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Development and characterization of fast dissolving tablets of doxazosin mesylate by using novel coprocessed super disintegrating technology

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ABSTARCT

In the present work, an attempt has been made to develop fast disintegrating tablets of Doxazosin mesylate. Novel method of co processed super disintegrates technology was employed to formulate the tablets. All the formulations were prepared by direct compression method. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F14 formulation showed maximum drug release i.e., 99.3% in 4 min hence it is considered as optimized formulation. The F14 formulation contains CP5 as super disintegrate in the concentration of 30 mg. (CP 5 contains Vivasole and polyplasdone XL in 3:1 ratio).

Keywords: Doxazosin mesylate, Co processed super disintegrates, Vivasole and polyplasdone XL.

INTRODUCTION

The concept of Fast dissolving drug delivery system (FDDS) emerged from the desire to provide patients with conventional means of taking their medication. Difficulty in swallowing (dysphasia) is a common problem of geriatrics and pediatrics, because of physiological changes associated with these groups of patients. Since the average life span is going–up considerably in this modern era, the number of geriatric patients is increasing and hence will have significant impact on development of drug delivery systems [1].

Fast dissolving tablet is one of such example, for the reason of rapid disintegration or dissolution in mouth with little amount of water or even with saliva. Significance of this drug delivery system includes administration without water, accuracy of dosage, ease of portability, alternative to liquid dosage forms, ideal for pediatric and geriatric patients and rapid onset of action. Superdisintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction which causes the tablet to burst or the accelerated absorption of water leading to promote disintegration. Proposed mechanism for the action of disintegrants include water uptake through wicking, swelling, deformation recovery and particle repulsion [2].

MATERIALS AND METHODS

Materials

Doxazosin mesylate, Vivasole, Polyplasdone XL were obtained from SD Fine Chemicals, Mumbai, India and all other chemicals/ solvents used were of analytical grade.

Formulation of Oro dispersible tablets of Doxazocin mesylate

Preparation of co processed super disintegrates

Co processed super disintegrates were prepared by using sodium Vivasole and polyplasdone XL. The super disintegrates were mixed in different concentrations and labeled as CP1,CP2,CP3.The blend of super disintegrates was mixed thoroughly for a period of 15 min, collected and used for preparing formulations in different concentrations [3].

Table 1: Composition of co processed super disintegrates

Ingredients	CP1	CP2	CP3	CP4	CP5
Vivasole (mg)	500	500	500	1500	1000
Polyplasdone XL (mg)	500	1000	1500	500	500

CP = Coprocessed super disintegrate

Preparation of tablets

Composition of Doxazosin mesylate Dispersible Tablet by direct compression is shown in table 6.4. All the ingredients were weighed. Required quantity of drug and excipient mixed thoroughly in a polybag. The blend is compressed using rotary tablet machine-8 station with 5mm flat punch, B tooling. Each tablet contains 8mg Doxazosin mesylate and other pharmaceutical ingredients [4].

Table no. 2: Composition of various tablet formulation

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13	F14	F15	F16	F17
Doxazosin mmmememesyl	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8	8
CP 1(mg)	10	20	30	-	-	-	-	-	-	-	-	-	-	-	-		
CP 2(mg)	-	-	-	10	20	30	-	-	-	-	-	-	-	-	-		
CP 3(mg)	-	-	-	-	-	-	10	20	30	-	-	-	-	-	-		
CP 4 (mg)	-	-	-	-	-	-	-	-	-	10	20	30	-	-	-		
CP 5(mg)	-	-	-	-	-	-	-	-	-	-	-	-	10	20	30		
Vivasole	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	10	
Polyplasdone	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	10
Mg St(mg)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3

Talc(mg)	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
MCC(mg)	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs	Qs
Total wt(mg	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**	**100**

Evaluation of Tablets

The formulations were evaluated for hardness, weight variation, thickness, friability, disintegration time, content uniformity, assay and *in vitro* dissolution study [5].

Tablet Hardness

Hardness is the crushing strength of tablet which determines the ease of handling and rigors of the transportation. For each formulation, 3 tablets were used for the study. The hardness of the tablet was determined and expressed in Kp [6].

Weight Variation Test

Weight variation test was done by weighing 20 tablets individually, calculating the average weight and comparing the individual tablet weight to the average. The data presented in Table 2 clearly show the weight variation tolerance for uncoated tablets [7].

Thickness

The thickness of the tablets was measured using Digital Vernier Caliper, and expressed in mm.

Friability

Friability test is performed to assess the effect of friction and shocks, which may often cause tablet to chip, cap or break. Roche friabilator was used for the purpose. This device subjects a number of tablets to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at distance of 6 inches with each revolution. Preweighed sample of tablets were placed in the friabilator, which was then operated for 100 revolutions. Tablets were dedusted and reweighed [8].

The percent friability was measured using the formula:

$\%F = \{(W - W_0)/W_0\}*100$

Where, %F = Friability in percent,

W = Initial weight of tablet.

W_0 = Weight of tablet after test.

Disintegration Time

One tablet was placed in each of six tubes of disintegration test apparatus. Disintegration test was carried out at 37 ± 2 ^{0}C according to USP XXII., Disintegration test apparatus without disc, time required for complete passage of tablet fragments through the sieve (#10) was considered as a disintegration time of a tablet [9].

Assay

For this, 30 tablets were randomly selected from all formulations. Out of 30 tablets 10 tablets were crushed into fine powder. The powder taken equivalent to label claim was weighed accurately, dissolved in their respective media and assayed individually at respective λ max against the reagent blank. The drug content should be within 90% to 110% of the labeled claim [10].

Uniformity of content

One tablet was powdered, shaken with 1 ml of dilute HCl and 40 ml of water for 15 min, and added sufficient water to produce 100 ml and mixed well. Centrifuged about 15 ml and to 10 ml of the clear, supernatant liquid 2 ml of 1M HCl and sufficient water were added to produce a solution containing about 0.005 % w/w concentrated HCl. The absorbance of the resulting solution was measured at the λmax. of 290 nm. Then the content corresponding to Doxazosin mesylate in the tablet was calculated [11].

In vitro Dissolution studies

The *in vitro* dissolution study was carried out in USP dissolution test apparatus Type 2 (paddle). Samples were withdrawn at 2, 4, 6, 8, 10, 15, 20,25 and 30 min time intervals by replacing with same dissolution medium and the dissolution of the drug was expressed as percentage drug dissolved by using following formula [12].

RESULTS & DISCUSSIONS

Table 3: Doxazosin mesylate FDT tablets characterization

Formulation code	Weight variation	Hardness (kg/cm^2)	Thickness (mm)	Disintegration Time (sec)	Friability (%)	Assay (%)
F1	105.9	2.5	4.59	20.33	0.43	97.23
F2	104.4	2.3	4.64	23.66	0.34	98.55
F3	110.7	2.5	4.59	25.33	0.49	98.16
F4	109.2	2.4	4.58	19.00	0.47	99.34
F5	99.4	2.3	4.59	20.33	0.49	98.16
F6	102.4	2.6	4.64	22.66	0.34	98.55
F7	101.3	2.5	4.59	20.33	0.49	98.16
F8	107.3	2.3	4.56	17.00	0.34	99.25
F9	102.32	2.3	4.56	19.45	0.34	100.26
F10	98.36	2.5	4.98	24.36	0.43	98.45
F11	95.34	2.4	4.73	23.72	0.52	99.36
F12	100.2	2.4	4.82	20.63	0.35	100.02
F13	101.3	2.2	5.03	18.34	0.64	97.34
F14	97.6	2.3	5.13	17.47	0.53	99.36
F15	99.4	2.5	5.32	19.35	0.48	98.63
F16	98.57	2.4	5.45	17.66	0.49	98.99
F17	100.07	2.5	5.09	18.76	0.49	98.76

Tablets of each batch were subjected to weight variation test, difference in weight and percent deviation was calculated for each tablet and was shown in the Table 3. The average weight of the tablet is approximately in range of 307 to 298.5, so the permissible limit is ±5% (>250mg). The results of the test showed that, the tablet weights were within the pharmacopoeia limit [13-16].

Hardness of the three tablets of each batch was checked by using Monsanto hardness tester and the data's were shown in Table-3. The results showed that the hardness of the tablets is in range of 2.0 to 2.5 kg/cm^2, which was within IP limits.

Thickness of three tablets of each batch was checked by using Vernier Caliper and data shown in Table-3 .The result showed that thickness of the tablet is raging from 4.56 to 5.34.

Tablets of each batch were evaluated for percentage friability and the data's were shown in the Table-3. The average friability of all the formulations lies in the range of 0.30 to 0.51% which was less than 1% as per official requirement of IP indicating a good mechanical resistance of tablets.

Tablets of each batch were evaluated for in vitro disintegration time and the data's were shown in the Table-3. The results showed that the disintegration time of prepared tablets were in the range of 17 to 25.33 seconds. Assay studies were performed for the prepared formulations. From the assay studies it was concluded that all the formulations were showing the % drug content values within 97.23 -100.26 %.

Invitro dissolution studies

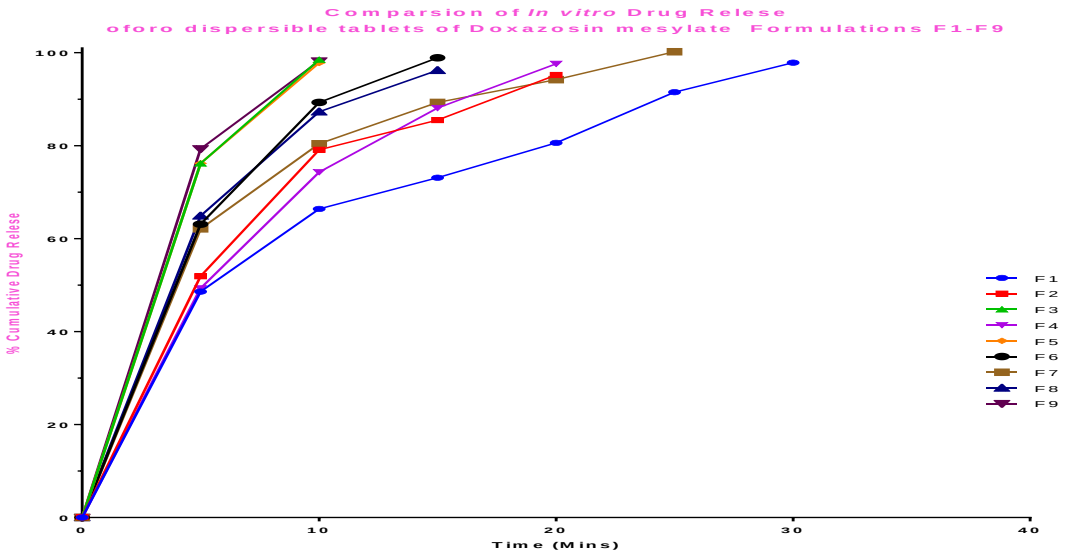

Fig no: 1 *In vitro* drug releases of F1- F9 formulations

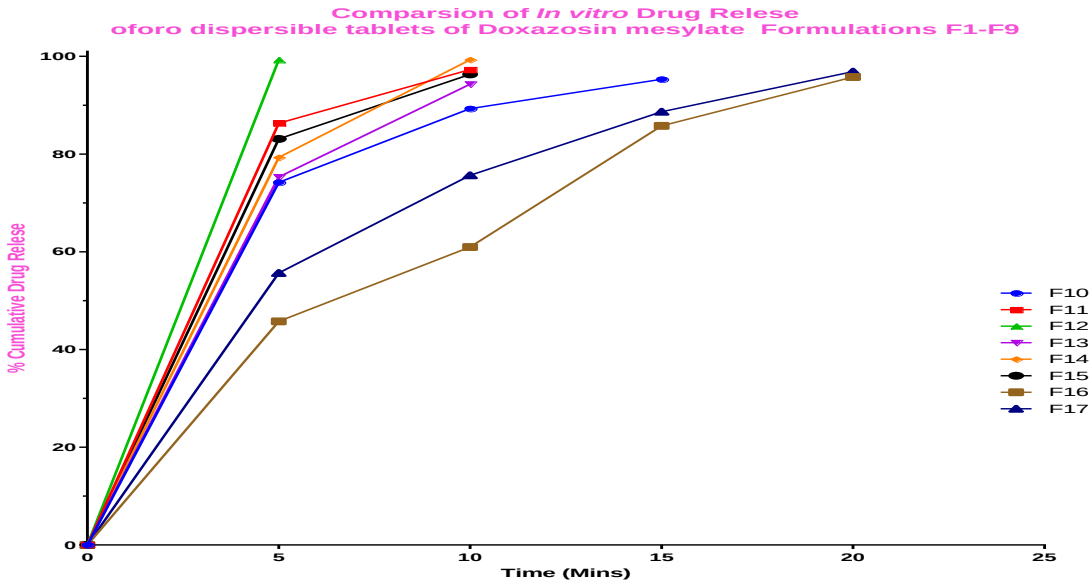

Fig no: 2 In *vitro* drug releases of F10- F17 formulations

Invitro dissolution studies were carried out by using 900ml of 6.8 pH phosphate buffer in USP dissolution apparatus by using paddle method. The dissolution studies were carried out for about 30 min. It was evident that the formulations prepared with super disintegrate CP5 showed maximum % drug release in 4 min i.e.99.3% (F14) formulations and the concentration of super disintegrate is 30mg). So the principle of coproceesed super disintegrates was found to be useful to produce FD tablets. F14 formulation was considered as optimized formulation as it contains less concentration of super disintegrants.

CONCLUSION

In the present work, an attempt has been made to develop fast disintegrating tablets of Doxazosin mesylate. Novel method of co processed super disintegrates technology was employed to

formulate the tablets. All the formulations were prepared by direct compression method. The blend of all the formulations showed god flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F14 formulation showed maximum drug release i.e., 99.3% in 4 min hence it is considered as optimized formulation. The F14 formulation contains CP5 as super disintegrate in the concentration of 30 mg. (CP5 contains Vivasole and polyplasdone XL in 2:1 ratio).

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