, rapid dissolving tablets, quick disintegrating tablets, rapimelt tablets, fast disintegrating tablets. This dosage forms allow high patients compliance, high drug loading, have a good mouth feeling and tastes, leaving minimal residue in the mouth after oral administration. Fast dissolving tablets enhances bioavailability of poorly water soluble drugs. This dosage forms offers combined advantages of dry and liquid dosage formulations. [12]

1.10.2 Requirements of fast dissolving tablet

- It should have pleasant mouth feel
- It should have Acceptable taste masking property
- Require no water for oral administration
- Be harder and less friable
- Less sensitive to environmental condition
- Allow high dose medicines

1.10.3 Salient feature of fast dissolving tablet

- Fast dissolving tablets does not require water for oral administration
- Fast dissolving tablets having sufficient hardness to withstand the rigor of the manufacturing process and handing during transportation.
- Allow high drug loading
- It should have pleasant mouth feel
- Cost effective

1.10.4 Advantages of fast dissolving tablets:

- Fast dissolving tablets is beneficial for the patients who cannot swallow, like elderly, bedridden stroke victims, patients suffering from renal failure and psychiatric patients.
- Rapid drug delivery intervention
- Convenient for administration
- Enhances bioavailability of poorly water soluble drugs through pre- gastric absorption of drug from mouth, esophagus as saliva passes down.
- Good mouth feel property which enhances patients acceptability
- The choking or suffocation during oral administration of conventional dosage forms is avoided.
- New business opportunity like product differentiation, promotion of product, patent extension and life cycle management.

1.10.5 Limitation of fast dissolving tablets:

- Careful handling is required due to insufficient mechanical strength.
- The tablets may leave grittiness in mouth if not formulated properly.[13]

1.10.6 Disadvantages of fast dissolving tablets:

- It is hygroscopic in nature so must be store in dry places
- Fast dissolving tablets also shows the fragile, effervesces granules property.
- It require special packing for stabilization of product [14]

1.10.7 Conventional method of preparation of fast dissolving tablets:

a) Lyophilization:

This method is also called as freeze drying method. The fast dissolving tablets prepared by lyophilization method are porous in nature so as to dissolve or disintegrate in saliva very easily. First step is material is frozen below its eutectic point which follow the primary drying to reduce the moisture to around 4% w/w of dry product. Finally secondary drying is done

to reduce the bound moisture up to the required volume.

b) Spray drying:

This method gives highly porous tablets. Tablet is compressed from spray dried powder obtained from spray drying which disintegrated within 20 seconds when come in contact with saliva. The formulation contains hydrolyzed or non-hydrolyzed gelatins as a supporting agent, sodium starch glycolate as a super disintegrate, and acidic material like citric acid and alkali material.

c) Sublimation:

The formulation consists of solid ingredients like ammonium carbonate, camphor that volatilize readily. These materials were removed via sublimation process which gives porous structure. Some solvents like benzene can also use as pore forming agents.

d) Direct compression method

This method is simple and cost effective. This method is commonly used method for manufacturing of fast dissolving tablets because of availability of improved excipients like superdisintegrates and sugar based excipients.

e) Superdisintegrants:

Superdisintegrants mainly affect the rate of disintegration and the dissolution. Sodium starch glycolate, croscarmellose sodium, crospovidone are some examples of commonly used superdisintegrants.

f) Sugar based excipients:

The sugar based excipients especially bulking agents like maltose starch dextrose fructose which are highly soluble in aqueous media and sweetness, and impart taste masking properties.

g) Mass extrusion method:

This method involves softening the active blend using solvent (mixture of methanol and polyethylene glycol) and subsequent expulsion through extruder or syringe to obtain cylinder of product which further cut into even segments by using heated blade.

h) Cotton candy process:

This method utilizes high spinning mechanism to produce floss like crystalline structure which mimics cotton candy. This method involves formation of matrix of polysaccharides by simultaneous process of flash melting or spinning. This matrix is partially recrystallised lead to improved flow properties or compressibility. Further obtained matrix is milled in appropriate size and blended with active ingredient

and other excipients and subsequently compressed to fast dissolving tablets.

i) Tablet molding method:

This method is of two types i.e. heat method and solvent method. In the solvent method, powder blend is moistens with hydro alcoholic solvents followed by compression at low pressure in molded plates. The solvent is removed by drying. In the heat molding method, preparation of suspension that contains drug agar and sugar then pouring the suspension into blister packaging wells, solidifying agar at too temperature to form a jelly and drying under vacuum.[15,16]

1.10.8 Patented technologies for preparation of fast dissolving tablets:

i. Zydus Technology:

The zydus tablet is prepared by freeze drying or lyophilization method in which drug is physically entrapped within the matrix of fast dissolving carrier material. When zydus tablet put into the mouth, the freeze dried structure disintegrate within the seconds. The zydus unit is very light weight and fragile and dispense in a special blister pack.

ii. Durasolv Technology:

It is the patented technology of CIMA labs. The tablet made by this method consists of active drug ingredients, filler, and a lubricant. Tablet is prepared by conventional manufacturing process and packed into conventional packaging. This method is required low amount of drug.

iii. Orasolv Technology:

Orasolv technology is developed by CIMA labs. The product is obtained by this method consists of taste masked active ingredients and effervescent superdisintegrating agent. Tablet is made by direct compression method at low compression force.

iv. Flash dose technology:

This technique is patented by Fuisz, Flash dose tablets consists of self binding shear form matrix named as floss which is prepared by flash heat processing. The Biovail Corporation launched a first commercial product manufactured by this method named as Nurofen meltlet (ibuprofen).

v. Wow tab technology:

This technique is patented by Yamanouchi Pharmaceuticals co. The meaning of WOW is without water. In this process, combination of high mouldability saccharides and low mouldability saccharides are used to obtain fast dissolving tablet.

Drug is mixed with low mouldability saccharides and granulated with high mouldability saccharides and compressed into tablet by conventional machines.

vi. Flash tab technology:

This technique is patented by Prographarm laboratories. Drug microgranules prepared by co - acervation, microencapsulation and extrusion spheronisation method and further compressed by conventional tablet punching machines. [17, 18]

1.10.9 Mechanism of action of disintegrants:

There are various mechanism of action of disintegrants are as follows

- a. By capillary action.
- b. By swelling.
- c. Because of heat of wetting.
- d. Due to release of gases.
- e. By enzymatic action.
- f. Due to disintegrating particle/particle repulsive forces.
- g. Due to deformation.

a) By capillary action:

When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. For these types of disintegrants, maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

b) By swelling:

Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.



Fig. No. 5: Disintegration by swelling
c) Because of heat of wetting (air expansion):

When disintegrants with exothermic properties gets wetted, localized stress is generated due to capillary expansion, which helps in disintegration of tablet

d) Due to release of gases:

Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. The tablet disintegrates due to generation of pressure within the tablet. This effervescent mixture is used when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablet.

e) By enzymatic reaction:

Here, enzymes present in the body act as disintegrants. These enzymes destroy the binding action of binder and helps in disintegration. Actually due to swelling, pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.

f) Due to disintegrating particle/particle repulsive forces:

Guyot-Hermann has proposed a particle repulsion theory based on the observation that non swelling particle also because disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.

g) Due to deformation:

Hess had proved that during tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. The swelling capacity of starch was improved when particles were extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet. This may be a mechanism of starch. [19]

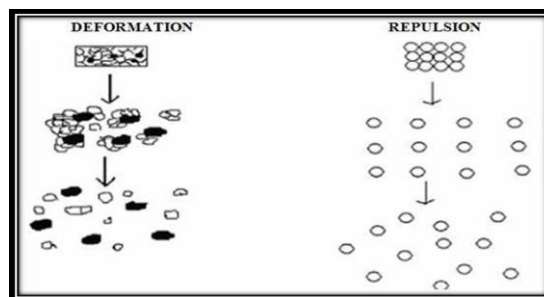


Fig.No.6: Disintegration by deformation and repulsion

2. SUMMARY AND CONCLUSION:

In the present research work, fast dissolving tablets of Cyclosporine are prepared by using solid dispersion technique and various superdisintegrants like croscopovidone, croscarmellose sodium are used with direct compression method.

3. ACKNOWLEDGEMENT

The authors are thankful to the management of the Smt. Sharadchandrika Suresh Patil College of Pharmacy for providing the necessary facilities to carry out the Research work..

4. CONFLICTS OF INTEREST:

Authors have no conflicts of interest to declare.

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