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CARVEDILOL SUSTAIN RELEASE FORMULATION USING HYDROPHILIC POLYMERS

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ABSTRACT

In the present study an attempt has been made to develop carvedilol matrix tablets using hydrophilic polymers (hydroxyl propyl methyl cellulose, ethyl cellulose and carbopol). The matrix tablets were prepared by direct compression method. All the physico chemical parameters like hardness, friability and drug content have been evaluated. Results of the present study demonstrated that combination of hydrophilic polymers could be successfully employed for formulating controlled release matrix tablets of carvedilol.

Key words: carvedilol, hydrophilic polymer, sustain release matrix tablet

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INTRODUCTION

Now a day's conventional dosage forms of drugs are rapidly being replaced by the new and the novel drug delivery systems. Amongst, these the controlled release/sustained release dosage forms have become extremely popular in modern therapeutics. Matrix system is the release system which prolongs and controls the release of the drug, which is dissolved or dispersed. A matrix is defined as a well-mixed composite of one or more drugs with gelling agent i.e. hydrophilic polymers. Introduction of matrix tablet as sustained release (SR) has given a new breakthrough over an extended time or denotes that the system is able to provide some actual therapeutic control whether this is of a temporal nature, spatial nature or both. Sustained release system generally do not attain zero order type release and usually try to mimic zero order release by providing drug in a slow first order. Repeat action tablet are an alternative method of sustained release in which multiple doses of drug are an alternative method of sustained release, in which, multiple doses are contained within a dosage form and each dose is released at a periodic interval. Delayed release system, in contrast, may not be sustaining, since often the function of these dosage forms is to maintain the drug in the dosage for some time before release, for example. Enteric coated tablet (2). A sustained release dosage form will provide a therapeutic concentration of the drug in the blood that is maintained throughout the dosing interval with a reduction in a peak concentration ratio (3, 4). Numerous drug delivery techniques have been developed to sustain the release of drugs, including triple-layered tablets (Geomatrix® technology) and

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osmotic pumps with laser drilled holes (OROS® technology). These technologies are intricate and relatively expensive to manufacture. Thus, there remains an interest in developing novel formulations that allow for sustained release of drugs using readily available, inexpensive excipients (5).

Carvedilol is a nonselective β-adrenergic blocking agent with α1-blocking activity. This is widely used as anti-hypertensive drug (6). Carvedilol is an antihypertensive drug with multiple mechanisms of action. It acts as a non-selective β and α-1 adrenergic receptor blocker and it also has vasodilating property that is attributed mainly to its α-1 receptor antagonist activity (7). Its conventional tablet dosage form is used to treat mild-to-moderate hypertension and angina pectoris. It exhibits poor absolute bioavailability of 25-35%. The half-life of the drug is 6 - 8 h. It's very poor aqueous solubility indicates that its absorption is dissolution rate-limited which results in irregular and delayed absorption. The aim of this work was to prepare matrix tablets containing carvedilol, hydrophilic polymer (hydroxyl propyl methyl cellulose, ethyl cellulose and carbopol) as matrix formers to control drug release.

MATERIALS AND METHODS

MATERIALS

Carvedilol (Arbindo Pharmceuticals Pvt Ltd.,) hydroxyl propyl methyl cellulose, ethyl cellulose and carbopol, magnesium state and talc from SD fine chemicals, Pvt Ltd, India

METHODS

Preparation of sustain release tablets

The matrix tablets were prepared by simple direct compression method. In this method, all the excipients and drug were geometrically mixed and that blend was directly used for compression. Different polymers were used in different concentrations to get good sustained release of drug, which imitate the drug release of the best formula. Different excipients were used, i.e., direct compressible excipients, lubricants and glidants to get good physical properties of the tablets. The weight of all tablets were kept constant i.e., 100 mg to minimize the effect of surface area/volume on the drug release pattern (8) Table-1.

Table-1 Drug, polymer and diluents concentration

Ingredients %w/w	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Drug	20	20	20	20	20	20	20	20	20	20
Ethyl cellulose	15	10	10	5	----	----	5	----	10	----
Carbopol	15	10	10	5		15	5	---	---	----
HPMC	----	10	----	15	10	15	10	10	5	5
Lactose	5	5	5	5	5	5	5	5	5	5
Talc	2	2	2	2	2	2	2	2	2	2
Magnesium streate	2	2	2	2	2	2	2	2	2	2
Total (%)	100	100	100	100	100	100	100	100	100	100

In vitro release studies

In vitro drug release studies of the matrix tablets were carried out using a six-station USP XXII type II dissolution test apparatus at 37 ± 0.5 °C and 100 rpm speed in 900 ml of 0.1M hydrochloric acid (gastric simulated fluid, pH 1.3) as a dissolution medium for the first 2 h and in intestinal simulated fluid (900 ml, pH 6.8) for the next 10 h.

Samples (10 ml) were withdrawn hourly over a period of 2 h, and the samples filtered The volume of dissolution medium was replenished with 10 ml of fresh dissolution medium. The absorbance of the samples was measured with a single-beam UV-spectrophotometer at 241 nm and the amount of drug released calculated. The release studies were conducted in triplicate, and mean values of drug released were plotted against time.

RESULTS AND DISCUSSION

The development of a successful formulation depends only on suitable selection of excipients. Hence the physical state of the drug (carvedilol) and the hydrophilic polymers (hydroxyl propyl methyl cellulose, ethyl cellulose and carbopol) individually and the admixture of drug and polymers used for sustain release preparation were studied by FTIR (Fig-1-2).

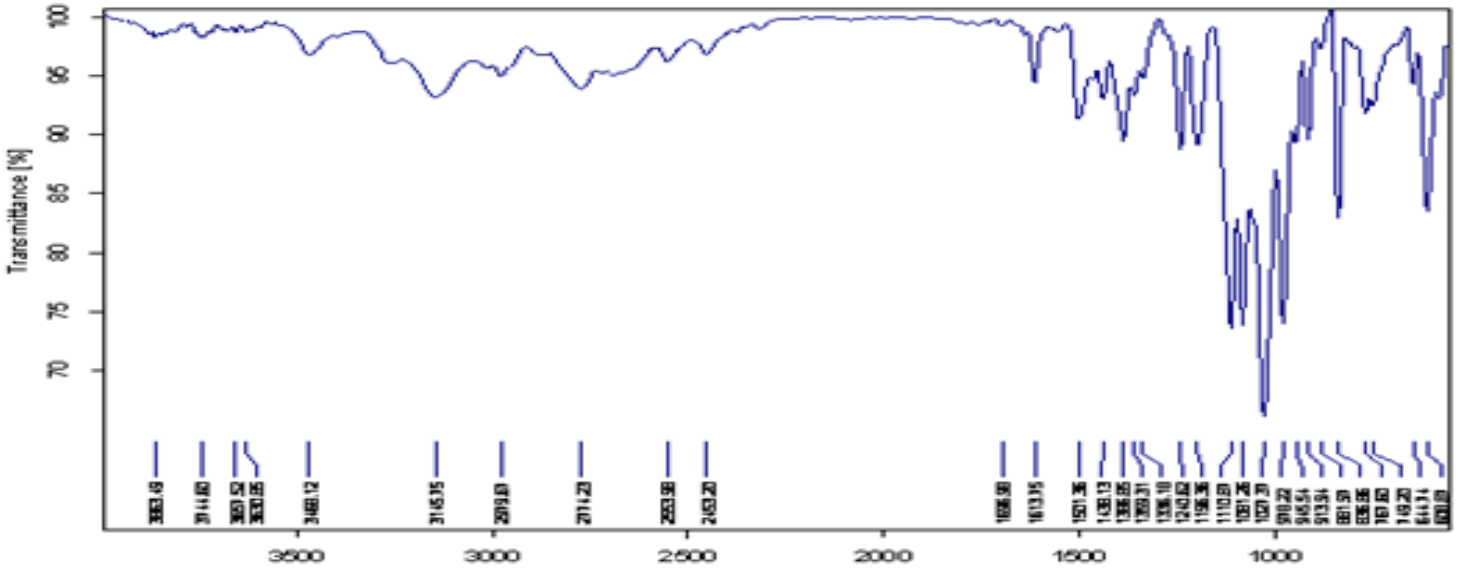

Fig-1 FT-IR of drug carvedilol

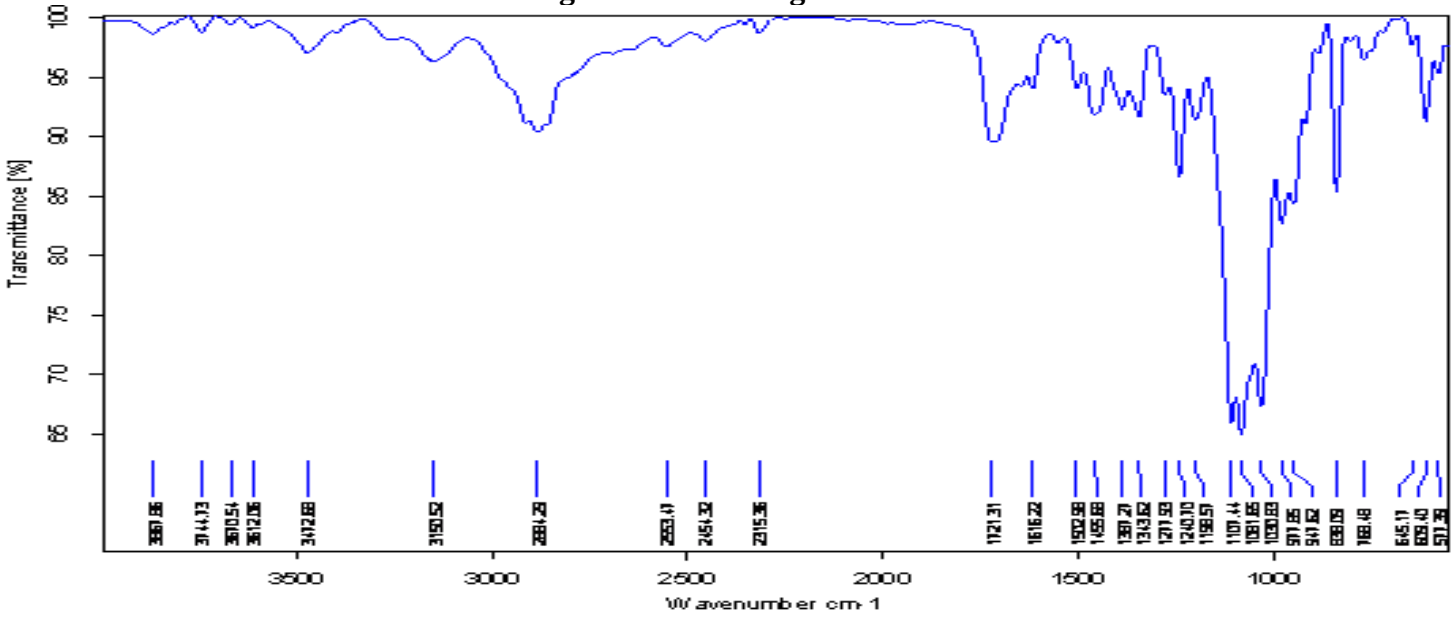

Fig-2 FT-IR of drug carvedilol + polymers

It was confirmed that no chemical modification of the drug has been taken place and thus they were proved to be compatible with each other and hence suitable for preparation of sustained release tablets.

The Flow properties of the granules were evaluated for angle of repose (Flow properties) and derived properties (Bulk density, Tapped density, Carr's index and Hausner's ratio) and the results were tabulated in table-1.

Table-1 Results for micrometric properties

S.NO	Angle of Repose	Bulk density	Tapped density	Carr's Index	Hausner's Ratio
F1	23.33 ± 0.17	0.455 ± 0.11	0.588 ± 0.02	22.61 ± 0.01	1.29 ± 0.11
F2	24.20 ± 0.12	0.445 ± 0.15	0.571 ± 0.11	14.36 ± 0.01	1.16 ± 0.02
F3	25.45 ± 0.11	0.435 ± 0.02	0.565 ± 0.2	16.21 ± 0.15	1.22 ± 0.2
F4	24.63 ± 0.2	0.475 ± 0.01	0.568 ± 0.3	15.61 ± 0..11	1.42 ± 0.3
F5	21.16 ± 0.5	0.445 ± 0.15	0.545 ± 0.15	15.22 ± 0.01	1.22 ± 0.02
F6	22.82 ± 0.15	0.455 ± 0.2	0.538 ± 0.19	19.12 ± 0.05	1.23 ± 0.11
F7	22.69 ± 0.26	0.435 ± 0.23	0.526 ± 0.03	20.12 ± 0.03	1.21 ± 0.07
F8	25.36 ± 0.15	0.485 ± 0.3	0.588 ± 0.2	21.61 ± 0.2	1.29 ± 0.3
F9	21.85 ± 0.26	0.456 ± 0.02	0.578 ± 0.5	22.61 ± 0.02	1.34 ± 0.001
F10	21.63 ± 0.3	0.476 ± 0.23	0.565 ± 0.12	20.61 ± 0.02	1.44 ± 0.02

INVITRO DRUG RELEASE STUDIES

The *in-vitro* drug release studies were conducted using pH 6.8 phosphate buffer solutions as dissolution medium and also represented graphically by taking Time (hrs) on X-axis and Cumulative percentage drug release on Y-axis (Table-2 and 3).

Table-2- *In-vitro* drug release data for F-7

Higuchi's data		Peppa's data	
Square root time	**Cumulative % drug release**	**Log time**	**Log cumulative % drug release**
0	0	0	0
1.414	25.56	0.30103	1.407
2	37.15	0.60206	1.569
2.44949	49.70	0.778151	1.696
2.828427	61.30	0.90309	1.787
3.162278	73.15	1	1.864
3.46402	85.75	1.079181	1.933

Table-3 *In-vitro* drug release data for F-7

In-vitro drug release		Zero order data		First order data	
Time (hrs)	**Cumulative % drug release**	**Time(hrs)**	**Mean % Release**	**Time(hrs)**	**Mean% log un release**
0	0	0	0	0	0
2	25.56	2	25.56	2	1.871
4	37.15	4	37.15	4	1.798
6	49.70	6	49.70	6	1.701
8	61.30	8	61.30	8	1.587
10	73.15	10	73.15	10	1.428
12	85.75	12	85.75	12	1.153

CONCLUSION

Based on the result F-7 was concluded as best. F-7 showed good linearity (r = 0.9768 to 0.9949), with slope (n) values ranging from 0.3318 to 0.4195, indicating that diffusion was the dominant mechanism of drug release, with these formulations indicative of quasi-fickian diffusion.

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