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Formulation and Evaluation of Mouth Dissolving Tablets Sildenafil Citrate

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Abstract:

Methods to improve patient's compliance have always attracted scientist towards the development of fancy oral drug delivery systems. Among them, mouth dissolving drug delivery systems (MDTs) have acquired an important position in the market by overcoming previously encountered administration problems and contributing to extension of patent life. MDTs have the unique property of rapidly disintegrating and/or dissolving and releasing the drug as soon as they come in contact with saliva, thus obviating the requirement of water during administration. Therefore, these dosage forms have lured the market for a certain section of the patient population which include dysphagic, bed ridden, psychic, geriatric and patients. Several techniques have been developed in the recent past, to improve the disintegration quality of these delicate dosage forms without affecting the integrity..

Keywords: Mouth dissolving, Fast disintegrating, Direct compression

Introduction:

The concept of MDTs emerged with an objective to improve patient's compliance. These dosage forms rapidly disintegrate and/or dissolve to release the drug as soon as they come in contact with saliva, thus obviating the need for water during administration, an attribute that makes them highly attractive for and geriatric patients. Difficulty in swallowing conventional tablets and capsules is common among all age groups, especially in elderly and dysphasic patients. This disorder of dysphagia is associated with many medical conditions including stroke, Parkinson's disease, AIDS, thyroidectomy, head and neck radiation therapy and other neurological disorders including cerebral palsy.

MDTs are known by various names such as "fast-melting, fast-dissolving, oral Disintegrating or orodisperse". The European Pharmacopoeia defines the term "orodisperse" as a tablet that can be placed in the mouth where it disperses rapidly before swallowing. Suitable drug candidates for such systems include neuroleptics, cardiovascular agents, analgesics, antiallergics and drugs for erectile dysfunction.

MDTs disintegrate and/or dissolve rapidly in saliva; therefore, water is not required during administration. Some tablets are designed to dissolve in saliva within few seconds, and are true fast-dissolving tablets.

Materials and Methods:

Materials:

Sildenafil Citrate a gift sample from Emcure Pharmaceuticals, Ltd., Pune, India. Sodium starch glycolate, croscarmellose sodium, crospovidone, microcrystalline cellulose, starch, magnesium state, mannitol, talc, were purchased from CDH Ltd, New Delhi, India. All chemicals used were of analytical grade and were used without further purification. Deionized distilled water was used throughout the study.

Techniques of MDT formulation:

Various manufacturing techniques for MDDDS include:

1. Lyophilization
2. Moulding
3. Direct Compression
4. Cotton Candy Process
5. Spray Drying
6. Sublimation
7. Mass Extrusion
8. Nanonization
9. Fast Dissolving Films

Direct Compression (DC)

DC is the simplest and most cost effective tablet manufacturing technique for MDTs as they can be fabricated using conventional tablet manufacturing and packaging machinery and also due to availability of tabletting excipients with improved flow, compressibility and disintegration properties, especially tablet disintegrants, effervescent agents and sugarbased excipients. In many MDT products based on

DC process, the disintegrants mainly affect the rate of disintegration and hence dissolution which is further enhanced in the presence of water soluble excipients and effervescent agents.

The introduction of superdisintegrants as croscarmellose sodium, crospovidone, sodium starch glycolate has increased the popularity of this technology.

Table 1: Formulation mouth dissolving tablets using Combination of two superdisintegrants- Direct compressions

Name of Ingredient	**Formulation in Quantity (in mg)**
	B_{10}
Sildenafil Citrate eq. to Sildenafil	35
CCS	16
CRP	4
Starch	60
MCC	40
Talc	0.12
Magnesium Stearate	0.12
Mannitol	44.8
Flavour (Vanilla)	qs
Total	**200**

Evaluation of mouth dissolving:

The tablets were evaluated for various quality control parameters like appearance, texture, taste, mouth feel, hardness, friability, weight variation, disintegration time, drug content, and drug release. Hardness of the tablets was determined by Monsanto hardness tester. Friability was determined by Roche's friability. The results of evaluation of formulation are depicted in table 2.

Disintegration Time

The test is carried out on the 6 tablets using the apparatus specified in IP buffer pH 6.8 at 37 ^{0} C ± 2 ^{0} C was used as a disintegration media and the time in second taken for complete disinigration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

Wetting time

A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petridish (ID = 6.5 cm) containing 6 ml of Sorenson's buffer pH 6.8. A tablet was put on the paper, and the time for complete wetting was measured. Three trials for each batch were performed and the standard deviation was also determined.

Water absorption ratio, R was determined using following equation.

$$R = (Wa - Wb/Wa) \times 100$$

Where, Wa = Weight of tablet after water absorption

Wb = Weight of tablet before water absorption.

Friability

It is measure of mechanical strength of tablets. Roche friabilator is used to determine the friability by following procedure.

Preweighed tablets are placed in the friabalator. Friabilator consist of a plastic chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets are rotated in the friabilator for at least 4 minutes. At the end of test tablets are dusted and reweighed; the loss in the weight of tablet is the measure of friability and is expressed in percentage as

% Friability = loss in weight / Initial weight X 100

Tablet hardness

Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation is determined by using Pfizer/Monsanto Hardness tester.

Content uniformity

Ten randomly selected tablets are weighed and average weight is calculated, the tablets are powdered in a glass mortar. The weight equivalent to tablet is weighed. The weighed amount is dissolved in solvent system in separate volumetric flask using magnetic stirrer, the volume is adjusted with Sorenson's buffer pH 6.8 and the solution was filtered. An aliquot of these solution are diluted with Sorenson's buffer pH 6.8 in separate volumetric flasks in Lambert's-Beer's Range. The drug content in formulation is determined spectrophotometrically very easily.

In vitro dissolution studies

In vitro dissolution studies for fabricated Mouth Dissolving tablet is carried out by using USP XXIV paddle method at 50 rpm in 900 ml of Sorenson's buffer pH 6.8 as dissolution media, maintained at 37±0.5 ^{0}C. 10 ml aliquots was withdrawn at the specified time intervals, filtered and assayed spectrophotometrically. An equal volume of fresh medium, which was prewarmed at 37 ^{0} C is replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test. Dissolution studies are performed in triplicate.

The various kinetic treatments are giving to the dissolution data. The in vitro dissolution data obtained

were subjected to a zero order and first order kinetics, Higuchi model as well as Hixson Crowell Cube Root Law to understand the release profile and release mechanism.

Result and discussion:

To optimize the parameters which is related to the formulation of Sildenafil citrate MDT, DT of formulation is shown in (Table 2) formulation were designed using and lower level of superdisintegrant and employing combination of two superdisintegrant at a time (Table 2) CRP, CCS, were as used superdisintegrant, MCC was used as diluents, which is also superdisintegrant,Tablets were prepared by direct compression technique.

Combination of two super disintegration CRP & CCS DT was 33 sec. at 4% concentration. While DT was 30 sec. at 2 & 8% concentration. Batch B_{10} containing combination of CRP and CCS exhibited lowest DT and wetting time 19 sec. The composition and result of (Batch B_{10}) it can be concluded that the optimum concentration of CCS and CRP is 16-4 mg respectively.

The hardness and friability of combination of two superdisintegrant are 2.6 kg/cm^2 and .60 batch B_{10} as shown in (table 2). The combination of two superdisintegrant CCS and CRP. Batch B_{10} tablets it showed the water absorption ratio and wetting time 76.6% and 19 seconds respectively.

Table 2 : Evaluation of Properties of tablets with combination of Crosscarmellose sodium and Crosspovidone (CCS&CRP)

Evaluation Properties	**B_{10}**
Weight Variation	Within Limit
Hardness (kg/cm^2)	2.6
Friability (%)	0.60
Uniformity of content(%)	97.65
Water absorption Ratio(%)	76.8
Wetting time(sec)	19
Disintegration time (sec)	30

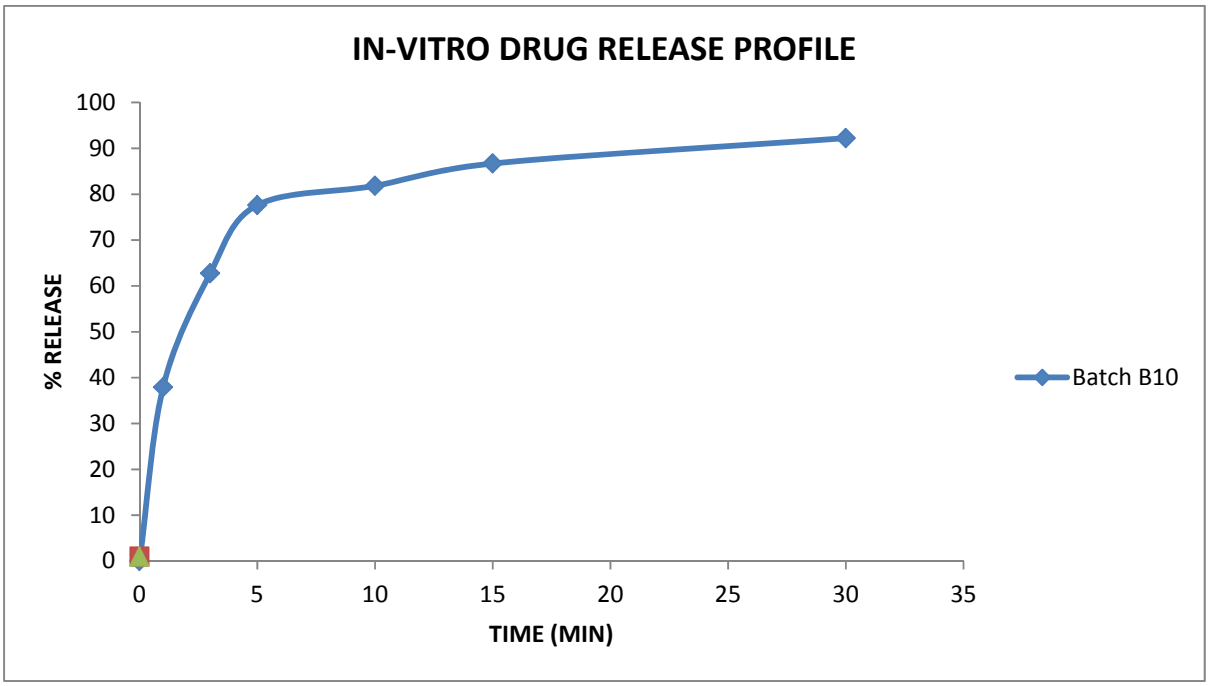

Figure 1: In-vitro drug release of batch B_{10} using CCS&CRP

Thus the result indicated that the Batch with minimum wetting time and more absorption ratio will take less time for disintegrating.

The combination of two superdisintegration tablet gave the better result in comparison to single superdisintegrant. The result of two superdisintegrant Crosscarmellose sodium (CCS) and Crosspovidone (CRP) is shown in table 2 the concentration of Crosspovidone has been kept constant and the concentration of Ac-Di-sol has been changed with 2%, 4%, 6%, and 8% and the disintegrant time of Batch B_{10} was found to be 30 seconds (Table 2).

The complete release of drug been has seen within 1 to 30 minutes. The Batch B_{10} complete drug was released within the 10 minutes. In the figure 1 the graph indicates that batch B_{10} tablets have better dissolution profile. The batch B_{10} shows the better results.

Conclusion:

It can also be concluded that crospovidone and crosscarmellose sodium are better disintegrants for formulation of MDTs of Sildenafil citrate. Over all result suggests that 2-8% of disintegrant concentration is suitable for the preparation of Sildenafil citrate, MDTs tablet the best allow combination of two superdisintegrant CCS and CRP (Batch B_{10}) release 81.82% drug, Show of DT 30 sec.

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