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FORMULATION, DEVELOPMENT & EVALUATION OF DISPERSIBLE TABLET OF ETHIONAMIDE

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The objective of this study was to develop an optimized stable dispersible tablet of the Ethionamide.
Ethionamide selected for the study acts by inhibition of mycolic acid synthesis by inhibition of enoyl reductase enzyme. The dispersible tablets were prepared by different binders, disintegrant and flavours finally optimized with a tablet weight of 270 mg. The Ethionamide was evaluated for pre formulation studies like DSC and by physical observation of binary mixture of drug and excipients. DSC study revealed that melting point of the drug was 161.70 C DSC thermograms and physical observation shown that both Ethionamide and were used in the formulation were compatible and have no significant change in the binary mixture of drug and excipients. The pre compressional and post compressional studies were carried out on dispersible tablets. The values were within the acceptance limit. The flow properties of the drug were improved by granulation. The post compressional parameters like Weight variation, Hardness, Thickness, Disintegration time, Fineness of dispersion, in -vitro dissolution study were performed and they found to be satisfactory. In order to evaluate the stability, the final optimized formulation was charged at long term and accelerated conditions of temperature and humidity as per ICH guidelines (25◦C/60% RH and 40◦C/75% RH) and the exposed samples were evaluated for physical parameters and in-vitro dissolution study.

KEYWORDS: Dispersible tablet, Ethionamide, Mycolic acid, Enoyl reductase enzyme.

1. INTRODUCTION

A solid dosage form is drug delivery system that includes tablets, capsules, sachets and pills as well as a bulk or unit dose powders and granules. Oral dosage form is the most popular route for drug therapy. Over 80 % of drugs formulated to produce systemic effects in the United States are produced as oral dosage forms. Tablets and capsules are currently accounted for the highest proportion of all drug presentations. this is because of several factors for example their simple and practical administration further more they have good chemical, physical and microbiological stability as well as relatively low cost of manufacturing.

Tablets are composed of a mixture of powders (drug and other functional excipients) which are highly compressed, beside the active drug there has to be fillers to make the tablet in more suitable size. To keep the powders together binders are used and to facilitate the making process of the tablet, glidants, and anti-adherents and lubricants are used. The glidant increases the flowability of the powder mass and reduces their interparticular friction. Anti-adherent is added to minimise the sticking of the powder to the faces of the punches and die wall while compaction, and a lubricant is added to minimise friction between powder and die.

Flavour and sweetener are primarily used to improve or mask the taste of drug. The tablets are also colored to make them easily to identify. Disintegrates are agents included in the tablet (and some capsule) formulations to increase the breakup of the tablet and capsule slugs into fine fragments in an aqueous environment, thereby increasing the available surface area and increase the more rapid release of the drug substance and there by the absorption. They increase moisture penetration and dispersion of the tablet matrix. This is especially very important for immediate release products because they need rapid release of drug substance.

- **Tuberculosis**

Tuberculosis[8] a disease caused by M. tuberculosis, it has been recorded in history since Egyptian, Greco-roman civilizations with evidence of spinal cord tuberculosis being recorded as long as ago 3400 BC. Description of tuberculosis spondylitis has been recorded

in ancient Indian scriptures at some time of 1500 and 700 BC. Tuberculosis has been postulated that it is unimportant pathogen to human until the coming of industrial evolution. With resulting of urbanization a new epidemic disease was evolved described as a great white plague. In the newly industrialised countries the incidence of tuberculosis probably increased sharply from the mid 1700 with subsequent pandemic spread throughout Western Europe over the next century and a peak incidence around 1800.

- **Epidemiology**[8]

There were 8.7 million new cases of active tuberculosis and 1.4 million deaths recorded worldwide in 2011, among patients 310,000 incident cases of multidrug-resistant tuberculosis, caused by organisms resistant to at least isoniazid and rifampin. More than 60% of these patients were in China, India, the Russian Federation, Pakistan, and South Africa, about of 84 countries have reported cases of extensively drug-resistant tuberculosis. The absolute number of cases is recorded highest in Asia, with India and China having the greatest burden of disease globally.

- **Pathogenesis**

Patients with active pulmonary tuberculosis are the source of Mycobacterium tuberculosis. There are two possible ways for occurrence of Tuberculosis in humans, either from a recent infection with M. tuberculosis; from the reactivation of dormant tubercle bacilli years or decades after initial infection resulting in tuberculosis disease.

Latent tuberculosis infection means patient is infected with Mycobacterium tuberculosis. But the patient does not have symptoms of tuberculosis.

Active tuberculosis is contagious while latent tuberculosis is not. There is no possibility to get infection TB from someone with latent tuberculosis. The main risk that approximately 10% of these patients will go on to develop active tuberculosis at a later stage of their life. It is particularly true under following conditions.

2. Drug Profiles

The Ethionamide selected for the formulation and development is used to treat Tuberculosis

- **Structure Of Ethionamide -**

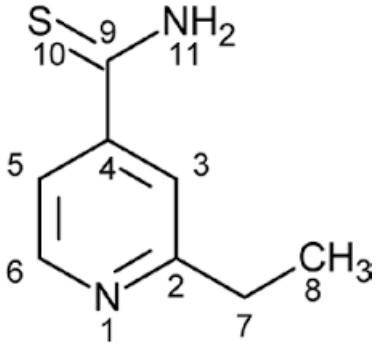

Table 2.1 Physicochemical properties of Ethionamide.

Molecular weight	166.2
Description	Yellow crystal powder with slight sulphide like odour
Solubility	Very sparingly soluble in water slightly soluble in chloroform soluble in methanol
Melting point	158-164
Bio availability	Approximately 100%
pKa	4.9
pH	6-7
Log P	0.739
Storage	Store in well air tight containers at less than 400C, preferably between 150-300 C

3. METHODOLOGY

Drug -excipients compatibility study requires 5 mg of drug, in 50 % mixture (1:1) with excipient, to maximize the likehood observing an interaction, while performing the test mixture should be examined under to avoid the oxidative, pyrrolytic effect at heating rates on apparatus.

Table 3.1: Calibration curve of Ethionamide.

Concentration (µg/ml)	Peak area
0	0
0.5	5003
1	99801
2	14980
3	23980
4	30040

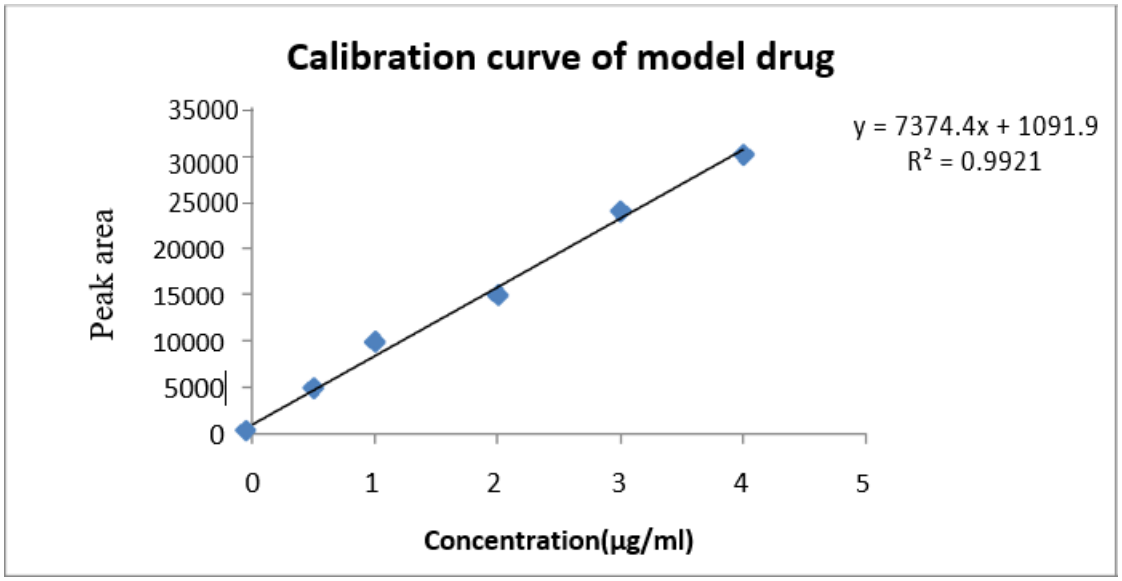

Fig 3.1: standard graph of Ethionamide in 0.1 N HCl.

Drug excipients compatibility studies Physical observation

Table 3.2: Drug excipients compatibility study of Ethionamide and individual excipients.

Ingredient	**Initial**	**400/75 % RH (7 days)**	**400/75 % RH (15 days)**	**400/75 % RH (30 days)**
Ethionamide	Yellow	Yellow	Yellow	Yellow
MCC PH 101	White	White	White	White
Crospovidone	White	White	White	White
Sucralose	White	White	White	White
Maize starch	White	White	White	White
PVPK 30	White	White	White	White
Sodium chloride	White	White	White	White
Aspartame	White	White	White	White
Menthol	White	White	White	White
Peppermint flavour	White	White	White	White
LHPC LH 11	White	White	White	White
Aerosil	White	White	White	White
Magnesium stearate	White	White	White	White
All excipients	White	White	White	White

4. Formulation and Evaluation

Table 4.1 : Formulation table.

Ingredients	F1	F2	F3	F4	F5	F6	F7
Dry mix							
Ethionamide	125	125	125	125	125	125	125
Crospovidone	5	7	10	10	10	15	16
MCC PH 101	70	64	57	57	57	52	48
Sucralose	1.5	3	4	4	4	4	4
Granulation							
Maize starch	_	_	5	15	10	10	12
PVPK 30	4	4	5	5	10	10	12
Purified water	QS	QS	QS	QS	QS	QS	QS
Prelubrication							
Crospovidone	10	13	12	12	12	16	17
MCC PH 102	23	19	15	5	5	19	17
Acacia	0.5	1	_	_	_	_	_

Sodium chloride	2	3	4	4	4	4	4
Aspartame	1.5	3	4	4	4	4	4
Menthol	1	2	2	2	2	2	2
Peppermint flavour	1.5	3	4	4	4	4	4
LHPC LH 11	_	_	_	_	_	2	2
Talc	2	_	_	_	_	_	_
Aerosil	1	1	1	1	1	1	1
Lubrication							
Magnesium stearate	2	2	2	2	2	2	2
Total weight	250	250	250	250	250	270	270

- **Preparation of binder solution Starch paste**

Divide the required quantity of water into 3 parts, maize starch disperse in the one part and Boil the another part, add the dispersion into boiling water under stirring until formation of Transparent paste then cool to room temperature. Dissolve the PVPK 30 in the remaining water then add into starch paste under stirring. Then add the binder solution to the dry mix under slow impellor speed in the Rapid mixture Granulator until formation of the smooth granules. Granules were dried in the fluidized bed dryer at 600C for 30 minutes, and then sifted through 40 meshes.

- **Pre lubrication**

MCC PH 102, Crospovidone, acacia, Sodium chloride, Menthol, Aspartame, Peppermint Flavour, L-HPC LH 11, Talc and Aerosil were sifted through 40 mesh then add to the dried Granules then mixed in the quanta blender for 10 minutes.

- **Lubrication**

Sift the magnesium stearate through the #60 mesh then added to mixture which was in the Octagonal blender and mixed for 3 minutes. The blend was collected in a poly bag and was compressed by Cadmech compression by using suitable tooling.

- **Evaluation[13-15]**

Pre compression parameters Characterization of drug substance and blend

The parameters like bulk density, tapped density, Hausner's ratio, compressibility index were performed to drug substance and blend and computed to all formulations of trial batches.

- **Bulk density**

Bulk density was determined by measuring the volume of known mass of powder sample which is passed through a screen into a graduated cylinder (USP method 1)

Approximately 10 gm of sample was weighed and introduced into 25 ml dry measuring cylinder without compacting. The powder levelled carefully without compacting and read the unsettled apparent volume Vo, the nearest graduated unit. The bulk density was expressed in gm/ml, and calculated by the formula

Bulk density = M/Vo

Generally replicate determinations are desirable for the determination of this property

- **Tapped density**

Tapped density was determined by mechanically by tapping a measuring cylinder containing powder sample. After measuring the initial weight and volume, the cylinder was mechanically tapped, and volume readings were taken until little further volume change is observed.

- **Procedure**

Cylinder containing powder sample was tapped mechanically by suitable mechanical tapped density tester that provide a fixed drop of 14±2 mm at an, initial rate of 300 drops per minute. Unless otherwise specified, the cylinder was tapped 500 times initially and tapped volume was measured, Va to a nearest graduated unit. The tapping was continued for additional 750 times and tapped volume was measured, Vb, to the nearest graduated unit. If the difference between the two volumes is less than 2%, Vb is the final tapped volume, Vf, it was repeated increments of 1250 taps, as need, until the succeeding measurements less than 2%, the tapped density expressed in gm/ml, and calculated by formula

Tapped density=M/Vf

Generally replicate determinations are desirable for the determinations of this property

- **Compressibility index**

The compressibility index and Hausner ratio are measure of the propensity of a powder to be compressed. As such, they are relative measures of the relative importance of interparticular interactions. In free flow in powder such interactions are generally less significant, and the bulk and tapped densities are will be closer in value. For poor flowing materials, there are frequently greater interparticular interactions, and greater difference between bulk and tapped densities will be observed. The differences are reflected in compressibility index and Hausner ratio.

Compressibility index -created by formula:

CI % = Vo-Vf/Vo

Hausner ratio-calculated by the formula:

HR = Vo/Vf

Where Vo-Bulk volume Vf-Tapped volume

Table 4.2: Scale of flowability (USP).

Compressibility index (%)	Flow character	Hausner's ratio
≤10	Excellent	1.00-1.1
11-15	Good	1.12-1.18
16-20	Fair	1.19-1.25
21-25	Passable	1.26-1.34
26-31	Poor	1.35-1.45
32-37	Very poor	1.46-1.59
>38	Very, very poor	>1.60

- **Angle of repose**

The angle of repose has been used to characterize the flow properties of solids. Angle of repose is a related to inter particular friction or resistant to movement between particles. Angle of repose formed on a fixed base with a retaining lip to retain a layer of powder on base. The base should be free of vibration the height of the funnel was varied to carefully build up a symmetrically cone of powder. Care should be taken to prevent vibration as the funnel is moved. The funnel height should be maintained approximately 2-4 cm from the top of the tip of the cone. I symmetrically cone of powder cannot be successfully or reproducibly prepared, this method is not appropriate. Angle of repose was determined by measuring the height of the v cone of powder and calculating the angle of repose, from the following equation:

$\tan\theta = h/r$

Table 4.3: Flow properties and corresponding angle of repose.

Flow property	Angle of repose(Degrees)
Excellent	25-30
Good	31-35
Fair-aid not needed	36-40
Passable-may hang up	41-45
Poor-must agitate, vibrate	46-45
Very poor	56-65
very, very poor	>66

Particle size determination: dry sieve analysis for particle size determination Dry sieve method

An accurately weighed quantity of test specimen was place on the top sieve and lid was replaced. Then the nest of sieves was agitated for 5 minutes. Then each was carefully removed from the nest without loss of material. Each was reweighed, and the weight of material on the each was determined. The weight of material in collecting pan also determined in similar manner. Then the nest of sieves were reassembled and agitated for 5 minutes. Each sieve was removed and weighed, as previously described. Upon completion of the analysis, the weights of material were reconciled. The total loss must not exceed 5T% of the total weight of original test specimen.

- **Post compression parameters**

As for pharmacopoeia standards all the batches of tablets were evaluated for various physical parameters like thickness, hardness, weight variation, friability, drug content, dissolution and fineness of dispersion.

- **Weight variation**

20 tablets were taken randomly and weighed individually on digital balance. Then average weight was calculated and then compared with each individual tablet. The tablets passed the U.S.P. test if not more than 2 tablets are outside the Percentage limits and if no tablet differs by more than 2 times the percentage limit.

Table 4.4 Acceptance criteria for tablet weight variation.

Average weight of tablet	% difference allowed
130 or less than	± 10
130-324	± 7.5
<324	± 5

- **Thickness**

Thickness of tablet is very important for uniformity of tablet size. Thickness of tablets can vary with no change in tablet weight because of pressure applied to the tablets and difference in density of granule blend, as well as speed of compression machine. Ten tablets select randomly and thickness was measured using vernier callipers and recorded.

- **Crushing strength**

Tablets should have sufficient strength or hardness to resist friability to withstand the mechanical shakes while

handling in manufacturing, packing and shipping. Hardness generally measures the crushing strength. Variation in hardness results in differences in disintegration and dissolution characteristics of tablet. The crushing strength of tablets was determined by using schleunger hardness tester.

- **Friability test**

This test is performed to evaluate the ability of tablets to withstand abrasion in handling, packing, Transporting. For tablets weighing 650 mg each, take a sample consisting of maximum number of tablets that makes a total mass of more than 6.5 gm. for tablets weighing more than 650 mg each take a sample of ten tablets. Dust should be removed from the tablets carefully before performing test. Accurately weigh the sample, and place the tablets in drum. Rotate the drum 100 times, at 24-25 rotations per minute and remove the tablets. Remove any loose dust from the tablets as before. if no tablets are cracked, split pr broken, accurately weigh the tablets, and determine the friability(mass percent of the loss mass with respect to the initial mass).

% Friability=Winitial - wfinal/winitial×100

- **Disintegration test**

Generally time limit for disintegration time is less than 3 minutes. The disintegration time is determined when the tablet has completely disintegrated and passed through the screen.

- **Fineness of dispersion**

This is a qualitative test specified by EP for dispersible tablets. It is an assessment of the grittiness which is arises due to disintegration of tablets into coarse particles. The test performed by pacing the 2 tablets in the 100 ml of water and stirring gently, till the tablets get disintegrated completely. The formulation considered comply the test if the dispersion passes through a sieve screen of nominal aperture 710µm without leaving any residue on the mesh.

- **Assay**

Weigh and powder 20 tablets. Weigh accurately a quantity equivalent to 100 mg of Ethionamide and transfer into 250 ml volumetric flask and then extract the drug with 100 ml of mobile phase then transfer 5ml of solution to a 200 ml of flask and dilute to volume with methanol and mix.

- **In vitro dissolution test**

Dissolution is a dynamic process by which the disintegrated solid particle enters into the solution.The test determines the time required for a definite percentage of the drug in a tablet to dissolve under specified conditions.Dissolution parameters: Medium: 0.1 N HCL Apparatus: USP-1(basket) Volume: 900ml RPM: 50
Temperature: 37±50C
Sampling times: 15, 30 and infinity
The samples were diluted and analyzed by HPLC HPLC parameters
Column: Inertsil ODS-3, (250×4.6 mm), 5 µm (GL Sciences Inc.) Pump mode: Isocratic
Flow rate: 1.0 ml/ min Injection volume: 20µl Sample temperature: Ambient Wavelength: UV, 290 nm ± 2 nm

5. Stability Studies

The stability studies are conducted to provide the proof on how the quality of a drug substance or drug product varies with time under influence of a variety of environmental factors such as light, temperature and humidity to found a re-test period for the drug substance or a shelf life for the dug product and recommended storage conditions.

Table 5.1: Stability conditions and their periods.

Study	Storage condition	Minimum time period covered by data at submission
Long term*	250±20C/60%RH±5% Or 300±20/65%RH±5%RH	12 months
Intermediate**	300±20C/65%RH±5%RH	6 months
Accelerated	400C±20/75%RH±5%	6 months

*It is up to applicant to decide whether long term stability studies are performed at 250±20C/60%RH±5% or 300±20/65%RH±5%RH.
**If 300±20/65%RH±5%RH is the long term condition, there is no intermediate condition.

If long term studies are conducted at 250±20C/60% RH±5% and "significant change" occurs at any time during 6 months testing at accelerated storage condition, additional testing at the intermediate storage condition should be conducted and evaluated against significant change criteria. The initial application should a minimum of 6 months data from a 12 month study at the intermediate storage condition.

In general "significant change" for a drug product is defined as:

- When using biological or immunological procedures Failure to meet the acceptance criteria for potency.
- A 5 % change in the assay from its initial value.
- failure to meet the acceptance criterion for pH
- Any degradation products exceeding its acceptance criterion;
- Failure to meet the acceptance criteria for physical attributes, appearance, and functionality test (e.g. phase separation, colour caking, resuspendability,

hardness, dose delivery per actuation); though, some changes in physical attributes (e.g. melting of creams, softening of suppositories) may be expected under accelerated conditions; and as appropriate for the dosage form.

- Failure to meet the acceptance criteria for dissolution for 12 dosage forms.

6. RESULTS AND DISCUSSION

- **Pre-formulation Solubility**

Table 6.1: Solubility study of the Ethionamide.

Media	Solubility
0.1 N HCl (Buffer)	Very soluble
pH 4.5 (Buffer)	Freely soluble
pH6.8(Buffer)	Soluble
Water(Buffer)	Springly soluble
pH 7.5(Buffer)	Slightly solubly

From the above table it was observed that solubility of the Ethionamide was increases with decreasing pH.
Particle size determination of Ethionamide dispersible tablet

Table 6.2: particle size determination of Ethionamide.

Sieve number	Sieve size(µm)	Mass of sample retained on each sieve(g)	Percentage of sample retained on each sieve (%)
80	177	1.05	2.10
100	149	2.03	4.06
120	106	46.09	92.18
Pan	-	0.23	0.46

From the above table it was observed that 92.18 % of the Ethionamide had particle size below 106µ.

- **Flowability of Ethionamide**

Table 6.3: Flow properties of Ethionamide.

Parameter	Observed values	
Tapped density(gm/ml)	0.791± 0.0038	
Bulk density(gm/ml)	0.465± 0.0052	
Carr's consolidation index (%)	41.176±	0.0036
Hauser ratio	1.700±	0.029

From the above table it was observed that Ethionamide had very poor flow properties so in order to improve the flow, Ethionamide was granulated through wet granution by Rapid mixture granulator.

- **Compatibility studies Physical observation**

From the table 6.2 and 6.3 it was observed that there was no change in the physically before and after 1 month compatibility study.

- **Analytical observation**

From the fig: 6.2 it was observed that DSC of the Ethionamide had two endothermic peaks at 161.700C and 217.280C. Among this 161.70 represents melting point which corresponded with melting point of Ethionamide. fig 6.3, 6.4 and 6.5 which were represents DSC thermograms of Ethionamide and all excipients mixture at initial, after one month and final product respectively, which shown meting point of Ethionamide at 161.110C, 161.110C and 161.10C respectively and also there is no appear and disappear of peaks in the thermograms, from this it was observed Ethionamide was compatible with all the excipients present in the formulation. From the above trial, it was observed that there is no improvement in the hardness and also slightly increased in disintegration time so previous trial was considered as optimized trial.

- **Evaluation**
- **Pre compression parameters**
- **Particle size distribution And Flow properties of final blend**

Table 6.4: Particle size distribution of final blend.

Sieve number	Sieve size (µm)	Mass of sample retained on each sieve(gm)	Percentage of sample Retained on each sieve
45	325	1.932	3.864

60	250	37.029	74.058
80	10077	8.820	17.64
100	149	1.939	3.878
Pan	-	0.05	0.1

Table 6.5: Flowability of final blend.

Parameter	**Ethionamide** ±SD*	
Tapped density(gm/ml)	0.55± 0.0035	
Bulk density(gm/ml)	0.46±	0.0052
Carr's consolidation inde0x (%)	16.36± 0.0036	
Hausner's ratio	1.19±	0.049
Angle of repose	31	

*Represents average value ± SD (n=3)

From the above table it was observed that 74 % of the final blend had particle size below 250 µm and from the knowledge of Carr's index, Hausner's ratio and Angle of repose results final blend had good flow properties.

- **Weight variation**

Table 9.13 weight variation test of all the formulations.

TRIAL	WEIGHT VARIATION ± SD*
F1	250±1.8
F2	250±1.81
F3	250±1.77
F4	250±1.65
F5	250±1.70
F6	270±1.76
F7	270±1.80

*Represents average value ± SD (n=20)

From the above results it was observed that all the formulation shown uniform in weight and found in within the limit.

- **Thickness**

Table 6.6: Thickness profile of all the formulations.

TRIAL	THICKNESS (mm)± SD*
F1	3.35 ± 0.35
F2	3.30± 0.32
F3	3.35 ± 0.41
F4	3.34 ± 0.37
F5	3.35±0.36
F6	4.03 ± 0.35
F7	4.03 ± 0.31

*Represents average value ± SD (n=5)

From then above results it was observed that Thickness of all the formulations was found to be uniform and within the limits.

Table 6.7: Hardness profile of different formulations.

TRIAL	**HARDNESS(N)** ± SD*
F1	2.8± 0.54
F2	3.0± 0.55
F3	3.2± 0.45
F4	4.0± 0.30
F5	4.6± 0.20
F6	3.5± 0.25
F7	3.8± 0.32

*Represents average value ± SD (n=5)

From the above table it was observed that F6 and F7 trials had sufficient hardness for dispersible tablets.

- **Disintegration**

Table 6.8: disintegration time of all the formulations.

TRIAL	DISINTEGRATION TIME(SEC) ± SD*
F1	70± 0.89
F2	80± 0.81
F3	75± 0.89
F4	85± 0.75
F5	90± 0.74
F6	45± 0.816
F7	80± 0.74

*Represents average value ± SD (n=6)

From the above results it was observed F6 formulation showed less disintegration time when compare remaining formulations.

- **Friability**

Table 6.9: % Friability all the formulations.

TRIAL	FRIABILITY (%) ± SD*
F1	1.5 ± 0.12
F2	1.4 ± 0.14
F3	1.06 ± 0.12
F4	1.03 ± 0.13
F5	0.6 ± 0.12
F6	0.26 ± 0.10
F7	0.35 ± 0.11

*Represents average value ± SD (n=3)

From the above results it was observed that formulations F1 to F5 were failed in friability due to insufficient hardness, but F6 and F7 formulation passed the friability test.

- **Dissolution test**

Above post-compression parameters revealed that F1, F2 and F3 trials were failed in the friability test, F4& F5 trials had insufficient hardness and F6 formulation shown better hardness and disintegration time compare to F7. So it was concluded that conduct the dissolution test and assay to F6 trial to determine the percentage of drug release.

Table 6.10: dissolution test of the optimized formulation.

Time(min)	% Drug release ± SD*
0	0
15	99 ± 1.16
30	100 ± 1.26
120	101 ± 1.40

*Represents average value ± SD (n=6)

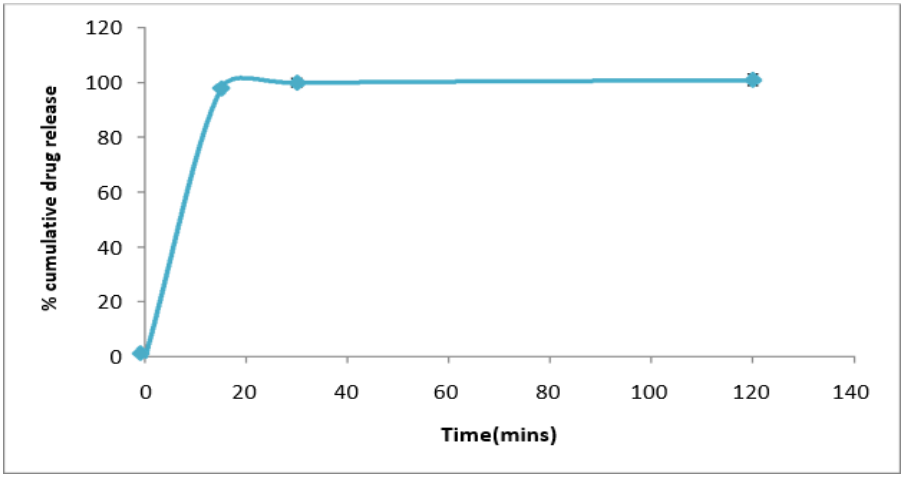

Fig 6.1: dissolution profile of optimized formulation.

From the above table and graph it was observed that F6 trial release 100% of the drug within 30 minutes which revealed that F6 formulation complies the limits prescribed in the USP so it was concluded that F6 trial as optimized formulation.

- **Assay**

Here assay was carried by HPLC and results were found to be 99.30%. This revealed that assay of dispersible tablets of Ethionamide within the limits.

- **Stability studies**

Physical parameters of the optimized formulation after 3 months of stability (250C/60% RH, 400C/75%RH) in the Alu-Alu strip pack.

Table 6.11: Physical parameters of optimized formulation in Alu-Alu- strip pack.

Parameters	Alu-Alu strip pack	
	250C/60%RH	400C/75%RH
Thickness ± SD*	4.03 ± 0.35	4.02 ± 0.30
Hardness ± SD*	49 ± 1.2	48 ± 1.5
DT ± SD**	43 ± 0.547	42 ± 0.816

*Represents average value ± SD (n=5)
**Represents average value ± SD (n=6)

- **Dissolution profile**

Dissolution profile of Ethionamide (400C/75%RH 3 months).

Table 6.12: dissolution profile of an optimized formulation after 3 months of stability.

Time(mins)	% cumulative drug release ± SD*
0	0
15	98 ± 1.1
30	100 ± 1.6
120	101 ± 2.0

Release profile of Ethionamide

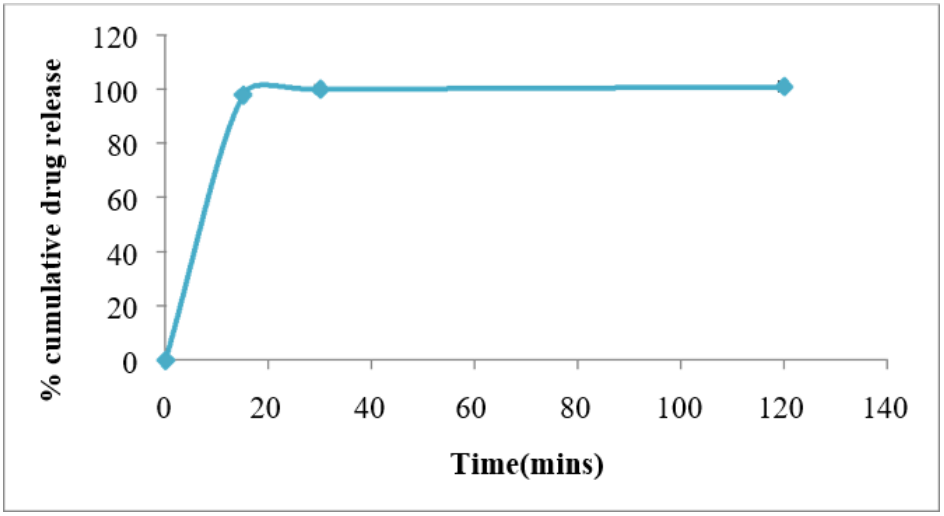

Fig 6.2 Dissolution profile optimized formulation after 3 months stability.

From the above tables it was observed that formulation was stable in Alu-Alu strip pack in terms of all parameters, so it was decided to pack the formulation within the Alu-Alu strip pack.

7. SUMMARY AND CONCLUSION

The objective of this study was to develop an optimized stable dispersible tablet of the Ethionamide. Ethionamide selected for the study acts by inhibition of mycolic acid synthesis by inhibition of enoyl reductase enzyme. The dispersible tablets were prepared by different binders, disintegrant and flavours finally optimized with a tablet weight of 270 mg. The Ethionamide was evaluated for pre formulation studies like DSC and by physical observation of binary mixture of drug and excipients. DSC study revealed that melting point of the drug was 161.70 C DSC thermograms and physical observation shown that both Ethionamide and were used in the formulation were compatible and have no significant change in the binary mixture of drug and excipients. The pre compressional and post compressional studies were carried out on dispersible tablets. The values were within the acceptance limit. The flow properties of the drug were improved by granulation. The post compressional parameters like Weight variation, Hardness, Thickness, Disintegration time, Fineness of dispersion, in -vitro

dissolution study were performed and they found to be satisfactory. In order to evaluate the stability, the final optimized formulation was charged at long term and accelerated conditions of temperature and humidity as per ICH guidelines (25◦C/60% RH and 40◦C/75% RH) and the exposed samples were evaluated for physical parameters and in-vitro dissolution study.

- **CONCLUSION**

From the knowledge of evaluated results it was revealed that the F6 formulation had Qualities sufficient to form a dispersible dosage form. So it was concluded that the F6 formulation as an optimized formulation.

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