Research Article

FORMULATION AND EVALUATION OF MOUTH DISSOLVING TABLETS OF LEVAMISOLE HYDROCHLORIDE.

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ABSTRACT:

The objective behind this research work was to formulate & evaluate mouth dissolving tablets of Levamisole Hydrochloride to improve patient compliance during administration, give faster onset of action and improve bio-availability. Levamisole Hydrochloride is class I anthelmintic drug and it is also used as immunostimulant and anti-neoplastic agent. Bitter taste of Levamisole Hydrochloride was masked and mouth dissolving tablet formulation were prepared by using excipient Sodium Starch Glycolate, Mannitol, Sucrose, et using direct compression method. The prepared tablets were evaluated forthickness, uniformity of weight, hardness, friability, disintegration, dissolution and drug content. Optimised batch was found to comply all parameters of specifications.

KEYWORDS: Levamisole Hydrochloride, Mouth Dissolving tablets(MDT) Disintegration, Dissolution , UV Spectrophotometer, FTIR Spectrum

INTRODUCTION:

Scientists have always been drawn to the creation of novel oral drug delivery systems in order to increase patient compliance. Mouth Dissolving Drug Delivery Systems (MDDDS) have risen to prominence in the market as a result of their ability to solve previously encountered administration issues and contribute to the extension of patent life. MDDDS have the unique ability of rapidly dissolving or releasing the drug as soon as it comes into contact with saliva, eliminating the need for water during administration. As a result, various dose forms have attracted a specific patient demographic, including dysphasic, bedridden, psychic, geriatric, and pediatric patients. Levamisole Hydrochloride is used to treat infections of the worm. Experimentally and historically, it has also been used to treat various autoimmune disorders and cancers in humans.[1,3]

MAERIALS AND METHODS:

Materials: Levamisole Hydrochloride(Research lab fine chem ,Mumbai), Mannitol (Analab fine chemicals ,Mumbai), SSG(research lab fine chem ,Mumbai), Aerosil (Analab fine chemicals, Mumbai) Magnesium Stearate(AG traders, Pune), Maize Starch (Analab fine chemicals, Mumbai). All chemicals were of analytical grade.

Methods

Analytical method for Levamisole Hydrochloride

Determination of ⅄max for Levamisole Hydrochloride:

Pure drug 100 mg was transferred into 100 ml of phosphate buffer pH 6.8 in a volumetric flask to prepare Std stock solution. This Std stock solution 10ml to 100 ml buffer 6.8 was scanned for the Levamisole Hydrochloride drug over range of 200-400 wavelength. The ⅄max was determined from this scan.

Standard calibration curve of Levamisole Hydrochloride in buffer pH 6.8 Accurately weighed 100 mg of LevamisoleHydrochloride was added to 100 ml volumetric flask volume made up to 100 ml with buffer this solution used as stock solution. This Std stock solution 10ml to 100 ml buffer 6.8 From this concentrations of 2,4,6,8,10 ppm were prepared. and absorbance was measured for each solution at ⅄max 214 nm using UV spectrophotometer. Graph was plotted for absorbance vs. Concentration.

Preparation of blend of MDT

Weigh all excipient except Magnesium Stearate, passedthem through Sieve No 40. Mixed one by one in geometrical proportion for 5 min. Levamisole Hydrochloride & excipient in poly bag to ensure mixing for 5 min. Then added Magnesium Stearate passed through sieve no 40 and mixed with here blend for 1 min in poly bag . unload in double poly bag and store tightly and label it. the blend is ready for compression.

Seven formulation of mouth dissolving tablet of Levamisole Hydrochloride using drug and Sodium Starch Glycolate ,Mannitol, sucrose and other excipient are shown in table below.

TABLE 1 : Formulation Trial Batches.

Sr.no	Ingredient mg/Tablet	F1	F2	F3	F4	F5	F6	F7
1	Levamisole Hydrochloride	50	50	50	50	50	50	50
2	Mannitol	40	50	50	50	50	50	50
3	Sodium starch glycolate	6	6	10	15	20	25	25
4	Maize Starch	10	10	10	10	10	15	20
5	Talc	-	8	8	8	8	8	8
6	Sucrose	192	173	169	164	159	154	154
7	Magnesium stearate	2	2	2	2	2	2	2
8	Aerosil	-	1	1	1	1	1	1

Pre-Compression Evaluation Parameters:

Prior to compression, the powder blends should be evaluated for their Bulk and Tapped density and Compressibility Index and Hausner's Ratio calculated.[4,5] The Angle of Repose was also determined.

Bulk Density(B.D):

It is the ratio of mass to bulk volume. It is required to decide appropriate packing of dosage forms. An accurately 10 gm of sample was weighed and transferred to a 50 ml measuring cylinder. The volume was noted. The Bulk densitywas obtained by dividing weight of the sample in grams by final volumeand it was determined by equation given below:

B. D=Mass/Bulk volume ----------(1)

Tapped Density(T.D):

Accurately weighed quantity of powder was carefully poured into graduated 50 ml measuring cylinder through large funnel. The cylinder was then tapped 100 times from a constant height and the tapped volume was read. This is expressed in gm / ml and determined by the following formula[4]

T.D=Mass/tapped volume ----------(2)

Angle of Repose:

A funnel was kept vertically in stand at a specified height above a paper placed on horizontal surface. The bottom was closed and 10 gm of sample powder was filled in funnel. The funnel was opened to release the powder on paper to form a smooth conical heap. The height of heap was measured using the scale. A border of heap was marked circularly and its diameter was measured at four points. The angle of repose was calculated using following formula: [4,6]

Tan θ=h/r ----------(3)

Where; θ= angle of repose

r=radius of the base

h=height from tip of funnel to the surface of graph paper.

Carr's Index:

It is also one of the simple method to evaluate flow property of a powder by comparing the bulk density and tapped density. Carr's index (CI) is an indication of the compressibility of a powder. It is expressed in percentage and determined by the following formula**:**

CI= (TD-BD)x100/TD ----------(4)

Hausner's Ratio:

A small index like percentage compressibility index has been defined by Hausner ratio. Values less than <1.25 indicates good flow, where as greater than 1.25 indicates poor flow. Added glidant normally improves flow of the material under study. Hausner's ratio(HR) can be calculated by;

H R=TD/BD ----------(5)

Post -Compression Evaluation Parameters.

Hardness:

Hardness (diametric crushing strength) is a force required to break a tablet cross the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The hardness was tested by using Monsanto hardness tester.[7]

Weight Variation: Individually weigh 20 tablets, which are selected at random and calculate the average weight. Then calculate difference of individual weigh from average weight.

Thickness:

The thickness in millimeters (mm) should be measured individually by vernier caliper.

Friability:

Roche friability test apparatus was used to determine the friability of the tablets. Twenty pre-weighed tablets were placed in the apparatus and operated for 100 revolutions and then the tablets were reweighed. The percentage friability was calculated according to the following formula.[7]

%Friability =(IW - FW) x 100/IW ----------(6)

Where IW = Initial weight

FW = Final Weight

Drug Content:

This is an important parameter and the efficiency can be evaluated by the assay. Ten tablets were powdered well and powder equivalent to 100mg of the drug was dissolved in 100ml of 6.8 buffer, filtered and with required dilution analyzed spectrophotometrically at 214nm. The concentration of drug was determined by using a standard calibration curve.[2]

Disintegration Test:

For this test, six tablets are employed in water at 37 ^{0}C using a tablet disintegration tester. The time required for disintegrating the tablets and passing completely through the sieve is recorded.[5]

In-vitro dissolution study:

In-vitro dissolution study will be carried out by using the USP dissolution test apparatus (Paddle II).
The dissolution medium consists of 900 ml 6.8 buffer and rotation speed at 50rpm. 5ml of sample is withdrawn at regular interval upto 30 minutes and replace with same quantity of the fresh dissolution medium. And withdrawn samples are analyzed spectrophotometrically at 214nm.[2]

Drug-Excipient Compatibility:

Compatibility studies were performed at 20°C, 30°C and 40°C by physical observation. The results showed that there was no change in physical appearance at various temperatures (20°C - 40°C) over 30 days and there was no interaction between drug and excipients.

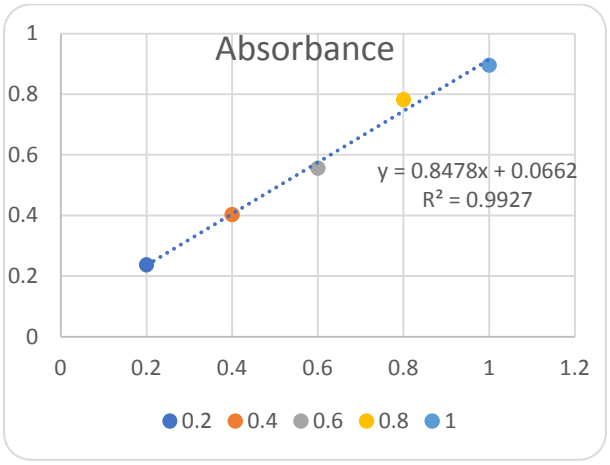
Stability studies: Stability studies were carried out on optimized formulation as per ICH specifications at 40° c±2 °c/75%± 5%RH for duration of three months. After an interval of one month samples were withdrawn and evaluated for percentage of drug release and moisture content[8]

RESULTS AND DISCUSSION

Determination of Calibration Curve of Levamisole Hydrochloride :

The concentration of solutions used, their absorbance and calibration curve graph are given below in table 3 and fig 2 respectively.

Table 3 concentration and Absorbance



Sr no	Conc	Absorbanc 214nm 6.8 buffer
1	2ppm	0.2136
2	4ppm	0.4032
3	6ppm	0.5563
4	8ppm	0.7126
5	10ppm	0.9355

Figure 1 Standard Calibration Curve

FTIR SPECTRA:

IR spectra of Levamisole Hydrochloride alone and its combination with excipients are shown in Figures given below spectrum of pure Levamisole Hydrochloride has characteristics peaks,whicharenotaffectedalongwiththecombinationofexcipients. From this, which indicate there is nointeractionbetweendrugandexcipients. Here NC=No Change

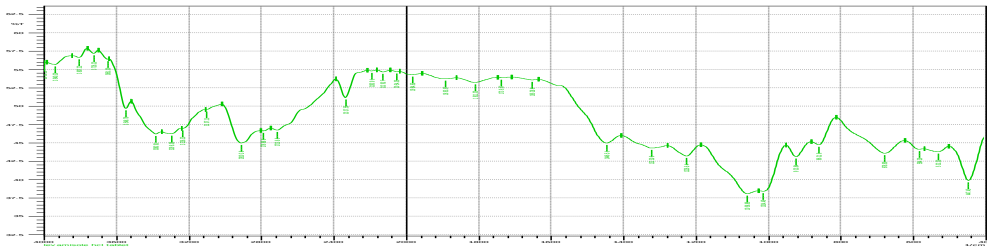


Figure 2 FTIR Spectra Tablet

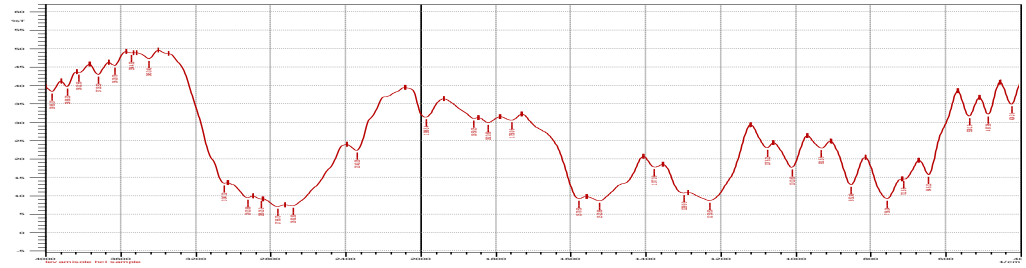


Figure 3 FTIR Spectra API + Excipient

Drug-Excipient Compatibility:

Table 4 : **Drug-Excipient Compatibility**

Sr. No	API+EXCIPIENT	INITIAL	At 30° c ±2 °c/60% ±5%RH	At 40° c ±2 °c/65% ±5%RH
1.	Levamisole Hydrochloride	Off White Powder	NC	NC
2.	API+SSG	Off White	NC	NC
3.	API+ Maize Starch	Off White	NC	NC
4.	API+ Mannitol	Off White	NC	NC
5.	API+ Mg Stearate	Off White	NC	NC
6.	API+ Talc	Off White	NC	NC
7.	API+ Sucrose	Off White	NC	NC
8.	API+MCC	Off White	NC	NC
9.	API+ Strawberry Flavor	Off White	NC	NC

Precompression parameters : the values of all precompression parameters are given in table

Formulation	**Angle of repose (θ)**	**Bulk density g/ml**	**Tapped density g/ml**	**% Compressibility**	**Hausner's Ratio**
F1	30.36±0.3	0.41±0.05	0.42±0.02	22.89±0.03	1.07
F2	26.55±0.4	0.49±0.04	0.62±0.03	16.63±0.05	1.26
F3	30.43±0.5	0.40±0.05	0.42±0.02	22.89±0.03	1.07

Table 3: Precompression parameters :

F4	25.66±0.02	0.69±0.03	0.81±0.01	19.57±0.03	1.19
F5	26.55±0.4	0.49±0.04	0.62±0.03	16.63±0.05	1.26
F6	26.55±0.4	0.49±0.04	0.62±0.03	16.63±0.05	1.26
F7	30.43±0.5	0.40±0.05	0.42±0.02	22.89±0.03	1.07

Table No 4 : Post compression Parameters

Sr.NO	FORMULATION CODE	Thickness(mm)	Friability (%)	Hardness (kg/cm2)	Disintegration Time(sec)
1	F01	3.9	0.6	4.5	80 to 90
2	F02	3.8	0.7	3.9	80 to 90
3	F03	3.9	0.8	3.7	52 to 60
4	F04	3.8	0.8	4.2	40 to 50
5	F05	3.7	0.7	3.8	25 to 30
6	F06	3.8	0.9	3.6	15 to 20
7	F07	3.9	0.8	4.4	15 to 20

F1 to F4 batches were prepared with SSG not achieved disintegration time. Hence rejected

TIME IN MINUTES	CUMULATIVE DRUG RELEASE		
	F05	**F06**	**F7**
5	47.61± 2.70	55.35±1 .12	59.61 ±2.70
10	68.32± 1.15	76.06±1 .12	78.48±1 .12
15	81.48± 1.12	81.48±1 .15	85.67±1 .12
20	88.25±	90.77±2	90.58±1

	1.15	.70	.12
30	90.58± 1.12	94.25±1 .23	94.25±1 .15

Table No 5 : Dissolution of F05 - F07

Sr. No.	Time in Months	Physical Changes	% Drug Release	% of Drug Release
1	Initial	Round W color uncoated	94.49 ±0.43	94.92 %
2	1 Month	No Changes	94.12 ±0.84	94.96 %
3	2 Month	No Changes	94.67 ±0.56	94.23 %
4	3 Months	No Changes	94.56 ±0.58	94.17%

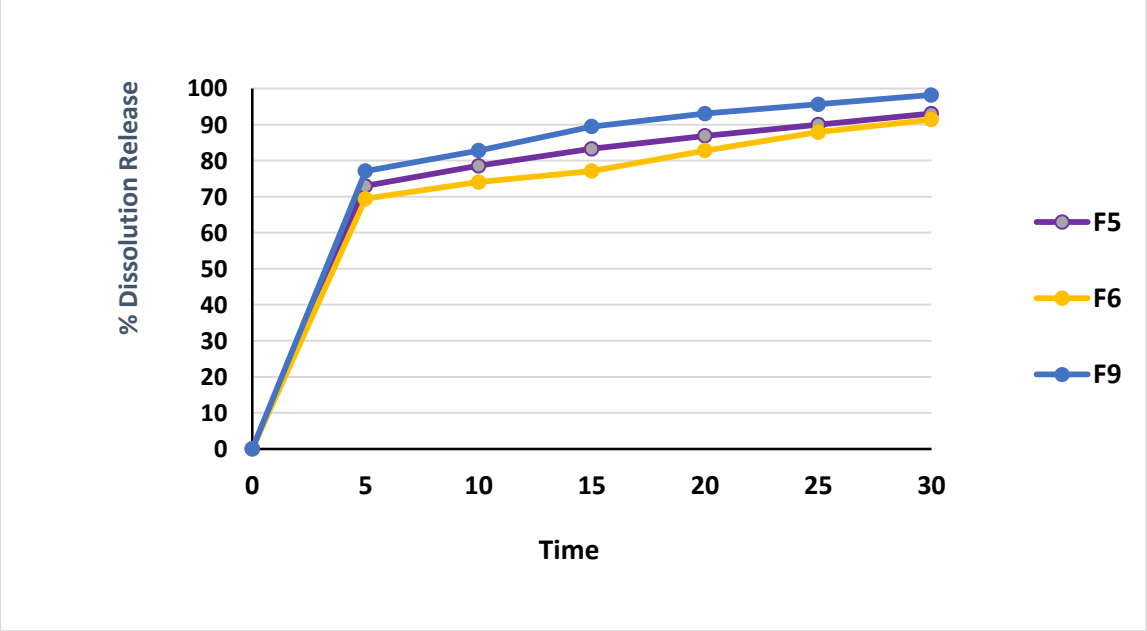
Table 6 Stability Study Results of MDT of Levamisole Hydrochloride

In-vitro drug release:

The in-vitro drug release profile of formulation (F5 – F7) depicted in table from the release data,

Maximum of 94% drug release was obtained at the end of 30 Minutes from the Mixtures. Formulation F6, F7 show best results in drug release. The rationale combination of Mannitol and SSG proves that these are good super disintegrant

Fig . Dissolution study graph.



Stability study:

The best formulation F7 was subjected for stability study and drug content, moisture content and % drug release are evaluated, and the result showed that the formula

conclusion:

As a result of this research there were seven different batches which were particularly evaluated. The optimized batch was found to be the F7 which had shown good properties. Mouth dissolving tablet dosage form of BCS Class I drug Levamisole Hydrochloride was successfully prepared to be used as a Antihelmintic drug.

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