

Formulation Optimization and Evaluation of Mouth Dissolving Tablet of Rupatadine Fumarate by Sublimation Technique

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ABSTRACT: The present study aimed to formulate, optimize, and evaluate mouth dissolving tablets of Rupatadine Fumarate by using the sublimation technique to achieve rapid disintegration and enhanced drug release. Mouth dissolving tablets were prepared by direct compression method using camphor as a sublimating agent to create a porous structure that improves tablet disintegration. Pregelatinized starch was used as a superdisintegrant to enhance the wetting and disintegration properties of the formulation. Drug-excipient compatibility studies were carried out using FTIR and DSC analysis, which confirmed the absence of any significant interaction between the drug and excipients. Different batches were formulated and evaluated for various pre-compression and post-compression parameters including hardness, friability, weight variation, wetting time, disintegration time, drug content, and in vitro drug release. Among all formulations, Batch B9 showed the best performance with a rapid disintegration time of 15.65 seconds and maximum drug release of 97.14%. The optimized formulation exhibited satisfactory physicochemical properties and good stability. The results demonstrated that the sublimation technique using camphor effectively improved the porosity and dissolution characteristics of the tablets. Therefore, the developed mouth dissolving tablet of Rupatadine Fumarate may provide rapid onset of action, improved patient compliance, and better therapeutic efficacy.

KEYWORDS: Mouth dissolving tablet, Rupatadine Fumarate, Sublimation technique, Camphor, pregelatinized starch, Drug release, Disintegration Time, stability study.

INTRODUCTION: Mouth dissolving tablets (MDTs) are oral solid dosage forms that rapidly disintegrate in the mouth without the need for water.

These tablets provide faster drug release, rapid onset of action, and improved patient compliance. MDTs are particularly useful for pediatric, geriatric, and dysphagic patients who have difficulty swallowing conventional tablets.

Several techniques are used for the preparation of MDTs, among which the sublimation technique is considered an effective method for producing highly porous tablets with rapid disintegration properties. In the present work, camphor was used as a sublimating agent to create pores within the tablet structure after sublimation. The porous nature of the tablets enhances saliva penetration and promotes faster tablet disintegration and drug release.

Due to their rapid action, ease of administration, and improved patient acceptability, mouth dissolving tablets prepared by the sublimation technique represent a promising approach in novel drug delivery systems.

Rupatadine Fumarate:

Rupatadine Fumarate is modern non-sedating H1-antihistamine, is also potent platelet-activating factor (PAF) inhibitor. It belongs to n-alkyl pyridine derivatives. Animal and human models have shown rupatadine to have dual antihistamine and PAF-antagonist properties. Rupatadine has been available in for the treatment of allergic rhinitis and chronic urticaria in adults and children aged over 12 years. Rupatadine is a dual histamine H1 receptor and platelet activating (PAF) receptor antagonist. During allergic response mast cells undergo degranulation, releasing histamine and other substances. Histamine acts on H1 receptors to produce symptoms of nasal blockage, rhinorrhea, itching, and swelling. PAF is produced from phospholipids cleaved by phospholipase A2. It acts to produce vascular leakage which contributes to rhinorrhea and nasal blockage. By blocking both the H1 receptor and PAF receptor, rupatadine prevents these mediators from exerting their effects with good safety and tolerability with minimal sedative

effect, so reduces the severity for long term management allergic symptoms.

MATERIAL & METHOD:

Materials:

Rupatadine Fumarate was purchased from SM pharma and Chemicals; Mumbai, Superdisintegrants Such as Pregelatinized Starch and MCC PH 102, Pearlitol SD 200 were procured From Medley Pharma Ltd; Andheri, Camphor was used as Sublimating an agent, other Excipients Aspartame, Talc, Orange Flavour, Magnesium Stearate were of analytical Grade and used as received. All chemicals and reagents used were of analytical or pharmaceutical grade.

Preformulation Studies:

Organoleptic Properties:

Organoleptic characters properties of Rupatadine Fumarate such as colour, odour, taste, were evaluated for tablets from each batch were randomly selected and taste tested, colour visually compared and odour checked.

Melting Point Determination:

Melting point determination of the obtained drug sample was done because it is a good first indication of purity of sample. Melting point of pure Rupatadine Fumarate was determined by open capillary method. The capillary was closed at one end and filled with Rupatadine Fumarate. The tube was placed in digital melting point apparatus. The rise in temperature was noted. The temperature at which the drug melt to clear liquid and then off the apparatus.

Solubility Study:

The approximate solubility of the substances was indicated by various Solvents such as methanol, ethanol, DMSO were used for the solubility study. a small quantity of drug sample was taken in a test tube and the solubility was determined by solving the drug in 1 ml of different solvents. Then the solubility was observed.

Determination of UV Spectrum of Rupatadine Fumarate (Estimation of λ_{max}):

Weigh accurately 10 mg drug of Rupatadine Fumarate and dissolved in 1 ml ethanol, then transfer into a 100 ml volumetric flask. Add some quantity of phosphate buffer pH 6.8 and shake the solution then make up the volume upto 100ml. Withdraw 1 ml of the solution from primary standard solution (100 ug/ml) and transfer into 10 volumetric flask and make up the volume up to 10 ml by using phosphate buffer pH 6.8. Rupatadine Fumarate solution (10ug/ml) was prepared in phosphate buffer pH 6.8. This solution scanned

under double beam UV visible spectrophotometer (Shimada 1800) and spectrum was recorded in the wavelength ranges between 200-400nm. The λ_{max} was observed to be 242 nm. Similarly, λ_{max} was also determined in phosphate buffer pH 6.8 and ethanol.

Determination of Standard Calibration Curve of Rupatadine Fumarate:

Weigh accurately 10 mg of Rupatadine Fumarate, transfer it into 100 ml volumetric flask add phosphate buffer pH 6.8 to obtained concentration 100 ug/ml. From this solution, pipette out 0.5, 1, 1.5, 2 & 2.5ml. transfer each to 10 ml volumetric flask and make up the volume up to 10 ml with phosphate buffer pH 6.8 to get 5, 10, 15, 20 & 25 ug/ml concentration of Rupatadine Fumarate respectively. Absorbance of each solution was measured at 242 nm using UV visible spectrophotometer (Shimadzu 1800) and phosphate buffer pH 6.8 as reference standard and the standard curve was generated.

FTIR Study:

It is an analytical technique used to identify organic, polymer, and in some cases, inorganic materials, The FTIR analysis method uses infrared light to scan test samples and observe chemical properties. The mixture of drug and excipients were subjected to FTIR studies to check whether there was any drug and excipients interaction. The FTIR Spectrum of Rupatadine Fumarate was recorded using FTIR 1-S Affinity. The Drug sample was placed in an FTIR sample holder and Scanned over the range 400 to 4000 cm^{-1} . The Spectrum conformed by comparing it with the IR spectra of Rupatadine Fumarate.

DSC Study:

Differential Scanning Calorimetry (DSC) is a thermoanalytical technique used to study the thermal behavior of drugs and excipients and to evaluate drug-excipient compatibility. In the present study, DSC analysis of the pure drug, excipients, and their physical mixture was carried out using a DSC-60 Plus thermal analysis instrument equipped with a nitrogen purge system. Accurately weighed samples (2-6 mg) were sealed in aluminium/ platinum pans and scanned at a heating rate of 10°C/min under nitrogen atmosphere. The obtained thermograms were evaluated for characteristic endothermic and exothermic peaks to confirm compatibility of the formulation components.

FORMULATION DESIGN OF MOUTH DISSOLVING TABLET:

The formulation optimization of Rupatadine fumarate mouth dissolving tablets was carried out using Central Composite Design (CCD) under

response surface methodology. The design was applied to study the influence of formulation variables on tablet characteristics and to obtain an optimized formulation with rapid disintegration and improved drug release. In the present study, pregelatinized starch (X1) and camphor (X2) were selected as independent variables. Pregelatinized

starch was used as a superdisintegrating agent, whereas camphor was employed as a sublimating agent to produce porous tablets after sublimation. The effect of these variables was evaluated on dependent responses such as Percentage Drug release (Y1) and Disintegration Time (Y2).

Table 1: Independent Variables

Independent Variable	Unit	Levels				
		- α	Low	Medium	High	+ α
Pregelatinized Starch (X1)	%	3.96447	5	7.5	10	11.0355
Camphor (X2)	%	2.92893	5	10	15	17.0711

Table 2: Composition of Batches Generated by Central Composite Design (CCD)

Ingredient (mg/tablet)	Batches									
	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10
Rupatadine Fumarate	10	10	10	10	10	10	10	10	10	10
Pearlitol SD 200	104	89	109	96.92 9	89.857 8	111.07 106	119	99	104	118.14 214
MCC PH 102	40	40	40	40	40	40	40	40	40	40
Pregelatinized Starch	15	20	20	22.07 1	15	7.9289 4	10	10	15	15
Camphor	20	30	10	20	34.142 2	20	10	30	20	5.8578 6
Aspartame	5	5	5	5	5	5	5	5	5	5
Talc	2	2	2	2	2	2	2	2	2	2
Orange Flavour	2	2	2	2	2	2	2	2	2	2
Magnesium Stearate	2	2	2	2	2	2	2	2	2	2
Avg. Wt(mg)	200	200	200	200	200	200	200	200	200	200

*All Ingredients are in mg

PREPARATION OF FORMULATION BLEND OF MDTs:

All the ingredients weighted Properly. Pass the Drug (Rupatadine Fumarate), Pearlitol SD-200, Pregelatinized Starch, Aspartame, Flavour, through # 60 mesh were passed individually to remove lumps and to ensure uniform particle size for proper mixing and flow properties. MCC PH 102 & Camphor were passed through a #22 mesh sieve. Pass Talc and Magnesium stearate Separately through # 60 mesh sieve. The drug was first mixed with a portion of Pearlitol SD 200 and MCC PH 102 to ensure uniform distribution of the active ingredient throughout the formulation blend. Subsequently, the remaining excipients were added and blended properly. Pregelatinized Starch added as superdisintegrants. Orange flavour was then incorporated into the mixture for taste masking. Finally, talc and magnesium stearate were added as glidant and lubricant, respectively, and mixed for few minutes prior to compression.

Pre-Compression Parameters:

1) Angle of Repose:

Angle of repose was determined by using funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The drug (as solid dispersion)-excipients blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation

$$\tan \theta = \frac{h}{r}$$

Where, h = height of the pile of the blend, r = radius of the pile

2) Bulk Density:

It is the ratio of total mass of powder to the bulk volume of powder. It was measured by pouring the weighed powder (passed through standard sieve # 20) into a measuring cylinder and initial weight was noted. This initial volume is called the bulk volume. From this the bulk density is calculated according to the formula mentioned below. It is expressed in g/ml and is given by

$$BD = \frac{\text{Mass of the powder (M)}}{\text{Bulk Volume of the Powder (Vb)}}$$

3) Tapped Density:

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2% (in a bulk density apparatus).

$$TD = \frac{\text{Mass of Powder (M)}}{\text{Tapped Volume of the Powder (Vd)}}$$

4) Carr's Index:

Compressibility index (CI) was determined by measuring the initial volume (VO) and final volume (V) after hundred tapings of a sample in a measuring cylinder. CI was calculated using equation

$$\text{Carr's Index} = \frac{V_0 - V}{V} \times 100$$

5) Hausner's Ratio:

A similar index to indicate the flow properties can be defined by Hausner's ratio. Hausner's ratio can be calculated by using following formula

$$\text{Hausner Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

PREPARATION USING DIRECT COMPRESSION TECHNIQUE:

The prepared powder blend was compressed into tablets by direct compression method using an 8 mm flat-faced punch mounted on a rotary tablet compression machine. The compression force was adjusted suitably to obtain tablets of uniform weight and adequate hardness. The compressed tablets were collected and stored for further studies.



Fig 1. Rupatadine Fumarate MDT Before Sublimation

SUBLIMATION TECHNIQUE:

placed the Compressed tablet in petri plates or trays. Tablet kept in hot air oven or Vacuum oven at Conditions: Temperature 80 C, Time: 2-6 hrs. The sublimation time depends on the sublimating agent, as camphor directly converts from solid to vapour on heating. Leave the tablet. Porous Mouth Dissolving Tablet of Rupatadine Fumarate was prepared.



Fig 2. Rupatadine Fumarate MDT After Sublimation

Post-Compression Parameters:

1) Tablet weight Variation:

To determine weight variation before and after sublimation, 20 tablets of each formulation were individually weighed using an electronic balance, the average weight was calculated, and the individual tablet weight was then compared to the average value. The tablets were said to pass the weight variation test if they complied with weight variation specification as per I.P.

2) Tablet thickness:

Tablet thickness is a crucial element in both duplicating appearance and counting with filling machinery. The uniform thickness of the tablets is used as a counting mechanism by some filling equipment. Micrometer was used to measure thickness.

3) Hardness:

The tablets' crushing strength was determined using a Monsanto hardness tester. Three tablets were randomly sampled from each formulation batch, and the average reading was recorded.

4) Friability:

For assessing the friability, Roche friabilator was utilized. Twenty tablets were precisely weighed before being inserted in the 25 rpm-revolving tumblers. After four minutes, the tablets were weighed and the % weight loss was calculated. The percentage friability was calculated by using this formula.

$$Friability = \frac{Initial\ Wt. - Final\ Wt}{Initial\ Wt} \times 100$$

5) Wetting Time:

Take a double folded tissue paper was placed in a petri dish containing & ml of methylene blue solution. Then the tablet was placed on tissue paper containing methylene blue and the time required for complete wetness of tablet was recorded as wetting time. The randomly three tablets were chosen from each formulation and the average wetting time was recorded.

6) Drug Content:

Drug content for Mouth Dissolving Tablet of Rupatadine Fumarate was done by the assay method. First the prepared tablet was crushed and added to 10 ml of phosphate buffer pH 6.8. After 30 min the solution was filtered through Whatman filter paper 42 and from 10 ml solution 0.2 ml solution was withdrawn diluted up to 10 ml with phosphate buffer pH 6.8 (10 µg/ml). The drug content was determined at A max 242 nm by UV-spectrophotometer against blank.

7) In-vitro Dissolution Studies:

In vitro dissolution studies of Rupatadine Fumarate mouth dissolving tablets were carried out using USP Type II (Paddle) dissolution apparatus. The dissolution medium consisted of 900 ml phosphate buffer pH 6.8 maintained at 37 ± 0.5°C with a paddle rotation speed of 50 rpm. Samples of 5 ml were withdrawn at predetermined time intervals of 0, 2, 4, 6, 8, and 10 min and replaced with equal volume of fresh dissolution medium. The samples were filtered through Whatman filter paper and analyzed at 242 nm using a UV-Visible spectrophotometer (Shimadzu-1800). The percentage drug release was calculated and dissolution profiles of different formulations were compared.

8) Disintegration Test:

The disintegration study was conducted to determine the time required for the tablets to break apart completely under specified conditions. The test was performed using a USP disintegration apparatus containing distilled water maintained at 37 ± 2°C. Six tablets were placed individually in the basket rack assembly and the apparatus was operated according to IP standards. The time required for complete disintegration of the tablets was observed and recorded in seconds.

9) Stability study:

The purpose of stability study is to provide evidence on the quality of a drug substance or drug product which varies with time under the influence of a

variety of environmental factors such temperature, humidity and light. The formulation was subjected to accelerated stability studies as per ICH (The International Conference of Harmonization) guidelines. The packed tablets were placed in stability chambers maintained at $30 \pm 2^\circ\text{C}$, $65 \pm 5\%$ RH and

at $40 \pm 2^\circ\text{C}$, $75 \pm 5\%$ RH for 3 months, in a stability chamber. Tablets were periodically removed and evaluated for physical characteristics & chemical characteristics drug content, in-vitro drug release etc

RESULTS AND DISCUSSION:

Organoleptic Properties:

Table No. 3 Organoleptic properties of Rupatadine Fumarate

Sr. No.	Properties	Observation	Standard	Conclusion
1	Colour	white or Slightly Pinkish powder	white or Slightly Pinkish powder	Complies With Standard
2	Odour	Odourless	Odourless	Complies With Standard
3	Taste	Bitter	Bitter	Complies With Standard

Melting Point Determination:

The melting point of the Rupatadine Fumarate was found in the ranges of 194°C – 200°C by capillary method using digital melting point apparatus.

Table No.4 Melting point of Rupatadine Fumarate

Sr. No	Drug (Rupatadine Fumarate)	Melting Point ($^\circ\text{C}$)
1.	Standard	194°C – 201°C
2.	Observed	193°C – 204°C

Solubility Study:

Table No.5 Solubility of Rupatadine Fumarate

Solvent	Solubility
Water	Slightly Soluble
Methanol	Freely Soluble
Ethanol	Soluble
DMSO	Freely Soluble

Determination of UV Spectrum of Rupatadine Fumarate (Estimation of λ_{max}):

A solution of Rupatadine Fumarate ($10\ \mu\text{g/ml}$) was prepared in phosphate buffer pH 6.8 & UV spectrum

was recorded using UV Visible spectrophotometer (Shimadzu 1800). The spectra of Rupatadine Fumarate in Phosphate Buffer pH 6.8 scanned in the range of 200-400 nm & Wavelength was observed at 242 nm.

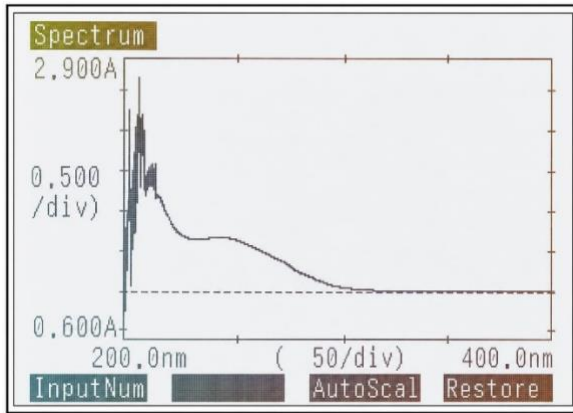


Fig. No. 3: UV Spectrum of Rupatadine Fumarate in Phosphate Buffer pH 6.8

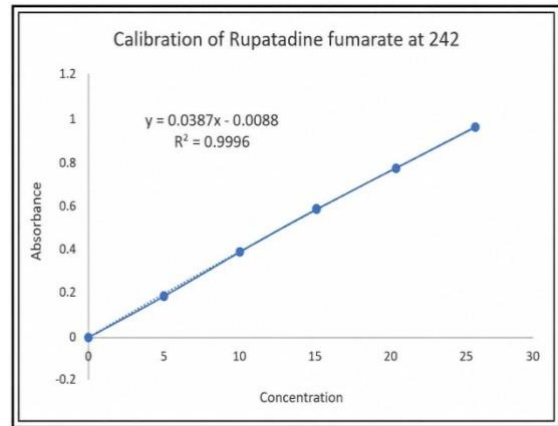


Fig. No. 4: Calibration Curve of Rupatadine Fumarate in Phosphate Buffer pH 6.8

Determination of Standard Calibration Curve of Rupatadine Fumarate:

Table No. 6 Observation Table for Calibration Curve of Rupatadine Fumarate

Sr. No	Concentration (ug/ml)	Absorbance (nm)
1.	0	0
2.	5	0.172
3.	10	0.377
4.	15	0.576
5.	20	0.766
6.	25	0.958
7.	Slop	0.0387
8.	Intercept	0.0088
9.	Coefficient Correlation (R ²)	0.9996

FTIR Study: (Fourier Transform Infrared Spectroscopy):

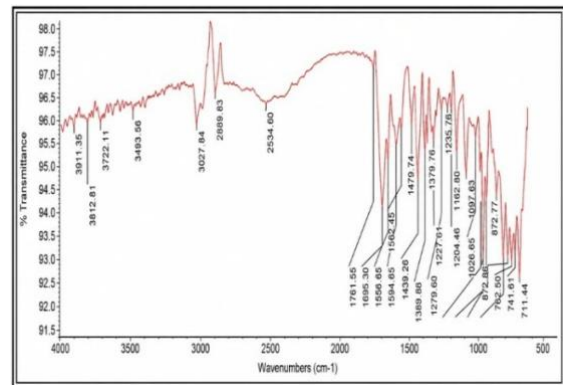


Fig. No. 5: FTIR Spectra of Rupatadine Fumarate

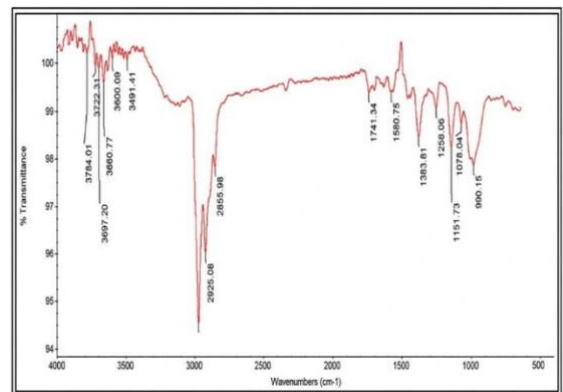


Fig. 6: FTIR Spectra of Pregelatinized

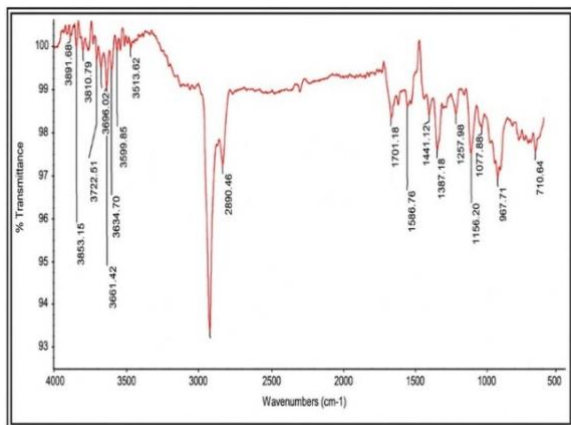


Fig. No. 7: FTIR Spectra of Rupatadine Fumarate + Pregelatinized Starch

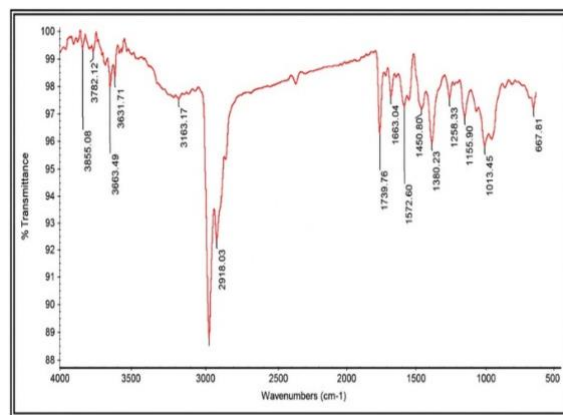


Fig. No. 8: FTIR Spectra of Rupatadine Fumarate + All Excipients

FTIR spectra of Rupatadine Fumarate, pregelatinized starch, drug-polymer mixture, and drug with all excipients confirmed that the characteristic peaks of the drug were retained without significant

shifting or disappearance. The study indicated absence of any chemical interaction or structural modification, confirming good compatibility of Rupatadine Fumarate with all polymers and excipients used in the formulation.

DSC Study: (Differential Scanning Calorimetry):

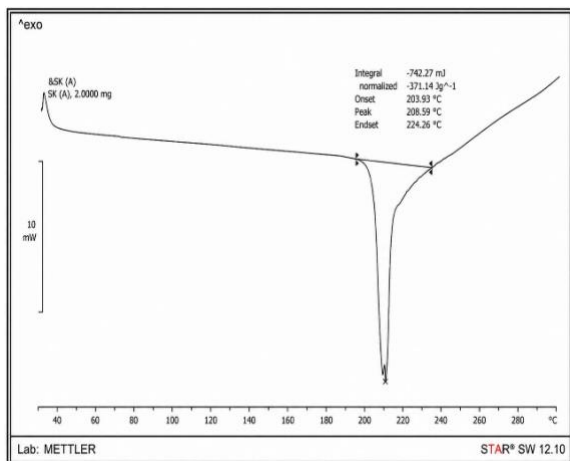


Fig. No. 9: DSC Thermogram of pure Rupatadine Fumarate

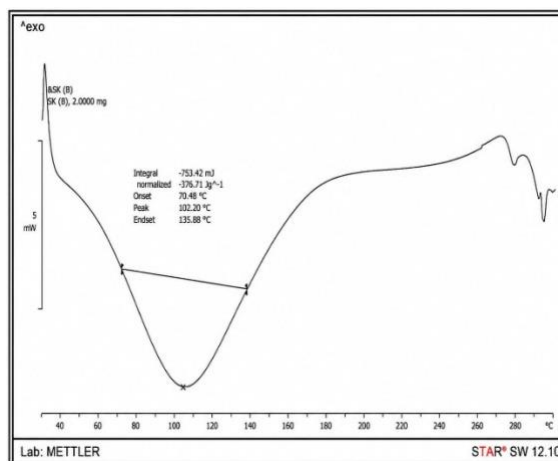


Fig. No. 10: DSC Thermogram of Rupatadine Fumarate + Pregelatinized Starch

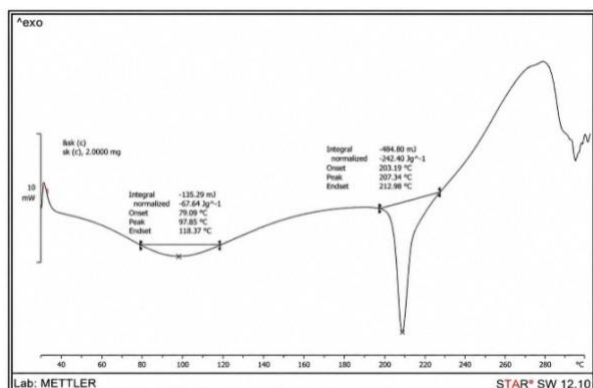


Fig. No. 10: DSC Thermogram of Rupatadine Fumarate + Pregelatinized Starch

The DSC study of Rupatadine Fumarate and its formulation exhibited characteristic endothermic peaks corresponding to the melting point of the drug. The presence of these peaks without significant shifting, broadening, or disappearance indicated that the drug remained stable and did not undergo any chemical interaction with the polymers and other excipients used in the formulation. Hence, the DSC analysis confirmed the compatibility and stability of Rupatadine Fumarate in the prepared formulation.

EVALUATION PARAMETERS:

Precompression Parameters:

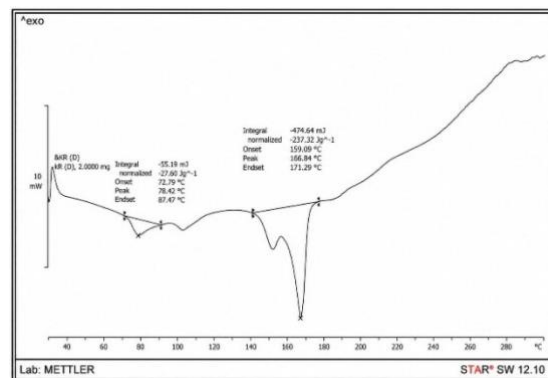


Fig. No. 12: DSC Thermogram of Rupatadine Fumarate + All Excipients

Pre-Compression Parameters: Pre-compression parameters such as bulk density, tapped density, Carr’s index, Hausner’s ratio, and angle of repose for formulation blends (B1–B10) were evaluated and all values were expressed as mean ± SD (n=3). The results were found in the range of 0.44±0.04 to 0.49±0.01 gm/ml for bulk density, 0.50±0.02 to 0.56±0.01 gm/ml for tapped density, 8.31±0.63 to 13.67±0.05% for Carr’s index, 1.03±0.03 to 1.18±0.06 for Hausner’s ratio, and 29.89±0.15 to 33.40±0.02° for angle of repose respectively. The obtained values indicated good flow properties and compressibility of the powder blends suitable for tablet compression.

Table No. 7: Precompression Parameter of Batches Generated By CCD

Precompression Parameter	Batches									
	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10
Bulk Density (gm/ml)	0.49 ±0.02	0.47±0.01	0.47±0.02	0.44±0.04	0.49±0.01	0.48±0.01	0.49±0.03	0.47±0.03	0.49 ±0.01	0.48 ±0.05
Tapped Density (gm/ml)	0.50 ±0.02	0.52±0.04	0.54±0.04	0.51±0.01	0.56±0.01	0.52±0.01	0.51±0.02	0.53±0.03	0.50 ±0.02	0.54 ±0.02
Carr’s Index (%)	11.61±0.07	13.38±0.08	13.52±0.06	13.67±0.05	12.33±0.17	8.90±0.21	8.31±0.63	11.23±0.09	11.62±0.08	13.38 ±0.15
Hausner’s Ratio	1.05±0.04	1.14±0.07	1.18±0.06	1.14±0.06	1.13±0.01	1.07±0.01	1.03±0.03	1.12±0.01	1.03±0.05	1.12 ±0.08
Angle of Repose	29.89±0.13	31.53±0.22	31.40±0.35	33.40±0.02	31.71±0.04	31.53±0.22	31.36±0.39	32.73±0.26	29.89 ±0.15	31.81 ±0.12

*All the Values were in mean ±SD, n=3

Post-Compression Parameters: Post-compression Parameters: Post-compression parameters such as weight variation before sublimation, weight variation after sublimation, thickness, diameter, hardness, friability, wetting time, disintegration time, drug content, and % drug release for formulation batches (B1–B10) were evaluated and all values were expressed as mean \pm SD (n=3). The results were found in the range of 196.6 \pm 0.4 to 199.7 \pm 0.2 mg for weight variation before sublimation, 166.4 \pm 0.43 to 194.7 \pm 0.30 mg for

weight variation after sublimation, 3.59 \pm 0.03 to 3.65 \pm 0.02 mm for thickness, 8.00 \pm 0.01 to 8.04 \pm 0.01 mm for diameter, 1.3 \pm 0.1 to 1.9 \pm 0.2 kg/cm² for hardness, 0.40 \pm 0.04 to 0.60 \pm 0.01% for friability, 15.08 to 24.45 sec for wetting time, 10.67 to 18.65 sec for disintegration time, 94.69 to 100% for drug content, and 93.96 to 99.33% for % drug release respectively. The obtained results indicated satisfactory post-compression characteristics of the prepared tablets.

Table No. 8: Post compression Parameter of Batches Generated By CCD

Post compression Parameters	Batches									
	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10
Weight Variation Before Sublimation (mg)	199.7 \pm 0.2	198.4 \pm 0.6	197.6 \pm 0.6	198.3 \pm 0.3	196.6 \pm 0.4	199.3 \pm 0.6	197.9 \pm 0.1	199.3 \pm 0.6	199.7 \pm 0.2	198.4 \pm 0.4
Weight Variation After Sublimation (mg)	179.7 \pm 0.3	169.3 \pm 0.67	189.6 \pm 0.3	179.4 \pm 0.40	166.4 \pm 0.43	179.7 \pm 0.2	189.7 \pm 0.30	169.6 \pm 0.34	180.06 \pm 0.06	194.7 \pm 0.30
Thickness (mm)	3.61 \pm 0.01	3.65 \pm 0.02	3.60 \pm 0.05	3.61 \pm 0.01	3.63 \pm 0.03	3.59 \pm 0.03	3.60 \pm 0.04	3.61 \pm 0.03	3.61 \pm 0.01	3.62 \pm 0.02
Diameter (mm)	8.04 \pm 0.01	8.01 \pm 0.02	8.02 \pm 0.03	8.04 \pm 0.01	8.03 \pm 0.04	8.00 \pm 0.01	8.01 \pm 0.05	8.02 \pm 0.01	8.04 \pm 0.01	8.01 \pm 0.01
Hardness (kg/Cm²)	1.6 \pm 0.1	1.5 \pm 0.1	1.8 \pm 0.2	1.9 \pm 0.1	1.7 \pm 0.15	1.8 \pm 0.2	1.3 \pm 0.1	1.9 \pm 0.2	1.6\pm 0.1	1.7 \pm 0.1
Friability (%)	0.50 \pm 0.03	0.60 \pm 0.01	0.40 \pm 0.04	0.49 \pm 0.06	0.50 \pm 0.05	0.46 \pm 0.05	0.60 \pm 0.03	0.40 \pm 0.05	0.50 \pm 0.02	0.45 \pm 0.02
Wetting Time (Sec.)	21.07	16.12	21.00	23.45	15.08	23.15	22.09	18.19	21.10	24.45
D.T (Sec.)	14.75	11.76	16.34	10.67	13.43	17.54	18.65	17.15	15.65	15.06
Drug Content (%)	97.34	99.11	98.23	99.11	100	96.46	94.69	96.46	99.11	97.34
% Drug Release	96.35	97.14	97.94	98.73	99.53	94.75	93.96	95.55	97.14	96.35

* All the values were in mean \pm SD, n=3

Table No. 9: % Drug Released of Batches generated by CCD

Time (min)	%Drug Released Batches									
	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10
0	0	0	0	0	0	0	0	0	0	0
2	45.38	39.22	42.99	46.98	44.59	39.01	38.22	42.99	46.18	48.57
4	56.53	54.14	51.75	57.33	59.72	46.98	52.55	48.57	57.33	56.53
6	71.66	63.70	71.66	72.46	70.07	62.90	69.27	60.51	70.07	64.49
8	82.01	79.62	86.79	82.81	88.38	79.62	80.42	76.44	83.60	81.22
10	96.35	97.14	97.94	98.73	99.53	94.75	93.96	95.55	97.14	96.35

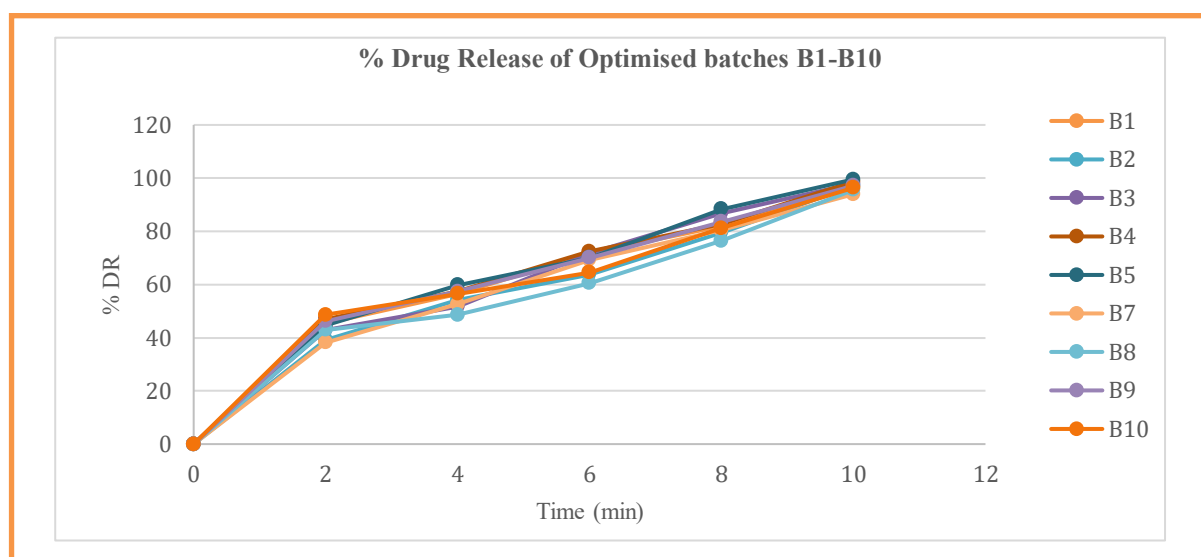


Fig No. 13: In-Vitro Drug Released Study of Optimized Batches of Rupatadine Fumarate MDTs Generated by CCD (B1-B10)

OPTIMIZATION AND DATA ANALYSIS:

1) Drug Released (%):

Final equation in terms of coded form

$$\% DR = + 96.74 + 1.40 X1 + 0.6609 X2$$

Concerning dissolution, the results of multiple linear regression analysis showed that the coefficients X1 and X2 bear positive sign. It revealed that % drug release increases with increases in both Pregelatinized Starch and Camphor as Sublimating agent. More amount of Pregelatinized Starch and Camphor as sublimating agent was expected to increase the % drug release due to faster disintegration of tablet. ANOVA was used to identify the significant effect. The result was found

to be significant at that level of probability ($p < 0.0128$)

2) Disintegration Time:

Final equation in terms of coded form

$$DT = + 15.10 - 2.18 X1 - 1.05 X2$$

Concerning disintegration time, the results of multiple linear regression analysis showed that the coefficients X1 and X2 bear Negative sign. It revealed that disintegration time decreases with increase in Pregelatinized Starch and Camphor. Further increase in concentration of superdisintegrant and sublimating agent led to decreases in disintegration time. ANOVA was used

to identify the significant effect. the result was found to be significant at that level of probability ($p < 0.0035$)

Table No.10: Result of Analysis of Variance for Batches by CCD of Rupatadine Fumarate of MDT Tablet

	DF*	SS*	MS*	F*	P value	
Y1=%DR						
Model	2	19.17	9.59	8.65	0.0128	Significant
Residual	7	7.74	1.11	--		
Total	9	26.91				
Y2=Disintegration						
Model	2	46.70	23.34	14.10	0.0035	Significant
Residual	7	11.59	1.66	--		
Total	9	58.26				

DF indicates degree of freedom; SS sum of square; MS mean sum of square and F is Fischer's ration

Graphical Representation: -

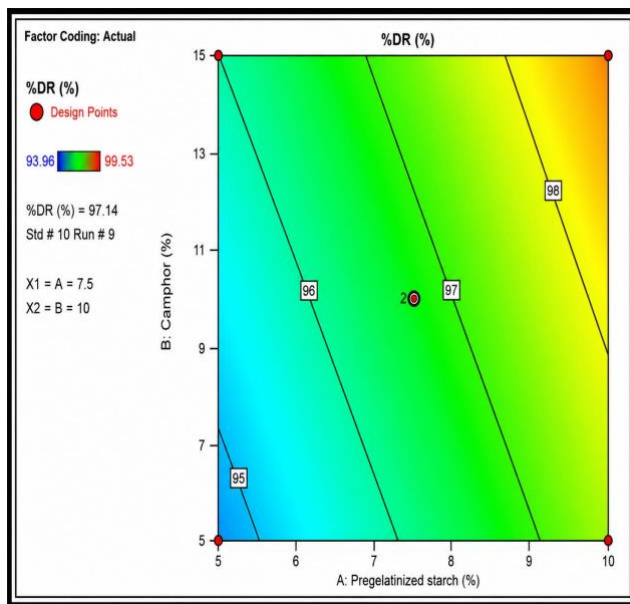


Fig. No. 14: Response Surface Contour Graph Showing the Influence of Pregelatinized Starch (X1) and Camphor (X2) on % Drug Release (Y1)

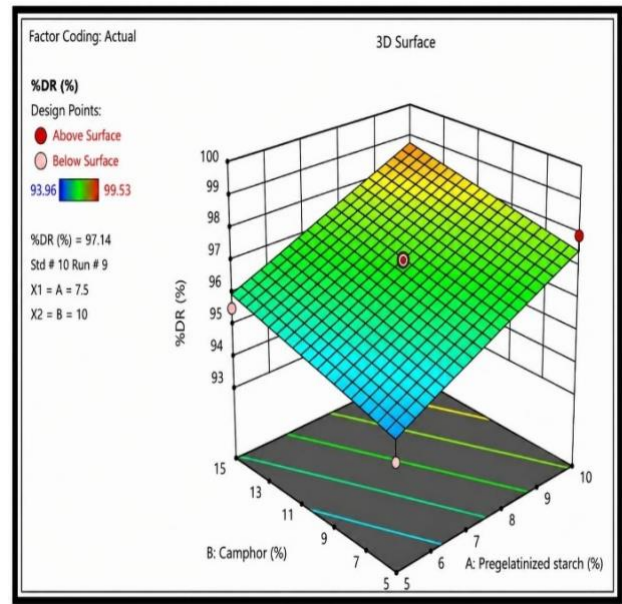


Fig. No. 15: 3D Response Surface Graph Showing the Influence of Pregelatinized Starch and Camphor (X2) on % Drug Release (Y1)

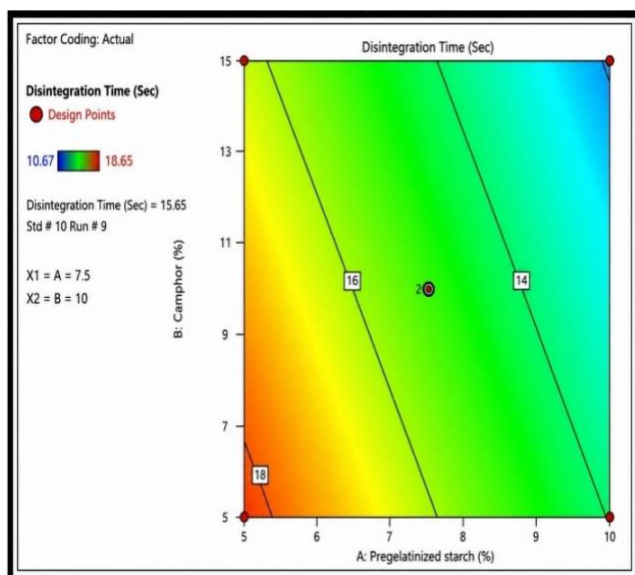


Fig. No. 16: Response Surface Contour Graph Showing the Influence of Pregelatinized Starch (X1) and Camphor (X2) on % Disintegration Time (Y2)

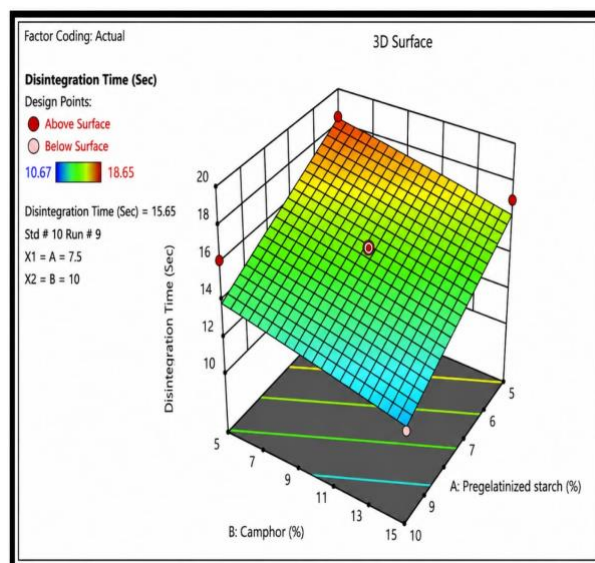


Fig. No. 17: 3D Response Surface Graph Showing the Influence of Pregelatinized starch (X1) and Camphor (X2) on % Disintegration Time (Y2)

STABILITY STUDY:

Stability Study for Optimized Batch Formulation B9

Table No 11 Stability Study of Optimized Batch of Rupatadine Fumarate MDTs

Parameters		Condition $40 \pm 2^\circ/75 \% \pm 5RH$		
		Initial	15 Days	1 Month
Physical	Average Weight after Sublimation (mg)	180	178	179
	Thickness(mm)	3.61	3.60	3.68
	Hardness (kg/cm ²)	1.6	1.5	1.5
	Friability (%)	0.49	0.48	0.50
Chemical	D.T. (Sec)	15.65	15.60	16
	Drug Release (%)	97.14	97.10	96.50
	Drug Content (%)	99.11	99.10	99.09

The optimized batch formulation (B9) showed good stability during the accelerated stability study carried out at $40 \pm 2^\circ C/75 \pm 5\% RH$ for one month. The formulation retained its physical appearance and evaluation parameters throughout the study period. Parameters such as average weight, thickness, hardness, friability, disintegration time, drug release, and drug content remained within acceptable limits with only negligible variations. These results confirmed that the prepared

formulation possessed satisfactory stability under the specified storage conditions.

CONCLUSION:

The present research work successfully developed and optimized Mouth Dissolving Tablets of Rupatadine Fumarate using the sublimation technique. Camphor was effectively utilized as a sublimating agent to produce porous tablets with rapid disintegration characteristics, while

pregelatinized starch enhanced the disintegration and drug release properties of the formulation. Compatibility studies by FTIR and DSC confirmed the absence of drug–excipient interactions, indicating stability of the formulation components. All prepared batches showed satisfactory pre-compression and post-compression evaluation parameters within acceptable limits. Among the formulations, batch B9 was found to be the optimized formulation showing rapid disintegration time (15.65 Sec) and high drug release (97.14%), satisfactory hardness and friability, uniform drug content. Stability studies demonstrated that the optimized formulation remained stable under accelerated storage conditions. Therefore, the developed mouth dissolving tablets of Rupatadine Fumarate prepared by sublimation technique can be considered a promising dosage form for rapid drug release, faster onset of action, enhanced patient compliance, and improved therapeutic effectiveness.

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