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FORMULATION PREPARATION AND PHYSICAL CHARACTERISTICS OF CR DILTIAZEM HCL WITH DIFFERENT POLYMER COMBINATIONS

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Abstract:

The drug delivery system (DDS) changes the formulation techniques and have made a great break-through progress. Started a simplest pill formulation and gradually improve the techniques regarding the new symptoms and indications and breakthrough in the developments of formulation to more sophisticated controlled release formulations. Polymers are the major components for the development of controlled release formulations. Chemicals included the magnesium stearate, Diltiazem HCl, lactose, polymers (Cabapol and Eudragit derivative) monobasic potassium phosphate, starch, CMC, and other of analytical grade. Friabilator, Disintegration Apparatus, Syringes, Beakers, Dissolution Apparatus, Balance, UV-Visible Spectrophotometer, PH-meter, Hardness tester, volumetric flasks, Test tubes, Single Punch Machine, Verniar caliper and pre-formulation studies done. This study concluded that he different types of polymers were used in different combination which showed its physical characteristics according to the specifications mentioned in standards.

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INTRODUCTION:

In the last few decades, the drug delivery system (DDS) changes the formulation techniques and has made a great break-through progress. Started a simplest pill formulation and gradually improve the techniques regarding the new symptoms and indications and breakthrough in the developments of formulation to more sophisticated controlled release formulations (1). The formulations now turned in to the targeted delivery on tissues and cells (2). To achieve therapeutic blood plasma level is now made possible by Control Release dosage form which also enhances the therapeutic efficacy and patient compliance of those drugs having very short half-life (3). As compare to the conventional dosage form the Controlled release drugs releases the active ingredient/ingredients at rates, which are significantly different (4). The active ingredient releases from the CR formulation systems is predictable, reproducible (5). It also releases at required rate as compare to the traditional dosage forms which releases the active ingredient by the process of dissolution and/or diffusion (6). Thus, in traditional drug delivery systems the amount of drug can fluctuate in plasma widely and it may cause side effects (7).

Polymers are the major components for the development of controlled release formulations (8). They may be synthetic or natural (9). Synthetic polymers like eudragit is non-biodegradable, amorphous non-toxic and non-absorbable (10). As carbopol is a natural polymer which is suitable for matrix structures (11). The formulations containing carbopol 974P was considerably prolonged in concentration (12). Diltiazem is widely used calcium antagonist for the treatment of both hypertension and angina pectoris (13). Diltiazem produces the antihypertensive effects by relaxing the vascular smooth muscles and it decreases the peripheral resistance. Diltiazem has shown to produce enhance in exercise tolerance. It is one of the abilities of Diltiazem which reduces the myocardial oxygen demand. The half-life of Diltiazem is in between 3.0-4.5 hours which is very suitable to formulate CR matrix tablets (13).

METHODOLOGY:

Chemicals

All Chemicals included the magnesium stearate, Diltiazem HCl, lactose, polymers (cabapol and eudragit derivative) monobasic potassium phosphate, starch, CMC, and other of analytical grade.

Instruments

Friabilator, Disintegration Apparatus, Syringes, Beakers, Dissolution Apparatus, Balance, UV-Visible Spectrophotometer, PH-meter, Hardness tester, volumetric flasks, Test tubes, Single Punch Machine, Verniar caliper.

Pre-formulation Studies

1. **Particles size distribution**
   Particle size was analyzed by the help of different sieves which were specified according to the official specification.

Construction of Standard Curve of the active ingredient

According to the specified specifications standard cure was done by the help of UV visible spectrophotometer.

2. **Solubility studies**

Formulation development

Each tablet would be prepared according to the specifications and dose, mixing the drug and polymer by different ratios i.e 10.1, 10.2, 10.3 and the polymers 50-50%.

Preparation CR Matrix tablets.

According to the specified standard protocol matrix CR tablet were prepared at different drug and polymers + polymer ratios prepared the matrix tablets on single punch tableting machine.

Physical Characterization of the double layered CR Tablets.

All following physical tests would be performed

1. Friability
2. Hardness
3. Thickness
4. Weight variation by standard procedure accordingly.

Table 1: Formulation development of Diltiazem HCl 100mg CR Matrix Tablets

Drug + Polymer Ratio	Drug Diltiazem HCl)	Polymers	Lubricant Mg St. 0.5%	Spray dried Lactose)
		Eudragit RS 100+Xanthan Gum+ Carbopol 934 P plus		
10 ratio1	60 mg	6mg	0.5mg	33.5mg
10 ratio2	60 mg	12mg	0.5mg	27.5mg
10 ratio3	60 mg	18mg	0.5mg	21.5mg

Table 2: Formulation development of Diltiazem HCl 100mg CR Matrix Tablets

Drug + Polymer Ratio	Drug Diltiazem HCl	Polymers	Lubricant (Mg St. 0.5%)	Filler Spray dried Lactose)
		Eudragit RS 100+Guar Gum+Carbopol 934 P plus		
10 ratio 1	60 mg	6mg	0.5mg	33.5mg
10 ratio 2	60 mg	12mg	0.5mg	27.5mg
10 ratio 3	60 mg	18mg	0.5mg	21.5mg

RESULTS AND DISCUSSIONS:

Result of diltiazem HCl standard curve

Different concentrations of Diltiazem HCl were plotted against respective absorbances and straight line was obtained showed linearity between concentration and absorbance. The R^2 (Co-efficient of determination was 0.9998 and regression equation y=3.5187x+0.0024 was resulted and was used for calculations of percent drug release of Diltiazem HCl from its different CR matrix tablets. results of standard curve which are shown figure 1.

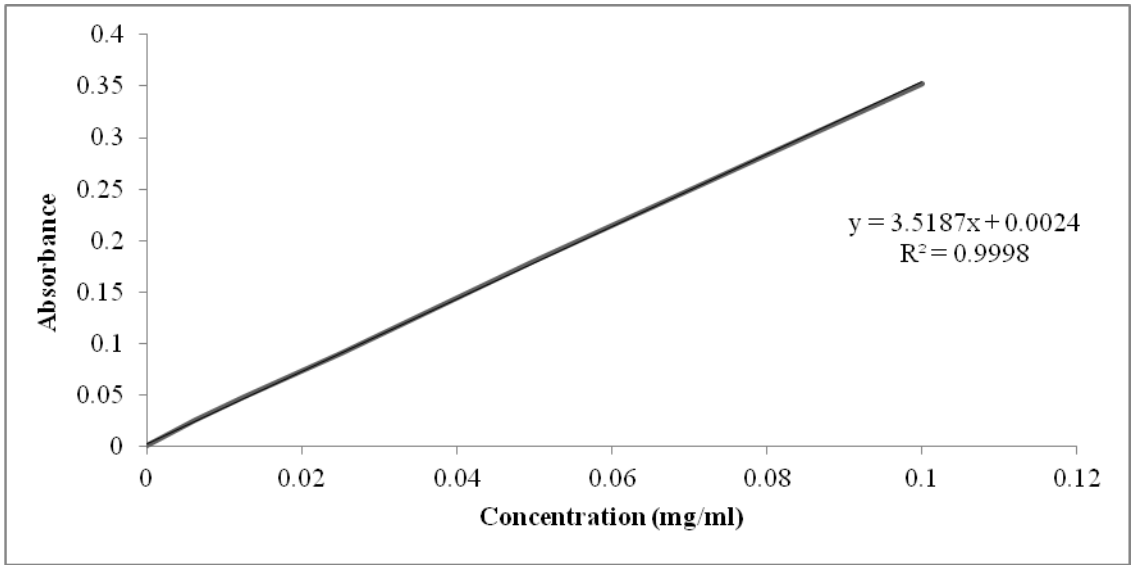

Fig.1: Diltiazem hydrochloride standard calibration curve

Diltiazem HCl solubility in Various Solvents

Solubility studies were conducted in different solvents and at different temperatures (25 ºC, 37 ºC and 40 ºC). Solubility was obtained in different solvents and highest (1.0mg/ml) in phosphate buffer (pH 7.2) and showed that Diltiazem HCl was freely soluble at this temperature and was selected as dissolution medium for *in-vitro* drug release studies.

Table 3: Diltiazem solubility in various solvents at different temperatures

S. No.	Solvent	pH	Temperature in C^0	Solubility (mg/ml)
1	Phosphate Buffer	6.8	40	0.82
2	Phosphate Buffer	6.8	37	0.80
3	Phosphate Buffer	6.8	25	0.79
4	Phosphate Buffer	7.2	40	0.92
5	Phosphate Buffer	7.2	37	1.1
6	Phosphate Buffer	7.2	25	0.89
7	Distilled Water	7.0	40	0.98
8	Distilled Water	7.0	37	0.997
9	Distilled Water	7.0	25	0.978

Table 4: Physical Characteristics of CR tablets

Formulations	Diameter	Thickness	Hardness	Friability	Weight variation
Eudragit RS 100 plus Carbopol 934P plus Xathan gum (10:1)	6.5	2.3±2.156	8.0	0.012	99.12
Eudragit RS 100 plus Carbopol 934P plus Xathan gum (10:2)	6.5	2.2	7.4	0.132	100.23
Eudragit RS 100 plus Carbopol 934P plus Xathan gum (10:3)	6.5	2.2	9.2	0.015	101.56
Eudragit RS 100 plus Carbopol 934P plus Guar gum (10:1)	6.5	2.3	9.6	0.038	102.45
Eudragit RS 100 plus Carbopol 934P plus Guar gum (10:2)	6.5	2.2	9.0	0.124	100.26
Eudragit RS 100 plus Carbopol 934P plus Guar gum (10:3)	6.5	2.3	8.9	0.006	100.34

Physical Characteristics of CR tablets

Tablets were elegant in appearance and the thickness ranged from 2.2±0.934 to 2.3±2.156, diameter ranged from 6.5±0.281 to 6.5±2.363, hardness ranged from 7.4±0.519 to 9.6±0.325, friability ranged from 0.006±0.238 to 0.132±1.107 and mean weight of CR tablets ranged from 99.12±0.282 to102.45±0.802. These results are within acceptable limits given by author Javaid, (1993). Results are shown in table 4.

CONCLUSION:

This study concluded that he different types of polymers were used in different combination which showed its physical characteristics according to the specifications mentioned in standards. The friability of the Diltiazem CR tablets was within the limits and the hardness is also within the limits. The thickness and Diameter showed its results near to the limits. Weight variations of all these formulations are within the limits. It is concluded that all the results of this study were within specified limits which showed that this study may further investigate the release profile and in-vivo studies.

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