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EFFECT OF DIFFERENT NATURAL AND SYNTHETIC SUPERDISINTEGRANTS USED IN DEVELOPEMENT OF AMIODARONE HYDROCHLORIDE FAST DISSOLVING TABLETS: A COMPARATIVE STUDY

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ABSTRACT

In the present work, fast disintegrating tablets of Amiodarone hydrochloride were prepared by subliming method with a view to enhance the patient compliance. Different natural and synthetic superdisintegrants were used in different ratio with camphor (30% W/W) as subliming agent. The prepared tablets were evaluated for various parameters like weight variation, hardness, friability, *in vitro* disintegration time, drug content, modified disintegration time, water absorption ratio, wetting time, *in vitro* dispersion time, *in vitro* wetting volume, measurement of tablet porosity, *in vitro* drug release, preliminary compatibility studies, FTIR, DSC studies, scanning electron microscopy before and after sublimation and short term stability studies. All the pre and post-compressional parameters are evaluated and found within the prescribed limits. The optimized formulation **(O F5)** and **(H F4)** showed good release profile with maximum drug being released at all time intervals. The result of the work concluded that the sublimation is a useful technique to enhance the solubility and dissolution rate of poorly water-soluble drugs. The release of Amiodarone from FDTs was found to follow non-Fickian diffusion kinetics.

Key words: Fast dissolving tablet, Direct compression, Amiodarone hydrochloride, Subliming agents, Superdisintegrants, Camphor.

INTRODUCTION

Many patients express difficulty in swallowing tablets and hard gelatin capsules, resulting in non-compliance and ineffective therapy. Recent advances in novel drug delivery systems (NDDS) aim to formulating a dosage form of drug molecules for convenient administration and to achieve better patient compliance. One such approach leads to development of fast dissolving/disintegrating tablets[1]. Advantages of these drug delivery systems include convenience of administration and accurate dosing as compared to liquids, easy portability and ability to provide advantages of liquid medication in the form of solid preparation, ideal for paediatric and geriatric patients and rapid dissolution/absorption of the drug, which may produce rapid onset of action. Some drugs are absorbed from mouth, pharynx and esophagus as the saliva passes down into the stomach and in such cases, bioavailability of the drug is increased: pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.

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One of the major problems with this drug is its very low solubility in biological fluids, which results into poor bioavailability after oral administration.

Amiodarone belongs to class II biopharmaceutical classification system (BCS), which is characterized by high membrane permeability and slow dissolution rate due to low aqueous solubility. It belongs to the class III anti-arrhythmic drugs, which prolong the duration of the action potential and the effective refractory period in both atria and ventricles. It would be advantageous to increase the solubility of such molecule. Further, it is important to enhance aqueous solubility and dissolution rate, which may lead to enhancement of bioavailability from its oral solid dosage form. From the formulation point of view conventional dosage forms (tablets and capsules) take higher disintegration time, so that the pharmacological action is delayed by 45-60 min from its administration.

Sublimation method[2]

In this method a subliming material like ammonium bicarbonate, ammonium carbonate, urea, benzoic acid, naphthalene, camphor etc. is removed by sublimation from compressed tablets and high porosity is achieved due to the formation of many pores, where camphor particles previously existed in the compressed tablets prior to sublimation of the camphor. These compressed tablets, which have high porosity (approximately 30%) rapidly dissolved within 15 sec in saliva.

Advantage: Tablets dissolved in 10-20 sec. and exhibit sufficient mechanical strength.

EXPERIMENTAL

Materials and methods

Amiodarone hydrochloride was procured from Madras Pharma Pvt. Ltd., Chennai, Crosspovidone, magnesium stearate and talc were obtained as gift sample from Microlabs (P) Ltd., Hosur. Orange peel powder, Plantago ovata husk, and Banana powder were purchased from Ayurveda Pharma, Madurai. Camphor and Menthol was purchased from Bose Laboratory, Madurai.

Methods of preparation of amiodarone hydrochloride fast dissolving tablets[3]

Various formulations of fast dissolving tablets of Amiodarone hydrochloride were prepared by using sublimation method. Accurately weighed quantity of Amiodarone hydrochloride, subliming agents (Camphor and menthol), synthetic superdisintegrants (crosspovidone), natural superdisintegrants (*plantago ovata* husk, orange peel and banana powder), starch and PVP were mixed and passed through the sieve No. 40. Finally, magnesium stearate and talc were added as lubricating agents. The tablets were prepared by direct compression method using 8 mm round shape punches on a single tablet compression machine. After compression, the tablets were heated in a hot air oven at 50^{o}C for 8 hrs. The composition of the each batches were shown in Table 1.

Table 1: Composition of formulation of sublimation method

Ingredients	F 1	F 2	F 3	F 4	F 5	F1	F2	F3	F4	F5
Amiodarone	100	100	100	100	100	100	100	100	100	100
Crosspovidone	-	4	6	8	10	-	-	-	-	-
Plantago Ovata husk	-	-	-	-	-	2	4	6	8	10
Orange peel extract	8	10	12	14	16	-	-	-	-	-

Cont…

Ingredients	F 1	F 2	F 3	F 4	F 5	F1	F2	F3	F4	F5
Banana powder	-	-	-	-	-	4	6	8	12	16
Camphor	60	60	60	60	60	60	60	60	60	60
Menthol	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
Starch	33.6	29.6	27.6	25.6	23.6	31.6	29.6	27.6	25.6	23.6
Magnesium stearate	2	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2	2
Polyvinyl pyrrolidine	2	2	2	2	2	2	2	2	2	2
Total weight (mg)	200	200	200	200	200	200	200	200	200	200

Drug – excipients compatibility studies[4]

Preliminary compatibility studies were performed in closed vial using hot air oven and autoclave. The physical mixture for all formulations were prepared in 1:1 ratio by triturating in mortar and pestle for 10 min. These samples were kept at 40^{o} for 1 month in hot air oven and at 121^{o}, 15 Ib pressure for 15 min in autoclave. Furthermore, samples were observed for their appearance and drug content was determined by assay.

Drug-excipients compatibility studies by IR spectroscopy[4]

IR spectra were recorded for Amiodarone, physical mixture, and compressed tablet using IR-spectrophotometer (Bruker alpha T, India). The samples were prepared in KBr dish and scanned over 400 to 4000 cm^{-1} (Fig. 2 a, 2b, 2c).

Differential scanning calorimetry[4]

Differential scanning calorimetry was used to characterize thermal properties. The DSC thermograms were recorded using TA-60 thermal analyzer (Shimadzu) for all formulations. The samples were hermetically sealed in aluminium pans and heated at a constant rate of 20^{o}/min over temperature range of 50 to 200^{o}. Inert atmosphere was maintained by purging nitrogen gas at flow rate of 50 mL/min.

Evaluation parameters of Amiodarone hydrochloride fast dissolving tablets

Pre-compression parameters[5]

Prior to compression, granules were evaluated for their flow and compressibility parameters. Flow properties of granules were determined by angle of repose method. Compressibility index of granules were determine by Carr's index and Hausner ratio.

Post- compression parameters[5]

The tablets were evaluated for the parameters viz, thickness, weight variation, hardness, friability, drug content, modified disintegration time, water absorption ratio, wetting time, *in vitro* wetting volume, modified disintegration time and measurement of tablet porosity.

***In vitro* disintegration time**

The *In vitro* disintegration time was determined using disintegration test apparatus. A tablet was placed in each of the six tubes of the apparatus and one disc was added to each tube. The time in seconds

taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

In vitro dispersion time

In vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 6 mL of distilled water. Three tablets from each formulation were randomly selected and *in vitro* dispersion time was performed. Standard deviation was also determined and *in vitro* dispersion time is expressed in seconds.

In vitro dissolution studies[6]

Dissolution rate was studied by using USP type–II apparatus (US XXIII dissolution test apparatus at 50 rpm) using 900 mL 1% SLS as dissolution medium. Temperature of the dissolution medium was maintained at 37 ± 0.5^{o}C, aliquot of dissolution of filtered was withdrawn at every 5 min interval and filtered, the absorbance of filtered solution was measured by UV spectrophotometer method at 251 nm and concentration of the drug determined from the standard calibration.

Scanning electron microscopy (SEM)[7]

The SEM analysis was conducted using Jeol, Japan (model-/JSM 5610 LV) company scanning microscope for the study of formation of pores within the tablets. As with SEM high vacuum is required for image formation and samples must be thoroughly desiccated before entering the vacuum chamber and, therefore samples were thoroughly dried after swelling for analysis. The dried samples were mounted on sample holder using double sided adhesive carbon tape. The SEM was operated at 15 KV. The condenser lens position was maintained at a constant level.

Stability studies as per ICH guidelines[8]

In the present study, stability studies were carried out at 40^{0}C ± 2^{0}C/75% ± 5% RH and 25^{0}C ± 2^{0}C/60% ± 5% RH for a specific time period up to 30 days for the selected formulations.

Application of release rate kinetics to dissolution data[9]

To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero order, first order, Higuchi and Korsmeyer-peppas release model.

RESULTS AND DISCUSSION

Calibration curve[10]

A standard calibration curve for the drug was obtained by measuring absorbance of the solution (1-10 µg/mL) at 251 nm by plotting the graph of absorbance vs concentration. The linear correlation coefficient was found to be $\gamma = 0.9998$. Amiodarone obeys Beer's law within the concentration range of 1 -10 µg/mL.

Evaluation of precompression properties[11]

For each designed formulation, blend of drug and excipients was prepared and evaluated for precompression properties shown in table. Bulk density was found to be between 0.867 ± 0.04 to 1.291 ± 0.01 g/cm^3 and tapped density between 0.951 ± 0.01 to 1.089 ± 0.04 gm/cm^3 for all formulations. From density data % compressibility was calculated and was found to be between 11.5 ± 0.02% to 15.81 ± 0.03%. Angle of repose was found to be in the range of 23.42 ± 0.03 to 27.29 ± 0.02. Hausner ratio was found below 1.13 ± 0.01 to 1.20 ± 0.01. All the formulations showed fair to good flow properties for direct compression and hence, tablets were prepared by using sublimation technique (Table 2).

Table 2: Evaluation of pre-compression parameters of fast dissolving tablets

Formulation code	Angle of repose (Ø)	Bulk density (G/Cm^3)	Tapped density (G/Cm^3)	Carr's index (%)	Drug content (%)	Hausner ratio	Flow
CF1	23.42	1.285	1.089	11.65	98.2	1.131	Good
CF2	24.13	1.289	0.955	11.85	99.2	1.135	Good
CF3	23.51	1.290	0.961	12.01	98.3	1.140	Good
CF4	24.55	1.286	0.958	11.99	98.3	1.134	Good
CF5	23.67	1.282	0.998	11.85	98.4	1.131	Good
HF1	27.01	1.292	0.845	15.2	97.1	1.17	Good
HF2	27.12	1.298	0.855	15.9	96.7	1.19	Good
HF3	27.19	1.295	0.847	15.5	98.5	1.21	Good
HF4	27.22	1.297	0.851	15.81	99.3	1.18	Good
HF5	27.29	1.291	0.854	15.66	98.8	1.22	Good
OF1	24.73	0.867	0.951	15.2	97.1	1.17	Good
OF2	24.56	0.872	0.957	15.8	99.1	1.19	Good
OF3	24.72	0.881	0.959	15.5	96.9	1.20	Good
OF4	24.75	0.871	0.961	15.4	99.1	1.19	Good
OF5	24.66	0.873	0.958	15.2	99.7	1.18	Good
BF1	25.65	0.965	1.081	11.6	97.4	1.13	Good
BF2	25.78	0.972	0.991	11.7	98.7	1.18	Good
BF3	25.81	0.966	0.989	11.65	99.2	1.14	Good
BF4	25.86	0.978	0.993	11.4	98.7	1.15	Good
BF5	25.79	0.981	0.987	11.5	98.1	1.16	Good

Evaluation of post compression properties of fast dissolving tablets[11]

Tablets were prepared using sublimation technique. Since the powder materials was free flowing, tablets were obtained of uniform weight due to uniform die fill. Tablets were obtained of uniform weight variations as per pharmacological specifications. The drug content was found in the range of 96.2-99.7% (acceptable limit) and the hardness of the tablets was between 3-4 Kg/cm^2. Friability of the tablets was found below 1% indicating a good mechanical resistance of tablets. Thickness of the formulations was varied from 3.5 ± 0.04 to 3.7 ± 0.04 mm. The dispersion time for the formulation prepared with crosspovidone, plantago ovata husk, and orange peel extract and banana powder were found in the range of 22 to 307 sec, 18 to 22 sec, 18.49 to 23.79 sec and 33 to 35 sec (Fig. 1). The formation of pores was confirmed by SEM analysis by subjecting tablet before and after sublimation. It was evident from the result presented in Fig. 4 that pores were formed on the surface of tablet after sublimation of camphor. The optimized formulation was found stable after evaluation of these parameters at different stability conditions and the results are given in Tables 4a and 4b. All the parameters were found well within the specified limit (Table 3).

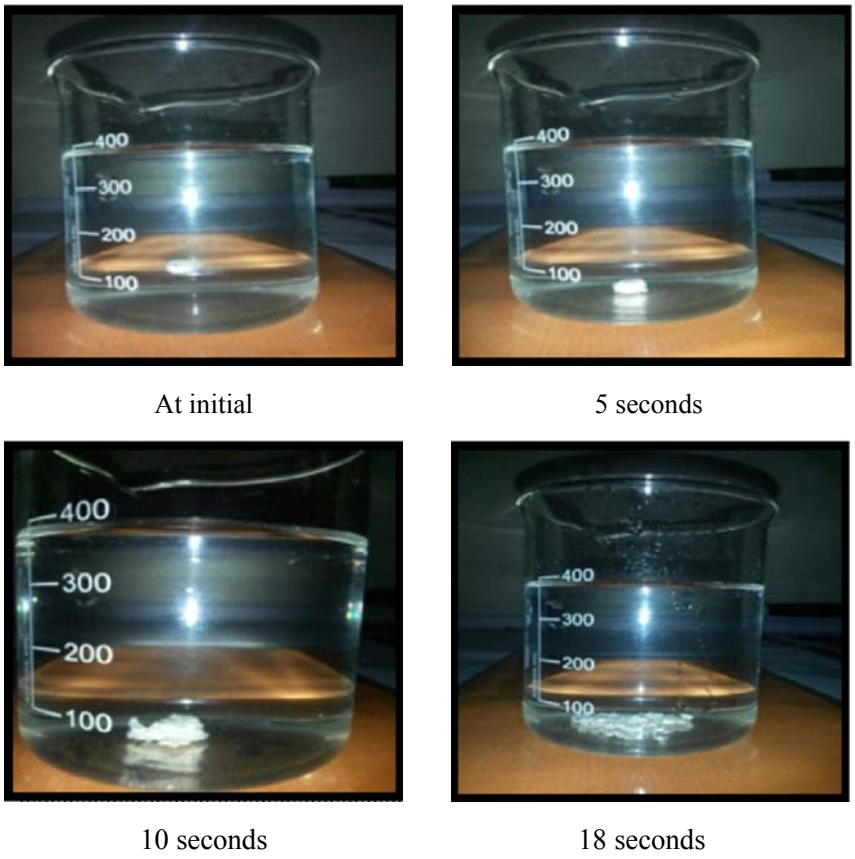


Fig. 1: *In-vitro* dispersion time image of HF4 optimized formulations

Effect of superdisintegrants on drug release[12]

The formulations OF1, OF2, OF3, O F4, and OF5 were prepared with 4%, 5%, 6%, 7%, 8% orange peel extract as a natural superdisintegrant, which showed the cumulative percentage of drug release 96.58%, 97.6%, 98.7%, 98.9%, 99.84%, respectively at 8.66 seconds. Formulation OF5 containing 8% orange peel extract shows maximum drug release (99.84%) at 8.66 seconds. This result indicated that the optimum concentration of orange peel extract was 8%.

Formulation HF1, HF2, HF3, HF4, and HF5 were prepared with 1%, 2%, 3%, 4%, 5% *plantago ovata* husk as a natural superdisintegrant, which showed the cumulative percentage of drug release 97.4%, 96.96%, 98.57%, 99.56%, 99.3%, respectively at 9.06 seconds. Formulation HF4 containing 4% *plantago ovata* husk shows maximum drug release (99.56%) at 9.06 seconds. This result indicated that the optimum concentration of *plantago ovata* husk was 4%.

The formulation BF1, BF2, BF3, BF4, and BF5 were prepared with 2%, 3%, 4%, 6%, 8% banana powder as a natural superdisintegrant, showed the cumulative percentage of drug release 95.9%, 96.9%, 98.07%, 98.24%, 99.07% respectively at 12.8 seconds. Formulation BF3 containing 8% banana powder shows maximum drug release (99.07%) at 12.8 seconds.

The formulation CF1, CF2, CF3, CF4, and CF5 were prepared with 0%, 2%, 3%, 4%, 5% crosspovidone as a synthetic superdisintegrant, showed the cumulative percentage of the drug release 56.68%, 97.46%, 97.69%, 98.7%, 99.07%, respectively at 11.4 seconds. Formulation CF5 containing 5% crosspovidone shows maximum drug release (99.07%) at 11.4 seconds. The formulation CF1 were prepared

without superdisintegrants, showed the cumulative percentage of drug release of (56.68%) at 274 seconds. From the results, the release rates of superdisintegrants were in the order:

Orange peel extract > *Plantago ovata* husk > Crosspovidone > Banana powder

The maximum percentage of drug release was achieved by the formulation containing orange peel extract OF5 (8%) as a natural superdisintegrant. It may be due to the results in the rapid disintegration of tablets in dissolution medium resulting in the maximum drug release. Among twenty formulations, formulation orange peel extract (OF5) and plantago ovata husk (HF4) was selected as a best formulation because of its lowest wetting time, disintegration time and highest water absorption ratio, drug release.

Infra red spectroscopy[13]

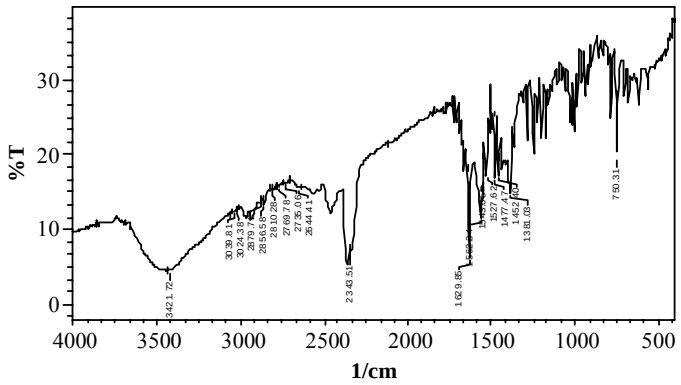


Fig. 2a: IR spectrum of Amiodarone hydrochloride

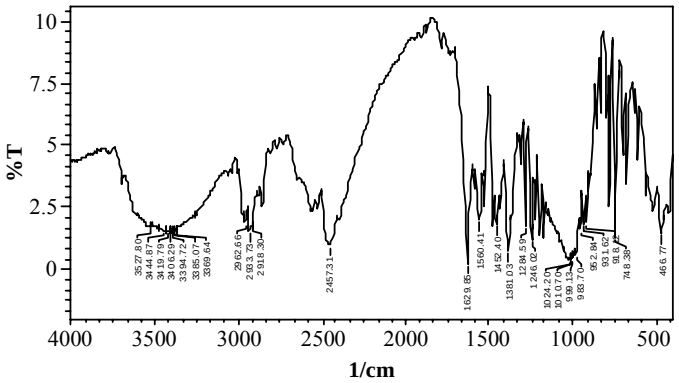


Fig. 2b: IR spectrum of optimized formulation of orange peel extract

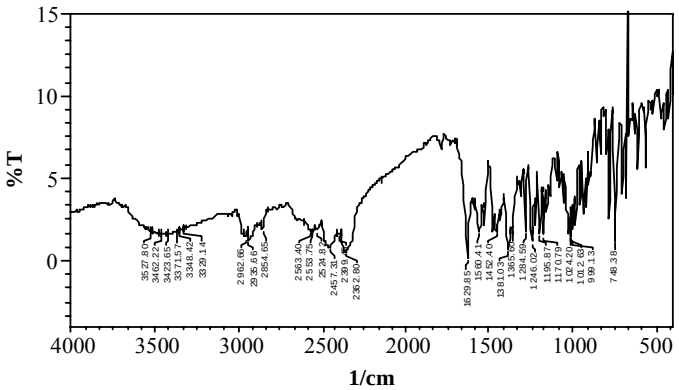


Fig. 2 c: IR spectrum of optimized *plantago ovata* husk

Influence of synthetic superdisintegrants on Amiodarone hydrochloride fast dissolving tablets

To study the influence of superdisintegrants on the performance of Amiodarone hydrochloride, a set of five formulations (CF1 to CF5) were prepared using superdisintegrants viz, crosspovidone (5%), respectively. The formulated tablets were subjected to various quality control tests and the results were shown in Table 3. All the tablets complied with the pharmacopoeial standards. The dissolution data was presented in Fig. 3a and 3b. The dissolution rate of Amiodarone hydrochloride was found to be affected by the synthetic superdisintegrants used in the preparation of tablets. The formulation prepared with crosspovidone was offered relatively slow release of Amiodarone hydrochloride when compared with natural superdisintegrants.

Influence of natural superdisintegrants on Amiodarone hydrochloride fast dissolving tablets

To study the influence of natural superdisintegrants on the performance of Amiodarone hydrochloride, a set of three formulations were prepared using three natural superdisintegrants viz, orange peel extract (OF1 to OF5), plantago ovata husk (HF1 to HF5), banana powder (BF1 to BF5) and crosspovidone (CF1 to CF5), respectively. The formulated tablets were subjected to various quality control tests and the results are shown in Table 3. All the tablets complied with the pharmacopoeial standards. The dissolution data are presented in Fig. 3a and 3b.

Table 3: Evaluation of post compression parameters of fast dissolving tablets

Formulation code	Content uniformity (%)	*In vitro* disintegration time (Sec)	Water absorption ratio (%)	Wetting time (Sec)	*In vitro* dispersion time (Sec)	% Porosity	Wetting volume (Ml)
CF1	97.7	274	23.3	251	307 ± 0.01	12.5	20 ± 0.2
CF2	98.7	11.4	79.8	23.6	23.67 ± 1.23	39.5	1.7 ± 0.1
CF3	98.0	11.7	81.8	22.87	24.67 ± 0.36	37.3	1.7 ± 0.04
CF4	98.1	12.0	85.08	23.2	22.00 ± 1.12	42.8	1.6 ± 0.04
CF5	98.1	11.8	97.9	23.03	28.33 ± 0.59	41.3	1.8 ± 0.08
HF1	96.2	11.6	77.7	22.6	25.33 ± 0.59	34.4	1.4 ± 0.1
HF2	96.3	11.8	79.3	22.8	26.00 ± 1.01	43.9	1.6 ± 0.1
HF3	98.2	11.6	81.1	22.8	22.33 ± 1.57	38.68	1.4 ± 0.09
HF4	98.9	9.06	98.5	15.2	18.00 ± 0.67	54.3	0.9 ± 0.04
HF5	98.4	11.5	90.3	22.3	21.00 ± 0.65	44.25	1.4 ± 0.04
OF1	96.0	11.2	77.01	18.8	23.79 ± 0.07	25.8	0.9 ± 0.08
OF2	98.5	11.6	75.7	18.8	23.7 ± 0.02	26.15	0.9 ± 0.04
OF3	96.1	11.8	85.0	19.7	23.53 ± 0.01	23.15	1.06 ± 0.04
OF4	98.7	11.5	93.4	20	23.91 ± 0.1	23.29	1.16 ± 0.04
OF5	99.1	8.66	98.7	14.9	18.49 ± 0.01	48.3	0.9 ± 0.1
BF1	97.4	13.2	77.01	30.1	33.45 ± 0.7	37.48	2.06 ± 0.04
BF2	98.1	12.6	79.8	27.2	33.70 ± 1.68	18.35	2.3 ± 0.09
BF3	98.4	12.2	81.5	28.03	35.62 ± 0.38	19.5	2.2 ± 0.04
BF4	98.5	12.7	82.2	28.1	35.52 ± 0.34	15.9	2.4 ± 0.04
BF5	97.9	12.8	85.7	22.3	34.45 ± 0.32	25.4	2.06 ± 0.09

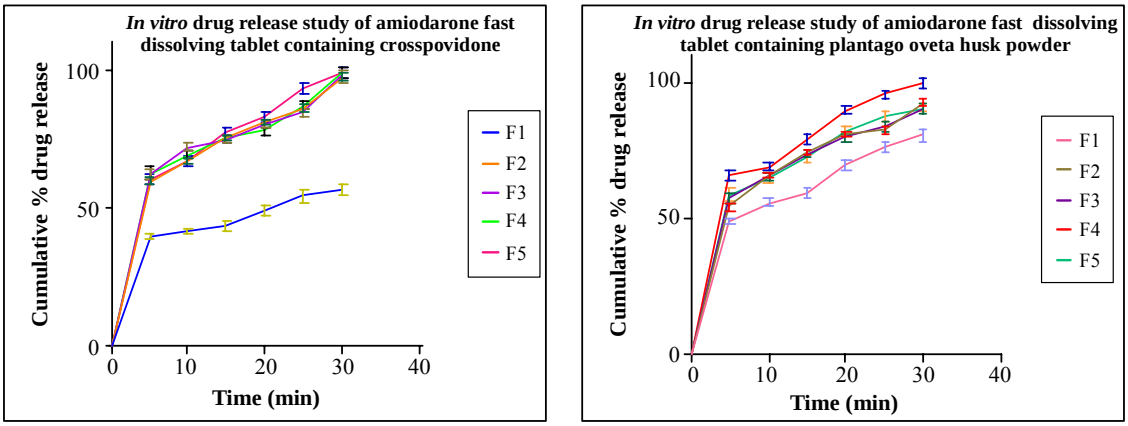


Fig. 3a: Comparison of *In vitro* release profile of Amiodarone containing different percentage of crosspovidone and plantago ovata husk

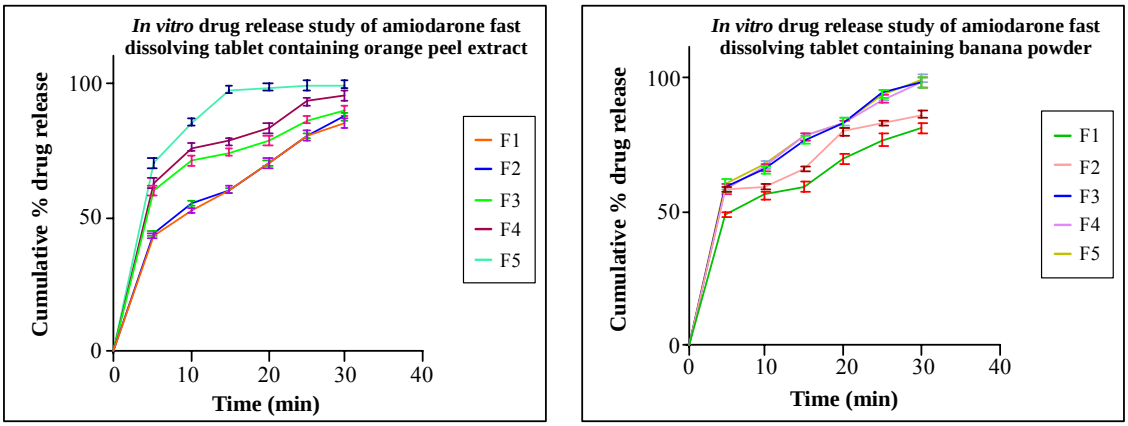
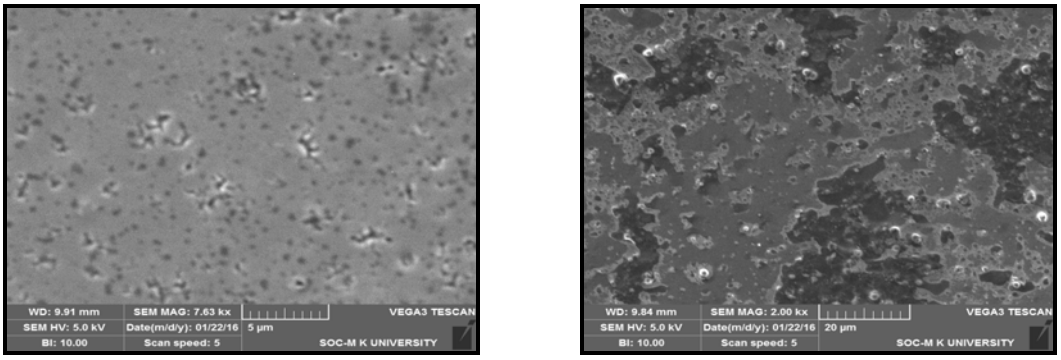


Fig. 3b: Comparison of *In vitro* release profile of Amiodarone containing different percentage of orange peel extract and banana powder

The dissolution rate followed first order kinetics (Fig. 5) as the graphs drawn between log % drugs unreleased Vs time were found to be linear. The dissolution rate of Amiodarone hydrochloride was found to be affected by nature of the natural superdisintegrants used in the preparation of tablets. Based on the dissolution rate, superdisintegrants can be rated as treated orange peel extract > *Plantago ovata* husk > Banana powder. The formulation prepared with orange peel (F5) was offered relatively rapid release of Amiodarone hydrochloride, when compared with other treated formulation.



(a) Before sublimation orange peel (OF5) **(b) After sublimation orange peel (OF5)**

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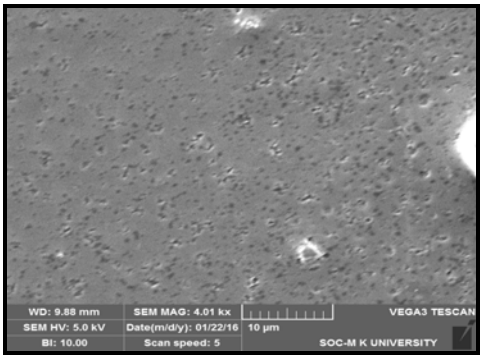
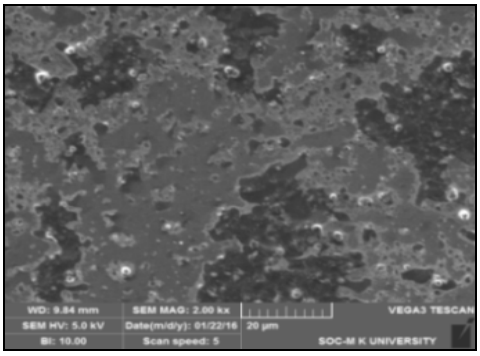


(a) Before sublimation *plantago ovata* husk (H F4)



(b) After sublimation *plantago ovate* (HF4)

Fig. 4: SEM of the formulation (a) before sublimation (b) after sublimation

Comparison of dissolution data of tablets containing synthetic superdisintegrants and natural superdisintegrants

The tablets with synthetic superdisintegrants showed maximum release for 11.4 seconds where as the Amiodarone hydrochloride tablets containing natural superdisintegrants showed the maximum release for 8.66 seconds.

Table 4 a: Selected formulations for stability studies orange peel extract (F5), *Plantago Ovata* husk (F4) stored At $25^0C \pm 2^0C/60\% \pm 5\%$ RH

S. No.	Formulation code	Tested after time (in days)	Drug content (%)	Disintegration time (sec)	Drug release (%) mean SD ± (n = 3)
1	Orange peel extract (F5)	0	99.1	8.66	99.84 ± 0.3
		10	98.9	8.59	99.7 ± 0.1
		20	98.1	8.46	99.0 ± 0.6
		30	98.1	8.47	99.3 ± 0.5
2	*Plantago ovata* husk (F4)	0	98.71	9.06	99.56 ± 0.4
		10	98.73	9.69	99.3 ± 0.7
		20	98.5	9.65	99.1 ± 0.5
		30	98.3	9.63	99.1 ± 0.5

Table 4 b: Selected formulations for stability studies orange peel extract (F5), *Plantago Ovata* Husk (F4) stored at $40^0C \pm 2^0C/75\% \pm 5\%$ RH

S. No.	Formulation code	Tested after time (in days)	Drug content (%)	Disintegration time (sec)	Drug release (%) Mean SD ± (n = 3)
1	Orange peel extract (F5)	0	99.1	8.66	99.84 ± 0.3
		10	99.2	8.69	99.86 ± 0.1
		20	98.8	8.62	99.76 ± 0.6
		30	98.9	8.62	99.79 ± 0.5

Cont…

S. No.	Formulation code	Tested after time (in days)	Drug content (%)	Disintegration time (sec)	Drug release (%) Mean SD ± (n = 3)
2	*Plantago ovata* husk (F4)	0	98.71	9.06	99.56 ± 0.4
		10	98.70	9.12	99.53 ± 0.7
		20	97.5	9.22	99.47 ± 0.5
		30	97.2	9.18	99.47 ± 0.5

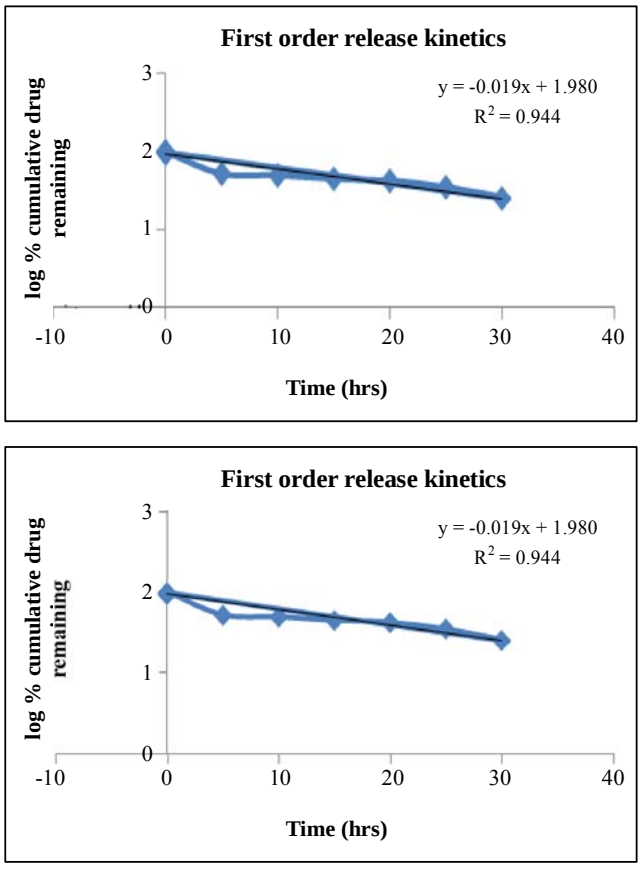


Fig. 5: Amiodarone drug release profile of OF5 and HF4 showing first order kinetics

CONCLUSION

In the present work, an attempt has been made to develop fast dissolving tablets of Amiodarone hydrochloride. Crosspovidone (synthetic superdisintegrants), orange peel extract, *plantago ovata* husk, and banana powder (Natural superdisintegrants) were employed as superdisintegrating agents to enhance the solubility and dissolution rate of selected drug molecules. Camphor was employed as sublimating agents, as due to presence of camphor, maximum pores will be formed. As the number of pores was more, the body fluid will penetrates more easily. All the formulations were prepared by direct compression method using 8 mm punch on single rotary tablet punching machine. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, and tapped density. Then all the formulations underwent sublimation technique. The prepared tablets were shown to have good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations, OF5 and HF4 formulation showed maximum percentage drug release i.e., 99.84 % in 30 min and hence, it is considered as optimized formulation.

The formulation OF5 containing 8% orange peel extract has shown the better results for disintegration time of 8.66 seconds and formulation HF4 containing 5% *plantago ovata* husk has shown the better result for disintegration time of 9.06 seconds.

The present work revealed that the natural superdisintegrants, orange peel extract and *plantago ovata* husk showed better disintegrating and dissolution property than the most widely used synthetic superdisintegrants in the formulation of fast dissolving tablets.

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