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REVIEW ARTICLE

An update on oral dispersible tablets

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Abstract

Oral solid dosage forms are by far the most preferable and widely used dosage form, although it still has some limitations, such as 1st pass metabolism, GI adverse effects, and prolonged onset of action as compared to injectable products. Oral dispersible tablet (ODT) system presents a solution to these problems, by providing rapid onset of action, reduce 1st pass metabolism, and prevent GI adverse effects. This is achieved by using superdisintegrants which decrease the disintegration time and provide rapid action and better bioavailability. This study is aimed at reviewing the various kinds of superdisintegrants and their action.

Keywords

1st pass metabolism
Bioavailability
Oral dispersible tablet

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Introduction

For most of the therapeutic agents that are intended to exert systemic effects that's why oral route is always preferred method of administration as it has high compliance of patient rate in comparison to all other routes (Valleri, 2004). Although it's major drawback is trouble in swallowing conventional tablets, especially by pediatrics and geriatrics (Tanmoy Ghosh, 2011; Jagadeesh Induru, 2012). Uptill now, more than half of the pharmaceutical preparations are administered orally due to several advantages (Sunita Kumari, 2010). A major setback for conventional solid oral dosage form is the protracted disintegration time which leads to delayed pharmacological action so effect of the medicine is achieved about 30-45 minutes after administration (J., 2011). This problem can be overcome with tablets which liquefy quickly when placed in the oral cavity leading to reduce the onset of action (Siddiqui, 2010).

After placing FDT in oral cavity, saliva rapidly penetrates through the pores producing swift disintegration (Puttewar, 2010). Based on literature, the absolute bioavailability of diclofenac sodium tablet is about 50-60%, this means that only around half of the original dose is available for systemic effect and the remaining half is unexploited by the liver (BJ., 2011).

Orodispersible tablets, sometimes known as fast-disintegrating tablets, orally disintegrating tablets and mouth-dissolving tablets. European Pharmacopoeia has now termed this system as orodispersible tablets. They can be described as an non-coated tablet system used to be placed in oral mucosa where they rapidly disperse, and then can be swallowed (Fu, 2004). The advantages offered by mouth dissolving tablet dosage form are now being known in industry as well as in academic research (Anupama Kalia, 2002). Although this system may not be able to fully solve all these compliance issues with conventional tablets, but it can be expected to create an advancement of sufficient therapeutic significance (Amit Modi, 2012).

They can be prepared by using various techniques including wet granulation (Ravi kumar, 2009; Suresh Kulkarni, 2011), direct compression (Jain, 2009), freeze drying (Ahmed, 2006), spray drying (Mishra DN, 2006) and sublimation. Various studies prove that orodispersible tablets prepared by direct compression comply to all parameters like weight variation, friability, content uniformity, hardness, dissolution and disintegration, and profile (Dandag P, 2006; Margret Chandira R, 2010).

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Advantages of ODT: They provide administration ease as mostly patients are unwilling to swallow conventional tablet especially paediatric and geriatrics (Habib W, 2000). Tablet disintegrates and dissolves within a matter of seconds leading to rapid onset of action of drug. FDT will be safer than conventional dosage forms as it eliminates choking or airway obstruction (Kushagra Khanna, 2016). Drug is primarily absorbed through oral mucosa so gastrointestinal adverse effects are minimized. Direct absorption through oral cavity can result in improved bioavailability. Minimum 1st pass metabolism lead to reduced dose which improve clinical performance by reducing side effects. Can be easily swallowed without water. Thus is highly convenient for patients while travelling or who can't have immediate access to water (Parakh, 2003). In case of drugs absorbed from the mouth, pharynx and oesophagus, bioavailability of drugs increases. ODTs have a good mouth feel which improves patient compliance, particularly in paediatric patients. It provides the advantages of liquid dosage form and the stability of solid preparation. Can be mostly prepared by direct compression, so easy to manufacture and cost effective (Priyanka Khokhar, 2014).

Disadvantages of ODT: Only those drugs can be formulated that are sufficiently absorbed through the oral mucosa at salivary pH. Only suitable for drugs with a small dose. Most excipients used in this system are hygroscopic so tablets should be stored at measured humidity and suitable temperature. Usually have less hardness than conventional tablets and low mechanical strength. Hence require careful handling. As they stay in mouth for a longer duration, they may leave bad taste or mouth feel if they're not formulated properly (Kushagra Khanna, 2016).

Mechanism of disintegration of ODTs: The mainstay of ODT system is superdisintegrants, whose predominant action is through interaction with available medium. There are different types of superdisintegrants used which follow one or more of the following mechanisms (Abhay Asthana, 2013).

Deformation: When the tablets are compressed, the dis-integrant particles may get deformed and upon coming in contact with aqueous medium, they regain their normal shape and size. So this changes the structure of the whole tablet, disintegrant particle repel each other and causes breakup of the whole tablet (Alexander Amit, 2010).

Swelling: Upon coming in contact with aqueous medium the particles swell, and repel each other leading to overcome adhesiveness of the particles and causes the breaking of tablets (kumar Shobhit, 2012b).

Wicking (capillary action): After coming in contact to the aqueous medium, the medium penetrates through the interparticulate spaces causing flagging of the bonding force among the particles of drug. This causes the tablet to break into sufficient fine particles (kumar Shobhit, 2012b).

Ideal characteristic of superdisintegrants: Poorly water soluble and having sufficient hydration capacity; Minimum gel formation; Good compressibility; Inert; Non-toxic; Good flow properties; Requirement of least quantity; Good mouth feel (Sharma V, 2010; Shihora H, 2011).

Technologies for ODTs Formulation: There are various techniques used in preparing ODTs, including direct compression, mass extrusion method, sublimation method, moulding method and freeze drying etc. Direct compression is a more simple and frequently used method as it employs commonly available excipients plus it involves limited steps (Chackol A.j, 2010). The low manufacturing budget is the utmost benefit of direct compression particularly at large scale production levels (kulkarni S.D, 2011).

Direct compression: Direct compression offers many advantages as it consists of fewer stages, minimum exposure to heat as well as moisture. That's why it is preferable process for hygroscopic drugs and thermo-sensitive substances(Mira J, 2000). Furthermore it increases the productivity and decreases the overall expense on the product thus reducing its final cost (Theresa B, 2001).

Sublimation: It involves mixing of drug, the volatilizing agent and excipients required to compress in tablet form. Then the volatile ingredient is evaporated by sublimation resulting in absorbent structure of the tablet. Volatilizing agents commonly employed are camphor, ammonium bicarbonate and ammonium carbonate (Fu Yourong, 2004).

Freeze-Drying: It is a process by which water is removed by sublimation process from the products containing heat sensitive substances. The tablet thus formed is brittle hence requiring distinct packing. Tablets made by this method have very low disintegration time but it is an expensive and comparatively time consuming (kumar Shobhit, 2012a).

Moulding: According to this method, hydro-alcoholic solvent is used to dampen or disperse the drug. This moist mixture is moulded to tablets. The solvent may be evaporated from this solution of drug by using hot-air drier. Moulding is frequently preferred for soluble drugs which lead to pleasant mouth feel and faster disintegration of the tablets(Khan Tarique, 2011).

Mass Extrusion: Active ingredient blend is make softer by polyethylene glycol and methanol. This softened mass is expelled through an extruder thus formed cylinder of the product can be cut into small even segments by help of heated blade to give them the form of tablets (Satpathy Tarun Kumar, 2007; Bandari Suresh, 2008).

Spray drying: In spray drying technique, the drug and other excipients is spray dried resulting in absorbent

powder material. This absorbent powder material being finally compressed to produce fast dispersing tablet (Sangale Shamrao S.).

Cotton candy process: In Cotton candy process, sugars matrix i.e. saccharides are formed by applying melting and spinning actions. Then re-crystallized of matrix is done to some extent in order to rend improper flow and compressibility properties. This material is then mixed with the active drug and other excipients and then compressed to form ODTs (kumar Shobhit, 2012b).

Challenges regarding ODTs formulation

Disintegration time and mechanical strength: If mechanical strength is more, disintegration time will extend so these two parameters should be properly assisted (Bharadwaj S, 2010).

Taste masking: Effectual taste masking should be done for nauseous drugs so drug taste should not be felt in oral cavity (Siden R, 2013).

Mouth feel: The particles produced after disintegration of the ODT should be very small. ODT should not leave any residue in the mouth after oral administration. Addition of flavors and cooling agents like menthol enhance the mouth feel (Vani R, 2014).

Sensitivity towards environmental conditions: ODTs must have low sensitivity towards various environmental conditions like temperature and humidity (Parijat Pandey, 2016).

Cost: The technology adopted for an ODT should be acceptable in terms of cost of the final product.

Amount of drug: The application of technologies used for ODTs is limited by the amount of drug that can be incorporated into each unit dose. According to USP, generally the ODT tablet weight should not exceed 500 mg. For lyophilized dosage form, the drug dose should be lower than 400 mg for insoluble drug and <60 mg for soluble drug. This parameter is principally perplexing during formulation of fast dissolving wafers or oral films (Chiman B, 2013).

Hygroscopicity: Numerous orally disintegrating dosage forms are hygroscopic and unable to withstand physical integrity below usual conditions of humidity and temperature. Hence, they require moisture protection which demands for dedicated product packaging (Roy, 2016).

Commonly used superdisintegrants

Natural superdisintegrants: These are the natural substances that have superdisintegrant property and mainly derived from plants. Various gums and mucilages swell significantly upon contact with water and this property can be used for disintegration of tablets. Some of the common natural superdisintegrants are discussed below:

***Planta goovata* Seed Mucilage (Isapghula):** Isapghulais the dried seeds of *Planta goovata* plant which contains a mucilage, present in the epidermis of its seeds. The mucilage is extracted from the seed and used as superdisintegrant. It is a recent innovation and when its super-disintegration property was compared with crosspovidone, it shows even better disintegration time as compared to the superdisintegrant, cross-povidone (P.S Mohanachandran1, 2013).

Xanthan gum: Xanthan Gum is the extract obtained from the plant Xanthomonascampestris. It is official USP compound having high hydrophilic property and low gelling character. It is poorly water soluble and extensively swellable resulting in fast disintegration of tablets.

***Lepidium sativum* Mucilage:** *Lepidium sativum* (family: Cruciferae) is known as Asaliyo and is widely used as herbal medicine in India. It is widely available in market and has very low cost (Dhiraj A. Khairnar, 2014).

Synthetic superdisintegrants: These are the synthetic compounds having remarkable disintegration properties. These are mostly prepared by cross-linking natural substances thus increasing their disintegration properties several times. Some commonly used superdisintegrants are as follows:

Sodium Starch Glycolate: Sodium starch glycolate, exists as sodium salt of carboxymethylester of starch (Shihora H, 2011), is available with brand names; Explosol, Explotab, Primojel etc. It is extensively used in oral pharmaceuticals preparations as tablet disintegrant whether prepared by wet granulation or direct compression (Ainley Wade; Rowe, 2009). The normal concentration range of sodium starch glycolate used in a product varies from 2% to 8%, while its optimum concentration is around 4%, although in various instances 2% also do the job.

Mechanism: Disintegration takes place by rapid water uptake leading to by fast and massive swelling (P.S Mohanachandran, 2011).

Crospovidone: Crospovidoneis a synthetic cross-linked homo-polymer of N-vinyl-2-pyrrolidinone, available as brand names Polyplasdone XL and Polyplasdone XL-10 (Amit Modi, 2012). It is basically insoluble in water, used as tablet disintegrant and also as dissolution agent and is employed in tablets made by direct compression as well as dry and wet granulation. Crospovidone, in addition to its disintegrant properties, also has solubility enhancing action (Rowe, 2009). The normal concentration range of crospovidone used in a formulation as disintegrant varies between 2-5%.

Mechanism: Crospovidone causes disintegration through high capillary activity and hydration capacity with slight chances of gel formation. Some studies found out that the optimum particle size of crospovidone has a strong influence on disintegration of analgesic tablets. It has also been found that larger particlesize provides a faster disintegration timeas compared to smaller particles (P.S Mohanachandran, 2011).

"Nitesh J. Patel et. al" formulated cinnarizine tablets using superdisintegrants such as croscarmellose

sodium, crospovidone, low-substituted hydroxy-propylcellulose (L-HPC), sodium starch glycolate, andpregelatinized starch. The formulation containing crospovidone (at 4.5% level) showed advanced organoleptic qualities accompanied with outstanding in-vitro drug release and disintegration time in comparison to other formulations (Nitesh J. Patel, 2011).

Croscarmellose sodium: Croscarmellose sodium is the cross-linked carboxy-methylcellulose as a sodium salt, also called Acdisol. Croscarmellose sodium can be used in oral solid dosage forms likecapsules, tablets, and granulesas a disintegrant (Priyanka Khokhar, 2014). In tablets preparations, it is widely used in tablets manufactured by both direct compression as well as wet granulation technique (Zhao N, 2006).

Mechanism: Croscarmellose sodium shows a combination of both wicking and swelling phenomena, leading to rapid disintegration of the dosage unit (Zhao N, 2006).

Concentration Range: Croscarmellose sodium can be used as a tablet disintegrant in a concentrations up to 5% w/w, although generally a 2% w/w concentration is also used in tablets that are prepared by using direct compression method and 3% w/w in tablets that are prepared by wet-granulation method (Ainley Wade; Rowe, 2009).

"Fulla M et al." formulated Prifinium bromide using different superdisintegrants. Results showed that formulation containingcroscarmellose sodium (CCS) as superdisintegrant, emerged as the best formulationwith respect to disintegration time, dissolution time and other organoleptic properties (Fulla M. Al-Ghabban, 2013).

"Yashpaul et. al" formulated zidovudine using Crospovidone, Crosscarmellose sodium and sodium starch glycollate as superdisintegrants by direct compression. ODTs prepared with Croscarmellose 6% gave least disintegration time (13.9), and dissolution profile was also better as compared to other formulations (Yash Paul, 2011).

Co-processed superdisintegrants: Co-processing is the process in which two or more excipients are combined by any suitable process (Michoel, 2002). Apparently the use of 2 or more superdisintegrants in combination can be expected to provide better results, to further improve their performance, these superdisintegrants may be co-processed instead of simple physical mixing (Gohel MC, 2005).

One advantage of using superdisintegrant in co-processed form is that it avoids segregation. Another good approach is to blend the superdisintegrants, one of which acts through swelling, and the other acts through wicking, this way the liquid medium will be more quickly brought inside the tablet, and swelling will occur more quickly (Sharma Shailesh, 2011).

Normally Co-processed superdisintegrantsare prepared by employing solvent evaporation process. In this technique2 different superdisintegrants are physically mixed and then added to about 10 ml of ethanol, after mixing thoroughly the ethanol is allowed to evaporate. The stirring is continued until most of the ethanol evaporates. Then this wet mass can be passed through a sieve of suitable size to obtain granules. After drying these granules they are stored in an airtight container (S.B Shirsand, 2010).

Co-processed superdisintegrants are believed to have better disintegration capacity than either of the superdisintegrants used alone. This is also elaborated in various studies, that co-processed superdisintegrants show better results than physically mixed superdisintegrants.

In a study by *"Swamy et.al"* the researcher prepared ODTs of Enalapril maleate containing three separate superdisintegrants and also a co-processed superdisintegrant that contained 50% crospovidone and 50% sodium starch glycolate. The formulation made with co-processed super disintegrant at a 5% w/w concentration emerged as their best formulation (Swamy NGN, 2012).

"S.B Shirsand et al" in their study found that out of all formulations designed by them, the formulation containing co-processed superdisintegrant (crospovidone and croscarmellose sodium1:1) 4% w/w emerged as the best formulation (S.B Shirsand, 2010).

Conclusion: Oral dispersible tablet dosage form has various preferences over conventional oral dosage forms, as it improves patient compliance, it has convenience of use, better bioavailability and faster onset of action. This makes them a great alternative for delivering a drug to geriatric as well as paediatric patients. They have the good properties of both solid as well as liquid dosage forms, as during storage they endure in solid state that is much more stable, and upon administration, within few seconds it transform into liquid dosage form. It can be concluded that due to simplicity and ease of use, ODT has a great opportunity for becoming the ideal system of drug delivery for majority of the drugs in coming years.

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