Asian Journal of Pharmaceutical and Clinical Research
Vol.2 Issue 3, July-September 2009 SSN 0974-2441

Research Article

FORMULATION AND EVALUATION OF NIFEDIPINE SUBLINGUAL TABLETS

SHEEBA F R, Mallige college of Pharmacy Chikkabanavara post, Bangalore-90,India
E-Mail: gilesheeba@yahoo.com
GILES D Acharya & B.M Reddy college of Pharmacy, Bangalore ,
RAMESHWARI S, JEYA ANANDHI J Arulmigu Kalasalingam College of Pharmacy, Tamilnadu

ABSTRACT

The aim of this study was to evaluate the effect of increasing nifedipine load on the characteristics of fast-disintegrating sublingual tablets for the potential emergency treatment of anginal pain and hypertension. Nifedipine undergoes first pass metabolism in liver and gut wall which has oral bioavailability of 43-77%. Sublingual dosage form bypasses the metabolism of the nifedipine in liver and offers a fast relieve from anginal pain and hypertension. An attempt has been made to prepare fast dissolving tablets of nifedipine using super distintegrants like cros carmellose sodium, sodium starch glycolate, cros povidone. Three different groups of formulations (A, R, and V) with variation in tablet excipients were prepared by direct compression method. Tablet weight variation, hardness, friability, drug content, disintegration time and dissolution time were evaluated for each formulation and found satisfactory. The studied sublingual tablet group V shows a lesser T50% compared to commercial oral tablet. The Group V also indicates the fast dissolution and disintegration rate of the optimized nifedipine sublingual tablet, which is prerequisite for rapid management of anginal and hypertension diseases.

KEY WORDS Sublingual Tablets, Nifedipine, Fast Drug Release, Hypertension, Anginal Pain.

INTRODUCTION

The sublingual route usually produces a faster onset of action than orally ingested tablets and the portion absorbed through the sublingual blood vessels bypasses the hepatic first-pass metabolic processes.[1-3]

Nifedipine is a dihydro pyridine calcium channel antagonist [4] originally introduced for the treatment of angina pectoris [5] hypertension and anti-atherosclerotic [6] activity.

The sublingual [7] dosage form offers fast release of drug from the formulation and it reaches the systemic circulation directly, which bypasses the metabolism of the nifedipine in the liver and offers a fast relive form the anginal pain, hypertension which will be worth in such conditions.

Various techniques can be used to formulate rapidly disintegrating or dissolving tablets. [8, 9] Direct compression is one of these techniques which require incorporation of a superdisintegrant into the formulation, or the use of highly water-soluble excipients to achieve fast tablet disintegration. Direct compression does not require the use of water or heat during the formulation procedure and is the ideal method for moisture and heat-labile medications.

Extremely fast tablet disintegration would be required to enhance the release of nifedipine from tablets for rapid absorption by the sublingual mucosa blood vessels. It was decided that nifedipine could be formulated into fast-disintegrating tablets for sublingual administration as potential emergency treatment of angina pectoris and hypertension. This could be achieved by selecting the appropriate pharmaceutical excipients in the correct proportion, in combination with optimal manufacturing techniques. The purpose of this study was to develop a sublingual nifedipine tablet formulation having good bioavailability.

MATERIALS AND METHODS

Materials

Nifedipine was obtained as gift sample from Sharan Biomedicine Ltd., Maharashtra. Avicel pH 101 was obtained from Wei Ming Pharmaceutical Mfg.Co.ltd, Taiwain. Mannitol, lactose DCL, magnesium stearate,

talc, saccharine sodium, aerosol and citric acid, were procured from s.d. Fine Chemicals Pvt.Ltd., Mumbai, India. Cros carmellose sodium, sodium starch glycolate and cros povidone were obtained from Amit Cellulose products, Puna. All the chemicals and solvents used were of analytical grade.

Preparation of sublingual tablets

Nifedipine sublingual tablets were prepared by the direct compression method using different excipients. [10] The excipients used were avicel PH101 (binding agent) mannitol and lactose DCL (diluents) saccharine sodium (sweetening agent) citric acid (antioxidant) cros carmellose sodium and sodium starch glycolate (disintegrant) and cros povidone (enhance dissolution rate).

Different concentration of excipients was used to prepare different group of sublingual tablets. Compositions of various formulations are shown in Table-1. All the ingredients of the sublingual tablets of nifedipine were weighed and mixed in mortar with the help of pestle, then finally 2mg magnesium stearate and 2mg talc and 1mg of Aerosil was added for lubrication and triturated well. Then the blended material was slightly compressed on the 6mm flat–faced punch using a Rimek MINI PRESS-II MT tablet machine (Karnawati Engg. Ltd., Mehsana, India). The total weight of the formulation was maintained 150mg.

Physical evaluation

All batches of tablets were evaluated for various parameters like weight variation, friability, hardness, drug content, disintegration and dissolution.

Table 1 - different formulation of Nifedipine sublingual tablets

INGREDIENTS (mg)	GROUP A					GROUP R					GROUP V				
	A1	A2	A3	A4	A5	R1	R2	R3	R4	R5	V1	V2	V3	V4	V5
Nifedipine	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Avicel pH101	20	30	40	50	60	20	30	40	50	60	20	30	40	50	60
Mannitol	22	22	22	22	22	22	22	22	22	22	30	30	30	30	30
Lactose DCL	85	75	65	55	45	89	79	69	59	49	75	65	55	45	35
Magnesium Stearate	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Talc	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Saccharine Sodium	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Aerosil	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Citric acid	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Cros carmellose sodium	2	2	2	2	2	-	-	-	-	-	2	2	2	2	2
Sodium starch glycolate	2	2	2	2	2	-	-	-	-	-	2	2	2	2	2

Weight variation test

Weight variation test was conducted by selecting 20 tablets at random as per I.P.

Friability test

Six tablets from each batch were examined for friability [11] using Roche friabilator (Tropical Equipment Pvt. Ltd., Mumbai, India) and the equipment was run for 4 min at 25 revolutions per minute. The tablets were taken out, dedusted and reweighed.

Hardness test

The hardness [12] of the tablet was determined using a Monsanto hardness tester (Campbell Electronics, Mumbai, India).

Disintegration time

The disintegration time of the tablets was determined as per Indian pharmacopoeia.

The test was carried out using tablet disintegration apparatus (scientific Engineering Corporation, Delhi, India). Distilled water was used as a disintegrating media at 24 ± 0.2°C. The time required to obtain complete disintegration of all the tablets were noted.

Drug content

Five tablets from each batch were finely powdered and the powder equivalent to 50mg of nifedipine was weighed and dissolved in suitable quantity of methanol. The solution was filtered, suitably diluted and the drug content was analyzed spectrophotometrically (Shimadzu, UV-1601) at 350nm.

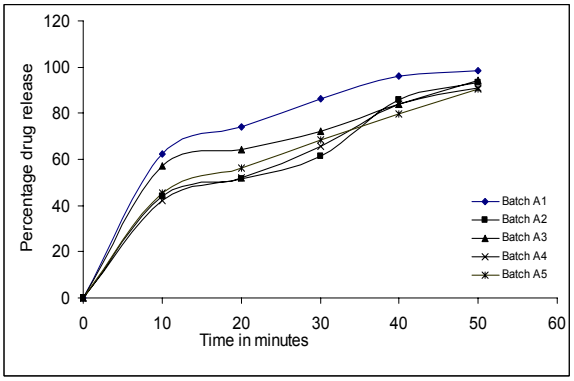

FIG 1. Drug release profile of group 'a' tablets

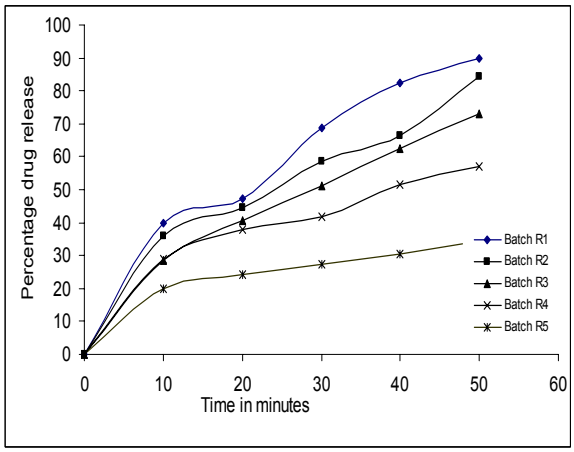

FIG 2. Drug release profile of group 'r' tablets

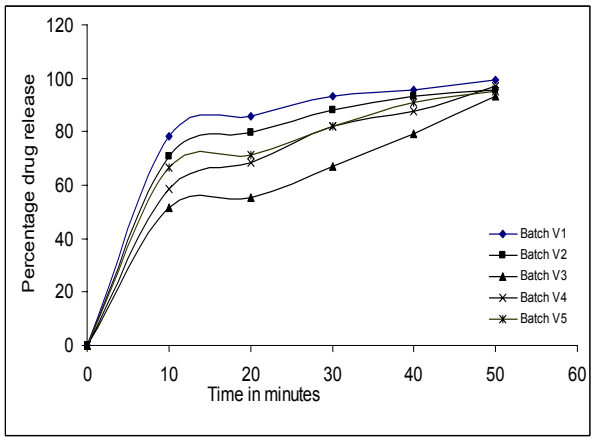

FIG 3. Drug release profile of group 'v' tablets

TABLE 2 EVALUATION DATA OF THE PREPARED NIFEDIPINE SUBLINGUAL TABLETS

Formu -lation	Hardness kg/cm^2	Friabilit y (%)	Drug content (%)	Disintegration time	Dissolution efficiency (%) (de50)	T50% drug release in min
A1	6.8±0.32	0.40	98.83	55sec	98.48	8
A2	6.2±0.29	0.33	98.18	2min2sec	93.00	10
A3	5.5±0.27	0.60	98.82	1min15sec	94.13	14
A4	4.9±0.49	0.74	99.05	1min49sec	90.98	18
A5	5.2±0.24	0.56	98.87	1min58sec	90.24	17
R1	6.3±0.21	0.23	100.87	2min58sec	90.03	22
R2	5.4±0.22	0.53	99.37	3min45sec	84.38	25
R3	6.7±0.15	0.44	99.78	3min	73.08	28
R4	6.4±0.24	0.47	100.18	3min50sec	57.05	38
R5	6.7±0.27	0.26	99.13	4min10sec	34.48	ND
V1	6.4±0.23	0.45	99.10	25sec	99.49	6
V2	6.0±0.11	0.34	99.50	32sec	95.82	7
V3	5.9±0.36	0.18	100.03	38sec	93.34	9
V4	6.1±0.10	0.37	99.05	29sec	96.98	8
V5	6.6±0.16	0.33	99.42	36sec	95.38	7

ND- not deducted only 34.48% drug release occurred during one-hour dissolution

In-vitro drug release study

Dissolution study was conducted for all the formulations using USP dissolution rate test apparatus type-II (Electrolab, Mumbai, India.). Nine hundred milliliters of phosphate buffer (pH 7.5) was taken as the dissolution medium at100rpm and 37^{o}C ± 0.5^{o}C for 50 min. Five milliliters of aliquots were periodically withdrawn, and the sample volume was replaced with an equal volume of fresh dissolution medium. The samples were analyzed spectrophotometrically at 350nm.

RESULTS AND DISCUSSION

Nifedipine sublingual tablets were prepared by direct compression method. Three different groups (A, R and V) of formulation with variation of tablet excipients were prepared with each group containing five different formulations. Table 2 shows the data obtained from the evaluation of tablets. All batches of the tablets were preliminarily evaluated for various physical parameters such as hardness, friability drug content, disintegration and dissolution which were reported in Table no 2. All above properties and value were near to boundary of standard limit. All the tablets maintained hardness in the range of 4.9 – 6.8kg/cm^2. The loss in total weight of the tablets due to friability was in the range of 0.18-0.6%. The drug content in different formulations was highly uniform and in the range of 98-100%. Formulation V was quickly disintegrated compared to other Formulation A, R and commercial tablets. From the *in-vitro* dissolution studies, it was observed that formulation V1 showed 99.49% dissolution efficiency in 50 min. The drug release patterns for different formulations were shown in Fig 1 to 3. The tablet group V1 showed a lesser T50% compared to the studied sublingual tablets and commercial oral tablets. Hence, the group V1 is selected as an optimized nifedipine sublingual tablet for subjecting into two different storage conditions over a period of 12 weeks. In conclusion, this study clearly indicated the fast disintegration and dissolution of the optimized nifedipine sublingual tablet, which is prerequisite for the rapid management of anginal hypertension diseases.

ACKNOWLEDGMENT

The authors thank the management and principal of Kalasalingam College of Pharmacy, Tamil Nadu, for providing various facilities to complete the work.

REFERENCE

1. Birudaraj R, Berner B, Shen S. Buccal permeation of buspirone: Mechanistic studies on transport pathways. J Pharm Sci 2005; 94: 70-78.
2. Ishikawa T, Koizumi N, Mukai B, Utoguchi N, Fujii M, Matsumoto M *et al.,* Pharmacokinetics of acetaminophen from rapidly disintegrating compressed tablet prepared using microcrystalline cellulose (PH-M-06) and spherical sugar granules. Chem Pharm Bull (Tokyo) 2001; 49: 230-232.
3. Price TM, Blauer KL, Hansen M, Stanczyk F, Lobo R, Bates GW. Single-dose pharmacokinetics of sublingual versus oral administration of micronized 17 beta-estradiol. Obstet Gynecol. 1997; 89: 340-345.
4. Croom, Katherine F, Wellington, Keri. Modified-release nifedipine: A review of the use of modified release formation in the treatment of hypertension and Angina pectoris. Drugs; 2006; 66 Suppl 4: 497-528.
5. Richard D Howland, Mary J Mycek Lippincott's Reviews pharmacology, 3rd ed. Philadelphia: Lippincott Williams and Wilkins; 1997. p. 211.
6. Anthony J Trevor, Bertram G Katzung, Usan B Masters Katzung and Trevor's Pharmacology, 7th ed. Singapore: McGraw Hill medical publishing; 2005. p.110.
7. Sean C Sweetman Martindale, The complete drug reference, Vol 34, USA: Pharmaceutical press; 2005. p.967.
8. Allen LV. Rapid-dissolve technology: an interview with Loyd V.Allen. Int J Pharm Technol. 2003; 7: 449-450.
9. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets: developments, technologies, taste-making and clinical studies. Crit Rev Ther Drug Carrier Syst. 2004; 21: 433-476.
10. Raymond C Rowe, Paul J Sheskey, Paul J Weller, Hand book of Pharmaceutical Excipients, 4th ed. London (UK): Pharmaceutical press; 2003. p.108-581.

11. Ketan A. Mehta, Serpil Kislalioglu M, Wantanee Phuapradit, Waseem Malick A, Navnit H. Shah. Multi-unit controlled release system of nifedipine and nifedipine: pluronic® F–68 solid dispersion: characterization of release mechanisms, Drug Dev Ind Pharm. 2002; 28 Suppl 3: 275-285
12. Mutaliksrinivas, Hiremath doddaya, Formulation and evaluation of chitosan matrix tablets of nifedipine, The Eastern Pharmacist 2000; 2, 137-139.