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Original Article

Formulation and Evaluation of Rapid Disintegrating tablet of α_1-Adrenoceptor Antagonist Drug

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ABSTRACT

The demand for fast disintegrating tablets has been growing, during the last decade especially for geriatric and paediatric patients because of swallowing difficulties. Urapidil is used to treat hypertension. Hence in present work an attempt has been made to formulate Fast dissolving tablet of Urapidil by direct compression technique using various concentration of Superdisintegrants like Crosscarmellose sodium (CCS), Cross povidone (CP) and Sodium starch glycolate (SSG). The formulated tablets were evaluated for Crushing strength, Friability, Thickness, Diameter, Weight variation, Drug content, Wetting time, Water absorption ratio, Disintegration time and Percentage of drug release. All formulations showed satisfactory result. Among them formulation F3 containing 3% of CCS exhibited complete release within 15 minute and disintegration time within 10 second. Accelerated stability study indicated no significant difference in assay and crushing strength. There was no chemical interaction between the drug and excipients during FT-IR study and DSC Study; considered in the present investigation.

Keywords: Fast disintegrating Tablet, Urapidil, Direct compression technique, Interaction.

1. INTRODUCTION

The most well-liked solid dosage forms area unit being tablets and capsules; one vital downside of those indefinite quantity forms for a few patients like geriatric, medicine or medical specialty patients is that the difficulty to swallow. For these reasons tablets which will quick dissolve or disintegrate within the oral cavity have attracted an excellent deal of attention. a fast dissolving tablet (FDT) system may be outlined as a indefinite quantity type for oral administration, that once placed in mouth, quickly spread or dissolved and may be enclosed in type of liquid. Recently quick dissolving formulation is popular as Novel Drug

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Delivery Systems as a result of their straightforward to administer and result in higher data patient compliance. As tablet disintegrates in mouth, this might enhance the clinical result of the drug through pre-gastric absorption through the mouth, tubular cavity and musculature, still as bioavailability of drug will considerably be increased by avoiding first pass liver metabolism. [1, 2, 3]

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, this was not substantiated in later studies that demonstrated it was devoid of agonist actions in the dog saphenous vein and the guinea-pig ileum. Unlike some other α_1-adrenoceptor antagonists. [4]

Thus, an attempt has been made to formulate the FDT of Urapidil by CCS, Cross povidone and Sodium starch glycolate (SSG). [5, 6]

2. MATERIALS AND METHODS

Materials

Urapidil was procured as gift sample from, Ahmedabad, India. Cross carmellose sodium and Sodium starch glycolate (SSG) were purchased from Signet chemical corporation Mumbai, India. All chemicals and solvents were used are of high analytical grade.

Method of preparation of FDT

Urapidil, CCS, CP, SSG, Mannitol were passed through were passed through #40 mesh and collected separately in polyethylene bag. 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 for 5 minutes in Octagonal Blender (Mevish engineering, India). Finally the blend was compressed to formulate tablets using tablet compression machine (Cadmach Machinery Pvt. Ltd, India) with 6.0 mm circular flat punch. The composition of various formulations designed in the present study is given in Table 1. [7, 8]

Micromeritic properties of blended powder

Prior to compression, granules were evaluated for their characteristic parameters. [8]Angle of repose was determined by funnel method. Bulk density (BD) and tapped density (TD) were determined by cylinder method. [9-11]

Physiochemical characterization of Tablets

The physical properties like crushing strength, friability, thickness, diameter, weight variation, drug content, and disintegration time for every formulation were determined. tablet crushing strength determined for 10 tablets victimization digital tablet hardness tester (Erweka TBH-28). friability determined by testing ten tablets in an exceedingly Roche friability tester for four min at twenty five revolutions per minute. The thickness and diameter of the tablets were measured by Vernier callipers (Mitatoyo, Japan). to check weight variation, twenty tablets were weighed victimization an balance (Contech Instruments CA 224, India). The drug content in terms of assay of every batch determined in triplicate. for every batch variety of twenty tablets were weighed and crushed to fine powder victimization mortar and pestle. associate accurately weighed of ten mg of the powder was taken and fittingly dissolved in methyl alcohol and analyzed by HPLC when creating acceptable dilutions. The procedure was disbursed on Shimadzu LC-10AT (Octadecylsilyl silicagel; 250 × four.00 mm) with rate of one.5 ml/minute at close temperature. double folded tissue was placed in an exceedingly dish having an inside diameter of 6.5 cm to it added six cubic centimetre of refined water. A pill was rigorously placed on the surface of the tissue within the dish. The time needed for water to achieve the side of the pill and to fully wet it absolutely was noted because the wetting time. Water absorption quantitative relation (R) was then determined according to the following equation

$$R= (Wa-Wb)/Wb\times100 \quad (3)$$

Where Wa and Wb are tablet weight after and before water absorption respectively.

In-vitro disintegration time was determined using a disintegration test apparatus (Lab Hosp, India). This test was carried out at 37 ± 2^0C in 900 mL of distilled water. [12-15]

In-vitro dissolution study

The procedure was determined using United States Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The dissolution test was performed using 900 ml of 0.1N HCl (pH-1.2) at 37 ± 0.5°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/Vis double beam spectrophotometer. [16-18]

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 31 to 39 which indicates optimal flow ability. In addition to that the tapped density and bulk density for all formulation granules ranged between 0.57±3.24 to 0.72±2.11 and 0.38±1.01 to 0.59±1.04 respectively. [19]

Physiochemical characterization of Tablets

The bodily homes of the designed formulations are presented in table 3. Those properties were studied by way of determining crushing energy, friability, thickness, diameter, weight version, drug content material, wetting time, water absorption ratio and disintegration time. Hardness or Crushing electricity of the prepared drugs ranged from 2.17 to 2.90 kg/cm2. It turned into observed that amongst all

formulations containing SSG exhibited better hardness than others. The EU and US pharmacopeias states that a loss up to at least one% is appropriate for friability. The friability of the prepared pills ranged from 0.2% to 0.5%. The thickness for all pills ranged among 2.31 to 2.67mm and diameter was similar for all tablets. In a weight variant test, the pharmacopoeial restriction for the share deviation for capsules of extra than one hundred fifty mg is ±3.5 %. The average percentage deviation of all pill formulations become determined to be within the above restriction, and as a result all formulations surpassed the take a look at for uniformity of weight as in keeping with legit requirements. common weight of every components drugs ranged from 190 mg to 192 mg. Uniformity in drug content become observed among unique batches of the tablets, and the percentage of drug content material became extra than 98%. The wetting time for capsules ranged between 12±2.02 to 38±2.19 2nd. It become discovered that because the superdisintegrants elevated proportionally the wetting time decreased. In this take a look at various disintegrants had been used at 1%, 2% and 4% stage. It was discovered that method F3 containing CCS at three% level took least disintegration time, due to the fact evolved porosity causes water uptake; consequently enables wicking action and brings about quicker disintegration. [20, 21]

In-vitro dissolution study

Different grades of superdisintegrants ranging 1, 2 and 3 percentage were used to formulate FDT of Urapidil tablets and those formulations were subjected to *in-vitro* drug dissolution studies. All formulation released 60 percentage of drug within 2 minute and 90 percentages within 15 minute. Formulations based on CCS at 3 percentage showed complete release within 10 minute. Whereas CP and SSG based formulations released complete drug within 15 respectively. Result showed that CCS based formulations exhibited quick drug release among all disintegrants. This could be the higher water uptake and formation of channel in the tablet. Among all formulation and on the basis of above result, F3 was selected as promising formulation for further studies.

Drug polymer interaction study

The drug - excipient interaction were studied using FTIR (FTIR 8400S, Schimazu). IR spectra for drug and powdered tablets were recorded in a Fourier transform infrared spectrophotometer with KBr pellets. The spectra were scanned over the 3600 to 400 cm-1 range. It was found that there was no chemical interaction between Urapidil and excipients used as cited in figure.

DSC Study

Differential scanning calorimetry (DSC) has shown to be an important tool to quickly obtain information about possible interactions between the active and the excipients, according to the appearance, shift or disappearance of endothermic or exothermic peaks. DSC study was performed using DSC 8000 Perkin Elmer instruments to determine the drug excepient compatibility study. During study a sharp endothermic peak for Urapidil was obtained at 170^0C corresponding to melting point. But in the formulation there was a slight change in peak temperature and peak shape, with an additional broad peak, which might be due to reduction of the purity level of component and interaction with excipients.

Table 1: Composition of tablet formulations (mg)

FORMULATIONS									
Sl no	**Ingredients (mg)**	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
1	Urapidil	40	40	40	40	40	40	40	40	40
2	Spray dried Lactose	10	10	10	10	10	10	10	10	10
3	Cross Carmellose sodium	2	4	6	-	-	-	-	-	-
4	Cross povidone	-	·	-	2	4	6	·	-	-
5	SSG	-	-	-	-	-	-	2	4	6
6	Avicel	90	88	86	90	88	86	90	88	86
7	Mannitol	43	43	43	43	43	43	43	43	43
8	Sodium saccharine	1	1	1	1	1	1	1	1	1
9	Aerosil	2	2	2	2	2	2	2	2	2
10	Talc	1	1	1	1	1	1	1	1	1
	Total weight (mg)	**191**	**191**	**191**	**191**	**191**	**191**	**191**	**191**	**191**

Table 2: Micromeritic properties of prepared powder blend

Formulations	Bulk density	Tapped density	Angle of repose
F1	0.38±1.01	0.67±2.12	37.72±1.11
F2	0.39±2.12	0.68±2.01	38.23±2.03
F3	0.45±1.04	0.72±2.11	39.45±2.46
F4	0.49±2.11	0.65±0.93	38.31±2.15
F5	0.59±1.04	0.67±1.03	33.26±2.27
F6	0.47±2.04	0.62±0.12	38.46±3.66
F7	0.48±1.12	0.58±2.04	31.38±1.17
F8	0.55±1.26	0.59±0.002	38.45±2.74
F9	0.48±1.28	0.57±3.24	37.52±1.54

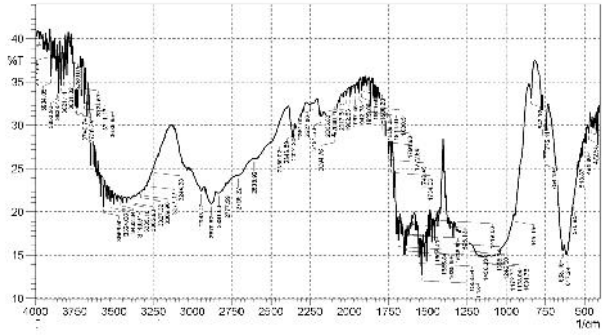

Fig 1: FTIR spectra of selected formulation

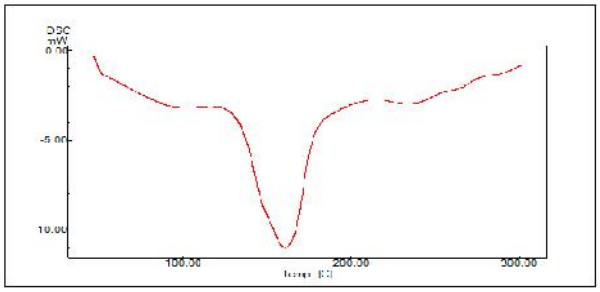

Fig 2: DSC Spectra of Selected formulation

4. CONCLUSION

The present investigation shows that the various superdisintegrants can effectively be be used to design Fast dissolving tablet of Urapidil employing direct compression technique. The use of superdisintegrants for preparation of FDT is highly effective and commercially feasible. These superdisintegrants accelerate disintegration/dissolution of tablets by virtue of their ability to absorb a large amount of water when exposed to an aqueous environment. It also concluded that, CCS was able to immediate release drug as compared to SSG and CP. Furthermore the *in-vivo* and pharmacokinetic study have to carry out.

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