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Formulation and Evaluation of Efavirenz Tablet using Moringa oleifera as a Natural Polymer

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ABSTRACT

This study describes a systemic approach for the formulation and evaluation of Efavirenz tablets and has been done in this work using Moringa Oleifera as a natural polymer at different concentrations. In order to identify the medication, melting point, solubility, and FTIR analysis were used. DSC was used for investigating the drug polymer interactions. Consequently, no interaction between the medicine and polymer used in the formulation was detected. The formulations were created by blending medication and excipients, then analysing them for Angle of repose, Bulk density, Tapered bulk density, Hausner's ratio, and Carr's compressibility index. The powder blends passed all of these tests with flying colours. Direct compression was used to make the seven batches of Efavirenz pills. Thickness, hardness, friability, weight variation, and drug content were all measured on the manufactured tablets. All of the values were found to be within the parameters. All seven batches were subjected to in-vitro dissolving tests. Because Formulation F7 has the largest percentage of medication release, it has been chosen as the best formulation. Stability tests were performed on the optimised formulation F7, and the findings showed no significant changes throughout the course of the three-month investigation.

Key words: Efavirenz, Moringa oleifera, Formulation, Evaluation studies.

1. INTRODUCTION

Efavirenz (EFV), also known as Sustiva, is an antiretroviral drug that is used to treat and prevent HIV/AIDS. It's usually safe to combine it with other antiretrovirals. It could be administered as a preventative measure following a needlestick injury or other possible exposure. Efavirenz/emtricitabine/tenofovir is a combination drug that is available as efavirenz/emtricitabine/tenofovir. It is taken orally. Rash, nausea, headache, exhaustion, and difficulty sleeping are all common adverse effects. Some of the rashes, such as Stevens–Johnson syndrome, can be dangerous. Depression, suicidal thoughts, liver issues, and seizures are among the more serious adverse effects. It is not recommended for use while pregnant. It's a non-nucleoside reverse transcriptase inhibitor (NNRTI) that operates by preventing reverse transcriptase from doing its job.

In the United States, efavirenz was approved for medical use in 1998, and in the European Union in 1999. It is listed as an essential medicine by the World Health Organization. It is now accessible as a generic drug as of 2016. [1]

1.1 HIV

HIV/AIDS (Human Immunodeficiency Virus Infection/Acquired Immunodeficiency Syndrome) is an immune system disease caused by infection with the human immunodeficiency virus (HIV). A person may experience a brief period of influenza-like sickness during the initial infection. This is usually followed by a period of time when there are no symptoms. As the condition continues, it wreaks havoc on the immune system, making the person far more susceptible to infections, including opportunistic infections and cancers that seldom harm persons with healthy immune systems.

HIV is a member of the Lentivirus genus, which belongs to the Retroviridae family. Many morphologies and biological features are shared by lentiviruses. Lentiviruses infect a wide range of organisms and are known for causing long-term diseases with a protracted incubation time. Lentiviruses are single-stranded, positive-sense, enclosed RNA viruses that are transferred.[2,3]

1.1.1 Types of HIV/AIDS

The considerable genetic heterogeneity of the Human Immunodeficiency Virus is one of the problems in treating it. HIV is split into two types: type 1 (HIV-1) and type 2 (HIV-2).

1.1.1.1 HIV-1

HIV-1 is the virus's most common and dangerous strain. HIV-1 is divided into three groups by scientists: a major group (Group M) and two or more lesser groups. Each group is thought to reflect a separate SIV transmission into humans (but subtypes within a group are not). All six potential reading frames (RFs) of the HIV-1 full genome sequence contain a total of 39 ORFs. However, just a few of them are operational.

1.1.1.2 HIV-2

HIV-2 is primarily connected to the simian immunodeficiency virus (SIV smm), which is found in the forests of coastal West Africa and is endemic in sooty mangabeys (Cercocebus atys). The viruses most closely linked to the two strains of HIV-2 that spread widely in people (HIV-2 groups A and B) are the SIV smm found in the sooty mangabeys of the Tai forest in Western Ivory Coast, according to phylogenetic study.[4,5]

1.2 Moringa Oleifera

[*Guilandina moringa* L, *Hyperanthera moringa* (L.) Vahl , *Moringa pterygosperma]*

The horseradish tree, Moringa oleifera, is a pan-tropical species with names like Benzolive, Drumstick Tree, Kelor, Marango, Mlonge, Mulangay, Nébéday, Saijhan, and Sajna. Moringa Oleifera is the most frequently cultivated species of the Moringaceae Monogeneric family, which is native to India, Pakistan, Bangladesh, and Afghanistan's sub-Himalayan regions. The ancient Romans, Greeks, and Egyptians used this fast-growing tree and it is now widely cultivated and has become naturalised in many tropical locations.[6,7]

2. METHODOLOGY

2.1 Materials and Methods

2.1.1 Preparation of Efavirenz Tablets

Accurately weighed amount of selected ingredients which is listed in table -1 [F1 –F7] reprenting 600 mg equivalent of drug was mixed using the direct compression method. All the ingredients with drug except magnesium stearate were taken in the mortar. The powder blend was then mixed well by using mortar and pestle for 15 to 30 minutes, and then each mixture was passed through #80 sieves. Finally, magnesium stearate was added as a lubricant and mixed thoroughly; lactose was used as diluents. The resultant mixture was compressed using 16 stations cadmach tablet compression machine to produce tablets.

Table No1: Composition of Various Efavirenz Tablet Formulations

S. No	Ingredients	Formulations						
		F1	F2	F3	F4	F5	F6	F7
1)	Efavirenz	350	350	350	350	350	350	350
2)	Mo rin	20	30	40	50	60	70	80
3)	Lactose	175	165	155	145	135	125	115
4)	Starch	40	40	40	40	40	40	40
5)	Magnesium	10	10	10	10	10	10	10
6)	Talc	5	5	5	5	5	5	5
Total		600	600	600	600	600	600	600

2.2 Evaluation

2.2.1 Micromeritic properties of powder blend

2.2.1.1 Angle of repose

Angle of repose is defined as the maximum angle possible between the surfaces of a pile of powder and horizontal plane and it was calculated using the following equation: [8,9]

$$\theta = \mathrm{Tan}^{-1}(h/r)$$

Where, ‘h’ is the height of powder blend cone

‘r’ is the radius of powder blend cone.

Table No 2: Flow properties and corresponding Angle of repose

S. No	Angle of Repose (θ)	Flowability
1	<20	Excellent
2	20 – 30	Good
3	30 – 35	Passable
4	>40	Very poor

2.2.1.2 Bulk density and tapped density:

An accurately weighed (10gms) powder blend from each formulation was taken and shaken lightly to break any agglomerates formed and it was introduced into a measuring cylinder. The volume occupied by the powder blend was measured which give bulk volume. The measuring cylinder was tapped until no further change in volume was noted which gave the tapped volume. Both bulk density (BD) and tapped bulk density (TBD) of powder blend was determined using the following formula. [8,9]

BD = Weight of the powder blend / Volume of the powder blend

TBD = Weight of the powder blend / Tapped volume of the powder blend

2.2.1.3 **Carr's Compressibility index**

The car's compressibility index was determined by using the following formula. [8,9]

Carr's Compressibility Index (%) =

[(TBD – LBD)/TBD] x 100

LBD = Loose Bulk Density,
TBD = Tapped Bulk Density

Table No 3: Standard Values for Carr's Index

S. No	% Compressibility	Flowability
1	May-15	Excellent
2	Dec-16	Good
3	18-21	Fair passable
4	23-35	Poor
5	33-38	Very poor
6	>40	Extremely Poor

2.2.1.4 Hausner's ratio:

Hausner's ratio is the ratio of the initial volume of the powder mass to the final volume of the powder mass obtained after the specified number of tapping. [8,9]

Table no 4**:** Scale of Flowability based on Hausner's Ratio

S. No	Hausner's ratio	Flow Property
1	0.0-1.25	Free flow
2	1.25-1.6	Cohesive flow

The above Micromeritic properties of powder blend was shown in TableNo-7

2.3 Physico-Chemical Properties Of Tablets

2.3.1. Appearance

The tablets were observed visually for any defect during compression and handling.

2.3.2. Size and Thickness

Due to differences in densities of different concentrations of polymer used in formulation, the size and thickness of a tablet can vary with no change in weight. A Vernier calliper was used to measure the thickness of the tablets.

2.3.3. Hardness

The ability of a tablet to survive mechanical shocks during handling, manufacturing, packaging, and shipping is referred to as hardness. The hardness of the tablets was measured using a Monsanto hardness tester. The Ketan tablet hardness tester, a sort of Monsanto hardness tester used to evaluate tablet hardness tester, was one of the first testers for this test. The tester is made out of a barrel with a compressible spring sandwiched between two plungers. The bottom plunger is pressed against the tablet, and a zero reading is obtained. By rotating a threaded bolt, the upper plunger is pressed against a spring until the tablet cracks. A pointer moves along a gauge in the barrel as the spring is squeezed, indicating the force. The fracture force is measured in kilogrammes. The hardness of the tablet should be between 5 and 10 kg/cm2.[10]

2.3.4. Friability

The strength of a tablet is measured by its friability. The Roche friabilator is used to perform this test. A sample of pre-weighed tablets was placed in the plastic chamber of a friabilator, which spun at 25 rpm for four minutes (100 revolutions), dropping the pills to a distance of six inches with each revolution. After that, the tablets were dusted and reweighed. Compressed pills with a weight loss of less than 0.5 percent to 1 percent are regarded acceptable.[10] The formula for calculating percent friability (percent F) was as follows.

% Friability = (Initial weight – Final weight / Initial weight) x 100

2.3.5. Weight Variation:

The weight variation test is randomly selecting 20 pills and weighing them individually. The average weight of a pill is calculated by multiplying the composite weight by 20. The percentage deviation of the individual weights from the average weight was then calculated. [11,12] Deviation should not exceed the values given in Table-5

Table-5- Percentage deviation allowed in weight variation

Average Weight of Tablet	% Deviation allowed
80mg or less	10
More than 80mg but less than	7.5
250mg or more	5

2.3.6. Drug content:

The drug content of the tablets must be closely monitored in order to forecast the formulation's potential and efficacy. Taking 10 tablets will establish the amount of active substance. 10 pills are powdered and weighed. A quantity of powder equal to 10mg of Efavirenz was properly weighed into a 100ml volumetric flask, dissolved in methanol, and the final volume was produced with 1% SLS. Filtration was done on the solution. The absorbance was measured at 247.6nm after 2.5ml of the filtrate was diluted to 10ml with 1 percent SLS.[13,14]

2.3.7. In-vitro disintegration test:

This test is used to check that tablets will dissolve in water if they are to be used as dispersible tablets. One tablet is placed in one tube of the USP disintegration test instrument, which is then filled with a disc. The tablet is suspended in distilled water in a beaker, and the equipment is run until the tablet disintegrates. When tested by the disintegration test for tablets, dispersible tablets must disintegrate within 3 minutes to meet IP criteria.

The apparatus consists of six glass tubes measuring 7.5 cm in length, 2 cm in internal diameter, and 2 mm in wall thickness. To determine disintegration time, one tablet was placed in each tube and the basket rack was placed in a 1 litre beaker of water kept at 37°0.5°C, such that the tablet remained 2.5 cm below the surface of the liquid on their upward movement and descended no closer than 2.5 cm from the beaker's bottom. The basket assembly was moved up and down by a typical motor-driven device at a frequency of 28 to 32 cycles/minutes over a distance of 5 to 6 cm. The time it took for the tablet to totally disintegrate was recorded.[15]

The above physical properties of powder blend were shown in Table No-8

2.4 *In vitro* Dissolution Studies

In 0.1N hydrochloric acid, the rate of dissolution of Efavirenz from tablets was investigated using USP XXIII dissolution test apparatus employing paddle stirrer. This is a single tablet. With 600mg of Efavirenz, a speed of 50 rpm, and a temperature of 37º -0.5ºC, employed. At different times, a 10ml aliquot of dissolving medium was removed. intervals, filtered, and spectrophotometrically measured for Efavirenz concentration at 246.5nm.[16,17]

2.5 Stability Studies

Stability testing is used to show how a product's quality has improved over time. Under the impact of a variety of factors, the drug substance or drug product changes over time. Temperature, humidity, and light are examples of environmental conditions that enable recommended practices. Storage conditions, re-test periods, and shelf-lives are all factors to consider. In general, the measurement of the rate at It takes a lengthy time for the product to deteriorate at room temperature. to stay away from the ideas of expedited stability investigations are used to avoid this unfavorable delay.

To determine the change in hardness, disintegration time, drug content, and other parameters,

The stability investigation of the optimized formulation F7 was carried out at 40°C in a humidity chamber with a 75% relative humidity. At regular intervals, samples were taken. during the 90-day research, the hardness of the optimized formulation F7 was tested. drug content and percentage drug release, as well as disintegration time

3. RESULT AND DISCUSSION

3.1 Colour and Appearance

White or almost white powder characterized the appearance and colour of the drug.

3.2 Melting point

A sample of Efavirenz was measured to have a melting point of 140.66±1.15 ºC. The reported melting point range for Efavirenz is given as 138 - 141ºC

3.3 Solubility Studies of the Drug

The solubility of Efavirenz in numerous solvents was disbursed and results were shown in Table no 6.

Table No:6 Solubility of Efavirenz

S. No	Solvent	Parts of solvent required per part of solute	Inference
1	Distilled water	>10000	Practically Insoluble
2	Methanol	2	Freely Soluble
3	Dichloromethane	4	Freely Soluble
4	1% w/v SLS	800	Slightly Soluble
5	0.1N HCl	80	Sparingly Soluble

3.4 Micromeritic properties

The results of the micrometric studies of powder blend was investigated and listed in Table No. 7

3.5 Physicochemical properties

The results of the Physicochemical properties of efavirenz tablet was investigated and listed in Table No. 8

3.6 Disintegration time

The result of the disintegration time of the different formulation of the efavirenz tablet was investigated and listed in the table no.9

3.7 Stability Studies

From the above results **F7** was found to be best formulation among the 7 formulations and hence it was selected for stability studies are listed in table no:10 and shown in the figure 1,2 and 3.

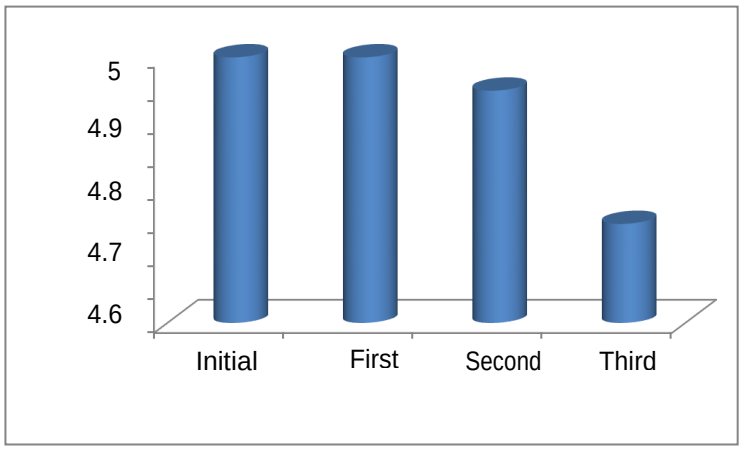

Fig . 1. Comparison for hardness before and after stability studies of best formulation F7

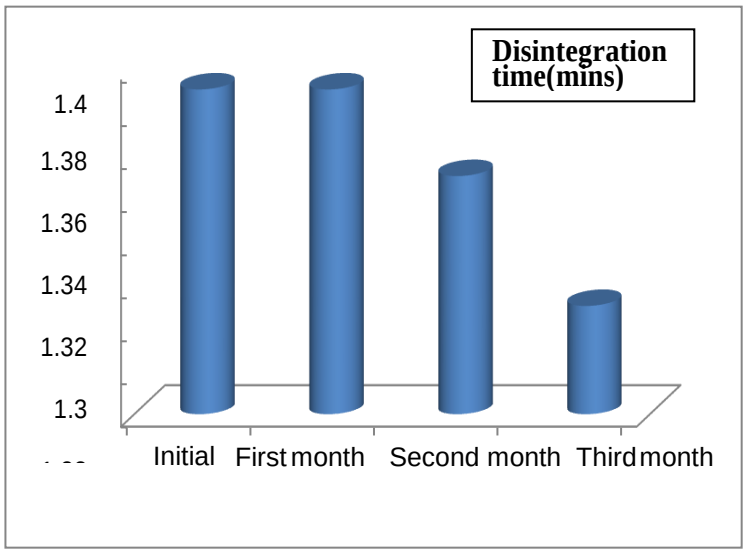

Fig.2. Comparison for disintegration before and after stability studies of best formulation F 7

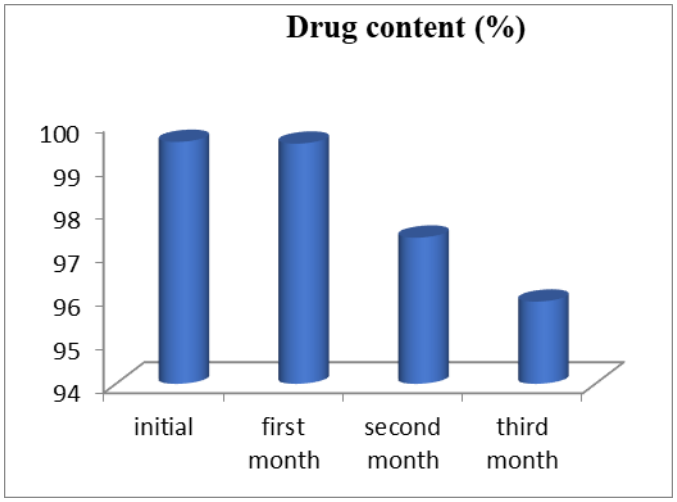

Fig.3 Comparison for percentage of drug content before and after stability studies of best formulation F7

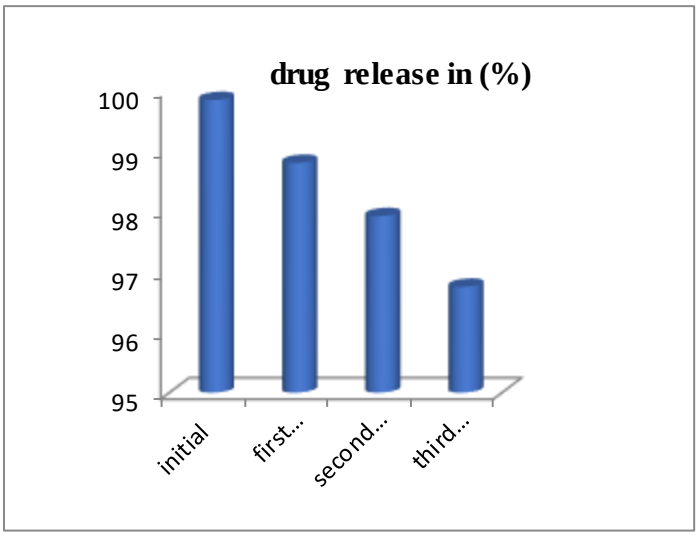

Fig 4: comparison for percentage of drug release before and after stability studies best formulation F7.

Table No. 7 Micromeritic properties of powder blend

Formulation Code	Angle of Repose (°)	LBD (gm/ml)	TBD (gm/ml)	Carr's Index (%)	Hausner's Ratio
F1	35.89±1.27	0.5457±0.26	0.6527±0.09	13.91±1.75	1.15±0.02
F2	34.86±1.12	0.5456±0.01	0.6528±0.005	15.42±3.32	1.18±0.04
F3	31.03±0.05	0.5484±0.005	0.6527±0.09	15.26±0.97	1.17±0.01
F4	31.56±1.24	0.5483±0.12	0.6526±0.024	14.63±3.36	1.17±0.04
F5	29.76±0.97	0.5416±0.14	0.6528±0.002	20.57±3.31	1.25±0.05
F6	28.03±0.01	0.5417±0.02	0.6527±0.015	15.65±3.29	1.18±0.04
F7	27.06±1.25	0.5199±0.016	0.6524±0.05	19.73±3.34	1.24±0.04

Table no-8 Physico-chemical properties

Formulation code	Thickness (mm)	Diameter (mm)	Weight Variation (%)	Hardness (kg/cm^2)	Friability (%)	Drug content (%)
F1	5.03±0.057	15.8±0.00	2.15±0.02	4.86±0.321	1.03±0.057	97.25±0.06
F2	5.06±0.057	15.8±0.00	3.62±0.02	4.43±0.568	0.27±0.000	97.48±0.01
F3	5.01±0.01	15.8±0.00	2.19±0.03	4.90±0.200	0.94±0.005	98.37±0.01
F4	5.06±0.057	15.8±0.00	3.41±0.02	5.06±0.288	1.06±0.015	96.53±.005
F5	5.03±0.057	15.8±0.00	2.26±0.02	4.83±0.404	0.81±0.016	97.25±.005
F6	5.06±0.057	15.8±0.00	3.40±0.01	4.56±0.152	0.78±0.020	98.38±0.01
F7	5.0±0.1	15.8±0.00	2.21±0.02	5.00±0.100	0.82±0.080	99.56±0.01

All the values are expressed as a mean ±SD, n=3

Table no:9 Disintegration time of different Formulation of Efavirenz Tablets

Formulation code	Disintegration Time (minutes)
F1	5.41±0.08
F2	5.45±0.06
F3	4.21±0.08
F4	3.31±0.08
F5	2.28±0.111
F6	2.31±0.140
F7	1.39±0.118

4. CONCLUSION

According to the findings, an efavirenz pill was developed employing moringa oleifera as a natural polymer, and several evaluation studies like thickness, friability ,hardness , drug content ,disintegration test etc., were evaluated and it delivers therapeutically relevant quantities of the active material to the target organ with minimal discomfort and side effects, boosting patient compliance with the therapies.

5. ACKNOWLEDGEMENT

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Table no: 10 Stability studies of best formulation

Stability Chamber	Time	Appearance	Hardness (kg/cm2)	Disintegration (mins)	Drug control (%)	% Drug release
40 ± 2ºCwith 75±5%RH	Initial	White	5.00±0.10	1.39±0.118	99.56±0.01	99.84±0.02
	1st month	No change	5.00±0.01	1.39±0.106	99.52±0.19	98.80±0.01
	2nd month	No change	4.9±0.15	1.35±0.120	97.36±0.02	97.92±0.01
	3rd month	No change	4.5±0.11	1.29±0.01	95.89±0.11	96.75±0.02

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