INTERNATIONAL RESEARCH JOURNAL OF PHARMACY
www.irjponline.com ISSN 2230 – 8407
Research Article

FORMULATION AND EVALUATION OF ORODISPERSIBLE TABLETS OF DIAZEPAM USING DIFFERENT SUPERDISINTEGRANTS

Patel Chirag J[1]*, Asija Rajesh[1], Mangukia Dhruv[1], Rathi Harish[1], Patel Kanu[2]
[1]Maharishi Arvind Institute of Pharmacy, Mansarovar, Jaipur, Rajasthan, India
[2]K.L.E. Collage of Pharmacy, Bangalore, Karnataka, India

Article Received on: 17/01/12 Revised on: 05/02/12 Approved for publication: 06/03/12

*Email: Chirag.bangalore@gmail.com

ABSTRACT
Diazepam orodispersible tablets were prepared to achieve quick onset of action and for maximum bioavailability. The purpose of the present research was to compare the effect of different superdisintegrants on the mouth dissolving property of diazepam tablets. Orodispersible tablets of diazepam were prepared using chitosan, sodium carboxy methyl cellulose, alginic acid, crospovidone and sodium starch glycollate as superdisintegrants by direct compression technique. Prepared tablets were evaluated for weight variation, hardness, friability, content uniformity, wetting time, in vitro dispersion time, in vitro disintegration time and dissolution studies. Disintegration time from all the prepared formulation was found to be in following order: F2<F5<F1<F4<F3. Disintegration time was found to be rapid in F2 formulation. The in vitro dissolution time was found to be 99.91% in 10 minutes for the formulation F2. Crospovidone showed faster disintegration of tablets among all other superdisintegrants.
KEY-WORDS: Diazepam, orodispersible tablet, direct compression, crospovidone, superdisintegrants

INTRODUCTION

The tablet is the most widely used dosage form because of its convenience in terms of self- administration, compactness, and ease in manufacturing. Orodispersible tablets are uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed. Orodispersible tablets undergo disaggregating in the mouth when in contact with the saliva in less than 60 seconds, preferably in less than 40 seconds, forming a suspension which is easy to swallow. The target population for these new fast-dissolving / disintegrating dosage forms has generally been pediatric, geriatric, and bedridden or mentally disabled patients. A major claim of some orodispersibles is increased bioavailability compared to traditional tablets. Because of dispersion in saliva while still in the oral cavity, there can be pregastric absorption from some formulation, in cases where the drug dissolves quickly. Buccal, pharyngeal and gastric regions are areas of absorption of the formulation[1-4]. Objective of present study was to develop such as novel drug delivery systems for diazepam by simple & cost effective direct compression method. Chitosan, sodium carboxy methyl cellulose, alginic acid, crospovidone and sodium starch glycollate were used as superdisintegrant in the formulation for faster disintegration. Micro crystalline cellulose (MCC) is used as diluents and disintigrant. It is one of the fastest growing segments in the pharmaceutical market[3,4,11].

Diazepam is an important member of the group of 1,4-benzodiazepine derivatives. Diazepam exerts anxiolytic, anticonvulsant, sedative, muscle-relaxant and amnestic effects. It is a colorless to light yellow crystalline compound insoluble in water [5,15].

MATERIALS AND METHODS

Materials

Diazepam was received as a gift sample from Ronak Pharmaceuticals pvt Ltd., Patan. Chitosan, magnesium stearate, talc, orange flavour, sodium carboxy methyl cellulose (sodium CMC), alginic acid, micro crystalline cellulose (MCC), crospovidone and sodium starch glycollate (SSG) were purchased from Central Drug House (P) Ltd., New Delhi.

Method [4,7,14,15]

Tablets were prepared by direct compression technique. The composition orodispersible tablet of Diazepam was shown in Table 1. Weighed quantities of Diazepam along with appropriate concentrations of superdisintegrants along with excipients were weighed and mixed in geometric progression in a dry and clean mortar. Then the blend was passed through sieve no 60 for direct compression. The powder blend for direct compression was then compressed into tablets using 8 mm convex faced punches in a 10 Station Rotary Tablet Machine. These Fabricated tablets were evaluated.

EVALUATION

Weight variation test[6,9,11]

20 tablets were selected at random, individually weighed and the average weight was calculated. None of the tablets deviated from the average weight by more than ±7.5%.

Hardness test[7,9]

Tablets require a certain amount of strength or hardness and resistance to friability to with stand mechanical shocks. The hardness of tablet was measured by Monsanto hardness tester.

Friability[6,8,11]

Twenty tablets were weighed and placed in a Roche friabilator and the equipment was rotated at 25 rpm for 4 min. The tablets were taken out, dedusted, and reweighed. The percentage friability of the tablets was calculated by

$$\% \text{ Friability} = \frac{\text{initial weight} - \text{final weight}}{\text{initial weight}} \times 100$$

Content uniformity[9,15]

The content of diazepam was determined according to the method described by BP for diazepam tablets. In brief, 1 ml of water was added to one diazepam tablet, stood for 15 min, then 80 ml of a 0.5% (w/v) solution of sulfuric acid in methanol. The obtained solution was stirred for 15 min and

the volume was adjusted to 100 ml with 0.5% (w/v) solution of sulfuric acid in methanol. The filtrated solution was diluted appropriately and the drug content was measured spectrophotometrically at 284 nm.

Wetting time[10,18]

A piece of tissue paper folded twice was placed in a small Petri dish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting was measured.

In Vitro Dispersion Time[11,12,15]

In vitro dispersion time was measured by dropping a tablet in a measuring cylinder containing 6 ml of phosphate buffer pH 6.8 (simulated saliva fluid). The time for the tablet to completely disintegrate into fine particles was noted. Six tablets from each batch were randomly selected and in vitro dispersion time was performed.

In Vitro Disintegration Time[11,13,15]

The disintegration time of the tablets was determined as per Indian Pharmacopoeia monograph. The time required for disintegration of six tablets from each batch placed in each tube of disintegration test apparatus were measured at 37±0.5°C using 900 ml of distilled water. The time required to obtain complete disintegration of all the six tablets was noted.

Dissolution Studies[14,15,16,17]

In vitro dissolution studies were performed using type II (paddle) dissolution apparatus at 100 rpm, and 900 ml of phosphate buffer (pH 6.8) was used as a dissolution medium. Temperature of dissolution medium was maintained at 37±0.5°C. Five milliliters aliquot of the dissolution medium was withdrawn at specific time intervals. Absorption of filtered solution was measured by UV–visible spectrophotometer at 275 nm, and the percent of drug released was determined using standard curve. Dissolution rate was studied for the prepared formulations.

RESULTS

Formulations were prepared by direct compression techniques using different disintegrating agents are shown in Table 1. Parameters like weight variation, hardness, friability, drug content, wetting time, in vitro dispersion time and in vitro disintegration are mentioned in Table 2. All formulations evaluated for variation in weight and results indicated that for all formulations exhibit very low weight variation which lies within the pharmacopoeia limits i.e. ± 7.5%. The tablets measured hardness was found to be in the range of 3.2 to 3.6 kg/cm^2. The percentage friability was less than 1% for all formulation ensuring mechanical stability of the formulated tablets. Content uniformity in all the formulations were found in the range of 9.61 ± 0.33 to 9.94 ± 0.65 indicating the compliance with the pharmacopoeia limits. In Vitro disintegration time was found to be in range of 18 to 31 second. According to the pharmacopoeia standards the dispersible tablet must disintegrate within 3 min but all formulated batches have shown very low disintegration time indicating suitability of formulation for fast dissolving tablet. Disintegration time from all the prepared formulation was found to be in following order: F2<F5<F1<F4<F3. Disintegration time of various formulations is mentioned in Figure 1. Wetting time was found to be in range of 24 to 36 second. In vitro dispersion time was found to be in range of 21 to 36 second. % Cumulative drug release from all the prepared formulation was found to be in following order: F2>F1>F3>F5>F4. % Cumulative drug release from F1, F2 and F5 formulations were found to be in 10 minute and from F3 and F5 formulations were found to be in 12 minutes. Formulation F2 shows fast disintegration and high % Cumulative drug release.

DISCUSSION

Different formulations were prepared using 10% superdisintegrant like chitosan, sodium carboxy methyl cellulose, alginic acid, crospovidone and sodium starch glycollate. The tablets prepared by direct compression technique were found to have adequate hardness, friability, content uniformity, wetting time and in vitro dispersion time. Prepared tablets disintegrate within few seconds without need of water; thereby enhance absorption resulting in increased bioavailability and increased patient compliance. Among all the superdisintegrant crospovidone showed maximum effect of disintigrantion. Effect of superdisintegrant from all the prepared formulation was found to be in following order: Crospovidone>SSG>Sodium CMC>Chitosan>Alginic acid. The formulated tablet F2 showed fast disintegration and in vitro dissolution. Therefore these tablets which possess rapid disintegration may be useful for pediatric and geriatric population.

ACKNOWLEDGEMENT

The authors are thankful to Narend Patel manager of Ronak Life Care pvt Ltd, Patan, India, for providing us gift sample of Diazepam. Our special thanks to honorable Rajesh Asija and Sangeeta Asija for providing us necessary support and facilities required for this research work. The authors also wish to acknowledge with thanks to the management of Maharishi Arvind Institute of Pharmacy, Mansarovar, Jaipur, for providing the infrastructure and facilities for our research project.

REFERENCES.

1. Jha SK, Vijayalakshmi P, Karki R and Goli D. Formulation and evaluation of melt-in-mouth tablets of haloperidol. Asian Jour. of Pharma. 2008; 2(4): 255-260.
2. J.J Hurani, D.A. Rathod and K.R.Vadalia. Orally disintegrating tablet. A review. Tropical journal of pharmaceutical research. 2009; 8(2): 161-172.
3. Bandari S, Mittapalli RK, Gannu R and Rao YM. Orodispersible tablets: An overview. Asian Jour. Of Pharma. 2008; 2(1): 2-11.
4. Chaudhri PD, Chaudhri SP, Lanke SD and Patel. Formulation and in vitro evaluation of taste masked orodispersible dosage form of Levocetirizine dihydrochloride. Indian Jour. of Pharm. Educ. Res.2007; 41(4): 319-328.
5. Inada T, Nozaki S, Inagaki A, Furukawa TA. Efficacy of diazepam as an anti-anxiety agent: metaanalysis of double-blind randomized controlled trials carried out in Japan. Hum Psychopharmacol Clin Exp. 2003; 18(6): 483–7.
6. D. M Patel, N. M Patel, R. R Shah, P. D Jogani, A. I Balapatel. Studies in formulation of orodispersible tablets of Refocoxib. Indian Journal of Pharmaceutical Sciences.2004; 66 (5): 621-625.
7. Kumaran V., Sathyanarayana D., Manna P.K., Chandrasekar G. Formulation development of acetaminophen tablets by direct compression and its pharmacoeconomics. Indian drugs 2004; 41(8): 473-477.
8. Jinichi F, Etsuo Y, Yasuo Y, Katsuhide T. Evaluation of rapidly disintegrating tablets containing glycine and carboxymethylcellulose. Int J Pharm. 2006; 310: 101–9.
9. British Pharmacopoeia Commission. Powder flow. London: British Pharmacopoeia Commission; 2007 (Appendix XVII N).
10. Margret CR, Jaykar B,Chakrabarty BL. Formulation and evaluation of Orodispersible tablets of terbutaline sulphate. Drug Invention Today. 2010; 2(1): 31-33.
11. Uma Vasi Reddy, Lakshmi Narasimha Reddy N, Poorna Chander T, Prashanth V. Formulation and evaluation of oral disintegrating tablets of salbutamol sulphate. Int. J. Pharm & Ind. Res. 2011; 1(1): 63-66.
12. Indian Pharmacopoeia, The Controller of Publication, 2, 1996, 735

13. Jinichi F, Etsuo Y, Yasuo Y, Katsuhide T. Evaluation of rapidly disintegrating tablets containing glycine and carboxymethylcellulose. Int J Pharm. 2006; 310(1-2): 101–9.
14. Sharma S, Gupta GD. Formulation and characterization of fast dissolving tablet of promethazine theocolate. Asian J Pharm. 2008; 70–72.
15. Khalid K. Abed, Ahmed A. Hussein, Mowafaq M. Ghareeb, Alaa A. Abdulrasool. Formulation and Optimization of Orodispersible Tablets of Diazepam. AAPS PharmSciTech 2010; 11(1): 356-361.
16. Nirav MK. D-Zolv mouth dissolves tablets. Ind. J. Pharm. Sci. 2000; 62(2): 527-528.
17. Kuchekar b et al mouth dissolving tablets of salbutamol sulphate: a novel drug delivery system, Indian drugs 2004; 41 (10): 592-598.
18. Singh J, Philip AK and Pathak K. Optimization Studies on Design and Evaluation of Orodispersible Pediatric Formulation of Indomethacin. AAPS Pharm Sci. Tech. 2008; 9(1): 60-66.

Table 1: Composition of orodispersible tablets of Diazepam

BATCH CORD	INGREDIANT (mg)										
	Diazepam	Sodium CMC	Crospovidone	Alginic acid	Chitoson	SSG	MCC	Mannitol	Orange flavour	Magnesium stearate	Talc
F1	10	20	-	-	-	-	55	109	2	2	2
F2	10	-	20	-	-	-	55	109	2	2	2
F3	10	-	-	20	-	-	55	109	2	2	2
F4	10	-	-	-	20	-	55	109	2	2	2
F5	10	-	-	-	-	20	55	109	2	2	2

Table 2: Evaluation of Diazepam orodispersible tablets

TESTS	BATCH CORD				
	F1	F2	F3	F4	F5
Weight variation (mg)	Pass	Pass	Pass	Pass	Pass
Hardness kg/cm^2	3.3	3.6	3.2	3.4	3.2
% Friability	0.49	0.35	0.62	0.42	0.66
Content uniformity (mg)	9.74 ± 0.43	9.94 ± 0.65	9.68 ± 0.25	9.85 ± 0.46	9.61 ± 0.33
Wetting time (second)	29	24	36	33	28
In Vitro dispersion time (second)	28	21	36	32	25
In Vitro Disintegration Time	24	18	31	27	22

Table 3: In vitro dissolution studies of orodispersible tablets of Diazepam

Time (min)	% Cumulative drug release				
	F1	F2	F3	F4	F5
2	54.34 ± 0.87	58.48 ± 0.65	48.76 ± 0.76	52.64 ± 0.66	50.33 ± 0.74
4	63.76 ± 0.46	67.75 ± 0.86	61.39 ± 0.39	65.73 ± 0.73	64.87 ± 0.63
6	78.65 ± 0.29	80.39 ± 0.48	75.58 ± 0.42	73.84 ± 0.26	79.64 ± 0.77
8	95.96 ± 0.84	97.57 ± 0.51	84.84 ± 0.63	83.33 ± 0.64	96.84 ± 0.45
10	98.87 ± 0.35	99.91 ± 0.23	92.76 ± 0.76	93.72 ± 0.54	97.99 ± 0.76
12	-	-	98.24 ± 0.65	97.47 ± 0.88	-

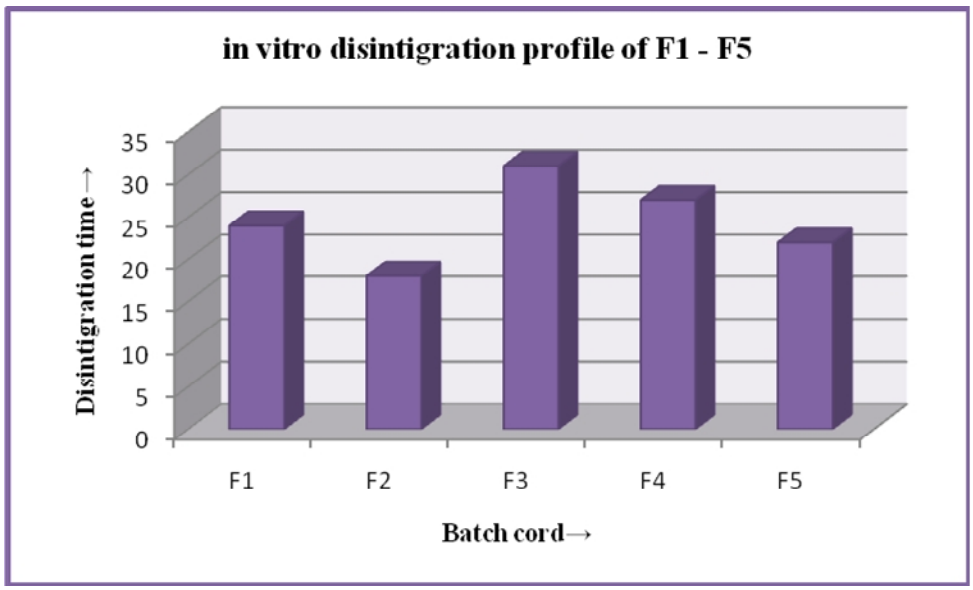

Figure 1: In vitro disintegration profile of F1 to F5.

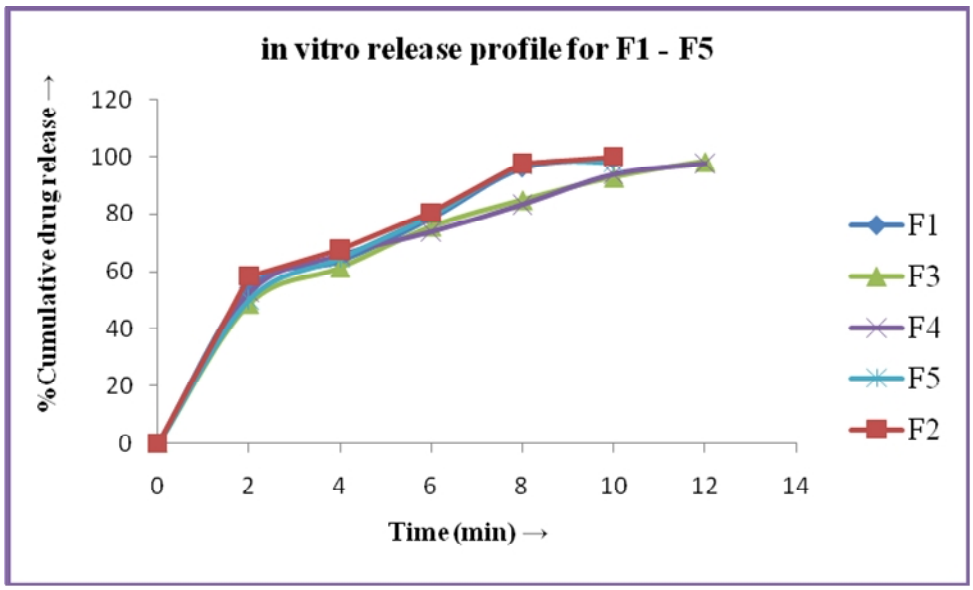

Figure 2: In vitro release profile for F1 to F5.

Source of support: Nil, Conflict of interest: None Declared