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Original Article

PREPARATION AND EVALUATION OF METOLAZONE SOLID DISPERSIONS AND FAST DISSOLVING TABLETS USING *STERCULIA FOETIDA* SEED STARCH AND PLASDONE K-29/32 AS SUPERDISINTEGRANTS

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ABSTRACT

Objective: The objective of the current study is to improve the solubility of the Biopharmaceutical Classification System (BCS) Class-II drug, Metolazone, using various superdisintegrants.

Methods: Starches were extracted from *Sterculia foetida* seed powder by water and alkali techniques i.e., sodium hydroxide at 0.1%, 0.25% and 0.5% concentrations. Several phytochemical and physicochemical parameters were evaluated on the extracted starches. Solid dispersions of Metolazone were prepared by the solvent evaporation technique using plasdone K-29/32 alone and by mixing plasdone K-29/32 with *Sterculia foetida* seed starch. Various physical parameters were evaluated for the prepared solid dispersions. Tablets were prepared using Metolazone solid dispersions and varying concentrations of *Sterculia foetida* seed starch by direct compression technique. Pre and post-compression parameters were evaluated along with *in vitro* drug release studies, characterization using Scanning Electron Microscopy (SEM) and stability studies.

Results: Phytochemical tests showed the presence of starch in all extracts. Starch prepared from 0.1% sodium hydroxide (SFS2) showed best physicochemical properties. *In vitro* dissolution studies revealed that solid dispersion MS4 containing Metolazone and plasdone K-29/32 in 1:3 ratios showed better drug release. Formulation MPT6 containing MS5 solid dispersion with 15% w/w of SFS2 showed enhanced drug release. SEM studies revealed no major interactions between drugs and excipients. Accelerated stability studies showed that all tablets were stable.

Conclusion: *Sterculia foetida* seed starch and plasdone K-29/32 have enhanced the solubility of Metolazone.

Keywords: Metolazone, Solid dispersions, Plasdone K-29/32, *Sterculia foetida*, Fast dissolving tablets

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INTRODUCTION

Solubility of drugs is an important pre-requisite in eliciting their pharmacological effect in the body. Most of the drugs are facing the problem of aqueous solubility. Enhancement of solubility of such drugs can be helpful for many patients. It is highly beneficial for geriatrics and paediatrics that prefer to take drugs through oral route [1]. The solubility can be enhanced by various techniques like preparation of solid dispersions, cyclodextrins, liposomes and fast-dissolving tablets. They change the properties of drugs and make them more soluble in water [2]. Solid dispersions are the dosage forms which have two main components; one is a hydrophobic drug and other a hydrophilic carrier. They were prepared by various techniques like physical mixing, solvent evaporation and fusion techniques [3]. Solid dispersions adopt many techniques to dissolve drug in water like making complexes, reducing the particle size, increasing wetting time etc [4].

Fast dissolving tablets (FDTs) are the formulations which releases the drugs immediately after taking into the mouth within seconds to 3 min. They contain special types of ingredients called superdisintegrants [5]. FDTs were formulated using different techniques like direct compression, wet granulation, lyophilization etc. Superdisintegrants are the agents which make the drug disintegrate rapidly in water by wicking or swelling or by any other mechanisms [6]. Till now, several synthetic and semi-synthetic superdisintegrants have been used in the preparation of dosage forms. Recent studies have suggested that usage of natural agents as superdisintegrants is beneficial [7]. Natural sources are gaining attention in the development of pharmaceuticals nowadays. Among those, starches stand on top because of their varying applications in the development of pharmaceutical formulations. Starches were used as binders, bulking agents and superdisintegrants [8].

In the current study, an attempt was made to extract starch from of *Sterculia foetida* seed powder and to use it as superdisintegrant for formulating fast-dissolving tablets. *Sterculia foetida* belongs to the family Malvaceae, grows in climates of India, Philippines and Indonesia. Their seeds have a black coat which can be easily removed. The central part contains the cotyledons. They contain starch and various significant phytochemical constituents [9]. Metolazone, which is a diuretic agent was selected for the present study. It is a BCS (Biopharmaceutical Classification System) class-II drug which is poorly soluble in water. It shows the diuretic effect by inhibiting the sodium-chloride symporter pump which is present in distal convoluted tubule of nephron. This it prevents the reabsorption of sodium, which favours its excretion [10]. Along with sodium, water also gets excreted from body. This is highly beneficial in case of hypertensive patients who have water retention as major obstruction. The bioavailability of metolazone is approximately 65%. Only 33% of the drug is bound to plasma proteins. It has an approximate elimination half-life of 14h. Based on pharmacokinetic and pharmacodynamic parameters, Metolazone is selected as drug of choice for present study.

MATERIALS AND METHODS

Materials

Metolazone and croscarmellose sodium were gift samples from M/s. NATCO Pharma Ltd. (Hyderabad, India). Plasdone K-29/32 and microcrystalline cellulose were gift samples from Pellets Pharma Ltd (Hyderabad, India). Sodium hydroxide, saccharin sodium, magnesium stearate and talc were procured form S. D Fine Chem. Ltd. (Mumbai, India). *Sterculia foetida* seeds were procured from the local market (Tirumala, Andhra Pradesh, India) and were identified and authentified by Dr. K. Ammani, Professor, Department of Botany, Acharya Nagarjuna University, Guntur and a voucher specimen (01/2017) was preserved in the Department of Pharmaceutics, Chebrolu Hanumaiah Institute of Pharmaceutical Sciences, Chowdavaram, Guntur, India.

Extraction of starch from *Sterculia foetida* seeds

Sterculia foetida seed starch was isolated using aqueous and alkali extraction methods [11]. 5g *Sterculia foetida* seed flour was added into 100 ml distilled water, 0.1%, 0.25% and 0.5% sodium hydroxide solutions separately and soaked (6 h and 8 h) at room temperature then stirred constantly. The slurry was filtered through 212 mesh stainless sieve and remaining sediment was washed with distilled water for three times. The filtrates were combined and precipitated overnight at 4 °C. The supernatant was discarded and the crude starch was cleaned with distilled water. This step was repeated three times and starch cake was dried at 40 °C for 24 h in oven dryer. The starch was ground with a mortar and pestle. The starches were packed in a plastic bag and stored at room temperature.

Phytochemical tests for *Sterculia foetida* seed powder and extracted starches

The raw *Sterculia foetida* seed powder and starches extracted were subjected to various phytochemical tests for the identification of carbohydrates, proteins, alkaloids, glycosides, steroids, flavonoids and saponins [12]. The results were indicated in table 1.

Evaluation of physicochemical properties of *Sterculia foetida* seed powder and extracted starches

Various physicochemical properties like gelatinization temperature, pH, viscosity, swelling index, water absorption index, total microbial load, acidity, fluorescence, presence of oxidizing substances, sulphated ash, loss on drying and amylose content were evaluated using suitable methods [13].

Acidity

One gram of starch was added to 100 ml of ethanol (70%), which was previously neutralized to phenolphthalein solution. This solution was shaken for 1h, filtered and 50 ml of the filtrate was titrated with 0.1M sodium hydroxide.

Fluorescence

500 mg of starch powder was dissolved in organic solvent, placed on a glass slide and was examined under UV cabinet for the presence of any fluorescent material.

Oxidizing substances

To 0.5g of the sample, 10 ml of water and 1 ml of acetic acid were added and stirred until a homogeneous suspension was obtained. 0.5 ml of a freshly prepared saturated solution of potassium iodide was added, mixed and allowed to stand for 5 min. Non-production of blue or blue colour indicates the absence of oxidizing substances.

Sulphated ash

1-2 g of the starch was placed in an accurately weighed crucible, ignited and thoroughly charred. Then it is cooled and the residue was moistened with 1 ml of sulphuric acid. It was heated gently until white fumes are no longer evolved and ignited at 800 °C until black particles have disappeared. The crucible was cooled and few drops of sulphuric acid was added and heated. Then it was weighed. This procedure was repeated until two successive weighing doesn't differ by more than 0.5 mg.

Loss on drying

Loss on drying is widely used to determine the moisture content of a sample, although occasionally it may refer to the loss of any volatile matter from the sample. Not more than 15% (for all starches except potato starch) and not more than 20% (for potato starch) of weight loss should be obtained. It was determined by drying 0.2g of starch in an oven at 105 °C.

Test for amylose content

To 100 mg of starch, 1 ml of ethanol and 9 ml of 1N sodium hydroxide were added and kept aside for overnight. The suspension was thoroughly mixed. The dispersed sample was transferred to a 100 ml volumetric flask and diluted to the mark with distilled water. 5 ml of this solution was pipetted into a 100 ml volumetric flask, 1 ml of 1N glacial acetic acid and 2 ml of Iodine solution (0.02N) were added. The volume was made up to 100 ml with distilled water and the absorbance was measured at 620 nm.

Preparation of metolazone solid dispersions by solvent evaporation method

Solid dispersions of Metolazone were prepared using plasdone K-29/32 in different ratios by solvent evaporation method [14]. Measured quantities of Metolazone and Plasdone K-29/32 were placed in a china dish, few ml of methanol was added and heated at low temperature until both gets melted. The mixture was allowed to evaporate by stirring. The solid mass was obtained after the solvent gets evaporated. The granules obtained were crushed and stored in desiccator for further studies. The results were given in table 3.

Evaluation of physical parameters

The prepared solid dispersions were evaluated for various physical parameters such as angle of repose, Carr's index, Hausner's ratio, particle size and drug content [15]. The results were indicated in table 4.

***In vitro* dissolution studies**

Dissolution studies for all solid dispersions were performed in a calibrated dissolution test apparatus (LABINDIA DS8000) equipped with paddles employing 900 ml of phosphate buffer pH 6.8 as dissolution medium. The paddles were operated at 75rpm and temperature was maintained at 37±1 °C throughout the experiment. The samples were withdrawn at 5, 10, 15, 20 and 30 min and replaced with equal volume of same dissolution medium to maintain the sink conditions. The amount of the drug dissolved in the dispersions was estimated by double-beam U. V spectrophotometer at 237 nm. The dissolution profiles were indicated in fig. 1.

Preparation of metolazone tablets

Metolazone tablets were prepared by direct compression technique using the solid dispersion, which showed maximum drug release. *Sterculia foetida* seed starch with the best physicochemical properties was selected as superdisintegrant for the preparation of tablets. The efficiency of starch was compared with croscarmellose sodium. The solid dispersion concentration was maintained constant, while the superdisintegrants concentration was increased. The raw materials were individually weighed and transferred to mortar. Using pestle, the components were mixed well and the prepared granules were passed through sieve no. 40. The granules were taken into a plastic bag and lubricated with talc and magnesium stearate. Then they were compressed as tablets under identical conditions. The compositions of various tablet formulations were given in table 5.

Evaluation of pre-compression parameters

The prepared granules were evaluated for pre-compression parameters such as angle of repose, Carr's index and Hausner's ratio [16]. The results were given in table 6.

Evaluation of post-compression parameters

The compressed tablets were further evaluated for post-compression parameters such as weight uniformity, hardness, friability, wetting time, dispersion test and drug content [17]. The results were given in table 7.

***In vitro* dissolution studies of metolazone tablets**

Dissolution studies for Metolazone tablet formulations were performed in a calibrated dissolution test apparatus (USP apparatus II method) using 900 ml of phosphate buffer pH 6.8 as dissolution medium. The paddles were operated at 75rpm and temperature was maintained at 37±1 °C throughout the experiment. Samples were withdrawn at 5, 10, 15, 20 and 30 min and replaced with an equal volume of same dissolution medium to maintain the constant conditions. The amount of drug dissolved was estimated using U. V spectrophotometer at 237 nm. The dissolution profiles were given in fig. 2 and 3.

Characterization studies

Based on dissolution studies, the optimized formulations were subjected to scanning electron microscopy (SEM) analysis to know surface characteristics. The results were shown in fig. 4.

Accelerated stability studies

Accelerated stability studies were carried out on optimized formulations as per International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) guidelines. These studies were carried out to investigate the effect of temperature on the physical properties and drug release of the tablets [18]. The results were given in table 8. The optimized tablets were also evaluated for *in vitro* drug release studies and indicated in fig. 5 and 6.

RESULTS AND DISCUSSION

Extraction of starch from *Sterculia foetida* seeds

The starches extracted from *Sterculia foetida* seed powder were white to creamish, with mild granules, free-flowing and stable in nature.

Phytochemical screening of *Sterculia foetida* seed flour and starch extracts

The raw *Sterculia foetida* **s**eed powder and starches extracted were subjected to phytochemical screening. The results were indicated in table 1.

Physicochemical parameters of *Sterculia foetida* seed flour and starch extracts

Physicochemical parameters were evaluated for all the starches. The results were indicated in table 2. The starch SFS2 showed high swelling index and water absorption index which made it suitable for selection of solid dispersions and tablets.

Preparation of metolazone solid dispersions by solvent evaporation method

Solid dispersions of Metolazone were prepared using plasdone K-29/32 as carrier in different ratios by the solvent evaporation method. The composition was given the table 3.

Evaluation of physical parameters

Various physical parameters for Metolazone solid dispersions were evaluated. All the parameters were found to be within I. P specified limits. The pure drug Metolazone is indicated as MP. The obtained results were indicated in table 4.

***In vitro* dissolution studies of metolazone solid dispersions**

Formulation MS4, prepared in 1:3 ratios of Metolazone and plans done K-29/32 showed maximum drug release proving that solid dispersions prepared by the solvent evaporation technique increases drug release. Usage of superdisintegrants has proved to increase dissolution efficiency [19, 20]. Past studies suggest that solvent evaporation technique has proved to be successful in preparation of solid dispersions for solubility enhancement [21, 22]. The dissolution profiles of Metolazone solid dispersions were given in fig. 1.

Table 1: Phytochemical screening of *Sterculia foetida* seed powder and starches (+indicates present; –indicates absent)

Test	SFSP	SFS1	SFS2	SFS3	SFS4
Carbohydrates	+	+	+	+	+
Polysaccharides	+	+	+	+	+
Proteins	–	–	–	–	–
Alkaloids	+	–	–	–	–
Glycosides	–	–	–	–	–
Steroids	–	–	–	–	–
Flavonoids	+	–	–	–	–
Saponins	+	–	–	–	–

Table 2: Physico-chemical properties of *Sterculia foetida* seed powder and starches

Properties	SFSP	SFS1	SFS2	SFS3	SFS4
Gelatinization temperature	194-200 °C	221-230 °C	232-240 °C	275-283 °C	225-232 °C
pH	6.40	7.01	7.21	7.79	7.98
Viscosity (in cps)	1.672	2.422	2.029	2.134	2.024
Swelling index	39	56	79	62	55
Water Absorption Index	186	262	294	255	240
Total Microbial Load	Absent	Absent	Absent	Absent	Absent
Acidity	Non acidified	Non acidified	Non acidified	Non acidified	Non acidified
Fluorescence	Nil	Nil	Nil	Nil	Nil
Oxidizing Substances	Nil	Nil	Nil	Nil	Nil
Sulphated Ash (%)	0.09	0.08	0.06	0.04	0.10
Loss on Drying (%)	3.6	3.3	2.4	6.2	4.4
Amylose Content	5.49	4.59	18.70	13.98	11.14

Table 3: Composition of metolazone solid dispersions prepared by a solvent evaporation method (*One part = 10 mg)

Formulation	Drug: Polymer (Metolazone*: Plasdone K-29/32)
MS1	1:0.5
MS2	1:1.0
MS3	1:2.0
MS4	1:3.0
MS5	1:4.0
MS6	1:5.0

Table 4: Physical parameters of metolazone solid dispersions (mean±SD; n=3)

Solid dispersion	Angle of repose (°)	Carr's index (%)	Hausner's ratio	Average particle size (µm)	Drug content (mg)
MP	34	22	1.27	45	09.54±1.11
MS1	27	19	1.24	185	10.02±1.38
MS2	24	17	1.21	176	09.98±1.27
MS3	22	15	1.19	170	10.07±0.97
MS4	20	12	1.15	163	10.01±1.01
MS5	23	14	1.17	168	09.87±0.59
MS6	23	15	1.18	172	10.11±1.19

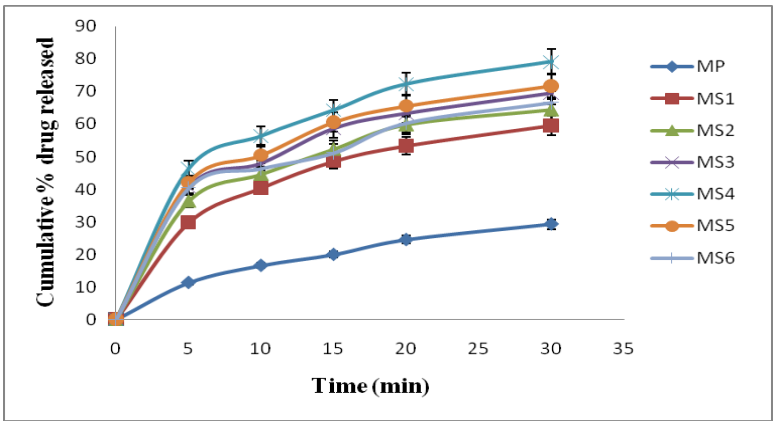

Fig. 1: Drug release profiles of metolazone solid dispersions prepared by a solvent evaporation method (mean±SD; n=3)

Preparation of metolazone tablets

Metolazone tablets were prepared using the optimized solid dispersions (MS4) along with various concentrations of *Sterculia foetida* seed starch (SFS2) and croscarmellose sodium (CCS) by direct compression technique. Formulations MPT1 to MPT6 were prepared using 2.5 to 15% of alkali extracted starch (SFS2). Formulations MPT7 to MPT12 were prepared using 2.5 to 15% of CCS. The formulation MPD contains only the solid dispersion MS4, but not any of the superdisintegrants. The compositions were given in table 5.

Table 5: Composition of metolazone tablets with different polymer concentrations (Q. S-quantity sufficient)

Ingredient (mg/tablet)	Formulations												
	MPD	MPT1	MPT2	MPT3	MPT4	MPT5	MPT6	MPT7	MPT8	MPT9	MPT10	MPT11	MPT12
MS4 Solid Dispersion	40	40	40	40	40	40	40	40	40	40	40	40	40
MCC (pH 102)	202.50	196.25	190	183.75	177.50	171.25	165	196.25	190	183.75	177.50	171.25	165
SFS2	-----	6.25	12.50	18.75	25	31.25	37.50	-----	-----	-----	-----	-----	-----
CCS	-----	-----	-----	-----	-----	-----	-----	6.25	12.50	18.75	25	31.25	37.50
Saccharin Sodium	5	5	5	5	5	5	5	5	5	5	5	5	5
Pineapple Flavour	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S	Q. S
Talc	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Magnesium Stearate	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25	1.25
Total Weight	250	250	250	250	250	250	250	250	250	250	250	250	250

Evaluation of pre-compression parameters

The pre compression parameter values obtained for various prepared granules were given in the table 6. The angle of repose, Carr's index and Hausner's ratio values for granules were within the range specified. Thus all the prepared granules were found to be stable and suitable for compression of tablets.

Table 6: Pre-compression parameters of granules prepared for tablet formulations

Formulation	Angle of repose (°)	Carr's index (%)	Hausner's ratio
MPD	31	21	1.22
MPT1	27	19	1.18
MPT2	25	17	1.16
MPT3	23	16	1.15
MPT4	23	15	1.13
MPT5	22	13	1.12
MPT6	22	12	1.12
MPT7	28	19	1.19
MPT8	27	18	1.17
MPT9	25	16	1.15
MPT10	24	14	1.14
MPT11	24	13	1.13
MPT12	22	12	1.12

Evaluation of post compression characteristics of metolazone tablets

The direct compression method was found to be suitable for preparation of fast dissolving tablets. Metolazone tablets were prepared and evaluated for post compression parameters. The results were given in table 7. Weight uniformity, hardness and friability loss of tablet formulations were within the specified limits and were found to be suitable for further studies.

Table 7: Post compression parameters of various metolazone tablet formulations (mean±SD; n=3)

Formulation	Weight uniformity (mg)	Hardness (kg/cm²)	Friability (% loss)	Wetting time (sec)	Dispersion test	Drug content (mg/tablet)
MPD	250±1.01	3.9±0.98	0.4	244	Passed	10.08±1.16
MPT1	249±0.91	3.3±1.17	0.3	84	Passed	09.98±0.68
MPT2	249±1.11	3.3±0.85	0.3	62	Passed	10.05±1.18
MPT3	250±1.20	3.2±1.06	0.2	54	Passed	10.10±1.57
MPT4	251±1.44	3.2±1.02	0.3	33	Passed	09.90±0.82
MPT5	250±1.32	3.3±0.75	0.3	25	Passed	10.05±0.93
MPT6	249±0.85	3.2±1.03	0.2	16	Passed	10.07±1.04
MPT7	251±1.04	3.4±1.09	0.3	90	Passed	09.94±1.37
MPT8	252±0.98	3.3±0.94	0.3	71	Passed	10.18±1.64
MPT9	251±1.13	3.3±0.73	0.2	59	Passed	10.02±0.99
MPT10	250±0.89	3.2±1.19	0.2	40	Passed	09.91±0.77
MPT11	250±1.51	3.2±1.35	0.3	29	Passed	10.18±1.11
MPT12	250±0.37	3.2±1.08	0.3	20	Passed	10.09±0.85

In vitro dissolution studies of metolazone tablets

Dissolution studies were carried on Metolazone tablets using U. S. P. paddle method (apparatus II) with phosphate buffer pH 6.8 as dissolution medium by maintaining the bath temperature at 37+1 °C and the paddles were operated at 75rpm. The dissolution profiles of tablets were given in table 8. The study clearly indicated that the concentration of starch as superdisintegrant has highly enhanced the dissolution parameters of the prepared tablet formulations. Formulation MPT6 containing 15% w/w of SFS2 as superdisintegrant exhibited closer dissolution profile with that of formulation MPT12 prepared by 15% w/w of CCS. Natural superdisintegrant has showed its solubility enhancement efficiency similar to earlier studies [23, 24]. The superdisintegrant potency of the starch was probably because of the rapid uptake of water, followed by swelling that leads to increase in hydrostatic pressure of tablet that ultimately disintegrates tablets faster [25]. This study thus strongly supports the usage of natural starches as superdisintegrants which was also shown in recent studies [26]. The results were shown in fig. 2 and 3.

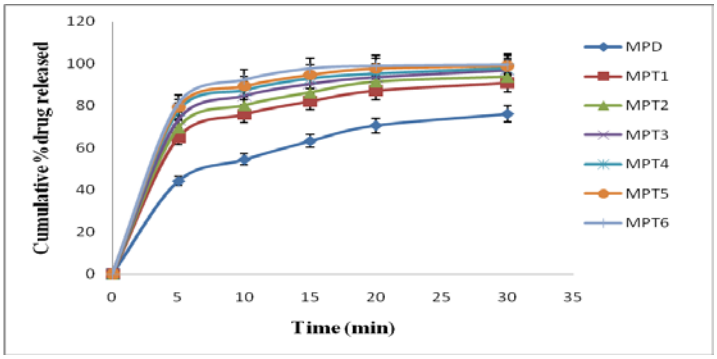

Fig. 2: Dissolution profiles of metolazone tablets prepared by direct compression method (MPT1–MPT6) (mean±SD; n=3)

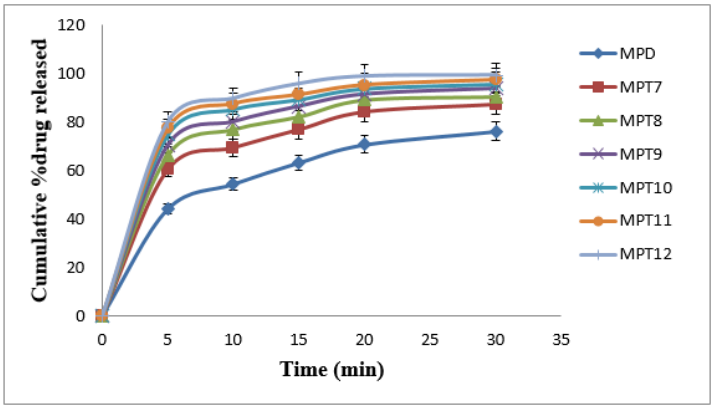

Fig. 3: Dissolution profiles of Metolazone tablets prepared by direct compression method (MPT7 – MPT12) (mean±SD; n=3)

Characterization of metolazone fast dissolving tablets

SEM studies

Scanning electron microscopy images were taken for Metolazone pure drug, SFS2, CCS, plasdone K-29/32, a blend of Metolazone with plasdone K-29/32, Metolazone with plasdone K-29/32 and SFS2 and Metolazone with plasdone K-29/32 and CCS. Metolazone pure drug exhibited crystalline form. The SFS2 starch exhibited spherical starch grains without any mucilage/resinous coverage. Plasdone K-29-32 exhibited clear granular structure. CCS exhibited blunt tubular shaped crystals. The SEM image of Metolazone with plasdone K-29/32 clearly exhibited uniform mixing of drug with granules. The SEM image of Metolazone with plasdone K-29/32 and SFS2 showed complete dispersion of drug with polymers, whereas Metolazone with plasdone K-29/32 and CCS showed uniform dispersion of drug with blunt tubular crystals of CCS. The detailed SEM images were shown in fig. 4.

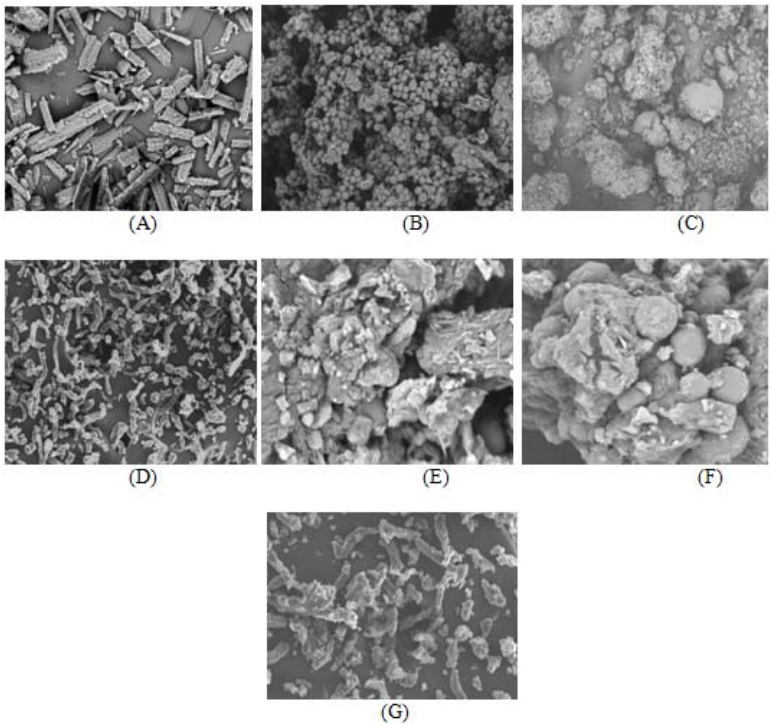

Fig. 4: SEM images: (A) Metolazone drug (B) SFS2 (C) Plasdone K-29/32 (D) CCS, (E) A blend of Metolazone with plasdone K-29/32 (F) A blend of Metolazone with plasdone K-29/32 and SFS2 (G) A blend of Metolazone with plasdone K-29/32 and CCS SFS2–*Sterculia foetida* seed starch extracted by 0.1% sodium hydroxide; CCS–Croscarmellose sodium

Accelerated stability studies of metolazone fast dissolving tablets

The fast dissolving tablets MPT6 and MPT12 containing Metolazone with MS4 solid dispersion in ratio of 1:3 mixed with SFS2 and CCS in 15% w/w respectively showed good *in vitro* dissolution and so was subjected to accelerated stability studies. The results were indicated in table 8.

No visible and physical changes were observed in the fast dissolving tablets after storage. Weight uniformity, hardness, friability, wetting time, dispersion test and drug content were found to be uniform before and after storage at different conditions. It was also observed that there was no significant change in drug release from the FDTs and was indicated in fig. 5 and 6. Thus the drug release characteristics of FDTs designed were found to be quite stable.

Table 8: Post compression parameters of metolazone fast dissolving tablet formulations (MPT6 and MPT12) under accelerated stability conditions (mean±SD; n=3)

Formulation	Storage condition	Hardness (kg/cm^2)	Friability (% loss)	Dispersion test	Wetting time (sec)	Drug content (mg/tablet)
MPT6	Before Storage	3.2±1.03	0.2	Passed	16	10.07±1.04
	25±2 °C, 60±5% RH	3.2±1.37	0.3	Passed	17	10.05±1.14
	40±2 °C, 75±5% RH	3.2±1.18	0.2	Passed	17	10.06±1.23
MPT12	Before Storage	3.2±1.08	0.3	Passed	20	10.09±0.85
	25±2 °C, 60±5% RH	3.3±1.17	0.3	Passed	22	10.11±0.99
	40±2 °C, 75±5% RH	3.2±1.49	0.3	Passed	21	10.10±1.20

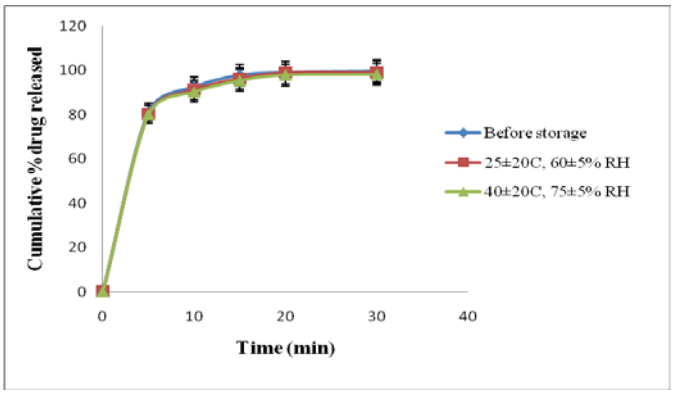

Fig. 5: Dissolution profiles of metolazone fast dissolving tablet formulation (MPT6) before and after storage at different conditions (mean±SD; n=3)

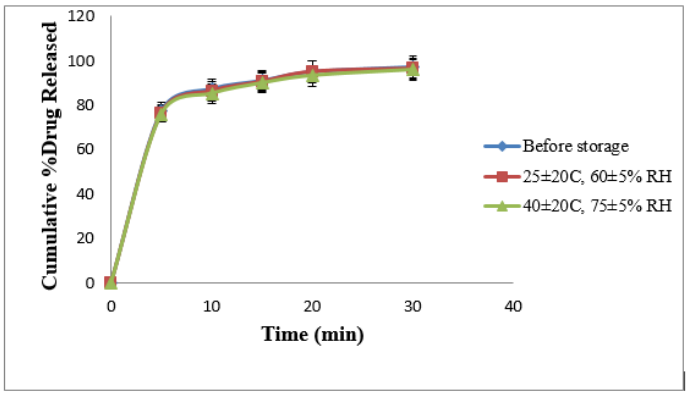

Fig. 6: Dissolution profiles of Metolazone fast dissolving tablet formulation (MPT12) before and after storage at different conditions (mean±SD; n=3)

CONCLUSION

The formulation MPT6 prepared with Metolazone solid dispersions using Plasdone K-29/32 along with *Sterculia foetida* seed starch (15%w/w) extracted using 0.1% sodium hydroxide. Similar dissolution profile was observed for formulation, MPT12 containing Metolazone solid dispersion (MS4) along with 15%w/w of CCS. The formulations MPT6 and MPT12 were also found to be stable even when subjected to accelerated stability studies. Based on above studies, it was concluded that Metolazone fast dissolving tablets prepared by *Sterculia foetida* seed starch extracted from 0.1% sodium hydroxide showed rapid drug release.

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AUTHORS CONTRIBUTIONS

Mr. Sandeep doppalapudi the guarantor of this study has designed, carried out the experiment, analyzed the results and contributed in preparation and revision of manuscript. Dr. Vidyadhara Suryadevara has designed, supervised the experimental process and reviewed the manuscript.

CONFLICTS OF INTERESTS

The authors declare no conflicts of interest

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