



A review on fast dissolving drug delivery system

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Received: 21-09-2014

Review completed: 11-11-2014

Accepted: 02-12-2014

Access this article online

QR Code



Website:
www.ijrpsonline.com

ABSTRACT

The development of pharmaceutical technology in past years has presented the development of dosage forms for patients who may have difficulty in swallowing of conventional tablets. Fast dissolving drug delivery systems (FDDDSs) are the system which disintegrate and release the active ingredient quickly and that do not require water to aid swallowing. Among the FDDDS, the fast disintegrating tablets (FDTs) are the more acceptable form of drug delivery system because of its convenience of self-administration and compactness. In the conditions (pediatric and geriatric patients, uncooperative patients, difficulty in swallowing), where the traditional capsules and tablets administration is inconvenient. The basic approach used in development of FDT is the use of superdisintegrants which provide immediate disintegration and thereby releasing the drug in saliva. Oral administration of bitter drugs with an adequate degree of palatability can be achieved by taste masking. These communication reviews the applications and technologies involved in formulation of FDDDS specially focused on FDTs.

Key words: Fast dissolving drug delivery system, Fast dissolving tablets (FDT), Evaluation

INTRODUCTION

In current decades, a variety of pharmaceutical research has been conducted to develop new dosage forms. Among the various dosage forms developed to improve the ease of administration, Fast dissolving tablet is the most widely preferred commercial product. The concept of Fast Dissolving Drug Delivery System emerged from the desire to provide patient with conventional means of taking their medicationally disintegrating tablets. This kind of fast dissolving tablet is good for those patients who have difficulty to swallow, especially geriatric & paediatric patients. The main criteria for fast dissolving tablet is to disintegrate or dissolve rapidly in oral cavity with saliva in 15 to 60 seconds without need of water and should have pleasant mouth feel. The concept of FDTs came into view with an objective of increased patient compliance. The main proposal of the present review is to study the practicability of fast dissolving drug delivery and briefly the ideal properties, limitations and advantages, conventional and patented technologies, assist marketed formulations in FDTs and evaluation.¹⁻³

Ideal characteristics of fast dissolving drug delivery system:

1. Ease of administration for patients who are mentally ill and uncooperative.
2. Requires no water.
3. Rapid disintegration and dissolution of the dosage form.
4. Overcomes unacceptable taste of the drugs.
5. Can be designed to leave minimum or no residue in the mouth after administration and also to provide a pleasant mouth feel.
6. Cost-effective.¹⁻³

Advantages of fast dissolving drug delivery system:

1. Improved patient compliance
2. No need of water
3. No need of chewing
4. Better taste
5. Improved stability
6. Suitable for controlled as well as fast release
7. Allow high drug loading
8. Cost effective
9. Ability to provide advantages of liquid mechanism in the form of solid preparation.¹⁻³

Disadvantages of fast dissolving drug delivery system:

1. The tablets usually have insufficient mechanical strength thus careful handling is required.
2. FDT requires special packaging for suitably stabilization and safety of stable product.¹⁻³

Fast dissolving drug delivery systems are broadly classified into three categories.

1. Orally disintegrating films
2. Fast disintegrating capsules
3. Fast disintegrating tablets

Fast disintegrating tablets are the most common dosage form in fast disintegrating drug delivery system. such tablets also called such as mouth dissolving, fast dissolving, fast melting, fast disintegrating tablets. According to European Pharmacopoeia or disperse tablets are those which dissolve quickly before swallowing, when placed in buccal cavity. Fast disintegrating tablets are characterized by high porosity, low hardness and low density. When administered, an in-situ suspension is created in the oral cavity as the tablet disintegrates and consequently swallowed. Recently the orally disintegrating tablet terminology has been approved by the nomenclature and Labeling Committee of USP. The US-FDA (Food and Drug Administration) has defined FDT as a solid dosage form composing drug.¹⁻³

Industry guidance: Orally disintegrating tablets

1. Orally disintegrating tablets should have dissolution time of approximately 30 sec or less.
2. The weight of orally disintegrating tablet should not more than 500 mg.¹⁻³

Method used in the preparation of fast disintegrating drug tablets**1. Freeze – drying (Lyophilisation technologies):**

In this process water is sublimed from the product after it is frozen. Lyophilisation is a pharmaceutical technology which allows drying of heat sensitive drugs and biological at low temperature under conditions that allow removal of water by sublimation. Lyophilisation results in preparations which have very high specific surface area with a highly porous, which dissolve fastly and show increased absorption and bioavailability. R.P. Scherer patented zydis technology by employing freeze drying process for the preparation of mouth dissolving tablet. On the basis of Gregory et al. Seager formation, process technology & bioavailability of fast dissolving tablets prepared by using zydis technology.⁶

2. Tablet molding method:

Moulded tablets are prepared by using water-soluble ingredients so that the tablet dissolve or disintegrate rapidly and completely. Powder is moistened with the help of hydro alcoholic solvent and then moulded into tablets under pressure less than the conventional form. The tablet possesses porous structures, which provide

easy dissolution. Adding sucrose, acacia or PVP k30 may increase the mechanical strength of the tablet.⁶

3. Sublimation techniques:

Inert solid ingredients (ex. urea, urethane, camphor, ammonium carbonate, naphthalene) are added to other tablet excipients and the blend is compressed into tablet. Removal of volatile substance by sublimation generated a porous structure. The tablets were dissolving in less than 20 sec. and exhibit sufficient mechanical strength. Conventional compressed tablets that consist highly water-soluble ingredients frequently fall to dissolve rapidly because of low porosity of the matrix. Hence to generate matrix volatile ingredients are used that are later subjected to a process of sublimation. The Heinemann and Rothe, Roser and Blair, Knitsch et.al inert solid ingredients that displayed high volatility (e.g., ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, hexa methonium tetramine, urea, phthalic anhydride, urethane and naphthalene) were compressed along with other excipients into a tablet. The volatile substance was then removed by sublimation, leaving behind a porous matrix.⁴

4. Spray drying technique:

Spray drying can produce highly porous and fine powders that dissolve rapidly. The formulations are included by hydrolyzed and non hydrolyzed mannitol as bulking agent, gelatine as supporting agents, sodium starch glycolate or croscarmellose sodium as disintegrating agent and an acidic material (e.g. citric acid) and/ or alkali material (e.g. sodium bicarbonate) to improve disintegration & dissolution.⁴

5. Direct Compression:

It is the easiest way to formulation of tablets. Conventional equipment, easily available excipients and a limited number of processing steps are involved in direct compression. High doses can be accommodated and final weight of tablet can easily exceed that of other production methods.⁵ the disintegration and solubilisation of directly compressed tablets depends on single or combined action of disintegrates, effervescent agents and water soluble excipients used. Breakage of tablet edges during handling and tablet crack during the opening of blister alveolus. To essential a high disintegration rate, choice of suitable type and an optimal quantity of disintegrate is important. Other components such as water soluble excipients or effervescent agents can promote improved dissolution or disintegration properties. But the main problem of using effervescent excipients is that they are highly hygroscopic in nature.³

6. Mass Extrusion:

This involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent removal of softened

mass through the syringe to get a cylinder of the product into even segments using heated blade to form tablet.⁴

Work done on fast dissolving drug delivery system:

Table No. 1: Work done on fast dissolving drug delivery system

S.No.	Author	Drug	Method	Inference
1.	Metkari VB et.al. (2014)	Carbamazepine	Direct Compression Using Solid Dispersion	Good Dissolution Profile with short disintegration time
2.	Pavan k. Rawat et.al. (2013)	Pioglitazone hydrochloride	Direct Compression	Improved patient compliance
3.	Kamal Saroha et.al. (2013)	Amoxicillin Trihydrate	Direct Compression	Better disintegration rate
4.	SavitaBhati et.al. (2013)	Metoclopramide hydrochloride	Direct Compression	Improved patient compliance in pediatric & geriatric
5.	Santosh R layer et.al. (2013)	Risperidone	Solvent Evaporation Method	Enhanced dissolution & increase bioavailability
6.	N.G.Raghavendra Rao et.al. (2012)	Fosinopril	Sublimation Method	Increase rate of dissolution & bioavailability
7.	N.G. RaghavendraRao et.al. (2012)	Fosinopril	Direct Compression	Used in treatment of various cardiovascular disorder
8.	Sanjay Kumar Bhupati et.al.(2012)	Terbutaline Sulphate	Direct Compression	Maintain Therapeutic concentration & enhance & improve bioavailability
9.	DewalkarHruskhi kesh et.al. (2012)	Ziprasidone	Direct Compression	Show better parameter by using crosspovidone as superdisintegrant
10.	N.G. RaghavendraRao et.al. (2012)	Baclofen	Direct Compression	Enhanced bioavailability
11.	Ankur Sharma et.al. (2011)	Aceclofenac	Direct Compression	Intended benefits
12.	SwathiDaram et.al. (2011)	Ketorolac Tromethamine	Direct Compression	Faster disintegration & drug release
13.	Kalpesh Gaur et.al. (2011)	Aceclofenac	Sublimation Method	Enhance patient compliance & using

				sublimating agent
14.	Rizwanulla et.al. (2011)	Oxcarbazepine	Direct Compression	Better patient compliance & Maximum dissolution rate
15.	A.S. Panwar et.al. (2011)	Piroxicam	Direct Compression	Prolonged therapeutic action
16.	N.G. RaghavendraRao et.al. (2010)	Carbamazepine	Direct Compression	Improved bioavailability & effectiveness
17.	Vijay Tiwari et.al. (2010)	Celecoxib	Holt Melt Extrusion	Enhanced bioavailability
18.	Narmada GY et.al. (2009)	Amlodipine Besylate	Sublimation Method	Acceptable Friability by design full factorial method
19.	Shailendra Kumar Singh et.al. (2009)	Combination of Omeprazole & Domperidone	Direct Compression	Enhance patient compliance
20.	Biraju Patel et.al. (2009)	Glipizide	Direct Compression	Enhance patient compliance
21.	D.M Patel et.al. (2008)	Etoricoxib	Sublimation Method	Improve dissolution

Table No 2 Patents on fast dissolving drug delivery system:

S.No	Author	Drug	Method/polymer	Inference
1.	Don Haeng Lee et.al. (2013)	Megestrol	Spray Drying	Quicker dissolve & mask the bitter taste of drugs
2.	Janos Szamosiet. al. (2013)	Phenyl PropanolamineHCl	Direct Compression	Melt at 37°C & low compression force
3.	Dominique Constantine (2011)	Ondasetron	Polyethylene Glycol	Used of bioactive agent & in treatment of dysphagia
4.	Amarjit Singh et.al. (2006)	Nimesulide	Sodium starch Glycolate	Dissolve or disintegrate in digestive organs
5.	Swati Aggarwal et.al.(2005)	Galanthamine	Direct Compression	Used in Alzheimer's disease
6.	Jacqueline Anne Callihan et.al.(2005)	Aspirin	Direct Compression	Mannose provide rapid disintegration & dissolution
7.	Janos Szamosi et.al.(2005)	Ibuprofen	Direct Compression	Provide excellent mouth feel
8.	A.Khawla et.al. (2004)	Ibuprofen	Melt Extrusion	Very low compression force

9.	Jacqueline Anne Callihan et.al. (2004)	Caffeine	Direct Compression	Rapid dissolution
10.	Langridge John et.al. (2003)	Active Substance	Freeze Drying	Rapid disintegration
11.	Abulzaza Kawla A. et.al. (2005)	Ibuprofen	Direct Compression	Low melting point of compound use
12.	William T. et.al. (2001)	Efavirenz	Wet Granulation	Used in HIV
13.	Paul Marie Victor Gilis et.al. (2000)	Galanthamine HBr	Direct Compression	Used in treatment of Alzheimer's Dementia
14.	Warner Lambert Co. et.al. (1998)	Active substance	Direct Compression	Use low density granules
15.	Tadashi Makino et.al. (1996)	Active substance	Compression Molding	High adequate strength disintegration & dissolving rate

Preformulation studies:⁴⁴

Preformulation is basic knowledge which essential to develop appropriate formulation.

1. Bulk Density (D b):

It is the ratio of total mass of powder and bulk volume of powder. It is determine by weigh accurately 10 gm of drug and transfer in 50 ml graduated cylinder. Calculate bulk density in gm/ml by following formula.

Bulk Density – Weight of Powder/Bulk Volume

It is expressed by:

$$D b = M / V b$$

Where

M -mass of powder

V b- bulk volume of the powder.

2. Tapped Density (D t):

It is the ratio of total mass of the powder and tapped volume of the powder. Calculate tapped density in gm/ml by following formula.

Tapped Density - Weight of Powder / Tapped Volume

$$D t = M / V t$$

Where,

M is the mass of powder

V t is the tapped volume of the powder.

3. Angle of Repose (θ):

It is calculated by:

$$\tan\theta = h/r$$

Table No 3: Flow properties of angle of repose

S.no	Angle of repose	Flow properties
1	<25	Excellent
2	25- 30	Good
3	30- 40	Passable
4	>40	Very poor

4. Carr's index or % compressibility:

It is measurement for observe tendency of powders to be compressed. It can be calculated as follows:

Carr's Index - (Tapped Density – Bulk Density) / Tapped Density × 100

Table No 4: Flow properties of carr's index

S.no	Carr's index	Flow properties
1	5-15	Excellent
2	12-15	Good
3	18-21	Fair to passable
4	23-30	Poor
5	33-38	Very poor
6	>40	Very very poor

5. Hausner ratio:

Hausner's Ratio = Tapped Density / Bulk Density

Table No 5: Flow properties according to hausner ratio

Hausner ratio	Flow properties
< 1.24	Good
>1.24	Poor

Evaluation of fast dissolving tablets:⁴⁴

Weight variation:

20 tablets is selected randomly from the group and weighted individually to check for weight variation as per I.P.

Table No 6: Weight variation limit

S.no	Average weight of tablet (mg)	Difference (%)
1	130 or less	10
2	130 – 322	7.5
3	325 or more	5

Hardness: Hardness (f c), it is measure using Monsanto tablet hardness tester. it is expressed in kg/cm².

Friability (F): It is determine by using USP friabilator. The friability (F) is expressed by:

$$F = (W_i - W_f) / W_i \times 100$$

Where,

W_i = initial weight

W_f = final weight

In-Vitro drug release: by USP dissolution test apparatus:

Dissolution test:

USP 2 Paddle apparatus was used and paddle was allowed to rotate at 50 rpm .phosphate buffer (PH 6.8) (900 ml) was used as a dissolution medium.

Crushing Strength:

It is an important parameter in formulation of mouth dissolve tablets because excessive crushing strength significantly reduces the disintegration time. The crushing

strength of the tablet is measure using Pfizer hardness testers.

Friability testing:

Friability of each batch is determined in “Electro lab friabilator”. 10 tablets are rotated at 25 rpm for 4 min or total 100 revolutions, the tablets are then again weighed and the percentage of weight loss is calculated.

Wetting time:

Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10 cm diameter. 10 mm of water-containing eosin a water-soluble dye was added to petridish. The tablet is carefully placed on the surface of the tissue paper. The time required for water to reached upper surface of the tablet is noted as a wetting time.

Modified disintegration test:

For this purpose, A petridish (10 cm diameter) is fill with 10 ml of water. The tablet is carefully put in the center of petridish and the time for the tablet to completely disintegrate into fine particles is noted. Disintegration in oral cavity.

Water absorption Ratio:

A piece of tissue paper folded twice is placed in a small Petri dish containing 6 ml of water. A tablet is put on the paper & the time required for complete wetting is determined. Water absorption ratio R is measured using following equation,

$$R=10(wa/wb)$$

where,

Wb is weight of tablet before water absorption

Wa is weight of tablet after water absorption.

In-vitro dispersion time:

Tablet is added to 10 ml of phosphate buffer solution, ph 6.8 at 37±0.5°C, Time required for complete dispersion of a Tablet is measured.

CONCLUSION

Fast dissolving drug delivery systems have better patient compliance and may propose improved biopharmaceutical properties, better efficacy and good safety. FDT dosage forms obtained by some of these technologies have sufficient mechanical strength, quick dissolution /disintegration in the mouth. However, geriatric and pediatric patients experience difficulty in swallowing conventional tablets, which leads to low patient compliance. To decrease this weakness, scientists have developed innovative drug delivery systems known as FDT. Their characteristic advantages such as administration without water where anytime lead to their suitability to geriatric and pediatric patients.

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