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Formulation and evaluation of sustained release matrix tablet of Nisoldipine

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ABSTRACT :

Controlled discharge and maintained discharge sedate conveyance has endedup the measures within the present day pharmaceutical plan and seriously investigate for accomplishing way better medicate item adequacy, unwaverinquality and security. Verbal supported discharge medicate conveyance (OSRDD) medicine will proceed to account for the biggest share (up to 80%) of medicate conveyance frameworks. The framework tablet planning shows up to be most attractive approach for the method improvement and scale-up point of see. A calcium channel blocker, Nisoldipine has found its appropriateness in cardiovascular infections exhorted to require the long term treatment of cardiovascular medicaments like anti-anginals, anti-hypertensives, etc. The calcium channel blockers are utilized as the potential operators for the treatment of these infections. They are considered as a moderate calcium channel blockers.

The coordinate compression strategy was received for the arrangement of maintained discharge network tablets with the 10mm punches and focused on weight of 450mg. The % medicate discharge considers for combined hypromellose and xanthan gum frameworks affirmed the group H2X2 (at the conclusion of 12 hours) as per USP criteria Test 2, which provide the 93.78% medicate discharge. Consequently, this definition was optimized and subjected to discharge dynamic consider and quickened steadiness ponders.

Keywords: Calcium channel blocker, Nisoldipine, Matrix tablet, Sustain release, Control releas

INTRODUCTION

SUSTAINED RELEASE SYSTEM

The goals of sustained drug delivery are to conserve and maintain effective drug concentration, to improve compliance and to decrease side effects. Oral sustained release formulations aim at releasing drug at zero order rate of release. Physicochemical nature of drug generally decides pharmacokinetic profile of drug. Sustain release drug delivery system are formulated by decreasing rate of absorption or modifying the structure of drug.

Advantages

- Improved therpy
- Patient Convenience/improved patient compliance
- Economy

Disadvantages

- Dose Dumping
- Less flexibility in acute dose adjustment
- Poor in vitro in vivo correlation
- Patient variation
- Sustained Release dosage forms are expensiveMaterial: Nisoldipine, HPMC K100LV, Eudragit L100-55, Microcrystalline cellulose, Lactose, Magnesium Stearate Experimental Work

Determination of melting point:

• Melting points of Nisoldipine and . were determined by capillary method.

Solubility:

The solubility of Nisoldipine and . in various media was observed.

FTIR Spectroscopy

• The FT-IR spectrum for the obtained gift sample of pure drug was obtained by KBr method and compared with the standard FT-IR spectra.

Compatibility studies:

• FT-IR spectroscopic studies were performed to check the compatibility between the drug and polymer in formulation and in final dosage form. The FT-IR spectra of drug alone and with formulation polymers were obtained by KBr method and compared with the standard FT-IR spectrum of the pure drug.

Determination of λ max:

From the stock solution, a suitable concentration of Nisoldipine (10 µg/ ml) was prepared in distilled water and UV scan was taken for the above stock solutions between the wavelengths of 200- 400 nm. The absorption maximum was found to be 237 nm and this wavelength was selected and utilized for further studies

COMPOSITION OF MATRIX TABLETS

Ingredients	All batch	All batches quantity in mg/tablet				
	and substates quantity in hig/more					
(mg)	F1	F2	F3	F4	F5	
Nisoldipine	90	90	90	90	90	
HPMC K100LV	45	90	180	270	-	
Eudragit L100-55	-	-	-	-	45	
Microcrystalline cellulose	155.25	132.75	87.75	42.75	155.25	
Lactose	155.25	132.75	87.75	42.75	155.25	
Magnesium Stearate	4.5	4.5	4.5	4.5	4.5	
Fotal weight	450	450	450	450	450	

PREPRATION OF MATRIX TABLETS

The corresponding amounts of active ingredient(drug-Nisoldipine), HPMC, Eudragit, microcrystalline cellulose and lactose were accurately weighed. The powders were sieved using screen #25. The screened powder was then transferred into the turbula mixer jar and mixed for 10 minutes. Magnesium stearate was accurately weighed, sieved through screen #25 and added to the turbula jar and mixed or an additional 2 minutes. The powder mix was then compressed into tablets using the instrumented tablet press, using a 7 mm round punch. Tablets were collected during compression for in-process testing (weight and hardness) The tablets were then stored in airtight high density polyethylene (HDPE) bottles until further testing.

EVALUATION OF MATRIX TABLETS

Pre-compressional Studies

Mixed powder were evaluated for various properties like bulk density, tapped density, compressibility index, Hausner ratio, flow properties (angle of repose) by using standard procedures. All studies were carried out in triplicate (n=3) and average values are reported with respective standard deviation.

Bulk Density and Tapped Density:

Both loose bulk density (LBD) and tapped bulk density (TBD) of prepared granules were determined. A quantity of 10 gm of blend from each formula, previously shaken to break any agglomerates formed was introduced in to 50ml measuring cylinder. The initial volume was noted, the cylinder was allowed to fall under its own weight on to a hard surface from a height of 2.5 cm by using bulk densitometer. The tapping was continued until no

further change in volume was noted. LBD and TBD were calculated using the following equations. (According to the USP-NF Guidelines 100 gm of sample was taken. If it is not possible to use 100 gm, the amount of the test sample and the volume of cylinder may be modified). LBD= Weight of the Granules/Untapped Volume of the packing TBD=Weight of the Granules/Tapped Volume of the packing

Compressibility Index:

The Compressibility Index of the blend was determined by Carr's compressibility index. It is a simple test to evaluate the LBD and TBD of a powder and the rate at which it is packed down. The formula for Carr's Index is as below: Carr's Index (%) = [(TBD-LBD) x100]/TB

Hausner's Ratio:

Hausner's Ratio was determined by Following Equation Hausner's Ratio = Tapped Density / Bulk Density

Angle of repose:

Angle of repose was determined by measuring the height and radius of the heap of the granules. A funnel was fixed to a stand and bottom of the funnel was fixed at a height of 3 cm from the plane. Granules were placed in funnel and allowed to flow freely and the height and radius of the heap of granules was measured. Similar studies were carried out after incorporating lubricants / glidants calculated using the equation.

POST-COMPRESSIONAL STUDIES

Hardness test:

It indicates the ability of a tablet to withstand mechanical shocks while handling. Hardness of tablets was determined using a validated Monsanto hardness tester. It is expressed in kg/cm^2 . Six tablets according to USP Guidelines were randomly picked from each batch and analyzed for hardness. The mean and standard deviation were also calculated.

Weight variation test:

According to USP-NF twenty tablets were selected randomly from each batch and weighed individually to check for weight variation.

Friability test:

Roche friabilator was used for friability test. According to IP guidelines Pre weighed tablet(WInitial) sample (20 tablets) were placed in the friabilator apparatus and rotated at 25 rpm for a period of 4 min. Tablets were again weighed (Wfinal) and the percentage weight loss in tablet was determined using formula. The % Friability of tablets less than 1% are considered acceptable.

DRUG CONTENT:

Nisoldipine:

Standard Solution:

100 mg of pure drug was weighed accurately and dissolved in 5 ml of distilled water. A sufficient quantity of distilled water was added to produce 100 ml and mixed well. From this 1 ml taken and distilled water was added to produce 100 ml.

• Sample Solution:

20 tablets were weighed accurately and finely powdered. To powder equivalent to 100 mg of Nisoldipine, 15 ml of distilled water was added and dispersed with the aid of shaker for 15 minutes. Sufficient quantity of distilled water was added to produce 100 ml, mixed well and filtered. To 1 ml of the filtrate distilled water was added to produce 100 ml and mixed well. The absorbance of the resulting solution was measured at the 237 nm using blank in the reference cell. The total content of Nisoldipine in the solution was calculated using the absorbance of a standard solution. The above test was done in triplicate.

Drug content was determined by crushing the tablet in a glass mortar and pestle and extracting the drug in phosphate buffer pH 7.4 with continuous shaking on a rotary shaker (Remi instruments Ltd, Mumbai, India) for 24 h. The drug content in extracted fluid was analyzed using a UV-Spectrophotometer (UV- 1601, Shimadzu, Japan) at 237nm against

IN VITRO DISSOLUTION STUDY

Dissolution Studies

To understand the release profiles of the drug from the tablets, dissolution experiments were performed in simulated gastric (0.1 N HCl, i.e., pH 1.2) and intestinal (pH 7.4) conditions. The release of Nisoldipine from the tablet was studied using USP XXIII paddle apparatus (Electrolab). Drug release profile was carried out in 750 ml of 0.1N HCl for 2 h and then in 900 ml of phosphate buffer solution (PBS) pH

7.4 maintained at 37 ± 0.5 °C and 100 rpm. Ten ml of samples were withdrawn at predetermined time intervals of every 1 h up to 12 h. The samples were replaced by its equivalent volume of dissolution medium and were filtered through 0.45 µm whatman filter paper and assayed at 237 nmby UV spectrophotometer (Evolution 201, UV-visible spectrophotometer, Thermo Fisher Scientific, USA).

RESULTS AND DISCUSSION

ANALYSIS OF DRUG

Description:

Dr	rug	Description
Ni	soldipine	A white, odorless, crystalline powder and has a bitter taste

Determination of melting point:

Melting point of Nisoldipine and . were determined by capillary method.

Drug	Melting pont
Nisoldipine	212 OC

Solubility:

Nisoldipine was found to be soluble in water, formic acid, methanol & chloroform. It was slightly soluble in ethanol.

Fourier Transformed Infrared (FT-IR) Spectroscopic Analysis:

• DETERMINATION OF λ max : Determination of λ max of Nisoldipine

The absorption maximum Nisoldipine was found to be 237 nm and this wavelength was selected and utilized for further studies.

Figure : IR spectra of pure Nisoldipine



PREPARATION OF CALIBRATION CURVE

Table: Absorbance values of Nisoldipine in 0.1 N HCl					
Sr. No.	Concentration in mcg/ml	Absorbance mean ± SD* (237nm)			
1	0	0			
2	2	0.116±0.002			
3	4	0.224±0.003			
4	6	0.332±0.004			
5	8	0.434±0.001			
6	10	0.536±0.001			

Standard deviation n=3



EVALUATION OF MATRIX TABLETS:

Evaluation of pre-compression parameters

Formul- ation	Bulk Density* (g/Cm3)	Tapped Density* (g/Cm3)	Compressib- ility Index* (%)	Hausner Ratio*	Angle of Repose*(O)
F1	0.517±0.004	0.564±0.004	8.33±0.021	1.09±0.08	23.62±0.12
F2	0.510±0.003	0.555±0.002	8.10±0.022	1.08±0.07	23.89±0.26
F3	0.513±0.006	0.575±0.007	10.78±0.026	1.12±0.10	22.84±0.62
F4	0.521±0.006	0.564±0.004	7.62±0.020	1.08±0.07	25.64±0.21
F5	0.500±0.002	0.553±0.002	9.58±0.024	1.10±0.10	21.58±0.15

POST-COMPRESSIONAL STUDIES

	Hardness*	Weight	Friability*	Content
Formulation	(kg/cm2)	Variation*(mg)	%	Uniformity (%)
F1	5.0 ± 0.04	449 ± 2.57	0.80 ± 0.02	98.6 ± 0.05
F2	5.2 ± 0.05	449 ± 2.28	0.51 ± 0.03	99.5 ± 0.03
F3	5.2 ± 0.08	448 ± 3.57	0.43 ± 0.02	99.5 ± 0.02
F4	5.4 ± 0.04	446 ± 2.39	0.42 ± 0.03	97.7 ± 0.03
F5	4.6 ± 0.04	439 ± 2.13	0.38 ± 0.01	98.5 ± 0.03

DISSOLUTION STUDIES OF MATRIX TABLET:

.Time (HRS)	Mean Cumulative % Drug Release of all Formulation (Mean 🗆 SD, n=3) Formulation						
	1	96.4±0.46	52.2±0.28	20.22±0.80	16.23±0.78	98.1±0.45	
2	98.4±0.79	82.2±0.90	30.12±0.10	22.26±0.36	98.1±0.64		
3	98.4±0.40	90.2±0.85	38.21±0.19	31.63±0.16	98.1±0.64		
4	98.4±0.40	94.6±0.92	50.14±0.69	39.67±0.92	98.1±0.64		
5	9.4±0.40	97.1±0.66	60.23±0.03	44. ±0.3576	98.1±0.64		



Figure :Nisoldipine release from SR matrix table

Conclusion

From the complete study, it is concluded that, HPMC K100LV & Eudragit® L100-55 at a concentration of 20% respectively produced sustained release Nisoldipine/ matrix tablets that are similar to the marketed product (Dilzem SR) in-vitro according to the f2 similarity factor.

PVAP & dibasic calcium phosphate at a concentration of 39.5% respectively, produced sustained release Nisoldipine matrix tablets that are similar to the marketed product (Dilzem SR) in vitro according the f2 similarity factor.

Optimized sustained release Nisoldipine . matrix tablets, showed square root of time dependent kinetics of drug release indicating a dissolution and diffusion controlled release mechanism.

Selected polymers and their concentrations are also capable of sustaining the release of drug Nisoldipine beside drug concentration.

The in-vivo X-ray study of selected sustained release HPMC and Eudragit and PVAP Nisoldipine matrix Tablets proved that the polymer utilized for the optimization of the formulation showed the sustaining activity in-vivo in rabbit by sticking to various sites in the GIT. Under long term storage conditions at 25oC and 60% RH, stability testing performed on the selected HPMC/Eudragit and PVAP tablets showed no significant change in the dissolution rates. Based on this finding, the recommended storage conditions are 25oC and 60% RH. Based on the above, it is concluded that sustained release Nisoldipine/. matrix tablets was developed using HPMC and Eudragit combination and PVAP as the release sustaining excipients. In vitro testing indicated that sustained release Nisoldipinete matrix tablets had similar dissolution behavior to the marketed product according to the model independent FA guideline (f2 factor).

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