MOUTH MELTING TABLETS: A PROMINENTLY UTILIZED TECHNOLOGY.

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Abstract
Oral administration of the drug is still considered to be the safest, most convenient, and most cost-effective method of providing the best route for patient compliance. However, in the case of pills, the biggest disadvantage is swallowing. To increase compliance with administration, a novel dosage form, i.e. Mouth Melting tablets (MMT) one that can be swiftly disintigrated without the use of water, has acquired importance. Within seconds, the fast dissolving drug delivery technology disintegrates/ disperses in saliva. As a result, they can be used instead of traditional tablets and gelatin capsules by people who have trouble swallowing, such as stroke victims, psychiatric, paediatric, and gediatric patients.Patients must adhere to a rigorous dosing regimen to avoid subtherapeutic effects as in case of epileptic patients, thus, oral dispersible tablets prevent missed doses even when travelling or in other situations when there is no access to water. Bioavailability is higher for Mouth Melting tablets(MMT). Since disintegration occurs within oral cavity. In order to be employed as an excipient in the MMT formulation, superdisintigrant must fulfil certain criteria in addition to its swelling qualities. It's utilised to make solid dose forms more effective. The application of superdisintigrants in tandem reduces disintegration time significantly. This review will provide data of various super disintigrants that deliver superior disintigration in less time especially for mouth melting tablets.

KEYWORDS: bioavailability, disintigration, mouth melting tablets, Oral administration, super disintigrants.

INTRODUCTION:

Oral medication delivery is widely accepted, accounting for 50-60% of total dosage forms. Solid dosage forms are popular because of their ease of administration, accuracy, self-medication, pain avoidance, and, most importantly, patient compliance. Tablets and capsules are the most common solid dose forms. For some patients, one of the most significant disadvantages of this dose form is the difficulty in swallowing it. The ingestion of oral dose forms is greatly aided by drinking water.[1] Because the melt-in-mouth tablets release the medication into the mouth, it can be absorbed by local oro-mucosal tissue as well as pre-gastric(oral cavity, pharynx, and oesophagus) and gastric(oral cavity, pharynx, and oesophagus) routes(stomach)The Gastro-Intestinal Tract is divided into pre-gastric (small and large intestine) and post-gastric(small and large intestine) segments. This dosage form is very beneficial for people who have trouble in swallowing regular tablets with water.[2] Sensual features such as tongue feel, swallowability, MMTs come in a variety of shapes, sizes, and flavours.

They also demonstrate differences in product performance, such as tablet mechanical strength, drug release, bioavailability, and stability. Mass extrusion, spray drying, cotton candy process, lyophilization, moulding, wet and dry granulation, direct compression and compaction are some of the manufacturing methods used to make MMTs.[3] Patented methods are Durasolv®, Orosolv®,Zydis®, WowTab®, Oraquick, Nano Crystal technology, Pharmaburst, Flash Tab, Frostatechnology, Advantol™ 20053, Advatab53, Quicksolv, Oraquick.[4]

Criteria for Fast dissolving Drug Delivery System:

1. The tablets should dissolve or disintegrate in the mouth in a couple of seconds without the need for water.
2. Be tolerant of flavour masking.
3. Be portable without being fragile.
4. Have a pleasant taste in the mouth.
5. After oral administration, there should be little or no residual in the mouth.
6. Should have a low sensitivity to environmental factors such as temperature and humidity.

All these dosage forms present some unique problems which include difficulty in scale up process (micro crystals), poor physical stability (micro emulsions), more number of processing steps and poor yield value (pelletization using solid dispersion technique)[5]

Super disintegrates [6]

MMT necessitates quick disintegration. As a result, pharmacists must develop superdisintegrants, which are effective at low concentrations, have higher dissolving efficiency, and are more effective intragranularly. However, because it is hygroscopic, it should not be used with moisture-sensitive medications.And this superdisintegrants act by swelling and 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.

Selection of super-disintegrates.[7]

The ideal super disintegrate should have,

1. Poor gel formation.

2. Good hydration capacity.
3. Good moulding and flow properties.
4. No tendency to form complex with the drugs.
5. Good mouth feel.
6. It should also be compatible with the other excipients and have desirable tableting properties.

MMT MECHANISM[8]

1. When saliva from the oral cavity comes in contact with a tablet containing quickly dissolving agents, the disintegrating chemicals swell and produce channels/pores for saliva to enter the tablet, causing swelling and pressure.
2. The tablet dissolves quickly in the mouth. Bitterness is disguised by resins and other sweets.
3. Drug substance's physicochemical and biological features contribute in solubilization and absorption via the gastro intestinal tract. To improve the efficacy of solid dose forms, superdisintegrants are utilized. This is accomplished by reducing the disintegration time, which improves the pace of medication dissolution. Disintegrates are compounds or mixtures of compounds added to a medicine formulation to aid in the breaking up or disintegration of tablet or capsule content into smaller particles that dissolve more quickly than without them. In the solid dosage form, superdisintegrants are normally employed at a modest level, approximately 1- 10% by weight compared to the total weight of the dosage unit. The current research focuses on the numerous types of superdisintegrants that are employed in therapeutic formulations to ensure patient compliance and safer, more effective medication delivery. Swelling, wicking, deformation, particle repulsive forces, and enzymatic response are five steps in the disintegration process with the help of superdisintegrants.

The proposed mechanism of action of disintegrates include;

1) Swelling [9]

The swelling of tablets due to increased porosity expression is the general mechanism of action for tablet disintegration. The lack of appropriate swelling force exerted in the tablet with insufficient porosity causes poor breakdown. It's worth noting that if the packing percentage is extremely high, fluid cannot penetrate the tablet, and disintegration slows down.

2) Porosity capillary action (wicking):[10] While placing the medicine in an appropriate aqueous medium, the medium enters the tablet and replaces the air absorbed in the particles, softening the intermolecular bond and causing the tablet to break down into fine particles.Water uptake, drug/excipient hydrophilicity, and tableting conditions Maintenance of porosity structure and interfacial tension toward aqueous fluid is required for these types of disintegrates, which aids in disintegration by creating a hydrophilic system around the particles.

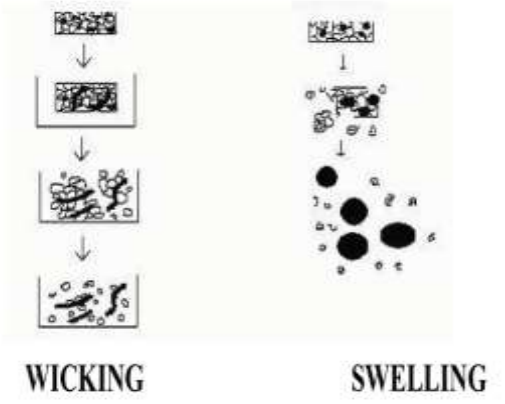

Fig.1 Disintegration of tablets by swelling and wicking mechanism.

3) Repulsion[11]

Another disintegrant mechanism tries to explain why tablets constructed with non-swellable disintegrants swell. Guyot-Hermann presented a particle repulsion theory based on the discovery that non-swelling particles are also responsible for tablet disintegration.The mechanism of disintegration is repulsive interactions between particles, and water is required for it. Researchers discovered that wicking plays second fiddle to repulsion.

4) Disintegration due to deformation[12]

Disintegrated particles are distorted during tablet compression, and when they come into touch with aqueous medium like water, they revert to their original structure.When starch granules were extensively distorted during compression, the swelling capacity of the starch was occasionally improved.The tablet breaks up due to the increased size of the distorted particles. This could be a mechanism of disintegration for starch that has only lately been investigated.Deformation cause tablet disintegration.

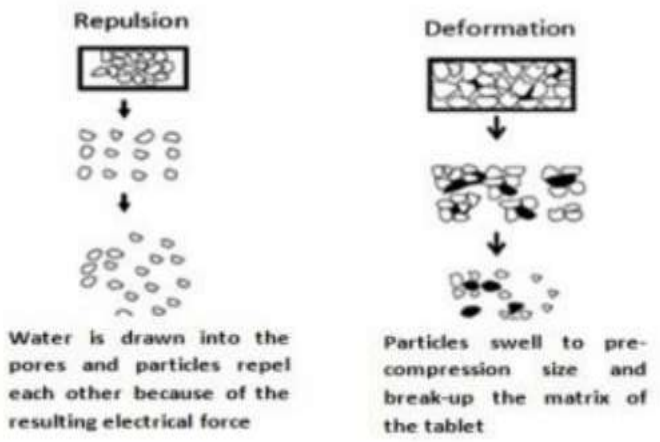

Fig.2 Disintegration of tablets by repulsion and deformation mechanism.

The methods used to make mmts are categorised as follows:

1) **Freeze drying[13]**

This process involves removing water from a frozen substance by sublimation.Lyophilization is a pharmaceutical process that permits heat-sensitive pharmaceuticals and biologicals to be dried at low temperatures under circumstances that allow water to be removed by sublimation. Lyophilization produces highly porous preparations with a high specific surface area that dissolve quickly and have better absorption and bioavailability.Molded tablets are made utilising water soluble components in this manner,allowing the tablets to dissolve completely and quickly.The powder mixture is wet with a hydro alcoholic solvent before being moulded into tablets at a lower pressure than traditional tablet compression. Air drying is used to remove the solvent.When compared to compressed tablets, moulded tablets are far less compact. These have a porous structure that helps them dissolve faster.

2) **Moulding[14]**

Moulding is a procedure that involves moistening,dissolving or dispersing the drug in solvents, then moulding the moist mixture into tablets while evaporating the solvent from the drug solution or suspension at ambient pressure.Because the compression force used in compression moulding is lower than that used in traditional tablets,the moulded tablets have a porous structure,which boosts the product's breakdown and dissolution rate.

3) Sublimation[15]

Rapid disintegration of MMT is aided by the presence of extremely porous components in the tablet matrix. Even though typical tablets include highly water soluble components, they frequently fail to disintegrate quickly due to its porosity.To improve this porosity,a volatile material such as camphor is utilised in the tablet manufacturing process and sublimates from the created tablets.

4) Spray drying[16]

This might result in porous, tiny particles that dissolve quickly. Hydrolyzed and non-hydrolyzed gelatin are used as supporting agents, and mannitol is used as a bulking agent. SSG, also known as croscarmellose sodium, is a dissolving, acidic, or alkali substance that aids in disintegration and dissolve.

5) Mass extrusion[17]

Softening the active blend using a solvent mixture of water soluble polyethylene glycol and methanol, then extruding the softened mass using an extruder or syringe to produce a cylinder-shaped extrusion,which is then cut into even segments with a hot blade to make a tablet.

6) Direct compression[18]

It's one of the most straightforward methods for producing tablets.Direct compression uses standard equipment, widely available excipients, and only a few processing stages.High doses can also be accommodated,and the final tablet weight can easily surpass that of other manufacturing methods.Disintegration and solubilization of directly compressed tablets is dependent on the individual and combined actions of disintegrants, water soluble excipients, and an effervescent agent.

Table 1 List of super disintegrants[19] [20] [21]

Superdisintegrants	Example	Mechanism of Action	Special comment
KyronT314 Kyron T-154 Kyron T- 104	Crosslinked	Swells 4-8 folds disintegrates In1.76 sec.	Swells in 2 dimensions Used for direct compression

Polyplasdone XL (Cross povidone)	Cross linked	Swelling,wicking Disintegrates in 15 sec.	spongy in nature so porous tablets
Primellose®Solutab® (cross caramellose sodium)	Cellulose	swelling disintegrate within 22-24 sec	
Explotab® (Sodium starch glycolate)	cross linked	wicking action disintegrate within 21-23 sec	
Combination of cross carmellose sodium and sodium starch		Disintegrate within 8-14 sec	
Combination of cross carmellose sodium and cross povidone		Disintegrate within 7 sec	

TECHNOLOGIES THAT HAVE BEEN PATENTED[22 23 24 25 26 27 28 29]

1) **Zydis® technology:**
The first marketed new technology tablet was Zydis, the most well-known of the fast dissolving/disintegrating tablet preparations. After being placed on the tongue for a few seconds, the tablet dissolves in the mouth. A Zydis tablet is made by lyophilizing or freeze drying the medication in a gelatin matrix. The product tablet is extremely light and delicate, and it must be distributed in a particular blister pack. Patients should be told that instead of pushing the tablets through the foil sheet, they should peel it back to release the tablet. The Zydis product is designed to dissolve in 2 to 3 seconds on the tongue. Because the ultimate water concentration in a freeze dried product is too low for microbiological growth, the Zydis formulation is also self-preserving. When compared to regular tablets, Zydis claims to have a higher bioavailability.It disperses and dissolves as a result of its dispersion and dissolution.This formulation can cause a significant quantity of pre-gastric absorption in saliva while still in the oral cavity.

2) **Orasolv® Technology:**
cima's initial dissolving dosage form was Orasolv. Unlike zydis, orasolv disperses in saliva with the help of nearly imperceptible effervescence.The orasolv technology is best defined as a fast-dissolving tablet; the tablet matrix dissolves in under one minute, leaving coated medication powder behind. The orasolv formulation provides two types of flavour masking. In orasolv, sweeteners and tastes aren't the only ways to disguise a drug's bad flavour; coating the powder and effervescence are also options. Over-the-counter medicines are commonly developed using this technology.

3) **Wow Tab®Technology:**
Wow is a word that implies "without water." Wow tab is a compressed intra buccally soluble tablet made out of saccharine granules with low and high moldability. When low- and high-moldable saccharine are used separately, the resulting tablets do not have the necessary attributes of quick disintegration and hardness, thus they are combined. When 150 mg of a low moldability saccharide is compressed under pressure of 10–50 kg/cm2 using a die 8 mm in diameter, tablets with hardness between 0 and 2 kg are produced. Lactose, mannitol, glucose, sucrose, and xylitol are examples of low-moldability saccharides. When manufactured under identical conditions, high-moldability saccharides generate tablets with a hardness of more than 2 kg. Maltose, manitol, sorbitol, and oligosaccharides are examples of high-moldability saccharides. It's utilised to make a tablet with a good hardness and a quick disintegration rate. Due to its significantly higher hardness than zydis and Orasolv, the wow tab formulation is more environmentally stable.The Wow tab product can be used in a traditional, bottle or blister form.

4) **Oraquick:**
K.V.Pharmaceuticals has a patent on this technology. It employs micro mask, a taste masking microsphere technology that gives great tongue feel, significant mechanical strength, and rapid product disintegration/dissolution. This method entails preparing micro particles in the shape of a matrix that protects the medicine and can be squeezed with enough mechanical strength. Low heat of manufacture allows for high medication dosages and enhanced mechanical strength.

5) **Nano Crystal technology:**
Elan's patented Nano Crystal technology (Nanomelt TM) helps boost compound activity and final product quality.The surface area of a particle increases as its size decreases, resulting in a faster dissolving rate. Using Nano Crystal technology, this can be done in a predictable and efficient manner.Nano Crystal particles are microscopic medicine

substance particles with a diameter of less than 1000 nm that are created by milling the medicinal ingredient using an unique wet milling method.

6) Pharmaburst technology:

This technology is patented by SPI Pharma, New Castle. The Pharmaburst MMT is made up of a proprietary disintegration (Pharmaburst) made up of mannitol and other tableting aids. It makes use of co-processed excipients to create ODT, which dissolves in 30-40 seconds. Dry blending of the medicine, flavour, and lubrication is followed by compression into tablets with this technology.

7) Flash Tab Technology:

The Flash tab technology has been patented by Ethypharm in Saint Cloud, France. This process involves granulating excipients using either a wet or dry granulation method, then compressing them into tablets. The usage of super disintegrates is crucial to this technique. Before compression, flash tab is a blend of wet and dry granulation.

8) Frostatechnology:

This technology is patented by Akina. The frostatechnology prepares rapid melting tablets by compressing highly plastic granules at low pressure. The extremely plastic granules are made up of three parts: a plastic substance, a plasticizer, and a plasticizer (Maltrin QD M580 and MaltrinM180 are maltodextrin and corn syrup solids) a wet binder (Mannogem EZ Spray) and a water penetration enhancer (sucrose, poly vinyl pyrolidone and hydroxyl propyle methylcellulose). Each of the three components is necessary for producing tablets with higher strength and faster disintegation time.

9) Quicksolv technology:

Janssen Pharmaceuticals has a patent on this technology. It creates a matrix out of two solvents that disintegrates instantly. The method entails dissolving medium components in water and freezing the solution or suspension. Then, using an excess of alcohol to remove water from the matrix, dry it (solvent extraction). As a result, the finished product has a consistent porosity and sufficient handling strength.

10) Ziplettechnology:

Water insoluble medications or pharmaceuticals in the form of coated micro particles are employed in ziplet technology. The addition of a reasonable proportion of water-insoluble inorganic excipients, along with Disintegrants, gave the oral dissolving tablet (MMT) outstanding physical conflict while maintaining optimal disintegration. In comparison to the most often used water soluble sugars or salts, the use of water-insoluble inorganic excipients improves disintegration. Tablets largely made up of water soluble ingredients frequently dissolve rather than disintegrate, forming a concentrated viscous solution that slows water diffusion into the tablet core.

CONCLUSION

1. Mouth melting tablets have the potential to be more effective than traditional solid dosage forms. This drug delivery technique is one of the most innovative of all revolutionary drug delivery systems. In comparison to traditional oral dosage forms, they may have higher patient acceptance and compliance, as well as superior biopharmaceutical characteristics, efficacy, quick beginning of action, and safety. MMT's best feature is its ability to disintegrate quickly in the oral cavity without the use of water, as well as its mechanical strength. Because of this, this formulation is a great choice for elderly and paediatric patients. Because of this, this formulation is a great choice for elderly and paediatric patients. Due to advancements in scientific research and discovery of new excipients, MMT is predicted to increase at a high rate in the near future, resulting in a future-ready, combative arena of pharmaceutical drug delivery systems.

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