



Original Article

Design and In-vitro Evaluation of Fast Dissolving tablet of Urapidil Hydrochloride

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An attempt has taken to formulate Urapidil Fast Dissolving tablet using various super disintegrants such as Cross povidone, Cross carmellose sodium and Sodium starch glycolate employing direct compression technique. Mannitol was added in the formulation to promote the cooling sensation of the prepared tablet. The physiochemical and micromeritic parameter were evaluated and all the formulations showed satisfactory result. The release characteristic was evaluated by dissolution study. Result showed the formulation containing Cross povidone exhibited faster release than all formulation. Drug polymer interaction study was conducted by FTIR and DSC. No such major interaction was found for the formulation

Keywords: Urapidil, Cross povidone, Cross carmellose sodium, Fast dissolving tablet, Invitro dissolution study.

1. INTRODUCTION

Oral drug delivery is the most widely utilized routes for administration that have been explored for systemic delivery of drug via various pharmaceutical products of different dosage form. Among them the most popular solid dosage forms are tablets and capsules, which are simple and convenient to use. One of the important drawbacks of these dosage forms is difficult to swallow for geriatric, pediatric, or psychiatric patients. Thus, great attention has been paid for designing of mouth dissolving drug delivery systems (MDDDS) with fast

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disintegrating and or dissolving properties to improve patient's .¹ A fast dissolving tablet (FDT) system can be defined as a dosage form for oral administration, which when placed in mouth, rapidly dispersed or dissolved and can be swallowed in the form of liquid.^{2,3} Recently, fast dissolving formulation is popular as novel drug delivery systems because they are easy to administer to the elderly patients and children having difficulty to swallow and also evident in travelling patients who may not have ready access to water.⁴ As the tablet disintegrates

in mouth, this could enhance the clinical effect of the drug through pre-gastric absorption through mouth, pharynx, and esophagus, as well as bioavailability of drug can be significantly increased by avoiding first pass liver metabolism.

Urapidil is a sympatholytic antihypertensive drug. It acts as an α_1 -adrenoceptor antagonist and as an 5-HT_{1A} receptor agonist. Although an initial report suggested that urapidil was also an α_2 -adrenoceptor agonist. Numerous studies have been carried out for the designing and fabrication of FDT formulations using super-disintegrants. Thus, an attempt has been made to formulate the FDT of Urapidil HCl by Cross-povidone, Cross carmellose sodium and sodium starch glycolate (SSG).^{5,6}

2. MATERIALS AND METHODS

Materials

Urapidil HCl was procured from Zydus Cadila Healthcare Ltd, Ahmedabad, India. Cross-povidone, and SSG were purchased from Signet chemical corporation Mumbai, India. Ltd, China. All chemicals and solvents used are of high analytical grade.

Method of preparation of FDT

Urapidil HCl, Crosspovidone, Cross carmellose sodium and SSG, were passed through #40 mesh and collected separately in polyethylene bag.⁷ Direct compression technique was adopted for batch

preparation of FDTs. The drug and diluents were mixed in a geometrical manner and blended for a period of 20 minutes. The resulted mixture lubricated with Aerosil-R 972. Finally the blend was compressed to formulate tablets using tablet compression machine (Cadmach Machinery Pvt. Ltd, India) with 6.5 mm circular flat punch. The composition of various formulations designed in the present study is given in Table 1.

Ingredients (mg)	Formulations								
	CP1	CP2	CP3	CCS1	CCS2	CCS3	SSG1	SSG2	SSG3
Urapidil	10	10	10	10	10	10	10	10	10
CP	2	4	6	-	-	-	-	-	-
CCS				-	2	4	6		
SSG							2	4	6
Avicel-102	90	88	86	90	88	86	90	88	86
Mannitol	43	43	43	43	43	43	43	43	43
Sodium saccharine	1	1	1	1	1	1	1	1	1
Aerosil R 972	2	2	2	2	2	2	2	2	2
Sodium behenate	2	2	2	2	2	2	2	2	2
Total weight (mg)	150	150	150	150	150	150	150	150	150

Micromeritic properties of blended powder

Prior to compression, granules were evaluated for their micromeritic parameters.⁸ Angle of repose was determined by funnel method. Bulk density (BD) and tapped density (TD) were determined by cylinder method, and Carr's index (CI) was calculated using the following equation:

$$CI = (TD - BD) / TD \times 100$$

Hausner's ratio (HR) was calculated by the following equation:

$$HR = TD / BD$$

Physicochemical characterization of tablets

The physical properties such as crushing strength, friability, thickness, diameter, weight variation, drug content, wetting time, water absorption ratio and disintegration time for each formulation were determined.

Crushing strength

Tablet crushing strength was determined by randomly selected 10 tablets using a digital crushing strength tester (Erweka TBH-28) and the data reported is the mean of three individual determinations.

Friability

Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap, or break. Preweighed randomly selected twenty tablets were placed in a Roche friability tester and operated for 4 min at 25 rpm. Compressed tablets should not loose more than 1% of their weight.^{9,10}

Thickness and diameter

Tablet thickness and diameter were measured by Vernier callipers (Mitatoyo, Japan).

Weight variation A weight variation test was performed according to USP30 NF25 on 20 tablets by taking samples from a batch after production of every 100 tablets and randomly from a total batch of 300 tablets using an electronic balance (Contech Instruments CA 224, India).

Drug content

The drug content in terms of assay of each batch was determined in triplicate. For each batch, a number of 20 tablets were weighed and crushed to fine powder using mortar and pestle.

Drug content

The drug content in terms of assay of each batch was determined in triplicate. For each batch, a number of 20 tablets were weighed and crushed to fine powder using mortar and pestle. An accurately weighed 10 mg of the powder was taken and suitably dissolved in methanol and analyzed by HPLC after making appropriate dilutions. The procedure was carried out on Shimadzu LC-10AT (Octadecylsilyl silicagel; 250 × 4.00 mm) with flow rate of 1.5 ml/minute at ambient temperature.

Wetting time and water absorption ratio

Twice folded tissue paper was placed in a Petri dish having an internal diameter of 6.5 cm to that 10 ml of purified water containing an eosin dye solution (0.05% w/v) was added to Petri dish. A tablet was carefully placed on the surface of the tissue paper in the Petri dish. The time required for dye to reach the upper surface of the tablet and to completely wet was noted as the wetting time. Water absorption ratio (R) was then determined according to the following equation:

$$R = (W_a - W_b) / W_b \times 100$$

Disintegration time

Many reports suggest that conventional DT apparatus may not give correct values of DT for FDTs. FDT is required to disintegrate in small amounts of saliva within a minute without chewing the tablet. In a simplest method to overcome these problems, 6 mL of phosphate buffer of pH 6.8 was taken in a 25-mL measuring cylinder. Temperature was maintained at $37 \pm 2^\circ\text{C}$. A FDT was put into it and time required for complete disintegration of the tablet was noted.¹¹

***In vitro* dissolution study**

The procedure was determined using United States Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method).¹² The dissolution test was performed using 900 ml of 0.1N HCl (pH-1.2) at $37 \pm 0.5^\circ\text{C}$ and 50 rpm. A sample of 10 ml of the solution was withdrawn from the dissolution apparatus at 2 minute interval with the replacement of fresh dissolution medium for 20 minute. The samples were passed through a 0.45- μm membrane filter and diluted to a suitable concentration with phosphate buffer. The absorbance of these solutions was measured at 268 nm using a Shimadzu UV-1601 UV/V is double beam spectrophotometer.

3. RESULTS AND DISCUSSION**Micromeritic properties of blended powder**

Result shows that all the formulations produced optimal flow properties calculated in terms of

compressibility. Table 2 depicts micromeritic properties of the designed formulations. The angle of repose ranged from 27.38 ± 0.07 to 30.52 ± 0.09 , which indicates optimal flow ability. In addition to that the tapped density and bulk density for all formulation granules ranged between 0.68 ± 0.02 to 0.73 ± 0.002 and 0.57 ± 0.04 to 0.61 ± 0.18 , respectively, whereas Hausner's ratio was obtained between 1.16 to 1.21.

Physiochemical characterization of tablets

The physical properties of the designed tablets are presented in Table 3. These properties were studied by determining crushing strength, friability, thickness, diameter, weight variation, drug content, wetting time, water absorption ratio, and disintegration time. Crushing strength of prepared tablets ranged from 69.3 ± 0.73 newton to 72.7 ± 0.83 newton. The results were compared and concluded on the basis of amount of superdisintegrants and Avicel-102 used. It was observed that those formulations contained SSG exhibited higher hardness than others. Moreover, the amount of Avicel-102 at 58% in all formulations showed higher crushing strength. The European and United States Pharmacopeia state that a loss up to 1% is acceptable for friability. Prepared tablets passed the friability test as values were ranged from 0.01% to 0.04% indicating the ability of tablet to withstand abrasion in handling packaging and shipment. The thickness for all tablets ranged between 2.80 ± 0.20 to 2.83 ± 0.25 mm and diameter was similar for all tablets. In a weight variation test, the pharmacopoeial limit for the percentage

Table 2: Micromeritic properties of prepared powder blend

Formulations	Bulk density	Tapped density	Angle of repose	Hausner's ratio	Carr's index
CP1	0.58 ± 0.01	0.68 ± 0.02	27.72 ± 0.11	1.17	14.7
CP2	0.59 ± 0.12	0.70 ± 0.01	28.23 ± 0.03	1.18	15.71
CP3	0.60 ± 0.04	0.72 ± 0.11	29.45 ± 0.26	1.2	16.66

CCS1	0.59 ± 0.11	0.70 ± 0.23	28.31 ± 0.05	1.18	15.71
CCS2	0.61 ± 0.04	0.71 ± 0.03	30.26 ± 0.27	1.16	14.08
CCS3	0.57 ± 0.04	0.69 ± 0.12	28.46 ± 0.46	1.21	17.39
SSG1	0.59 ± 0.02	0.68 ± 0.04	27.38 ± 0.07	1.15	13.23
SSG2	0.60 ± 0.06	0.73 ± 0.002	29.45 ± 0.34	1.21	17.8
SSG3	0.61 ± 0.18	0.73 ± 0.24	30.52 ± 0.09	1.19	16.43

Data are represented as mean \pm standard deviation (SD), n = 3

In-Vitro Dissolution study

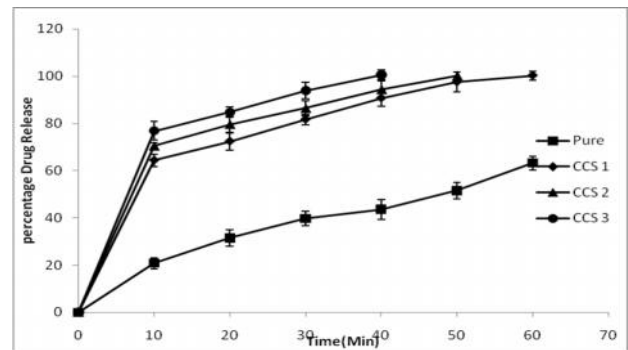


Fig 1: In-vitro Dissolution study of Formulation F1-F3

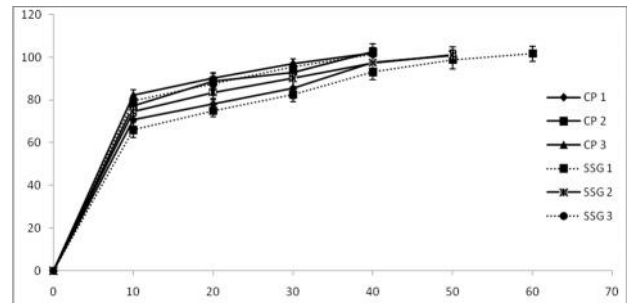


Fig 2: In-vitro Dissolution study of Formulation F6-F9

Drug polymer interaction study

The drug-excipient interaction were studied using FTIR (FTIR 8400S, Shimadzu) and By DSC study.

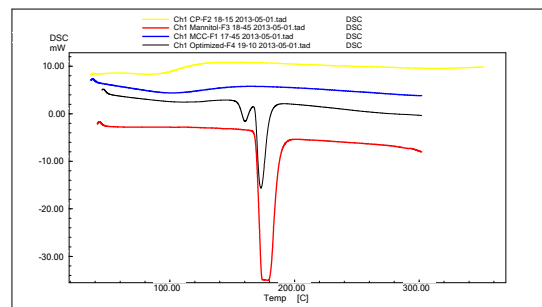


Fig 3: DSC study of formulation.

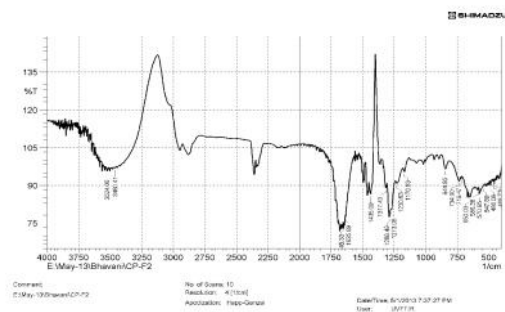


Fig 3: FTIR study of formulation.

4. CONCLUSION

The present investigation shows that the various superdisintegrants can effectively be used to design fFDT of Urapidil utilizing direct compression technique. The use of superdisintegrants for preparation of FDT is highly effective and commercially feasible. These superdisintegrants accelerate disintegration or dissolution of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment. The physiochemical characterizations of all formulations were found to be satisfactory.

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Conflict of Interest: None

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