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Research Article

DEVELOPMENT OF FAST DISSOLVING ORAL FILMS AND TABLETS OF CINNARIZINE: EFFECT OF SUPERDISINTEGRANTS

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ABSTRACT

Objective: present study was to formulate and evaluate fast dissolving oral films (FDOFs) and fast dissolving tablets (FDTs) of Cinnarizine using different superdisintegrants; sodium starch glycolate, crospovidone and croscarmellose sodium.

Methods: FDOFs were prepared by solvent casting method and FDTs were prepared by direct compression technique. The FDOFs were evaluated for weight variation, thickness, drug content, folding endurance, flatness and tensile strength. FDTs were evaluated for weight variation, hardness, friability and drug content.

Results: Both the formulations were compared by their *in vitro* release studies. The results revealed that 4% crospovidone was found to be more promising superdisintegrant in the preparation of FDOFs and FDTs.

Conclusion: It was concluded that FDOFs were preferred over FDTs in terms of more release, flexibility and patient compliant dosage form. It can be concluded that cinnarizine FDOFs and FDTs offer more stable, robust, predictable and faster drug release/absorption than the corresponding conventional formulations.

Keywords: Fast dissolving oral films, Tablets, Cinnarizine, Superdisintegrants, Crospovidone.

INTRODUCTION

Fast dissolving drug delivery system was first came into existence in 1970 as an alternative to tablets, syrups and capsules, for pediatric and geriatric patients, which rapidly disintegrate and dissolve in saliva and then easily swallowed without need of water which is a major benefit over conventional dosage form [1]. They also impart unique product differentiation, thus enabling use as line extensions for existing commercial products. This novel drug delivery system can also be beneficial for meeting the current needs of industry are improved solubility/stability and bioavailability enhancement of drugs.

Nearly 35-50% of the general population, especially the elderly and children suffer from dysphagia or difficulty in swallowing, which results in high incidence of non-compliance and ineffective therapy. Swallowing problems also are very common in young individuals because of their poorly developed muscular and nervous systems. Other groups who may experience problems in swallowing conventional oral dosage forms are the patients with tremors of extremities, mentally ill, developmentally disabled, non-cooperative and patients with reduced liquid intake or patients suffering from nausea, as well as patients travelling or who do not have access to water [2].

Even with these differences, most of the existing fast dissolving drug delivery systems are in the form of solid tablets as fast dissolving tablets (FDTs), designed to dissolve/disintegrate in the patient's mouth without the need to drink or chew in short disintegration/dissolution times. However, to overcome fear of taking solid tablets and the risk of choking for certain patient population, a new drug delivery system was introduced as fast dissolving oral films (FDOFs). FDOFs are the most advanced form of oral solid form due to more flexibility and comfort.

Cinnarizine is a piperazine derivative, antiallergic with antihistamine, sedative, and calcium-channel blocking activity. It is used for the symptomatic treatment of nausea and vertigo caused by Meniere's disease and other vestibular disorders and for the prevention and treatment of motion sickness. Cinnarizine is absorbed from the gastrointestinal tract, peak plasma concentrations occurring 2 to 4 hours after oral doses. It has a half-life of 3 to 4 hours. The dose for vertigo and vestibular disorders is 30 mg three times daily by mouth and for motion sickness a dose of 30 mg is taken 2 hours before the start of the journey and 15 mg every 8 hours during the journey if necessary [3]. The available marketed dosage form of cinnarizine is 25 mg and 75 mg conventional tablets which can be given according to the requirement.

On this basis, there is always a need of better drug delivery system of cinnarizine for immediate effect, uniform plasma concentration profile and enhanced patient compliance. Thus the present research is focused in making fast dissolving drug delivery system of cinnarizine to enhance the bioavailability, dissolution of the drug and increasing the patient compliance. Fast dissolving films of cinnarizine can be considered suitable for clinical use in the treatment of allergic rhinitis and other conditions of allergies, where a quicker onset of action for a dosage form is desirable along with the convenience of administration.

MATERIALS AND METHODS

Materials

Cinnarizine was purchased from TasMed Pharma Pvt. Ltd., Baddi, India. HPMC (E15), HPMC (E15) was purchased from CDH, New Delhi. Sodium starch glycolate (Explotab®), crospovidone (Polyplasdone®), croscarmellose sodium (Ac-di-sol), mannitol, microcrystalline cellulose, talc and Magnesium stearate were purchased from S.D. fine chemicals Ltd, India.

Methodology

Formulation of Fast dissolving oral film

FDOFs were prepared by solvent casting method. 400 mg of hydrophilic polymers (HPMC and PVA) were dissolved in 10 ml solvent (distilled water: glacial acetic acid, 7:3). Superdisintegrants were added in the polymeric solution in concentrations (2%, 4%, 6% and 8% w/w) in different formulations. Drug (20% w/w) was added to the polymer solution and mixed thoroughly to obtain a homogeneous solution, PEG-400 (15% v/v) was added as plasticizer. The resulting polymeric solution was casted into glass moulds of 4×4 cm^2 area and dried in an oven at 50 ^{o}C for 48 hrs. The films were packed in an aluminium foil and stored in an air tight glass container to maintain the integrity and elasticity of the films.

Physicochemical Characterization of FDOF

FTIR Studies

Compatibility of drug and polymers was studied using Fourier Transform Infrared (FTIR) spectroscopy. FTIR Spectrum was

recorded in between 600-4000 cm^{-1} using Shimadzu 160a, Kyoto, Japan by KBr Disc method.

Physical appearance, Weight and Thickness

All the films were visually inspected for color, clarity, flexibility and smoothness by feel or touch. The assessment of weight and film thickness was done in 10 different randomly selected films from each batch. Films were directly weighed on a digital balance [4]. Thickness of the films was measured using micrometer with a least count of 0.01mm at different spots of the films. The thickness was measured at three different spots of the films and average was taken.

Drug Content determination

Drug content uniformity was determined by dissolving the $2cm^2$ film in 100 ml of phosphate buffer (pH 6.8) for 8 h by homogenization under occasional shaking. Then 5 ml solution was taken and diluted with phosphate buffer pH 6.8, and the resulting solution was filtered through a 0.45 µm Whatman filter paper. The drug content was then determined after proper dilution at spectrophotometer at λ_{max} 254 nm [5, 6].

Flatness

For flatness determination, one strip was cut from the center and two from each side of the film. The length of each strip was measured and variation in length was measured by determining percent constriction. Zero percent constriction is equal to 100% flatness [7, 8].

Folding Endurance and Tensile strength

The folding endurance of the films was determined by repeatedly folding one film at the same place place until it break. The number of times the film could be folded at the same place without breaking was the folding endurance value [6]. Tensile strength was determined by weight pulley method [9].

Formulation of fast dissolving tablets

FDTs prepared by Direct compression method, In this powder blends of active ingredient and suitable excipients, which flow uniformly in the die cavity and forms a firm compact. Powdered drug were mixed/blended with superdisintegrants in 2%, 4%, 6% and 8% w/w, Microcrystalline cellulose as diluent, talc as glidant, magnesium stearate as lubricant and Mannitol as filler was used. All blends passed through mesh #60. Before compression, hardness was adjusted. Each tablet weighed 200 mg.

Micromeritic properties of powdered blend

The formulation blend was evaluated for the following micromeritic parameters viz., bulk density, tapped density, Carr's index and Hausner's ratio and angle of repose as per the official procedure [10].

Physicochemical characterization of fast dissolving tablets

General appearance

Tablets of different formulations were randomly selected and organoleptic properties such as color, odor, taste, shape, were evaluated [11].

Uniformity of weight and Hardness

Twenty tablets were selected randomly from each formulation and weighed individually to check for weight variation [11]. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm^2.

Friability: The friability of the tablets was measured in a Roche friabilator. Tablets of a known weight or a sample of 20 tablets are dedusted in a drum for a fixed time (100 revolutions) and weighed again. Percentage friability was calculated from the loss in weight as given in equation as below. The weight loss should not be more than 1%. Determination was made in triplicate [12].

$$\text{Percentage friability} = \frac{\text{initial weight} - \text{final weight}}{\text{initial weight}} X\ 100$$

Drug content

Twenty tablets from each batch were weighed accurately and powdered tablet equivalent to 100 mg cinnarizine was shaken with 100 ml of phosphate buffer pH 6.8 in 100 ml volumetric flask and from this 1 ml was pipette out and then dilute up to 100 ml. Resulting solution was filtered and assayed at 254 nm using UV/Visible spectrometer and content of Cinnarizine was calculated [13].

***In vitro* release study of FDOFs and FDTs**

The release studies of cinnarizine from the prepared FDOFs (2x2 cm) and FDTs were carried out using dissolution apparatus Type II, in 900 ml phosphate buffer (pH 6.8) at 37 ± 0.5º C with a paddle rotation speed of 50 rpm. At specified time intervals, 5 ml of dissolution medium was withdrawn and assayed spectrophotometrically at 254 nm [13].

Determination of drug release kinetics

To analyze the *in vitro* release data various kinetic models zero-order, first order and Higuchi's, Hixon Crowell and Korsmeyer-Peppas models were used to describe the release kinetics [13].

Selection of batches from FDOFs and FDTs

Selection of batches was done on the basis of results obtained from *in vitro* release studies

Comparative study of FDOFs and FDTs

This study involved the comparison of *In vitro* drug release profile of the best formulations of FDOFs and FDTs. The study involved the plottation of data, will give us the actual increase in dissolution of drug.

RESULTS AND DISCUSSION

Drug Excipient Compatibility Studies

FTIR studies of pure drug and drug with polymers indicated that there is no interaction between drug and superdisintegrants used [Fig. 1]. Pure cinnarizine displays a peak characteristic of O-H stretching vibration at 3432 cm^{-1}, C-H stretching at 2957 cm^{-1}, C=O stretching of acid at 1777 cm^{-1}, C=O stretching of ketone at 1653cm^{-1}, C=C stretching of aromatic ring 1594, 1490 cm^{-1}, C-H deformation of CH_3 (symmetric) at 1278, 1179 cm^{-1}, C-H deformation of CH_3 (asymmetric) 1447, 1370 cm^{-1} and C-H deformation of aromatic rings 861-564 (several bands), The spectra of drug with different polymers showed all characteristic peaks of drug indicating that the drug is compatible with polymers.

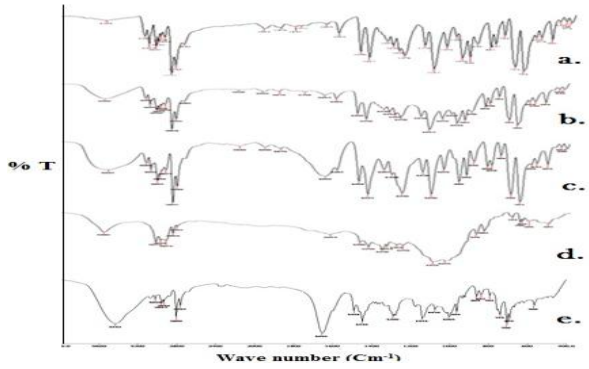

Fig. 1: Fourier transform infrared spectra of (a) cinnarizine, (b) cinnarizine with HPMC (c) cinnarizine with PVA (d) physical mixture for films; of cinnarizine, HPMC and PVA (e) physical mixture for tablets; of cinnarizine, MCC, CP, SSG and CCS.

Physicochemical characterization of FDOFs

The results of physicochemical characterization of films are shown in Table 1. The average weights ranged between 121.67 ± 0.15 to 142.36 ± 0.33 mg, which indicates that different batches varied in weights. This is due to addition of superdisintegrants. As the concentration of disintegrants was increased, weight of films was

increased. The thickness of the films was measured by micrometer and film thickness was found to lie between 0.45 ± 0.08 to 0.71 ± 0.04 mm. Again due to addition of superdisintegrants, thickness was found to be increased. Accepted uniformity of drug content among the batches was observed with all formulations and ranged 95 to 99%.

The results indicated that the process employed to prepare fast dissolving oral films in this study was capable of producing formulations with uniform drug content. The flatness study showed that all the formulations had the same strip length before and after their cuts, indicating 100% flatness. Thus, no constriction was observed indicating all films had a smooth and flat surface. Tensile strength was observed from 0.31 to 0.42 kg/mm^2. Folding endurance ranged between 176 ± 09 to 204 ±10. This is due to the reason that more is the thickness, lower will be the folding endurance. Results indicated that the films would not break and would maintain their integrity with general folding when applied.

Table 1: Composition and physicochemical characterization of fast dissolving oral films

Code	HPMC:PVA (Total weight 400mg)	Superdisintegrant (% w/w of polymer weight)	Average Weight variation (mg)* of 2x2 cm^2	Thickness (mm)	Drug content (%)	Folding endurance	Flatness (%)	Tensile strength (kg/mm^2)
A1	1:0	-	121.67 ± 0.15	0.45 ± 0.08	96.43 ± 0.47	204 ± 10	100 ± 0.00	0.325 ± 0.02
A2	1:1	-	125.29 ± 0.27	0.48 ± 0.02	95.88 ± 0.21	198 ± 07	100 ± 0.00	0.315 ± 0.03
A3	1:2	-	122.07 ± 0.13	0.48 ± 0.01	98.07 ± 0.33	201 ± 09	100 ± 0.00	0.329 ± 0.03
A4	1:3	-	127.55 ± 1.29	0.49 ± 0.01	97.07 ± 0.33	195 ± 10	100 ± 0.00	0.349 ± 0.06
A5	3:1	-	130.83 ± 0.27	0.56 ± 0.01	99.54 ± 0.22	182 ± 15	100 ± 0.00	0.425 ± 0.04
A6	2:1	-	131.35 ± 0.42	0.57 ± 0.08	95.18 ± 1.21	179 ± 08	100 ± 0.00	0.428 ± 0.03
A7	0:1	-	133.76 ± 0.54	0.57 ± 0.01	97.87 ± 0.46	176 ± 09	100 ± 0.00	0.421 ± 0.04
B1	3:1	SSG (2%)	139.12 ± 1.25	0.63 ± 0.05	97.29 ± 0.06	180 ± 10	100 ± 0.00	0.383 ± 0.03
B2	3:1	SSG (4%)	140.93 ± 0.10	0.65 ± 0.02	97.28 ± 0.33	179 ± 07	100 ± 0.00	0.358 ± 0.03
B3	3:1	SSG (6%)	141.47 ± 0.14	0.68 ± 0.07	98.12 ± 0.79	177 ± 14	100 ± 0.00	0.361 ± 0.02
B4	3:1	SSG (8%)	142.36 ± 0.33	0.71 ± 0.04	97.13 ± 0.33	174 ± 10	100 ± 0.00	0.356 ± 0.03
C1	3:1	CP (2%)	123.43 ± 0.23	0.58 ± 0.07	97.88 ± 0.39	180 ± 12	100 ± 0.00	0.338 ± 0.04
C2	3:1	CP (4%)	123.80 ± 0.44	0.58 ± 0.02	97.20 ± 0.31	180 ± 08	100 ± 0.00	0.336 ± 0.02
C3	3:1	CP (6%)	126.91 ± 0.17	0.59 ± 0.05	96.78 ± 0.08	179 ± 05	100 ± 0.00	0.333 ± 0.05
C4	3:1	CP (8%)	127.88 ± 0.22	0.59 ± 0.45	98.29 ± 0.22	177 ± 15	100 ± 0.00	0.331 ± 0.02
D1	3:1	CCS (2%)	136.14 ± 0.12	0.60 ± 0.05	99.33 ± 0.12	181 ± 07	100 ± 0.00	0.374 ± 0.03
D2	3:1	CCS (4%)	136.76 ± 1.12	0.61 ± 0.35	97.35 ± 0.88	164 ± 10	100 ± 0.00	0.366 ± 0.02
D3	3:1	CCS (6%)	138.80 ± 0.43	0.62 ± 0.05	98.68 ± 1.01	187 ± 05	100 ± 0.00	0.363 ± 0.03
D4	3:1	CCS (8%)	139.91 ± 0.27	0.63 ± 0.25	95.18 ± 0.21	190 ± 07	100 ± 0.00	0.360 ± 0.04

Concentration of drug (20% w/w of polymer weight) was kept constant in all formulations; HPMC is hydroxy propyl methyl cellulose, PVA is polyvinyl alcohol, SSG is sodium starch glycolate, CP is crospovidone and CCS is croscarmellose sodium. *n = 10 for weight; n=6 for other parameters.

Total volume of solvent (glacial acetic acid: distilled water, 7:3) was 10 ml.

***In vitro* Drug Release Study of FDOFs**

Effect of hydrophilic polymers (without superdisintegrants)

The robustness of the film mainly depends on the type and the amount of polymer used in the formulation. The drug release with different formulations (A1 to A7) without any superdisintegrant ranged from 44.87±0.32 to 61.45±0.98% within 2 minutes. Formulation A4 (1:3) met the maximum drug release profile, 61.45±0.98% (Fig. 2), as rapid release and enhanced bioavailability, due to the reason that HPMC/PVA with composition ratio 1:3 is completely solubilized in the medium that simulates the pH of saliva, stomach and intestine [14].

It was required that the developed formulations should have the rapid drug release profile, *i.e.* more than 70% for 2 minutes. For these reasons, it was decided to incorporate superdisintegrants in different ratios for fast dissolving films.

Effect of sodium starch glycolate (SSG)

Among formulations containing SSG, B4 with 8% SSG showed maximum drug release. It indicated that the drug release from the formulation increases with increase in concentration of superdisintegrant. According to Bolhuis *et al.,* 1997; SSG (Explotab®) shows its better disintegrating property, when it is used in 2-10% w/w concentration. It swells 7-12 folds in less than 30 seconds, by wicking action (porosity and capillary mechanism) (Fig. 3) [15].

Effect of Crospovidone (CP)

Among formulations containing CP, C2 with 4% CP superdisintegrant showed maximum drug release. According to Zhao *et al.,* 2005; Crospovidone (Polyplasdone®) shows its best disintegration property if it is used in 2-4% w/w concentration. It swells very little and disintegration act by capillary action [16].

Effect of croscarmellose sodium (CCS)

Formulation D3 with 6% superdisintegrant indicated maximum drug release. According to Rowe *et al.,* 1997; Croscarmellose sodium (Ac-di-sol) shows its best disintegration property if it is used in more than 5% w/w concentration. It swells 4-8 folds in less than 10 seconds by swelling and wicking mechanisms [17].

Fig. 2: *In vitro* release profile of Cinnarizine FDOFs without superdisintegrants

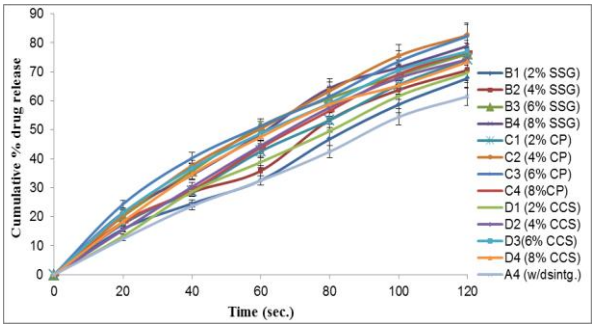

Fig. 3: *In vitro* release profile of Cinnarizine FDOFs

Drug Release Kinetic Study of FDOFs

The mechanism and kinetics of drug release of cinnarizine were determined by the application of Korsmeyer-Peppas model, Higuchi's model, zero order and first order kinetics as shown in the Table 2. In FDOFs the release kinetics of best formulations, was best fitted in first order release kinetics for cinnarizine FDOFs. It means the drug follows the linear kinetic process.

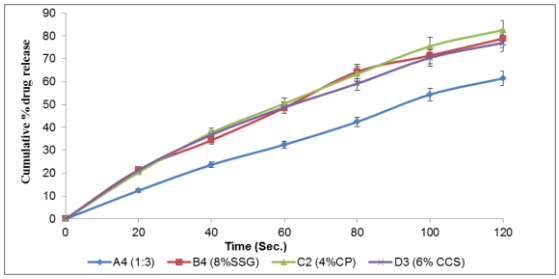

Fig. 4: Comparative *in vitro* release of best formulations of FDOFs

The value of n was more than 0.5 suggesting non-fickian diffusion (anomalous transport) with "n" value less than 1. This indicates that the drug release depends upon swelling and diffusion mechanism of release.

Physicochemical characterization of FDTs

Micromeritic properties of powder blend

Powder blends were evaluated for their micromeritic properties such as angle of repose, bulk density, tapped density, Carr's compressibility index and Hausner ratio as per official requirement. Bulk density was found to be in the range of 0.45 to 0.57 gm/cm^3, tapped density was in the range of 0.50 to 0.66 gm/cm^3, Carr's index was found to be in the range of 9.26 to 14.75 %, Hausner ratio was found to varying between 1.11 to 1.22 and angle of repose was found to varying between 18^0.94' and 24^0.89'. All parameters were found to be in acceptable limits indicating fair to good flow properties [Table 3].

Table 2: Release Kinetics of best formulations of FDOFs

Code	Zero order (r^2)	First order (r^2)	Higuchi model (r^2)	Hixon Crowell (r^2)	Korsemeyer and Peppas (n)	Release Model
W (w/dtg.)	0.640	0.838	0.811	0.814	0.361	**First order,** non fickian
X3 (8%SSG)	0.753	0.943	0.936	0.917	0.365	**First order,** non fickian
Y2 (4% CP)	0.684	0.882	0.857	0.859	0.354	**First order,** non fickian
Z3 (6%CCS)	0.789	0.895	0.891	0.885	0.445	**First order,** non fickian

Table 3: Micromeritic properties of fast dissolving tablets

Code	Angle of Repose (Θ)	Loose Bulk Density (gm/cm^3)	Tapped Bulk Density (gm/cm^3)	Carr's Compressibility Index (%)	Hausner ratio
W	21.08	0.52	0.62	16.16	1.22
X1	24.89	0.50	0.58	13.79	1.16
X2	23.12	0.48	0.53	09.43	1.10
X3	21.70	0.52	0.61	14.75	1.17
X4	20.23	0.49	0.54	9.26	1.10
Y1	20.79	0.53	0.59	10.16	1.19
Y2	19.86	0.47	0.52	09.61	1.10
Y3	18.95	0.45	0.50	10.00	1.11
Y4	17.35	0.48	0.54	11.11	1.12
Z1	22.08	0.57	0.64	10.93	1.12
Z2	20.31	0.46	0.54	13.63	1.17
Z3	19.42	0.57	0.66	13.72	1.15
Z4	18.27	0.51	0.57	10.52	1.11

Table 4: Composition and Physicochemical characterization of fast dissolving tablets

Code	Superdisintegrant (% w/w of polymer weight)	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
W	----	201 ± 1.04	3.6 ± 0.42	0.34 ± 0.33	99.12 ± 0.40
X1	SSG (2%)	206 ± 1.14	3.5 ± 0.01	0.32 ± 0.03	98.38 ± 0.32
X2	SSG (4%)	199 ± 1.13	3.7 ± 0.31	0.29 ± 0.16	97.72 ± 0.04
X3	SSG (6%)	201 ± 2.14	3.6 ± 0.12	0.29 ± 0.01	99.46 ± 0.05
X4	SSG (8%)	202 ± 1.21	3.5 ± 0.05	0.31 ± 0.03	97.51 ± 0.12
Y1	CP (2%)	202 ± 2.15	3.9 ± 0.31	0.37 ± 0.07	96.58 ± 0.24
Y2	CP (4%)	201 ± 0.70	3.8 ± 0.27	0.34 ± 0.03	98.43 ± 0.03
Y3	CP (6%)	205 ± 1.06	3.8 ± 0.51	0.29 ± 0.25	99.32 ± 0.60
Y4	CP (8%)	204 ± 2.23	3.7 ± 0.33	0.28 ± 0.43	98.29 ± 0.03
Z1	CCS (2%)	198 ± 0.63	3.7 ± 0.41	0.37 ± 0.03	99.29 ± 0.02
Z2	CCS (4%)	202 ± 1.04	3.6 ± 0.18	0.34 ± 0.42	98.61 ± 0.06
Z3	CCS (6%)	204 ± 1.66	3.7 ± 0.26	0.32 ± 0.08	96.47 ± 0.07
Z4	CCS (8%)	204 ± 2.17	3.7 ± 0.47	0.36 ± 0.19	97.61 ± 0.32

Concentration of drug (20 mg), Microcrystalline cellulose (120 mg), Starch (20 mg), Talc (4 mg) and Magnesium stearate (2 mg) was kept constant in all formulations; SSG is sodium starch glycolate, CP is crospovidone and CCS is croscarmellose sodium.

Evaluation of FDTs

Tablets showed flat, circular shape and white in color. Table 4 presents the results of physicochemical evaluation of all batches of cinnarizine FDTs. All prepared tablets were located within the acceptable limit as per IP specifications (±7.5%). Drug content was found to be in the range of 96 to 99%, hardness of the tablets was found to be in the range of 3.5 to 3.9 kg/cm^2. Friability was found to be below 1% (0.29-0.37). Mannitol (q.s. 200 mg) maintained in all formulations.

***In vitro* drug release of FDTs**

Effect of normal disintegrants (without superdisintegrants)

The drug release from the formulation W (without superdisintegrant) was 57.33 ± 0.30% within 2 minutes (Fig. 5). According to Fukami *et al.,* 2006, that the addition of mannitol with micro crystalline cellulose in the preparation of FDTs, decrease the disintegration time of tablets [18].

Effect of sodium starch glycolate (SSG)

In Formulation containing SSG X3 with 6% SSG showed maximum drug release. Further increase in the superdisintegrant concentration showed insignificant change in disintegration time ($p>0.05$, t-test). These results are in agreement with the results of Ringard *et al.,* 1988. The suggested mechanism is based on combined measurement of swelling force and more water absorption [19].

Effect of crospovidone (CP)

Formulation Y2 with 4% CP showed maximum drug release. These results were in agreement with that of Murakami *et al.,* 1999, who explained the mechanisms, due to either disintegrant swelling in contact with water, release of gases when in contact with water or increasing the uptake of aqueous liquids inside tablets [20].

Effect of croscarmellose sodium (CCS)

Formulation Z3 with 6% CCS showed maximum drug release. 6% CCS is a critical concentration; more than 6 to 10% gave same disintegration time (Ringard *et al.,* 1988). Due to high uptake of liquids, leads to decreasing tablets strength and fast disintegration (Fu *et al.,* 2005) [21].

Comparison of effect of superdisintegrants

Formulations having superdisintegrants, X3 (6%), Y2 (4%) and Z3 (6%) significantly ($p<0.05$, t-test) has higher drug release as compared to W formulation (without disintegrants) (Fig. 6). This is the effect of superdisintegrants, which disintegrated the films fast and eroded them to release drug. When different superdisintegrants were compared, it was found that crospovidone (C2) revealed maximum release within 2 minutes. This may be due to, its disintegration act by capillary action, swells very little and reduces the physical bonding forces between the particles.

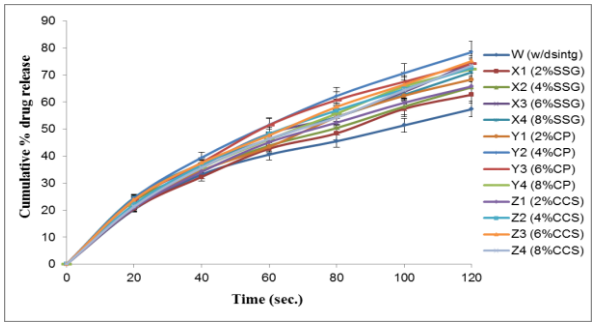

Fig. 5: *In vitro* release profile of Cinnarizine FDTs

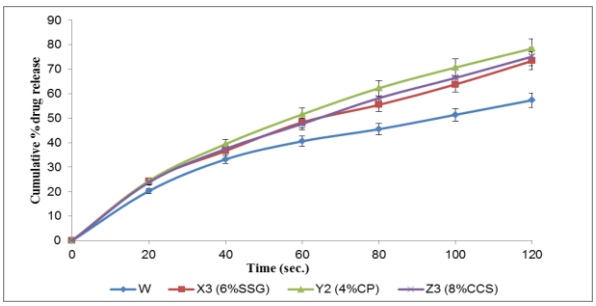

Fig. 6: Comparative *in vitro* release of best formulations of FDTs

Drug Release Kinetic Study of FDTs

In FDTs the release kinetics of best formulations, (X3, Y2 and Z3) was best fitted in different models for cinnarizine FDTs. Formulation X3 and Z3 showed first order release and formulation Y2 followed Hixon crowell which showed that there was a change in surface area and diameter of particles (Table 5).

Table 5: Release Kinetics of best formulations of FDTs

Code	Zero Order (r^2)	First order (r^2)	Higuchi Model (r^2)	Hixon Crowell (r^2)	Korsemeyer and Peppas (n)	Release Model
W (w/dtg.)	0.850	0.968	0.972	0.951	0.769	**Higuchi,** non fickian
X3 (6%SSG)	0.741	0.974	0.945	0.938	0.759	**First order,** non fickian
Y2 (4% CP)	0.713	0.954	0.927	0.957	0.748	**Hixon Crwl,** non fickian
Z3 (6%CCS)	0.728	0.964	0.935	0.926	0.752	**First order,** non fickian

Comparison between FDOF and FDT formulations: Selected best formulations of cinnarizine FDOFs and FDTs of cinnarizine were compared with the selected best formulations and results are reported

Fig.7: From the comparison, it was found that formulation C2 (4% CP) in FDOFs and Y2 (4% CP) in FDTs are more effective formulations of the system.

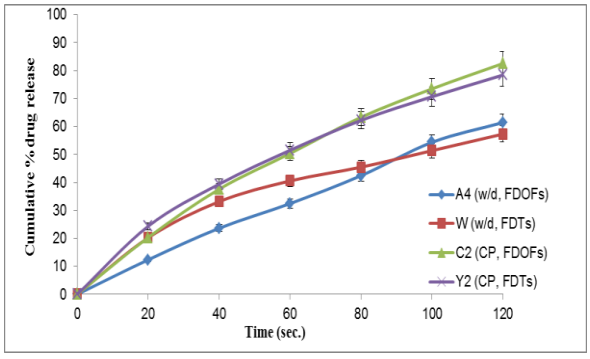

Fig. 7: *In vitro* Comparison of FDOFs and FDTs

CONCLUSION

The objective of the present investigation has been achieved by preparing fast dissolving oral films and tablets of cinnarizine for the solubility and bioavailability enhancement using different superdisintegrants. The results revealed that crospovidone (4%) was a promising superdisintegrant. Because it quickly wicks saliva to generate volume of expansion and hydrostatic pressure, this is necessary to provide rapid disintegration in the mouth. Unlike other superdisintegrant, rely principally on swelling for disintegration. On comparison of both the formulations, FDOFs were preferred over FDTs in terms of more flexibility and comfort dosage form. It can be concluded that cinnarizine FDOFs offer more stable, robust, predictable and faster drug release/absorption than the corresponding conventional formulations. The results from the study showed the utility of FDOFs to enhance solubility and dissolution of sparingly soluble compounds like cinnarizine. The present exploratory work successfully illustrates the potential utility of FDDDs for the delivery of poor water-soluble compounds.

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