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Review article

Co-Processed Superdisintegrants: Novel Technique for Design Orodispersible Tablets

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Abstract

Researchers throughout the world are focusing intensively on the methods for the development of new drug delivery systems to enhance patient's compliance. The oral route is the most convenient route for administration of solid dosage form, about 85% of solid dosage administered by oral route because of advantages over others. The oral route however still remained as the best administration route of therapeutic agents for its ease of ingestion, pain avoidance and versatility. Hence, fast dissolving tablets become an emerging trend in the pharmaceutical industry. Fast dissolving tablets are ideal for all types of people, including for people who have swallowing difficulties, paediatric, geriatric, and bedridden patients. The objective of the present article is to highlight traveller friendly orodispersible tablet by direct compression using superdisintegrant materials, the various kinds of superdisintegrants along with their role in tablet disintegration and drug release, which are being used in the formulation to provide the safer, effective drug delivery with patient compliance.

Key words: Disintegrants, Superdisintegrants, Fast Dissolving Tablet (FDT), Co-Processed.

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1. Introduction

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. The reason that the oral route achieved such popularity may be in part attributed to its ease of administration as well as the traditional belief that by oral administration the drug is as well absorbed as the food stuffs that are ingested daily. In fact, the development of pharmaceutical products for oral delivery, irrespective of physical form involves varying extents of optimization of dosage form characteristics within the inherent constraints of GI physiology. Therefore, a fundamental understanding of various disciplines, including GI physiology, pharmacokinetics, pharmacodynamics and formulation design are essential to achieve a systemic

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approach to the successful development of an oral pharmaceutical dosage form. The more sophisticated a delivery system, the greater is the complexity of these various disciplines involved in the design and optimization of the system. In any case, the scientific frame work required for the successful development of an oral drug delivery system consists of a basic understanding of the following three aspects:

1. Physicochemical, pharmacokinetic and pharmacodynamic characteristics of the drug
2. The anatomic and physiologic characteristics of the GIT and
3. Physicochemical characteristics and the drug delivery mode of the dosage form to be designed [1].

Many patients find it difficult 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 traveling. Other groups that may experience problems using conventional oral dosage form include the mentally ill, developmentally disable and patients who are uncooperative [2].

Difficulty in swallowing (dysphasia) is common among all age groups, especially in elderly, and is also seen in swallowing conventional tablets and capsules. This disorder is associated with many medical conditions, including stroke, Parkinson's, AIDS, thyroidectomy, head and neck radiation therapy and other neurological disorders, including cerebral palsy [3].

Due to a society that is becoming increasingly aged, the development of an appropriate dosage form for the aged patients is most desirable. Because the changes in various physiological functions related with aging including difficulty in swallowing, current dosage forms like capsules are impractical. The most desirable formulation for use by the elderly patients is one that is easy to swallow and easy to handle [4].

To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage forms known as orally disintegrating tablets (ODTs) or Fast disintegrating tablets (FDTs) or mouth melting tablets (MMTs) or mouth dissolving tablets (MDTs) which disintegrate rapidly in saliva, usually in a matter of seconds, without the need to take water [5].

Oro dispersible tablets (ODT) are solid single-unit dosage forms that are placed in the mouth, allowed to disperse/dissolve in the saliva and then swallowed without the need for water [6].

Oro dispersible tablets have been developed, which combine hardness, dosage uniformity, stability and other parameters, with extremely easy administration, since no water is required for swallowing the tablets and they are thus suitable for geriatric, pediatric and traveling patients [7].

The solution containing the active ingredients is swallowed and the active ingredients are then absorbed through the gastrointestinal epithelium to reach the target and produce the desired effect. In addition to improving patient compliance, ODTs have been investigated for their potential in increasing the bioavailability of poorly water soluble drug through enhancing the dissolution profile of the drug. Moreover, pharmaceutical companies also have commercial reasons for developing ODTs. As a drug formulation comes to the end of its patent, the development and formulation of the drug into new dosage forms allows pharmaceutical companies to extend the patent life and 'market exclusivity'. This allows pharmaceutical companies to attract new consumers

through advertisement and product promotion plans, and increase profits in the long term [8].

However, due to the rapid ODT disintegration, the active substance comes in contact with the taste buds and the need for a pleasant taste becomes a key aspect for patient palatability. Thus the taste-masking of bitter active substances is a critical hurdle to overcome for the successful development of ODT formulations. In general, oral administration of bitter active substances through ODT formulations should provide an improved degree of palatability, increased patient compliance and beneficial therapeutic effect. In the past, the methods of taste-masking in orodispesible tablets included sweeteners and flavors. Nevertheless, these additives were not a sufficient means for complete taste-masking. Recent advances in technology have presented viable dosage alternatives to taste-mask bitter drugs. Several approaches have been reported which involve complexation freeze-drying, micro encapsulation, fluidized-bed coating and supercritical fluids for taste-masking purposes [9].

Recently, the European pharmacopoeia adopted the term orodispersible tablet as a tablet to be placed in the oral cavity where it disperses rapidly before swallowing and which disintegrates in less than 3 min. There was no specification concerning neither the hardness nor the friability of this kind of tablets. That is why we find certain ODT in the market that disintegrate in less than 1 min or may be 30 sec. Commercially available ODT are prepared by various techniques, mainly lyophilisation, molding and direct compression. The lyophilisation and molding techniques produce ODT which disintegrate within about 30 sec, but that have low physical resistance and high friability. On the other hand, tablets obtained by direct compression are less friable but disintegrate in a longer time [10].

The ODT tablets of diluent and amorphous saccharide mixture are prepared at low compression pressure and stored for the crystalline transition. The diluents and amorphous saccharides include mannitol, erythritol, xylitol, microcrystalline cellulose, etc. and sucrose, maltose, lactose, etc. respectively. In our previous study, the factors affecting the properties of tablets prepared by CT method were clarified. As an alternative technique for preparing ODTs, molded tableting technique that compresses wet granules at low compression force has been developed to achieve rapid disintegration in conjunction with high tablet hardness compared with those prepared by standard compression method. Molded tablets have high porosity; thereby allowing greater water penetration into the tablets and accelerating tablet disintegration [11].

Co-processed superdisintegrants

In recent years drug formulation scientists have recognized that single-component excipients do not always provide the requisite performance to allow certain active pharmaceutical ingredients to be formulated or manufactured adequately. Hence, there is a need to have excipients with multiple characteristics built into them such as better flow, low/no moisture sensitivity, superior compressibility and rapid disintegration ability. One such approach for improving the functionality of excipients is co-processing of two or more excipients. Co-processing is based on the novel concept of two or more excipients interacting at the sub particle level, the objective of which is to provide a synergy of functionality improvement as well as masking the undesirable properties of individual. Co-processing excipients leads

to the formulation of excipient granules with superior properties compared with physical mixtures of components or individual components [12].

In the present investigation, the preparation and evaluation of orodispersible tablets by using co-processed superdisintegrants containing crospovidone and sodium starch glycolate was studied. The reasons for selection of crospovidone are high capillary activity, pronounced hydration capacity and little tendency to form gels. Sodium starch glycolate was chosen because of its high swelling capacity. The concept of formulating orodispersible tablets using co-processed superdisintegrants which increase the water uptake with shortest wetting time and thereby decrease the disintegration time of the tablets by simple and cost effective direct compression technique.

Requirements of fast dissolving tablets [13]

An ideal fast dissolving tablet should:

- Require no water for oral administration, yet dissolve/disperse /disintegrate in mouth in a matter of seconds.
- Have a pleasing mouth feel.
- Have an acceptable taste masking property.
- Should be harder and less friable.
- Leave minimal or no residue in the mouth after oral administration.
- Exhibit low sensitivity to environmental conditions such as humidity and temperature.
- Allow the manufacture of tablet using conventional processing and packaging equipments.

Salient features of fast dissolving tablets [14]

- Ease of administration to patients who refuse to swallow a tablet such as, pediatric, geriatric and psychiatric patients.
- Convenience of administration and accurate dosing as compared to liquids.
- No need of water to swallow the dosage form, which is highly convenient especially for patients who are traveling and do not have immediate access to water.
- Good mouth feel property of MDDS helps to change the basic view of medication as “bitter pill”, particularly for pediatric patients.
- Rapid dissolution and absorption of drug, which may produce quick onset of action.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach; in such cases bioavailability of drugs is increased.
- Ability to provide advantages of liquid medication in the form of solid form.
- Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.

Advantages of fast dissolving tablets [15]

- Ease of administration to patients who cannot swallow, such as the elderly, stroke victims and bedridden patients; patients who should not swallow, such as renal failure patients; and who refuse to swallow, such as pediatrics, geriatric and psychiatric patients.
- Patient’s compliance for disabled bedridden patients and for travelling and busy people who do not have ready or easy access to water.
- Good mouth feel property of mouth dissolving drug delivery system helps

to change the basic view of medication drugs.
- Convenience of administration and accurate dosing as compared to liquid formulations.
- Benefit of liquid medication in the form of solid preparation.
- More rapid drug absorption from the pre-gastric area i.e. mouth, pharynx and esophagus which may produce rapid onset of action.
- Pre-gastric absorption can result in improved bioavailability, reduced dose and improved clinical performance by reducing side effects.
- New business opportunities: product differentiation, line extension and life-cycle management, exclusivity of product promotion and patent-life extension.

Challenges in formulating FDTs [16]

Palatability:
Most orally disintegrating drug delivery systems disintegrate or dissolve in patient's oral cavity, thus releasing the active ingredients which come in contact with the taste buds; hence, taste-masking of the drugs becomes critical to patient compliance.

Mechanical strength
In order to allow FDTs to disintegrate in the mouth, they are made with very low compression force, which makes the tablets friable and/or brittle, difficult to handle, and often requiring specialized peel-off blister packing that may increase the cost. Only few technologies such as Wowtab® by Yamanouchi Shaklee and Durasolv® by CIMA labs can produce tablets that are sufficiently hard and durable to allow them to be packaged in multidose bottles.

Hygroscopicity
Several FDTs are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need protection from humidity which calls for specialized product packaging.

Amount of drug
For lyophilized dosage forms, the drug dose must be lower than 400 mg for insoluble drugs and less than 60 mg for soluble drugs.

Aqueous solubility
Water-soluble drugs form eutectic mixtures, which result in freezing-point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimation process.

Size of tablet
It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve.

Drug selection criteria [17]
The ideal characteristics of a drug for oral dispersible tablet include
- Ability to permeate the oral mucosa.
- At least partially non-ionized at the oral cavity pH.
- Have the ability to diffuse and partition into the epithelium of the upper GIT.
- Small to moderate molecular weight.
- Short half life and frequent dosing drugs are unsuitable for ODT.
- Drug should have good stability in saliva and water.

- Very bitter or unacceptable taste and odor drugs are unsuitable for ODT.

Excipients commonly used for FDT preparation [18,19]
The following excipients are used in preparation of ODT:

Superdisintegrants
Now, demand for faster disintegrating formulation is increased. So, pharmacists need to formulate disintegrants i.e. superdisintegrants which are effective at small concentration and have greater disintegrating capacity and they are more effective intragranularly. This superdisintegrants act by swelling and as result of 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. The mechanism of disintegration is as shown in figure 1.

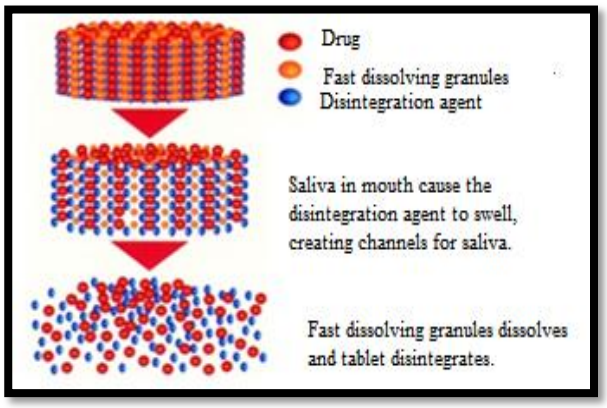


Figure 1. Mechanism of disintegration

Various types of superdisintegrants used are as follows:
- Crospovidone
- Microcrystalline cellulose
- Sodium starch glycolate
- Sodium carboxy methyl cellulose or cross carmellose sodium
- Pregelatinzed starch
- Calcium carboxy methyl cellulose
- Modified corn starch, Sodium starch glycolate has good flowability than cross carmellose sodium.

Factors to be considered for selection of superdisintegrants for use
- It should dissolved in mouth when comes in contact with saliva.
- It should be compactable as enough to produce less-friable tablets.
- It should produce good mouth feel to the patient. Thus, small particle size is preferred to acquire patient compliance.
- It should have good flow since it improve the flowability of the total blend.

The tablet breaks into primary particles by one or more of mechanisms as given below:
By capillary action
Disintegration by capillary action is always the first step. 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. Water uptake by tablet depends upon hydrophilicity of the drug/excipient and on tableting conditions. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration.

By swelling
The most widely accepted general mechanism of action for tablet disintegration is 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. The mechanism of disintegration using wicking and swelling is shown in figure 2.

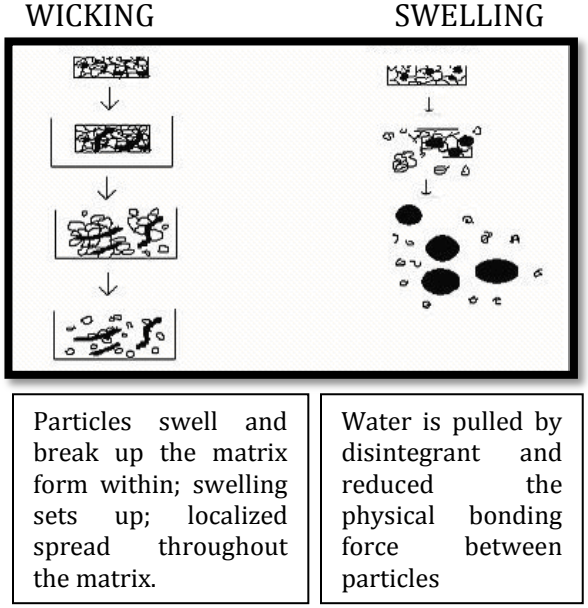


Figure 2. Disintegration of tablet by wicking and swelling

Because of heat of wetting (air expansion)

When disintegrants with exothermic properties gets wetted, localized stress is generated due to capillary air expansion, which helps in disintegration of tablet. This explanation, however, is limited to only a few types of disintegrants and can not describe the action of most modern disintegrating agents.

Due to disintegrating particle /particle repulsive forces

Another mechanism of disintegration attempts to explain the swelling of tablet made with 'non-swellable' disintegrants. Guyot-Hermann has proposed a particle repulsion theory based on the observation that nonswelling particle also cause 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.

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. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a break up of the tablet. This may be a mechanism of starch and has only recently begun to be studied. The disintegration mechanism by using deformation and repulsion is shown in figure 3.

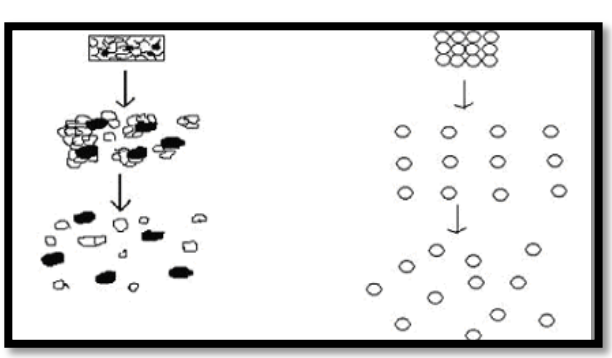


Figure 3. Disintegration by deformation and repulsion

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 tablets. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during manufacturing of the tablets. The effervescent blend is either added immediately prior to compression or can be added in to two separate fraction of formulation.

By enzymatic reaction

Here, enzymes presents in the body act as disintegrants. These enzymes destroy the binding action of binder and helps in disintegration.

Taste masking agents

These agents are used for masking the bitter taste of drug. Taste-masking of bitter or with objectional tasting drug substances is critical for any orally administered dosage form drugs for ODT. Less commonly, active pharmaceutical ingredients to be incorporated are tasteless and do not require taste masking. Sugar based excipient are used for taste masking and as bulking agents. Most of the drugs are having unpleasant or bitter taste and the basic requirement for designing ODTs is that the drug should not have disagreeable taste. So taste masking is necessary in most of the cases, sorbitol, mannitol, xylitol, dextrose, fructose, etc. are mainly used. There are various approaches of taste masking of bitter drugs for ODT.

Binders

Main role of binders is to keep the composition of these fast melting tablets together during the compression stage. Binders commonly used are cellulosic polymers, povidones, polyvinyl alcohols and acrylic polymers. Among the cellulosic polymers it will be advantageous to select ethylcellulose, hydroxyl propyl cellulose (HPC) and hydroxy propyl methyl cellulose alone or in admixtures and the most commonly acrylic polymers are used such as the ammonio-methacrylate copolymer (Eudragit RL and RS), polyacrylate (Eudragit.NE) and polymethacrylate (Eudragit E). The right selection of a binder or combination of binders is essential to maintain the integrity and stability of the tablet. The temperature of the excipient should be preferably around 30-35^{0}C for faster melting properties. Further, its addition imparts smooth texture and disintegration characteristics to the system.

Technologies used to manufacture mouth dissolving tablets

The technologies used to manufacture mouth dissolving tablets can be classified as:

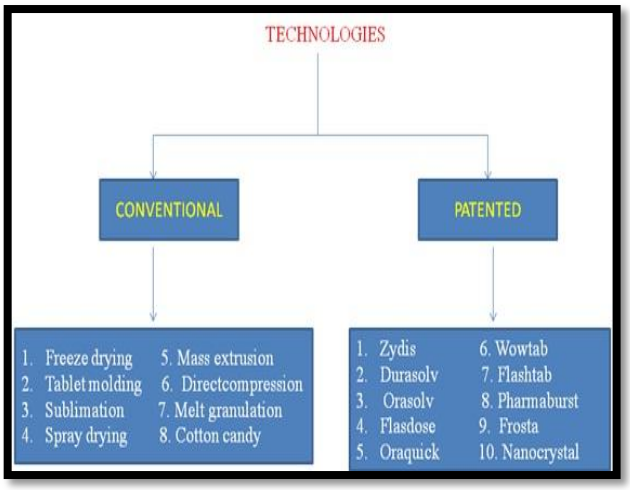


Figure 4. Various technologies used to manufacture mouth dissolving tablets.

Conventional technologies for preparing mouth dissolving tablets [20-23].

Freeze drying

It is a process in which water is sublimated from the product after freezing. Lyophilization is a pharmaceutical technology which allows drying of heat sensitive drugs and biological products at low temperature under conditions that allow removal of water by sublimation. Lyophilization results in preparations, which are highly porous, with a very high specific surface area, which dissolve rapidly and show improved absorption and bioavailability.

Tablet molding

Molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying. Molded tablets are very less compact than compressed tablets. These possess porous structure that enhances dissolution. They disintegrate very quickly because these are made from water soluble excipients. These properties are enhanced with porous structures or are physically modified by the molding process. In comparison to lyophilization process, tablets produced by molding technique are easier to adapt to the industrial scale.

Sublimation

The basic principle involved in preparing fast dissolving tablets by sublimation technique is addition of a volatile salt to the tabletting component, mixing the components to obtain a substantially homogenous mixture and volatizing salt. The removal of volatizing salt creates pores in the tablet, which help in achieving rapid disintegration when the tablet comes in contact with saliva. The tablets were then subjected to vacuum at 80ºC for 30 minutes to eliminate volatile components and thus create pores in the tablet. Volatile salts such as camphor, ammonium bicarbonate, naphthalene, urea, etc. were also used as sublimable components to prepare porous tablets of good mechanical strength. Schematic diagram of sublimation technique is shown in figure 5.

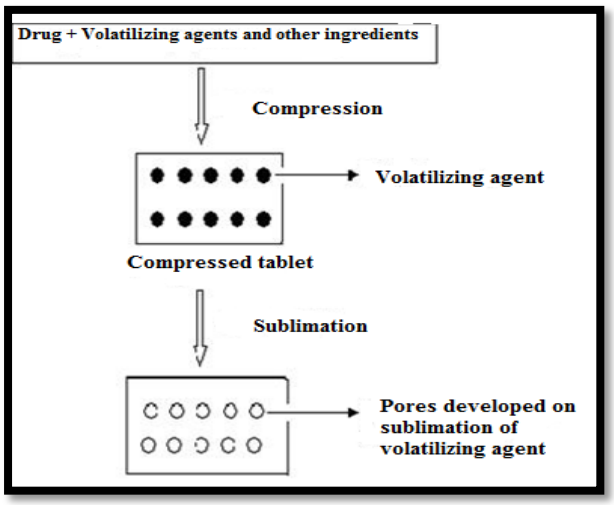


Figure 5. Schematic diagram of sublimation technique.

Spray drying

Spray drying process is widely used to provide products with high porosity in fine powder because the processing solvent can be easily dried. Hence rapidly disintegrating tablets can be prepared where tablets disintegrate in less than 20 seconds. This technique is based on particulate support-matrix, which is prepared by spray drying the solvent. This matrix then becomes the carrier for the active ingredients. The formulations are incorporated by hydrolyzed and non hydrolyzed gelatins as supporting agents,

mannitol as bulking agent, sodium starch glycolate or cross carmellose sodium as disintegrating agent and an acidic material (e.g. citric acid) and/or alkali material (e.g. sodium bicarbonate) to enhance disintegration and dissolution.

Mass extrusion

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

Direct compression

It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. The mixture to be compressed must have adequate flow properties and coherent under pressure thus making pretreatment as wet granulation unnecessary. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods. Directly compressed tablet's disintegration and solubilization are strongly affected by tablet size and hardness. This technique can now be applied to fast dissolving tablets because of the availability of improved tablet excipients, especially superdisintegrants like cross carmellose sodium, microcrystalline cellulose, crospovidone, sodium starch glycolate and partially substituted hydroxypropyl cellulose, effervescent agents (citric acid, sodium bicarbonate) and sugar-based excipients (dextrose, fructose, isomalt, maltitol, maltose, mannitol, sorbitol, starch hydrolyse, polydextrose and xylitol).

Melt granulation

It is a unique method for the preparation of orodispersible tablets by incorporating superpolystate. Superpolystates are hydrophilic waxy binders with a melting point 33-37°C and hydrophilic - lipophilic balance value is 9. They play a dual role as a binder that increases the physical resistance of the tablets and also as a disintegrants, which help the tablet to melt in the mouth, and solubilize rapidly leaving no residue in the mouth. Superpolystates were introduced in the formulation of orodispersible tablets by melt-granulation method. Here, granules are formed by the molten form of this material. Crystallized paracetamol was used as a model drug along with mannitol and crosscarmellose sodium.

Cotton candy process

This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to ODT. This process can accommodate high doses of drug and offers improved mechanical strength. However, high process temperature limits the use of this process.

Patented technologies for mouth dissolving tablets [24-26].

Zydis technology

Zydis formulation 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 into the mouth, the freeze-dried structure disintegrates instantaneously and does not require water to aid swallowing. The zydis matrix is composed of many materials designed to achieve a number of objectives. To impart strength during handling, polymers such as gelatin, dextran or alginates are incorporated. These form a glossy amorphous structure, which imparts strength.

To obtain crystallinity, elegance and hardness, saccharides such as mannitol or sorbitol are incorporated. Water is used in the manufacturing process to ensure production of porous units to achieve rapid disintegration. Various gums are used to prevent sedimentation of dispersed drug particles in the manufacturing process. Collapse protectants such as glycine prevent the shrinkage of zydis units during freeze drying process or long term storage. Zydis products are packed in blister packs to protect the formulation from moisture in the environment.

Durasolv technology

Durasolv is the patented technology of CIMA labs. The tablets made by this technology consist of a drug, fillers and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity. These can be packaged into conventional packaging system like blisters. Durasolv is an appropriate technology for products requiring small amounts of active ingredients**.**

Orasolv technology

CIMA labs have developed orasolv technology. In this system active medicament is taste masked. It also contains effervescent disintegrating agent. Tablets are made by direct compression technique at low compression force in order to minimize oral dissolution time. Conventional blenders and tablet machine is used to prepare the tablets. The tablets prepared are soft and friable.

Flashdose technology

Flashdose utilizes a unique spinning mechanism to produce a floss-like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the active drug and be compressed into a tablet. This procedure has been patented by Fuisz. Instead of a floss-like material, small spheres of saccharides can be produced to carry the drug. The process of making microspheres has been patented by Fuisz, and is known as Ceform and serves as an alternative method of taste masking.

Oraquick technology

The Oraquick fast dissolving/ disintegrating tablet formulation utilizes a patented taste masking technology. The taste masking process does not utilize solvents of any kind and therefore leads to faster and more efficient production. Also, lower heat of production than alternative fast dissolving/ disintegrating technologies makes oraquick appropriate for heat-sensitive drugs. Oraquick claims quick dissolution in a matter of seconds, with good taste masking. There are no products using the oraquick technology currently on the market, but KV Pharmaceutical has products in development such as analgesics, scheduled drugs, cough and cold, psychotropics, and anti-infectives.

Wowtab technology:

Yamanouchi patented this technology. WOW means without water. This technology utilizes conventional granulation and tabletting methods to produce FDTs employing low- and high-moldability saccharides. Low moldability saccharides are lactose, mannitol, glucose, sucrose and xylitol. High-moldability saccharides are maltose, maltitol, sorbitol and oligosaccharides. When these low- and high-moldable saccharides are used alone tablets obtained do not have desired properties of rapid disintegration and hardness, so combinations are used. This technology involves granulation of low-moldable saccharides with high-moldable saccharides as a binder and compressing into tablets followed by moisture treatment. Thus tablets obtained showed adequate hardness and rapid disintegration.

Flashtab technology:

This is patented by Ethypharm France. This technology includes granulation of excipients by wet or dry granulation method and followed by compressing into tablets. Excipients used in this technology are of two types. Disintegrating agents include reticulated polyvinylpyrrolidine or carboxy methylcellulose. Swelling agents include carboxy methylcellulose, starch, modified starch, microcrystalline cellulose, carboxy methylated starch, etc. These tablets have disintegration time is within 1 min and also shows satisfactory physical resistance.

Pharmaburst technology:

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

Table 1: List of some patented technologies based branded products. [27]

Patented technology	Basis of technology	Technology developed by company	Active ingredient (Brand names)
Zydis	Lyophilization	R.P.Scherer,Inc.	Loratidine (Claritin Reditab)
Orasolv	Direct Compression	Cima Labs,Inc.	Paracetamol (Tempra Quicklets), Zolmitriptan (Zolmig Repimelt)
Durasolv	Direct Compression	Cima Labs, Inc.	Hyoscyamine Sulfate (NuLev), Zolmitriptan (Zolmig ZMT)
Flashtab	Direct Compression	Ethypharm	Ibuprofen (Nurofen Flashtab)
Wowtab	Direct Compression	Yamanouchi Pharma Tech. Inc.	Famotidine (Gaster D)
Oraquick	Micromask taste masking	KV Pharm.Co.,Inc.	Hyoscyamine Sulfate ODT
Quicksolv	Lyophilization	Janssen Pharmaceutics	Cisapride monohydrate (Propulsid Quicksolv), Risperidone (Risperdal MTab)
Lyoc	Lyophilization	Farmalyoc	Phloroglucinol Hydrate (Spasfon Lyoc)

Table 2: Marketed products of MDTs[28]

Trade name	Active drug	Manufacturer
Nimulid-MD	Nimesulide	Panaca biotech
Zyrof meltab	Rofecoxib	Zydus Cadila
MOSID-MT	Mosapride Citrate	Torrent Pharmaceuticals
Feledine Fast Melt	Piroxicam	Pfizer
Maxalt MLT	Rizatritan	Merck
Remeron Sol Tab	Mirtazapine	Organon
Romilast	Montelukast	Ranbaxy
Torrox MT	Rofecoxib	Torrent Pharmaceuticals
Olanex Instab	Olanzepine	Ranbaxy
Zopran ODT	Ondansetron	Glaxo
Febrectol	Paracetamol	Prographarm
Zelaper TM	Selegiline	Amarin Corp

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