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Formulation and invitro evaluation of amiodarone orodispersable tablets.

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ABSTRACT

The oral disintegrating tablets of Amiodarone with sufficient mechanical strength, acceptable taste and smaller disintegration time were achieved employing suitable superdisintegrants and other excipients at optimum concentration. FTIR studies revealed that there was no shift in peaks, indicating there is no interaction between Amiodarone and other ingredients used. Among three super disintegrants used Croscaramellosesodium and SLS combination showed better performance in disintegration time when compared to crospovidone and sodium starch glycolate used alone. In the *invitro* dissolution study comparison among all formulations, F10 showed best results. So the formulation of F10 was found to be best among all other formulations, because it has exhibited good taste and faster disintegration time when compared to all other formulations.

Keywords: Croscaramellosesodium, Crospovidone and Sodium Starch Glycolate

INTRODUCTION

The oral route of administration still continue to be the most preferred route due to its manifold advantages including ease of ingestion, pain avoidance, versatility and most importantly patient compliance[3]. The most popular dosage forms being tablets and capsules. Even few of the drawbacks of these dosage forms like swallowing and some drugs resist comparison in dense compacts, owing to their amorphous nature or flocculent, low-density characteristics (*VikasAgarwal et al.,)*. Drugs with poor wetting, slow dissolution properties, intermediate to large dosage, and optimum absorption in the gastrointestinal tract or any combination of these features may be difficult or impossible to formulate and manufacture as a tablet that will still provide adequate or full drug bioavailability[1]. Bitter tasting drugs, drugs with an objectionable odor, or drugs that are sensitive to oxygen or atmospheric moisture may require encapsulation or entrapment prior to compression[2].

Desired criteria for mouth dissolving drug delivery system

The tablets should

1. Not require water to swallow, but is should dissolve or disintegrate in the mouth in matter of seconds.
2. Be compatible with taste masking.
3. Be portable with taste masking.
4. Have a pleasing mouth feel.
5. Leave minimal or no residue in the mouth after oral administration.
6. Exhibit low sensitivity to environmental conditions as humidity and temperature[6].

7. Allow the manufacture of tablet using conventional processing and packaging equipment at low cost (*SudhirBhardwaj.,).*

Salient features of mouth dissolving tablet

a. Ease of administration to patient who refuses to swallow tablets, such as pediatric, geriatric and psychiatric patients.
b. No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
c. Rapid dissolution and absorption of drug, which will produce quick onset of action.
d. Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach (*Dali Shukla et al.,)* in such cases bioavailability of drugs is increased[8].
e. Pregastric absorption can result in improved bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwanted effects.

OBJECTIVE

Need for the study

The concept of mouth dissolving drug delivery system emerged from the desire to provide patient with more conventional means of taking their medication. It is difficult for many patients to swallow tablets and hard gelatin capsules. Hence, they do not comply with prescription, which results in high incidence of non-compliance and ineffective therapy. In some cases such as motion sickness, sudden episodes of allergic attacks or coughing and unavailability of water, swallowing conventional tablets may be difficult. Such problems can be resolved by means of mouth dissolving tablets when put on tongue these tablets disintegrate and dissolve rapidly in saliva without need of drinking water. The faster the drug disintegrates in to solution, the quicker the absorption and onset of clinical effect. Some drugs are absorbed from the mouth, pharynx and esophagus as saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablet dosage form. Hence, in the present study an attempt will be made to formulate oro dispersible tablets of Amiodarone is an antiarrhythmic agent used for various types of cardiac dysrhythmias, both ventricular and atrial.

Objectives of the study

1. Preparation of orodipersible tablets of Amiodarone by direct compression using different concentration of Superdisintegrants like cros-carmellose sodium (AC-di-sol), sodium starch glycolate (Explotab) and Cros-Povidine (polyplasdone XL)[5].
2. Oro dispersible tablets of Amiodaronewere also prepared by direct compression and using cros-carmellose sodium (Ac-di-sol), sodium starch glycolate (Explotab) and crosprovidone (polyplasdone XL) as superdisintegrants[4].
3. Oro dispersible tablets of Amiodarone were evaluated for hardness, friability, weight variation, disintegration time, drug content, water absorption ratio, water absorption time, drug-excipients interaction studies (IR spectroscopy).
4. Study *invitro* dissolution of Amiodarone from the formulated Oro dispersible tablets.

METHODOLOGY

Drug-excipient compatibility studies

Fourier Transform Infrared (FTIR) Spectroscopy

The Fourier transform infrared (FTIR) spectra of samples were obtained using FTIR spectrophotometer (Perkin Elmer). Pure drug, individual polymers and optimised formulations were subjected to FTIR study. About 2–3 mg of sample was mixed with dried potassium bromide of equal weight and compressed to form a KBr disk. The samples were scanned from 400 to 4000 cm^{-}.

Preparation of Oro Dispersible Tablets by Physical Mixture

Direct Compression

Amiodorone (100mg) and all the ingredients were accurately weighed and passed through sieve #40. Amiodorone was well mixed with weighed quantity of ingredients i.e., Sodium starch glycolate, Cros-carmellose sodium, Cros-povidone, Mannitol, Aspartame, citric acid, and Microcrystalline cellulose in geometric proportions. Mixed homogeneously in a

polybag for about 5 -10min. Then the lubricated blend was subjected to compression on a sixteen station rotary tablet punching machine using 8mm circular standard flat faced punches.

Table (1): Formulation of Amiodorone tablets Prepared by Direct Compression

Compo sition (%)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Amiodorone(mg)	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**
Sodium starch glycolate	5	**5**	--	--	--	--	--	--	--	--
Cross povidone	--	--	**5**	**5**	--	--	--	--	--	--
Cros-carmellose sodium	--	--	--	--	5	**5**	**7.5**	10	**7.5**	10
PVP	**5**	-	**5**	-	**5**	-	**5**	**5**	**7.5**	**7.5**
SLS	--	--	--	--	--	--	--	--	**0.25**	**0.25**
Starch	-	**5**	-	**5**	-	**5**	-	-	-	**5**
Magnesium stearate	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**
Talc	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**	**2.5**
Aspartame	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**
Mannitol	**20**	**20**	**20**	**20**	**20**	**20**	**20**	**20**	**20**	**20**
Citric acid	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**	**0.2**
MCC	**qs**	**qs**	**qs**	**Qs**	**qs**	**qs**	**qs**	**qs**	**qs**	**qs**
Total weight	300	300	300	300	300	300	300	300	300	300

RESULTS AND DISCUSSION

Preformulation parameters

Table: 2 Preformulation parameters of amiodorone tablets Prepared by Direct Compression method.

S.no	Formulations	Bulk Density (gm/ml)	Tapped Density (gm/ml)	Compressibility index (%)	Angle of repose (^{0})	Haunser ratio
1	F1	0.45	0.52	15.19	23^0 44	1.15
2	F2	0.42	0.49	14.54	25^0 08	1.17
3	F3	0.45	0.51	13.48	21^0 45	1.13
4	F4	0.710	0.873	19.714	26 ^{0}34	1.251
5	F5	0.721	0.870	17.126	23 ^{0}09	1.206
6	F6	0.510	0.583	12.52	21 ^{0}96	1.14
7	F7	0.44	0.50	12.58	$23^0$25’	1.13
8	F8	0.416	0.482	13.69	$24^0$5’	1.15
9	F9	0.309	0.353	12.46	$26^0$01’	1.14
10	F10	0.510	0.583	12.52	$24^0$24’	1.14

EVALUATION OF TABLETS

Thickness

Tablet mean thickness was almost uniform in all the formulations.

Hardness

The prepared tablets in all the formulations possessed good mechanical strength with sufficient hardness in the range of 2.5-3.2kg/sq cm.

Friability

Friability values below 1% were an indication of good mechanical resistance of the tablets.

Weight variation

All the tablets from each formulation passed weight variation test, as the % weight variation was within the pharmacopoeial limits of ±7.5% of the weight. The weight variation in all the six formulations was found to be 298-302mg, which was in pharmacopoeial limits of ±7.5% of the average weight.

Invitro disintegration

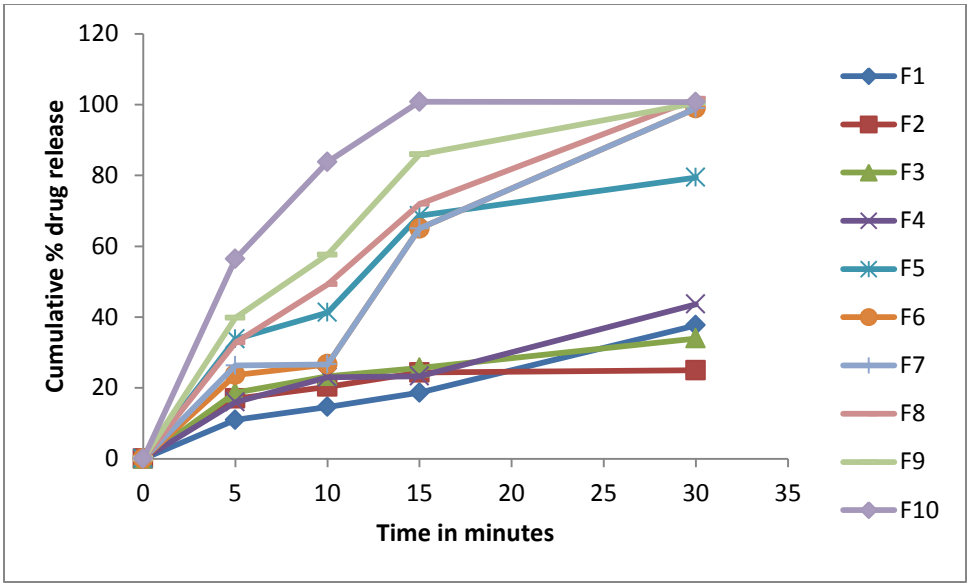
All formulations containing Amiodorone showed disintegration time below 1min.

Table (3): Post formulation parameters of amiodorone tablets

Formula code	Hardness (Kg/cm^2)	Thickness	Weight variation (mg)	Friability (%)	Invitro Disintegration Time(sec)
F1	2.5	3.99	300	0.22	43 sec
F2	2.5	4.64	299	0.23	59 sec
F3	3.5	4.43	301	0.2	30 sec
F4	3	4.68	298	0.21	32 sec
F5	3	4.39	300	0.24	120 sec
F6	3	4.51	299	0.19	123 sec
F7	2.5	3.94	299	0.25	97 sec
F8	3.2	4.4	300	0.29	40 sec
F9	2.9	3.39	302	0.34	45 sec
F10	2.5	4.1	298	0.23	34 sec

Table (4): Cumulative Percent Drug Release of tablets

Time (mins)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
0	0	0	0	0	0	0	0	0	0	0
5	10.99	16.99	18.66	15.99	33.81	23.66	26.33	32.81	39.8	56.4
10	14.66	20.33	23.33	22.99	41.28	26.66	26.66	49.25	57.6	83.8
15	18.66	24.33	25.66	23.33	68.6	64.99	64.99	71.91	85.9	100.8
30	37.66	24.99	33.99	43.66	79.4	98.93	98.93	101.6	100.4	100.7



DISCUSSION

The prepared tablets in all the formulations possessed good mechanical strength with sufficient hardness in the range of 2.5-3.2kg/sq cm. and thickness 3.39 to 4.68. Friability values below 1% were an indication of good mechanical resistance of the tablets. All the tablets from each formulation passed weight variation test, as the % weight variation was within the pharmacopoeial limits of ±7.5% of the weight. The weight variation in all the formulations was found to be 298-302mg, which was in pharmacopoeial limits of ±7.5% of the average weight.

CONCLUSION

The oral disintegrating tablets of Amiodarone with sufficient mechanical strength, acceptable taste and smaller disintegration time were achieved employing suitable superdisintegrants and other excipients at optimum concentration. FTIR studies revealed that there was no shift in peaks, indicating there is no interaction between Amiodarone and other ingredients used. Among three superdisintegrants used Croscaramellose sodium and SLS combination showed better performance in disintegration time when compared to crospovidone and sodium starch glycolate used alone. In the *invitro* dissolution study comparison among all formulations, F10 showed best results. So the formulation of F10 was found to be best among all other formulations, because it has exhibited good taste and faster disintegration time when compared to all other formulations.

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