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DEVELOPMENT, FORMULATION AND EVALUATION OF ETHAMBUTOL HYDROCHLORIDE AND ISONIAZID COMBINATION TABLETS

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ABSTRACT

Tuberculosis is a chronic disease and a major health problem in developing countries. About 1/3rd of the world's population is infected with Mycobacterium tuberculosis. Ethambutol and isoniazid drugs are used as anti-tuberculosis agent in the initial treatment of pulmonary tuberculosis. Combination preparation plays an important role in tuberculocidal clinical treatment because of its better and wider curative synergism and weaker side effects. In the present study combination tablet containing ethambutol and isoniazid were prepared by the wet granulation method using a different binder such as starch paste, PVP-IPA, gelatine, HPMC and HPC. In the study common tablet properties like thickness, hardness, weight variation, friability, percent release and assay were done. Among these different formulations with different binders, batches F1 to F5 with wet granulation, the formulation batch F5 shows the satisfactory in vitro drug release and other evaluation parameter as compared to innovator formulation. The cumulative percentage drug release of optimized formulation ethambutol and isoniazid was found to be **99.23%** and **99.28%** respectively. The result of stability study of optimized formulation batch F5 shows that it is stable at 40^0C±2^0C. /75% RH. ± 5% RH as there was no significant changes in assay, physicochemical parameters and release pattern observed after two month.

KEYWORDS: Anti tuberculosis Agent, Effect of different binders, % drug release, Assay.

1. INTRODUCTION[1,2,3]

Ethambutol is a white crystalline powder, soluble in chloroform, water[1], it has pKa 9.35, chemically called 2, 2'-(1, 2-Ethylenediimino) bis- 1-butanol **[**Fig.1]. It is an oral chemotherapeutic agent which is specifically effective against mycobacterium, which was the recent discovered (1961) first line treatment as anti-TB drug.[1] It has been found to inhibit arabinosyl transferees involved in arabinogalactan synthesis and to interfere with mycolic acid incorporation in mycobacterial cell wall.[2,3] It has excellent activity in vitro and in vivo against Mycobacterium tuberculosis.

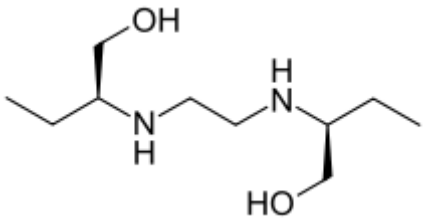

FIG. 1: Chemical Structure of Ethambutol.

Isoniazid (INH) was introduced in 1952 as a drug that is quite effective in the treatment of tuberculosis.[2,3] Isoniazid is a white crystalline powder, soluble in water, rather difficult to dissolve in ethanol, difficult to dissolve in chloroform and ether[1], it has pKa 13.61, chemically called is pyridine-4- carbohydrazide **[**Fig.2]. The primary mechanism of action of INH is inhibition of synthesis of mycolic acids which are unique fatty acid components of mycobacterial cell wall. Based on the germicidal properties of its tuberculosis, to obtain the effectiveness of treatment, shortness of treatment and prevent the emergence of resistance by the combinations with other 1st first line antituberculosis agents. One such combination is an INH and Ethambutol hydrochloride. These combination is definitely shows the synergistic effect.[4]

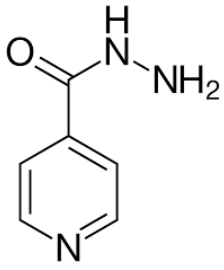

FIG. 2: Chemical Structure of Isoniazid.

Ideal properties of Tablets[5]

The objective of the developed and manufactured of the compressed combination tablet is to deliver orally the correct amount of drug in the proper form, at or over the proper time and in desired location. Besides the physical and chemical properties of the medicinal agents formulated as a tablet, it should posses following properties.

i. A tablet should have elegant product having its own identity, while beings free defects such as chips, cracks, discolouration and contamination.
ii. Must be uniform in weight, and drug content.
iii. Should have the sufficient strength to withstand difficulties of mechanical shock in its encountered in production, packaging, shipping, and dispensing.
iv. Should have physical and mechanical stability to maintain its physical/chemical attributes over time.
v. It must be release the medicinal agents in the body in a predictable and reproducible manner.
vi. Must have suitable chemical stability over a time so as not to allow alteration of the medicinal agents.

2. AIM AND OBJECTIVES

The aim of the present study was to Develop, Formulate and Evaluate of Ethambutol hydrochloride and Isoniazid tablets.

1. To formulate Ethambutol and Isoniazid tablet by using different binders and disintegrants
2. To evaluate the formulations as per standard IP evaluation methods.
3. The select optimized formulation in terms of product efficacy.
4. To compare the dissolution profile, assay and HPLC profile of selected formulations with their working standard and marketed preparations.
5. To carry out the stability studies of selected formulations.
6. To minimizes or eliminates side effects, increase patient compliance and to provide economical short term treatment for the tuberculosis.
7. It can be achieved by planning for trails until the desired release pattern obtained.

3 MATERIALS AND METHODS

Ethambutol was procured by Lupin Tarapur (Aurangabad, India), Isoniazid was procured by AMSAL Chem. Talc was gifted by Alfa Chemicals, Magnesium stearate was gifted by Aristo raw Pharma Pvt. Ltd; HPC was gifted by Aristo raw Pharma pvt. Ltd (India); Maize

starch was gifted by Alfa Chemical; PVP K30 was gifted by GC Chemical Pharma; HPMC, gelatin was gifted by Dow Chemical's (India).

Facility for formulation provided by Hindustan Antibiotic Ltd. Pimpri, Pune.

4 PREFORMULATION STUDY

The preformulation study of the pure drugs were done with the following evaluations

Flow Properties.[1, 5-9]

i. **Angle of repose:** The fixed funnel and free standing cone methods employ a funnel that is secured with its tip at a given height, h, which was kept 2cm above graph paper that is placed on a flat horizontal surface. With r being the radius, of base of conical pile, angle of repose can be determined by following equation:

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

Where, θ is the angle of repose, h is height of pile; r is radius of base of the pile

ii. **Bulk density and tapped density:** Both loose bulk density and tapped bulk density were determined. A quantity of 10gm of granules/powder from each formula, previously light Shaken for the break of any agglomerates formed, was introduced into the 10ml of measuring cylinder. After the initial volume was observed, the cylinder was allowed to fall down its own weight from the hard surface from a height of 2.5cm at 2 sec Intervals. The tapping was continued until no further change in the volume was noted. BD and TD were calculated using the following formulas:

BD: Weight of the powder/volume of the packing.

TD: Weight of the powder/Tapped volume of the packing.

iii. **Compressibility index:** The compressibility index of the granules was determined by Carr's Compressibility index.

Carr's index (%) = [(TD-BD) × 100] / TD

Where, BD: Weight of the powder/volume of the packing.

TD: Weight of the powder/Tapped volume of the packing.

iv. **Hausner's ratio:** Hausner's ratio can be determined by the following equation,

Hausner's ratio = TD / BD

Where, TD -Tapped densities & BD- Bulk densities

The results of preformulation study shown in table 4

v. **Infra-red spectroscopy:**[10-12] The results shown in Fig. 3 and Table 5 for ethambutol hydrochloride and Fig. 3 and Table 5 for isoniazid.

vi. **DSC:**[10-12] The results shown in Fig. 5 for ethambutol hydrochloride and Fig. 6 for isoniazid

5 FORMULATION OF ISONIAZID AND ETHAMBUTOL TABLETS[13,14]

Table 1: Formulation of Isoniazid and Ethambutol Tablets (Innovator)

Sr. No.	Ingredients	Unit Formula (mg)
01	Ethambutol	800
02	Isoniazid	300
03	Dibasic calcium phosphate	90.50
04	Maize Starch	36.157
05	Maize Starch Paste	2.22
06	Lake of sunset yellow	0.80
07	Gelatin	20
08	Magnesium Stearate	13.33
09	Talc	10
10	Maize Starch	12
Total Weight of Tablet		**1285**

Table 2: Optimized Batches of each Formulation of Ethambutol and Isoniazid Tablets.

Sr. No.	Ingredient	F1 (mg)	F2(mg)	F3 (mg)	F4 (mg)	F5 (mg)
1.	Ethambutol	800.00	800.00	800.00	800.00	800.00
2.	Isoniazid	300.00	300.00	300.00	300.00	300.00
3.	Dicalcium Phosphate	100	90.50	70	-	100
4.	Maize starch	70	21.55	20	50	-
5.	MCC	-	20	20	40	50
6.	Gelatin 10%	10	-	-	-	-
7.	Starch paste	-	36.15	-	-	-
8.	Pvpk-30	-	-	55	-	-
9.	HPC	-	-	-	40	-
10.	HPMC 5CPS	-	-	-	-	10
11.	Lake of sunset yellow		0.80	01.00	02.00	02.00
12.	Magnesium stearate	05.00	14.00	08.00	10.00	08.00
13.	Talc	04.00	10.00	05.00	15.00	04.00
14.	Aerosil	03.00	-	03.00	05	-
15.	SSG	10	10	10	30	10
16.	Cross Povidone	-	-	10	10	08
	Total weight of Tablet	1302	1302	1302	1302	1302

6 EVALUATION OF GRANULES AND TABLETS[1,5,7]

The granules were evaluated for following official and unofficial parameter

i. Angle of repose:
ii. Bulk density and tapped density:
iii. Compressibility index:
iv. Hausner's ratio**:**

The results of evaluation of granules are shown in Table 7

All the tablets were evaluated for following official and unofficial parameter

1) Weight variation
2) Thickness
3) Hardness
4) Friability Test
5) Disintegration Test
6) Assay
7) Dissolution study

1. Weight variation

20 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 tablets weight derivative from the average weight by more than the percentage shown. (Table 8)

Table 3: Percentage deviation allowed under weight variation as per IP standard.

Percentage deviation allowed under weight variation test	
Average weight of tablets (X mg)	**Percentage deviation allowed**
X< 80mg	10
80 < x < 250 mg	7.5
x> 250 mg	5

2. Thickness

Five tablets were selected at random from individual formulations and thickness was measured by using vernier caliper scale, which permits accurate measurement. Thickness should be controlled within a ± 0.5% variation of standard value.

The results are shown in Table 8.

3. Hardness

Five Tablets was selected at random from individual formulations and hardness was measured using Monsanto hardness tester. The results are shown in Table 8.

4. Friability Test

Tablet select 20 tablets from pooled sample, weight. The tablets on calibrated balance and note down weight of 20 tablets (w1). add these tablets to the friability test apparatus, operate apparatus for 100 rotations, upon completion examine the tablets for the physical changes and remove the half broken tablets from the sample and weight on the calibrated balance.(w2). Calculate the friability in % as follow:

$$\%F = \frac{Loss\ in\ weight}{Initial\ weight} \times 100$$

The results are shown in Table 8.

5. Disintegration Test

Disintegration time for Tablets was determined using 6 tablets. Place one tablet in each six tubes of the basket, add disc to each tube and operate the apparatus using water at $37^0 \pm 2^0$C as the immersion fluid at the end of 15 mins, lifts the basket from the fluid and observe the tablets. All the tablets should disintegrate. Record the disintegration time in min. and seconds. Disintegration time for the Tablets should not be more than 15min.

The results are shown in Table 8.

7 ASSAY[1]

A. Assay of Isoniazid

Chromatographic conditions

i. Column: 15cm x 4.6 cm**,** packed with octadecyisilyl silica gel
ii. Column temperature: 30 c
iii. Wavelength: 254 nm
iv. Flow rate: 1 ml /min
v. Injection volume: 20 µl

Buffer solution PH 6.8

Dissolve 1.4 g of disodium hydrogen orthophosphate anhydrous in 1000 ml of water; adjust pH 6.8 with dilute phosphoric acid.

a) Mobile phase

Mix 960 ml of buffer solution with 40 ml of acetonitrile Filter through 0.45µ filter and degas.

b) Test solution

Weight and powder 20 tablets.171.0 mg powdered tablets containing about 40 mg of isoniazid, dissolve in 50.0 ml of methanol and dilute to 500 ml diluents.

c) Diluents

Dissolve 1.4 g of disodium hydrogen orthophosphate anhydrous in 1000 ml of water; adjust pH 6.8 with dilute phosphoric acid and sufficient water to produce 1000ml.

d) Reference solution

Weight accurately about 40 mg of isoniazid WS, dissolve in50.0 ml of methanol and dilute to 500.0 ml with the diluents.

e) Procedure

Inject the reference solution in five replicate into the chromatograph and measure responses for the major peaks. If system suitability passes then inject test solution .Record the responses for the major peaks and calculate the content of tablet.

f) System suitability

Tailing factor: NMT2.0 Theoretical Plates: NLT1500

R.S.D: NMT2.0%

g) Calculation

Calculate the Isoniazid content in tablets as % as follows

$$\%\ Assay\ of\ Isoniazid = \frac{AT \times WS \times 500 \times P \times W \times 100}{AS \times 500 \times WT \times 100 \times 300}$$

The results are shown in Table 7.

B. Assay of Ethambutol Hydrochloride

Chromatographic conditions

i. Column: 15cm x 4.6 cm**,** packed with nitrile groups chemically bounded to porous silica particles.
ii. Wavelength: 200nm
iii. Flow rate: 1.0 ml /min

iv. Injection volume: 50 µl

Buffer solution PH 7.0

1000 ml of water add 1.0 ml triethylamine, mix thoroughly adjust pH to 7.0 with phosphoric acid.

a. Mobile phase

Prepare a mixture of above buffer 7.0&Acetonitrile (50:50) filter and degas.

b. Test solution

Weight and powder 20 tablets. Weight accurately 96.0 mg powdered tablets into 100 ml volumetric flask. Add about70 ml of diluents, dissolve and dilute to 100 ml with diluents shake well.

c. Diluents

Dissolve 1.4 g of disodium hydrogen orthophosphate anhydrous in 1000 ml of water; adjust pH 6.8 with dilute phosphoric acid and sufficient water to produce 1000ml.

d. Reference solution

Weight accurately about 60 mg of Isoniazid WS into 100 ml volumetric flask. Dissolve in 70 ml of diluent and dilute to 100 ml with diluents and mix.

e. Procedure

Inject 50 µl the reference solution in five replicate into the chromatograph and measure response for the major peaks. If system suitability passes then inject test solution .Record the response for the major peaks and calculate the content of tablet.

f. System suitability

Tailing factor: NMT3.0 Theoretical Plates: NLT1500

R.S.D: NMT2.0%

g. Calculation

Calculate the Ethambutol Hydrochloride content in tablets as% as follows:

$$\%\ \text{Assay}\ of\ Ethambutol = \frac{AT \times WS \times 100 \times \mathrm{P} \times W \times 100}{AS \times 100 \times \mathrm{WT} \times 100 \times 800}$$

Where,

AT = Mean area of test preparation

AS = Mean area of standard preparation

WS= wt. of standard in mg

WT= wt. of sample in mg P = Potency of standard

W = Avg. weight of tablets

The results are shown in Table 8.

8 DISSOLUTION STUDY[1,15]

USP Dissolution apparatus: Type II (Paddle)

i. Media: Water
ii. Volume of dissolution medium: 900ml
iii. Speed of paddle rotation: 100RPM
iv. Temperature: $37^0 \pm 0.5^0C$
v. Sampling point: 5, 10, 15, 20, 30, 45 min.

PART 1

Test solution

In vitro dissolution study was carried out using USP II apparatus Paddle assembly in 900ml water for 45 mins. Temp of the dissolution medium was kept at 37 ± 0.5^0C and paddle was set at 100 rpm. At the end of specific interval time withdraw 10 ml of sample solution from a zone midway between the surface of medium, top surface of the rotating paddle and not less than 1 cm from bowl wall. Filter through Whatmann filter paper, discarding first few ml of filtrate, in separate marked test tubes. dilute 10 ml of filtrate to 20 ml with water.

Reference solution

Weight accurately 44 mg of Ethambutol Hydrochloride WS into 100ml volumetric flask, dissolve in 70 ml of dissolution medium and diluted to 100 ml with the same solvents and mix.

Procedure

Inject the reference solution in five replicate into the chromatograph and measure responses for the major peaks. If system suitability passes then inject test solution. Record the response for the major peaks and calculate the content of tablet.

Calculation

$$\%\ Drug\ Release = \frac{AT \times WS \times 900 \times 20 \times XP \times 100}{AS \times 100 \times 1 \times 10 \times 100 \times 800}$$

The results are shown in Table 9

PART 2

Test preparation

Dilute 2 ml of the filtrate obtained in part A to 50 ml.

Procedure

In vitro dissolution study was carried out using USP II apparatus Paddle assembly in 900ml water for 45 mins. Temp of the dissolution medium was kept at 37 ± 0.5^0C and paddle was set at 100 rpm. Determine the amount of isoniazid dissolve from ultraviolet absorbance at the wavelength at 263 nm of the test solution. The concentration was determined from the standard curve of isoniazid. Cumulative percentage of drugs release was calculated using the equation obtained from a standard curve.

The results are shown in Table 10.

The all % drug release / dissolution profile shown in fig. 7 to fig. 12

9 STABILITY STUDIES[16]

The results of accelerated stability studies shown in Table 12 carried out according to ICH guidelines indicated that the tablets did not show any physical changes (colour change, friability and hardness), assay and dissolution characteristics during the study.

10 RESULT AND DISCUSSION

a. Pre-formulation studies

1) Evaluation of powder

Preformulation study was done initially and results directed for the further course of formulation. Based on preformulation studies different batches of Isoniazid and Ethambutol HCL were prepared using selected excipients.

Powder were evaluated for tests Angle of repose, bulk density, tapped density, compressibility index, Hausner's ratio before punched of tablet.

Table 4: Preformulation study (Flow Properties) of pure drug.

Sr. No.	Test	Results	
		Ethambutol	Isoniazid
01	Bulk Density	0.28g/ml	0.66g/ml
02	Tapped Density	0.39g/ml	0.90g/ml
03	Compressibility Index	30%	26.66%
04	Hausner's Ratio	1.42	1.36

2) Fourier Transferred Infra-red Spectroscopy (FT-IR)

a. IR Spectra of Ethambutol

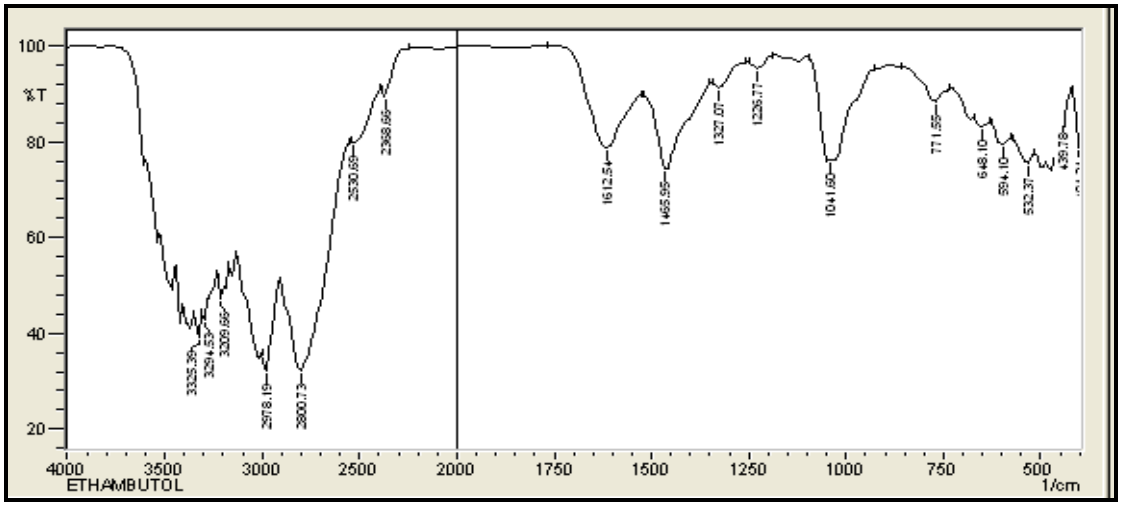

Fig. 3: IR Spectrum of Ethambutol Hydrochloride.

Table 5: Interpretation of IR Spectrum for Ethambutol Hydrochloride.

Sr. No.	Reference peak Wave number (cm^{-1})	Observed Peak Wave number (cm^{-1})	Functional group
1	3200-3600	3325.29	OH
2	3300-3500	3294.53	NH
3	3000-3200	3209.66	C-H
4	1600-1300	1465	C-H Bending
5	1250-1020	1041.60	C-H Stretching

The above FTIR spectrum shown the characteristics peak of Ethambutol hydrochloride shown in **(Fig. 3 and Table 5)** from this result it was conclude that the sample of Ethambutol hydrochloride was pure.

b. IR Spectra of Isoniazid

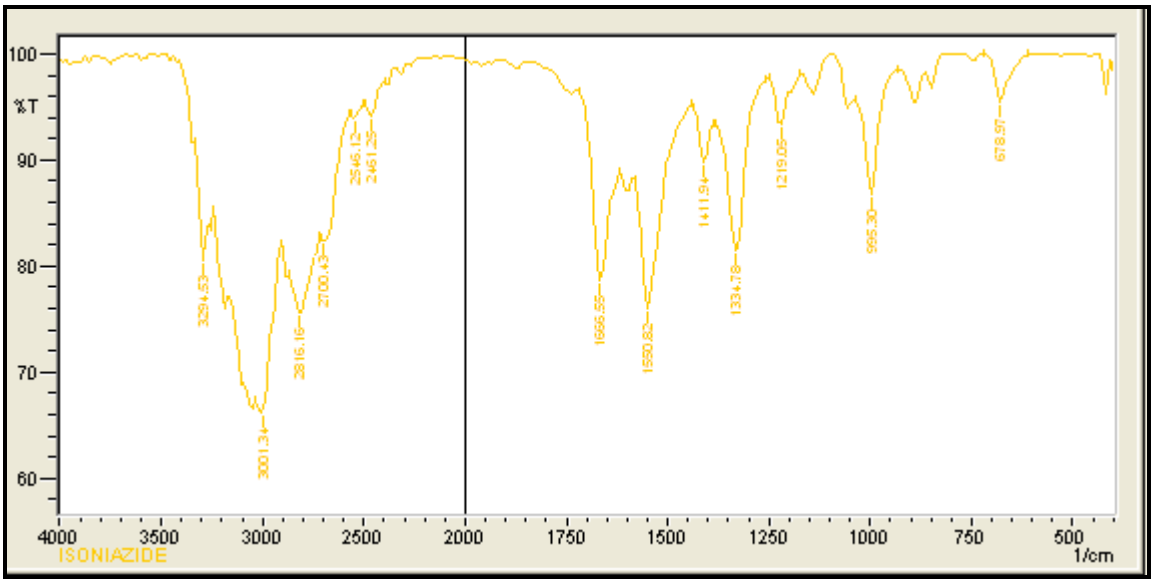

Fig. 4 IR Spectra of Isoniazid.

Table 6: Interpretation of FT-IR Spectrum of Isoniazid.

Sr. No.	Reference Peak Wave Number (cm^{-1})	Observed Peak Wave Number (cm^{-1})	Functional Group
1	1870-1540	1666.55	C=O
2	1650-1580	1550.82	NH
3	1250-1020	1219.05	C-N
4	995-985	995.30	C≡C
5	3000-2800	2816	N-H Stretching

The above FTIR spectrum shown the characteristics peak of Isoniazid shown in **(Fig. 4 and Table 6)** from this result it was conclude that the sample of Isoniazid was pure.

3) Differential Scanning Colorimetry (DSC)

a) DSC Thermogram of Ethambutol

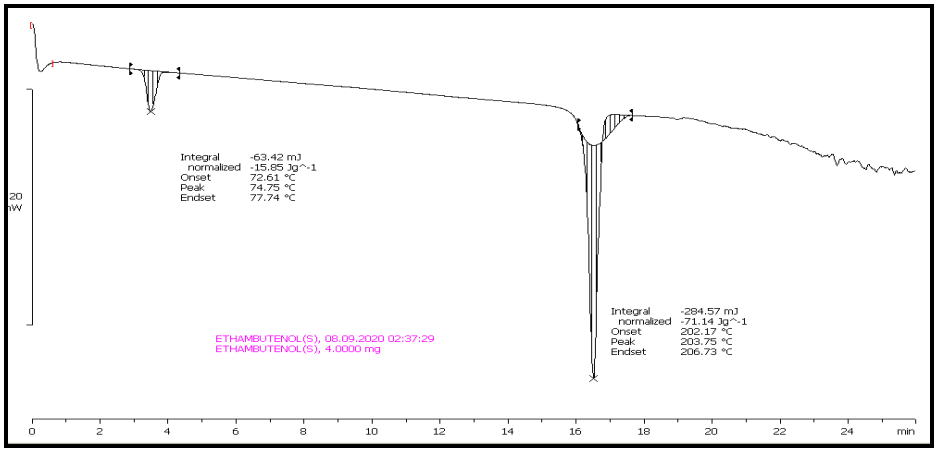

Fig. 5 DSC Thermogram of Ethambutol.

DSC Thermogram of given sample of Ethambutol shown in fig. 5. Thermogram shows sharp endotherm at 202.17˚C which is corresponding to the melting point of Ethambutol. From this it is conclude that the given sample of Ethambutol Hydrochloride is in pure form.

a. DSC Thermogram of Isoniazid

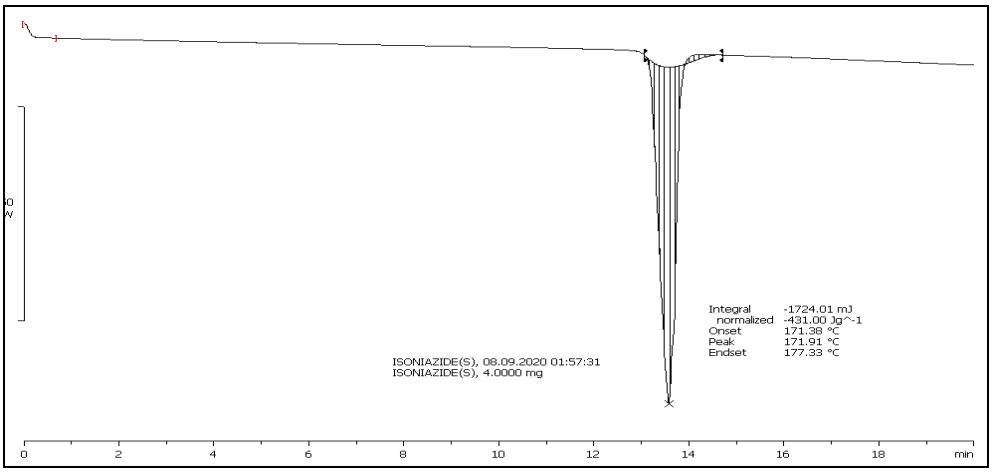

Fig. 6 DSC Thermogram of Isoniazid.

DSC Thermogram of given sample of Isoniazid is shown in Fig. 6 the Thermogram shows sharp endotherm at 171.38˚C which is corresponding to the melting point of Isoniazid. From this it is conclude that the given sample of Isoniazid is in pure form.

b. Flow properties of granules

Table 7: Flow properties of blend/granules.

Batch No.	% LOD	Angle of Repose	Bulk Density(g/ml)	Tapped Density(g/ml)	Carr's Index (%)	Hausner's Ratio
INNOVATOR	0.55	28.56	0.586	0.671	9.69	1.07
F1	0.34	39.23	0.34	0.39	17.02	1.20
F2	0.75	36.51	0.37	0.45	17.77	1.21
F3	0.93	39.46	0.34	0.43	20.93	1.26
F4	0.18	27	0.40	0.50	20	1.25
F5	0.22	23.7	0.45	0.542	16.16	1.20

c. Evaluations of combination tablets

Table 8: Physico-chemical Evaluation of combination tablets.

Batch No.	Weight variation	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Disintegration time	Assay	
						ETH	INH
INNOVATOR	1288±0.3	6.7±0.2	6.4±0.3	0.22±0.09	9min17sec	99.14	100.03
F1	1302.5±0.2	6.9±0.2	6.2±0.2	0.18±0.09	7min55sec	98.17	100.71
F2	1303±0.3	7.0±0.3	6.3±0.1	0.2±0.08	8min05sec	99.54	98.91
F3	1303.2±0.5	6.8±0.2	6.2±0.3	0.30±0.05	7min37sec	98.94	99.15
F4	1303.5±0.3	7.0±0.3	6.5±0.4	0.32±0.07	9min47sec	99.02	100.16
F5	1302±0.5	6.9±0.2	6±0.2	0.12±0.08	7min23sec	99.56	100.39

d. Dissolution studies

In Vitro Dissolution studies

Table shows the data for in Cumulative % release of Ethambutol HCL from tablet batches F1, F2, F3, F4 and F5 respectively. (Table 8)

In Vitro Dissolution studies

Table shows the data for in Cumulative % release of isoniazid from tablet batches F1, F2, F3, F4, and F5 respectively. (Table 9)

Table 9: Cumulative % release study of Ethambutol of various Formulation.

Time	% Cumulative Release					
	INNOVATOR	F1	F2	F3	F4	F5
0	0	0	0	0	0	0
5	35.30	33.49	32.85	37.45	34.61	35.95
10	49.57	55.01	52.03	50.32	55.41	51.55
15	60.67	67.19	68.15	61.88	64.69	61.95
20	78.60	75.52	72.30	76.85	74.55	71.61
30	88.3	86.90	87.23	81.55	82.84	85.89
45	97.36	95.51	97.43	94.61	96.8	99.23

Table 10: Cumulative % release study of Isoniazid various formulation.

Time in min	% Cumulative Drug Release					
	INNOVATOR	F1	F2	F3	F4	F5
0	0	0	0	0	0	0
5	36.4	31.54	35.84	32.71	30.5	32.54
10	55.3	55.63	54.23	53.91	57.88	51.78
15	68.9	63.84	65.54	67.27	68.24	64.55
20	79.7	77.64	75.14	76.45	76.83	74.57
30	89.4	86.18	87.92	83.90	87.64	89.4
45	97.46	95.57	97.87	96.25	97.78	99.28

Table 11: Cumulative % release study of (F5 and Innovator).

Time in min	% Cumulative Drug Release			
	INNOVATOR		F5	
	ETB	INH	ETB	INH
0	0	0	0	0
5	35.30	34.43	35.95	32.54
10	49.57	55.3	51.55	51.78
15	60.67	68.9	61.95	64.55
20	78.60	79.7	71.54	74.57
30	88.3	87.81	82.48	89.4
45	97.36	97.46	99.23	99.28

e. Dissolution profiles

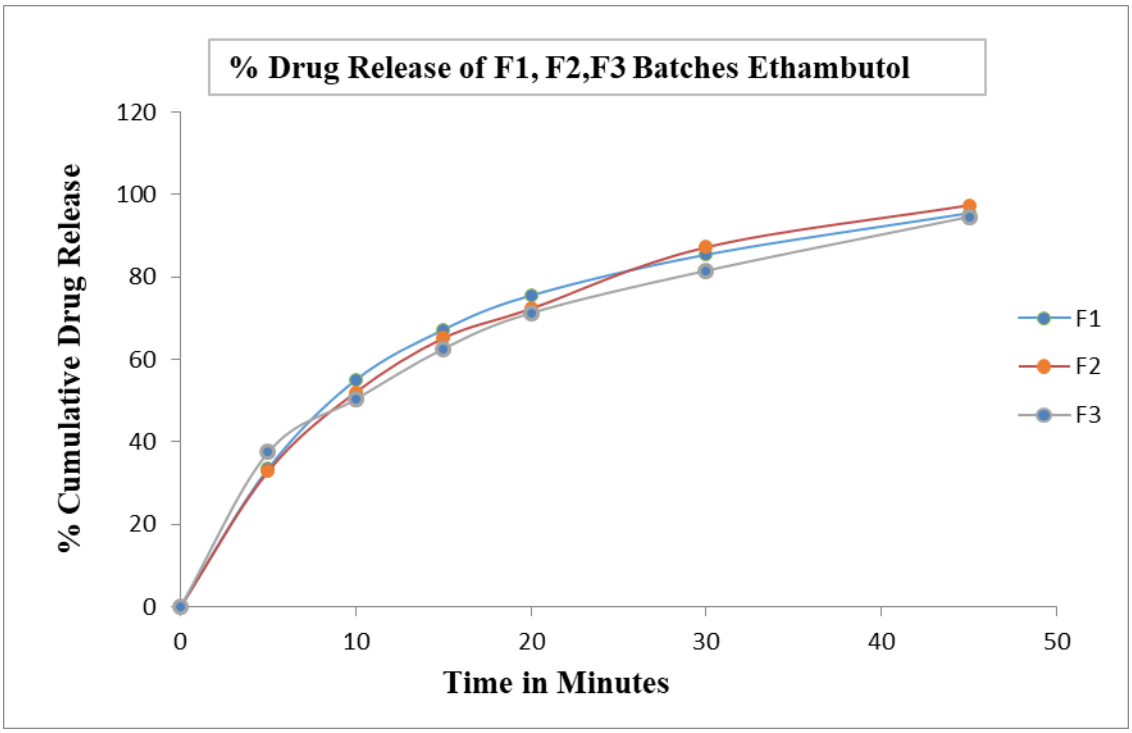

Fig 7: Graph of cumulative % drug release for F1, F2, F3 batches (ETB)

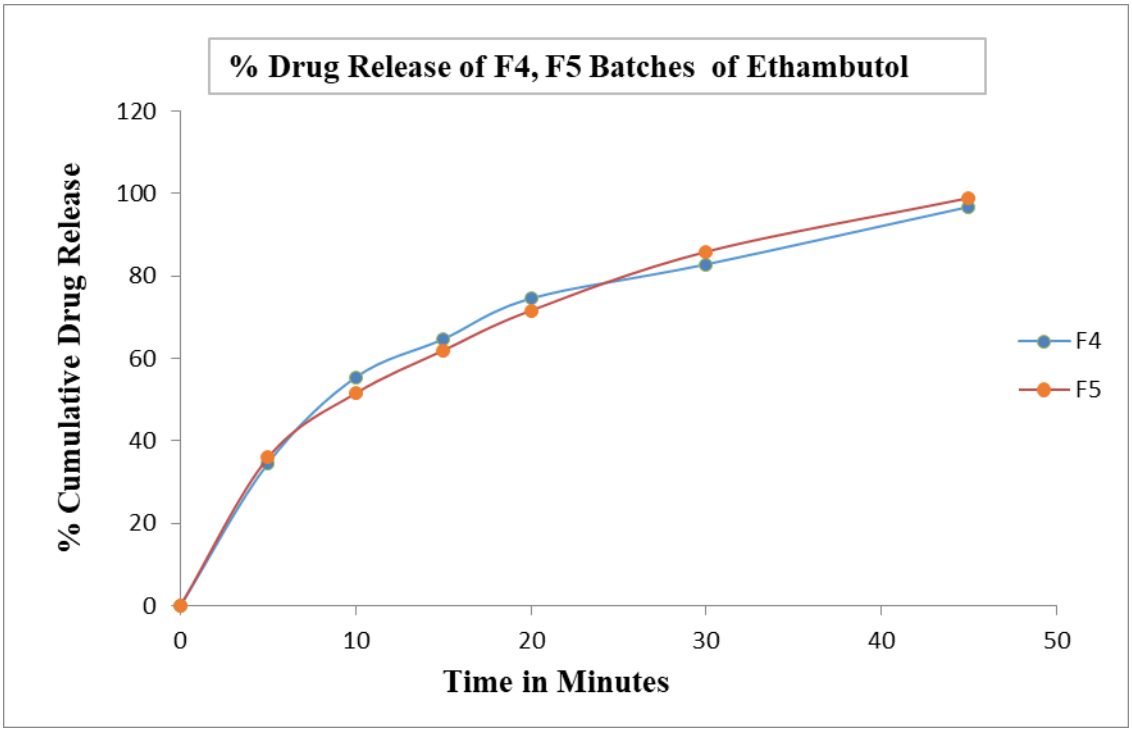

Fig 8: Graph of cumulative % drug release for F4, F5 batches (ETB)

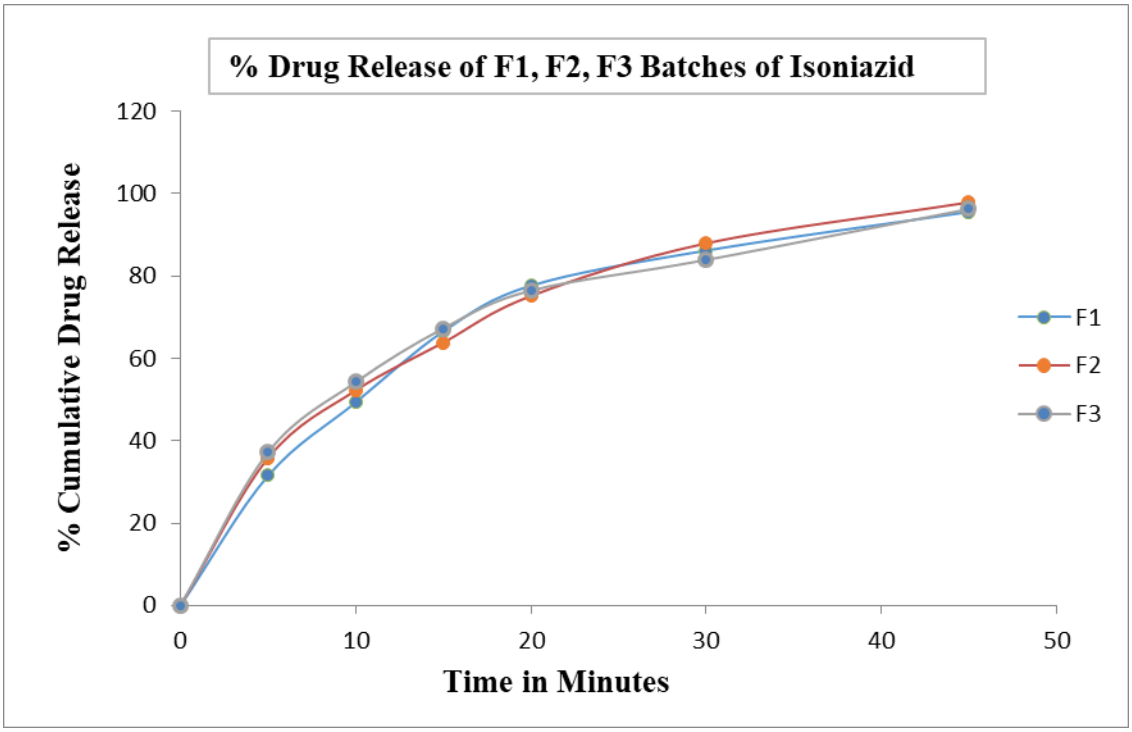

Fig. 9: Graph of cumulative % drug release for F1, F2, and F3 batches (INH)

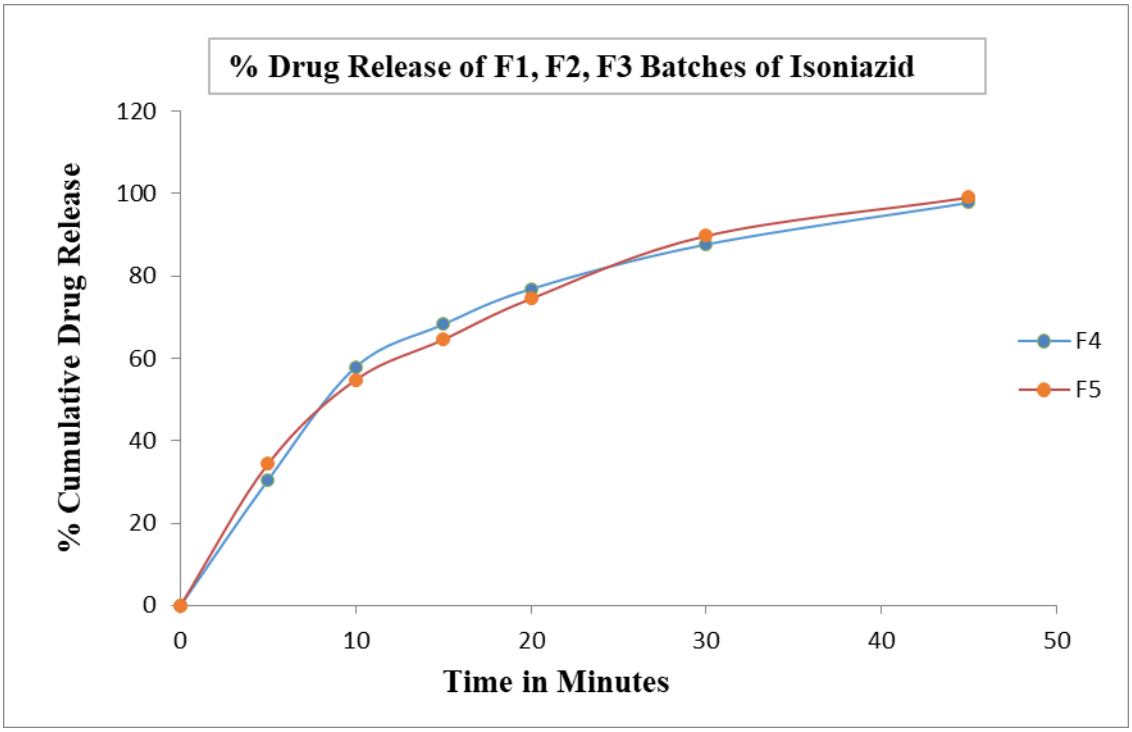

Fig. 10: Graph of cumulative % drug release for F4, F5 batches (INH)

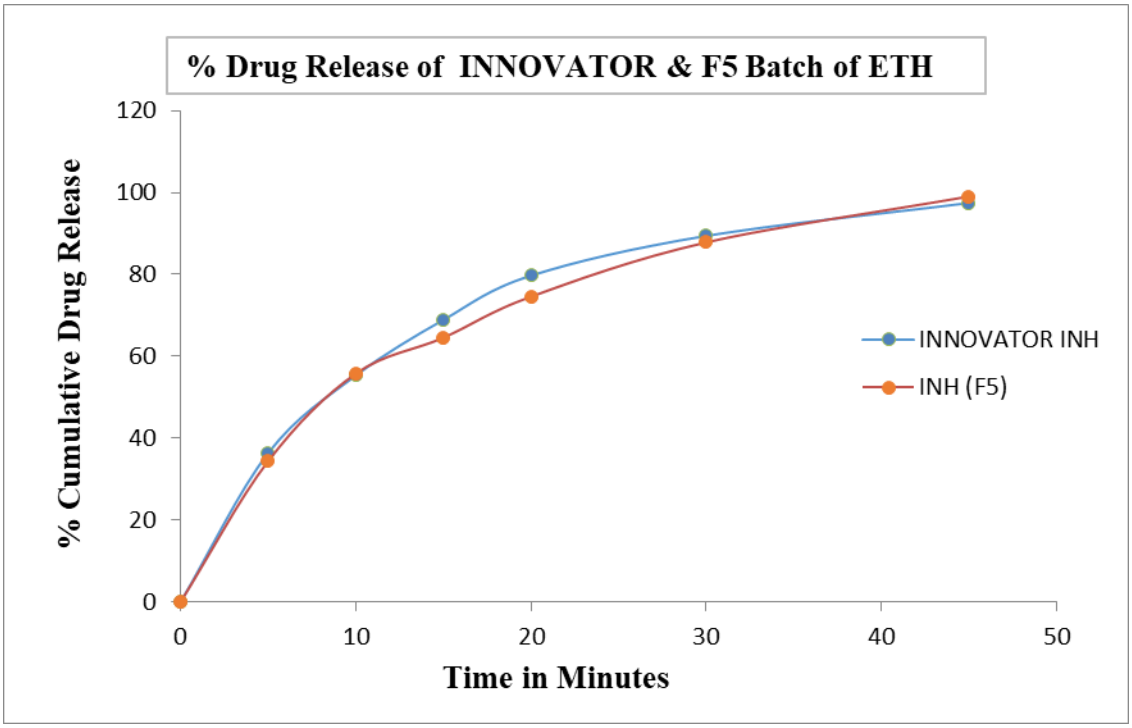

Fig. 11: Graph of cumulative % drug release for INNOVATOR & F5batches (ETH)

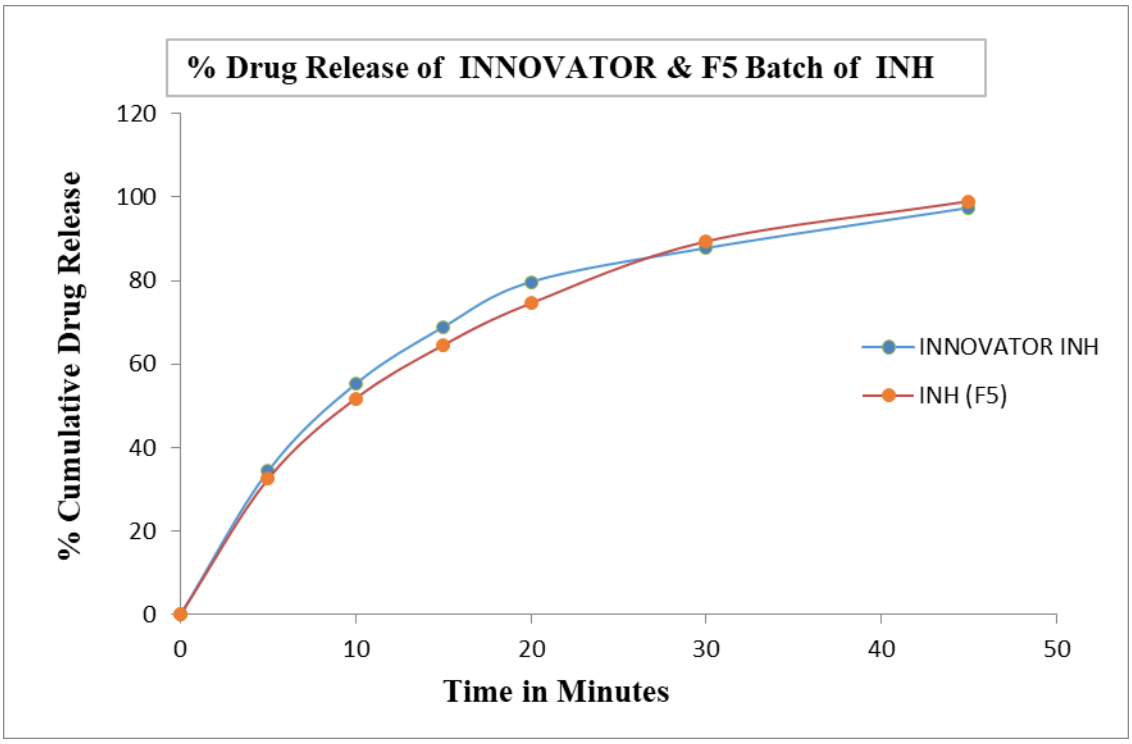

Fig. 12: Graph of cumulative % drug release for INNOVATOR & F5 batches (INH)

f. Stability Study

Table No. 10: Stability Study of Optimized Formulation F27.

Sr. No.	Parameter	Initial	After Two Months
01	Hardness	6	6
02	Thickness	6.9±0.3	6.9±0.3
03	Friability	0.12±0.08	0.18±0.09%
04	Weight Variation	1302±0.15%	1302 ±0.11%
05	Disintegration Time	7 Min 23 Sec.	7 Min 39 Sec.
06	% Drug Release	99.23 & 99.28	99.13 & 98.89
07	% Assay	99.56 & 100.39	99.07 & 100.08

11 SUMMARY AND CONCLUSION

The present study was undertaken with an aim to develop, formulate and evaluate ethambutol hydrochloride and isoniazid combination tablets using different binders. Preformulation study was done initially and result directed for the further course of formulation. Based on preformulation studies different batches of ethambutol and isoniazid were prepared using selected excipients. Powders were evaluated for tests angle of repose, bulk density, tapped density, compressibility index, and Hausner's ratio before being punched as tablets. Various formulations of tablets of ethambutol and isoniazid were developed using various binders viz, starch paste, gelatin, HPMC, PVPK -30, HPC in different proportions and combinations by wet granulation technique. The tablets were evaluated for physical characterization, in vitro release study and stability studies. Result of in vitro release profile indicated that formulation (F5) was the most promising formulations as the drug release from this formulation was high as compared to others formulations. The cumulative % of drug release of formulation F5 (INH) and F5 (ETB) were 99.28 and 99.23 respectively. Stability study was conducted on tablets of Batch F1 stored at $40^0 \pm 2^0$C/75±5% RH for one month. Tablets were evaluated for hardness, friability, in-vitro release profile and drug content. After one month no significant changes were observed in any of the studied parameters during the study period, thus it could be concluded that formulation was stable. From the above results and discussion it is concluded that formulation of tablets of ethambutol and isoniazid containing HPMC batch F5 can be taken as an ideal or optimized formulation compressed tablet as it fulfils all the requirements for tablet.

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