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Research Article

Formulation and evaluation of chewable tablet of levamisole

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ABSTRACT

Levamisole is a synthetic imidazothiazole derivative that has been widely used in treatment of worm infestations in both humans and animals. As an anthelmintic, it probably works by targeting the nematode nicotinergic acetylcholine receptor. In the market, levamisole tablets are available in the form of tablets. Geriatric and paediatric patients find it difficult to swallow these tablets. So in order to avoid this problem, chewable tablets are most preferable. The chewable tablets of levamisole were prepared by using lactose or mannitol along with sodium starch glycolate in concentration ratios especially for paediatric use. Sodium saccharin and vanilla were used as sweetening agent and flavouring agent respectively. From the disintegration studies, it was observed that the formulation containing 1.6% w/w of sodium starch glycolate shows minimum disintegration time whereas formulation having no or less concentration of sodium starch glycolate shows increase in disintegration time. It was observed that the formulation containing lactose shows less disintegration time than formulation containing mannitol.

Keywords: Levamisole; Chewable tablet; paediatric use; sodium starch glycolate; lactose; mannitol; disintegration time.

INTRODUCTION

Levamisole is a synthetic imidazothiazole derivative that has been widely used in treatment of worm infestations in both humans and animals (Tripathi, 2008; Moens, 1978). As an anthelmintic, it probably works by targeting the nematode nicotinergic acetylcholine receptor. These are intended to be chewed in the mouth prior to swallowing and are not intended to be swallowed intact. These tablets provide additional advantages like greater absorption and increased patient's compliance (Suzuki et al., 2003). Levamisole is available in dose of 50mg and 150 mg. In present work, 50 mg levamisole is taken.

EXPERIMENTAL

Materials

Levamisole was gifted by Harsh Pharma, Palampur. All other chemicals and reagents used were of analytical grade.

Methods

Preparation of levamisole chewable tablet

The granules are prepared by wet granulation. It involves weighing ingredients, preparing a damp mass, screening the damp mass into granules by passing through sieve no.14, drying of granules, adding lubricants (stearic acid & magnesium stearate) and blending and tablet formation by 8 station rotary press tablet compression machine (Liberman et al., 1989; Lachman et al., 1987)

Evaluation of granules

Angle of repose

The angle of repose is a relatively simple technique for estimation of the flow property of a powder. Powders with low angle of repose are free flowing and those with a high angle of repose are poorly flowing powders.10 gm of granules were passed through funnel and the pile was formed. The angle of repose was calculated by using the formula

Angle of repose (θ) = $\tan^{-1}$ height /radius.

Carr`s compressibility index

The Carr's compressibility index was calculated by calculating the tapped and bulk density using the 100 ml measuring cylinder. Compressibility is calculated by the formula,

$$C = 100 \times (1 - \frac{\rho_B}{\rho_T})$$

where ρ_B is the freely settled bulk density of the powder, and ρ_T is the tapped bulk density of the powder. A carr`s index greater than 25 is considered to be an indication of poor flowability, and below 15, of good flowability.

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Table 1: Formulation of chewable tablets of levamisole

Ingredients	LM_1	LM_2	LM_3	LM_4	LM_5	LM_6
Levamisole	50 mg	50 mg	50 mg	50 mg	50 mg	50 mg
SLS	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg
PVP	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg
Lactose	218 mg	221 mg	224 mg	-	-	-
Mannitol	-	-	-	218 mg	221 mg	224 mg
SSG	6 mg	3 mg	-	6 mg	3 mg	-
Magnesium stearate	10 mg	10 mg	10 mg	10 mg	10 mg	10 mg
Stearic acid	5 mg	5 mg	5 mg	5 mg	5 mg	5 mg
Starch	47 mg	47 mg	47 mg	47 mg	47 mg	47 mg
Vanilla flavour	15 mg	15 mg	15 mg	15 mg	15 mg	15 mg
Sodium saccharin	4 mg	4 mg	4 mg	4 mg	4 mg	4 mg
Total weight	380mg	380mg	380mg	380mg	380mg	380mg

Particle Size distribution

The particle size distribution of granules was evaluated by sieve analysis using standard sieves in the range of sieve no. 10-36. The fraction was collected and weighed (Gaud et al., 2007; Mullarney et al., 2003).

Evaluation of tablets

Hardness

The hardness test is performed to provide a measure of tablet strength. Tablets should be hard enough to withstand packaging and shipping but not so hard as to create undue difficulty upon chewing. Tablet hardness is determined using equipment from various suppliers that measure the force needed to break up the tablets. The Pfizer tester is commonly used. This tester operates on the same mechanism principle as a pair of pliers. As the plier's handles are squeezed, the tablet is compressed between a holding anvil and a piston connected to a direct force reading gauge. The dial indicator remains at the reading where the tablet breaks and is returned to zero by depressing a reset button.

Disintegration

This test initially may not appear appropriate for chewable tablets as these tablets are to be chewed before being swallowed. However, patients, especially pediatric and geriatric, have been known to swallow these chewable dosage forms. This test would thus indicate the ability of tablet to disintegrate and still provide the benefit of the drug if it is accidentally swallowed. Tablets should preferably pass the USP disintegration test for uncoated tablets. Procedure for USP disintegration test for uncoated tablet

Organoleptic properties

The colour, odour and taste characteristics were evaluated.

Diameter and Thickness

It was measured by using vernier calliper scale.

Weight variation

The USP weight variation test is run by weighing 20 tablets individually, and comparing individual weight to the average. The tablets meet the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit. The weight variation tolerances for uncoated tablets differ depending on average tablet weight.

Assay of drug content

Spectrophotometric method was used to determine the active drug content on a representative sample. The recovered amount of active drug is the expressed as percent of labeled drug content. The obtained value of drug content should be within established limits (Allen et al., 2005; USP 27).

Calibration Curve

Dissolve 10mg of drug in a solution containing 2ml of ethanol and 8 ml of distilled water. Pipette out 1 ml from this solution and dilute with distilled water upto 10ml. Then pipette out sufficient quantity of this solution and dilute with distilled water to get concentrations of 5 ppm, 10 ppm, 15 ppm, 20 ppm &25 ppm. Then carry out uv sphectrophotometric determination by using uv spectrophotometer at 214 nm note down the absorbance Plot a graph of absorbance against concentration.

Preparation of sample solution

Triturate the tablet. Weigh 10mg of powder. Dissolve it in a solution containing 2ml of ethanol and 8ml of distilled water. Filter solution using whatman filter paper. Then, sufficiently dilute filtrate and carry out uv spectrophotometric determination at 214 nm. Note down absorbance and find out content uniformity using suitable formula.

FTIR study was carried out to check the compatibility of the drug and excipients.

Table 2: Evaluation of granules

Sr. No.	Parameter	LM_1	LM_2	LM_3	LM_4	LM_5	LM_6
1	Angle of repose						
a)	Before adding lubricant	$16^0 25'$	$16^0 45'$	$15^0 38'$	$24^0 24'$	$23^0 42'$	$19^0 57'$
b)	After adding lubricant	$13^0 22'$	$15^0 41'$	$13^0 47'$	$14^0 11'$	$17^0 13'$	$18^0 24'$
2	Hausner's ratio	1.024	1.07	1.026	1.07	1.07	1.03
3	% compressibility	2.38	6.6	2.5	6.6	6.54	3.22

Table 3: Sieve analysis of batch LM_1

Sieve no.	Aperture size (µm) (d)	Weight retained (n) (gm)	% weight retained	cumulative % weight retained	nd
14	1180	0.25	1.99	9.12	295
16	1000	0.27	23.90	9.85	270
18	850	0.4	20.72	14.60	340
22	710	0.19	9.56	6.93	134.9
36	425	1.3	36.65	47.45	552.5
Fines	-	0.33	7.17	12.04	
		∑n=2.74			∑nd=1592.4

From above table, it is clear that maximum granules were retained on sieve no.36

Table 4: Sieve analysis of batch LM_2

Sieve no.	Aperture size (µm) (d)	Weight retained (n) (gm)	% weight retained	cumulative % weight retained	nd
14	1180	0.05	1.99	1.99	59
16	1000	0.6	23.90	25.89	600
18	850	0.52	20.72	46.61	442
22	710	0.24	9.56	56.17	170.4
36	425	0.92	36.65	92.82	391
Fines	-	0.18	7.17	100	
		∑n=2.51			∑nd=1662.4

From above table, it is clear that maximum granules were retained on sieve no.36

Table 5: Sieve analysis of batch LM_3

Sieve no.	Aperture size (µm) (d)	Weight retained (n) (gm)	% weight retained	cumulative % weight retained	nd
14	1180	0.21	9.46	9.46	247.8
16	1000	0.94	42.34	51.8	940
18	850	0.16	7.21	59.01	136
22	710	0.15	6.76	65.77	106.5
36	425	0.62	27.93	93.7	263.5
Fines	-	0.14	6.31	100	-
		∑n=2.22			∑nd=1693.8

From above table, it is clear that maximum granules were retained on sieve no.16.

RESULTS AND DISCUSSION

Evaluation of granules

The granules thus prepared were evaluated and the results thus obtained are given in table 2.

As granules in all the batches have the angle of repose (before adding lubricant &after adding lubricant) value less than 25°, all batches show excellent flow. After adding lubricant, all batches shows considerable decrease in angle of repose. This causes increase in flowability of granules. The maximum change in angle of repose after addition of lubricant was shown by batch LM_4. This shows presence of less air space between granules of all batches. The hausner's ratio value was found to be less than 1.25 which indicates excellent flowability. As value of % compressibility is found to be less than 15, it indicates good flowability.

Table 6: Sieve analysis of batch LM_4

Sieve no.	Aperture size (µm) (d)	Weight retained (n) (gm)	% weight retained	cumulative % weight retained	nd
14	1180	0.05	2.86	2.86	59
16	1000	0.18	10.29	13.15	180
18	850	0.14	8.00	21.15	119
22	710	0.42	24.00	45.15	298.2
36	425	0.75	42.86	88.01	318.75
Fines	-	0.21	12.00	100	-
		∑n=1.75			∑nd=974.95

From above table, it is clear that maximum granules were retained on sieve no.36.

Table 7: Sieve analysis of batch LM_5

Sieve no.	Aperture size (µm) (d)	Weight retained (n) (gm)	% weight retained	cumulative % weight retained	nd
14	1180	0.21	8.57	8.57	247.8
16	1000	0.76	31.02	39.59	760
18	850	0.6	24.49	64.08	510
22	710	0.22	8.98	73.06	156.2
36	425	0.47	19.18	92.24	199.75
Fines	-	0.19	7.76	100	-
		∑n=2.45			∑nd=1873.75

From above table, it is clear that maximum granules were retained on sieve no.16.

Table 8: Sieve analysis of batch LM_6

Sieve no.	Aperture size (µm) (d)	Weight retained (n) (gm)	% weight retained	cumulative % weight retained	nd
14	1180	0.26	14.29	14.29	306.8
16	1000	0.7	38.46	52.75	700
18	850	0.13	7.14	59.89	110.5
22	710	0.08	4.40	64.49	56.8
36	425	0.51	28.02	92.31	216.75
Fines	-	0.14	7.69	100	-
		∑n=1.82			∑nd=1390.85

From above table, it is clear that maximum granules were retained on sieve no.36.

Table 9: Determination of average particle size

Batch no.	LM_1	LM_2	LM_3	LM_4	LM_5	LM_6
Average paticle size (µm)	581.16	662.31	762.97	557.11	764.79	763.73

From above figure, it is clear that average particle size was found to be in the range of 557-765 µm. The maximum average particle size was found to be for batch LM_6 and minimum average paticle size was found to be for batch LM_4.

From table 10 it is clear that, all batches showed no variation in colour, odour, taste, diameter and thickness of tablets. They showed % weight variation within given limits (< 5%). Hardness value was found to be in the range of 2.6-4.2 Kg. The maximum hardness was obtained for batch LM_2 which is 4.2 kg. Disintegration time ranges from 14-25 min. The tablets of batch LM_1 disintegrated rapidly (i.e. in14 min.) than any other batch. The batches of tablets containing sodium starch glycolate disintegrated rapidly than batches of tablets devoid of it.

In FTIR analysis there is no change in peaks for the drug which indicate no interaction between drug and excipients resulting in formation of new structure.

Table 10: Evaluation of tablets

Sr. No	Parameter	LM_1	LM_2	LM_3	LM_4	LM_5	LM_6
1	Colour	White	White	White	White	White	White
2	Odour	Pleasant	Pleasant	Pleasant	Pleasant	Pleasant	Pleasant
3	Taste	Vanilla like	Vanilla like	Vanilla like	Vanilla like	Vanilla like	Vanilla like
4	%Weight variation	1.3195 ±0.7905	1.3205 ±0.2575	1.3255 ±0.2525	1.3195 ±0.7905	1.3575 ± 0.5875	1.3205 ±0.2575
5	Diameter (cm)	0.9±0.05	0 .9±0.05	0 .9±0.05	0 .9±0.05	0 .9± .05	0 .9± .05
6	Thickness(cm)	0.5±0.02	0.5 ±0.02	0.5 ±0.02	0.5 ±0.02	0.5 ±0.02	0.5 ±0.02
7	Hardness	3 kg	4.2 kg	2.6 kg	3.8 kg	3 kg	3.2 kg
8	Disintegration time (min.)	14 min	18 min	21 min	17 min	20 min	25 min

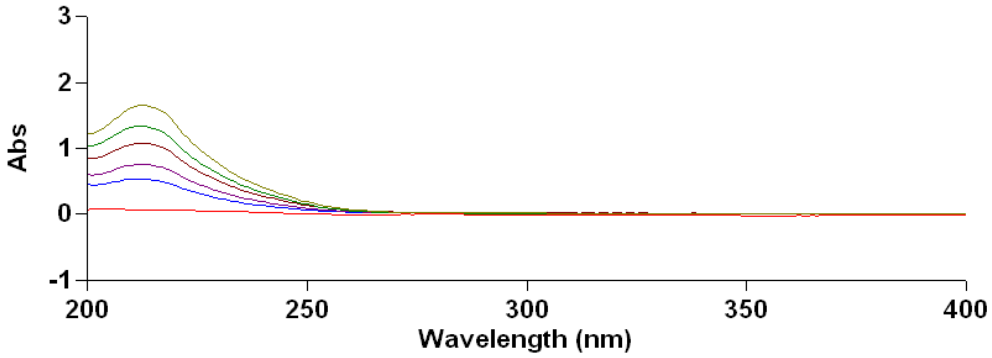

Figure 1: Standard curve for assay of drug content

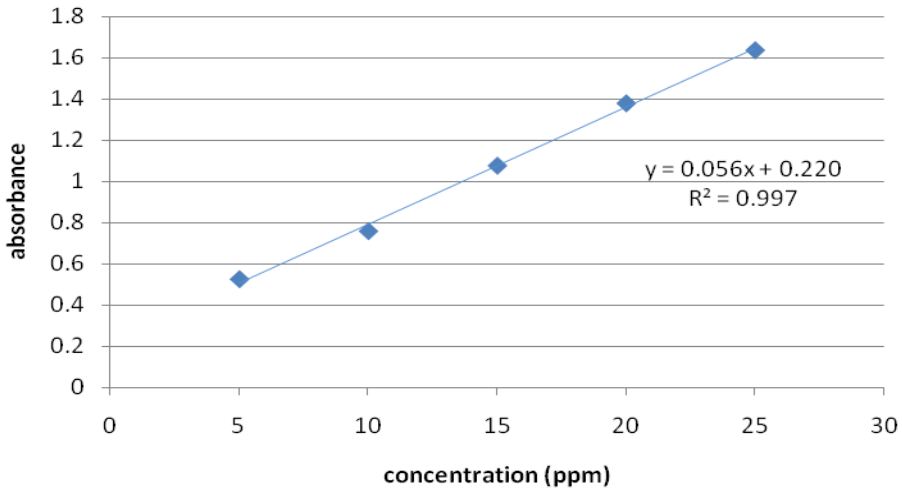

Figure 2: Calibration curve for assay of drug content

Table 11: Comparison of % drug content of different batches of levamisole

Batch no.	LM_1	LM_2	LM_3	LM_4	LM_5	LM_6
% Drug content	93.16	96.47	100.81	98.78	97.56	102.58

From above table, it is clear that the % drug content of tablet was found to be within USP limits i.e. between 90 to 110 %.

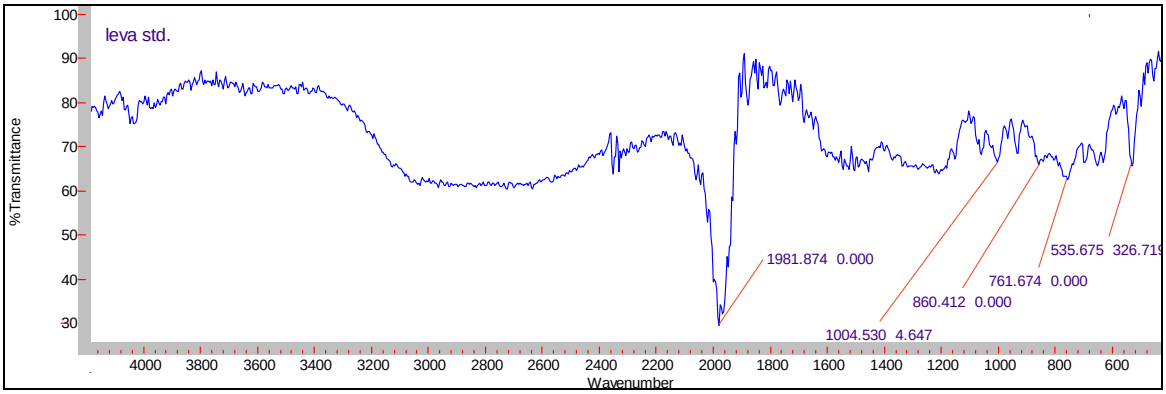

Figure 3: FTIR of levamisole

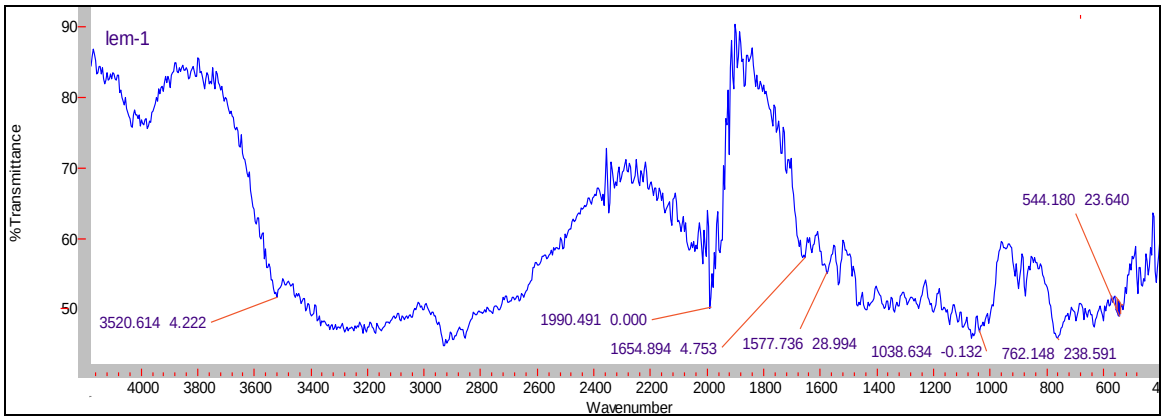

Figure 4: FTIR of tablet of batch LM_1

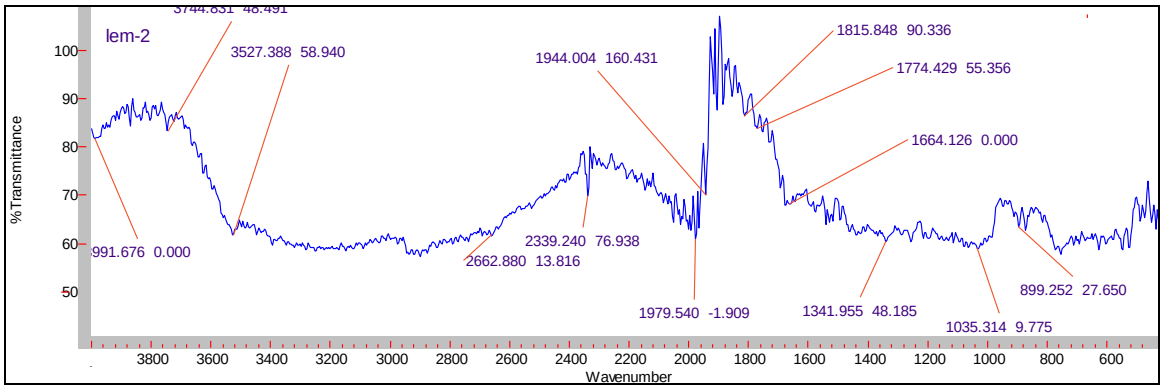

Figure 5: FTIR of tablet of batch LM_2

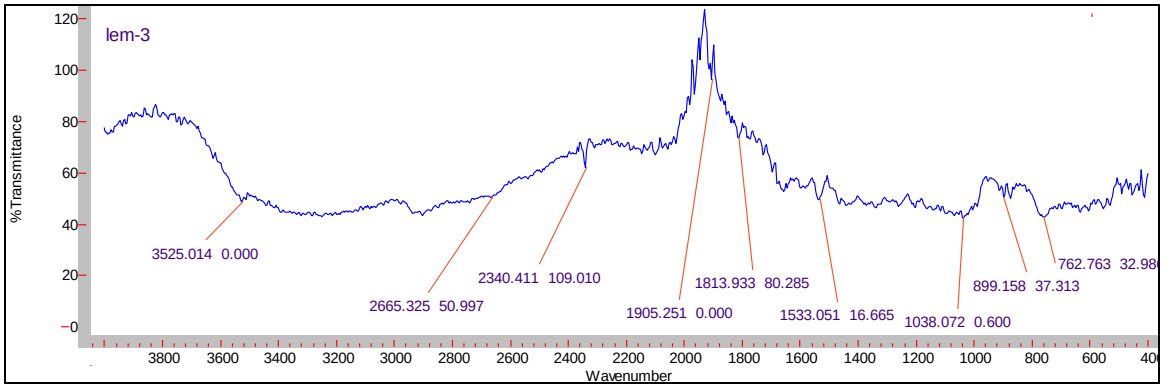

Figure 6: FTIR of tablet of batch LM_3

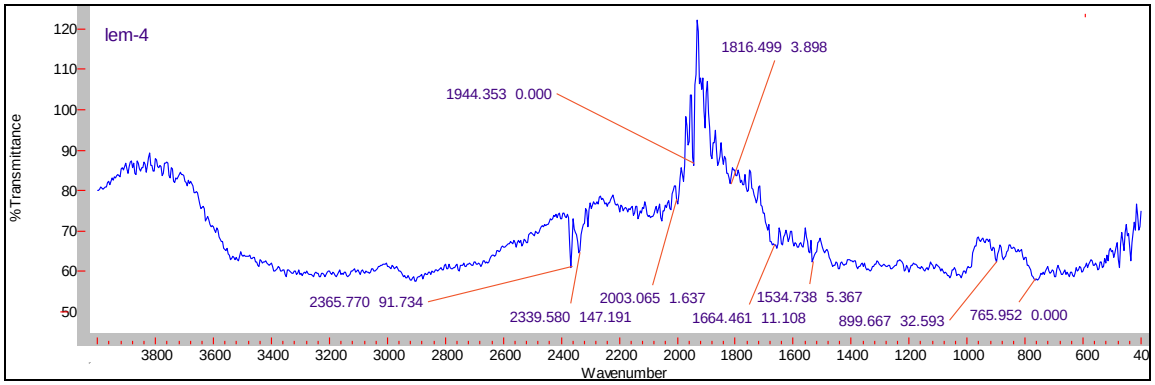

Figure 7: FTIR of tablet of batch LM_4

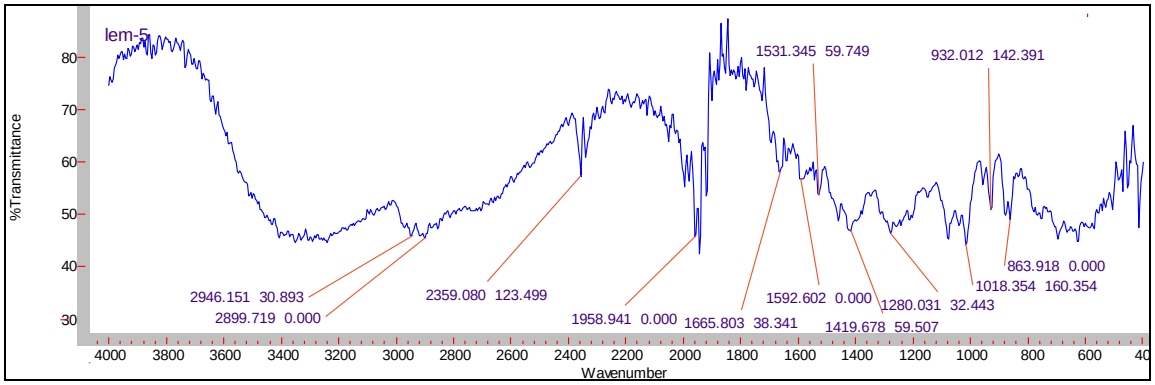

Figure 8: FTIR of tablet of batch LM_5

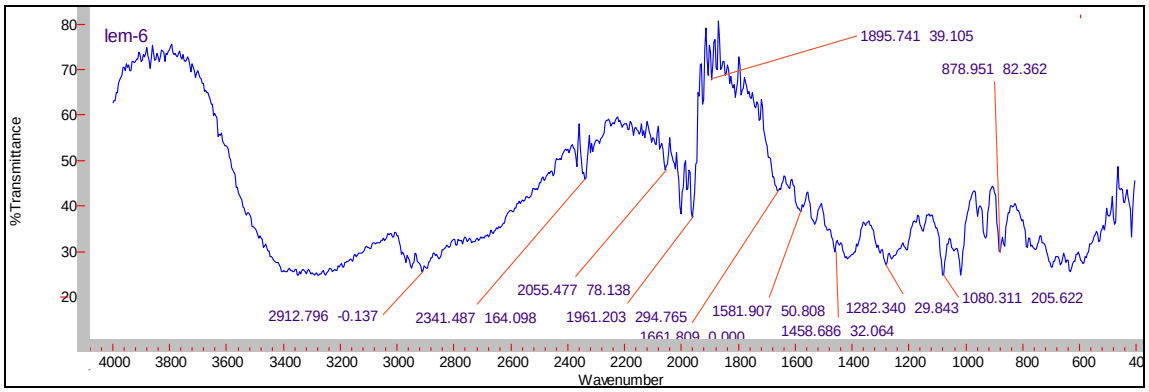

Figure 9: FTIR of tablet of batch LM_6

SUMMARY AND CONCLUSION

The evaluation of granules and tablets indicate successful formulation of chewable tablet of levamisole. From the disintegration studies, it was observed that the formulation containing 1.6% w/w of sodium starch glycolate shows minimum disintegration time (14 min.) whereas formulation having no or less concentration of sodium starch glycolate shows increase in disintegration time. It was observed that the formulation containing lactose shows less disintegration time than formulation containing mannitol. The tablet containing lactose and sodium starch glycolate (1.6% w/w) is the best levamisole chewable tablet with minimum disintegration time, sufficient hardness, pleasant taste and meeting all USP limits. Therefore, this can be the formulation for paediatric use in future.

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