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Formulation and Evaluation of Mouth Dissolving Tablets of Amiodarone

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Abstract

Mouth dissolving tablets are a vital tool in keeping our children and senior population healthy. Their ease of use and accurate dosing allow advanced patient compliance and further dependable remedial goods. Super disintegrants are the abecedarian element contained in Mouth dissolving tablets and are responsible for their unique capability to snappily disintegrate and dissolve on the face of the lingo without the use of any fresh liquid. In order to determine the most effective type and optimal quantum of super disintegrants for orally disintegrating tablets manufactured by direct contraction, the following tablet parameters were tested hardness, consistence, frangibility, decomposition time, and wetting down time. Three super disintegrants were tested, videlicet Kyron T- 314, Ac- Di- Sol, and Banana Powder and the most effective superdisintegrant was named grounded on the below mentioned studies. From the results attained, it can be concluded that the tablet expression(F3) showed the promising expression also the hardness, frangibility, decomposition time and dissolution rate of set tablets were set up to be respectable according to standard limits.

Keywords: Amiodarone; Kyron T-314, Ac-Di-Sol; Banana Powder and Mouth Dissolving Tablets

Introduction

The oral route of administration is considered as the most considerably accepted route because of its convenience of tone- administration, conciseness and easy manufacturing. But the most apparent disbenefit of the generally used oral capsule forms like tablets and capsules is difficulty in swallowing, leading to cases incompliance particularly in case of paediatric and elderly cases, but it also applies to people who are ill in bed and to those active working cases who are busy or travelling, especially those who have no access to water.

For these reasons, tablets that can swiftly dissolve or disintegrate in the oral depression have attracted a great deal of attention. Mouth disintegrating tablets are not only indicated for people who have swallowing difficulties, but also are ideal for active people [1].

An Mouth disintegrating tablet (MDT) is a solid capsule form that contains medicinal substances and disintegrates swiftly(within seconds) without water when placed on the lingo. The drug is released, dissolved, or dispersed in the saliva, and also swallowed and absorbed across the GIT [2].

The definition by USFDA for MDT tablets as "A solid capsule form containing medicinal substances which disintegrates swiftly generally within a matter of seconds, when placed upon the lingo".

Recently European Pharmacopoeia used the term 'Orodispersible tablet as a tablet that is to be placed in the mouth where it disperses swiftly before swallowing.

Mouth disintegrating tablets are also called as mouth-dissolving tablets, presto disintegrating tablets, fast dissolving tablets, orodispersible tablets, rapimelts, porous tablets, quick dissolving tablet [3-7].

Mechanism of Action of Mdt in Oral Mucosa [8-11]

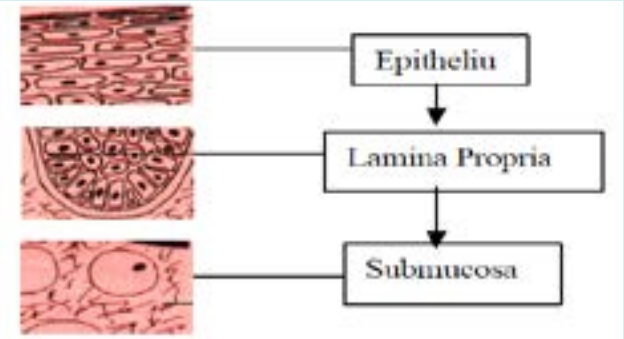

Figure 1: Different layers of oral mucosa.

Mechanism of Action

The MDT is placed upon patient's tongue or any oromucosal tissue. It instantly get wet by saliva due to presence of hydrophilic polymer and other excipients, then the tablet rapidly hydrates and dissolves to release the medication for or omucosal absorption.

Methodology

Analytical method development for Amiodarone:

Determination of absorption maxima: A spectrum of the working norms was attained by scaning from 200- 400 nm against the reagent blank to fix Absorption maxes. The λmax was set up to be 353 nm. Hence all farther examinations were carried out at the same wavelength.

Construction of standard graph: 100 mg of Amiodarone was dissolved in 100 mL of pH 6.8 phosphate buffer to give a concentration in 1mg/mL (1000µg/mL) 1 ml was taken and diluted to 100 ml with pH 6.8 phosphate buffer to give a concentration of 0.01 mg/ml (10µg/ml). From this stock solution aliquots of 0.5 ml, 1 ml, 01.5 ml, 2 ml, 2.5 ml, were pipette out in 10 ml volumetric flask and volume was made up to the mark with pH 6.8 phosphate buffer to produce concentration of 5, 10, 15, 20 and 25µg/ml respectively. The absorbance of each concentration was measured at respective (λmax) i.e., 353nm.

Formulation development

Drug and different concentrations of super disintegrants (Kyron T-314, Ac-Di-Sol and Banana Powder)and required ingredients were accurately weighed and passed through a 40-mesh screen to get uniform size particles and mixed in a glass motor for 15 min.

- The attained mix was lubricated with magnesium stearate and glidant (Talc) was added and mixing was continued for farther 5min
- The attendant mixture was directly compressed into tablets by using punch of rotary tablet compression machine. Compression force was kept constant for all formulations.

Ingredients	Formulation Codes								
(MG)	F1	F2	F3	F4	F5	F6	**F7**	**F8**	**F9**
Amiodarone	100	100	100	100	100	100	100	100	100
Kyron T-314	25	50	75	-	-	-	-	-	-
Ac-Di-Sol	-	-	-	25	50	75	-	-	-
Banana Powder	-	-	-	-	-	-	25	50	75
Sodium saccharin	20	20	20	20	20	20	20	20	20
Talc	5	5	5	5	5	5	5	5	5
Mg stearate	4	4	4	4	4	4	4	4	4
MCC	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total Weight(mg)	300	300	300	300	300	300	300	300	300

Table 1: Formulation table showing various compositions.

Results and Discussion

- **Preparation of Calibration Curve of Amiodarone:**
  The regression coefficient was found to be 0.999 which indicates a linearity with an equation of Y= 0.059 X-0.002. Hence Beer-Lambert's law was obeyed.

Concentration	Absorbance
0	0
5	0.181
10	0.327
15	0.468
20	0.611
25	0.758

Table 2: Calibration curve data of Amiodarone in pH 6.8 phosphate buffer.

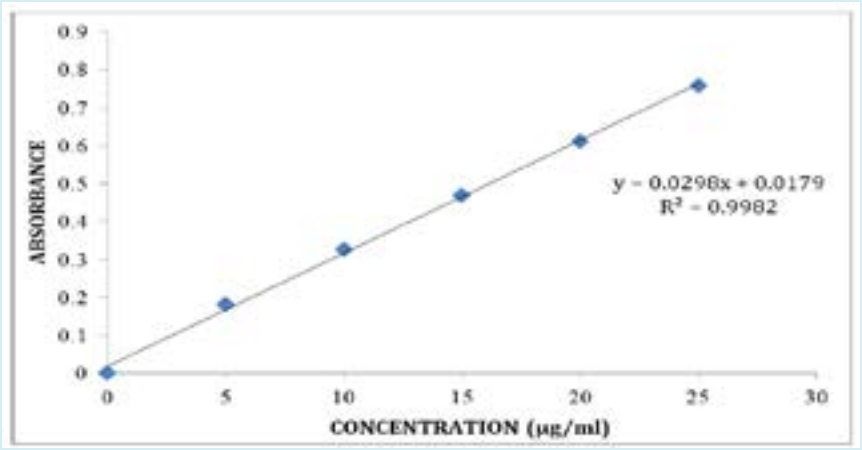

Figure 1: Standard curve of Amiodarone.

Ftir Results

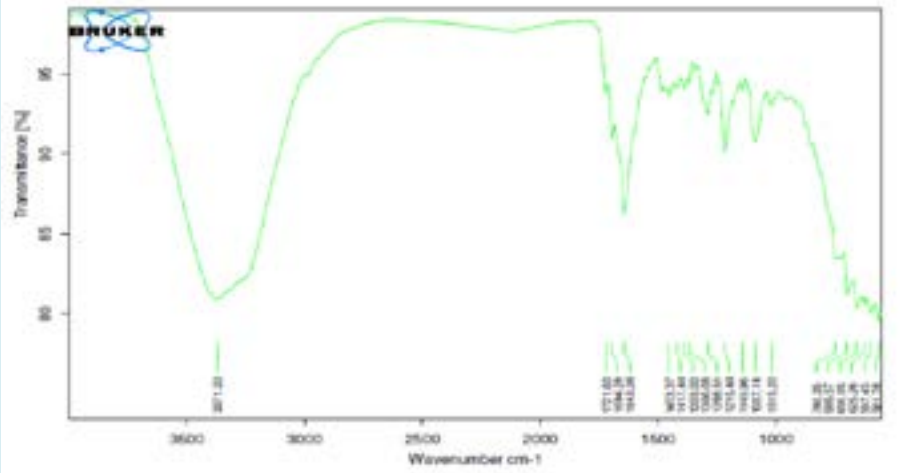

Figure 2: FTIR of Amiodarone Pure drug.

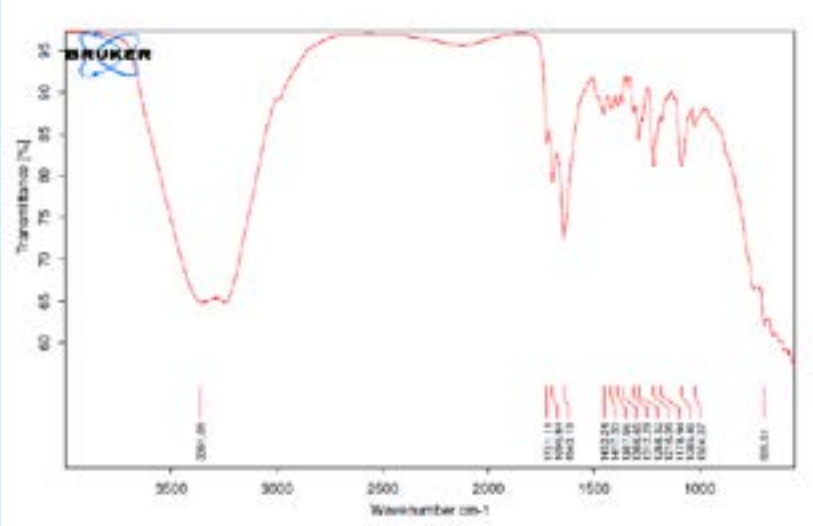

Figure 3: FTIR of Amiodarone optimized formulation.

- **Evaluation of Pre-Compression Parameters of Powder Blend**

Formulation Code	Angle of Repose	Bulk Density(gm/mL)	Tapped Density (gm/mL)	Carr's Index(%)	Hausner's Ratio
F1	25.92±0.04	0.326±0.076	0.354±0.06	7.998±0.04	1.086±0.03
F2	24.56±0.02	0.37±0.04	0.408±0.03	9.524±0.07	1.095±0.03
F3	26.93±0.06	0.350±0.065	0.382±0.02	8.444±0.02	1.090±0.02
F4	27.25±0.04	0.37±0.04	0.387±0.02	5.541±0.06	1.045±0.05
F5	27.82±0.04	0.272±0.076	0.314±0.03	13.33±0.04	1.153±0.08
F6	26.93±0.03	0.324±0.05	0.337±0.03	8.76±0.04	1.041±0.03
F7	27.82±0.04	0.382±0.087	0.404±0.06	5.547±0.03	1.047±0.04
F8	25.07±0.06	0.236±0.06	0.266±0.04	11.428±0.03	1.129±0.05
F9	24.39±0.02	0.259±0.054	0.286±0.02	9.406±0.02	1.103±0.03

Table 3: Evaluation of pre-compression parameters of powder blend.

Evaluations of post compression parameters of Amiodarone mouth dissolving tablets

Formulation codes	Weight variation (mg)	Hardness (kg/cm^2)	Friability (%loss)	Thickness (mm)	Drug content (%)
F1	298.47	3.9	0.54	4.96	98.12
F2	300.01	3.4	0.46	4.89	99.47
F3	299.36	3.6	0.65	4.45	96.35
F4	295.47	3	0.47	4.58	100.02
F5	300.03	3.9	0.51	4.7	98.41
F6	299.98	4.1	0.63	4.46	96.54
F7	299.63	3.8	0.42	4.24	98.68
F8	298.21	3.5	0.5	4.99	97.42
F9	299.2	3.2	0.28	4.54	99.67

Table 4: Evaluation of post compression parameters of Amiodarone Mouth dissolving tablets.

Formulation	Disintegration time*(seconds)	Wetting time* (seconds)	*In vitro* dispersion time*(sec)	% Water absorption ratio*
F1	48	51	48	94
F2	36	43	30	98
F3	28	36	24	99
F4	40	55	51	95
F5	36	45	38	97
F6	30	39	32	99
F7	42	60	56	98
F8	38	52	44	98
F9	30	43	32	97

Table 5: Evaluation of post compression parameters of Amiodarone mouth dissolving tablets.

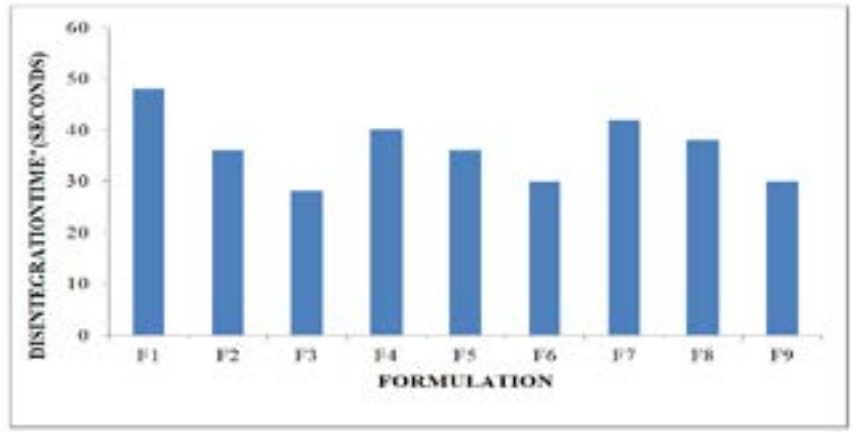

Figure 4: *In vitro* Disintegration time graph.

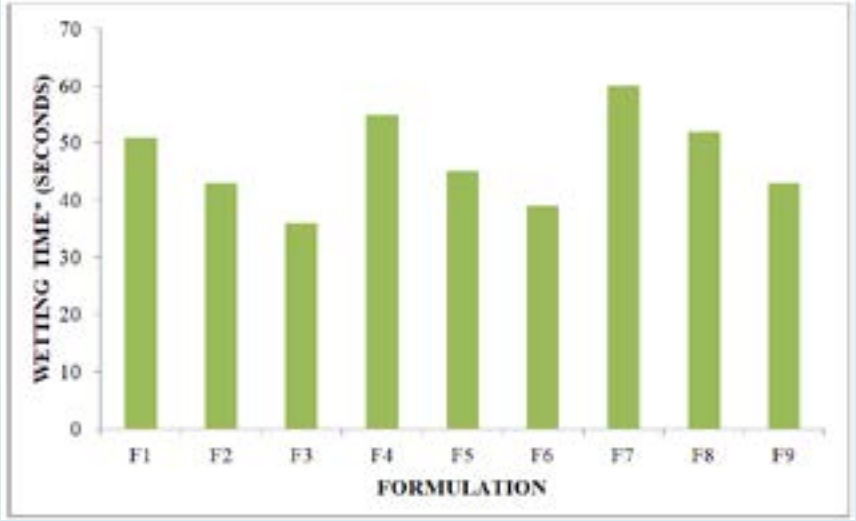

Figure 5: Wetting time graph.

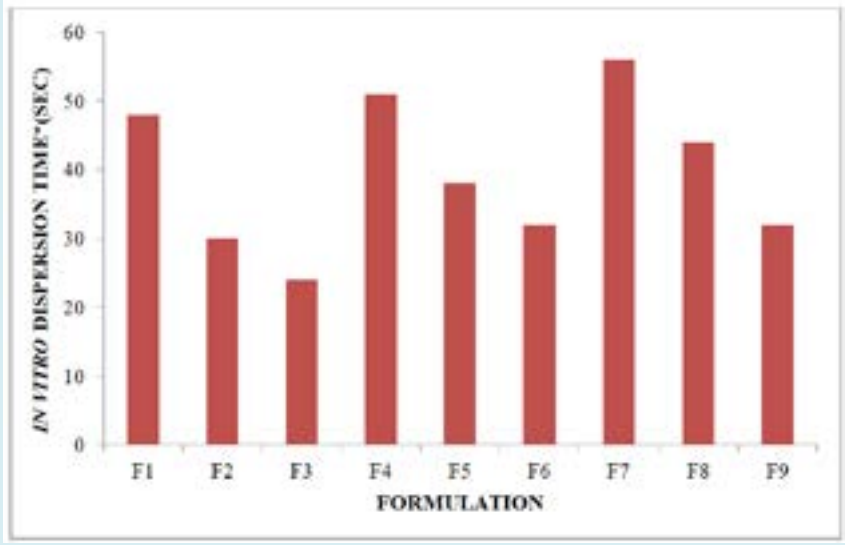

Figure 6: *In vitro* dispersion time.

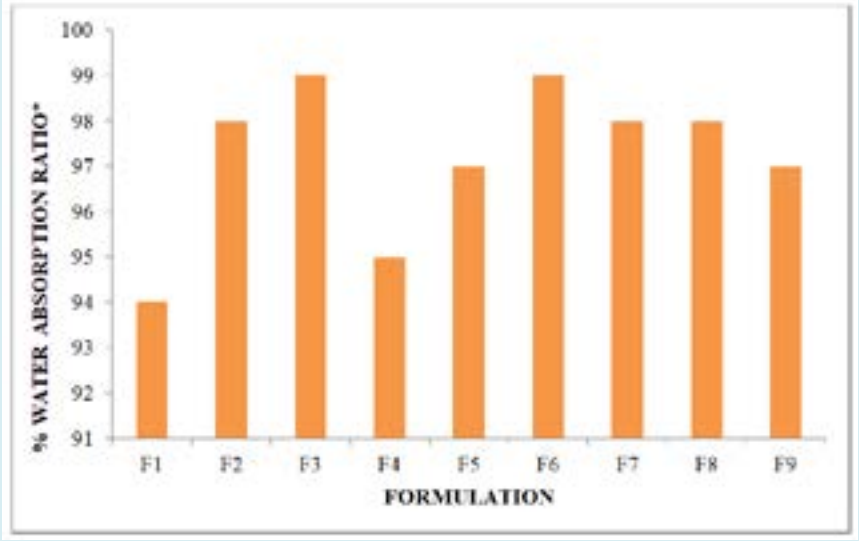

Figure 7: Water absorption ratio graph.

- ***In vitro* drug release studies of Amiodarone**

Time(Min)	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	34.15	45.93	52.87	41.56	50.92	56.25	29.93	46.92	52.54
10	47.93	58.2	61.38	65.24	65.01	67.42	38.65	57.16	62.3
15	58.71	65.14	76.11	73.98	83.36	78.71	61.57	75.34	68.17
20	74.24	81.96	87.96	81.47	90.28	85.98	76.19	84.25	89.25
30	84.31	92.83	99.72	89.34	95.17	96.03	87.21	90.17	97.51

Table 6: Dissolution data of Amiodarone.

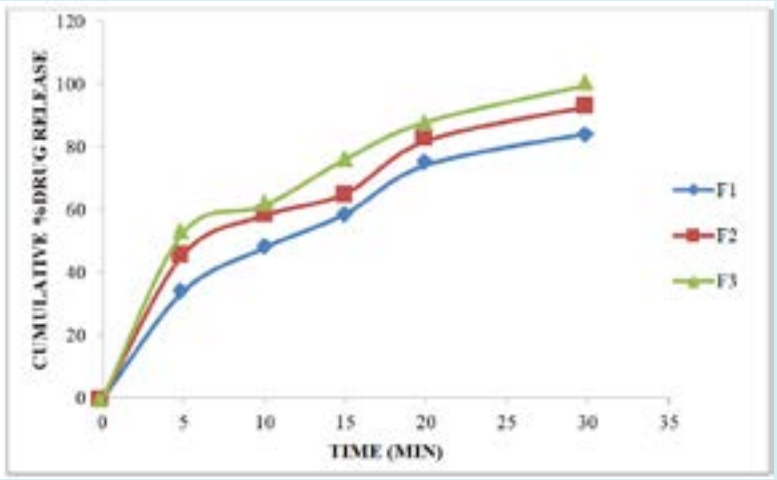

Figure 8: Dissolution profile of formulations F1, F2, F3.

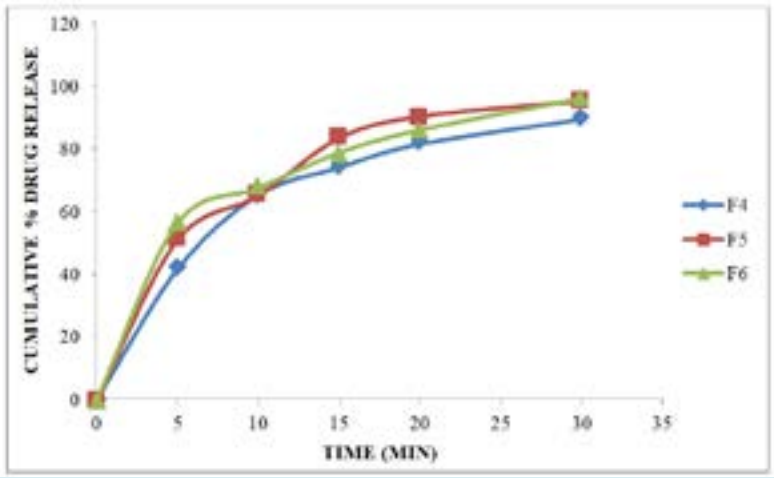

Figure 9: Dissolution profile of formulations F4, F5, F6.

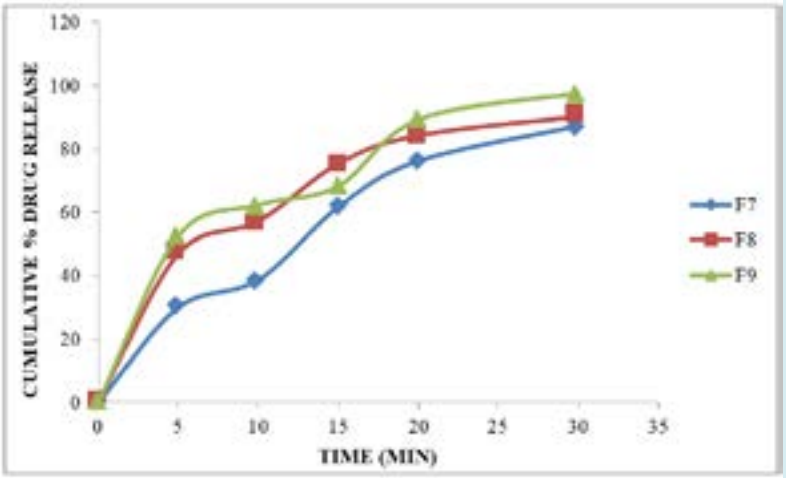

Figure 10: Dissolution profile of formulations F7, F8, F9.

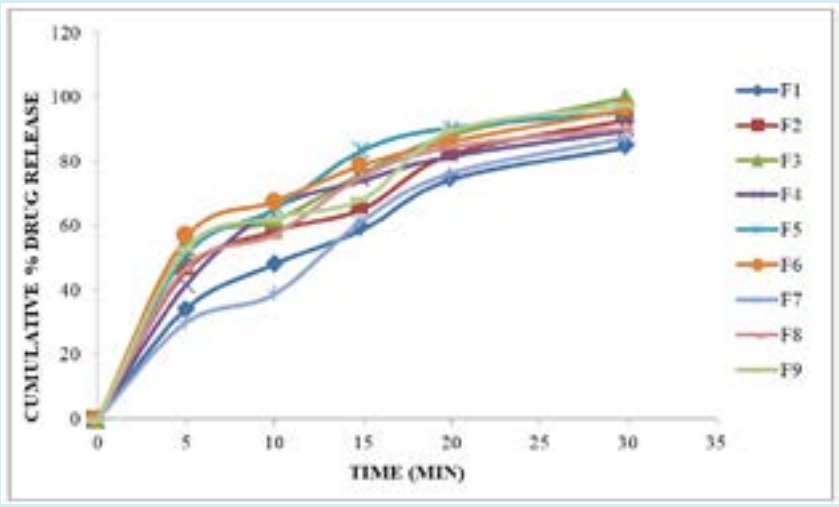

Figure 11: Dissolution profile of all formulations F1-F9.

Summary

- The purpose of the study was to formulate and evaluate mouth dissolving tablets of Amiodarone.
- The results of Fourier Transmission Infra-Red spectroscopy confirm that both drug and excipients are compatible with each other and are devoid of interactions.
- The results of precompression studies like angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio reveals that the prepared powder blends of all formulations possess good flow properties.
- The tablets were prepared by direct compression method using superdisintegrants like Kyron T-314 (F1 to F3), Ac-Di-Sol (F4 to F6), and Banana Powder (F7 to F9) in different concentrations. Aspartame is used as sweetener for additional taste masking and microcrystalline cellulose as diluent. The tablets obtained were of uniform shape and size.
- The prepared tablets were subjected to post compression evaluations and the results indicate that, the hardness, thickness and Friability of all the tablets are uniform, which ensures that all the tablets were of uniform size and shape with good resistance against mechanical damage.
- The tablets of all formulations contains uniform amount of drug, which ensures content uniformity for tablets of all formulations.
- The tablets were found within the limits of weight variation test, which in turn indicate uniform distribution of contents of the powder blends of each formulations.
- The friability of all the tablets was found to be < 1%, which indicates the good mechanical resistance.
- The tablets of all formulations were found to have minimum wetting time and maximum water absorption ratio which is the desired characteristic of fast dissolving tablets, which enables faster disintegration of tablets.
- The disintegration time of all tablets were found to be less than 48 sec, which ensures faster disintegration.
- Amongst all the formulations, formulation containing Kyron T-314as superdisintegrants is fulfilling all the parameters satisfactorily. It has shown very good in vitro disintegration compared to other superdisintegrants.
- Apart from all the formulations, F3 formulation showed maximum drug release (99.72%) at the end of 30 min.

Conclusion

It was concluded, that Amiodarone can be successfully formulated as mouth dissolving tablets using various superdisintegrants in different concentrations by direct compression method. The formulation F3 containing 1:3 ratio of Kyron T-314 as superdisintegrant was found to be outstanding than other formulations in terms of disintegration time and rate of dissolution.

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