Journal of Comprehensive Pharmacy

Research Article

Available Online at: www.jcponline.in

ISSN NO: 2349-5669

Preparation and Evaluation of Nifedipine sustained release Tablet by using Natural Gums as release retardant

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ARTICLE INFO

Article history:

Received 27 August 2014
Accepted 15 September 2014
Available online 27 October 2014

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ABSTRACT:

Aim: The present investigation has been aimed to design and evaluate oral sustained drug release matrix tablets of Nifedipine using natural hydrophilic gums like Xanthane gum and guar gum as rate retarding agents.

Method: The matrix tablets were prepared by Direct compression method and were evaluated for Hardness, Friability, Weight variation, Drug content uniformity, swelling index and to study the mechanism of drug release by applying kinetic parameters and to determine the best batch of drug release profile as per USP.

Result: Nifedipine containing Xanthane gum, Guar gum and combination of Xanthane and Guar gum as rate controlling polymer demonstrated slow release. But formulations F11-F12 showed drug release as per USP limit.

Conclusion: The present study clearly indicated a promising potential of extended release Nifedipine tablets containing combination of Xanthane gum and Guar gum as rate controlling polymers for effectively treating CVD's.

KEY WORDS: Nifedipine, Xanthane gum, Guar gum, Sustained release, Natural gums.

INTRODUCTION:

Among various dosage forms, matrix tablets are widely accepted for oral sustained release (SR) as they are simple and easy to formulate. Matrix system is the release system which prolongs and controls the release of drug i.e., dissolved or dispersed [1]. Gums of natural sources are biodegradable and non-toxic which hydrates and swell on contact with aqueous media and these have been used for the preparation of single unit dosage forms. In fact matrix is defined as a well composite of one or more drugs with a gelling agent i.e. hydrophilic polymer.

Xanthane gum is a polysaccharide with β -D glucose back bone like cellulose but every second glucose unit is attached to a tri-saccharide consisting of mannose

and glucuronic acid. Xanthane gum is produced by the bacterium *xanthomonas campestris* which is found on cruciferous vegetables such as cabbage and cauliflower [2]. Xanthane gum is used as thickener for sauces, to prevent ice crystal formation in ice cream. Xanthane gum is frequently mixed with Guar gum because the viscosity of the combination is greater than when either one is used alone.

Chemically Guar gum is a polysaccharide composed of sugars galactose and mannose. Guar gum based matrix tablets are currently being evaluated as a method of administering sustained released drugs for colonic drug delivery of corticosteroids to patients with inflammatory bowel disease [3]. Nifedipine (NFD) is a yellow crystalline powder, practically in soluble in

water and sparingly soluble in absolute ethanol. Nifedipine is extremely light sensitive drug and breaks down rapidly upon exposed to day light to a nitrosophenyl pyridine, hence assay and test should be performed in either dark or under golden fluorescent or other low- actinic light [4].

MATERIALS AND METHODS:

Nifedipine was obtained from Aurobindo pharmlabs, HYD. Xanthane gum and guar gum were obtained from Finar chemicals Pvt.Ltd. Microcrystalline cellulose, Magnesium stearate were obtained from Otto, Mumbai, Potassium di hydrogen phosphate, sodium lauryl sulphate were obtained from Finar chemicals Pvt.Ltd.

Preparation of matrix tablets:

Drug, polymers and other excipients were weighed separately for 100 tablets for each formulation as shown in Table 1. The proposed formulations were coded as F1, F2, F3, F4, F5, F6, F7, F8, F9, F10, F11, and F12. The tablets were prepared by direct compression method. Active ingredient (Nifedipine) and polymers (Xanthane gum and Guar gum) were Passed through #24 sieve and placed in a poly bag. They were hand blended for 20 minutes. Talc (1%) and Magnesium Stearate (1%) were passed through #40 sieve and placed in the same poly bag and were blended for another 5 minutes. Blended powder were compressed using 8 station tablet compression machine equipped with 8.0 mm round flat punch and die set. After compression, all the tablets were stored in double polythene bags at room temperature for further study [5].

Compatibility study:

One of the requirement for the selection of suitable excipients or carrier for pharmaceutical formulation is its compatibility. Therefore, in the present work a study was carried out by using FT-IR spectrophotometer to find out if there is any possible chemical interaction of Nifedipine with Xanthane gum and Guar gum. As shown in Table 2 & Figures 1- 6.

Evaluation of matrix tablets:

All prepared matrix tablets were evaluated for weight variation test (electronic balance), hardness test (Monsanto hardness tester), and friability was determined using friabilator, Thickness was measured by Verniercaliper as shown in Table 3.

In-Vitro Drug release studies (Dissolution studies):

Dissolution study development and setting specifications for a drug with low aqueous solubility create problems. As it is difficult to maintain sink condition during their dissolution studies using conventional dissolution methods and procedures. Various modification in dissolution test method such as use of large volume of dissolution medium, use of two phase medium or modification of dissolution test equipment have been discussed [6, 7, 8]. However addition of surfactants in the dissolution medium to provide sink condition is considered to stimulate physiological environment more closely than other approaches [9, 10]. So, the SLS concentration of 1% W/V was added in dissolution medium at pH 6.8 to provide sink condition for Nifedipine [11]. The study was carried out using 6.8 pH Phosphate buffer with 1% SLS using USP apparatus type – II with 50 RPM, the dissolution medium 900 ml maintained at $37^{\circ} \pm 0.5^{\circ}\text{C}$ as shown in Table 4 & Figure 7.

Table 1: Composition of 20 mg Nifedipine tablet

S.No	Ingredients (in mg)	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12
1.	Nifedipine	20	20	20	20	20	20	20	20	20	20	20	20
2.	Xanthane gum	5	10	15	20	--	--	--	--	2.5	5	7.5	10
3.	Guar gum	--	--	--	--	5	10	15	20	2.5	5	7.5	10
4.	Micro crystalline cellulose	12	11	11	10	12	11	11	10	12	117	112	107
5.	Magnesium stearate	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5
6.	Talc	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5	1.5

Table 2: IR Spectroscopy Data

S.No.	Nifedipine	Nifedipine + Xanthane gum	Nifedipine + Guar gum	Nifedipine + Guar+ Xanthane gum
N-H	3331.38	3331.41	3331.91	3332.56
C-H	2953.06	2952.88	2953.26	2922.38
C=O	1678.89	1678.86	1679.33	1678.97
C-O	1226.72 & 1120.75	1226.95 & 1120.76	1226.80 & 1120.82	1227.31 & 1121.00
NO ₂	1529.35	1529.42	1529.55	1529.78

Figure 1: R Spectrum of Nifedipine

Figure 2: IR Spectrum of Xanthane gum

Figure 3: IR Spectrum of Guar gum

Figure 4: IR Spectrum of Formulation

Figure 5: IR Spectrum of Formulation

Figure 6: IR Spectrum of Formulation

Table 3: Data's for physical evaluation of oral sustained-release tablets of Nifedipine

S. No.	Formulation Code	^a Diameter (mm)	^b Thickness (mm)	^c Weight variation (mg)	^d Hardness (Kg/Cm ²)	^e Friability (%)	^f Drug content (%)
1.	F1	8.03±0.016	2.52±0.026	151±7.5	5.1±0.124	0.120	99.355±0.361
2.	F2	8.02±0.004	2.55±0.030	150±7.5	5.4±0.248	0.066	98.820±0.478
3.	F3	8.03±0.004	2.53±0.034	154±7.5	5.3±0.210	0.133	99.530±0.410
4.	F4	8.03±0.008	2.54±0.028	145±7	5.2±0.232	0.132	99.425±0.314
5.	F5	8.06±0.012	2.53±0.017	147±7.5	5.9±0.126	0.166	97.860±0.618
6.	F6	8.05±0.012	2.52±0.020	151±7.5	5.2±0.142	0.232	99.443±0.489
7.	F7	8.04±0.016	2.54±0.015	152±7.5	5.4±0.180	0.146	98.548±0.724
8.	F8	8.03±0.012	2.55±0.015	149±7.5	5.3±0.228	0.191	99.234±0.463
9.	F9	8.02±0.012	2.61±0.010	148±7.5	5.9±0.219	0.149	98.906±0.226
10.	F10	8.03±0.012	2.55±0.041	153±7.5	5.8±0.160	0.193	98.026±0.624
11.	F11	8.03±0.016	2.63±0.026	150±7.5	6.2±0.126	0.154	99.477±0.354
12.	F12	8.05±0.016	2.61±0.030	148±7.5	6.1±0.113	0.046	99.240±0.162

* All values are expressed as mean ± S.D, n(a) =3 n(b)= 6 n(c)=20 n(d)= 6 n(e)= 20 n(f)=1

Table 4: Kinetic analysis of In vitro release rates of sustained release tablets of Nifedipine

Formulations	Zero order release		First order release		Higuchi release		Korsmeyer-Peppas	
	r ²	K ₀	r ²	K ₀	r ²	k _n	r ²	n
F ₁	0.9941	11.767	0.9096	-0.3109	0.9085	33.579	0.9876	0.9523
F ₂	0.951	7.846	0.9886	-0.1957	0.9479	28.787	0.9983	0.9484
F ₃	0.9525	6.5978	0.9974	-0.1252	0.9577	24.314	0.9882	0.9841
F ₄	0.9607	5.9019	0.9946	-0.1	0.9543	21.618	0.9805	0.9864
F ₅	0.9343	10.937	0.9897	-0.2828	0.9769	33.38	0.9967	0.7507
F ₆	0.8956	7.8579	0.9886	-0.2802	0.976	30.146	0.9753	0.6768
F ₇	0.9503	7.7973	0.9974	-0.2291	0.9699	28.949	0.9593	0.6496
F ₈	0.9525	6.9438	0.9946	-0.1526	0.9543	25.82	0.9766	0.7142
F ₉	0.9705	11.675	0.9387	-0.3728	0.9628	34.709	0.9778	0.6759
F ₁₀	0.9431	8.1937	0.9502	-0.2991	0.9596	30.375	0.9776	0.7146
F ₁₁	0.9569	7.7833	0.9786	-0.1989	0.9461	28.444	0.9842	0.833
F ₁₂	0.9676	7.5955	0.9813	-0.2802	0.9305	27.373	0.9904	0.9621

The USP dissolution requirements for Nifedipine 20mg sustained release tablets for 3, 6, and 12 hours are 10-30%, 40-65% and not less than 80% respectively [12].

Figure 7: Percentage cumulative drug release of matrix tablets.

Swelling studies:

Pre weighed tablets with wire mesh basket were placed in the medium (Phosphate buffer pH 6.8 containing 1% SLS). At different time intervals the weight of the swollen tablet was recorded after wiping of excess of water. The swelling index was calculated by using the following equation as shown in Figure 8.

$$\text{Swelling index} = \frac{(W_t - W_0)}{W_0}$$

Where,

W_0 – Initial weight of tablet and

W_t – weight of the tablet at time's (t)

Study of release kinetics:

In order to investigate the *in-vitro* release profile obtained from all formulations was analyzed with the following mathematical models

Zero order: $Q = K_0t$

First order release: $\ln(100-Q) = \ln Q - K_1t$

Higuchi equation [13]: $(Q = K_t^{1/2})$

Korsmeyer and Peppas equation [14]

$(Q = K_p t^n)$

Where,

Q is the percentage of drug release at time t and K_0 and K_t are the coefficients of the equation. K_p is constant incorporating structural and geometric characteristics of the release device and n is the release exponent indicating the release mechanism.

Figure 8: Comparative swelling index for F1 to F12

RESULT AND DISCUSSION:

The IR studies revealed that there was no interaction between polymers and drug. When the characteristic peaks of Nifedipine were compared with the combination of Nifedipine and polymers, it was found that the similar fundamental peaks and patterns were also present. All the formulations showed excellent flow ability as expressed in terms of micrometric parameters. The formulated tablets possessed uniform thickness in the range 2.52-2.63 mm and hardness 5.1-6.2 Kg/cm². The tablets complied within the IP limit in terms of weight variation and the tablets passed the friability test. Drug content in different formulations was estimated by UV Spectrophotometric method. The standard deviations among the three values were found to be small. That indicates the drug was distributed almost uniformly throughout in all the formulations. The formulated matrix tablets met the Pharmacopoeial requirement of drug content uniformity, hardness, thickness, percentage friability and weight variation. Swelling index was studied in 6.8 phosphate buffer with 1% SLS, all the formulations containing xanthane gum, Guar gum and combination of xanthane gum and Guar gum showed gradual increase in the swelling index as the time increase. Swelling index was increased, because weight gain by tablet was proportional to rate of hydration upto 6 hrs, later on it decreases gradually due to dissolution of outermost gelled layer of tablet into dissolution medium.

Formulation F1, F2, F3, and F4 contains xanthane gum as rate controlling polymers in the drug: polymer ratio 1:0.25, 1:0.50, 1:0.75, 1:1 respectively, and microcrystalline cellulose as diluents. The tablet showed drug release of 92.846% at the end of 8th hour

89.630, 76.736, and 70.165 at the end of 12th hour for F1, F2, F3, and F4 respectively. As the amount of Xanthane in the matrix increase a greater retardation of the drug is observed. This may be due to the greater swelling of Xanthane gum. To analyse the release mechanism of the drug through the matrix peppas equation was used. In formulations F1, F2, F3, and F4 the n value is between 0.9484-0.9864 indicating Anomalous transport or non-fickian drug diffusion which suggested that the drug release occurs by swelling as well as erosion. Drug release was not found to be within the limit as per USP. Drug release was less when compared with USP limits.

Formulation F5, F6, F7, and F8 contains Guar gum as rate controlling polymers in the drug: polymer ratio 1:0.25, 1:0.50, 1:0.75, 1:1 respectively, and microcrystalline cellulose as diluents. The tablet showed drug release of 90.020 at the end of 8th hour 96.963, 94.070, 83.998, at the end of 12th hour respectively. When the guar gum is used as the retarding agent a higher initial release as well as increased drug release is absorbed. To analyze the release mechanism of the drug through the matrix peppas equation was used. In formulation F5, F6, F7 and F8 the n value is between 0.6496-0.7507 indicating Anomalous transport or non-fickian drug diffusion which suggested that the drug release occurs by swelling as well as erosion. Drug release was not found to be within the limit as per USP.

Formulation F9, F10, F11, and F12 contains combination of Xanthane gum and Guar gum as rate controlling natural polymers in the drug: polymer : polymer ratio of 1:0.125:0.125, 1:0.25:0.25, 1:0.375:0.375 & 1:0.50:0.50, respectively and microcrystalline cellulose as diluents. The tablet from F9 formulations showed drug release of at 95.449 the end of 8th hour respectively. F10, F11, F12, showed the drug release of 97.243, 90.184, and 86.365 at the end of 12 hours respectively. Drug release from F9, and F10, was not found to be within the limit as per USP. The drug release from formulation F11 and F12 was found to be within the limit as per USP at end of 3rd hour, 6th hour and 12th hour. All the formulations were best fit in first order release except the F9 was best fit in zero order. The 'n' values for F9, F10, F11, and F12 were found to be more than 0.5 which indicates the Non-Fickian Diffusion mechanism or anomalous transport which means the drug release shows a combination of diffusion and erosion mechanisms.

CONCLUSION:

From all the parameters studied, it can be concluded that formulation F11 was found to be best formulation regarding all the properties evaluated. The drug release

was found to be within the limit as per USP at the end of 3rd, 6th and 12th hour. Thus the results of the present study clearly indicated a promising potential of extended release Nifedipine tablets containing combination of Xanthane gum and Guar gum as rate controlling polymers for effectively treating CVD's.

REFERENCES:

1. Chien YW. Concept and system design for the rate controlled drug delivery. In: Chien YW, editor. Novel Drug Delivery Systems. 2nd ed. New York, NY: Marcel Dekker, Inc; 1992. pp. 1-42.
2. Girish K Jani, Dhiren P Shah, Vipul D Prajapati etc .Gums and mucilages: versatile excipients for pharmaceutical formulations. *AJPS* 2009;**4(5)**:308-322.
3. Chourasia MK, Jain SK. Pharmaceutical approaches to colon targeted drug delivery systems. *J Pharm Pharm Sci* 2003;**6(1)**:33-66.
4. Panchagnula R, Singh R, Ashokraj Y. *In vitro* evaluation of modified release formulations of nifedipine from Indian market. *Indian J Pharm Sci* 2007;**69**:556-561.
5. Pratheep Jose, Venkatesh Kumar K, Mohamed Saleem TK, Dilip C and Azeem AK. Sustained release drug delivery systems of Cefuroxime Axetil, Scholars Research Library, Der Pharmacia Litte 2011;**3(3)**: 325-332.
6. Crison JR, Weiner ND, Amidon GL. Dissolution media for in vitro testing of water-insoluble drugs: effect of surfactant purity and electrolyte on in vitro dissolution of carbamazepine in aqueous solutions of sodium lauryl sulfate. *J Pharm Sci* 1997;**86(3)**:384-388.
7. Grundy JS, Anderson KE, Rogers JA, Foster RT. Studies on dissolution testing of the nifedipine gastrointestinal therapeutic system. I. Description of a two-phase in vitro dissolution test. *J Control Release* 1997;**48**:1-8.
8. Pillay V, Fassihi R. Evaluation and comparison of dissolution data derived from different modified release dosage forms: an alternative method. *J Control Release* 1998;**55(1)**:45-55.
9. Shah VP, Konecny JJ, Everett RL, McCullough B, Noorizadeh AC, Skelly JP. In vitro dissolution profile of water-insoluble drug dosage forms in the presence of surfactants. *Pharm Res.* 1989;**6(7)**:612-618.
10. Shah VP, Noory A, Noory C, McCullough B, Clarke S, Everett R, Naviasky H, Srinivasan BN, Fortman D, Skelly JP. *In vitro* dissolution

- of sparingly water-soluble drug dosage forms. *Int J Pharm* 1995;**125**:99-106.
11. Rajeev Gupta, Soneil Guptha, Krishna Kumar Sharma, Arvind Gupta, and Prakash Deedwania Regional variations in cardiovascular risk factors in India: India heart watch *World J Cardiol* 2012;**4(4)**:112–120.
 12. United States Pharmacopeia 30 and National Formulary 25. The United States Pharmacopeial Convention, CD ROM; 2007.
 13. Higuchi t. Mechanism of sustained-action medication. Theoretical analysis of rate of release of solid drugs dispersed in solid matrices. *J Pharm Sci* 1963;**52**:1145-1149.
 14. Korsmeyer RW, Gurny R, Doelker E, Buri P, Peppas NA. Mechanisms of solute release from porous hydrophilic polymers. *Int J Pharm* 1983;**15**:25-35.

Cite this Article as: Medisetty GD, Botta GB, Yamana UM, Avasarala A. Preparation and Evaluation of Nifedipine sustained release Tablet by using Natural Gums as release retardant. *J Compr Phar* 2014;1(3):78-84