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Research

Formulation Development And Evaluation Of Azilsartan Medoxomil Sustained Release Tablet

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Abstract

The purpose of the study was To design, formulate and evaluate sustained release tablets of Azilsartan Medoxomil which is expected to deliver the drug in controlled and sustained release manner with reduce frequency of drug administration, reduce GI tract side effects and improve patient compliance. The present work is aimed at preparation and evaluation of Sustained Release matrix tablets of Azilsartan Medoxomil using using HPMC, Vinyl pyrrolidone vinyl acetate as polymers in varying ratios. The tablet were evaluated for its Thickness, Hardness, Friability, Friability, Disintegration and in vitro drug release studies. The FTIR studies revealed no chemical interaction between the drug molecule and polymers and found that drug was compatible with used polymer. In vitro drug release study confirms that formulation F4 was the best formulation as it releases 98.87 % at the end of 12 hr. This confirms the developed Azilsartan Medoxomil tablet are promising for sustained release drug delivery system.

Keywords: Azilsartan Medoxomil, Disintegration, Administration, Hydroxy Propyl Methyl Cellulose.

INTRODUCTION

Sustained release tablets and capsules are commonly taken only once or twice daily, compared with counterpart conventional forms that may have to take three or four times daily to achieve the same therapeutic effect. Typically, sustained release products provide an immediate release of drug that promptly produces the desired therapeutic effect, followed by gradual release of additional amounts of drug to maintain this effect over a predetermined period. The sustained plasma drug levels provide by sustained release products often times eliminates the need for night dosing, which benefits not only the patients but the care given as well.[1]

The basic rationale of a sustained drug delivery system is to optimize the Biopharmaceutical, Pharmacokinetic and Pharmacodynamics properties of a drug in such a way that its utility is maximized through reduction in side effects and cure or control of condition in the shortest possible time by using smallest quantity of drug, administered by the most suitable route.[2]

The novel system of drug delivery offer a means of improving the therapeutic effectiveness of incorporated drugs by providing sustained, controlled delivery and / or targeting the drug to desired site. The goal of any drug delivery system is to provide a therapeutic amount of drug to the proper site in the body to achieve promptly and then maintain the desired drug concentration. There is a continuously growing interest in the pharmaceutical industry for sustained release oral drug delivery systems. There is also a high interest for design a dosage formulation that allows high drug loading, particularly for actives with high water solubility. Oral route has been the most popular and successfully used for sustained delivery of drugs because of convenience and ease of administration, greater flexibility in dosage form design and ease of production and low cost of such a system.[3,4]

MATERIALS AND METHODS

Material

Azilsartan Medoxomil was obtained as gift- sample from Mankind Pharma, Verna Pvt. Ltd. Verna Goa and Ethyl cellulose, HPMC of pharmaceutical grade were procured from Oxford Laboratories, Mumbai and Talc, Magnesium stearate, Micro crystalline Cellulose from SD Fine chemicals.

Pre-formulation studies

Pre- formulation is considered as important phase where researcher characterizes the physical and chemical properties of drug substance which helps to develop stable, effective and safe dosage forms and also check possible interaction with various excipients. The absorbance of above solutions was recorded at □max (248 nm) of the drug using double beam UV-Visible spectrophotometer.[5]

Compatibility Study FT-IR Spectra Analysis[6]

The FTIR analysis of Azilsartan Medoxomil was carried out for qualitative compound identification. The FTIR spectra for pure drug and with other excipients was obtained by placing the drug directly into the cavity and was determined by FTIR spectrophotometer in the wave number region of 4000-400 cm-

Preparation of tablet

The hydrophilic matrix tablets were prepared by either direct compression or wet granulation technique. In the direct compression, sustained-release matrix tablets were formulated to contain 80 mg of Azilsartan Medoxomil. The drug polymer ratio was developed to adjust drug release as per theoretical release profile and to keep total weight of tablet constant for all the fabricated batches under experimental conditions of preparation. Then add microcrystalline cellulose was incorporated as filler excipients to maintain the tablet weight constant. Powder were mixed and lubricated with 1% (W/W) magnesium stearate and then directly compressed on a sixteen station compression machine tablet machine at a tablet weight of 270 mg, with a flat, non-beveled punch of 12-mm diameter.[7,8]

Table 1: Formulation Designs of Sustained Release Tablets of Azilsartan Medoxomil

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
AM	80	80	80	80	80	80	80	80	80
HPMC	40	80	120	-	-	-	-	-	-
KOLLIDON -SR	-	-	-	40	80	120	-	-	-
EC	-	-	-	-	-	-	40	80	120
PVP	8	8	8	8	8	8	8	8	8
MCC	137.2	97.2	57.2	137.2	97.2	57.2	137.2	97.2	57.2
MS	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6
TALC	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2	3.2
Total	270	270	270	270	270	270	270	270	270

AM : Azilsartan Medoxomil
HPMC : Hydroxy Propyl Methyl Cellulose
EC : Ethyl Cellulose
PVP : Poly Vinyl Pyrrolidone
All the quantities are taken in mg.
Evaluation of Tablet

The evaluation of tablet was carried out on different parameter.

a) Angle of Repose

The angle of repose of granules was determined by the funnel-method. The accurately weighed granules were taken in a funnel. The height of the funnel was adjusted in such a manner that the tip of the funnel just touched the apex of the heap of the granules. The granules were allowed to flow through the funnel freely onto the surface. The diameter of the powder cone measured and angle of repose was calculated using the following equation.

$\tan \theta = h/r$

b) Determination of Bulk Density and Tapped Density

An accurately weighed quantity of the granules/ powder (W) was carefully poured into the graduated cylinder and volume (V_0) was measured. Then the graduated cylinder was closed with lid and set into the tap density tester (USP). The density apparatus was set for 100 tabs and after that the volume (V_f) was measured and continued operation till the two readings were equal.

The bulk density and the tapped density were calculated using the following formula.

Bulk density = $\mathbf{W/V_0}$

Tapped density = $\mathbf{W/V_f}$

c) Compressibility Index (Carr's Index)

Carr's index (CI) is an important measure that can be obtained from the bulk and tapped densities. In theory, the less compressible a material the more flowable it is.

CI = (TD-BD) x 100/TD

where, TD is the tapped density and BD is the bulk density

Table 2: In Process Evaluation of Granules

S. No.	Formulation	Bulk density (g/cm^3)	Tapped density (g/cm^3)	Carr's Index (%)	Hausner's ratio
1	F1	0.214	0.451	14.74	1.17
2	F2	0.308	0.464	15.38	1.18
3	F3	0.276	0.522	14.28	1.16
4	F4	0.341	0.488	12.11	1.13
5	F5	0.324	0.476	13.82	1.16
6	F6	0.320	0.597	15.39	1.24
7	F7	0.264	0.532	13.24	1.11
8	F8	0.282	0.498	16.75	1.21
9	F9	0.362	0.567	14.32	1.19

RESULT AND DISCUSSION

Compatibility Study FT-IR Spectra Analysis

The comparative FTIR studies of Drug and excipients combination revealed that no chemical interaction between the drug molecule and polymers and found that drug was compatible with used polymer. The FTIR spectra of pure drug and drug with excipients are shown in the Fig 1 & 2.

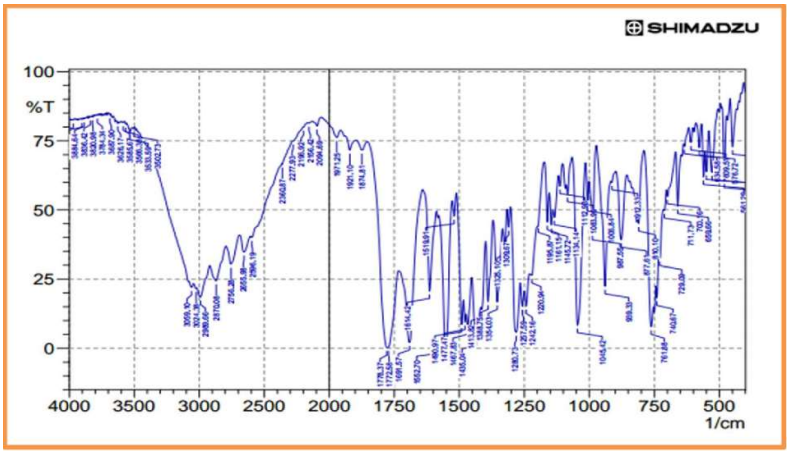

Fig 1: FT-IR Spectra of Pure drug (Azilsartan Medoxomil)

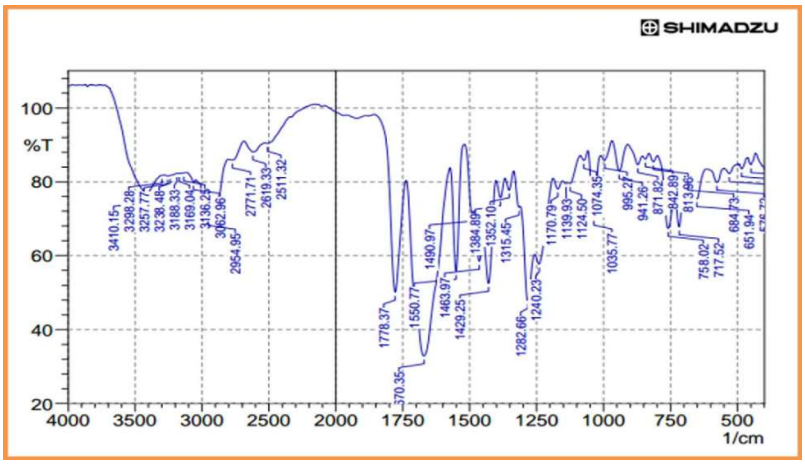

Fig 2: FT-IR Spectra of Azilsartan Medoxomil + Excipients

Evaluation of Prepared Tablets

The Evaluation of tablet carried out on thickness, Hardnesss, Friability and weigh Variation. The Parameter of evaluation are given in table no.3

Table 3: Evaluation of Prepared Tablets

S. No.	Formulation	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Weight Variation (mg)
1	F1	6.22	5.50	0.36	349.8±1.48
2	F2	6.37	5.50	0.39	350± 0.54
3	F3	6.14	5.58	0.12	349.6±0.41
4	F4	6.20	5.66	0.41	348.8±1.64
5	F5	6.08	4.25	0.54	348.6±1.14
6	F6	6.33	4.08	0.58	349.2±0.83
7	F7	6.13	4.12	0.34	347.2±0.12
8	F8	6.21	5.42	0.46	348.9±0.23
9	F9	6.25	5.31	0.51	349.3±0.39

In vitro dissolution study

The in-vitro drug release profile for all batches was shown in Fig. 3. Drug release from Azilsartan Medoxomil tablet were slow, controlled release and dependent upon the nature and concentration of polymers used. The tablet were subjected to in-vitro drug release rate by dissolution profiles are shown inTable 4. In vitro

drug release study confirms that the formulation F4 was the best formulation as it releases 98.87 % at the end of 12 hr. in controlled manner.[9,10]

Table 4: In vitro release of Cumulative % Drug Release Vs Time

	Cumulative Percentage Drug Release								
Time (hrs)	**F1**	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
1	7.47	9.44	5.19	8.34	6.811	6.05	10.10	7.03	7.13
2	10.7	18.01	14.92	15.60	16.40	15.57	16.04	14.6	15.36
4	12.30	26.36	24.01	28.12	21.53	26.17	21.48	21.09	26.82
6	24.07	31.42	32.66	43.20	30.32	35.04	41.08	27.90	38.50
8	53.61	51.85	42.83	62.84	43.50	65.92	64.16	47.02	46.08
10	70.42	74.70	70.52	86.13	59.10	80.48	84.81	79.54	77.66
12	94.92	92.50	91.08	98.87	94.04	96.05	96.89	92.06	94.54

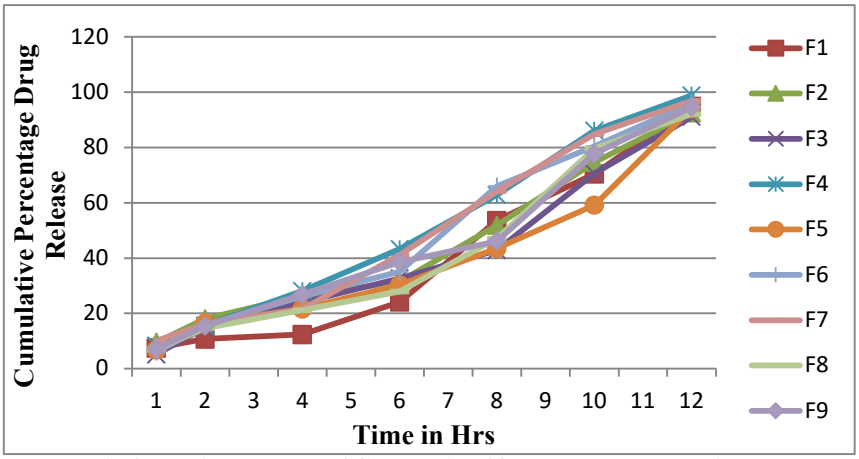

Fig 3: In vitro release of Cumulative % Drug Release Vs Time

CONCLUSION

The formulation with Ethyl Cellulose has shown low drug release and has the problem of dose dumping. The formulation with HPMC has shown similar drug release as that of Vinyl pyrrolidone vinyl acetate but does not follow the theoretical drug release profile. Micro crystalline cellulose used as diluents does not show any effect on the drug release pattern. Optimized formulation F4 which includes Vinyl pyrrolidone vinyl acetate has successfully sustained the drug release for 12 hours and the drug release pattern was similar to theoretical release profile.

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