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FORMULATION AND *IN-VITRO* EVALUATION OF ARIPIPRAZOLE ORAL DISPERSION TABLETS

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ABSTRACT

The objective of present study is to design and develop a stable solid oral dosage form of Aripiprazole oral dispersible tablets to deliver with optimum concentration of drug at desired site at specific time comparable to the innovator product with better stability, high production feasibility, and excellent patient compatibility. The tablets were prepared by wet granulation method. *In-vitro* dissolution studies showed that F_7 has better release profiles compared to the other formulations. Though F_4 showed release within 45 minutes, the drug release was not constant. *In-vitro* drug release from the dosage form has been increased with the increase in the quantity of xylitol in the formulation.

KEY WORDS: Aripiprazole, Xylitol, oral dispersible tablet, Hydroxy propyl cellulose

1. INTRODUCTION

Pharmaceutical suspensions are uniform dispersions of solid drug particles in a vehicle in which the drug has minimum solubility. These are usually formulated to improve chemical stability of drug, mask the unpleasant taste and in instances where a liquid dosage form is preferred (easier to swallow, flexibility of administration in a range of doses) over a solid dosage form. Suspension as a dosage form however is associated with issues such as microbial growth, sedimentation and non-uniformity of dose, high cost of manufacturing, difficult to carry etc. For administration of suspensions to children a special oral syringe or dosator needs to be provided which requires care during administration such as proper calculation of the dose, cleaning of the syringe after use, etc. Therefore an alternative dosage form is desired.

Solid oral dosage forms are most convenient from patient as well as from manufacturing chemist's perspective. They ensure uniformity of dosage; have less microbiological issues compared to liquid dosage forms. However immediate release tablets cannot act as a substitute for suspension. Thus, there is a need for a formulation, which overcomes the problems associated with the swallowing of solid dosage forms and act as a viable substitute for suspensions. One such dosage form is dispersible tablet. Dispersible tablets can be defined as uncoated or film coated tablets intended to be dispersed in water before administration giving a homogeneous dispersion. Typically a dispersible tablet is dispersed in about 5-15 ml of water (e.g. in a tablespoonful or a glass of water) and the resulting dispersion is administered to the patient. However, they can also be placed directly on the tongue and sucked.

Dispersible tablets are required to disintegrate within 3 minutes in water at 15-25°C. Also the dispersion produced from a dispersible tablet should pass through a sieve screen with a nominal mesh aperture of 710 microns. The dispersion properties of dispersible tablets can be facilitated by the inclusion of an acid/base couple in which the base liberates carbon dioxide when the components of the couple are dissolved in water.

2. MATERIALS AND METHODS

Aripiprazole, Xylitol, Aspartame, Acesulfame Potassium, Iron oxide yellow, Silicon dioxide, Cross povidone, Microcrystalline cellulose, Croscarmellose sodium, Ethyl vanillin, Tartaric acid, Magnesium stearate ,Calcium silicate and Hydroxy propyl methyl cellulose was obtained from Signet chemicals, Chennai.

2.1. PREPARATION OF ARIPAPRAZOLE FAST DISSOLVING TABLET

2.1.1. Sifting: Aripiprazole, calcium silicate, microcrystalline cellulose, croscarmellose sodium, crospovidone, xylitol, and colloidal silicon dioxide were sifted together through sieve number 40.

2.1.2. Dry mixing: Mixture was loaded into rapid mixer granulator (RMG) and mixed for 15 minutes with impeller slow speed and chopper off.

2.1.3. Preparation of Binder Solution: Binder solution was prepared by dissolving hydroxy propyl cellulose in purified water under stirring and stirred well till the clear solution was formed.

2.1.4. Wet granulation: Binder solution was added over a period of 2 minutes to the dry mix in RMG with impeller and chopper at slow speed. Impeller and inner walls of the bowl was scraped using a scraper and checked for complete formation of granules. The wet mass was kneaded for sufficient time with Impeller and Chopper at slow speed. The wet mass was unloaded from the granulator.

2.1.5. Drying: Wet granules were loaded in to fluidized bed dryer (FBD) bowl and dried at 55 ± 5°C. Proper fluidization was ensured for the timely and uniform drying of the granules. The process was continued until loss on drying (LOD) limit 2.0- 3.0 % w/w was reached.

2.1.6. Sizing of dried granules: Sifted the dried granules through sieve number 20 and the oversize granules (retained granules) were milled using multi mill with 2 millimeter screen initially then 0.5 millimeter screen finally at medium speed and knives forward configuration. Milled granules were passed through sieve number 20.

2.1.7. Sifting of extra granular ingredients: Microcrystalline cellulose, aspartame, acesulfame potassium, tartaric acid, ethyl vanillin, iron oxide yellow and magnesium stearate were sifted through sieve number 40.

2.1.8. Blending: Sifted excipients in the above step were added to dried and milled granules which were previously loaded in the octagonal blender and blended for 15 minutes.

3. RESULTS AND DISCUSSION

3.1. Preliminary studies: Seven formulations were prepared with different types and quantities of excipients and named F1 to F7 (Table 1&2). Micromeritics of blends of various formulations were determined and represented in table 3. The bulk density was found in the range 0.468 – 0.568 g/cm^3. The Tapped density was found in the range 0.697 – 0.757 gm/cm^3. The compressibility index was found in the range 24 - 39%. The Hausner's ratio was found in the range 1.23 – 1.643. The angle of repose was found to be in the range $23^0 13^{'}$ – $40^0 13$'.

Table no1 Representation of various trials (Excipients for wet granulation)

SNo	Ingredients	Formulation code						
(All the quantities are in milligrams)		F1	F2	F3	F4	F5	F6	F7
1	Aripiprazole	10	10	10	10	10	10	10
2	Calcium silicate	60.47	44.71	42	39.97	45.36	48.03	34.44
3	Microcrystalline cellouse	6.66	13.33	10	13.33	13.33	13.33	20
4	Croscarmellose sodium	5	2.66	5.0	5	3	3.33	3.33
5	Cross Povidone	5	2.66	5	5	3	3.33	3.33
6	Xylitol	7	6.66	10	11	10	10	16.66
7	Silicon dioxide	0.66	1	1	1	1	1	1
8	Hydroxy propyl celluose	--	--	--	0.26	0.4	0.4	0.66

Table no 2 Excipients for blending

SNo	Ingredients	Formulation code						
(All the quantities are in milligrams)		F1	F2	F3	F4	F5	F6	F7
1	Microcrystalline cellulose	--	13.33	9.1	6.66	6.66	3.33	3.33
2	Aspartame	1.33	1.33	1.2	2	2	2	2
3	Acesulfame Potassium	2	2	3	2.66	2.66	2.66	2.66
4	Tartaric Acid	0.66	0.66	0.7	0.46	0.46	0.46	0.46
5	Iron Oxide Yellow	0.26	0.13	1	0.66	1	0.13	0.13
6	Magnesium Stearate	0.63	1	1	1	1	1	1
7	Ethyl Vanillin	0.33	0.53	1	1	0.13	1	1

Table no 3 Micromeritic properties

Formulation code	Bulk density (g/cc)	Tapped density (g/cc)	Compressibility index (%)	Hausner's ratio	Angle of repose (degrees)
F1	0.468	0.697	32	1.486	$37^0 41$'
F2	0.468	0.697	32	1.486	$37^0 41$'
F3	0.434	0.714	39	1.643	$40^0 13$'
F4	0.568	0.757	25	1.333	$32^0 31$'
F5	0.546	0.712	24	1.23	$27^0 35$'
F6	0.490	0.701	23	1.412	$23^0 13$'
F7	0.52 0	0.735	29	1.412	$29^0 13$'

3.2. Evaluation of Aripiprazole tablets: Tablets were prepared using 16 station Cadmach compression machine at 22 rotations per minute speed. Weight variation, hardness, thickness and disintegration were evaluated and tabulated in table 4. All the results were found to be within the limits. Assay of the tablets was also calculated for the amount of drug in the tablets and it was found to be in the in the range 98.3 – 102.7%. The IR spectrum of drug and excipients showed nil interference. *In- vitro* drug release studies were conducted for the formulations using USP dissolution apparatus type-II (paddle), at 75 rpm. The percentage drug release at the end of 45 minutes was found in the range 80 – 100 % (Table 5). From the *in vitro* data it was found that Formulation F7shows the same pattern of release as such of innovator product (Figure.1).

5. CONCLUSION

By considering the above data the design and develop a stable solid oral dosage form of Aripiprazole oral dispersible tablets to deliver with optimum concentration of drug at desired site at specific time comparable to the innovator product with better stability, high production feasibility, and excellent patient compatibility.

Table no 4 physical evaluation of ODT tablets

Formulation code	Thickness (mm)	Hardness (Kg/cm^2)	Weight variation(mg)	Disintegration time(Seconds)
F1	3.0-3.4	3.2	101±2%	14
F2	3.0-3.4	3.2	99±2%	12
F3	3.0-3.4	3.2	101±2%	8
F4	3.0-3.4	3.2	101±2%	11
F5	3.0-3.4	3.2	102±2%	12
F6	3.0-3.4	3.2	99±2%	7
F7	3.0-3.4	3.2	101±2%	7

Table no 5 *In–vitro* drug release data

Sno	Time in minutes	% Drug Release							
		Innovator Product	F1	F2	F3	F4	F5	F6	F7
1	0	0	0	0	0	0	0	0	0
2	10	64	62	59	67	85	67	67	95
3	20	81	75	73	79	96	74	83	98
4	30	88	79	80	86	98	79	86	99
5	45	93	80	88	89	100	85	94	100

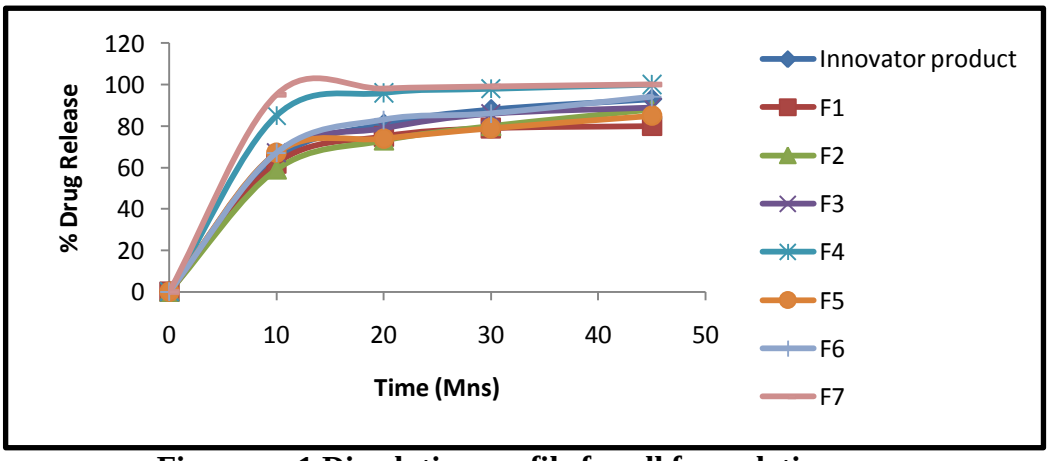

Figure no 1 Dissolution profile for all formulations

5. References:

Aulton M, Pharmaceutics: The Science of Dosage Form Design, International Student Edition, 2002, 304-321, 347-668.

Brown D, Orally disintegrating tablets-taste over speed, Drug Delivery technol, 2001, 3(6), 58-61.

Keberle H, The biochemistry of Desferrioxamine and its relation to iron metabolism, Ann NY, Acad Sci., 119, 1964, 758-775.

Lachman L, Liberman H, Kanig J, The Theory and Practice of Industrial Pharmacy, 3rd ed, 2005, 293-345, 346-373.

Mendes Al, Ferro A, Martin R, Non-classical hereditary haemochromatosis in Portugal: novel mutations identified in iron metabolism-related genes, Ann Haematol, 88(3), 2009, 229-34.

Nash R A, Metals in medicine,Alternative Therapies in Health and Medicine, 2005, 11(4), 18-25.

Reddy LH, Ghosh B, Rajneesh, Fast dissolving drug delivery systems: A Brief Overview. Indian J Pharm Sci., 64(4), 2002, 331-336.

Sreenivas SA, Dandagi PM, Gadad AP, Godbloe AM, Hiremath SP, Mastiholimath VS, Orodispersible tablets: New-fangled drug delivery systems-A review, Indian J Pharm Educ Res, 39(4), Oct 2005, 177-81.

Choudhry V P, Rahul Naithani, Current Status of Iron Overload and Chelation with Deferasirox, Indian J Pediatr, 74(8), 2007, 759-764.