

The technologies used for developing orally disintegrating tablets: A review

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Orally disintegrating tablets (ODTs), also known as fast melts, quick melts, fast disintegrating and orodispersible systems, have the unique property of disintegrating in the mouth in seconds without chewing and the need of water and are thus assumed to improve patient compliance. Conventional methods like direct compression, wet granulation, moulding, spray-drying, freeze-drying and sublimation were used to prepare ODTs. New advanced technologies like Orasolv[®], Durasolv[®], Wowtab[®], Flash-tab[®], Zydys[®], Flashdose[®], Oraquick[®], Lyoc[®], Advatab[®], Frosta[®], Quick-Disc[®] and Nanomelt[®] have been introduced by some pharmaceutical companies for the production of ODTs. The main objective of this review is to give a comprehensive insight into conventional and recent technologies used for the preparation of ODTs.

Keywords: orally disintegrating tablet, orodispersible tablet, superdisintegrant, drug delivery, fast disintegrating tablet

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An orally disintegrating tablet (ODT) is defined as a solid dosage form that dissolves or disintegrates quickly in the oral cavity without the need for administration of water. The *EP* describes ODTs as »uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed« and as tablets which should disintegrate within 3 min (1). *FDA* defines ODT as »a solid dosage form which contains a medicinal substance or active ingredient which disintegrates rapidly within a matter of seconds when placed upon a tongue« (2). Orally disintegrating tablets are claimed to be a better solution than conventional solid oral dosage forms (tablets and capsules) as the latter create problems for pediatric, geriatric, bedridden, nauseous or non-compliant patients (3). After coming in contact with saliva ODTs disintegrate immediately and produce a suspension that can be easily swallowed by the patient (4). The active ingredients in solution are more rapidly absorbed through the pre-gastric route from the mouth, pharynx and esophagus and through gastrointestinal epithelium to produce the desired effect (5). ODTs are preferred for people suffering from dysphagia, institutional psychi-

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atric patients as well as hospitalized patients suffering from a variety of disorders such as stroke, thyroid disorder, Parkinson's disease and other neurological disorders like multiple sclerosis and cerebral palsy. Dysphagia is a condition marked by the difficulty in swallowing and it has been reported that about 35 % of the general population, in addition to 30–40 % of elderly institutionalized patients and 18–22 % of all persons in long-term care facilities, suffer from dysphagia (6, 7). ODTs have also been found to be the dosage form of choice for patients suffering from nausea, vomiting or motion sickness (8). Popularity of ODTs depends on factors such as patient preference and life cycle management. Reasons for patient acceptance of this dosage form include its oral disintegration, good mouth-feel, easy handling, easy swallowing, no need of water and effective taste masking.

Also, to give a new lease of life to a patented product whose patent term is about to expire, the formulation and development of the drug into a new dosage form like ODT allows pharmaceutical companies to enjoy market exclusivity (9).

Formulation of ODT has been studied as one of the ways to improve the bioavailability of poorly water soluble drugs and it has been observed that ODT increase the bioavailability of such drugs (10). Although there are various challenges involved in the formulation and development of ODTs, a number of techniques have been tried so far to develop this dosage form; these challenges are:

- i)* it is difficult to achieve sufficient mechanical strength of ODTs (11);
- ii)* it is a challenge to achieve rapid disintegration of a tablet (3);
- iii)* selection of polymer and its concentration for the coating of drug particles is a complicated task since the thickening of drug particle coating or pH dependent solubility of coated polymers such as methacrylate of polyvinyl pyrrolidone affect the dissolution profile (3);
- iv)* to achieve better patient compliance, it is expected that no residue should remain in the mouth, after swallowing (3);
- v)* some active pharmaceutical ingredients (APIs) have a bitter taste and it is a big challenge for the formulation scientist to achieve acceptable taste masking for such ingredients (3);
- vi)* selection of the proper method for taste masking amongst the available methods is a forbidden challenge for formulators (3, 11).

Taste masking is the first and foremost task in the preparation of ODTs. A number of taste masking techniques are available and are listed below. Details of each technique can be found elsewhere in the literature (12, 13). The taste masking techniques are:

- i)* layering the drug onto inert beads using a binder and its subsequent coating with a taste masking polymer (14, 15);
- ii)* granulating the drug and its subsequent coating with a taste masking polymer (8, 15, 16);
- iii)* spray-drying the drug dispersed or dissolved in a polymeric solution to get taste-masked particles (17, 18);
- iv)* complexation by inclusion in cyclodextrin or drug-resinate complex formation (19–22);

- v) co-acervation to make the drug microencapsulated within a polymer (23, 24);
- vi) formation of pellets by extrusion spheronization or mass extrusion (25–27).

The following section deals in detail with the different techniques used to prepare ODTs.

TECHNIQUES/PROCESSES INVOLVED IN PREPARATION OF ODTs

Lyophilization/freeze-drying

The principle of the lyophilization technique is drying carried out at low temperature under conditions involving removal of water by sublimation (28). In this technique, the material is initially frozen below $-18\text{ }^{\circ}\text{C}$ and then reducing the pressure of the system and giving the necessary heat allows the sublimation process. This technique is extremely useful for heat sensitive drugs and biologicals. Here, the drug is physically entrapped in a water soluble matrix, which is then freeze-dried to give a product that is highly porous and has a large surface area. Due to the porous nature of the product, the liquid medium penetrates into the interior surface of the tablet thereby enhancing its disintegration. The tablets prepared by lyophilization disintegrate rapidly in less than 5 s due to quick penetration of saliva in pores when placed in the oral cavity (4, 29). The lyophilization process gives a glassy amorphous structure to the bulking agent and sometimes to the drug.

In the lyophilization process, the API is dissolved or dispersed in an aqueous solution of a water-soluble excipient, such as gelatin, mannitol, starch or hydrophilic gum and the resultant mixture is poured onto the blister film. The filled blisters are passed through a cryogenic freezing process, specially designed to control the ultimate size of ice crystals. These frozen units are then transferred to large-scale freeze dryers for the sublimation process, where the remaining moisture is removed from the tablets. Finally, the freeze-dried open blisters are sealed *via* a heat-seal process to ensure stability and to protect the product from varying environmental conditions (30). The main advantage of lyophilization is elimination of the adverse effect of heat on the pharmaceutical product as APIs are not exposed to the elevated temperature. The ideal drug candidate for formulating ODTs by lyophilization is a tasteless, water insoluble drug with particle size preferentially smaller than $50\text{ }\mu\text{m}$. Particle size plays an important role as larger particles than the mentioned ones might produce sedimentation problems during manufacturing (31). Water insoluble drugs are generally preferred because incomplete freezing or collapse may occur with water soluble drugs at low eutectic freezing temperature. Low-solubility drugs are weakly bonded to the solvent and are hence more easily converted into the freeze-dried form. Moreover, weakly soluble drugs form less palatable formulations and do not require any taste masking. Water soluble drugs are sometimes converted into a less soluble form with the help of ion-exchange resin or converted to the base form or the polymorphic form may be changed to carry out lyophilization.

Freeze-dried products have shorter dissolution time compared to other solid products (32). The ODT of ketoprofen, a poorly water soluble drug, was prepared by dispersing the drug in aqueous solution of a highly water soluble carrier material such as gela-

tin, glycine or sorbitol. The results of this study show that ketoprofen solubility was increased nearly three times for the lyophilized matrix as compared to the plain drug, which could have been due to the supersaturation generated by the amorphous form of the drug (10).

Corveleyn and Remon (33) studied the influence of various formulation and process parameters on the characteristics of ODT made by lyophilization using hydrochlorothiazide as a model drug. Maltodextrin, gelatin, xanthan gum and hydroxyethylcellulose (HEC) were used as excipients for ODT preparation. The resulting tablets were then analyzed for mechanical strength, porosity, disintegration time and residual moisture. The concentration of maltodextrin, used as the matrix forming agent, was found to affect the integrity and strength of the tablets, their disintegration time as well as the pore size of the product. Increasing the maltodextrin concentration resulted in stronger tablets. The strength of the tablets was also observed to be dependent on the xanthan gum concentration. The disintegration time of the ODTs containing HEC was much shorter compared to those containing xanthan gum as a binder in the same concentration. Incorporation of HEC in the formulations induced a decrease in the strength of the tablets. Addition of polyethylene glycol (PEG) 6000 (1 %, *m/V*) resulted in an increase in drug release from the ODTs within 10 min; however, it decreased the strength of the tablets.

Although the research suggests that the ODTs prepared using freeze-drying showed optimum characteristics, this process has some disadvantages, like the high production cost and longer processing time. ODTs prepared using freeze-drying were found to be fragile, to lack physical resistance in standard blister packs and to have limited capacity or ability to incorporate high concentrations of active drug. ODTs prepared using freeze-drying were difficult to handle due to low mechanical strength and also exhibited poor stability on storage under stressed conditions (34). To improve stability associated with freeze-dried formulations, Blank *et al.* (35) used a mixture of mannitol and natural gum such as acacia gum, guar gum, xanthan gum or tragacanth as carrier material for preparation of an open matrix network structure. The mannitol concentration in stable ODT was reported to be at least 50 % (*m/m*) and the natural gum concentration of the solid dosage form was about 0.07 to 3.2 % (*m/m*). This study revealed an improvement in the properties of ODTs when the open matrix structure comprised mainly mannitol.

Molding

ODTs prepared by molding, also known as solid dispersion, disintegrate within 5 to 15 s (32). Compression molding and heat molding are the two approaches to preparing ODTs by the molding technique. Compression molding involves moistening of the powder blend with a hydro-alcoholic solvent, followed by compression into mold plates to form a wetted mass. The wetted mass is then air-dried to remove the solvent. The compression force involved in compression molding is lower than that used for conventional tableting and hence molded tablets are less compact than conventional compressed tablets and possess highly porous structure, which in turn increases disintegration and dissolution rates.

In the heat molding process for the preparation of ODTs, molten mass containing a dispersed drug and/or dissolved drug is used (36). In this process, suspension of the drug with water-soluble sugars such as mannitol, lactose, sucrose, glucose, sorbitol or

xylitol and agar is prepared and then poured onto blister packaging. The dispersion is then dispensed into molds where the agar solution is solidified at room temperature to form a jelly and dried at 30 °C under vacuum. ODTs developed in this way are found to improve the mouth feel due to the presence of water soluble sugars (32). The physical form of the drug present in ODTs prepared using the molding process depends on whether and to what extent it is dissolved in the molten carrier or molten matrix. Drugs can be present as micro particles or discrete particles dispersed in the matrix. If the drug dissolves totally in the molten carrier, then it forms a solid solution, or a dispersion in the matrix if it dissolves partially in the molten carrier. The disintegration time and dissolution rate of ODTs prepared using molding depend upon the dissolution or dispersion type of the drug.

Modi and Tayade (37) prepared valdecoxib ODT using the molding or solid dispersion method. The drug was kneaded with polyvinyl pyrrolidone (PVP K-30) and compressed into a tablet. The dissolution profile of the developed ODT was then compared with that of commercial products. A phase solubility method was used to evaluate the effect of various water soluble polymers on aqueous solubility of valdecoxib. The outcome of their study showed that the molding technique can be successfully used for improvement of valdecoxib dissolution.

Laitinen *et al.* (38) studied the dissolution rate of perphenazine (PPZ), a poorly water soluble drug, by the solid dispersion technique using 0.1 mol L⁻¹ HCl solution. PVP K-30 and PEG 8000 were selected as carriers and their 5/1, 1/5 and 1/20 mixtures with PPZ were prepared. The dissolution rate of PPZ was improved with all drug/polymer mixture ratios compared to crystalline or micronized PPZ. Considerable dissolution rate improvement was seen with 1/5 PPZ/PEG formulation with PPZ dissolved completely within one minute. DSC and FTIR studies suggested that PPZ dihydrochloride salt was formed and hydrogen bond formation occurred between PPZ and the polymers. Laitinen *et al.* also suggested that formation of a solid solution of PPZ may not be the only factor enhancing the drug dissolution from solid dispersions; the presence of PPZ hydrochloride in the solid dispersions also created a microenvironment around the dissolving particles that led to a high supersaturation of PPZ. This promoted the dissolution of PPZ, especially in the case of high drug-loaded dispersions (5/1 PPZ/polymer). Simultaneous modulation of the micro-environmental pH and drug crystallinity in solid dispersions was also found to be a useful way to increase the dissolution rate of an ionizable drug.

Hence, it can be said that the ODTs preparation using the molding process is easy and convenient at an industrial scale although cannot achieve disintegration time compared to that of lyophilized forms. The molded tablets typically do not possess great mechanical strength and can break during handling or when blister packs are opened. However, the addition of binders (acacia, polyvinylpyrrolidone, PEG) gives sufficient consistency to the formulation and prevents tablet breaking (39).

Cotton candy process

Cotton candy process utilizes a unique spinning mechanism to produce floss of crystalline structure. The process involves formation of a matrix of saccharides or polysaccharides by simultaneous flash melting and spinning. This results into formation of the

candy floss matrix, which is then milled and blended with active ingredients and excipients and subsequently compressed into ODTs. To improve the flow properties and compressibility, the candy floss matrix may sometimes partially recrystallize, which imparts good mechanical strength and can accumulate a large quantity of drug. However, this process is not suitable for thermolabile drugs (40, 41).

Compaction

In the compaction process, a mixture of particulate matter is fed to a compression device which promotes agglomeration due to pressure. Continuous sheets of solid material or solid forms such as briquettes or tablets are produced. Compaction processes range from confined compression devices such as tableting to continuous devices such as roll presses, briquetting machines and extrusion. The following different techniques are based on the compaction mechanism.

Crystalline transition process. – ODTs are prepared by crystalline transition through compressing two saccharides having high and low compressibility/moldability indices and are then subjected to the conditioning process (42). Transition from the amorphous to crystalline state is intentionally done by the conditioning process after tablet compression to achieve sufficient hardness and fast disintegration time. Fluidized bed granulator is commonly used for the crystalline transition process. Particle modification can be carried out by coating or granulating a low compressible saccharide with high compressible saccharides.

Mizumoto *et al.* (42) studied the properties of the tablets prepared using the combination of low and high compressible saccharide. Mannitol was used as a low compressible saccharide and maltose as a high compressible saccharide and binder for granulation. Recrystallization of maltose was done by conditioning the tablet containing amorphous maltose at 25 °C and 70 % RH. The amorphous maltose present on the surface of mannitol particles absorbs moisture during the conditioning process. When crystallization of maltose occurs, particles adhere to each other firmly, which results in increasing the tablet hardness. The disintegration time and tablet hardness were found to be 10–15 s and 4.0–5.8 kg cm⁻², respectively. The authors recommended sucrose, lactose, glucose, xylitol, mannitol, erythritol as low compressible saccharides and maltose, sorbitol, trehalose and multitol as high-compressibility saccharides in increasing order of their compressibility.

Sugimoto *et al.* (43, 44) developed a manufacturing method for ODTs using crystalline transition of amorphous sucrose. Fluidized bed granulation of mannitol was carried out using a sucrose solution as binder and the resultant granules were then compressed into the tablet. The tablet obtained was subsequently conditioned at 25 °C and 51 % RH for two days in a container and the effect of formulation ingredients such as diluents, active drug substances and amorphous sugar on ODTs was studied. Their results revealed that highly water soluble active drug substances were more suitable than low water-solubility active drug substances for the formulation of ODTs and the appropriate formulation was obtained when erythritol, mannitol and xylitol were used as diluents.

Melt granulation. – Abdelbary *et al.* (45) prepared ODTs by incorporating the hydrophilic waxy binder PEG 6-stearate (Superpolystate[®]) in the formulation. Superpolysta-

te[®] has the melting point around 33–37 °C and hydrophilic-lipophilic balance value (HLB) of 9. It acts as a binder and increases the physical resistance of the tablet and also helps in its fast disintegration when placed in the mouth. Crystalline paracetamol was used as a model drug. The formulation also contained mannitol as a water soluble excipient and croscarmellose sodium as disintegrating agent. Granules were prepared in a high speed mixer equipped with a heated jacket. The temperature for granulation was maintained at 42 ± 2 °C throughout the procedure. Initially, the mixture of powders was blended for 3 min at 330 rpm and subsequently Superpolystate[®] was added and phase mixing was continued for further 10 min at 480 rpm. The granulation takes place once the waxy binder melts inside the mixer. At the end of the granulation process, the granules were dried using tray dryers. The sieving process was conducted to get uniform granules, which were then compressed into a tablet with other ingredients like 8.6 % croscarmellose as an external phase disintegrant, 2.9 % aspartame and 0.5 % magnesium stearate. The resultant ODT showed excellent hardness with the disintegration time of just 67 s. In yet another study, Abdelbary *et al.* (46) reported melt granulation as the technique to develop emulsion granulation tablet. The study involved ODT preparation by using emulsion granulation. 12 % emulsion of Superpolystate[®] was used as wetting liquid for the emulsion granulation tablet, which was then added to the internal phase made up of paracetamol, D-mannitol and sodium carboxymethyl cellulose. It was observed that the incorporation of Superpolystate[®] improved the physical resistance and decreased the friability of ODTs.

Perissutti *et al.* (47) developed the ODTs of carbamazepine (CBZ) by the melt granulation technique. The granules of CBZ were prepared using PEG 4000 as a melting binder and lactose monohydrate as hydrophilic filler without using solvents or water. The potential of using crospovidone as a dissolution enhancer and a disintegrating agent was also evaluated. The CBZ granules so prepared displayed a significant improvement in the *in vitro* drug dissolution behavior. The subsequent step encompassed the preparation and evaluation of the tablets, including the effect of extragranular introduction of crospovidone. Besides the remarkable enhancement of the drug dissolution rate of granules in comparison with physical mixtures and the pure drug, no significant differences were found between the dissolution profiles of the granules containing lactose or crospovidone. The dissolution profiles of granules containing crospovidone were found to be superimposable to those prepared without disintegrants. However, the intragranular addition of crospovidone was found to be necessary to produce tablets with a satisfactory disintegration time and a remarkable increase of the drug dissolution rate. Difficult disintegration and bad dissolution performance of the tablets not containing intragranular crospovidone showed the necessity for this disintegrant in the granulating mixture. Moreover, the extragranular addition of a small amount of crospovidone gave rise to further amelioration of the disintegration and dissolution performances (47).

Phase transition. – Kuno *et al.* (48) studied the effect of the preparation method on the properties of ODTs. They manufactured ODTs using phase transition of sugar alcohol (SA). This method was mainly dependent upon the melting point of SA. The process involves compressing the powder containing two SAs of high and low melting points and subsequently heating the compressed mass at the temperature between their melting points. Before the heating process, tablets did not have sufficient hardness because of low compressibility and higher inter-particle bonds. However, tablet hardness was

found to be increased after heating due to diffusion and solidification of SA. While using the wet granulation compression method (WGCM), Kuno *et al.* sprayed a low melting point sugar alcohol (LMPSA) solution onto erythritol particles in a fluidized-bed granulator and the obtained granules were then compressed into tablets. The authors hypothesized that the WGCM may form more complete inter-particle bonds and pore structures compared to the direct compression method (DCM) because of the ease of LMPSA diffusion during the heating process. The result of their study showed that WGCM enables ODTs to maintain rapid disintegrating properties with greater hardness after short heating. The effect of particle size of SA on the hardness and oral disintegrating time of erythritol-trehalose tablets in DCM was also studied (48). The tablets containing small-sized particles of LMPSA became harder after a short period of heating compared to the tablets containing large-sized particles of LMPSA. This could be due to the reduction in LMPSA size that in turn increased the bonding surface area in the tablet, leading to an increase in tablet hardness.

In another similar study, Kuno *et al.* (49) used a combination of two SAs: either erythritol as the high melting point sugar alcohol (HMPSA) (melting point 126 °C) and tetrahalose as the LMPSA (melting point 93–95 °C). They evaluated the effect of lubricant on the characteristics of ODTs manufactured using phase transition of the mixture of lactose and xylitol. The disintegration time of the tablet containing magnesium stearate or sodium stearyl fumarate (SSF) was increased with increase in tablet hardness. However, in case of talc, oral disintegration time did not change with an increase in hardness. Among the three lubricants studied, *i.e.*, magnesium stearate, sodium stearyl fumarate and talc, talc was recommended as the most desirable lubricant for preparation of ODTs by phase transition of SA.

Sublimation. – Conventional tablets with high water soluble ingredients fail to disintegrate rapidly because of their low porosity and this suggests that the presence of a highly porous particle structure in the tablet matrix is an important factor for fast disintegration of ODT. In the sublimation process, volatile substances like camphor, ammonium carbonate, ammonium bicarbonate, benzoic acid, hexamethonium tetramine, naphthalene, phthalic anhydride, urea and urethane were used along with other excipients. Solvents such as cyclohexane/benzene were sometimes also used for further enhancement in the porous matrix formation. Volatilization of these materials eliminates the complicated process associated with the lyophilization process, that is, sublimation of frozen water.

Patel and Patel (50) developed ODTs of etoricoxib using the sublimation technique. Granules containing etoricoxib, aspartame, sublimating agent (camphor/ammonium bicarbonate), intragranular fraction disintegrants (crospovidone) and mannitol were prepared by the wet granulation technique. Menthol was sublimed by exposing granules to the vacuum and the resultant porous granules were then subjected to tableting. Results obtained showed that the sublimation technique effectively improves etoricoxib dissolution.

Suresh *et al.* (51) prepared and evaluated salbutamol sulphate ODTs for asthma. They prepared ODTs by using a volatile substance like camphor/ammonium bicarbonate. Study results showed that physicochemical properties of the ODT evaluated were within the official limits and disintegration time was 5–40 s.

A rapidly soluble tablet made with anhydrous trehalose was described by Roser and Blair (52). Trehalose, which unlike lactose does not undergo Maillard reaction with amino compounds, was incorporated as diluent with the active agent. The obtained tablets had an increased surface area, decreased mass and increased dissolution rate compared to solid tablets of similar dimensions without trehalose. It was also observed that anhydrous trehalose can impart stability to moisture sensitive active ingredients.

Conventional methods. – Different conventional methods such as direct compression, wet granulation and dry granulation are used in the preparation of ODTs. Yamamoto *et al.* (53) studied the effect of tablet characteristics on tablet disintegration. The relationship between disintegration time in the mouth and stationary time of upper punch displacement (STP) was studied using a tableting process analyzer. As the value of bulk density increased, STP became longer and disintegration time in the mouth was shorter. A formulation with bulk density greater than 0.5 g mL^{-1} with the chosen compression force of 5 kN produced a tablet which gave a disintegration time of less than 60 s. Also, the hardness of the tablet was found to be greater than 3 kg if at least one compressible excipient was used in the formulation.

Direct compression method. – Few drugs can be directly compressed into tablets of acceptable quality with good flow properties and stability under pressure. This technique is now applied to the preparation of ODTs if good tablet disintegrants, superdisintegrants and sugar-based excipients are available. Disintegration of the tablets prepared by direct compression depends upon the single or combined effect of disintegrants, water soluble excipients and effervescent agents. Superdisintegrants are a family of disintegrants that are superior to the traditional disintegrant in promoting the tablets to disintegrate into their primary particles when placed in an aqueous environment and are efficient at concentrations as low as 2–5 %.

The commonly used superdisintegrants in ODTs are summarized in Table I.

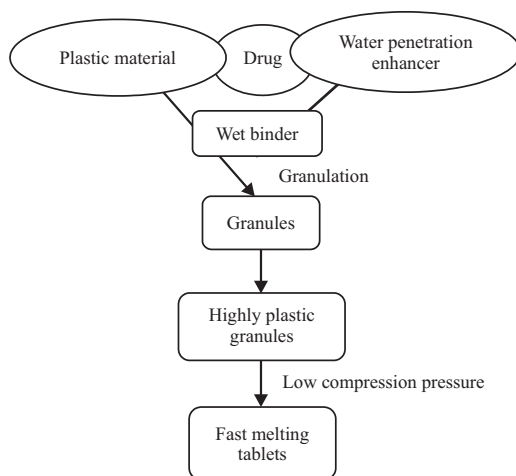


Fig. 1. A general processing step for making highly plastic granules and fast-melting tablets.

Table I. Superdisintegrants employed in ODTs (54–65)

Superdisintegrant	Chemical structure	Physical properties	Mechanism of action
Crospovidone (Kollidon CL, Polyplasdone XL)	Synthetic homopolymer of cross-linked <i>N</i> -vinyl-2-pyrrolidone	Water insoluble, spongy in nature so gives a porous tablet, smoother mouth feel	Capillary action absorbs water leading to swelling
Croscarmellose sodium (Ac-Di-Sol [®] , Nymce ZSX [®] , Primellose [®] , Solutab [®] , Vivasol [®])	Crosslinked form of sodium CMC	Swells in two dimensions, swells 4–8 folds in < 10 s	Swelling
Sodium starch glycolate (Explotab [®] , Primogel [®] , Vivastar P)	Sodium salt of carboxymethyl ether of starch	Swells in three dimensions and at high concentration, serves as sustained-release matrix, Insoluble in organic solvents, disperse in cold water	Water uptake followed by rapid and enormous swelling
Sodium alginate (Kelcosol, Keltone, Protanal)	Sodium salts of alginic acid	Hygroscopic in nature and slowly soluble in water	Swelling
Acrylic acid derivatives	Poly(acrylic acid) super porous hydrogel		Wicking
Soy polysaccharides (Emcosoy [®])	Natural polysaccharide	Does not contain any starch or sugar	
NS-300 (carmellose)	Carboxy methyl cellulose	Particle size 106 μm, disintegration time 20 s	Wicking
ECG-505 (carmellose calcium)	Calcium salt of CMC	Disintegration time 80 s	Swelling
L-HPC (LH-11)	Low hydroxypropyl cellulose	Disintegration time 90 s	Both swelling and wicking
Ion exchange resin (Indion 414, Indion 234, Tulsion 234, Tulsion 344, Amberlite IPR 88)			Swelling
Gas evolving disintegrants (citric acid, tartaric acid, sodium bicarbonate)	Effervescence substance	Evolution of CO ₂ after contact with fluid	In contact with water liberates CO ₂ that disrupts the tablet
Isphagula husk		<i>Plantago ovata</i> seed husk has high swellability and gives uniform and rapid disintegration	Swelling

Wet granulation method. – Fu *et al.* (66) developed a new method for fast melting tablets formed by wet granulation based on highly plastic granules. If a plastic material is polymeric, then it is essential to prevent formation of a viscous layer of the material at tablet surface when it dissolves in aqueous medium. One way of making such tablets is to mix the plastic material with water penetration enhancers at certain ratios and compress them at low pressure. This results in plastic deformation of plastic materials, creating intimate contact among the particles required for forming bonds between the particles. In this process, the plastic particles are separated by water penetration enhancing particles, which prevent formation of a viscous layer on the tablet surface. Highly plastic granules were produced by the wet granulation method. Mannogem EZ spray (spray-dried mannitol) was used as the plastic material and Maltrin QD 580 (maltodextrine in quick dispersing porous form) was used as the water penetration enhancer and sucrose solution (10 to 70 % *m/V*) was used as binder. The plastic material chosen was porous, water soluble or water dispersible and pharmaceutically regarded as safe. Highly plastic granules retain the porous structure even after compression which results in fast disintegration due to fast absorption of water into the compressed tablet (Fig. 1).

Shery *et al.* (67) prepared ODTs of glibenclamide using a modification of the non-reactive liquid based wet granulation technique. Orally dissolving effervescence tablets of glibenclamide were based on highly plastic granules. In the effervescent system, we had to protect the various acids and the carbonate source for the purpose of effervescence. Citric acid was coated with plastic material such as PEG in absolute alcohol (95 %) as vehicle, which provided a physical barrier to the reaction. PEGs can provide a stabilizing effect because of their hygroscopic nature that could decrease the moisture of the effervescence mixture. Also sodium bicarbonate blended with sugar alcohol like mannitol would give a protecting coating over granules of citric acid.

PATENTED TECHNOLOGIES USED FOR MANUFACTURING ODTs

Orasolv[®]. – This is a direct compression technology, which involves effervescent material and taste masked APIs. Effervescence causes a tablet to disintegrate rapidly in less than 1 min on contact with water or saliva, leaving coated drug powder. This technique is frequently used to develop over-the-counter formulations. *Orasolv*[®] is Cima's first orally disintegrating dosage form. *Orasolv*[®] technology can accommodate a wide range of APIs from less than 1 mg to as high as 500 mg. The effervescent mixture comprises two dry ingredients: an effervescent acid (malic acid, tartaric acid, citric acid) and an effervescent base (sodium carbonate, potassium carbonate, potassium bicarbonate). They undergo an effervescent reaction when they come in contact with aqueous solutions resulting in the generation of CO₂ (68).

The microparticles prepared by this newer technique include the dispersion of API into suitable polymers together with other excipients such as mannitol and magnesium oxide. The polymers used for this purpose are ethyl cellulose, methyl cellulose, acrylate and methacrylic acid resins. The API and mannitol were added to the polymeric dispersion under stirring and after that magnesium oxide was added. Mannitol and magnesium oxide act as release promoters for the release of APIs from polymeric coating. The

resulting mixture was dried for 1 h at 50 °C, delumped and again dried for 1 h under similar temperature conditions. The material was then screened through 2.36 mm aperture and dried for 1 h at 60 °C. The formed microparticles, effervescent agents and other ingredient such as flavor, sweeteners, colorants and lubricants were blended and compressed at a low degree of compaction into tablets having 1.0–2.0 kg hardness (69, 70). Tablets developed were fragile and this promoted fast disintegration. To impart physical protection and impermeability to moisture, the tablets were packed in dome-shaped aluminum foil blisters (8).

A novel method, known as particulate effervescence couple was utilized, to overcome the issue of tablet friability associated with the above described technique. The ingredients involved in this technique include polyols as fillers, disintegrants which include effervescence couple, flavor, colorant, sweetener and lubricant. In this method, organic acid crystals are coated by the base material. The particle size of organic acid crystals is greater than the base material for uniform coating of the base material on acid crystals. For the initiation of the coating process, purified water is required as reaction initiator. The reaction end point is determined by measuring CO₂ evolution. The resulting effervescent couple can be used for tablet preparation by mixing with polymer coated APIs and other excipients (8, 71).

Durasolv[®]. – *Durasolv*[®] is Cima's second-generation orally disintegrating tablet formulation manufactured in a similar fashion to *Orasolv*[®], but the tablets produced contain non-directly compressible fillers (sugars and SAs, such as dextrose, mannitol, sorbitol, lactose and sucrose) and a lubricant. The ingredients are fine particles that provide a large surface area for improving the dissolution rate. Disintegrants are avoided in the formulation but wicking agents such as carbopol, gums (gum arabic and xanthan), and hydroxyalkylcelluloses (hydroxyethylcellulose and hydroxypropylmethylcellulose) are added to assist water entry into the tablet. *Durasolv*[®] has much higher mechanical strength than *Orasolv*[®] due to the use of higher compaction pressure during tableting and hence the product can be packed in either traditional blister packs or vials. The newest *Durasolv*[®] formulation, *NuLev*[®], is actually dispensed in stock bottles. However, care must be taken at the time of dispensing tablets from stock bottles because excess exposure to high RH conditions may introduce enough moisture to initiate dissolution of the tablet matrix. The advantage of this technique includes its low cost of production, faster production rate, standard manufacturing technique, standard material, packaging format and low cost and risk dependence. A disadvantage of *Durasolv*[®] is that the technique is not applicable for a large dosage of APIs. As the formulation is subjected to high pressure during the compaction process, the bitter taste of the drug is exposed to the patient's taste buds and therefore *Durasolv*[®] technology is suitable for formulation of small dose tablets of APIs. Other disadvantage is that *Durasolv*[®] has a slightly longer disintegration time (8).

Wowtab[®]. – *Wowtab*[®] technology was developed by Yamanouchi Pharma Technologies, USA. *Wowtab* tablets have sufficient hardness to maintain the physical characteristics of the dosage form during the production and distribution. *Wowtab*[®] technique utilizes saccharides because they possess the properties of fast dissolution in water or saliva and achieve the required tablet hardness upon compaction. However, no single individual saccharide possess both these properties. They either possess fast disintegra-

tion properties or good hardness upon compaction. For example, mannitol, lactose, glucose, sucrose and erythritol showed very quick dissolution characteristics and low compressibility and were called low moldable sugars. Maltose, sorbitol, trehalose and maltitol were called high moldable sugars as they show adequate hardness upon compression, good binding and slow *in vivo* disintegration time (1, 8). The term moldability is defined as the capacity of the compound to compress and dissolve rather than formation of a true molding by solvent wetting and melting (32). A new formulation composition was generated by granulation of a low moldable sugar with a high moldable sugar. The tablet prepared by compression of the above composition, exhibited both fast disintegration and adequate hardness characteristics after humidification and drying. The resulting tablet had a hardness of at least 1.0–2.0 kg and disintegration time of 1–40 s. The taste masking technique utilized in Wowtab® is proprietary but it offers superior mouth feel due to smooth melt action (8).

Flashtab®. – Flashtab® tablets were developed by Prographarm, France. In this technique, most of the excipients are used as for conventional compressed tablets. A disintegrating agent and a swelling agent are used in combination with coated drug particles to produce a tablet that disintegrates in the mouth in one minute. Flashtab® matrix tablet contains a swelling agent such as modified starch or microcrystalline cellulose and a superdisintegrant such as croscopolvidone or croscarmellose. The system may also contain a highly water soluble polyol such as mannitol, sorbitol, maltitol or xylitol with binding properties if no swelling agent is used. The direct coating procedure is used for taste masking of the active ingredient. In the Flashtab® technique, the excipients are first granulated using wet or dry granulation. Then they are mixed with coated drug particles and compressed into tablets using conventional processing equipment. Tablets containing hygroscopic materials can be also blister packed using high quality polyvinyl chloride (PVC) or aluminum foils. These packing materials provide a higher degree of moisture protection than normal PVC or polypropylene foils (1, 8).

Zydis®. – Zydis® technique is owned by R P Scherer, a subsidiary of Cardinal Health. A Zydis® tablet is produced by lyophilizing or freeze-drying the drug in a water soluble matrix material, usually consisting of gelatin. Freeze-drying is done in blisters, where sublimation removes water, which are then sealed and further packed. The resultant product is very porous, light, fragile and disintegrates immediately on contact with saliva. The Zydis® formulation is also self-preserving since the final water concentration in the freeze-dried product is very low and prevents microbial growth. The ideal drug candidates for Zydis® are the ones showing relatively low water solubility, with fine particles and good aqueous stability in the suspension (32). For water soluble drugs, the upper limit for drug loading is very low (approx. 60 mg). The basic problem of water soluble drugs is the formation of a eutectic mixture, which results in freezing point depression and formation of glossy solids on freezing, leading to supporting structure collapse during sublimation. This problem can be solved by adding a crystal forming agent such as mannitol. Mannitol induces crystallinity and ultimately imparts rigidity to the amorphous structure (32, 72). Another way to prevent the collapse of the structure is complexation of soluble drug with ion-exchange resin. Ion-exchange resin also helps in masking the bitter taste of APIs. The appropriate particle size is less than 50 µm. The large particle size of APIs is obtained by using a suspending agent such as gelatin or a flocculating

agent such as xanthan gum. The matrix consists of polymers such as gelatin, dextran or alginates providing structural strength; saccharides such as mannitol or sorbitol to provide crystallinity or hardness, water as a manufacturing process vehicle. The formulation also contains sweeteners, flavors and a preservative such as paraben for drug suspension stability prior to the freeze-drying step. pH adjustment of the suspension is done with citric acid.

The manufacturing and packaging of freeze-dried products is done in PVC or PVDC plastic packs or Aclar laminates or an aluminum foil-foil preparation to protect the product from moisture (32). A disadvantage of the Zydis® technique is that it is relatively expensive. The formulation has poor stability at higher temperature and RH. It readily absorbs water at RH greater than 65 % and results in a collapsed lyophilized product. Patients should use Zydis® formulations within 6 months of opening the laminated foil pouch and immediately after opening the blister pack (31).

Flashdose®. – Flashdose® technology was invented by Fuisz Technologies, USA, now owned by Biovail (Canada). Fuisz Technologies has developed three oral drug delivery systems that involve fast dissolution. The first two generations are quick-dissolving Soft Chew and EZ Chew tablets which require some chewing. Most recently Fuisz also developed Flashdose® technology, which uses a unique spinning mechanism to produce a flash-like crystalline structure, much like cotton candy. These crystalline sugars can then incorporate APIs and be compressed into tablets. Flashdose® dosage form utilizes the shearform technique in association with Ceform™ to mask the bitter taste of the medicament. Ceform™ technique which produces uniform microspheres with very narrow particle size distribution has been patented by Fuisz.

The shearform technology used in the preparation of the matrix is known as floss, which is made from a combination of excipients (73). The floss cotton candy-like fibers are made up of saccharides such as sucrose, dextrose, lactose and fructose. Sucrose required a temperature of 82–130 °C to be transformed into fibers while other polysaccharides such as polymaltodextrins and polydextrose require 30–40 % lower temperature than sucrose. Hence, it is used for incorporation of thermolabile drugs into the formulation (74).

Highly porous and hydrophilic tablets were produced by Flashdose® because of relatively low compression pressure during the tableting. Flashdose® tablets containing a matrix of sugar fibers disintegrate very rapidly within few seconds on contact with saliva (8).

The Flashdose® manufacturing process can be divided into four steps:

1. *Floss blend*. Approximately 80 % of sucrose in combination with mannitol or dextrose and 1 % of surfactant (approx.) are blended to form the floss mixture, in which the surfactant acts as a crystallization enhancer for maintaining the structure and integrity of floss fibers. Also, the enhancer helps conversion of amorphous sugars into crystalline sugar. In this process, dispersed API is retained in the matrix by minimizing its migration out of the mixture (75).

2. *Floss processing*. The floss formation machine consisting of a spinning head and heating element is similar to the cotton candy type. The matrix is produced by subjecting the carrier material to flash heat and flash flow processing. In the flash heat process, the carrier material is heated sufficiently to create the internal flow condition and then

exit through the spinning head, which throws the floss by centrifugal force. Sufficient centrifugal force is generated by spinning head rotation at approximately 2000–3600 rpm. The heating blocks are positioned around the circumference of the crown and are outlined outside on the rim of the heaters. Narrowing the width of the aperture and increase in the path length of the existing material result in the production of fibers. The fibers produced are usually amorphous (76–78).

3. *Floss chopping and conditioning.* The fibers are conditioned to smaller particle size in a high shear mixer granulator by chopping and rotation. The conditioning is performed by partial crystallization, which is carried out by spraying ethanol (< 1 %) on the floss. The resultant evaporated floss fibers possess the cohesive properties and improved flow properties (73).

4. *Tablet blend and compression.* The resultant floss fibers are then blended with API along with other required tablet excipients and compressed into tablets. A modification of this process is a curing step. The curing step is added to improve the mechanical strength of the barely molded flashdose dosage form in plastic blister pack dispersion. The curing step involves exposure of the dosage form to elevated temperature and humidity conditions such as 40 °C and 85 % RH for 15 min. The curing step is carried out for crystallization of the floss material.

Oraquick[®]. – *Oraquick*[®] formulation was developed by utilizing patented taste masking technologies such as FlavourTech and MicroMask. In MicroMask technology, the taste masking process is done by incorporating the drug into the matrix microsphere and KV Pharmaceutical claims that MicroMask has good taste masking compared to FlavourTech. In *Oraquick*[®] technique, tablets are prepared by dissolving the sugar (sucrose, mannitol, sorbitol, xylose, dextrose, fructose or mannose) and protein (albumin or gelatin) in a suitable solvent such as water, ethanol, isopropyl alcohol and ethanol-water mixture. The matrix solution is then spray-dried to give highly porous granules. Porosity of the resultant granules depends upon the quantity of solvent used in the process. These granules are then mixed with the drug and other tablet ingredients or excipients and compressed at low compression pressure. The compressed tablets are treated in a sintering step. Tablets are sintered in an oven at about 50 to 100 °C for a few minutes to a few hours or subjected to 90 °C for 10 min. When a tablet is compressed it achieves significant mechanical strength without disturbing the taste masking (31).

Lyoc[®]. – *Lyoc*[®] technique is owned by Cephalon Corporation. CIMA is a subsidiary of Cephalon and it currently manages the *Lyoc* R&D efforts. This was the first freeze-drying technique used for the manufacturing of ODTs. The liquid solution or suspension preparation involves fillers, thickening agents, surfactants, non-volatile flavoring agents and sweeteners along with APIs. The resultant homogeneous liquid is placed in blister cavities and subjected to freeze-drying. *Lyoc*[®] tablets do not contain preservatives (80). To prevent inhomogeneity due to sedimentation during this process, the formulation requires a large proportion of undissolved inert filler (mannitol) in order to increase the viscosity of the in process suspension. The high proportion of filler reduces the potential porosity of the dried dosage form and results in denser tablets, with disintegration rates comparable to the loosely compressed oral melt formulations.

Advatab[®]. – Eurand's Advatab[®] is a new generation ODT. Advatab[®] is based on an external lubrication system patented by Eurand Technologies (Italy). The lubricant is only applied to the tablet surface, which produces hard and durable tablets without the need of high compression forces during manufacturing. In this technology, the microencapsulation process completely envelopes individual drug particles with gastro-soluble polymer barrier coating between the drug and taste buds in the mouth. Microencapsulation restricts the dissolution of API in the mouth but allows rapid dissolution in the gastrointestinal tract. Polymers used for microencapsulation of bitter drugs include ethylcellulose, cellulose acetate phthalate and hydroxypropyl methylcellulose phthalate, depending upon the solubility in water or cyclohexane. Co-acervation process is used for coating of the polymeric membrane and there is no need of plasticizer to form membranes on active cores for effective taste masking. Advatab[®] tablets disintegrate rapidly in the mouth, typically in less than 30 s to allow for convenient oral drug administration without water. These tablets are especially suited to patients that experience difficulty in swallowing capsules and tablets. Advatab[®] is different from other ODT technologies in that it can be combined with Eurand's complimentary particle technologies like Microcaps[®] (world leading taste masking technology) and Diffucaps[®] (controlled release technology). A combination of Advatab[®] and Microcaps[®] creates products that offer the dual advantage of a patient's preference together with superior taste and smooth mouth feel. This is critical advantage as the unpleasant taste of drugs restricts application of other ODT technologies (34).

Frosta[®] (*Akina*). – The Frosta[®] approach utilizes conventional wet granulation processing and tablet machines for extremely cost effective production of fast-melting tablets. In this technique, plastic granules are formulated and compressed at low pressure to produce strong tablets with high porosity. Plastic granules are composed of three components – porous and plastic material, water penetration enhancer and binder. The process involves mixing of the porous plastic material with water penetration enhancer followed by granulation with binder. The tablets obtained have excellent hardness and rapid disintegration time, ranging from 15 to 30 s depending on the size of the tablet (34).

Quick-Dis Technology[®]. – The novel intraoral drug delivery system, trademarked Quick-Dis[™], is Lavipharm's proprietary patented technology and is a thin, flexible and quick-dissolving film (81). The film is produced by the solvent casting method. In this technique, water-soluble hydrocolloids like gelatin, pectin, gum acacia, gum arabic, hydroxypropylmethylcellulose or starch were completely dissolved in water to form a homogenous viscous solution. Other ingredients such as emulsifying agents, solubilizing agents, wetting agents, taste-modifying agents, plasticizers, water-soluble inert fillers, preservatives, buffering agents, coloring agents, and stabilizers along with APIs were dissolved in a small portion of aqueous solvent using a high-shear processor. The active mixture was then added to the viscous hydrocolloid solution to form a homogeneous viscous solution. This viscous solution was degassed under vacuum and the resulting bubble-free solution was then coated on a non-treated casting film with typical coating thickness of 5–20 μm . The coated film was subsequently sent into an aeration drying oven. The dry film was then cut into the desired shape and size for the intended application (82).

The film is placed on the top or on the floor of the tongue and retained at the site of application; it rapidly releases the API for local and/or systemic absorption.

The typical disintegration time is only 5 to 10 s for the Quick-Dis™ film of 2-mm thickness. The dissolving time, which is defined as the time at which not less than 80 % of the tested film is dissolved in aqueous media, is around 30 s for Quick Dis™ film of 2-mm thickness. The typical release profile of an API by Quick-Dis™ drug delivery system is 50 % of the drug released within 30 s and 95 % within 1 min. The thickness of a typical film is 1–10 mm and its surface area can be 1–20 cm² for any geometry. The Quick-Dis™ drug delivery system can be dispensed in various packaging configurations, ranging from unit-dose pouches to multiple-dose blister packages.

Nanocrystal Technology/nanomelt®. – For ODT, Elan’s proprietary Nanocrystal® technology improves compound activity and final product characteristics. Decreasing the particle size increases the surface area, which in turn leads to an increase in the dissolution rate and this is the main principle behind the Nanocrystal™ technology. This technique is especially used for poorly water-soluble drugs. Nanocrystal™ particles are nano-sized drug substances, typically less than 1000 nm in diameter, which are produced by milling

Table II. Some of promising drug candidates for ODTs

Category of API	Examples of APIs
Antibacterials	ciprofloxacin, tetracycline, erythromycin, rifampicin, penicillin, doxycyclin, nalidixic acid, trimethoprim, sulphacetamide, sulphadiazine
Anthelmintics	albendazole, mebendazole, thiabendazole, ivermectin, praziquantel, pyrantel embonate, dichlorophen
Antidepressants	trimipramine maleate, nortriptyline · HCl, trazodone · HCl, amoxapine, mianserin · HCl
Antidiabetics	glibenclamide, glipizide, tolbutamide, tolazamide, gliclazide, chlorpropamide
Analgesics/anti-inflammatory agents	diclofenac sodium, ibuprofen, ketoprofen, mefenamic acid, naproxen, oxyphenbutazone, indomethacin, piroxicam, phenylbutazone
Antihypertensives	amlodipine, carvedilol, diltiazem, felodipine, minoxidil, nifedipine, prazosin · HCl, nimodipine, terazosin · HCl
Antiarrhythmics	disopyramide, quinidine sulphate, amiodarone · HCl
Antihistamines	acrivastine, cetirizine, cinnarizine, loratadine, fexofenadine, triprolidine
Anxiolytics, sedatives and hypnotics	alprazolam, diazepam, clozapine, amylobarbitone, lorazepam, haloperidol, nitrazepam, midazolam phenobarbitone, thioridazine, oxazepam
Diuretics	acetazolamide, clorthiazide, amiloride, furosemide, spironolactone, bumetanide, ethacrynic acid
Gastro-intestinal agents	cimetidine, ranitidine · HCl, famotidine, domperidone, omeprazole, ondansetron · HCl, granisetron · HCl
Corticosteroids	betamethasone, beclomethasone, hydrocortisone, prednisone, prednisolone, methyl prednisolone
Antiprotozoals	metronidazole, tinidazole, omidazole, benznidazole

using a proprietary wet milling technique and are stabilized against agglomeration to create a suspension that behaves like a solution.

Nanocrystal™ orally dissolving technology provides for:

- i) pharmacokinetic benefits, which mainly include bioavailability of orally administered nanoparticles (< 2 µm) in the form of a rapidly disintegrating tablet matrix;
- ii) product differentiation based upon a combination of proprietary and patent-protected technology elements;
- iii) exceptional durability, enabling use of conventional packaging equipment and formats (*i.e.*, bottles and/or blisters);
- iv) wide range of doses (up to 200 mg of API per unit);
- v) use of conventional, compendial inactive components;
- vi) employment of non-moisture sensitive inactives.

Nanocrystal colloidal dispersions of drug substance are combined with water soluble, generally regarded as safe (GRAS) ingredients, filled into blisters and lyophilized. The resultant wafers dissolve in very small quantities of water in seconds. This approach is mainly used when working with highly potent or hazardous materials because it avoids a number of manufacturing steps such as granulation, blending and tableting, which generate large quantities of aerosolized powder and constitute a much higher risk of toxicity.

Table II summarizes suitable drug candidates for developing ODTs, and commercially available ODT products are listed in Table III.

Table III. Commercially available ODTs

Trade Name	Active Drug	Manufacturer
Nimulid-MD	Nimesulide	Panacea Biotech, New Delhi, India
Feldene Fast Melt	Piroxicam	Pfizer Inc., NY, USA
Zyrof Meltab	Rofecoxib	Zydus Cadila, India
Pepcid RPD	Famotidine	Merck and Co., NJ, USA
Romilast	Montelukast	Ranbaxy Labs Ltd., New Delhi, India
Torrox MT	Rofecoxib	Torrent Pharmaceuticals, Ahmedabad, India
Olanex Instab	Olanzapine	Ranbaxy Labs Ltd., New Delhi, India
Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK
Mosid-MT	Mosapride citrate	Torrent Pharmaceuticals, Ahmedabad, India
Febrectol	Paracetamol	Prographarm, France
Maxalt MLT	Rizatriptan	Merck and Co., NJ, USA
Zelapar TM	Selegiline	Amarin Corp., London, UK

CONCLUSIONS

The introduction of ODTs has solved some of the problems encountered in administration of drugs to pediatric and elderly patients, who constitute a large proportion of the world's population. Large numbers of companies are in the ODT drug delivery market, which is evident from the number of products launched as ODTs and of patents approved. Amongst other drug delivery companies, those in the ODT market possess a tremendous potential of extending the drug product life cycle and extending the profitability of existing products. Owing to ODT flexible nature, molecules of a wide variety of doses and chemical characteristics can be incorporated into an ODT. The different technologies such as fine particle layering/coating or adding flavors/sweeteners into the tablet matrix for taste masking, spray-drying, granulation, freeze-drying and molding are now widely accepted in the industry for developing ODTs. It is reasonable to expect that future trends in drug delivery system innovation will continue to bring together different technological disciplines to create novel technologies.

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S A Ž E T A K

Pregled tehnologija pripreve oralno raspadljivih tableta

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Oralno raspadljive tablete (ODT), poznate i kao lako topljive tablete, brzo raspadljive i kao orodisperzibilni sustavi, imaju jedinstveno svojstvo trenutnog raspadanja u ustima, bez žvakanja i bez potrebe uzimanja vode, što poboljšava pacijentovu suradljivost. U pripravi ODT koriste se uobičajene metode kao što su izravna kompresija, vlažna granulacija, kalupljenje, sušenje sprejanjem, sušenje smrzavanjem i sublimacija, a u njihovoj proizvodnji napredne tehnologije kao što su Orasolv[®], Durasolv[®], Wowtab[®], Flashtab[®], Zydis[®], Flashdose[®], Oraquick[®], Lyoc[®], Advatab[®], Frosta[®], Quick-Disc[®] i Namomelt[®]. Cilj ovog rada je dati uvid u uobičajene i novije tehnologije u pripravi ODT.

Ključne riječi: oralno raspadljive tablete, orodisperzibilne tablete, superdezintegratori, isporuka lijekova, brzo raspadljive tablete

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