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Comparative Study of Evaluation Parameters of Marketed and Formulated Rifampicin Tablet using *Ricinus Communis Oil* as a Binder

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ABSTRACT

The purpose of the study was comparative study of various parameters of marketed and formulated rifampicin tablet using castor oil. Rifampicin is used as 1st line anti-tubercular drug for the treatment of tuberculosis. Tablets were prepared by direct compression containing castor oil as a binder and various excipients. Both the marketed and prepared tablets were evaluated parameters such as Hardness, Thickness, Friability, Weight variation, Dissolution studies. The formulation of rifampicin tablet batch F1 shows optimized release of drug within 45 minutes.

KEYWORDS: *Rifampicin, Ricinus Communis oil, Anti Tubercular, Tuberculosis, In-vitro Dissolution studies*

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INTRODUCTION

Tuberculosis is a ubiquitous, highly contagious chronic granulomatous bacterial infection caused by the Mycobacterium tuberculosis. Mycobacterium tuberculosis is rod shaped bacteria called as Koch's bacillus.[1] Tuberculosis is the world's commonest cause for death after HIV/AIDS. According to WHO about 1/3rd of world population are infected with TB. More than 8 million people are commonly infected with TB annually in developing countries like sub-Saharan Africa and Asia. The prevalence of TB in India accounts for 30% of global burden and when combined with cases from china constitute 40% of all cases globally. Approximately 10% of the infected people develop active TB.[2] TB spreads through droplets of secretions such as sputum or aerosols released by coughing from the infected persons. Its eradication requires prevention, early diagnosis and effective treatment of the infection. A vaccine called BCG is administered in many parts of the world where TB is common.[3] Tuberculosis is one of the most chronic and infectious disease occurring world wide ranging from developing countries to developed countries. Tuberculosis infection is caused by Mycobacterium tuberculii.[4] Rifampicin is a critical component in the therapeutic armamentarium for tuberculosis Rifampicin is a semi synthetic derivative of macro cyclic antibiotic derived from Streptomyces Mediterranean. Rifampicin act by inhibiting DNA dependent RNA polymerase. The bioavailability of rifampicin in FDC may be reduced owing to chemical reaction with isoniazid in acidic gastric environment; pyrazinamide and ethambutol catalyzes the reaction.

Treatment of TB involves administration of combination of rifampicin, isoniazid, pyrazinamide and ethambutol for initial 2 months followed by rifampicin and isoniazid for 4 months.[5] Isoniazid and rifampicin are the most potent anti-TB drugs kills more than 99% tubercular bacilli within 2 months of initiation therapy.[6]

MATERIALS AND METHODS

Materials: [7]

Rifampicin was supplied by Aarti Pharmaceuticals, Mumbai. Ricinus communis oil, Lactose, Sodium Bicarbonate, Stearic acid, Silicon dioxide were supplied by Research lab fine chem Industry, Mumbai.

Method:

Identification of pure drug. [8]

Identification of pure drug was carried by Fourier Transform Infra-red Spectrophotometry (Shimadzu 8400s) scanned in the range of 200-400nm.

Drug excipient compatibility study.

Studies of drug excipient compatibility are important to ascertain that the drug and excipients are compatible with each other. DSC graph and IR spectra are used to study drug-excipient compatibility.

FTIR study.

FTIR (Shimadzu 8400s) spectrophotometer was used in the range of 400-4000cm^{-1} using potassium bromide discs (Mixing ratio 1:1). The samples were hermetically sealed in aluminum pans and heated at a constant rate of 10°C/min over a temperature range of 40 to 300°C.

DSC study

The DSC thermogram of Rifampicin in combination with various excipients shows the peak onset temperature at 146.27°C and peak transition temperature at 151.48°C.

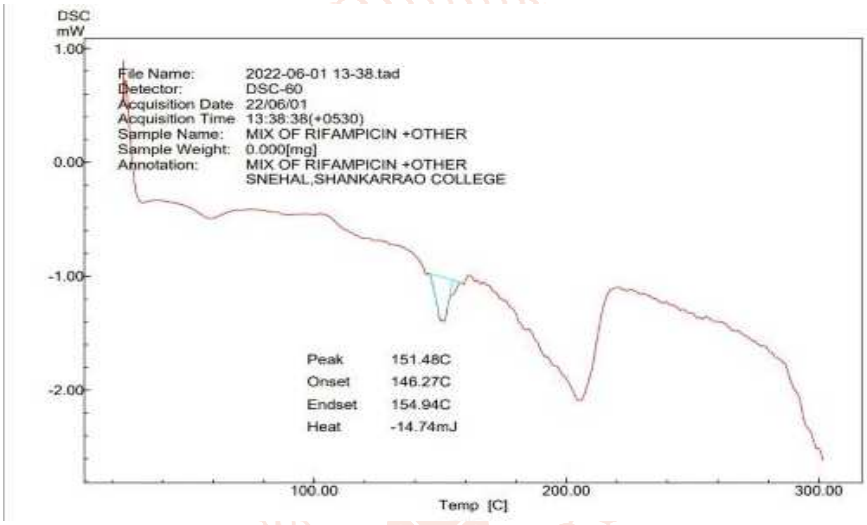
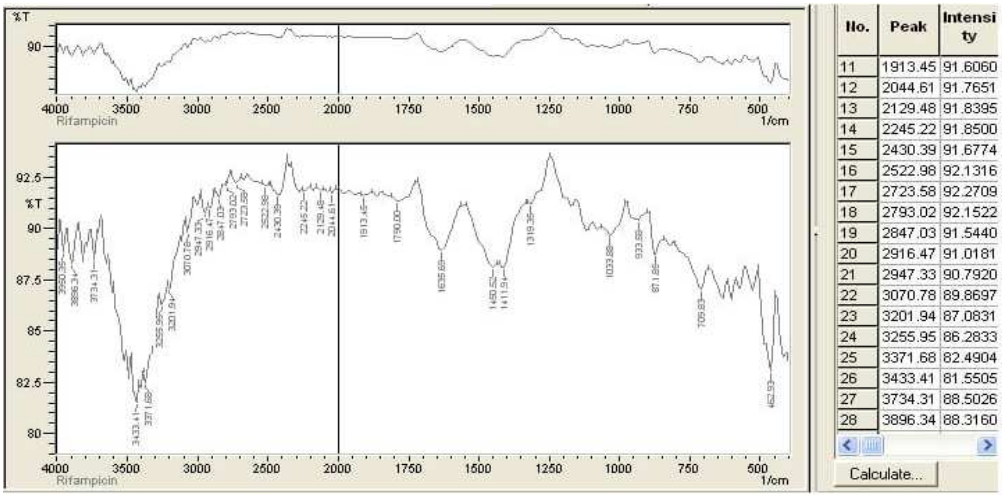


Figure 1: DSC graph of Rifampicin

FTIR spectroscopy

The FTIR spectra of pure Rifampicin was studied. It was observed that there are no major shifts in the main peaks of the drug. Rifampicin shows peaks at 1750.00 cm^{-1} (C=O Stretching), 3070.78 cm^{-1} (C-H Stretching), 1635.69 cm^{-1}(C-N Stretching), 3371.68 cm^{-1}(O-H Stretching), 3433.41 cm^{-1}(N-H Stretching), 3255.95 cm^{-1}(R-OH Stretching) and 2129.48 cm^{-1}(C-C Stretching) as shown in figure 2.



No.	Peak	Intensity
11	1913.45	91.6060
12	2044.61	91.7651
13	2129.48	91.8395
14	2245.22	91.8500
15	2430.39	91.6774
16	2522.98	92.1316
17	2723.58	92.2709
18	2793.02	92.1522
19	2847.03	91.5440
20	2916.47	91.0181
21	2947.33	90.7920
22	3070.78	89.8697
23	3201.94	87.0831
24	3255.95	86.2833
25	3371.68	82.4904
26	3433.41	81.5505
27	3734.31	88.5026
28	3896.34	88.3160

Figure 2: FTIR spectra of Rifampicin

UV spectroscopy [9]

The linearity of the response of the drug was verified at 2-10µg/ml concentrations. The calibration curve was obtained by plotting the absorbance versus concentration data and was treated by linear regression analysis. The equation for linearity curve of Rifampicin obtained was y = 0.8689x + 0.0113. The linearity curve was found to be linear and the correlation coefficient (R^2) was found 0.9981 as shown in figure 3

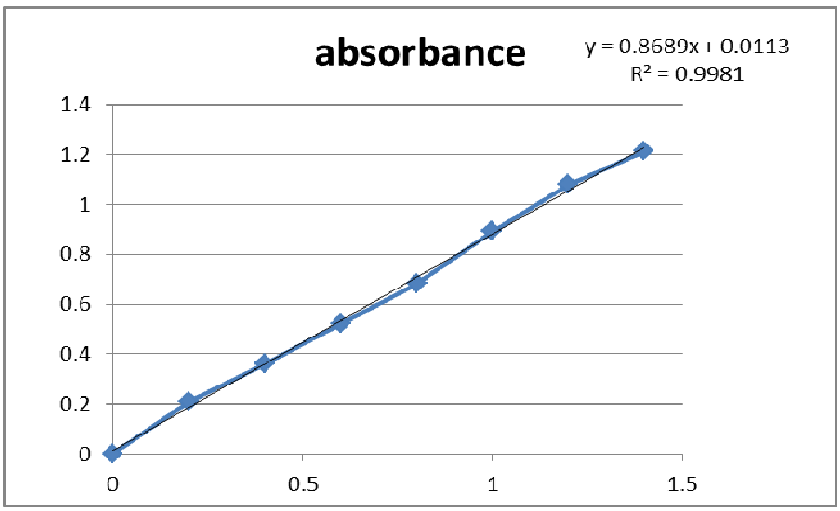


Figure 3: Calibration curve of Rifampicin

Preparation of Tablets:

Accurate quantity of drug and all ingredients were weighed according to formula and was blended homogeneously in mortar and pestle for 15 minutes. Prepared powder blend was passed through sieve No.#60. Finally, castor oil was added and further mixed for 10 minutes. The tablets were prepared using the formula as shown in table no 1.

Table 1: Formulation of Rifampicin tablets

Formulations	F1 (mg)	F2 (mg)
Ingredient		
Rifampicin	450	450
Ricinus communis oil	4.5	4.5
Lactose	19	28
Sodium bicarbonate	9	-
Stearic acid	5	5
Silicon dioxide	13	13
Total	500	500

Evaluation of powder blend

1. Angle of Repose [10,11]

The flow characteristics are measured by angle repose. Angle of repose is defined as the maximum angle possible between the surface of a pile of the powder and the horizontal plane.

$\Theta = \tan^{-1}(r/h)$

Where,

Θ= Angle of repose

r = Radius of pile in centimeter

h= Height of pile in centimeter

when the angle of repose is less than 25° the flow is said to be excellent and when the angle of repose is more than 40° the flow is considered to be poor.

2. Bulk density [12]

Apparent bulk density was determined by pouring blend into a graduated cylinder. The bulk volume and weight of the powder (M) was determined. The bulk density was calculated using the formula

BD = M/Vb

Where,
BD= Bulk density
M= Weight of powder
Vb= Bulk volume

3. Tapped density [13]

The minimum volume (Vt) occupied in the cylinder and the weight (m) of the blend was measured. The tapped density (ρt) was calculated using the following formula.

TD=M / ρt

Where,
TD= Tapped density
M= Weight of powder
ρt= Tapped volume

4. Compressibility Index

The simplest way for measurement of free flow of powder is compressibility, a indication of the case with which a material can be induced to how is given by compressibility index (I) which is calculated as follows;

Carr's compressibility index (%) = TD-BD/ TD x100

5. Hausner's ratio

Hausner's ratio is an indirect index of ease of powder flow. It is calculated by the following formula;

Hausner's ratio= ρ t/ρ b

Where,
ρ t is tapped density
ρ b is bulk density

EVALUATION OF MARKETED TABLETS AND PREPARED RIFAMPICIN TABLETS:

1. Appearance

The tablets were visually observed for capping, chipping and lamination

2. Weight Variation Method

Twenty tablets were randomly selected from each batch and individually weighed. The average weight and standard deviation of 20 tablets was calculated. The batch passes the test for weight variation test if not more than two of the individual tablet weight deviates from the average weight.

3. Thickness

Three tablets were selected randomly from each batch and thickness was measured by using Vernier Calliper.

4. Hardness [14]

Hardness or tablet crushing strength (Fo) the force required to break a tablet in a diametric compression was measured using Pfizer Hardness Tester. For each formulation, the hardness of 6 tablets was determined using the Pfizer hardness tester. The tablet was held along its oblong axis in between the two jaws of the tester. At this point, reading should be zero kg/cm2. Then constant force was applied by rotating the knob until the tablet fractured. The value at this point was noted in kg/cm^2.

5. Friability [15]

Friability of the tablets was determined using Roche Friabilator. This device subjects the tablets to the combined effect of abrasions and shock in a plastic chamber revolving at 25 rpm and roping the tablets height of 6 inches in each revolution.

Pre-weighed sample of tablets was placed in the Friabilator and were subjected to 25 revolutions. Tablets were dedusted and reweighed, the friability (F) is given by the formula.

% F = (Initial wt. - Final wt. / Initial wt.) x 100.

6. Content uniformity

The rifampicin content was estimated as follows.

Method

20 tablets were finely powdered and weight equivalent to 10 mg of rifampicin was dissolved in 100 ml of 0.1N HCL and assayed for drug content using UV-Visible spectrophotometer at 256 nm.

7. In-vitro Dissolution studies [16]

Method

Dissolution profiles of Marketed tablets and prepared rifampicin tablets were determined using the USP Type II Dissolution test apparatus set with a paddle speed of 100 rpm. Dissolution was performed in 900 ml of 0.1N HCl maintained at 37± 0.50°C. Aliquot of dissolution medium, 5 ml was withdrawn at 0, 5, 10, 15, 30 and 45 min. The amount of drug dissolved was determined by UV-Visible spectrophotometer by measuring the absorbance of the sample at 336nm. An equal volume of fresh medium, pre-warmed at 37^0C was replaced into the dissolution medium after each sampling to maintain the constant volume throughout the test.

RESULTS AND DISCUSSION

Table 2: Physical appearance of Tablet blend

Formulations	Physical Appearance	
	Colour	Appearance
F1	Red brown	Powder
F2	Red brown	Powder

Table 3: Evaluation of tablet blend

Formulations	Angle of repose (Θ)	Bulk Density (gm/cm^3)	Tapped Density (gm/cm^3)	Hausner's Ratio (H_R)	Carr's Compressibility index (%)
F1	18.27±0.78	0.33±0.014	0.47±0.005	1.25±0.05	15.41±0.12
F2	21.99±1.72	0.30±0.011	0.48±0.005	1.23±0.005	14.5±0.24

Table 4: Evaluation of Marketed Tablets

Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Drug Content (%)	Weight Variations (mg)
3.6 ± 0.11	4.8 ± 0.17	0.8±0.005	98.04±3.41	449±0.57

Table 5: Evaluation of Prepared Tablets

Sr. No	Formulations	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Drug Content (%)	Weight variations (mg)
1	**F1**	3.33±0.57	4.63 ± 0.45	0.6±0.31	98.75±0.01	499± 1.15
2	**F2**	4.5±1	4.56± 0.63	0.8±0.41	98.50±0.11	501±2.51

In Vitro Dissolution studies

Dissolution Profile of Marketed Tablets:

Dissolution study of marketed tablets carried out in 0.1N HCL and analysed Spectro -photometrically at 336nm. Each preparation was tested in triplicate and then mean values were calculated. The Table 6 indicates the % drug release of marketed tablets at the end of 45 min. And graph was plotted to show % drug release which is represented in figure 4.

Table 6: - Dissolution profile of marketed tablets.

Sr. No.	Time (min)	Cumulative % drug release
1	0	00
2	5	12.78±0.21
3	10	29.15±0.25
4	15	42.80±0.13
5	30	69.99±0.18
6	45	92.87±0.94

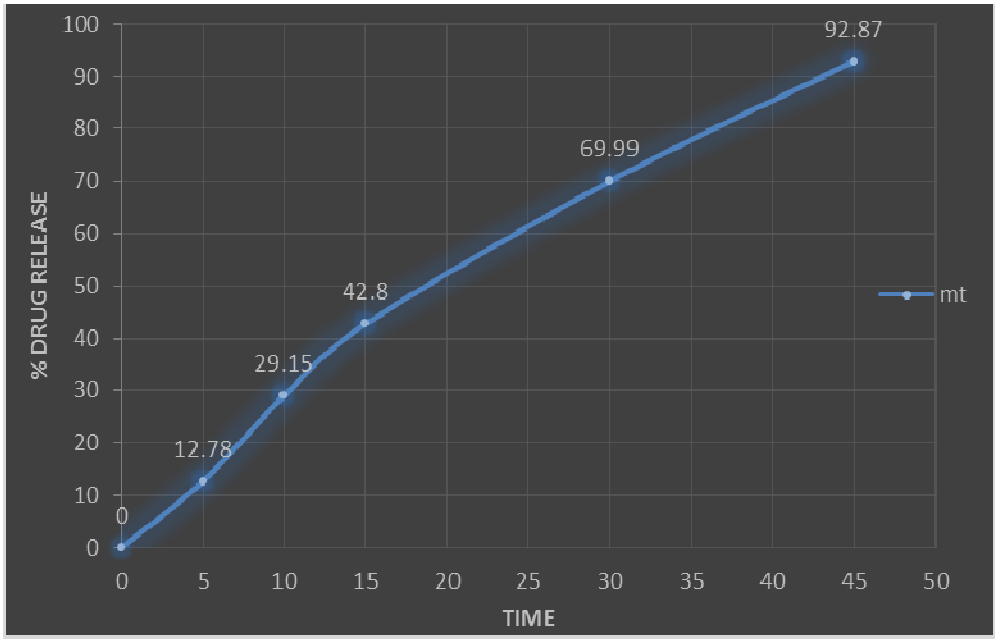


Figure 4: - Dissolution profile of marketed tablets

Table 7: Dissolution profile of Prepared tablets

Sr. No	Time (min)	Cumulative % drug release	
		F1	F2
1	0	00	00
2	5	18.71±0.14	13.72±0.17
3	10	32.65±0.06	24.52±0.46
4	15	44.54±0.65	34.88±0.06
5	30	67.11±0.02	52.47±0.27
6	45	81.89±0.15	69.87±0.42

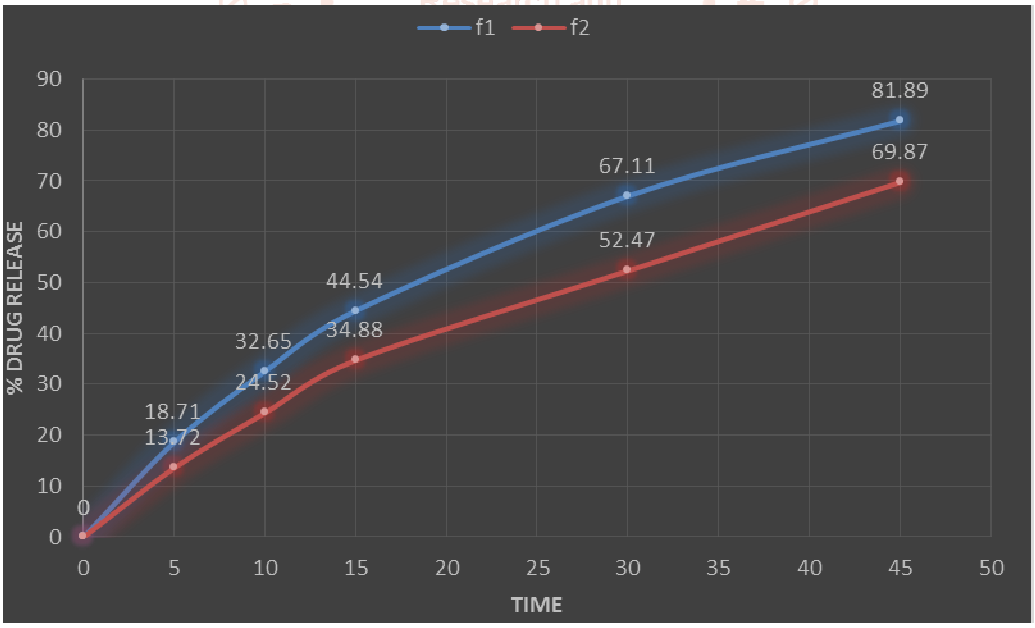


Figure 5: Dissolution Profile of Rifampicin Tablet F1 and F2.

CONCLUSION

Overall, the results concluded that suitable formulated batch F1 of Rifampicin tablets prepared by conventional method improved the dissolution rate. It was decided to prepare Rifampicin tablets by direct compression method. In the formulation of tablets, *Ricinus Communis Oil* was used as a binder. Prior to compression, the tablet blend was evaluated for angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio. Both, MARKETED TABLETS and PREPARED TABLETS were also evaluated for weight variation, hardness, friability, drug content, in vitro drug release. In the above studies, F1 batch showed promising results. It was further supported by FTIR analysis which showed that it had no interaction. So F1 formulation was considered as the optimized formulation. The comparative study indicated that the

formulated product has a comparative good result when compared with the standard formulation. The percentage drug release of drug was calculated. Dissolution profiles of marketed tablets and prepared rifampicin tablets were studied. Out of two batches of Rifampicin tablets, F1 showed optimum drug release i.e. 81.89 %.

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