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Formulation and Evaluation of Orodispersive Tablets of "Ebastine" Using Natural Super Disintegrant by Molecular Dispersion Technique

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Abstract:- Ebastine is a 2nd generation H1 receptor antagonist that is mainly indicated for allergic rhinitis and chronic idiopathic urticaria. In allergic conditions the patient become panic and will have difficulty to swallow tablet with a glassful of water. In such cases Orodispersive tablets will be a good solution for patient compliance and efficient dose regimen. Ebastine tablets are available in different strength i.e. 10 mg and 20 mg. The main objective of this project work was to developed and designed an Orodispersive tablets (ODTs) containing Ebastine 20 mg, using "Natural Super Disintegrants'' by molecular dispersion technique including various pharmaceutical excipients with different strengths to enhance patient compliance and therapeutic value as compare with the available market brands. Orodispersive Tablets of Ebastine were formulated by molecular dispersion technique and using Natural Superdisintegrants such as Agar and Guar gum and other excipients like gelatin, sodium lauryl sulphate, microcrystalline cellulose, sweetening agent as Sodium saccharine, talc and magnesium stearate as lubricants, clove oil and lemon flavor as flavoring agent. Drug - excipients compatibility tests performed before start the formulation. The selection and the rejection of excipients for experimental formulation was considered after getting the result of drug excipients compatibility study. The flowability of the powder mixtures were evaluated using Carr's index, Angle of Repose and the Hausner's ratio. The tablets were evaluated according to the standards prescribed by British Pharmacopoeia like weight variation, thickness, hardness, friability, disintegration time, a simulated wetting test and in-vitro dissolution. Prepared tablets after Optimization showed disintegration time less than 30 seconds and drug dissolution of about 75% within 30 minutes. The prepared tablets of optimized batch tested for stability 40 degree Celsius and 75% RH for 3 months and were found to be stable. Prepared Orodispersive tablets of Ebastine 20 mg from optimized batch were found bioequivalent under fasting and fed conditions with the available market products. The determination and evaluation were made for the most effective type and optimal amount of "Natural Super Disintegrants'' for the manufacture of Orodispersive Tablets by molecular dispersion & direct compression technique.

I. INTRODUCTION

Tablet measurements structure is the most well-known medication conveyance frameworks which are viewed as the least demanding and most reasonable method of organization of the medication to a patient with the utilization of a glass of water. So, tablets are the most best measurements structure involves the biggest and the most critical spot as contrast with other dose structures. There are various sizes relating to the portion of the medication which can be given just as the state of the tablet. A few tablets may contain as low as 1 mg or less of the medication, and others contain 1.5 g. of the dynamic medication per tablet, which gives an immense scope of medication content. Tablet dose structures can be made in various sizes and shapes, and the medication fixing may contain 0.1% to 90% of a tablet mass. The assembling of tablets is very simple when contrasted with other measurements structure. The soundness issues are extremely less too. Creation yield is likewise high and is the most affordable. Especially in the event of present-day mechanical strategies including the cycle of Direct Compression Technique (DC).

Direct Compression is the most straightforward, monetary and financially savvy producing procedure which would now be able to be applied to Orodispersive tablets, Fast dissolving Tablets, Mouth dissolving tablets and so on due to the accessibility of huge scope of exceptionally improved excipients like tablet normal super disintegrants, semi engineered disintegrants, manufactured excipients, strands and sugar-based excipients.

ISSN No:-2456-2165

"Orodispersive Tablets" (ODTs) can be characterized as strong single-unit measurement structure that is expected to be set on the tongue where it disintegrates quickly within the sight of salivation inside couple of moments and afterward gulped without the need of water. Quicker the medications breaking down, scattering and disintegration happen, the faster the ingestion and beginning of clinical impact.

As indicated by the US-FDA, the ODTs were characterized as "A strong measurements structure containing restorative substances which breaks down quickly, for the most part inside only seconds, when set upon the tongue". It has been demonstrated measurably that (ODTs) have a few focal points over regular tablets to upgrade persistent consistence and acknowledgment in light of its attainability and comfort. Practically half of the populace experiences trouble gulping while at the same time taking traditional tablets and hard gelatin containers. These populaces incorporate pediatric and geriatric populaces who experience issues gulping enormous tablets. So as to defeat these issues, Orodispersive tablets (ODTs) have been created as elective oral measurements structures. Likewise, ODTs turned into a phenomenal decision as another medication conveyance framework, since they are anything but difficult to regulate and prompt better patient consistence, particularly in the older and kids.

The goal of this investigation was to create and plan an Orodispersive tablet dose type of dynamic medication Ebastine, utilizing different drug organizations including super disintegrants from characteristic sources to improve tolerant consistence basically for pediatric and geriatric patients. It is a histamine-H1 receptor obstructing specialist with anticholinergic and narcotic property utilized for its insect unfavorably susceptible properties. Consequently, it is basically utilized in the administration of hypersensitivity manifestations like unfavorably susceptible rhinitis, urticaria, skin rashes, irritated/watery eyes, runny nose, and regular virus.

In the current investigation, Orodispersive tablets (ODTs) of Ebastine was planned utilizing Natural Superdisintegrants by molecular dispersion technique. Direct compression method was applied to compress the tablets due to generally helpful, straightforward, savvy. The excipients were utilized in the detailing, for example, Gelatin, Sod. Lauryl sulfate, Agar, Guar gum, microcrystalline cellulose, Sod. Saccharine, Colloidal Silicon di oxide and magnesium stearate. The planned tablet definitions will be assessed for as indicated by the British Pharmacopeia for weight variety, thickness, hardness, friability, breaking down time, a recreated wetting test, and in-vitro disintegration. The dependability of test item was assessed according to the ICH Q8 rules.

Justification of Research

Super disintegrants are the key material for a successful brand and the best therapeutic results in the form of Orodispersive tablets. The existing market brands containing Ebastine 20 mg or 10 mg were developed and designed using superdisintegrants obtained from other than natural sources or synthetic sources. In the current research work it has been proven that natural superdisintegrants are superior as compared to superdisintegrants obtained from synthetic process. Commercially, the Natural Superdisintegrants are freely available in market. The price of Natural superdisintegrants are very competitive and cheaper than synthetic superdisintegrants. Although the superdisintegrants obtained from natural sources categorized safer ingredients in comparison to synthetic superdisintegrants. The molecular dispersion technique utilized to increase the bioavailability of active constituent 'Ebastine' which is poorly soluble in water. Molecular dispersion of micronized form of Ebastine with gelatin and Sodium Lauryl Sulphate increased its solubility which get dissolved faster in presence of Natural superdisintegrants when comes in contact with saliva after placing the tablet in oral cavity and get quick absorbed in blood stream. The onset of action of drug start faster than a conventional tablet. The preparation of Orodispersive tablets using Natural superdisintegrants by Molecular dispersion technique is completely satisfies the regulatory requirements and the manufacturing process is commercially feasible. The optimized formulation was robust, following all the parameters of standards and no issues were faced with respect to organoleptic attributes, blend uniformity, content uniformity, tableting, stability and bioequivalence etc.

II. MATERIAL AND METHODS

Drug and Excipients used in the formulation

Material	Gifted By
Ebastine	Bal Pharma Ltd.
Gelatin	Bal Pharma Ltd.
Sodium Lauryl Sulphate	Bal Pharma Ltd.
Agar	Bal Pharma Ltd.
Guargum	Bal Pharma Ltd.
Microcrystalline Cellulose	Bal Pharma Ltd.
Sod. Saccharine	Bal Pharma Ltd.
Clove Oil	Bal Pharma Ltd.
Lemon Flavor	Bal Pharma Ltd.
Colloidal Silicon-di-Oxide	Bal Pharma Ltd.

Equipment and instruments used during formulation

Equipment and instruments	Make and Model
Weighing Machine	PS6000/C/1 manufactured by LCGC RADWAG
Vibrosifter	Gansons Engineering
Electromagnetic Sieve Shaker	EM8-08 Plus manufactured by Electrolab
Tap Density Testing Apparatus;	ETD-1020 manufactured by Electrolab
Double Cone Blender with interchangeable bowls	manufactured by Sams Technomech;
Loss on Drying Mositure Analyzer	Model MB 45 manufactured by Ohaus
Comminuting Mill equipped with 0.5mm Screen	Manufactured by Cadmach Machinery;
16 Station Single Rotary Tablet Compression Machine	Manufactured by Cadmach Machinery
Hardness Tester	Type: TBH 125 manufactured by Erweka
Thickness Tester Vernier Caliper	Absolute Dogmatics manufactured by Mitutoyo
Friabilator	EF-1W manufactured by Electrolab
Disintegration Test Apparatus	Model ED 2L manufactured by Electrolab
6.35 mm Round Flat Faced Bevel Edged Punch Tooling	manufactured by ACG PAM Pharma Technology
pH Meter	H12215 manufactured by Hanna Instruments
UV Visisble Spectrophotometer	manufactured by Perkin Elmer Lambda 25
Lab Stirrer	RQ126D manufactured by Remi
Dissolution Apparatus	TDT-08L manufactured by Electrolab
40°C / 75% RH Stability Chamber	manufactured by Thermolab Scientific Equipment

Disintegration and dissolution parameters

Disintegration test was performed in USP disintegration test apparatus in purified water at 37+ 0.5-degree celcius. Specification NMT 30 Seconds. Dissolution is performed in purified water. The parameters include USP-II (Paddle) 50 RPM, 900 ml, purified water at 37+ 0.5-degree celcius, Time Points 0, 0.08, 0.16, 0.25, 0.33, 0.41, 0.5, 0.66, 0.83, 1.0, 2.0, 4.0 and 6.0 minutes. Specification NLT 75% (Q) of the labelled amount in 60 minutes.

III. METHOD OF ASSAY, BLEND UNIFORMITY, CONTENT UNIFORMITY/UNIFORMITY OF DOSAGE UNITS AND DISSOLUTION

Method for Bulk Density, tapped density, Angle of Repose and Friability

USP guidelines followed in the measurement of Bulk Density, Tapped Density, Compressibility Index, Hausner's Ratio, Repose Angle and % Friability measurements.

Experimental Methodology

Molecular dispersion technique with micronized active drug Ebastin by using Natural superdisintegrants, the process will be the same for every trial batch from Batch No. F1 – Batch No. F13 for the manufacturing of Orodispersive Tablets.

- **Step -1: - Material Sifting**
  - Ebastin, Sod. Lauryl Sulphate, Guar gum, Agar, Microcrystalline Cellulose shall be sifted through #60 separately.
  - Colloidal silicon dioxide and Magnesium Stearate shall be sifted through #60 separately.
- **Step – 2:- Manufacturing Process**
  - Take Gelatin and SLS in a china dish according to the formula and melt at 70 degrees Celsius.
  - Now transfer the whole qty of Ebastin into china dish and mix properly.
  - Keep the homogenous mixture in a refrigerator for 5-8 hrs.
  - Cooled mass shall be milled and mixed with previously sifted MCC, Agar/Guar gum and blend until proper mixing of all ingredients.
- **Step - 3:- Lubrication**
  - Finally add previously sifted colloidal silicon dioxide, Mag. Stearate, Sod. Saccharine, Flavors and lubricate for 5 min.
- **Step – 4:- Compression**
  - The lubricated blend is compressed into tablets as per pre-planned formulation by using a rotary compression machine.
- **Step – 5:- Analysis**
  - Compressed tablets shall be analyzed as per the official guidelines for all parameters and a comparative study shall be done with the existing market brand

Parameters Fixed for the tablet

The following parameters were mixed for the final tablets obtained:

- Punch size: 7.14 mm
- Thickness: 3.2 – 3.6 mm
- Hardness: 20 – 100 Newton
- Weigh variation: +/- 2 %

ISSN No:-2456-2165

Proposed Formulations For Experiments

(Table 1.0) F1-F6 with Natural Superdisintegrants alone

Sr. No.	Ingredients	Unit Formula (mg/tablet)					
		F-1	F-2	F-3	F-4	F-5	F-6
1	Ebastine	20	20	20	20	20	20
2	Gelatin	1.5	1.5	1.5	1.5	1.5	1.5
3	Sodium Lauryl Sulphate	1.5	1.5	1.5	1.5	1.5	1.5
4	Agar	5	--	9	--	13	--
5	Guargum,	--	5	--	9	--	13
6	MCC	117	117	113	113	109	109
7	Sod. Saccharine	2	2	2	2	2	2
8	Colloidal Silicon-di-oxide	1.5	1.5	1.5	1.5	1.5	1.5
9	Mag. Stearate	1.5	1.5	1.5	1.5	1.5	1.5
Net Wt. / Tab. in mg		150	150	150	150	150	150

(Table 2.0) F7-F9 with the combination of 2 Natural Super disintegrants

Sr. No.	Ingredients	Unit Formula (mg/tablet)		
		F-7	F-8	F-9
1	Ebastine	20	20	20
2	Gelatin	1.5	1.5	1.5
3	Sodium Lauryl Sulphate	1.5	1.5	1.5
4	Agar	3	5	9
5	Guargum*	3	5	9
6	MCC	116	112	104
7	Sod. Saccharine	2	2	2
8	Colloidal Silicon-di-oxide	1.5	1.5	1.5
9	Mag. Stearate	1.5	1.5	1.5
Net Wt. / Tab. in mg		150	150	150

(Table 3.0) F10-F13 with organoleptic additive
(After getting results of previous formulations from F1 – F9)

Sr. No.	Ingredients	Unit Formula (mg/tablet)			
		F-10	F-11	F-12	F-13
1	Ebastine	20	20	20	20
2	Gelatin	1.5	1.5	1.5	1.5
3	Sodium Lauryl Sulphate	1.5	1.5	1.5	1.5
4	Agar	9	9	9	9
5	Guar gum,	9	9	9	9
6	MCC	101	101	101	101
7	Sod. Saccharine	2	2	2	2
8	Clove Oil	2	--	3	--
9	Lemon Flavor	--	2	--	3
10	Colloidal Silicon-di-oxide	1.5	1.5	1.5	1.5
11	Mag. Stearate	1.5	1.5	1.5	1.5
Net Wt. / Tab. in mg		150	150	150	150

Preformulation studies

All the excipients were evaluated with the drug for compactability studies. The preformulation studies were performed according to the formula and results were recorded based on the data was obtained accordingly.

Characterization of Active Drug

The active drug was evaluated for various parameters through the standard test and accordingly the results have been mentioned in Table 4.0

ISSN No:-2456-2165

Table 4.0 Result analysis of Ebastine

Test	Specification	Observation	Conclusion
Description	White color powder	White color powder	Complied
Odor	Odorless	Odorless	Complied
Solubility	Insoluble in water	Practically Insoluble in water	Complied
	Sparingly soluble in methyl alcohol; freely soluble in methylene chloride.	Practically it is sparingly soluble in methyl alcohol; freely soluble in in methylene chloride.	Complied

Drug-excipient compatibility studies

The drug was evaluated along with all the excipients for compatibility studies and the results were recorded as per the data obtained after completion of the studies in Table 5.0.

The FT-IR spectrum of Ebastine and excipient individually and their mixtures of drug and excipient are shown in Fig. 1.0 to 1.10

Table 5.0 Drug-excipient compatibility data

S. No.	Drug+ Excipient	Condition		
		Room Temperature	Hot air oven	Freezing Temperature
1	EBASTINE (API)*	Stable	Stable	Stable
2	API + GELATIN	Stable	Stable	Stable
3	API + SODIUM LAURYL SULPHATE	Stable	Stable	Stable
4	API + MCC	Stable	Stable	Stable
5	API + AGAR	Stable	Stable	Stable
6	API + GUAR GUM	Stable	Stable	Stable
7	API + COLL. SILI. DI. OXIDE	Stable	Stable	Stable
8	API + MAG. STEARATE	Stable	Stable	Stable
9	API + SOD. SACCHARINE	Stable	Stable	Stable
10	API + CLOVE OIL	Stable	Stable	Stable
11	API + LEMON FLAVOR	Stable	Stable	Stable

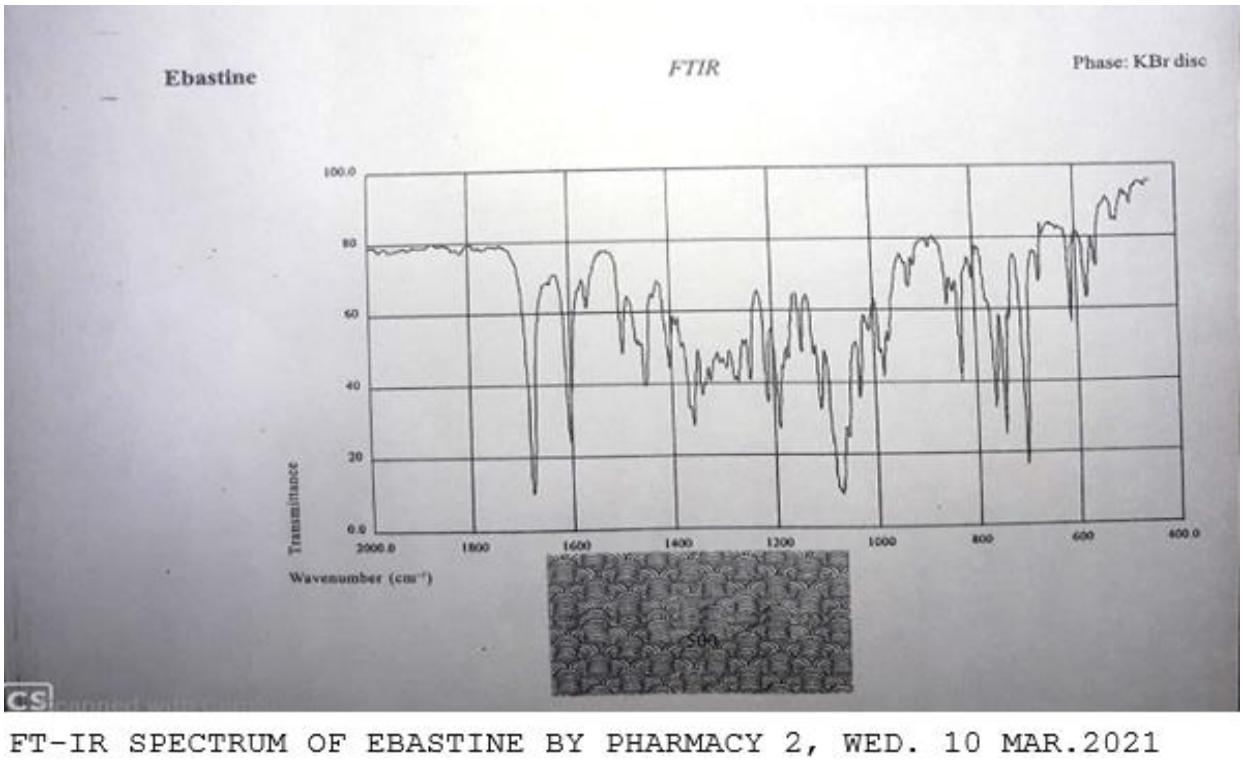
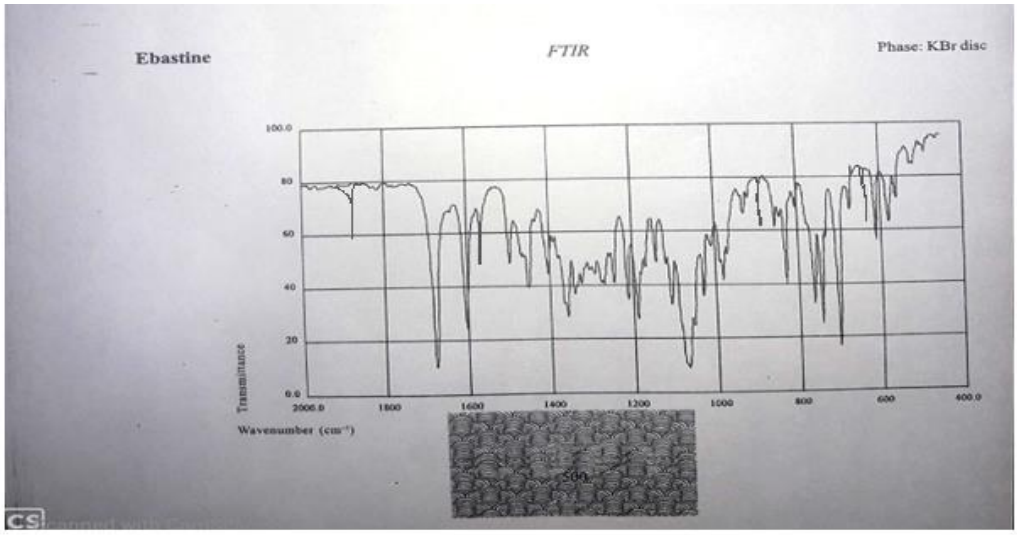


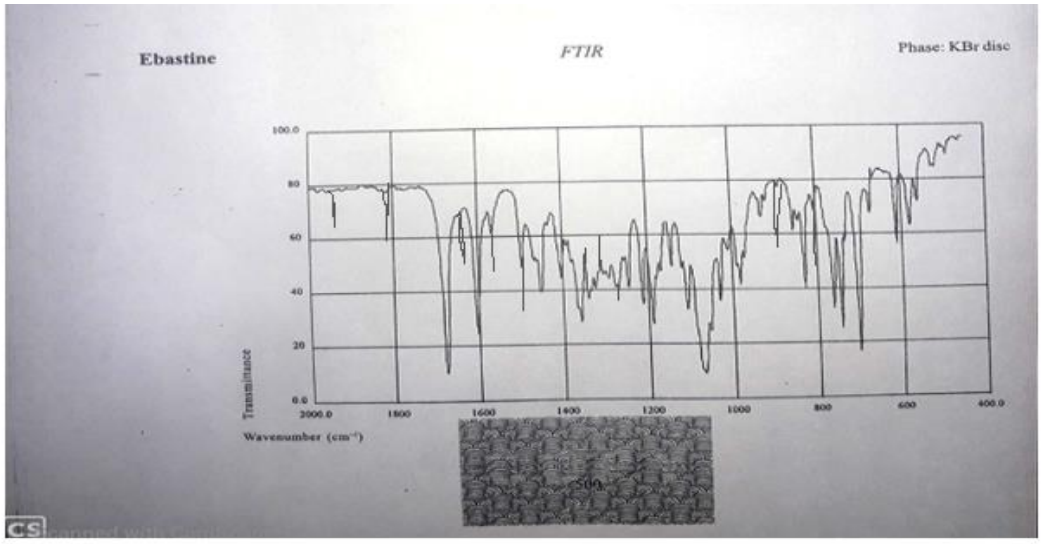
Fig. 1.0 FT-IR spectrum of "EBASTINE"

ISSN No:-2456-2165



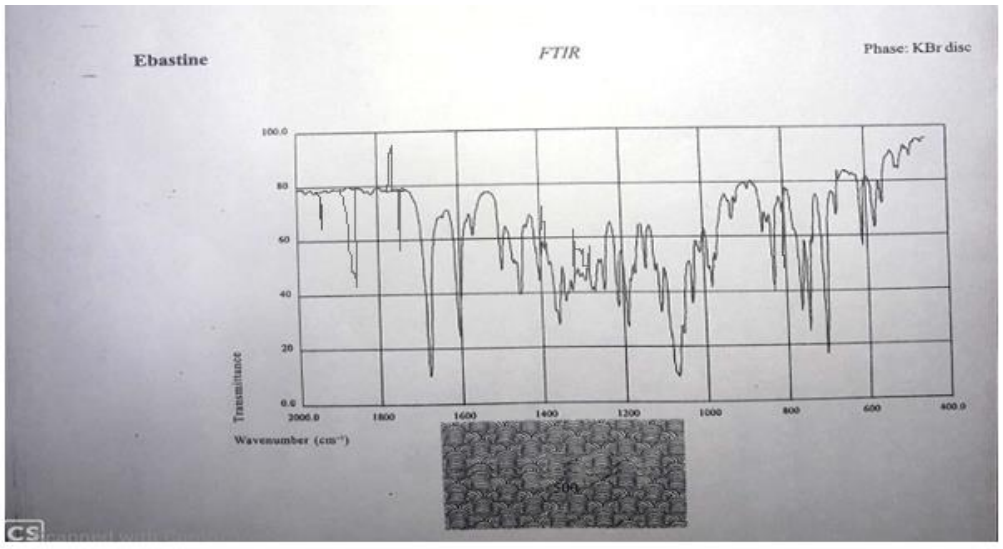
FT-IR SPECTRUM OF EBASTINE AND GELATINE BY PHARMACY 2, WED. 10 MAR.2021

Fig. 1.1 FT IR spectrum of API+GELATIN



FT-IR SPECTRUM OF EBSTINE AND SLS BY PHARMACY 2, WED. 10 MAR. 2021

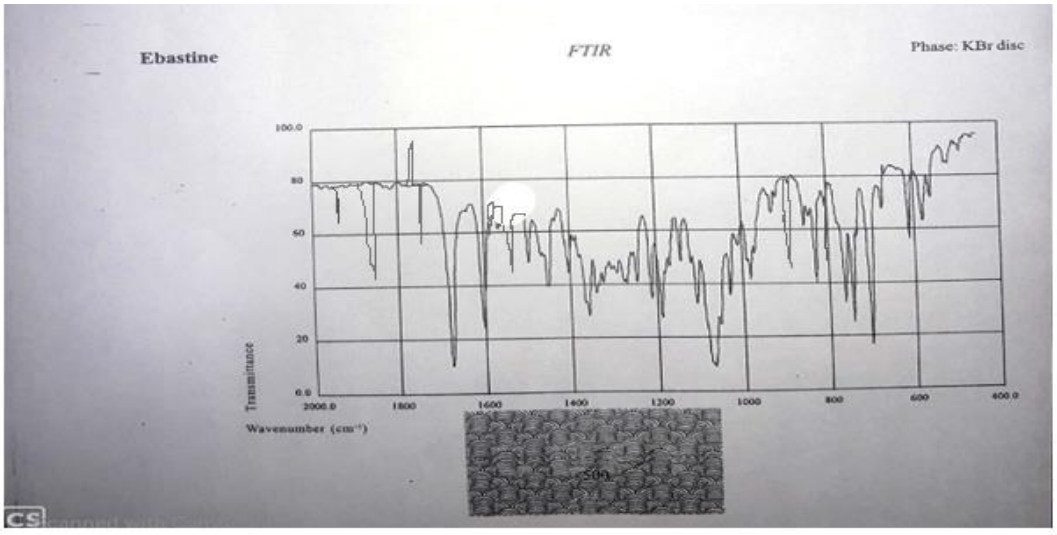
Fig. 1.2 FT IR spectrum of API + SODIUM LAURYL SULPHATE



FT-IR SPECTRUM OF EBASTINE AND AGAR BY PHARMACY 2, WED. 10 MAR. 2021

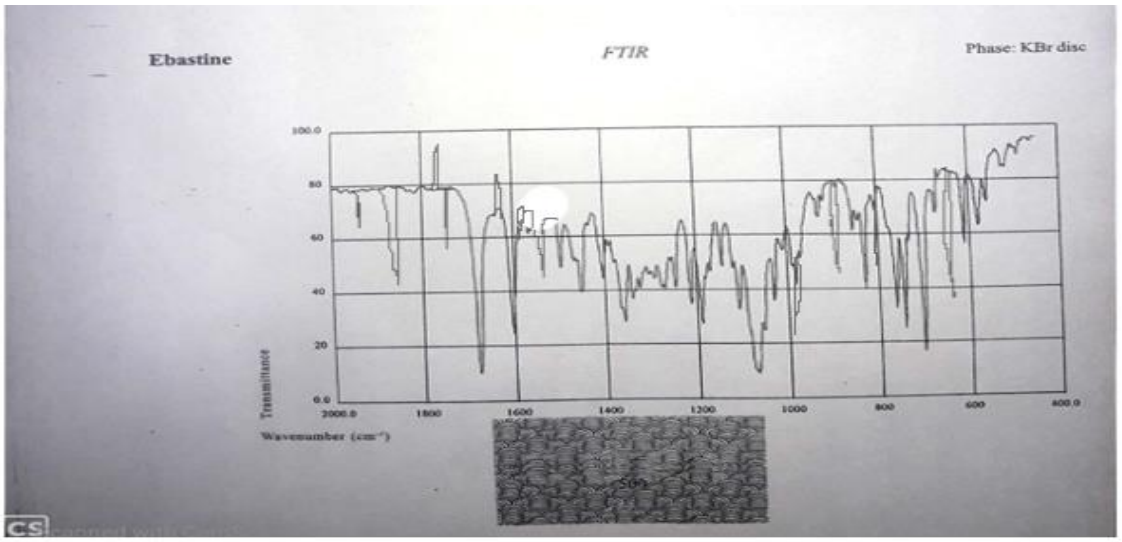
Fig. 1.3 FT IR spectrum of API+AGAR

ISSN No:-2456-2165



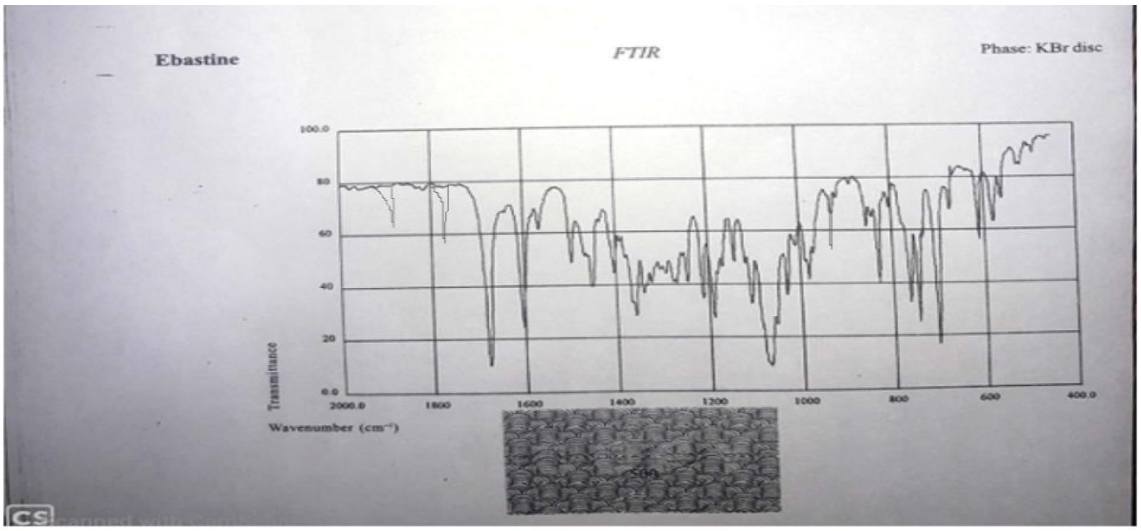
FT-IR SPECTRUM OF EBASTINE AND GUARGUM BY PHARMACY 2, WED. 10 MAR. 2021

Fig. 1.4 FT IR spectrum of API+GUARGUM



FT-IR SPECTRUM OF EBASTINE AND MCC BY PHARMACY 2, WED. 10 MAR. 2021

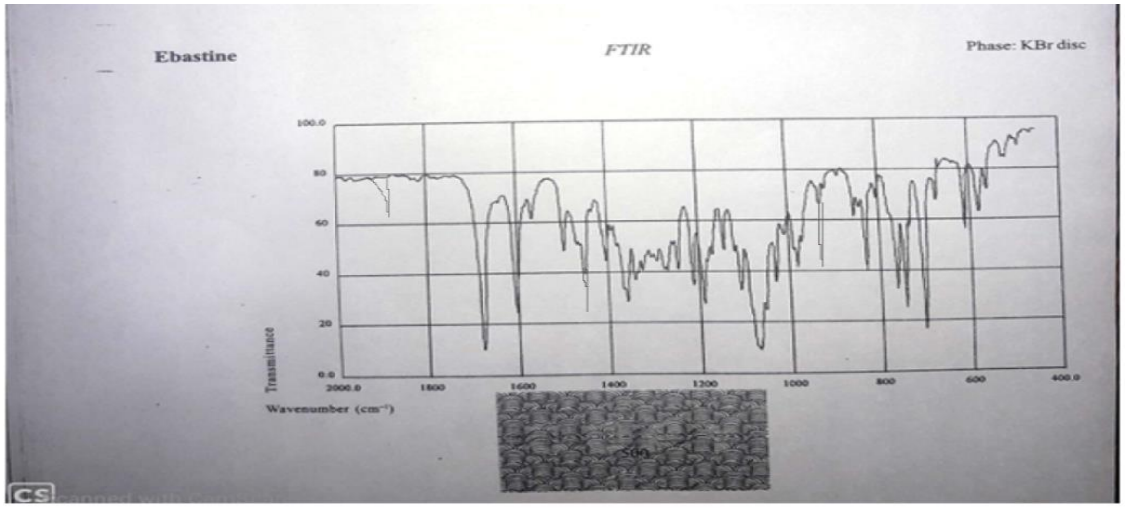
Fig. 1.5 FT IR spectrum of API+MICRO CRYSTALLINE CELLULOSE



FT-IR SPECTRUM OF EBASTINE AND COLLOIDAL SILICON DI OXIDE BY PHARMACY 2, WED. 10 MAR. 2021

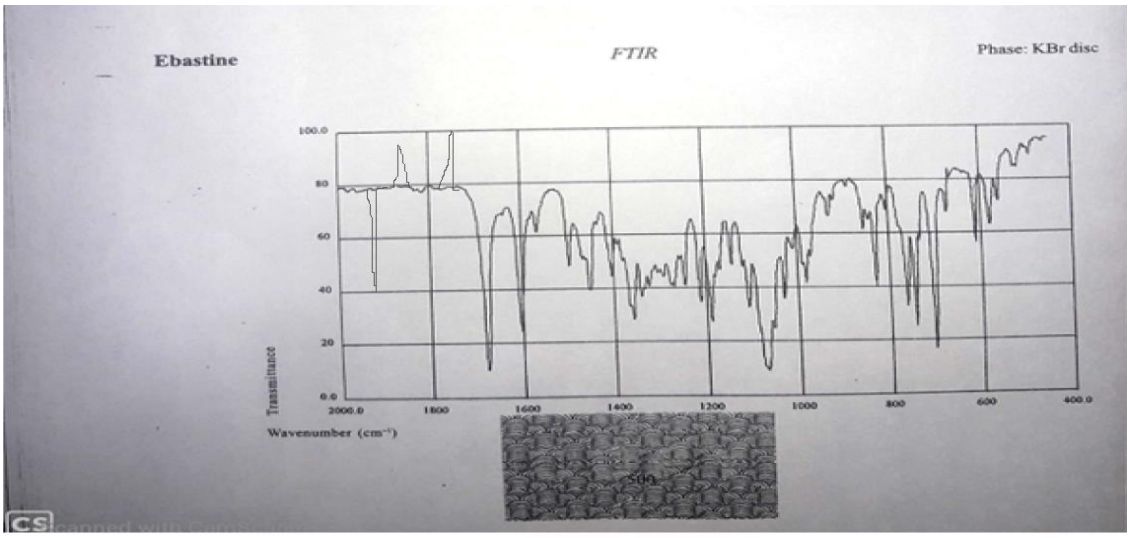
Fig. 1.6 FT IR spectrum of API + COLLOIDAL SILICON DIOXIDE

ISSN No:-2456-2165



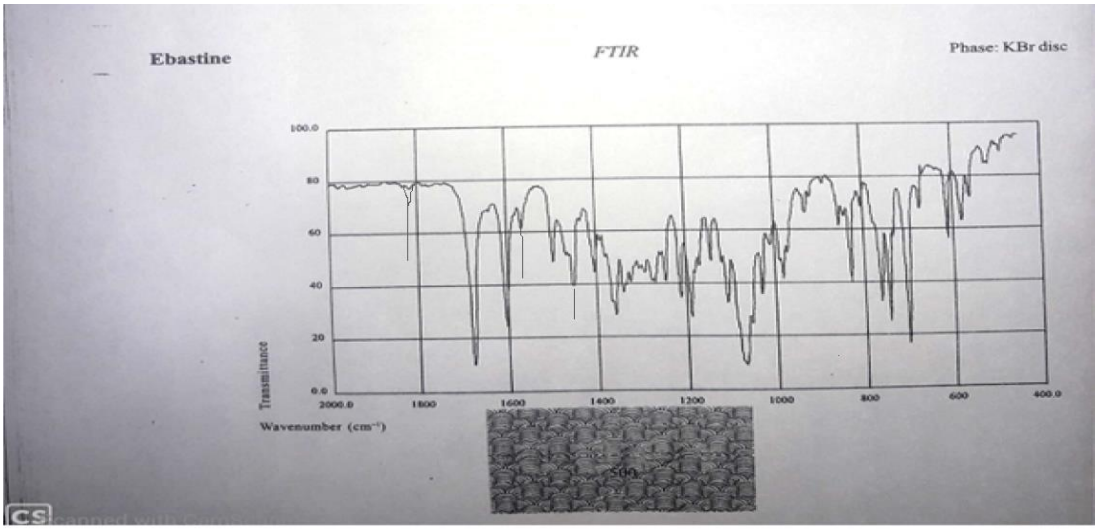
FT-IR SPECTRUM OF EBASTINE AND MAG. STEARATE BY PHARMACY 2, WED. 10 MAR. 2021

Fig. 1.7 FT IR spectrum of API + MAGNESIUM STEARATE



FT-IR SPECTRUM OF EBASTINE AND SOD. SACCHARINE BY PHARMACY 2, WED. 10 MAR. 2021

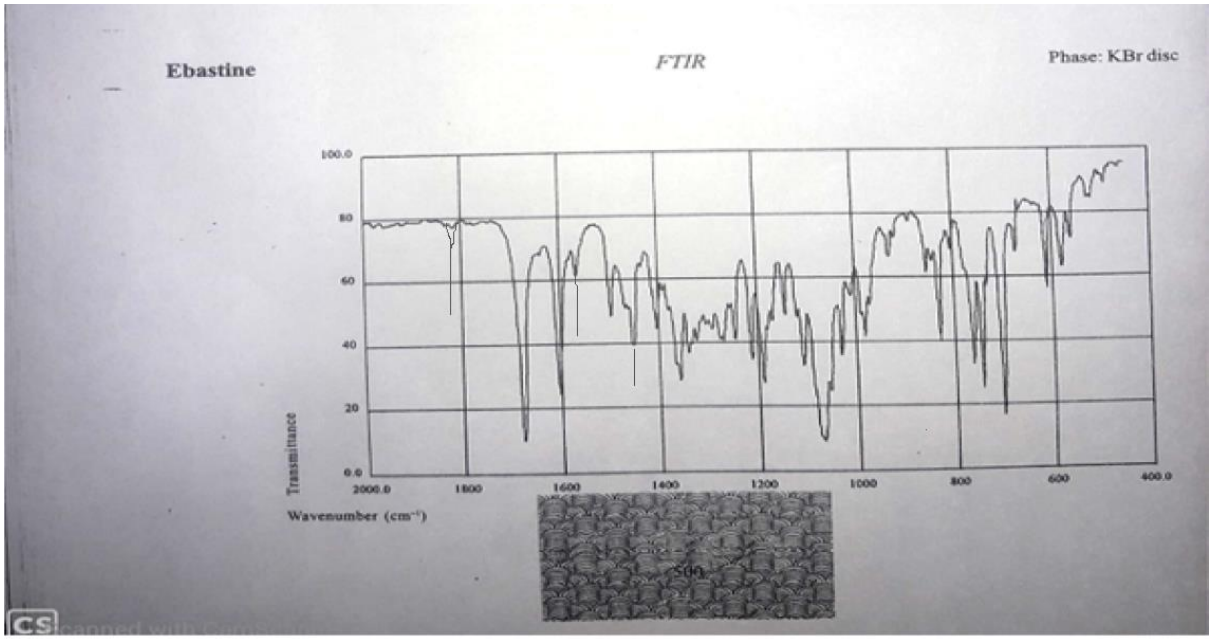
Fig. 1.8 FT IR spectrum of API + SODIUM SACCHARINE



FT-IR SPECTRUM OF EBASTINE AND CLOVE OIL BY PHARMACY 2, WED. 10 MAR. 2021

Fig. 1.9 FT IR spectrum of EBASTINE + CLOVE OIL

ISSN No:-2456-2165



FT-IR SPECTRUM OF EBASTINE WITH LEMON FLAVOR BY PHARMACY 2, WED. 10 MAR. 2021

Fig. 1.10 FT IR spectrum of API + LEMON FLAVOUR

Determination of λmax of Ebastine using a UV spectrometer

The λmax of Ebastine was found to be 252 nm.

Results of pre-compression studies

Precompression studies generally involve the evaluation of the blend in terms of bulk density, tapped density, compressibility index, Hausner's ratio, and so on (Table 5.3). These also determine the flow property of the powder.

Table 6.0 Physical properties of the prepared blend

BATCH	BULK DENSITY	TAPPED DENSITY	ANGLE OF REPOSE	CARR'S INDEX	HAUSNER'S RATIO
F1	0.49±0.002	0.65±0.001	31.96±0.38	24.62 ± 0.160	1.33± 0.003
F2	0.45±0.001	0.60±0.001	32.49±0.80	25.00 ± 0.660	1.33± 0.003
F3	0.49±0.001	0.69±0.001	32.58±0.46	28.99 ± 0.360	1.41± 0.009
F4	0.51±0.002	0.70±0.001	34.81±0.86	27.14 ± 0.890	1.37± 0.016
F5	0.53±0.001	0.71±0.001	34.58±0.58	25.35 ± 0.450	1.34± 0.014
F6	0.52±0.002	0.69±0.001	34.31±0.36	24.64 ± 0.860	1.33± 0.006
F7	0.55±0.001	0.71±0.001	32.58±0.46	22.54 ± 0.360	1.29± 0.009
F8	0.53±0.002	0.73±0.001	34.81±0.86	27.40 ± 0.890	1.38± 0.016
F9	0.50±0.001	0.71±0.001	34.58±0.58	29.58 ± 0.450	1.42± 0.014
F10	0.55±0.002	0.69±0.001	34.31±0.36	20.29 ± 0.860	1.25± 0.006
F11	0.52±0.001	0.73±0.001	34.58±0.58	28.76 ± 0.450	1.35± 0.014
F12	0.52±0.002	0.68±0.001	34.31±0.36	23.53 ± 0.860	1.31± 0.006
F13	0.51±0.001	0.71±0.001	32.58±0.46	28.17 ± 0.360	1.39± 0.009

Results of post compression studies

Orodispersive tablets of all set of batches were evaluated after the compression for several pre-prescribed pharmacopeial and in-house standards and parameters like average weight, Hardness, Friability, Drug Content, Tablet thickness, dispersion, drug content, wetting time, water absorption ratio, and in vitro disintegration time.

- After the completion of analytical tests, the obtained results are shown in Table 7.0 and 8.0.
- In-vitro dissolution rate study is shown in Table. 9.0.

ISSN No:-2456-2165

Table 7.0 Evaluation parameter of the tablet

BATCH	Average weight (mg)*	Hardness (N)**	Friability (%)	Drug content (%)**	Thickness (mm)
F1	148.99	34.8±4.57	0.89	98.57	3.26±0.05
F2	149.00	36.8±4.87	0.46	100.52	3.23±0.02
F3	150.02	36.8±2.67	0.51	101.18	3.44±0.04
F4	150.50	41.8±3.17	0.49	102.73	3.34±0.04
F5	151.40	39.8±2.58	0.79	101.34	3.46±0.03
F6	150.20	38.8±3.87	0.76	100.48	3.45±0.04
F7	150.02	36.8±2.67	0.70	99.88	3.24±0.04
F8	150.50	42.8±3.17	0.57	99.43	3.34±0.04
F9	149.40	39.8±2.58	0.59	101.24	3.36±0.03
F10	150.20	37.8±3.87	0.36	100.48	3.35±0.04
F11	150.50	43.8±3.17	0.87	101.33	3.54±0.04
F12	151.40	39.8±2.58	0.49	101.24	3.46±0.03
F13	150.20	37.8±3.87	0.86	99.68	3.34±0.04

* Average weight of 20 tablets was taken into consideration ** Average of 3 readings

Table 8.0 Evaluation parameter of the tablet

Batch	Wetting Time (Sec.)	Disintegration Time (Sec.)
F1	0.87±0.052	17.0±1.00
F2	2.17±0.032	14.0±1.50
F3	0.67±0.352	17.0±1.20
F4	0.68±0.042	30.0±1.80
F5	0.97±0.059	29.0±1.80
F6	0.67±0.012	23.0±2.10
F7	2.17±0.032	25.0±1.50
F8	0.67±0.352	15.0±1.20
F9	0.47±0.059	12.0±1.80
F10	0.67±0.012	27.0±2.10
F11	0.67±0.012	29.0±2.10
F12	2.17±0.032	19.0±1.50
F13	0.67±0.352	16.0±1.20

**Average of 3 readings

In-Vitro Dissolution Study Results

The result of in vitro dissolution study is given in below Tables

Table 9.0 In-Vitro Dissolution Rate Study

Time (min)	Cumulative Percent Drug Release of All Formulation					
	AGAR (F1)	AGAR (F2)	AGAR (F3)	GUAR GUM F4)	GUAR GUM (F5)	GUAR GUM (F6)
0	0	0	0	0	0	0
0.08	4.43±1.96	4.63±1.16	5.93±1.26	5.86±2.96	6.40±0.96	6.43±1.26
0.16	6.43±2.47	6.83±1.47	6.83±1.42	6.93±2.47	7.43±2.47	669±3.67
0.25	13.01±2.19	21.01±1.11	16.01±2.69	6.01±0.19	11.01±2.19	7.96±2.34
0.33	30.27±0.73	42.17±0.13	45.27±1.13	8.07±2.73	14.27±9.78	9.57±9.94
0.41	48.79±8.55	53.79±4.55	63.79±8.55	12.79±7.55	20.79±8.55	15.79±8.55
0.5	71.88±5.49	75.88±6.49	78.88±5.49	16.88±2.49	28.88±1.49	34.88±8.49
0.66	83.95±3.20	87.95±4.60	87.95±3.20	23.95±7.20	51.95±8.20	49.95±6.20
0.83	90.82±2.45	97.82±1.45	92.82±2.45	38.82±5.45	62.82±2.45	66.82±8.45
1	**91.40±1.32**	**92.50±3.32**	**96.40±1.32**	**54.40±1.32**	**74.40±8.32**	**79.40±7.82**
2	96.74±4.89	99.74±1.8	99.74±4.89	79.74±2.89	97.74±9.89	80.74±9.89
4	100.19±5.50	101.19±1.50	101.11±1.50	86.19±1.5	100.1±7.5	87.19±8.5
6	100.9±6.03	102.9±1.03	102.2±7.03	98.9±3.03	101.9±3.03	94.9±0.03

*Average of 2 reading

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Market Presence

Brand Name:	Ebal 20
Dosage Forms:	Fast Dissolving Tablets
Manufacturer:	**Bal Pharma Ltd.**

IV. CONCLUSION

The Orodispersive tablets of Ebastine were successfully formulated using various ratios of different types of natural super disintegrants and the formulation was prepared by molecular dispersion and direct compression technique. The natural super disintegrants Agar and Guargum were added in the formulations in various concentrations to achieve the optimized batch. The Orodispersive tablets of Ebastine were prepared using natural super disintegrants along with the other excipients. All the set of product formulation (F1-F13) were evaluated for

- Pre formulation parameters such as Drug-excipients compatibility studies.
- For flowability and compressibility analysis pre-compression parameters such as Bulk & Tapped density of blend, Carr's index, Hausner's ratio, and angle of repose obtained.
- Initially, the powder blend for all set of batches was evaluated for their flowability property. The values obtained through Carr's index were satisfactory suggested that the blends have good compressibility and the values obtained by Hausner's ratio were showing a good sign for flow property for the powder blend.
- Other tests like weight variation, hardness, friability, disintegration time, wetting time, dissolution analysis, drug content uniformity was performed as post-compression parameters study.
- Finally, the optimized batch was also evaluated for accelerated stability studies & bio equibalance study.

Orodispersive tablets of Ebastine were formulated to have the adequate mechanical strength to withstand during their handling, packaging, shipping, storage, and transportation. The tablets were prepared following the standards as prescribed by guidelines. Formulation F9 were showing fast disintegration and dissolution profile. Drug dissolution further impact on bioavailability and therapeutic effect of formulation. The optimized formulation was considered for stability studies. The data obtained from stability studies demonstrated that Orodispersive tablets of Ebastine were steady and stable under various natural environmental storage conditions.

SUMMARY

Orodispersive Tablets (ODTs) drug-delivery systems were developed for patient compliance, especially for pediatric, geriatric, dysphagia, tremor, or physically disabled and travelers. Sometimes it is impractical to access water which is required to administer the drug in the form of a tablet or capsules. Those patients who feel difficulty in swallowing or engaged at such places where it is not easy to approach water supply. Sometimes the patients may be in a condition like the unconscious, travelers, minors, or old aged so fast disintegrating tablets may resolve such issues to administer the dose without providing them a sense to swallow a drug. Such patients can be given a single tablet to keep it in their mouth where the Orodispersive tablet is dispersed in a few seconds and starts to absorb in the bloodstream.

Orodispersive tablets are developed and designed for quick dispersion and rapid disintegration in the saliva generally less than 30 seconds. ODTs having some major advantages over other formulations. ODTs disintegrate quickly in saliva within few seconds and this is an advantage that there is no need to take water.

There were mainly two techniques used to develop ODTs

- The first technique is to use super disintegrants like croscarmellose sodium (CCS), sodium starch glycolate (SSG), crospovidone & other polymers as disintegrants.
- And the second technique is increasing the pore size within tablets by freeze-drying or vacuum drying process.

In this present research, Superdisintegrants were used from Natural origin. Pre gastric absorption and quick absorption of the drug from an oral cavity after the dispersion of ODTs in saliva may increase the therapeutic value or bioavailability of drugs. The test formulation containing Ebastine as a model drug is a second-generation H1 receptor antagonist. Ebastine is an ethanolamine derivative H1 blocker. It competes with the free histamine to bind at the HA receptor site. After placing an Orodispersive tablet in the oral cavity, it disintegrates within a few seconds and quickly gets absorbed in the blood. Orodispersive tablets of Ebastine after oral administration has an onset of action within a few minutes which is present for the next 10-12 hrs. The elimination of the drug is by the renal and metabolic routes. So it is important to reduce the dose of the drug for patients having metabolic disorders, kidney, or renal failure.

Orodispersive Tablets (ODTs) of Ebastine were prepared by using natural super disintegrants with different concentrations such as Agar, Guar gum. Gelatine, Sodium lauryl sulfate, Micro Crystalline Cellulose, Sodium saccharine, Lemon Flavor, Clove Oil, Colloidal silicon dioxide, Magnesium Stearate were used in formulations as other excipients. A total of 13 formulations were designed with molecular dispersion. To compress Orodispersive

tablets, the direct compression method was preferred. All the set of batches were evaluated for Pre formulation parameters like

Precompression Studies

- Drug excipients compatibility studies, Angle of repose for flowability of powder blend, bulk, and tapped density of powder blend, compressibility index, Hausner's ratio was analyzed for each formulation.

Compression Parameters Studies

- Similar conditions were followed for all the sets of formulations. The average weight of Orodispersive tablets was within the range of 149.99 to 150.4 mg.
- Other parameters were found within the prescribed limits such as weight variation, friability within the range 0.36 – 0.89 % of all formulation.
- The hardness of tablets from all set of 13 batches was found satisfactory and within the range of 34.8 to 43.8 Newton.
- Disintegration time is most of the important parameter for ODT's, quick dispersion or disintegration help in swallowing of dispersed tablets & drug absorption in the oral cavity, thus promoting therapeutic value by increasing bioavailability of the drug.
- ODTs showing disintegration time within the time limit. Practically the values were observed within the range of 12 sec to 30 seconds. The percent drug content of the Orodispersive tablet of formulation F9 was found to the 98.57%, which has the best percent drug content among all the sets of formulations & Formulation F4 was found with the percent drug content of 54.40%, which has the least percent drug content among all the formulations. *In vitro* dissolution studied of ODT's was performed in the 0.1N HCL using the USP paddle-type dissolution apparatus. It was observed that formulations with the natural super disintegrants in optimum concentration having better drug release as compared to the product with super disintegrants from synthetic sources due to the swelling and wicking effect of its combination. The best in-vitro dissolution profile was obtained from the formulations containing super disintegrants from the natural origin when the results were compared with the preexisting formulations containing super disintegrants from the synthetic origin. The optimized batch F9 was considered for a long time on stress conditions to determine the shelf life of the product.

FUTURE PROSPECTS OF CURRENT RESEARCH WORK, BIOEQUIVALENCE STUDY AND CLINICAL TRIAL

The prospects of Orodispersive formulations are promising and the market demand is increasing day by day. Several techniques were applied with different kinds of material that were used to formulate the ODTs. Natural Superdisintegrants are the best option to produce satisfactory and safer ODT formulation which has been proven with the existing study. ODTs with natural super disintegrants were found stable during Drug Excipients stability studies. Disintegration time and dissolution profiles were found more challenging as compared with the available ODTs with synthetic disintegrants. The optimized batch can be considered for human trials to investigate the In-vivo drug release. Bioequivalence studies can be done for test formulation with the brand drug "Ebay 20" or with other brands as available in the market.

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