



## Formulation Development and Evaluation of Effervescent Tablets of N-Acetylcysteine and Acebrophylline

Zeba Shaikh<sup>2</sup>, Satish Nangude<sup>1</sup>, Minakshi Nehete<sup>2\*</sup>

<sup>1</sup>Research and Development Department, SciTech Specialities Pvt Ltd., A/43, STICE, Musalgaon, Nashik - Shirdi Rd, Sinnar, Nashik- 422112, Maharashtra, India.

<sup>2</sup>C. U. Shah College of Pharmacy, S.N.D.T Women's University, Juhu Tara Road, Santacruz (W), Mumbai-400049, Maharashtra, India.

\*Corresponding author's E-mail: [minakshi.nehete@cushapharmacy.sndt.ac.in](mailto:minakshi.nehete@cushapharmacy.sndt.ac.in)

Received: 16-07-2025; Revised: 23-10-2025; Accepted: 29-10-2025; Published online: 20-11-2025.

### ABSTRACT

**Objective:** This study aimed to develop and evaluate an effervescent tablet containing acebrophylline and N-acetylcysteine using a specific flavor to enhance the palatability and make it easier to swallow by dissolving it in water before administration.

**Methods:** The preformulation studies were performed using various parameters such as organoleptic properties, melting point determination, solubility analysis, Fourier transform infrared spectroscopy (FTIR) and drug-drug and drug-excipient compatibility studies. The pre-compressible blend was evaluated using various parameters such as the angle of repose, bulk density, tapped density, Hausner's ratio, and Carr's index. The formulation was evaluated for weight variation, thickness, hardness, solution time, pH and content uniformity.

**Results:** Identification of drugs using FTIR confirmed the identity of both drugs based on characteristic absorption peaks. The observed melting point values closely match reported values, confirming the quality and authenticity of both drugs. The assay of pure drugs fell within the reported range, indicating sample purity and potency. The compatibility study showed there is no incompatibility between drug-drug and drug-excipient. Evaluation of pre-compression characteristics of powder blend showed that optimized formulation exhibited excellent flowability, good compressibility and suitable bulk and tapped densities. Optimized formulation was found to comply with pharmacopeial and In-house standards. Results of stability testing showed no significant changes in all the parameters tested, confirming the stability of tablets.

**Conclusion:** The N-acetylcysteine and acebrophylline effervescent tablet represents a promising pharmaceutical formulation with enhanced patient acceptability and potential therapeutic benefits in managing chronic obstructive pulmonary disease symptoms and reducing bronchial obstructions.

**Keywords:** N-Acetylcysteine, Acebrophylline, Effervescent Tablet, Evaluation, Bronchial Asthma.

### INTRODUCTION

The most common and popular route of drug delivery is through the oral dose form. However, it has some drawbacks, including slow absorption and delayed onset of an effect, which can be overcome by administering the drug in liquid form. Numerous active pharmaceutical ingredients (APIs) exhibit limited stability when incorporated into a liquid formulation. Consequently, effervescent tablets present a viable option for overcoming these challenges in oral dosage formulations.<sup>1</sup>

Effervescent tablets, as defined by the US FDA, are those that are meant to be dissolved or distributed in water before administration.<sup>2</sup> Further to active ingredients, it typically contains a combination of acids, acid salts, carbonate, and hydrogen carbonates, which when combined with water, release carbon dioxide.<sup>3</sup> Effervescence is the chemical reaction that causes gas bubbles to emerge from a liquid.



Citric acid + Sodium bicarbonate  $\longrightarrow$  Sodium citrate + Water + Carbon dioxide

In the reaction as mentioned above, citric acid and sodium bicarbonate combine with water to form sodium citrate, carbon dioxide, and water. Even a small amount of water

can catalyze this reaction, and because water is one of the reaction products, the presence of water enhances the rate of the process, making it difficult to halt. Due to this, the whole manufacturing and storage of effervescent products is planned by minimizing the interaction with water.<sup>3</sup> Tartaric and citric acids undergo a chemical reaction with alkali metal carbonates or bicarbonates in the presence of water. This reaction leads to the production of carbon dioxide, resulting in the rapid disintegration of the tablet. Uncoated effervescent tablets commonly contain acids, bicarbonates, or carbonates.<sup>4,5</sup> These components are beneficial for medications that impact the stomach or are susceptible to the stomach's pH levels. Additionally, effervescent tablets of the medicines frequently recommended in high doses may be employed.<sup>6</sup> Some patients prefer effervescent tablets over traditional tablets or capsules, which can be challenging to consume because they are administered in liquid form and are simple to swallow. However, one dose of effervescent tablet is typically diluted in 3–4 ounces of water. The gastrointestinal system is not directly exposed to effervescent tablets since they have been dissolved in a buffer solution first. As a result of decreased gastrointestinal irritation, they might be well tolerated in the stomach and intestine. Another advantage associated



with the effervescent tablets is that when they are taken by the patient, exactly the taken amount enters the stomach. In actuality, the CO<sub>2</sub> generated during an effervescence enhances the penetration of active compounds into the paracellular route and, as a result, their absorption.<sup>7,8</sup>

Acebrophylline is classified under the Biopharmaceutics Classification System (BCS) as a Class I compound, characterized by high solubility and high permeability. Conversely, N-acetylcysteine falls under BCS Class II, indicating low solubility but high permeability. Both agents function as bronchodilators and are commonly employed in the management of bronchial asthma and chronic obstructive pulmonary disease (COPD). N-acetylcysteine acts as a mucolytic agent by reducing mucin viscosity through the cleavage of disulfide bonds within mucin glycoproteins. Additionally, it is used as a therapeutic intervention for paracetamol (acetaminophen) overdose. Despite their therapeutic efficacy, both drugs are associated with similar palatability issues.<sup>9,10</sup>

The objective of this study was to develop and evaluate an effervescent tablet containing acebrophylline and N-acetylcysteine. This effervescent formulation aims to enhance patient compliance and bioavailability compared to conventional marketed tablets. The effervescent tablet facilitates faster absorption of the active pharmaceutical ingredients, potentially improving both bioavailability and patient palatability.

## MATERIALS AND METHODS

### Materials

N-acetylcysteine, acebrophylline, citric acid, sodium bicarbonate, maltodextrin, sucralose, acesulfame potassium, guava flavor, strawberry flavor, lubricant "A" and lubricant "B" were supplied by SciTech Specialities Pvt. Ltd., Sinnar, Nashik, Maharashtra, India.

### Methods

#### Preformulation studies

The preformulation studies were performed as follows:

#### Organoleptic properties

The samples of N-acetylcysteine and acebrophylline were examined for organoleptic properties such as taste, color and odour.<sup>11,12</sup>

#### Melting Point Determination

Melting points of N-acetylcysteine and acebrophylline were determined using a capillary tube along with small quantities of the drug samples, with the tube closed at one end and placed into the melting point apparatus. The melting point was mentioned in triplicate.<sup>11,12</sup>

#### Solubility analysis

Solubility of N-acetylcysteine and acebrophylline was determined by dissolving 1g of the drug in 100ml of solvents such as water, ethanol and methanol.<sup>11,12</sup>

### Fourier transform infrared spectroscopy (FTIR)

FTIR studies were carried out on individual pure drugs and a physical mixture consisting of the drug and excipients together. A Fourier Transform spectrophotometer (Agilent Technologies) was utilized to record the infrared absorption spectrum of both pharmaceutical actives and excipients over a frequency range 4000–400 cm<sup>-1</sup>.

### Drug-drug and drug-excipient compatibility study

The compatibility studies were performed using Fourier Transform Infrared Spectrophotometer (Agilent Technologies). N-acetylcysteine and acebrophylline were mixed in a polybag in an appropriate ratio (1:1) to test drug-drug compatibility. For the drug-excipient compatibility studies, drugs and excipients were mixed in a polybag in an appropriate ratio (1:1). The above mixture was passed through a #60 sieve before being packed in sachets and kept at controlled conditions (40 ± 2°C/ 75 ± 5% RH) inside the stability chamber. These samples were withdrawn at the end of the fourth week and reanalysed.<sup>11,12</sup>

### Evaluation of pre-compressible blend

The mass uniformity of a dose is significantly influenced by an important parameter known as flow properties. Flow properties are commonly assessed using various parameters such as the angle of repose, bulk density, tapped density, Hausner's ratio, and Carr's index.

#### Bulk density

The bulk density of the powder blend was determined using the Veego Tapped Density Apparatus following the USP-II method.<sup>13</sup> By pouring the previously weighed powder into a measuring cylinder, the bulk density was determined. This first volume is known as bulk volume and is measured in g ml<sup>-1</sup>.

$$\text{Formula: } \rho_b = M/V_0$$

where,  $\rho_b$  = Bulk density (g ml<sup>-1</sup>)

M = Mass of powder (g)

V<sub>0</sub> = Bulk volume of powder (ml)

#### Tapped density

Tapped density was determined by mechanically tapping a measuring cylinder containing a powder blend that had previously been weighed using the Veego Tapped density apparatus.<sup>13</sup> The final volume after tapping was measured and expressed in g ml<sup>-1</sup>.

$$\text{Formula: } \rho_t = \frac{M}{V_t}$$

where,  $\rho_t$  = Tapped density (g ml<sup>-1</sup>)

M = Mass of powder (g)

V<sub>t</sub> = Tapped volume of powder (ml)

#### Angle of repose

The fixed funnel method was used to measure the angle of repose.<sup>14</sup> In this method, a funnel is positioned above a



blank sheet of paper placed on a horizontal surface. The tip of the funnel is set at a specific height. Granules are then poured through the funnel until they form a pile beneath, with the tip of the pile touching the bottom of the funnel. The height and radius of the resulting powder blend pile are measured and determined, and the angle of repose was determined as follows:

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

$$\theta = \tan^{-1}h/r$$

where,  $\theta$  represents the angle of repose in degrees,  $h$  denotes the height of the pile in centimeters, and  $r$  signifies the radius of the pile in centimeters.

### Compressibility or Carr's index (%)

Carr's index depicts the ability of the powder to contract under pressure. It is used to predict flow properties using bulk and tapped density results. The flowability of powder may be evaluated by comparing the bulk density ( $\rho_b$ ) and tapped density ( $\rho_t$ ) of powder and the rate at which it

compacts.<sup>15</sup> The Carr's index was determined using following formula:

$$\text{Carr's index} = \frac{\text{Tapped density} - \text{Bulk density}}{\text{Tapped density}} \times 100$$

### Hausner's ratio

Hausner's ratio is a measure of the ease with which powder flows. It can be calculated by considering the bulk density and tapped density of a substance.<sup>16</sup> The following formula is used to calculate Hausner's ratio:

$$\text{Hausner's ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

### Formulation development:

Each Effervescent tablet contains N-acetylcysteine (600mg) and acebrophylline (100mg). Formulation development involved the utilization of various excipients and different manufacturing techniques while optimizing the formulation. Optimization of the concentration of excipients was done as shown in Table 1.

**Table 1:** Formulation trials for optimization of concentration of excipients from batch F1 to F10

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
<b>Blend A</b>										
N-Acetylcysteine	600	600	600	600	600	600	600	600	600	600
Acebrophylline	100	100	100	100	100	100	100	100	100	100
Citric acid	125	129.20	125.77	124.05	124.91	406.8	602.8	592.8	592.8	588.80
Sodium bicarbonate	637	622.80	606.23	597.95	602.09	610.2	904.2	889.2	889.2	883.2
Maltodextrin	163	163	163	163	163	163	163	163	163	163
Purified water	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
<b>Blend B</b>										
Sucralose	5	10	15	20	15	15	15	15	15	15
Acesulfame Potassium	--	--	5	5	5	10	15	15	10	10
Strawberry flavour	30	30	35	40	40	50	55	60	50	40
Guava flavour	--	5	10	10	10	5	5	5	10	10
<b>Blend C</b>										
Lubricant "A"	40	40	40	40	40	40	40	40	40	40
Lubricant "B"	--	--	--	--	--	--	--	20	30	50
Total	1700	1700	1700	1700	1700	2000	2500	2500	2500	2500

\*All values are expressed in mg/tablet.

### Selection of excipients

Different excipients were studied and tested for compatibility with the active ingredients. Only the excipients that demonstrated compatibility with the active ingredients were selected and incorporated into the final formulation.

Flavor: A combination of strawberry flavour and guava flavours was selected.

Sweetener: Sucralose, acesulfame potassium was used.

Diluent: Maltodextrin was used.

Acidic source: Citric acid was selected.

Alkaline source: Sodium bicarbonate was selected.

Lubricant: All the excipients were studied and tested for compatibility with the active ingredients and only those excipients were used in the formulation which is found to be compatible with drugs.

Punch Tooling: 20mmroundshapepunch was used.

### MANUFACTURING PROCESS DEVELOPMENT

The flow of the manufacturing process for N-acetylcysteine and acebrophylline effervescent tablets was as follows:

#### Dispensing

The required active raw material and excipients were dispensed under controlled conditions and with proper



labelling and were further packed with double polybags by the doers-checkers system.

### Sifting

The material was sifted using the specified sieves (#20 & #60) in the sequence specified. The sieve's integrity is checked both before and after sieving.

### Granulation- Blend A

Citric acid and sodium bicarbonate were added to the Rapid Mixer Granulator (RMG) and the RMG was run for 5 min at slow mixer speed. Then, 5 ml of binder solution (purified water) was added to the above material, and the RMG was operated for 5 more min at a slower mixer speed. Finally, 20 ml of binder solution was added to the above blend, and it was mixed for another ten min at a slower mixer speed. After the granulation procedure was completed, the blend was unloaded into a polybag.

### Drying

The Fluidized Bed Dryer (FBD) was pre-heated for 15 min at 50-55 °C inlet temperature. Blend 'A' was then dried in FBD at 50-55°C for an estimated time of 8 min to achieve the parameters. The dried granules' Loss on Drying (LOD) was evaluated after drying.

Limit for Loss on Drying (LOD): NMT 0.2%

### Sieving

Blend A was thereafter passed through sieve #20.

Retained material of 'Blend A' on sieve #20 was then further passed through Multimill for particle size reduction and to attain uniformity.

### Blending

An octagonal blender was filled with an accurately weighed amount of Blend A, all other ingredients except lubricants and blended for 10 min at 8 RPM.

### Final Blending

The above blend was then mixed for 15 min at 8 RPM with an accurately weighed quantity of lubricants Blend C after blending was completed; the appearance and loss on drying were recorded.

### Compression

Transferring the final blend into the hopper of the Accura D4, 12-station tablet compression machine and using a 20mm round shape punch for tablet compression resulted in compression of the powder blend and tablet punching.

### Packaging

The compressed tablets were filled into high-density polyethylene (HDPE) tubes and packed in a manner where each tube accommodated 10 tablets.

## EVALUATION OF EFFERVESCENT TABLET FORMULATION

Formulated effervescent tablets were evaluated by performing various physicochemical tests such as drug

content uniformity, weight variation, tablet hardness, thickness and diameter, pH and disintegration test.<sup>17,18</sup>

### Uniformity of weight

Twenty tablets were chosen at random and weighed individually. The average weight of the sample was then calculated. To pass the weight variation test, the tablets must meet specific criteria. Typically, the test requires that no more than two tablets are outside the specified percentage limit, and none of the tablets should differ by more than twice the specified percentage limit.

### Drug content uniformity

The amount of N-acetylcysteine and acebrophylline in each of the ten dosage units was determined at random using a suitable analytical method.

### Thickness and diameter

Tablet thickness and diameter are critical for tablet size uniformity. The thickness and diameter of each of the five tablets were measured using a digital Vernier calliper and expressed in millimetres.

### Hardness

The hardness of tablets is an important parameter that determines their ability to withstand external forces and resist breakage during storage, transportation, and handling before they are used by consumers. Tablets with appropriate hardness are less prone to damage, ensuring that they reach the end-users in a safe and intact condition. The hardness of each of the five tablets was measured with a Veego Hardness Tester and expressed in kilograms per square centimetre.

### Disintegration time

The disintegration time of the tablet was determined using the disintegration test apparatus. The disintegration time of a tablet refers to the duration it takes for the tablet to fully disintegrate in a specified volume of water (typically 150 ml) at a controlled temperature range of 20-30 °C after the effervescent reaction is completed, the evolution of gas bubbles stops, and a clear solution is obtained. This time is calculated as a disintegration time for a specific tablet and is recorded. The procedure was repeated for a total of 5 tablets.<sup>9</sup>

### Determination of pH

After the disintegration time, the pH of the solution of one tablet was measured in a volume of 150 ml of purified water, maintaining a controlled temperature range of 20 ± 1 °C using a pH meter (HI2211 model by Rihanna).

### Assay of N-Acetylcysteine

The assay was performed using the potentiometric titration method. The average weight of the tablet was taken in a 250ml beaker and 60ml water was added to it. 10ml potassium iodide and 10 ml dilute HCl were added to the beaker. The beaker was placed on the potentiometer for titration. 0.05M Iodine was used as a titrant. The % content



was determined by using the following formula<sup>17</sup>:

$$\% \text{ Content} = \frac{\text{Burette Reading} \times \text{Normality of iodine} \times \text{Factor} \times \text{Average weight}}{0.05 \times \text{sample weight}}$$

### UV Visible spectroscopy method of analysis for acebrophylline

Acebrophylline standard and sample were scanned within the UV range of 200nm to 400nm and  $\lambda_{\text{max}}$  of acebrophylline standard and sample was determined.<sup>19</sup>

#### Preparation of standard solution (100 ppm)

100 mg of acebrophylline was added to a 100 ml conical flask. 10 ml methanol was added to it and the volume was made with purified water. 10 ml of the above solution was diluted to 100 ml with purified water in volumetric flask. The absorbance of resulting solutions was measured at obtained  $\lambda_{\text{max}}$  against purified water as a blank.

#### Preparation of Sample Solution (100ppm)

The average weight of the tablet was taken and added to a 100 ml volumetric flask. 10ml methanol was added to it and the volume was made with purified water. 10 ml of the above solution was diluted to 100 ml with purified water in volumetric flask. The absorbance of resulting solutions was measured at obtained  $\lambda_{\text{max}}$  against purified water as a blank. Content in percentage was determined.

$$\% \text{Content} = \frac{\text{Sample absorbance}}{\text{Standard absorbance}} \times \frac{\text{Standard weight}}{100} \times \frac{10}{100} \times \frac{100}{\text{Sample weight}} \times \frac{100}{10} \times \frac{\text{Average weight}}{\text{Label claim}}$$

#### Determination of linearity of acebrophylline

The absorbance of different concentrations of acebrophylline was measured at 308 nm. The tablet was powdered and the amount of powder equivalent to 100mg of acebrophylline was weighed. The content was diluted to get a 100ppm concentration. Solutions of different concentrations were scanned between 200-400 nm and absorbance at 308 nm was measured for acebrophylline.

#### Stability studies

The product was subjected to all three temperature and humidity conditions. The optimized formulations were

packaged in tubes and kept in walk-in humidity chambers for a month at temperatures of 25°C/60% RH, 30°C/65% RH and 40°C/75% RH, respectively. After a month, ten tablets were randomly selected for withdrawal. The physical appearance, hardness, disintegration time, pH of the solution, and drug content of these samples were then determined.

## RESULTS

The results of the preformulation study were as follows:

#### Organoleptic properties

The given sample of N-acetylcysteine powder was found to be white and that of acebrophylline was found to be off-white in color. The results are shown in Table 2.

#### Melting point

The melting point of N-acetylcysteine and acebrophylline was found to be 110°C and 215°C, respectively and both melting points comply with the standard. The melting points of N-acetylcysteine and acebrophylline are given in Table 3.

#### Solubility analysis

The solubility of N-acetylcysteine and acebrophylline was determined in different solvents. N-acetylcysteine was found to be soluble in water, ethanol and methanol. Acebrophylline was found to be soluble in ethanol and methanol and insoluble in water. The results are shown in Table 3.

#### Drug-drug and drug-excipient compatibility study

Drug-drug and Drug-excipient compatibility studies were carried out using Infrared absorption spectroscopy. Infrared absorption spectra of N-acetylcysteine + acebrophylline and N-acetylcysteine + acebrophylline + excipients were recorded over the frequency range of 2000 to 400  $\text{cm}^{-1}$  using Fourier Transform Infra-red Spectrophotometer (Agilent Technologies) as shown in Figure 1(a) and Figure 2 (a). The infrared spectra of above-mentioned samples were again recorded after 1-month storage at 40°C/75% stability conditions as shown in Figure 1(b) and Figure 2 (b). Interpretations of IR spectra are shown in Table 4 and Table 5.

**Table 2:** Organoleptic properties of N-Acetylcysteine and Acebrophylline

Properties	N-Acetylcysteine	Acebrophylline
State	Solid	Solid
Colour	White	White to off white
Odour	Characteristic	Characteristic

**Table 3:** Melting point and solubility of N-acetylcysteine and acebrophylline

Drug	Melting Point (°C)		Name of solvent		
	Literature	Observed	Water	Ethanol	Methanol
N-Acetylcysteine	104-110°C	110±0.361	Soluble	Soluble	Soluble
Acebrophylline	213-215°C	215±0.458	Insoluble	Soluble	Soluble

N=3, Values are expressed as Mean±SD

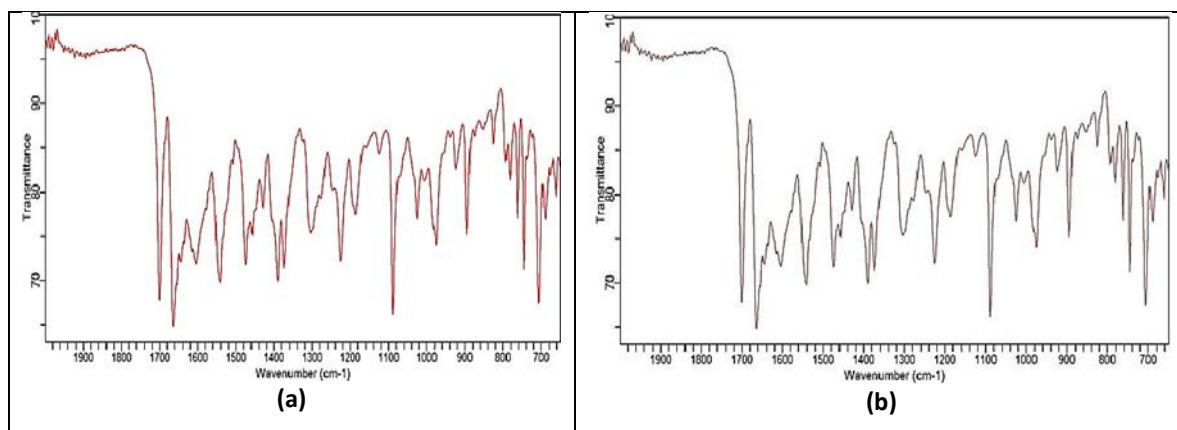


**Table 4:** Functional group identification based on wavenumber of initial and final IR spectrum of N-acetylcysteine and acebrophylline

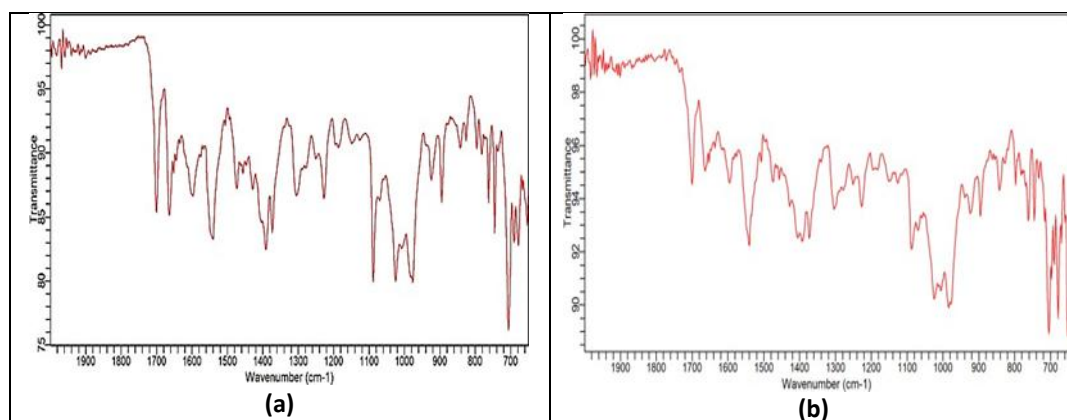
Functional Group	Wavenumber (cm <sup>-1</sup> ) initial IR spectrum of N-acetylcysteine and acebrophylline	Wavenumber(cm <sup>-1</sup> ) of final IR spectrum of N-acetylcysteine and acebrophylline after 1 month of storage at 40°C/75% stability
C-O Stretch	1276, 1069	1269,1066
C=O Stretch	1699	1694
C=C Stretch	1935	1932
N=O Bending	1543	1541
N-H Bend	1474, 1302	1470,1300
C-H Bend	973, 730	976,924

**Table 5:** Functional group identification based on wavenumber of initial and final IR spectrum of N-acetylcysteine + acebrophylline + excipients

Functional Group	Wavenumber (cm <sup>-1</sup> ) initial IR spectrum of N-acetylcysteine + acebrophylline+ excipients	Wavenumber(cm <sup>-1</sup> ) of final IR spectrum of N-acetylcysteine + acebrophylline+ excipients after 1 month of storage at 40°C/75% stability
C-O Stretch	1226,1185,1125, 1088, 1025	1226,1185,1125, 1088, 1025
C=O Stretch	1699,1662,1602	1699, 1662, 1602
C=C Stretch	1935	1935
N=O Bending	1543	1543
N-H Bend	1474,1429,1390, 1373, 1304	1474,1429,1390, 1373, 1302
C-H Bend	976,928,894,782,762,745,706,689,661	976,924,894,782,762,745,706,689, 661



**Figure 1:** Initial IR Spectrum of N-acetylcysteine and acebrophylline (a) and Final IR spectrum of N-acetylcysteine +acebrophylline after 1 month of storage at 40 °C/75 % stability conditions (b)



**Figure 2:** Initial IR Spectrum of N-acetylcysteine +acebrophylline + excipients (a) and Final IR Spectrum of N-acetylcysteine + acebrophylline+ excipients after 1 month of storage at 40 °C/75 % stability conditions (b)

**Table 6:** Evaluation of precompression blend of optimized batch F1 to F10

Properties	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10
Bulk density (g ml <sup>-1</sup> )	0.789±0.004	0.738±0.004	0.746±0.007	0.790±0.005	0.723±0.005	0.755±0.004	0.765±0.003	0.753±0.004	0.765±0.003	0.752±0.005
Tapped density (g ml <sup>-1</sup> )	0.887±0.005	0.868±0.005	0.857±0.004	0.89±0.006	0.811±0.004	0.890±0.005	0.867±0.004	0.834±0.006	0.86±0.004	0.862±0.004
Compressibility index (%)	13.567±0.05	12.448±0.04	14.876±0.002	12.456±0.01	10.558±0.10	12.586±0.02	12.790±0.05	12.574±0.02	12.620±0.03	12.765±0.04
Hausner's Ratio	1.186±0.003	1.189±0.002	1.901±0.001	1.877±0.003	1.980±0.001	1.908±0.0015	1.790±0.003	1.765±0.002	1.654±0.001	1.146±0.0015
Angle of Repose (°)	41±0.917	39±0.529	34±0.400	40±0.529	35±0.721	38±0.872	36±0.721	34±0.529	38±0.800	32±0.693

N=3, Values are expressed as Mean±SD

### Powder flow properties

The powder blend (batches labeled as F-1 to F-10) was evaluated for bulk density, tapped density, carr's index, hausner's ratio, and angle of repose. The F-10 Batch was chosen as an optimized formulation because it had the best overall properties when compared to the other formulations. The results are shown in Table 6.

### Evaluation of N-acetylcysteine and acebrophylline effervescent tablet

The formulated tablet of N-acetylcysteine (NAC) and acebrophylline was evaluated for the post-compressional parameters. The obtained results are shown in Table 7.

**Table 7:** Post compression parameters of N-acetylcysteine and acebrophylline effervescent tablet (optimized F10 batch)

Parameter	Batch F-10
Uniformity of Weight (g)	2.529±0.13
Diameter(mm)	20.20±0.050
Thickness (mm)	5.586±0.006
Hardness (kg cm <sup>-2</sup> )	14.200±0.529
Disintegration time(sec)	140±5.292
pH	5.700±0.053

N=3, Values are expressed as Mean±SD

### % Content of N-acetylcysteine

The % content of N-acetylcysteine and acebrophylline was found to be within the acceptable range. The results are mentioned in Table 8.

**Table 8:** % Content of N-acetylcysteine

Burette Reading (ml)	% Content of N-Acetylcysteine	Assay
8.106	100.32%	100.317 % ±0.035
8.250	100.28%	
8.301	100.35%	

### % Content of acebrophylline

The % content of acebrophylline was found to be within specified acceptance limit criteria. The results are shown in Table 9.

### Linearity

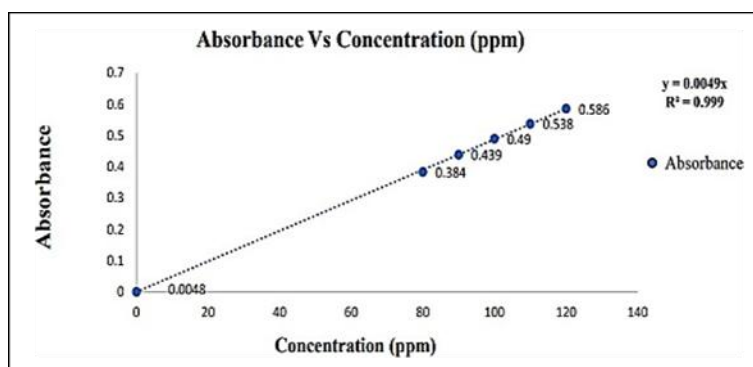
The graph of absorbance and concentration of different concentrations of acebrophylline was found to be linear (R<sup>2</sup>=0.99) at 308 nm. The obtained results are shown in Figure 3.

### Stability Studies

The formulation was tested for the stability study by placing it in a walk-in stability chamber for a month at 25°C/60% RH, 30°C/65% RH and 40°C/75% RH conditions. Batch F-10 of the formulation was found to be stable. There is no discernible change in the characteristics. The results are shown in Table 10. The formulation of the optimized Batch F-10 was found to be stable. It doesn't show any significant change in the physical characteristics.

**Table 9:** Absorbance of acebrophylline at different concentrations

Concentration (ppm)	Absorbance of std	Absorbance of sample	Assay	Average assay
80	0.384	0.496	101.26%	101.26% ±1.22
90	0.439		102.48%	
100	0.490		100.04%	
110	0.538			
120	0.586			



**Figure 3:** Calibration curve of acebrophylline API at 308 nm

**Table 10:** Stability study of optimized formulation (F-10) at different conditions

Parameter	Initial	After one month		
		25°C/60% RH	30°C/65%RH	40°C/75%RH
Uniformity of Weight (gm)	2.530±0.0005	2.528±0.007	2.529±0.002	2.526±0.005
Diameter (mm)	20.20±0.050	20.20±0.000	20.20±0.000	20.20±0.050
Thickness (mm)	5.589±0.045	5.586±0.009	5.583±0.006	5.585±0.008
Hardness (kg/cm <sup>2</sup> )	16±0.365	14.2±0.529	16.4±0.40	18±0.436
Disintegration Time (sec)	150±3	139±7	153±2	170±3
% Content of N-acetylcysteine (Assay)	100.26±0.384	100.30±0.330	100.28±0.421	100.27±0.360
% Content of acebrophylline	100.12±0.125	100.09±0.136	100.05±0.095	100.00±0.164

N=3, Values are expressed as Mean±SD

## DISCUSSION

An effervescent tablet containing acebrophylline and N-acetylcysteine was developed in the current study. The organoleptic characteristics, melting point, UV, FTIR, and DSC analysis of the procured sample of N-acetylcysteine and acebrophylline confirmed the purity. There is no chemical interaction between the drug and excipients, as confirmed by the DSC analysis, which revealed no apparent shift in the endothermic peak, and the FTIR analysis, which revealed no distinctive peaks of the pure drug.

Each batch pre-compression mixture was subjected to a thorough evaluation of various powder flow properties, including bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio. The results of flowability studies show that the powder mixture has outstanding flow characteristics. When compared to the other formulations, the F-10 Batch exhibited the best overall attributes, which led to its selection as an optimal formulation.

The effervescent composition consisted of citric acid and sodium bicarbonate, which when in contact with water, created a fizzing reaction. This reaction aided in the disintegration of the tablet and facilitated the rapid release of the active ingredients. Purified water was used as a binder, ensuring the cohesion of the tablet components during the manufacturing process. In addition to the effervescent composition and binder, other ingredients were incorporated to enhance the sensory attributes and overall palatability of the tablets. Sucralose and acesulfame

potassium were used as sweetening agents to provide a pleasant taste. Strawberry and guava flavors were included to impart desired flavors to the tablets. Lubricating agents were also used in varying ratios to improve tablet flowability and prevent sticking during manufacturing and packaging processes.

After being characterized for a number of physical characteristics, including thickness, hardness, friability, weight fluctuation, and disintegration time, the prepared tablets were found to be within the acceptable range. Because of the uniform die fill, acceptable flow characteristics, consistent pressure, and suitable punch movement, the thickness of tablet indicates uniformity. The ideal formulation falls within the weight fluctuation range. According to pharmacopeial specifications, the content uniformity of acebrophylline and N-acetylcysteine is within the acceptable range. It shows that the recommended dose remains uniform across all formulations.

The findings of the stability studies showed that even after three months of storage at different temperatures and humidity levels, there was no significant change in the physiochemical characteristics. It can be inferred that the formulation did not degrade or change. This indicates that the optimized formulation maintained its integrity and stability under the specified humidity and temperature conditions, suggesting its suitability for storage and potential use.

## CONCLUSION

In this research, N-acetylcysteine and Acebrophylline effervescent tablets were prepared by using Citric acid and sodium bicarbonate, as an effervescent composition. Water soluble maltodextrin was used as a diluent and water as granulation fluid. Acesulfame potassium and Sucralose were used as a calorie free sweetener. Strawberry flavor and Guava flavor were used to improve the palatability of N-acetylcysteine and Acebrophylline effervescent tablets. Stoichiometric ratio of acid base is modified to get sour taste to the product than salty. Water-soluble, generally regarded as safe (GRAS) recommended lubricants were used to improve the flow properties of the final blend. The N-acetylcysteine and acebrophylline effervescent tablet is designed for oral administration, offering a significant advantage in avoiding gastrointestinal disorders that may arise from other administration routes. Overall, the N-acetylcysteine and acebrophylline effervescent tablet represent a promising pharmaceutical formulation with enhanced patient acceptability and potential therapeutic benefits in managing COPD symptoms and reducing bronchial obstructions.

## ACKNOWLEDGMENTS:

I would like to express my heartfelt gratitude to Mr. Pradip Gadre, Managing Director, and Mr. Satish Nangude, General Manager of Product Development at SciTech Specialities Pvt. Ltd., Sinnar. Their invaluable guidance, encouragement, and moral support played a crucial role throughout this research project. I am also deeply grateful to them for providing the essential facilities required to carry out this work.

**Source of Support:** The author(s) received no financial support for the research, authorship, and/or publication of this article

**Conflict of Interest:** The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

## REFERENCES

- Derle D, Khandekar S, Bhavsar A, Derle N, Formulation development and evaluation of effervescent tablet of paracetamol and N-acetylcysteine, Indo American Journal of Pharmaceutical Research, 2017;7(03):7946-7954.
- Prabhakar CH, Krishna KB, A review on effervescent tablet, International Journal of Pharmacy and Technology, 2011;3:704-12.
- Patel SG, Siddaiah M, Formulation and evaluation of effervescent tablets: A Review, Journal of Drug Delivery and therapeutics, 2018;8(6):296-303.
- Srinath KR, Chowdary CP, Palanisamy P, Krishna A, Aparna S, Ali SS, Swetha K, Formulation and evaluation of effervescent tablets of paracetamol, International Journal of Pharmaceutical Research and Development, 2011 May12;3(3):76-104.
- Palanisamy P, Abhishekh R, Yoganand Kumar D, Formulation and evaluation of effervescent tablets of aceclofenac, International Research Journal of Pharmacy, 2011;2(12):185-90.
- Aslani A, Jahangiri H, Formulation, characterization and physicochemical evaluation of ranitidine effervescent tablets, Advanced Pharmaceutical Bulletin, 2013;3(2):315.
- Wadhvani AR, Prabhu NB, Nandkarni MA, Amin PD, Consumer friendly mucolytic formulations, Indian Journal of Pharmaceutical Sciences, 2004;7:506-7.
- Bandeline FJ, Pharmaceutical Dosage Forms: Tablets, New York: Marcel Dekker Inc. 1989. p. 287-292.
- British Pharmacopoeia, London: Medicines and Healthcare Products Regulatory Agency: N-acetylcysteine; 2018.01. p.12.
- The United States Pharmacopoeia. National Formulary, Rockville (MD): United States Pharmacopoeial Convention: N-acetylcysteine; 2017. 01. p.27.
- Desu PK, Vaishnavi G, Divya K, Lakshmi U, An overview on preformulation studies, Indo American Journal of Pharmaceutical Sciences, 2015;2(10):1399-407.
- Chaurasia G, A review on pharmaceutical preformulation studies in formulation and development of new drug molecules, International Journal of Pharmaceutical Sciences and Research, 2016;7(6):2313-20.
- Fiese EF, Hagen TA. In Lachman, Leon, Liberman HA, Knig JL, Eds., The theory and practice of industrial pharmacy. 3rd edn. Mumbai: Varghese Publishing House;1987. p.183.
- Thoke SB, Sharma YP, Rawat SS, Nangude SL, Formulation development and evaluation of effervescent tablet of Alendronate sodium with vitamin D3, Journal of Drug Delivery and Therapeutics, 2013;3(5):65-74.
- Akhtar SE, Hussain SO, Mandal SK, Formulation development and characterization effervescent tablets along with levocetirizine dihydrochloride, Asian Journal of Pharmaceutical and Clinical Research, 2020;13(8):124-30.
- Patil MG, Kakade SM, Pathade SG, Formulation and evaluation of orally disintegrating tablet containing tramadol hydrochloride by mass extrusion technique, Journal of Applied Pharmaceutical Science, 2011;01(06):178-81.
- Indian Pharmacopoeia, Ghaziabad, The India Pharmacopoeial Commission Official Tests for Evaluation of Tablet; 2019. 01(Addendum). p.309.
- Banker GS, Anderson NR. In Lachman L, Lieberman HA, Kanig JL, The theory and practice of industrial pharmacy, 3rd edn. Mumbai: Varghese Publishing House; 1987. p.297-300.
- Patel A, Patil R, Patil S, Sonar KV, Development and validation of UV spectroscopic method for estimation of acebrophyllinein tablet dosage form, American Journal of PharmTech Research, 2019;9(02);2249-3387.

For any questions related to this article, please reach us at: [globalresearchonline@rediffmail.com](mailto:globalresearchonline@rediffmail.com)  
 New manuscripts for publication can be submitted at: [submit@globalresearchonline.net](mailto:submit@globalresearchonline.net) and [submit\\_ijpsrr@rediffmail.com](mailto:submit_ijpsrr@rediffmail.com)

