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Research Paper

Formulation and Evaluation of Sustained Release Matrix Tablet of Efavirenz

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ABSTRACT

In this study, matrix tablets of efavirenz were made using the direct compression method, which is currently thought to be a straightforward and economical manufacturing process. It is regarded as a suitable technique for compounds that are thermolabile and hygroscopic. A total of six formulations with varying amounts of polymers were created. Using a Monsanto hardness tester, the average hardness values were determined for each composition. From each formulation, twenty tablets were chosen at random and examined. Nearly consistent data were collected. Since the percentage of weight variation was within the USP Pharmacopoeia's bounds of $\pm 5\%$ of the weight, all of the tablets passed the weight variation test. All of the prepared tablets' drug contents were found to be within the acceptable range. The findings that fall within the range show that the mixing is uniform.

INTRODUCTION

As is well known, the phrase "sustained release" has been used for a long time in pharmaceutical and medical literature. The therapeutic drug's release has been constantly postponed by sustained release in order to prolong its plasma profile and guarantee its ongoing presence in the bloodstream. Despite having a long-lasting therapeutic impact, its pharmacological activity usually takes some time to begin. Sustained release (SR) dose forms

have garnered ongoing attention in recent years because of their enhanced patient compliance and lower incidence of adverse medication reactions. Drug delivery techniques that continually release medication for an extended period of time after administration in an effort to generate a significant therapeutic impact are referred to as sustained release, sustained action, prolonged action, and extended action.

Benefits of Sustained Release Matrix Tablet:

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- Drug administration frequency is decreased;
- Patient compliance can be increased
- There is a reduction in the blood level oscillation that occurs with multiple dosing of traditional dosage forms; also, drug administration can be made easier.
- Since the high blood level peaks that may be seen following the administration of a dose of a high availability medicine can be decreased, better control of drug absorption can be achieved.
- It is possible to lessen the typical blood level volatility brought on by repeated dosing of traditional dose forms.

The term "sustained release," "sustained action," "prolonged action," and "extended action" refer to drug delivery methods that aim to produce a substantial therapeutic impact by continuously releasing medication over a long period of time

after administration of a single dose. The United States Food and Administration approved anti-retroviral drug Lamivudine, a nucleoside thymidine analog, is used exclusively for treating HIV AIDS and its related conditions. In recent years, sustained release (SR) dose forms have garnered ongoing interest due to their increased patient compliance and decreased frequency of adverse drug responses.

MATERIAL AND METHOD

In the present study chemical are required to use in that efavirenz containing dosage form, hydroxy propyl methyl cellulose (HPMC), Magnesium Stearate, Microcrystalline Cellulose, Sodium alginate, Polyethylene oxide.

Composition of matrix tablets containing efavirenz

Table No 1: Composition of sustained released Matrix Tablet Containing Efavirenz (FD1 to FD6)

Ingredients (mg)	All batches quantity in mg/tablet					
	FD1	FD2	FD3	FD4	FD5	FD6
Efavirenz	90	90	90	90	90	90
HPMC K100LV	45	90	180	90	-	45
Microcrystalline cellulose	155.2	132.7	87.7	87.7	155.2	132.7
Lactose	155.2	132.7	87.7	87.7	155.2	132.7
Magnesium Stearate	4.5	4.5	4.5	4.5	4.5	4.5
Total weight	450	450	450	450	450	450

Preparation of Matrix Tablets Containing Efavirenz

The corresponding amounts of active ingredient (drug-Efavirenz, HPMC, microcrystalline cellulose and lactose) were accurately weighed. The powders were sieved using screen #25. The screened powder was then transferred into the turbula mixer jar and mixed for 10 minutes. Magnesium stearate was accurately weighed, sieved through screen #25 and added to the turbula jar and mixed for an additional 2 minutes. The

powder mix was then compressed into tablets using the instrumented tablet press, using a 7 mm round punch. Tablets were collected during compression for in-process testing (weight and hardness) the tablets were then stored in airtight high-density polyethylene bottles until further testing.

RESULT AND DISCUSSION

Evaluation of matrix tablets:



Table No. 2: Pre-compression evaluation parameter.

Formulation	Bulk Density (g/Cm3)	Tapped Density (g/Cm3)	Compressibility Index (%)	Hausner Ratio	Angle of Repose
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	0.515±0.003	0.573±0.005	10.12±0.026	1.11±0.10	22.15±0.21
FD5	0.500±0.002	0.553±0.002	9.58±0.024	1.10±0.10	21.58±0.15
FD6	0.526±0.004	0.555±0.002	5.22±0.018	1.05±0.05	22.46±0.21

Results of the pre-compression parameters performed on the blend for batch. The angle of repose of all the formulations was in the range of 21.580 ± 0.15 to 26.480 ± 0.12 . The Compressibility Index for all formulations was in range of 5.22 to 14.23%, bulk density 0.490 to 0.526 g/cm³. The angle of repose for all

formulations was < 30 indicating good flow properties of the powder. This was further supported by lower compressibility index values. Compressibility index values up to 15% results in good to excellent flow properties.

Post-compressional studies

Table No.3: Post-compression evaluation of Formulated Efavirenz SR Matrix Tablet.

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	5.2 ± 0.07	450 ± 2.47	0.38 ± 0.01	99.8 ± 0.03
FD5	4.6 ± 0.04	439 ± 2.13	0.38 ± 0.01	98.5 ± 0.03
FD6	4.8 ± 0.04	441 ± 2.58	0.45 ± 0.01	99.1 ± 0.01
Marketed (Estiva) Hetero drug ltd.	5.0 ± 0.08	188 ± 2.57	0.28 ± 0.01	99.4 ± 0.02

Matrix tablets of Efavirenz were prepared by the dry granulation method and subjected to different evaluation tests reported in table No.21. As per IP, drug content of each tablet should be in the range of 90-110% of the theoretical label claim. All formulations showed good uniformity in drug content and the percentage of drug content was 97.7 ± 0.03 to 99.8 ± 0.03 %. Tablets hardness for all formulations were in the range of 4.6 ± 0.04 to 5.4 ± 0.04 kg/cm². The formulations containing only HPMC at 10 to 60% levels generated tablets with hardness values of 5.0 ± 0.04 kg/cm² to 5.4 ± 0.04 kg/cm² respectively. The hardness of tablets containing only HPMC was higher than that of tablets. The higher hardness of

HPMCK100LV is the result of relatively low methoxy and also the high moisture content resulting in stronger hydrogen bonds lets. For all the prepared formulations, friability percentage was less than 1% and results were in acceptable limit. For tablets weighing more than 250 mg, 5% deviation from the mean weight is acceptable. The average weight variation percentage of 20 tablets taken from each formulation was less than $\pm 0.5\%$. The effect of the amount of HPMC 10, 20, 40 and 60 % on the Efavirenz release. The Efavirenz release decreased as the percent amount of HPMC level in the tablet increased. Drug release is controlled by the hydration of HPMC, which forms a gelatinous barrier layer at the surface of



the matrix. By using viscosity grade of the HPMC the resistance of such a gel layer to erosion is controlled. HPMC K100LV is a low viscosity polymer (100 cps), therefore, 10% and 20% polymer level showed a fast drug release from the matrix. It was observed that for the 10% HPMC level, within 1 hour, near about 100% of the Efavirenz was released while for the 20% HPMC level after 3 hours, 90.2 % of the Efavirenz was released in the dissolution media. An increase in polymer amount causes an increase in the viscosity of the gel and gel layer with a longer diffusional path. The ultimate effect was a decrease in the effective diffusion coefficient of the drug with a

reduction in the drug release rate. The results from the HPMC polymer show this predictable behavior. The Efavirenz release from the formulations containing 40% and 60% HPMC was found to be 99.22% and 84.18%, respectively at 12 hours. Release rate data from table 29 shows a very high r^2 for the HPMC 40 and 60% formulations suggesting diffusion release kinetics. The gel thickness might have prolonged the drug release from the formulations. (Release kinetics) - shows the release rate data. Dissolution profiles of the HPMC alone SR matrix tablets showed that at levels of 40% and 60%, the profiles were close to the profile obtained by the marketed product.

Table No 4: Effect of long-term stability storage on the physical properties of HPMC/Efavirenz tablets (Optimized Batch FD4)

Physical Property	Initial	1 month	3 months	6 months	9 months
Weight	450±2.4767	449±2.5726	450±2.5726	451±2.2820	451±3.5703
Hardness	5.2±0.07071	5.2±0.0836	5.3±0.0894	5.4 ± 0.0447	5.5±0.0894

(* **significantly different from initial at 0.05 level**)

CONCLUSION

From the complete study, it is concluded that, hpmc k100lv at a concentration of 20% respectively produced sustained release Efavirenz matrix tablets that are similar to the marketed product (Estiva). Optimized sustained release Efavirenz matrix tablets, showed square root of time dependent kinetics of drug release indicating a dissolution and diffusion-controlled release mechanism. Selected polymers and their concentrations are also capable of sustaining the release of drug Efavirenz beside drug concentration.

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