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Formulation and Evaluation of sustained release Matrix Tablet of Cardizem HCL

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ABSTRACT :

The controlled and continuous drug distribution system has become necessary in modern drug development due to their ability to increase medical efficacy, improve patient compliance and ensure drug safety and reliability. Of these, oral continuous release drug delivery (OSRDD) systems represent an important part - about 80% - all drug distribution technologies are currently in use.

Matrix tablets are one of the most promising approaches for continuous drug delivery, especially from a formulation and scale-up perspective. In this study, continuous release of cardizam hydrochloride, a calcium channel inhibitor was usually prescribed for long -term management of heart conditions such as hypertension and angina. Calcium channel blockers classified as slow acting agents, widely used in cardiac.

The tablet was designed using the direct compression method, which employs 10 mm punches with a target tablet of 450 mg. Various Yogas- especially Hypromalose and Zanthan Gum- were evaluated for their drug release profiles involving a combination of hydrophilic polymers. Amid tested yogas, the batch H2X2 demonstrated optimal continuous release, according to the USP Test 2 criteria, achieving 93.78% drug release in 12 hours.

Based on these results, the H2X2 formulation was selected for further investigation, including the drug release canteix and quick stability tests.

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

INTRODUCTION

SUSTAINED RELEASE SYSTEM

The ongoing goal of drug collection is to maintain and maintain effective drug concentrations, improve compliance and reduce side effects. The purpose of oral yogas for continuous release is to release the drug at the rate of zero release. The physical chemical properties of a drug are usually determining the pharmacocinetic profile of a drug. The Sustain release pharmaceutical delivery system is developed by reducing the absorption rate or by changing the composition of the drug.

Benefit

1. Better bag
2. Patient facility/better patient compliance
3. economy

Loss

1) dose dumping
2) Low flexibility in acute dose adjustment
3) Poor in these vitro - in vivo correlation
4) Patient variation
5) Constant release doses are expensive
6) Materials: Cardizam hydrochloride, HPMC K100LV, EUDRAGIT L100-55, Microcystline Cellulose, Actose, Magnesium Steal Experimental Work

Determination of melting point:

Cardizem hydrochloride and melting points of metopolol succinate were determined by the capillary method.

Solubility:

The solubility of cardiops hydrochloride and metoprolol was observed in various media.

Bro -boroscopy

The FT-IR spectrum was obtained by the KBR method for the gift sample obtained and compared with the standard FT-IR spectra.

Compatibility Studies:

The FT-RI spectroscopic studies were performed to confirm the compatibility between the drug and the drug and the polymer in the form of final doses. This was preserved by the KBR method with the drug-cavalry FT-RI spectra and oral polymer and compared to the standard FT-Ritra of pure drugs.

Determination of λ_{max}:

From the stock solution, a suitable concentration of cardiosam hydrochloride (10 µg/ ml) was prepared in distilled water and UV scan was taken for the above stock solutions between the wavelength of 200–400 nm. Absorption was found to be maximum 237 Nm and this wavelength was selected and used for further studies.

COMPOSITION OF MATRIX TABLETS

Table No : Composition of Cardizem Hydrochloride

Ingredients (mg)	**All batches quantity in mg/tablet**				
	FD1	**FD2**	**FD3**	**FD4**	**FD5**
Cardizem Hydrochloride	**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**
Total weight	**450**	**450**	**450**	**450**	**450**

PREPRATION OF MATRIX TABLETS

Accurate weight measurements were made up of the correct amount of lactose, microcystline cellulose, HPMC, eudragit and active ingredients (drug, cardizom hydrochloride). Screen #25 was used to sieve particles. After the screen was performed, the powder was put into the turbula mixer jar and stirred for ten minutes. After being properly weighed and sieve through screen #25, the magnesium steerate was added to the turbula jar and shaken for two and minutes. A 7 mm round punch was then used to compress the powder mixture in the tablet using an instructed tablet press. During compression, pills were collected for in-processes test (hardness and weight). Before undergoing additional tests, tablets were placed in bottles of Airtight High Density Polyethylene (HDPE).

EVALUATION OF MATRIX TABLETS

Pre-compressional Studies[95]

Mixed powder was evaluated using standard procedures for various properties such as bulk density, tap density, compressed index, hoosar ratio, flow properties (angle of reposes). All studies were performed in three copies (n = 3) and reported with the average value related standard deviation.

Bulk Density and Tapped Density:

Both the tapped bulk density (TBD) and loose bulk density (LBD) were measured. A 50 ml measuring cylinder was filled with 10 grams of a mixture of each formula, which was shaken to break any aglomerates formed. Using a wholesale densitometer, the cylinder was allowed to fall 2.5 cm on a hard surface under its own weight after entering the initial volume. Tapping was placed until there was no more audio variation. The following formulas were used to determine LBD and TBD. According to the USP-NF guidelines, a sample weighing 100 grams was collected. If 100 grams cannot be used, the testing samples and the volume of cylinder can be changed.

Lbd = Unused amount of granules of granules tbd = Volume of Volume of Weight/Packing

Compressibility Index:

The compress of the mixture was determined by the compressed index of the index Carr. It is a simple test to evaluate LBD and TBD of a powder and the rate at which it is packed. The formula for Carr's index is like 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:

The angle of reposes was determined by measuring the height and radius of the pile of granules. A funnel was fixed for a stand and was fixed at a height of 3 cm from the aircraft below the funnel. The corpuscles were placed in the funnel and allowed to flow independently and measured the height and radius of the pile of granules. Similar studies were conducted after the inclusion of calculated lubricants / glidants using the equation.

POST-COMPRESSIONAL STUDIES

Hardness test:

It indicates the ability of a tablet to withstand mechanical shock when handling. The stiffness of tablets was determined using a valid monsanto hardness tester. It is expressed in kg/cm2. According to the USP guidelines, six tablets were randomly raised from each batch and analyzed for rigidity. Media and standard deviations were also calculated.

Weight variation test:

According to the USP-NF, twenty pills were selected randomly from each batch and were personally weighed to check weight variation.

Farability test:

The Rosh Fibilateer was used for the Feribility Test. According to IP guidelines, pre -walled tablet (winematial) sample (20 tablets) were placed in a fibilater equipment and rotated at 25 rpm for a 4 -minute period. The tablet was re -weighed (wfinal) and the percentage weight loss in the tablet was determined using the formula. Feruability of less than 1 % tablet is considered acceptable.

DRUG CONTENT:

Cardizem Hydrochloride:

Standard Solution:

The 100 mg of pure drug was accurately weighed and dissolved in 5 ml distilled water. Adequate amount of distilled water was added to 100 mL and mixed well to produce well. This was taken from 1 mL and the distilled water was added to produce 100 mL.

A) Sample solution:

20 bullets were weighed accurate and finely powder. To powder equal to 100 mg of cardium hydrochloride, 15 mL of distilled water was added for 15 minutes and spread with the help of a shaker for 15 minutes. 100 mL, adequate amount of distilled water added for mixed well and filtered production. 1 mL of filtrate distilled water was added to 100 mL and mixed well. The absorption of the resulting solution was measured at 237 Nm using the blank in the reference cell. The total content of cardium hydrochloride in the solution was calculated using the absorption of a standard solution. The above test was done in three copies.

The drug content was determined by crushing a glass mortar and tablet in pestle and in the phosphate buffer pH 7.4, by taking out a constant shakes on a rotary Sheker (Remy Instruments Limited, Mumbai, India) for 24 hours. The analysis of drug material in extracted fluids was analyzed against 237Nm using a UV-spectrophotometer (UV-1601, Shimdzu, Japan)

IN VITRO DISSOLUTION STUDY

Dissolution Studies

To understand the release profiles of the drug from tablets, dissolution experiments were performed in fake gastric (0.1 N HCL, ie, pH 1.2) and intestines (pH 7.4). The release of cardiosam hydrochloride from the tablet was studied using USP XXIII paddle equipment (electrolab). The drug release profile was done in 750 mL of 0.1n HCL for 2 hours and then 900 mL phosphate buffer solution (PBS) in pH

7.4 37 kept at 37 ± 0.5 .c and 100 rpm. Ten mL samples were withdrawn for 12 hours at a pre -determined time interval of each 1 hour. The samples were replaced by its dissolve amount of its disintegration medium and was filtered via 0.45 µm Whatsan filter paper and tested in 237 NMBY UV spectrophotometer (Evolution 201, UV-Druce Spectrophotometer, Thermo Fisher Scientific, USA).

RESULTS AND DISCUSSION

ANALYSIS OF DRUG

Description:

Drug	Description
Cardizem Hydrochloride	A white, odorless, crystalline powder and has a bitter taste

Determination of melting point:

Melting point of Cardizem Hydrochloride and Metoprolol Succinate were determined by capillary method.

Drug	Melting pont
Cardizem Hydrochloride	212 ^{0}C

Solubility:

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

Fourier Transformed Infrared (FT-IR) Spectroscopic Analysis:

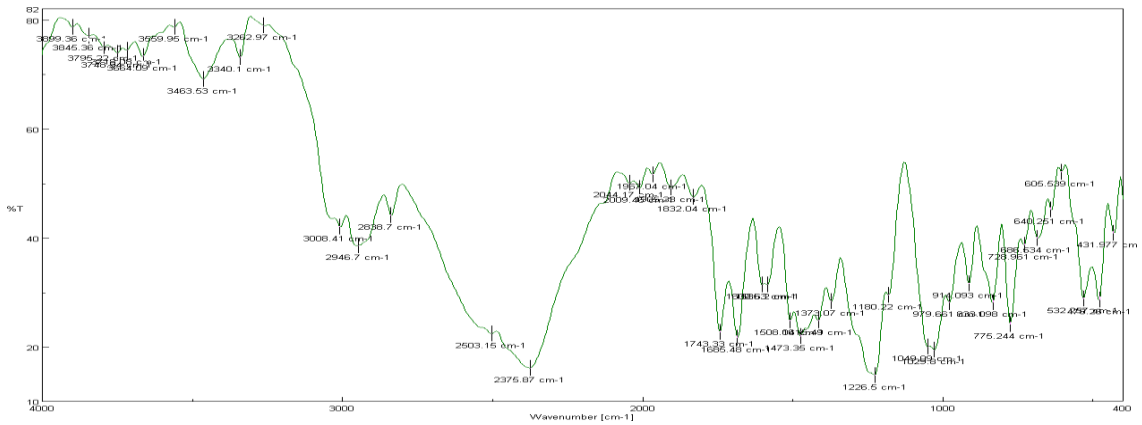


Figure : IR spectra of pure Cardizem hydrochloride

DETERMINATION OF λ max : Determination of λ max of Cardizem Hydrochloride

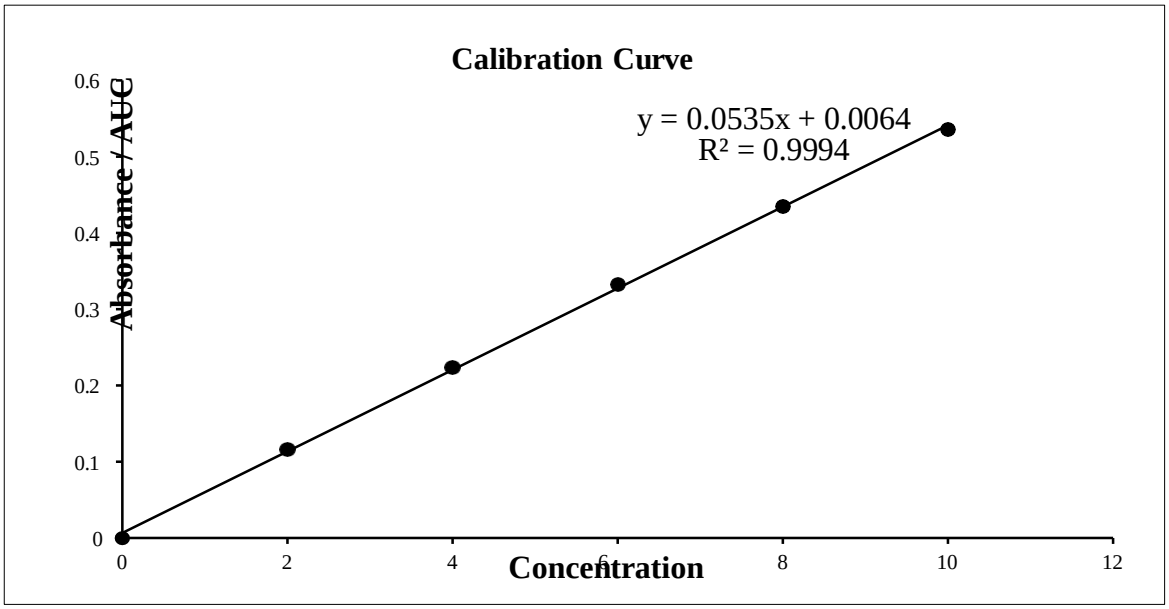
The absorption maximum Cardizem Hydrochloride was found to be 237 nm and this wavelength was selected and utilized for further studies.

PREPARATION OF CALIBRATION CURVE

Table: Absorbance values of Cardizem Hydrochloride 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/Cm^3)	Tapped Density* (g/Cm^3)	Compressib- ility Index* (%)	Hausner Ratio*	Angle of Repose*(^{O})
FD1	0.517±0.004	0.564±0.004	8.33±0.021	1.09±0.08	23.62±0.12
FD2	0.510±0.003	0.555±0.002	8.10±0.022	1.08±0.07	23.89±0.26
FD3	0.513±0.006	0.575±0.007	10.78±0.026	1.12±0.10	22.84±0.62
FD4	0.521±0.006	0.564±0.004	7.62±0.020	1.08±0.07	25.64±0.21
FD5	0.500±0.002	0.553±0.002	9.58±0.024	1.10±0.10	21.58±0.15

*mean (n = 3)

POST-COMPRESSIONAL STUDIES

Formulation	Hardness* (kg/cm^2)	Weight Variation*(mg)	Friability* %	Content Uniformity (%)
FD1	5.0 ± 0.04	449 ± 2.57	0.80 ± 0.02	98.6 ± 0.05
FD2	5.2 ± 0.05	449 ± 2.28	0.51 ± 0.03	99.5 ± 0.03
FD3	5.2 ± 0.08	448 ± 3.57	0.43 ± 0.02	99.5 ± 0.02
FD4	5.4 ± 0.04	446 ± 2.39	0.42 ± 0.03	97.7 ± 0.03
FD5	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				
	FD1	FD2	FD3	FD4	FD5
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

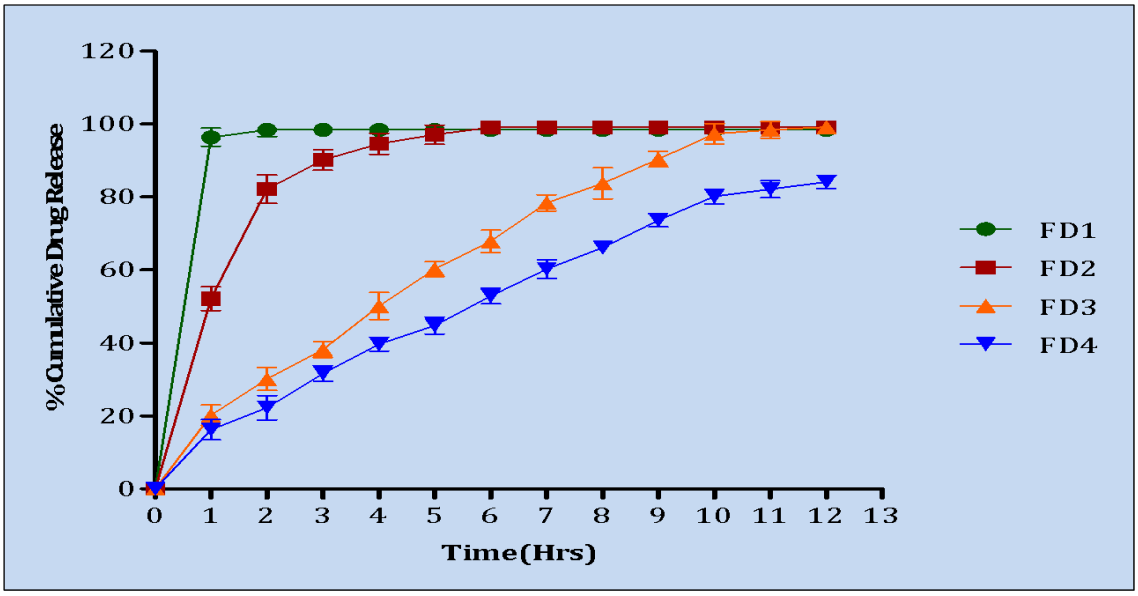


Figure : Cardizem hydrochloride release from SR matrix table

Conclusion

Based on a complete investigation, it was determined that, at 20% concentration, HPMC K100LV and EUDRAGIT® L100-55 created continuous release-release cardizom hydrocholoride/matrix tablets, which in the in vitro, are similar to the Dilzem sr on the basis of F2 equality.
Element.
The F2 is compared to the continuous release cards, the constant release cards made with PVAP and debacic calcium phosphate, in the respective concentrations of 39.5% generated in the vitro, compared to the Dilzem SR.
The drug release was displayed using a constant release cardiosum hydrochloride metoprolol-matrix tablets, which suggested a disintegration and dissemination-controlled release mechanism.
In addition to the drug concentration, some polymers and their concentrations may also maintain the release of cardiozam hydrochloride.
Polymer used the in-Vivo X-ray research of specific continuous continuous release HPMC and Eudragit and PVAP Cardium Hydrochux Matrix Tablets, used to optimize continuous activity in vivo in vivo in rabbits, demonstrating continuous activity in vivo in rabbies. The stability test on HPMC/UDRGIT and PVAP tablet selected under long -term storage settings on 25 ° C and 60% relative humidity did not make any admirable changes to the rates of disintegration. The suggested storage conditions are 25 ° C and 60% relative humidity in the light of this conclusion. According to the above information, the continuous release cardizam was made with hydrochloride/metoprolol successful matrix tablets PVAP as a mixture of exempia and HPMC and Eudragit was released.

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