A Comprehensive Review: Antihypertensive Fast Dissolving Tablet

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Abstract:

Hypertension, commonly known as high blood pressure, is a widespread health issue that poses substantial risks to cardiovascular health and overall well-being. Effectively managing this condition is vital, and antihypertensive medications play a pivotal role in regulating blood pressure and decreasing the likelihood of serious complications such as heart disease, stroke, and kidney problems. This detailed analysis delves into a range of topics related to hypertension treatment, including the advantages of fast-dissolving tablets and their impact on patient adherence to prescribed regimens. It also examines traditional preparation techniques that have been historically used in the development of antihypertensive therapies. A thorough exploration of various classes of antihypertensive medications is featured in this analysis. These classes encompass beta-blockers, which help reduce heart rate; angiotensin II receptor blockers (ARBs), which relax blood vessels; angiotensin-converting enzyme (ACE) inhibitors, known for preventing the conversion of angiotensin I to angiotensin II; calcium channel blockers (CCBs), which inhibit calcium entry into cells to decrease blood pressure (B. P.); and thiazide diuretics, which aid in reducing fluid retention. Additionally, the analysis outlines specific

criteria for evaluating the effectiveness and quality of fast-dissolving tablets, highlighting their importance in improving medication compliance among patients with hypertension. This comprehensive review aims to provide valuable insights into emerging trends in the management of high blood pressure.

Keywords:

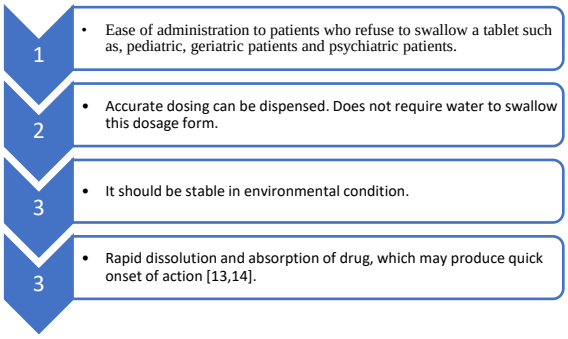
Fast-dissolving tablets, Hypertension, Angiotensin-converting enzyme (ACE) inhibitors, Blood pressure.

Introduction:

The oral route remains a preferred method for administering therapeutic agents, despite significant advancements in drug delivery systems. This preference is due to several factors: it allows for accurate dosage, offers low-cost therapy, supports self-medication, is non-invasive, and is easy to administer, all of which contribute to high patient compliance. However, pediatric patients may experience

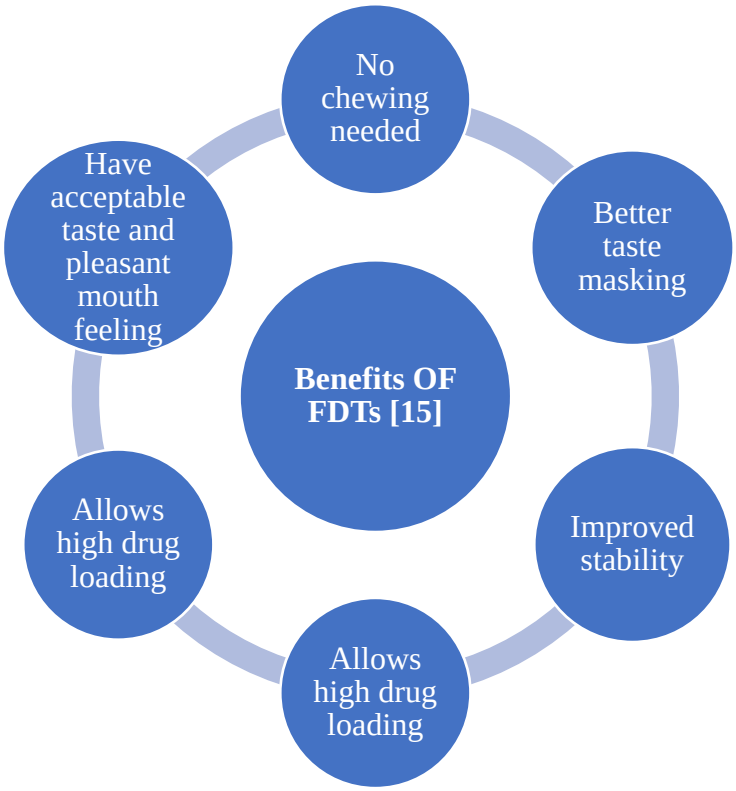
difficulties with ingestion due to underdeveloped muscular and nervous control. Additionally, patients traveling with limited or no access to water may find it challenging to use conventional tablets or capsules that are taken orally [1, 2, 3]. Fast-dissolving tablets (FDT) are highly preferred commercial products. The oral route is the most desired and accepted method of drug delivery by patients. [1]. The most well-known dosage forms are tablets and capsules. One significant disadvantage of these forms is that they can be difficult to swallow. Fast-dissolving tablets offer several advantages: they do not require water for administration, provide a rapid onset of action, reduce the risk of choking, and bypass hepatic first-pass metabolism [4]. Many patients struggle to swallow tablets and hard gelatin capsules, which leads to noncompliance with their medication regimens. It's estimated that about 50% of the population experiences this issue, resulting in a high rate of noncompliance and ineffective treatment [5, 6]. There is a growing demand for solid dosage forms that can be easily dissolved or suspended in water, chewed, or quickly dissolved in the mouth. This trend is especially relevant in the pediatric and geriatric markets, but it also appeals to other patients who prefer a convenient way to take their medication. As the average human lifespan increases and swallowing ability declines with age, administering oral tablets has become a significant challenge and is gaining public attention [7]. Before being ingested, these dose forms are put in the mouth and dissolved or scattered in saliva. In certain instances, they are made to pass through the esophageal and buccal mucosa when saliva enters the stomach. Under such circumstances, a drug's bioavailability from fast-dispersing formulations may surpass that of conventional dose forms [8]. One of the main challenges with fast-dissolving tablets (FDT) is the bitterness of the medication, which can be detected by taste buds as the tablet disintegrates in the mouth. To address this issue, taste masking techniques are essential. These may include methods such as forming inclusion complexes, applying polymer coatings, and utilizing resin complexes.

Ideal characteristics of FDTs



According to the European Pharmacopeia, "Oral Dispersible Tablets (ODTs) should disperse or dissolve in less than three minutes when placed on the tongue." The concept of a fast-dissolving drug delivery system (FDDDS) integrates the benefits of both liquid and solid formulations while providing advantages over traditional dosage forms. [11, 12].

This review provides clear information about fast-dissolving tablets (FDT).



Conventional techniques used in the preparation of FDTs:

1. Freeze drying/ Lyophilization

The method of lyophilization entails sublimating water out of materials while drying them at low temperatures. This technique produces a very porous structure by encasing the medication in a water-soluble matrix and then freeze-drying it. Because saliva enters the pores of tablets made by lyophilization so quickly, they

dissolve quickly—often in less than five seconds—when put in the oral cavity [16].

2. Molding

This method works especially well for medications that are heat-sensitive, or thermolabile. By employing water-soluble components to prepare molded tablets, this approach guarantees that the pills dissolve quickly and fully. After being wet with a hydroalcoholic solvent, the powder mixture is formed into tablets using less pressure than is typically required for tablet compression. After it has formed, the solvent is eliminated by air-drying [17]. Molded tablets are less dense than compressed tablets, featuring porous structures that enhance dissolution. However, the mechanical strength of molded tablets is a significant concern. To address this, binding agents that improve mechanical strength need to be included in the formulation [18]. Additionally, tablets produced using the molding technique are easier to scale up for industrial manufacturing when compared to those made using the lyophilization technique. [19].

3. Direct Compression

Direct compression represents the most cost-effective and simplest tablet manufacturing technique. Because of the accessibility of improved excipients especially super disintegrants and sugar-based excipients, this technique can now be used for the preparation of Fast Dissolving Tablets [20].

4. Spray drying

The process of spray drying creates thin, highly porous powders that dissolve quickly. In this procedure, an aqueous composition comprising the support matrix and additional ingredients is spray-dried to create a particulate support matrix. The end product is a fine, very porous powder that is combined with active substances before being compacted into tablets. Mannitol is used as a bulking agent in the formulations, while hydrolyzed and non-hydrolyzed gelatins are used as supporting agents. To enhance disintegration and breakdown, disintegrating agents like sodium starch glycolate or croscarmellose sodium are added, as well as acidic (like citric acid) or alkaline (like sodium bicarbonate) substances. In an aqueous media, tablets crushed from the spray-dried powder can dissolve in 20 seconds [21].

5. Mass Extrusion

In this technique, a blend of active drugs and other ingredients is softened with a solvent mixture containing water-soluble polyethylene glycol and methanol. The softened mass is then extruded through an extruder or syringe to form a cylinder of product. This cylinder is subsequently cut into uniform segments using heated blades to create tablets. The dried cylinder can also be used to coat granules of bitter-tasting drugs, effectively masking their unpleasant taste [22, 23].

6. Sublimation

This technique involves adding inert solid ingredients that readily volatilize, such as camphor, ammonium bicarbonate, naphthalene, urea, and urethane, to other tablet excipients. The mixture is then compressed into tablets. The volatile material is subsequently removed through sublimation, resulting in a porous structure. Koizumi et al. applied this sublimation technique to create highly porous compressed tablets that dissolve quickly in saliva. In their study, mannitol served as the tablet matrix material, while camphor was used as the sublimating agent. The sublimation of camphor was

conducted in a vacuum at 80 °C for 30 minutes to develop the pores in the tablets [24].

Potential Candidates for Antihypertensive Fast Dissolving Tablet

A. Antihypertensive agents

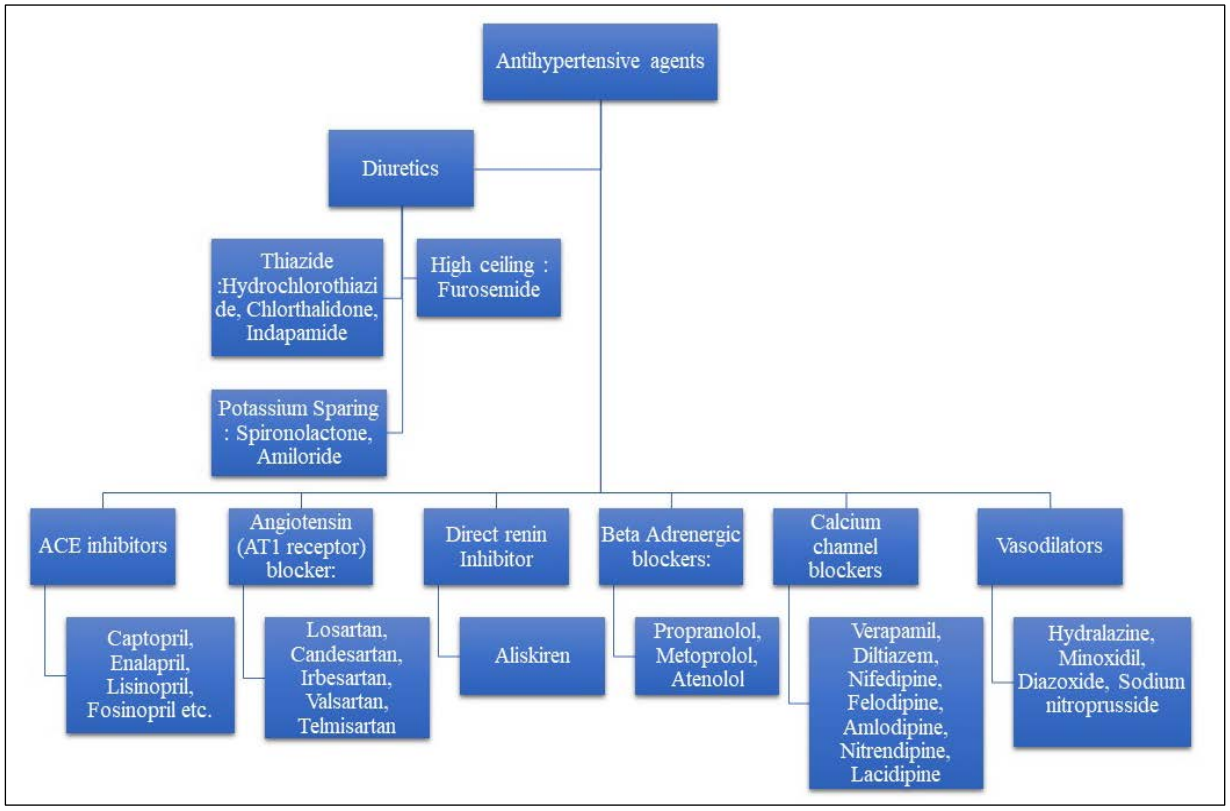


Figure 1 Classification of Antihypertensive drugs

B. Excipients

To balance the characteristics of the active ingredients in fast-melting tablets, excipients are essential. To avoid any possible interactions with the active ingredients, formulators must possess a thorough understanding of the chemistry of these excipients. Additionally, determining the cost of these ingredients is another important consideration for formulators.

Excipients, which are typically inert food-grade substances, aid in improving the intended organoleptic qualities and overall product efficacy when used in the formulation of fast-melting tablets. Although the majority of excipients can be used with a variety of active components, masking agents may be necessary for some particular active substances. [26].

a) Bulking materials:

Bulking materials play a crucial role in the formulation of fast-melting tablets. These materials serve multiple functions, including acting as a diluent, filler, and cost reducer. They enhance the textural characteristics of the tablets, which in turn improves disintegration in the mouth. Furthermore, adding bulk 1 lowers the formulation's active component

concentration. Sugar-based bulking agents, such as mannitol, polydextrose, lactitol, direct compressible lactose (DCL), and starch hydrolysate, are advised for use with this kind of delivery system. These agents are favored for their higher aqueous solubility and favorable sensory perception. Mannitol, in particular, is known for its excellent aqueous solubility and sensory properties. Typically, bulking agents are incorporated into the final composition at levels ranging from 10% to 90% by weight [26].

b) Emulsifying agents:

Emulsifying agents are essential excipients in the formulation of fast-melting tablets. They enable rapid disintegration and drug release without the need for chewing, swallowing, or drinking water. Additionally, these agents help stabilize immiscible blends and improve the drug's bioavailability. Various emulsifiers can be utilized in fast-melting tablet formulations, including alkyl sulfates, propylene glycol esters, lecithin, and sucrose esters. These emulsifying agents can be incorporated at levels ranging from 0.05 percent to approximately 15 percent by weight of the final composition [26].

c) Lubricants:

Lubricants, although not essential excipients, can improve the palatability of tablets after they dissolve in the mouth. They help reduce grittiness and facilitate the drug's transport from the mouth to the stomach [26].

d) Flavors and sweeteners:

Flavoring and taste-masking agents enhance the palatability of products, making them more appealing to patients. These ingredients help mask the bitterness and unpleasant tastes associated with certain active ingredients. Both natural and synthetic flavors can be utilized to improve the taste and overall sensory experience of fast-melting tablets. Formulators have a variety of sweeteners to choose from, including sugar, dextrose, and fructose, along with non-nutritive options like aspartame, sodium saccharin, sugar alcohols, and sucralose. Including sweeteners not only adds a pleasant taste but also provides bulk to the formulation [26].

e) Super disintegrants

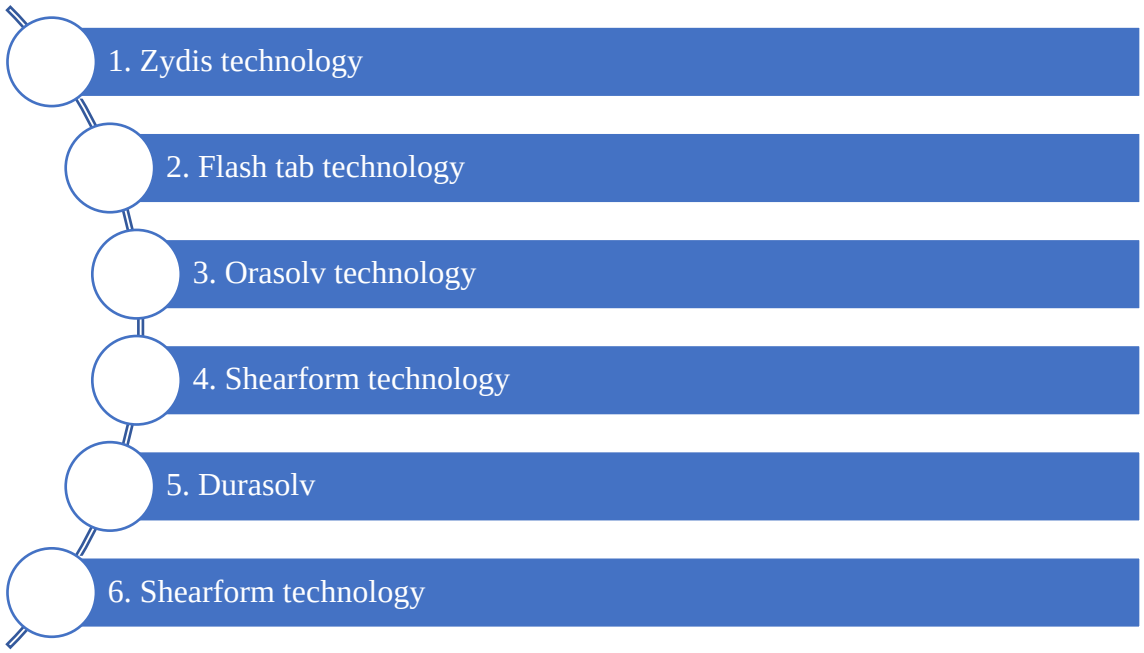
A disintegrant is an excipient, which is added to a tablet or capsule blend to aid in the break up of the compacted mass when it is put into a fluid environment [27].

Table no. 1 List of super disintegrants used in FDTs

super disintegrants	Synonym	Mechanism of action
Sodium-Starch Glycolate	(Explotab, primogel)	Significant and widespread swelling occurs with little to no gelling.
Microcrystalline cellulose	(Avicel, celex)	Water wicking.

Cross-linked Povidone	Crospovidone, Kollidone)	The disintegrant has the highest rate of swelling compared to other disintegrants and possesses a greater surface area-to-volume ratio.
Low-substituted hydroxyl propyl cellulose	(LH-11, LH-21)	Offer binding properties while maintaining the ability to disintegrate.
Cross-linked carboxy methyl cellulose sodium	(Ac-Di-sol, Croscarmellose sodium)	The fibrous structure allows for effective wicking, while also enabling swelling with minimal gelling.

Patent techniques for preparation of FDTs



1. Zydis Technology

The medicine is either entrapped or dissolved in a rapidly dissolving carrier matrix in the special freeze-dried tablet known as Zydis. These tablets dissolve immediately in the mouth with no demand for water. For strength and durability, the matrix contains polymer compounds such as gelatin, dextran, or alginates; for crystallinity and hardness, it contains sweeteners like sorbitol or mannitol. Gums aid in preventing medication particle sedimentation, and water is employed in production to generate porous units for quick breakdown. Glycine and other collapse protectants prevent shrinkage

during storage and freeze-drying. Blister cases are used to protect Zydis goods from dampness [28, 29].

Durasolv Technology

CIMA Labs created the proprietary Duracell technology. A medication, fillers, and a lubricant are all included in tablets made with this technology. They have a high degree of stiffness and are produced using standard tableting equipment. Blisters and other conventional packaging methods can also be used to package these pills. Durasolv works best for items that need minimal levels of active chemicals [28, 29].

Orasolv Technology

Orasolv Technology has been developed by CIMA Labs. This system involves taste-masking the active ingredient and includes an effervescent disintegrating agent. The tablets are produced using a direct compression technique with low compression force to minimize oral dissolution time. Conventional blenders and tablet machines are utilized for tablet production. The resulting tablets are soft and friable, and they are packaged using specially designed pick-and-place systems [28, 29].

Wowtab Technology

Yamanouchi Pharmaceutical Company is the patent holder of Wowtab Technology. "WOW" is an acronym for "Without Water." A combination of low and high-moldability saccharides is used in this novel approach to produce a tablet that melts quickly without losing its structural integrity. A low-moldability saccharide is combined with the active component, which is subsequently granulated with a high-moldability saccharide and compressed into tablet form [28, 29].

Flash Dose Technology

Fuisz is the patent holder of flash dosage technology. Nurofen Meltlet, a novel form of ibuprofen that Biovail Corporation introduced as melt-in-mouth tablets, is the first commercial product to use this technology. The self-binding shear form matrix that makes up flash tablets is called "floss." Flash heat processing is the method used to manufacture these shear-form matrices [28, 29].

Flashtab Technology

Prographarm Laboratories has patented a technology called Flashtab. Tablets produced with this system contain the active ingredient in the form of microcrystals. The drug micro granules can be prepared using conventional techniques such as coacervation, microencapsulation, and extrusion-spheronization. All the processes involved use standard tableting technology [28, 29].

Oraquick Technology

OraQuick is a fast-dissolving tablet that utilizes a patented taste-masking technology. KV Pharmaceutical's microsphere technology, known as Micro Mask, enhances the mouthfeel without the use of solvents, allowing for faster and more efficient production. Additionally, its lower heat production makes OraQuick suitable for heat-sensitive medications. The pliable matrix surrounding the drug powder enables strong tablet compression while effectively preserving taste. OraQuick claims to dissolve in seconds while effectively masking any unpleasant flavors [30].

Evaluation of fast-dissolving tablets

1. Shape and Size:

A tablet's dimensions can be precisely defined, tracked, and managed. When employing filling equipment, tablet thickness is an essential feature for maintaining a consistent appearance and

for efficient counting. Certain filling machines use the consistent thickness of the tablets as a counting mechanism. For instance, ten tablets are chosen, and a micrometer is used to test their thickness [31, 32, 33].

2. Hardness:

One of the main advantages of orally disintegrating tablets (ODTs) can be difficult to achieve due to the specialized processes and ingredients required for their production. To ensure that these tablets dissolve quickly in the mouth, their hardness is usually kept within a lower limit. The hardness of ODTs can be measured using standard hardness testing equipment [32].

3. Friability:

For orally disintegrating tablets (ODTs), formulators may find it difficult to achieve the required friability % within predetermined bounds. A higher proportion of friability is frequently the result of different production techniques. To keep the findings within the allowed range of 0.1% to 0.9%, this parameter must be evaluated. For orally disintegrating tablets (ODTs), formulators may find it difficult to achieve the required friability % within predetermined bounds. A higher proportion of friability is frequently the result of different production techniques. Assessing this parameter is therefore essential to ensuring that the outcomes remain within the permissible range of 0.1% to 0.9% [33, 34].

4. Wetting time:

A 12 cm by 10.75 cm piece of tissue paper is folded twice and placed in a 6.5 cm diameter Petri dish containing 6 ml of Sorenson's buffer at pH 6.8. A tablet is placed on the paper, and the time taken for it to become completely wet is recorded. Three trials are conducted, and the standard deviation is calculated. [33, 34].

5. In-vitro disintegration test

The test is performed on six tablets using the apparatus specified in I.P.-1996. Distilled water at a temperature of 37°C ± 2°C is used as the disintegration medium. The time, measured in seconds, is recorded for the complete disintegration of the tablet, ensuring that no remnants of the tablet remain in the apparatus [27, 28, 29].

6. Dissolution test:

The USP monograph usually specifies the dissolving conditions for drugs. Orally disintegrating tablets (ODTs) should be evaluated using other media, such as pH 4.5, pH 6.8, and 0.1 N HCl buffers. Testing ODT dissolution is best done with the USP II paddle equipment, which is typically set at 50 rpm. In these circumstances, ODTs often dissolve rapidly, therefore comparison profiles might benefit from slower rates. Increasing the paddle speed can help prevent a mound from forming in the vessel from larger tablets, especially those weighing more than one gram and containing dense particles. Therefore, 25 to 75 rpm is the ideal stirring speed range [30, 31].

Conclusion:

FDTs, or fast-dissolving tablets, are dosage forms designed to dissolve or disintegrate rapidly in saliva, typically within a few seconds. They offer several advantages over conventional dosage forms, including improved efficacy, enhanced bioavailability, rapid onset of action, and increased patient compliance. FDTs are particularly beneficial for pediatric and geriatric patients as they are easier to administer. These tablets can be formulated using various methods, depending on the specific drug and additives involved. While FDTs generally

have lower mechanical strength, recent advancements in technology and the use of specific additives have made it possible to produce FDTs with sufficient mechanical strength.

Abbreviations:

FDTs- Fast dissolving/ disintegrating tablet

ARBs- Angiotensin II receptor blockers

ACE- Angiotensin-converting enzyme inhibitors

CCB- Calcium channel blocker

B. P- Blood pressure

ODT- Oral dispersible tablet

FDDDS- Fast dissolving drug delivery system

DCL- Direct compressible lactose

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