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FORMULATION AND EVALUATION OF BILAYERED TABLETS OF LOVASTATIN AS IMMEDIATE RELEASE AND ATENOLOL AS CONTROLLED RELEASED TABLET

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ABSTRACT

In this present study bilayered tablet of Lovastatin and Atenolol were designed. lovastatin is a antihyperlipoprotienemic agent which acts as a cholesterol -lowering agent, Due to its short duration of action makes the drug suitable for immediate release, and it has poor solubility in water. lovastatin was incorporated as immediate layer and atenolol as controlled release layer. Bilayered tablet contains two layers. We can formulate first layer into immediate release and second layer into sustained release for desired action. Lovastatin have half-life 2-4hrs make the drug suitable for immediate release. Atenolol have half-life 6-7hrs make the drug suitable for sustained release. Lovastatin has poor solubility in water, Solid dispersions method is used to enhance the solubility of lovastatin. In this formulation using super disintegrants for immediate release, HPMC and ethyl cellulose as a polymers for Controlled release. In this study Bilayered tablets of lovastatin and Atenolol tablets were evaluated for weight variation, hardness, thickness, drug content and In-vitro studies.

KEYWORDS: Lovastatin, Atenolol, HPMC, Ethylcellulose, PEG6000, Avicel PH102, PVA, Lactose.

MATERIALS AND METHODS

Lovastatin, atenolol, HPMC, Ethlcellulose, PEG6000 from Gautham college of pharmacy.

INTRODUCTION

Oral drug delivery is most suitable route of administration because of its high patient satisfactoriness, flexibility in formulation and stability. Factors that often impact the

absorption of orally administered drugs include frequent dosing which results in fluctuation of plasma drug concentration and finally toxicity.[1] The fluctuations in plasma level by conventional oral drug delivery system that delivers drug for an extended period of time was developed. This system has many difficulties due to physiological problems like drugs with narrow absorption window, alteration in emptying time of stomach, drugs that have stability issues in intestine and drugs that are transported via active transport mechanism.[2,3] Hypolipidemic agents, or antihyperlipidemic agents, are a diverse group of pharmaceuticals that are used in the treatment of high levels of fats (lipids), such as cholesterol, in the blood (hyperlipidemia).[4] They are called lipid-lowering drugs. Lovastatin comes under classification natural statin. Statins are particularly well suited for lowering LDL, the cholesterol with the strongest links to vascular diseases.[5] In studies using standard doses, statins have been found to lower LDL-C by 18% to 55%, depending on the specific statin being used. Lovastatin is poorly soluble in water. soluble in organic solvent ethanol and DMSO. Usually conventional dosage form produce fluctuations in plasma drug concentration levels in blood stream and tissues, with poor toxicity and therapeutic effects.[6] The goal of designing sustained or controlled delivery system is to reduce the frequency of the dosing and increase effectiveness of the drug by localization at the site of action, reducing the dose or providing uniform drug delivery. Bi-layer tablet is suitable for sequential release of two drugs in combination, separate to incompatible substances and also for immediate release as initial dose and sustained release as maintenance dose (Shiyani et al., 2008).[6] In Bi-layer tablets drug release is unidirectional, if the drug can be incorporated in the upper non-adhesive layer.

Atenolol, a cardio selective beta-1 adrenoreceptor. It belongs to antihypertensive agent and helps in reducing high blood pressure. The drug has half-life 6-7hrs which make the drug suitable for controlled release. controlled release layer maintain uniform drug levels over a longer period to reduce dosing intervals, side effects, increase the safety margin for highly potent drugs and thus offer better patient compliance. Acacia, HPMC, Sodium alginate, Methyl cellulose, Ethyl cellulose used as polymers for controlled release.

Preparation of solid dispersions

Solubility of lovastatin was improved by preparing solid dispersions by solvent evaporation method. The required quantity of drug was dissolved in the solvent (dichloromethane) to get a clear solution in a dry mortar. The carrier starch was when added to the clear drug solution

and dispersed. The solvent was then removed by continuous trituration. Trituration was continued until a dry mass was obtained. The mass obtained was further dried at 45ºC for 1-2 hours in a oven. The dried product was powdered and passed through mesh no.100 in each case. Solid dispersions were prepared using different carriers like PEG6000, Starch, PVP at ratios of drug: carrier, namely All with 1:1 ratios. A total of three solid dispersions were prepared. In the above formulation solid dispersion with PEG6000 shows good release.

Preparation of Immediate Release layer

Lovastatin is poorly Soluble in water. To enhancing the solubility of Lovastatin using super disintegrants Avicel PH 102 and lactose in different concentrations. Magnesium stearate acts as a lubricant. To get the desired tablets granules were prepared by using wet granulation method.

Preparation of Sustained Release Tablets

Atenolol has half-life 6-7hrs suitable for formulation into sustained release dosage form. To get desired action different ratios of HPMC and Ethyl cellulose are used as a polymers. Ethyl cellulose acts as a binder. Binder plays an important role in the controlled formulations. Atenolol is supposed to be granulated with water. Magnesium stearate used as a lubricant. These granules were prepared by wet granulation method.

Preparation of Bilayered Tablet

In this process, the first step controlled release granules are weighted accurately and fed in to die cavity of tablet punching machine. The next step involves immediate release granules are fed in to die cavity and compressed so that final hardness can be achieved. After preparation of tablets, the tablets are subjected for evaluation. Evaluation parameters are weight variation, hardness, thickness, drug content and In-vitro studies.

Table 1: Formulation of Solid dispersions (1:1).

Pure drug	**40**	**40**	**40**
starch	40	-	-
PVP	-	40	-
PEG6000	-	-	40

Table 2: Formulation of Immediate release layer.

Formulation	Lovastatin(mg)	Avicel PH 102 (mg)	lactose	Magnesium stearate (mg)	Total weight (mg)
IR-F-1	40	10	48	2	100
IR-F-2	40	15	43	2	100
IR-F-3	40	20	38	2	100

Table 3: Formulation of Sustained release layer.

Formulation	Atenolol (mg)	HPMC(mg)	Ethyl cellulose (mg)	Magnesium stearate (mg)	Total weight (mg)
CR-F-1	50	80 (20%)	262	8	400
CR-F-2	50	160 (40%)	182	8	400
CR-F-3	50	240 (60%)	102	8	400

Table 4: Formulation of Bilayered tablet.

Layers	Ingredients	F-1	F-2	F-3
Immediate release layer	lovastatin	40	40	40
	Avicel PH 102	10	15	20
	Lactose	48	43	38
	Magnesium stearate	2	2	2
Sustained release layer	Atenolol	50	50	50
	HPMC	80	160	240
	Ethyl cellulose	262	182	102
	Magnesium stearate	8	8	8

In-vitro dissolution studies

Dissolution study was carried out by USP dissolution apparatus II (Paddle type), rotational speed 50rpm with 900ml 6.8pH Phosphate buffer as a dissolution medium maintainted at 37 ± 0.5°C. Samples were withdrawn for a period of 12hrs. 5ml of sample was withdrawn. By using UV/Visible spectrophotometer at 248 & 235nm for the estimation of Lovastatin and Atenolol concentration.

Table 5: Dissolution profile of Nifedipine tablet.

Time (min)	IF-1 (% drug released)	IF-2 (% drug released)	IF-3 (% drug released)
5	49	58	59
10	71	77	80
15	94	97	99

Table 6: Dissolution profile of Atenolol tablet.

Time (min)	CR-F-1 (% drug released)	CR-F-2 (%drug released)	CR-F-3 (% drug released)
10	6	3	4
30	35	28	33
60	68	63	76
2hrs	72	68	78
4hrs	76	71	78
6hrs	88	79	89
8hrs	92	86	97
10hrs	96	91	98
12hrs	97	96	99

Table 7: Evaluation parameters.

Bilayered Tablet	Weight variation (mg)	Hardness (kg/cm)	Thickness (mm)	Drug content (lovastatin)	Drug content (Atenolol)
F-1	493 ± 0.8	5.3	2.38	97	101
F-2	495 ± 1.2	6.1	2.31	98	99
F-3	497± 0.6	6.4	2.42	99	102

RESULTS AND DISCUSSION

Lovastatin poorly soluble in water. So in order to improve the solubility, solid dispersion of lovastatin with super disintegrants Avicel PH 102 was used. For immediate release formulation IR-F-1, IR-F-2, IR-F-3 were prepared with different concentration ratios (5%, 10%, 20%) of Avicel. Lactose gives bulkiness to the formulation. To get the controlled effect Atenolol with HPMC and Ethyl cellulose were prepared. The evaluation parameters were estimated. In Immediate release formulation, IR-F-3 formulation gives 98% release within 15min. This formulation is used for Bilayered tablet to combine with sustained released tablet. For sustained effect CR-F-1, CR-F-2 gives 97-98% release within 10-12hrs. CR-F-3 gives 99% release within 10-12hrs for a longer period of time. HPMC 40% gives more retardant effect over a period of time. This may be due to increase in concentration of polymer and binder.

CONCLUSION

The aim of this study is to Design and Evaluate Bilayered tablet of Lovastatin and Atenolol. Lovastatin comes under classification natural statin. Atenolol belongs to antihypertensive agents which helps in reducing blood pressure. In this Bilayered tablet lovastatin released the drug for immediate action because of short duration of action. For controlled release HPMC, Ethyl cellulose are used with Atenolol. The evaluation parameters are weight variation, hardness, thickness, drug content and In-vitro studies were carried out. In-vitro dissolution

studies are performed using pH 6.8 Phosphate buffer, F-2 formulation shows good sustained effect for a longer period of time up to 10-12hrs.

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