

# Review on Formulation Development: Mucolytic and Expectorant in Pediatric Wet cough.

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## Abstract

Mucus hypersecretion is a clinical feature of severe respiratory diseases such as asthma, cystic fibrosis and chronic obstructive pulmonary disease. Airway mucosal infection and/or inflammation associated with these diseases often gives rise to inflammatory products, including neutrophil-derived DNA and filamentous actin, in addition to bacteria, apoptotic cells and cellular debris, that may collectively increase mucus production and viscosity. Coactive agents have been the medication of choice for the treatment of respiratory diseases in which mucus hypersecretion is a clinical complication. The main purpose of coactive drugs is to increase the ability to expectorate sputum and/or decrease mucus hypersecretion. Many coactive drugs are currently available and can be classified according to their putative mechanism of action. Coactive medications include expectorants, mucoregulators, mucolytics and microkinetic. By developing our understanding of the specific effects of coactive agents, we may result in improved therapeutic use of these drugs. The present review provides a summary of the most clin relevant coactive drugs in addition to potential mechanism of action.

In healthy individuals, mucus secretion is not excessive and mucus continuously removed by epithelial ciliated cells, then propelled towards the larynx for swallowing [1]. However, an increase in airway mucus secretion can be problematic, especially if the rate of secretion exceeds the rate at which it can be removed by normal ciliary action. Increased mucus secretion (hypersecretion) is a clinical feature of severe respiratory diseases, such as asthma, cystic fibrosis (CF) and chronic obstructive pulmonary disease (COPD). Typically, during infection and/or inflammation, the airway mucosa responds by increasing the volume of mucus hat is secreted. This response is mainly due to hyperplasia and hypertrophy of goblet cells and the submucosal gland, a phenomenon recognized as secretory hyperresponsiveness [2]. The inflammatory process results in loss of cells and ciliary function, destruction of the surfactant layer by airway phospholipases and alteration of the biophysical properties of the mucus [3, 4]. In addition, by-products accumulated during the inflammatory process include neutrophil-derived DNA and filamentous actin (F-actin), dead/apoptotic cells, bacteria and cell debris. Collectively, these factors contribute to mucus purulence, and when expectorated, this mucus is termed sputum [5].

In healthy individuals, mucus secretion is not excessive and mucus continuously removed by epithelial ciliated cells, then propelled towards the larynx for swallowing [1]. However, an increase in airway mucus secretion can be problematic, especially if the rate of secretion exceeds the rate at which it can be removed by normal ciliary action. Increased mucus secretion (hypersecretion) is a clinical feature of severe respiratory diseases, such as asthma, cystic fibrosis (CF) and chronic obstructive pulmonary disease (COPD). Typically, during infection and/or inflammation, the airway mucosa responds by increasing the volume of mucus hat is secreted. This response is mainly due to hyperplasia and hypertrophy of goblet cells and the submucosal gland, a phenomenon recognized as secretory hyperresponsiveness [2]. The inflammatory process results in loss of cells and ciliary function, destruction of the surfactant layer by airway phospholipases and alteration of the biophysical properties of the mucus [3, 4]. In addition, by-products accumulated during the inflammatory process include neutrophil-derived DNA and filamentous actin (F-actin), dead/apoptotic cells, bacteria and cell debris.

Collectively, these factors contribute to mucus purulence, and when expectorated, this mucus is termed sputum [5].

**Keywords:** - mucoactive agents, expectorants, COPD, cystic fibrosis, Chronic cough, microkinetic agent, mucolytic agent.

## Introduction Mucolytics

Mucolytics are medications that decrease the thickness (viscosity) and breakdown mucus in the respiratory system making it easier to cough up and clear from the airway Ex: - Ambroxol Bromhexine

## Expectorants

Expectorants is a medication that promotes the discharge or expulsion of mucus from. The respiratory tract by thinning and loosening it, making it easier to cough up from the lungs and airways.

Ex: - Guaifenesin, Honey.

Mucus hyperaccretion is a clinical feature of asthma, cystic fibrosis, and chronic obstructive pulmonary diseases Air ways mucosal infection and/or inflammation associated with these diseases often gives rise to inflammation

associated with this disease Often gives rise to inflammatory product including. Neutrophil derived DNA and inflammatory action its addition to bacteria, apoptotic Cell and Cellular debris that may collectively increase mucus production and viscosity[6].

mucoactive agents have been medication of choice for the treatment of respiratory disease in which mucus hypertension is a clinical complication. The main purpose of mucoactive drugs is to increase the ability to expectorant sputum and Oregon decrease mucus hypersecretion. Mucoactive medication include expectorants mucoregulators, Mucolytic and Microkinetic. In conditions like COPD and asthma chronic irritation of the Airways leads to mucus hypersecretion[7,8].

## Advantages and disadvantages Mucolytics

Effective for severe conditions

Advantages of mucolytics: -

Highly effective for chronic respiratory disease like cystic fibrosis in (CF), Chronic Obstructive pulmonary disease (COPD) And bronchiectasis, where mucus is thick and sticky.

Disadvantages of Mucolytics: -

Requires a prescription and a direct delivery to the lungs via nebulizer for maximum effect, which less convenient than oral medications.

Breaks down Mucus directly

Advantages of Mucolytics: -

The active ingredient yen acetyl cysteine (NAC) Breaks down the disulfide bonds in the mucus proteins, and dornase alpha breaks down DNA in Purulent mucus Direct action provide powerful relief.

Disadvantages of mucolytics: -

Can cause side effects, including nausea, vomiting, stomach upset and skin rash. In some cases, it can cause more serious reactions like bronchospasms especially in patients with asthma.

Antioxidant and anti-inflammatory effects

Advantages of Mucolytics: -

The mucolytics s yen acetyl cysteine also has antioxidant and anti-inflammatory properties, offering additional benefits for patients with chronic lung inflammation.

Disadvantages of Mucolytics

Can worsen respiratory Distress, particularly in young children who may struggle to clear a newly thinned secretion.

Aids clearance of purulent secretion

Advantages of Mucolytics: -

For condition involving thick, infected mucus, Such as CF, Mucolytics that target DNA (Like Dornase Alfa are very useful)

Disadvantages of Mucolytics

Intravenous yem acetyl cysteine can trigger anaphylactic reactions, through this is rare.

### **Advantages and disadvantages of Expectorants**

Over-the- Counter (OTC) availability

Advantages of Expectorant: -

The most common expectorant, Guaifenesin (Pound in Mucinex and Robitussin), is widely available over the counter, making it easy to access for treating common congestion.

Disadvantages of expectorant: -

Effectiveness is often debated and poorly researched, with some studies questioning its clinical benefits beyond the effects of staying hydrated

Effective for short term illness

Advantages of expectorant: -

Useful for congestion associated with common short-term illnesses, such as colds, the flu or acute bronchitis.

Disadvantages for expectorant: -

Not suitable for chronic coughs, which should be evaluated by a healthcare provider to rule out more serious causes like asthma or COPD.

Makes coughing more productive

Advantages for expectorant: -

By thinning secretions and adding moisture to the airways, expectorants help turn a dry, non-productive cough into a more effective one. This helps clear irritants and bacteria.

Disadvantages of expectorant: -

Can cause mild side effects like headache, and nausea, and vomiting. In combination products, the other ingredients may cause additional side effects.

Open used with other medications

Advantages of expectorant: -

The most common expectorants are generally considered safe and can be used in combination with other cough and cold medications.

Disadvantages of expectorant: -

Individuals with underlining health issues like kidney liver, or heart problems should use expectorant with caution and consult a

doctor.

### Mucolytics common composition

This agent breaks down or loosens thick mucus in the Airways, making it easier to clear.

Active ingredient	Mechanism of action
N acetylcysteine	Breaks disulfide bonds in mucus, reducing viscosity
Carbocation	mucus composition and reduce viscosity
Ambrosoli	stimulates surfactant production, mucolytics action.

### Expectorant- common compositions

This agent increases the volume or hydration of airways secretion, helping expel mucus via coughing

Active ingredient	mechanism of action
Guaifenesin	increases respiratory tract fluid; decreases mucus adhesiveness
Ammonium chloride	irritates gastric mucous—reflex increase in bronchial secretion

### Significance of mucolytics and expectorant

#### 1. Aid in airways clearance

Both classes help remove mucus from lungs and bronchi. This improves ventilation and reduces airways obstruction. Especially important in conditions where mucus is thick and difficult to expel, like:

Bronchitis  
Bronchiectasis  
Cystic fibrosis  
Pneumonia (in some cases)  
COPD (in older children or adolescents)

#### 2. Reduce cough severity and frequency

By clearing secretions, these drugs can;

Lessen the irritation caused by mucus buildup  
Make coughing more productive and efficient  
Sometimes reduces night-time coughing in older children

#### 3. Improve comfort and quality of life

Children with wet coughs often have chest congestion, difficulty sleeping, and fatigue. These agents can relieve the symptoms, make breathing and rest easier.

#### 4. Prevent complications of mucus stasis

Thick or retained mucus can lead to:

Secondary infections

Atelectasis (Collapsed lung segments) Worsening of chronic disease

Mucolytics especially in chronic condition help prevent these complications

#### 5. Supportive roles in chronic respiratory disease

Mucolytics like young acetylcysteine or carbocysteine are often part of long-term therapy in; Cystic fibrosis

Primary ciliary dyskinesia Bronchiectasis

They enhance airway hygiene and reduce exacerbation frequency

## Significance

### 1 Acute respiratory tract infection (RTIs)

Example; Acute bronchitis, Viral lower respiratory infection, Pneumonia (in recovery phase) Expectorants may help make curve more productive by hydrating secretions.

Mucolytics may reduce mucus thickness to ease Clearance.

### 2 Chronic respiratory diseases

Condition Role of mucolytics/ Expectorant

Cystic fibrosis Mucolytics like eon acetyl cysteine or Dornase alpha not a classic mucolytics help breakdown thick sticky mucus.

Bronchiectasis Regular use of mucolytics example carbocisteine add chest physiotherapy help reduce mucus Statis.

### 3 Post infectious cough with residual mucus

After recovery from pneumonia or bronchiolitis, children may have lingering in wet cough due to mucus residue. Short term use of mucolytics and expectorant may help clear secretions through not always necessary.

### 4 Sinopulmonary condition

Examples; chronic sinusitis with Post nasal drip process media with effusion,

Mucolytics like carbocisteine sometimes used to reduce mucus viscosity in ENT condition. May help clear middle ear fluid or nasal mucus, through evidence in mixed.

### 5 Supportive use in Airways clearance techniques

In physiotherapy best based Airways clearance

(e.g., CF or bronchiectasis) mucolytics are used before chest physiotherapy or nebulization to facilitate mucus expulsion.

### 6 Nebulized formulation for inhalation

Nebulized N-acetylcysteine (NAC) used in hospital to manage thick secretion example in ventilated patients, severe pneumonia, asthma with mucus plugging.

### 7 Age consideration and caution

Age of group	Application	Caution
<2 years	Rarely use	Risk of mucus retention, Airways obstruction
2-6 years	limited Use	Only clinically indicated

>6 years                      More common                      Especially in chronic ENT condition

## Classification of mucolytic and expectorants

### 1. mucolytics

These agents break down the structure of mucus, making it less viscous and to expel.

#### A. True mucolytics

Act by breaking chemical bond in mucus. Acetylcysteine

Breaks disulfide bonds in mucoproteins

Also used as an antidote for acetaminophen overdose. Carbocysteine (carboxymethyl cysteines)

Modulates mucus viscosity and improves mucociliary clearance. Mense (sodium 2-mercaptoethane sulfonate)

Used more often for cryoprotection but has mucolytic properties.

#### B. peptide mucolytics

Breaks down DNA / protein in purulent sputum. Dornase alfa (rhodanese)

Used in cystic fibrosis to break down extracellular DNA in mucus

### 2. Expectorant

These agents increase the volume or hydration of secretions, promoting easier removal through coughing

#### A. Direct Expectorants

Stimulate bronchial blends directly to increase mucus output Potassium iodide

Sodium citrate

#### B. Reflex expectorants

Irritate the gastric mucosa to stimulate vagal reflex, increasing respiratory tract Secretions. Guaifenesin (Most common OTC expectorant) Ipecacuanha (Low doses)

### Parts/Components(The example of mucolytics): Drug name                      How it works

N- Acetylcysteine                      Brakes disulfide bonds in mucus

NAC   Proteins

Carbocysteine                      Reduce mucus viscosity can help its drainage

Bromhexine /ambroxol                      Enhance mucus clearance and has anti-inflammatory effect

### Function

Breaks down thick mucus in the lung's bronchi or trachea. Makes coughing more productive by loosening mucus.

Used in chronic respiratory disease like:

Chronic bronchitis

COPD chronic obstructive pulmonary disease Cystic fibrosis

May also have antioxidant properties e.g.; NAC

### Parts/Components/(Examples of expectorants)

Drug name                      How it works

Guaifenesin                      Increase mucus volume and reduces viscosity

Potassium iodide                      Stimulates blends to secrete thinner mucus

Water vapor                      Natural expectorant that moistens Airways

## Functions

Stimulate secretion of thinner mucus from the respiratory tract lining Help clear mucus from the Airways by making coughing more effective. Often used for productive coughs in condition like;

Common cold Acute bronchitis

Mid respiratory infections

## Introduction to Ambroxol

Ambroxol is a mucolytic agent commonly used to treat respiratory conditions associated with excessive or thick mucus. It is metabolite of bromhexine with a more potent and direct effect on thinning mucus and improving its clearance from the respiratory tract [9].

Ambroxol work by breaking down the structure of mucus, making it less sticky and easier to expel through coughing. It also stimulates the surfactant production and enhances the ciliary activity which helps to move mucus of the lungs and Airways.

Due to its expectorant, anti-inflammatory, and mid local anesthetic properties, Ambroxol is widely used in the management of;

Productive weight cough

Acute and chronic bronchitis, Chronic obstructive pulmonary disease COPD [10].

## Ambroxol-Detailed drug information

Generic name: - Ambroxol hydrochloride

Drug class: - Mucolytic agent (also has mild local anesthetic and anti-inflammatory properties) Common brand names: -

Mucosolvan, Ambroxol, Losolven, Ambrodil, Broxol Mechanism of action

Stimulate surfactant production and activities Ciliary motility, enhancing mucociliary clearance. Breaks down mucus viscosity, making it thinner and easier to expel via coughing.

Has antioxidant and local anesthetic effects, which may help reduce throat irritation and pain during cough [11].

## Indications (Uses)

Condition	Use
Acute and chronic	To clear thick mucus and is productive cough respiratory disease
Bronchitis (active/	Symptomatic relief Chronic)
Pneumonia	As in adjunct to help with mucus clearance
Bronchiectasis	Chronic management
Asthma (COPD in	Supportive in mucus clearance older children adult)

## Pediatric Dosing (syrup)

Ambroxol syrup (15 mg/5 ml)

Children two to five years: 1.25 ML to 2.5 ML Two to three times daily Children 6 to 12 yrs 5ML two to three times daily

Children >12 years and adults : 10ML three times daily

## Other formulations

### Syrup

Drop for infants Nebulizer solution

Injectable (for hospital use) Lozenges (for sore throat relief)

## Onset and duration

On set with 30 minutes oral Duration of action ~6-12 hours

## Types of ambroxol

1 Ambroxol syrup/ Oral suspension Use mainly for children or adults Who prefer Easy to swallow

Typically available in different concentrations e.g.; 15ml/5ml



**2      Ambroxol tablets/capsules**

Available in immediate release for sustained release forms Convenient for adults

Usually comes in doses like 30MG or 75MG

**3      Ambroxol drops**

Concentrated liquid forms

Often used for children who have difficulty swallowing syrup or tablets

**4      Ambroxol inhalation solution**

Use in nebulizers

Direct delivery to the lungs

Effective for acute chronic respiratory disease with mucus retention

**5      Ambroxol lozenges**

Throat lozenges containing ambroxol

Used for smoothing irritated throat and easing cough

**7      Ambroxol injectable**

Registered via injection or infusion

**Contraindication**

Hypersensitivity to Ambraxol

A caution in Gastric ulcer Disease

Non recommended infants under six months without medical supervision

**Precautions**

Renal or Hepatic impairment: use with caution

Pregnancy use only if clearly needed (especially in first trimester) Location: precise into breast milk in small amounts; caution advised

**Drug interaction**

No significant interactions with commonly used medications

May increase penetration of antibiotics Example amoxicillin, Cefuroxime into bronchial secretion sometimes considered beneficial

**Storage**

Store below 25°C

Keep out of reach of children Protect from light and moisture

**Clinical notes**

Works best when taken with plenty of fluids, which aids mucolytic action

Often combined into syrup with bronchodilator example: -Salbutamol, terbutaline, or expectorant example: - guaifenesin In lozenges, from it can help relief sore throat pain due to local anesthetic effect

**Introduction to guaifenesin**

Guaifenesin I commonly used expectorant that helps manage productive (wet) cough by making mucus in that airway thinner and easier to expel. It works by increasing the volume and reducing the viscosity of respiratory tract secretions, which facilitates mucociliary clearance [12].



Originally derived from guaiac tree resin, guaifenesin has been widely used for decades and is especially effective in condition involving chest congestion and thick phlegm, such as;

Acute bronchitis

Upper respiratory tract infections, Common cold with chesty cough, Chronic bronchitis[13].

Guaifenesin- detailed drug information Generic name

(also known as glyceryl guaiacolate)

Drug class

Expectorant(microkinetic agent)

### Common brand names

Benylin expectorant Robitussin

Tixylix Mucinex

Corex expectorant

### Mechanism of action

Guaifenesin acts by

Increasing the volume and reducing the viscosity of bronchial secretion.

Irritating the gastric mucosa mildly, which stimulates the vagal reflex, increasing respiratory tract fluid production. This results in easier expectoration (coughing up) of mucus, making the cough more productive.

It does not suppress the cough reflex, unlike antitussives [14].

### Indications (therapeutic uses)

Condition

purpose

Acute bronchitis

To, thin and loosen mucus

Productive (wet) cough

To, helps expel mucus more effectively Common cold with chest

Symptomatic relief

Congestions

COPD (chronic bronchitis

Adjunct to help mucus clearance Post-infectious cough

useful

in

lingering wet cough Sinusitis with post-nasal drip

may help reduce mucus viscosity

### Pediatric dosing as expectorant

Age Typical dose in syrup

2-5 years

2.5-5 ML (Typically 50-100mg per dose Every 6-8 hours

6-12 years

5-10 ml every 6-8 hours

>12 Years and adults

10-15 every 6-8 hours

Other formulations

Syrup (most common)

Iv oral solution used for acid base imbalance, not cough Tablets (rarely used in modern practice)

Onset and duration

Onset: ~30 Minutes (oral) Duration :4-6 hours

### Types of guaifenesin

1 immediate-release guaifenesin

This is the standard form that starts working shortly after injections Usually available in liquid syrups, tablets, or capsules Typically, those multiple times a day because it's metabolized relatively quickly.

2 extended-release (ER) guaifenesin Designed to release guaifenesin Slowly over time Usually come in tablet forms

Allow for less frequent dosing example every 1 hours

### 3 combination products

Guaifenesin is often combined with other active ingredient for broader symptom relief: Guaifenesin + dextromethorphan (a cough suppressant)

Guaifenesin + Phenylephrine (a nasal decongestant) Guaifenesin + Acetaminophen (Pain relief fever reducer)

Others with antihistamines or additional cold and flu Symptoms relievers.

### 4 Liquid syrups and solutions

Often use for children are people who prefer liquid medications

## Contraindication

Severe liver or kidney disease Metabolic or respiratory acidosis

Patients on sodium restricted diet, Hypersensitivity to ammonium salt

## Precautions

Caution in children under two years (risk of mucus accumulation or choking) Use carefully in asthma or COPD -excessive secretions may worsen symptom Avoid overdose -higher doses may cause toxicity

Monitor in patients with electrolyte imbalance

## Drug interaction

may interact with urinary alkalinizes (e.g. Sodium bicarbonate)

Use with caution alongside diuretics may affect electrolyte balance No significant interactions in standard low dose expectorant use

## Storage

Store at room temperature 15 to 25°C Keep tightly closed

## Clinical notes

Always taken with fluid to help thin mucus

Commonly used in multi-ingredient cough syrup, often with empty Antihistamine, bronchodilators, or decongestant. Not effective alone for chronic cough or severe mucus retention

Avoid prolonged or unsupervised Use, especially in young children.

## Summary table

Parameter	Details
Drug class	Expectorant
Mechanism	Reduce increase in bronchial secretion
Form	Syrup often in combinations
Pediatric use	Common in 2+ years age-appropriate dosing
Side effects	GI upset, Nausea, Rare CNS symptoms
Use infants	Not recommended under 2 years
Pregnancy / Lactation	Caution advice limited data

## Clinical case example

A 4-year-old Presents with a wet, chesty cough for 4 days, no fever, normal appetite and cough syrup containing ammonium chloride + diphenhydramine + sodium citrates every 8 hours for 5 days, along with hydration saline nasal drops. After follow-up the child shows reduce mucus thickness and cough frequency.

## Introduction to Carbocisteine

Carbocisteine Also Known as carboxymethyl cysteine Is a mucolytic agent used to treat respiratory conditions where thick sticky mucus is a problem It works by breaking down the chemical bonds in the mucus reducing its viscosity and elasticity which makes it easier to cough up and clear from the lungs and Airways [14].

### Carbocisteine He is commonly prescribed for:

Chronic bronchitis Productive (wet) cough

Chronic obstructive pulmonary disease (COPD) Sinusitis

Otitis media with effusion

Cystic fibrosis (as adjunctive therapy)

Unlike some other mucolytics carbocisteine Also help normalize mucus production not just team heat and it considered well tolerated in both children usually over two years adults.

It is available in syrup, capsule and tablet forms and is most effective when used with plenty of plenty and aids mucus clearance

**Carbocisteine Detail drug information** Generic name (Also known as carboxymethylcystin) Drug class Mucolytic agent

Common brand names:

Mucodyne Rhinathiol Solmux Bornklyn

### Mechanism of action Carbocysteine

Words by modifying the structure of mucus it reduces the viscosity and elasticity of sputum by breaking down mucoprotein bonds.

Promotes normalization of mucus secretion making it thinner and easier to expel. Help restore the functions of mucosillary transport, Adding in Airways clearance.

Unlike NAC it does not break disulphide bonds directly but alters mucin composition [14].

### Therapeutic indications

Conditions	Use
Acute chronic bronchitis	Facilitates mucus clearance Productive wet cough Symptomatic relief
Chronic obstructive pulmonary disease	Reduces frequency and severity of Exhibition
Cystic fibrosis	adjunct to add sputum expectoration
Sinusitis And Otitis	Help reduce mucus statis Media with infusion
Post infections cough	short term use for mucus clearance

### Pediatric dosing

Carbocisteine Syrup 250MG/5 ml/ Or 125MG/5ML

Age group	Dose
2-5 Years	2.5 ML (125MG) 3 times daily (Max 750MG per day)

6-12 day)	5ML (250MG) 3 times daily (Max 1500 EMG per	years
>12 years C syrup	750MG Dash 1500 EMG per day in divided doses adults	capsule

### Available formulations

Syrup commonly 125MG/ 5ML or 250MG/ 5ML Capsule (375MG, 500MG)

Tablets

Oral solution

### Onset and duration

Onset; Within one to two hours of oral intake.

Duration: Where is affect last for several hours, hence dosed two to three times per day.

### Types of carbocisteine

1 Immediate release carbocisteine

Available as syrups, Capsules, Tablets Starts working shortly after administration. Typically taken multiple times per day (example 3 times daily)

2 Extended-release ER carbocisteine Formulated to release the drug slowly overtime Usually available in capsule or tablet forms Allow for less frequent dosing (example two wise daily) Provides more consultant blood levels and symptoms control

3 Syrups and liquid suspensions

Often preferred for children or people who have difficulty swallowing tablets Dosage is major with a spoon or cup for accuracy

4 Combinations product

Sometimes carbocisteine is combined with other medicines, such as:

Carbocisteine + Cough suppressant (less common since carbocysteine helps clear mucus)

### Contraindications

Hypersensitivity to carbocysteine or excipients Active Peptic Ulcer disease

Severe renal or hepatic impairment Children <2 years risk of mucus Retention

### Precautions

Use with caution in patience with history of bleeding or ulcers. Monitor in patients with asthma or chronic lung disease.

Ensure adequate hydration to optimize mucolytic effect.

### Drug interaction

Minimal clinically significant interaction

Can we safely, administered with antibiotics, bronchodilators, and corticosteroids first stop.

Avoid with anti-tissue cup suppressants may leads to mucus accumulation due to reduce cough reflex

### Storage

Store at room temperature 15 to 25°C Project from moisture and direct sunlight

### Clinical notes

Best taken with plenty of flutes to assist mucus thinning. May take a few days to show full effect in chronic cases

Use regularly in chronic Bronchitis COPD and ENT infections with thick secretions.

Often preferred Over yen N-acetylcysteine in children due to better taste and GI tolerance

### Summary table

Parameters	Details
Drug class	Mucolytics
Mechanism	Reduces mucus viscosity by altering mucoprotein
Indications	Wet cough, Bronchitis, COPD, sinusitis
Onset	One to two hours
Common dose	250 to 1500 MG per day age dependent
Formulation	Syrup, capsule, tablet
Side effects	GI upset, rash, rarely bleeding
Age restriction	Not for <2 years

### Clinical case example

Oh 7-year-old child presents with a wet persistent add nasal congestion after a viral infection. Examination reveals post nasal drip and thick mucus on throat exam. The Dr Prescribe.

Carbocisteine 250M Purify ML syrup 5ML 3 times a day Saline nasal drops, steam inhalation, and hydration Follow up after 5 days show

Thinner mucus

Reduced coughing spell No adverse effect

### Introduction ammonium chloride

Ammonium chloride is a traditional expectorant commonly used in combination curve syrups to treat productive (wet) cough. It works by irritating the gastric mucosa, which reflexively stimulates the bronchial glands to increase respiratory secretions, thereby helping the loosen and expel mucus from the air ways [15].

Through rarely use alone, ammonium chloride is often found in multi-ingredient formulations with antihistamines, decongestants, bronchodilators or other expectorant like guaifenesin.

In addition to its respiratory use at higher doses ammonium chloride also functions as systemic acidifier and has been used in the treatment of metabolic alkalosis and two acidify urine [16].

Because of its mechanism, it is most effective when combined with adequate fluid intake and is not recommended for use in infants under two years due to the risk of mucus retention [17,18].

### Ammonium chloride detailed drug information

Generic name: - Ammonium chloride

Drug class: - Expectorant (at low doses)

Systemic acidifier at higher doses used in different clinical contexts

### Common brand combinations

Ammonium chloride is rarely used alone as a drug. It, key found in combination cough syrups with other agents like: Diphenhydramine

Guaifenesin Phenylephrine Terbutaline

Example combination products Corix

Tixylix Benadryl

### Mechanism of action (as an expectorant)

Text by Pittie irritating the gastric mucosa, which triggers a reflex stimulation of bronchial glands via the vague nerve. This leads to increased respiratory tract secretions, making mucus thinner and easier to expel [19].

### Indications (in respiratory use)

Condition	Purpose
Wet / Productive cough Upper respiratory tract infection (URTIs)	to assist in mucus clearance Acute bronchitis Adjunct to relief congestion in combination with antihistamines or decongestant
Post nasal drip or sinusitis	Help Thin secretion
Bronchitis with thick sputum	Expectorant effect in combination syrup

### Pediatric dosing (as expectorant);

Age group	Typical dose in syrup
2 to 5 years	2.5 to 5ML Typically 15 to 100 MG per dose every 6 to 8 hours
6 to 12 years	5 to 10ML every 6 to 8 hours
>12 years and adults	10 to 15ML every 6 to 8 hours

### Other formulations:

Syrup (most common)

Iv or oral solution used for acid base imbalance not cough Tablets (Rarely used in modern practice)

### Onset and duration

Onset~30 minutes (oral) Duration: 4 to 6 hours

### Types of ammonium chloride

1 Industrial grade ammonium chloride

Used mainly in manufacturing such as in fertilizers batteries metalwork like shouldering and metal cleaning and pharmaceuticals

Usually less pure than food or pharmaceutical grades

May contain some impurities acceptable for industrial uses

2 Pharmaceutical grade ammonium chloride

High purity suitable for medical or pharmaceutical use

Use as an expectorant in cough medicine or to acidify the urine in certain medical treatments. Must meet strict quality standards.

3 Food grade ammonium chloride

Approved for use in food products as flavoring agents (example licorice candy) or acidity regulator. High purity and safe for human consumption

It has a different regulatory standards depending on the country

4 Analytical grade Ammonium chloride

Very high purity used for laboratory and research purposes Suitable for chemical analysis and experiments

Usually comes with the certificate of analysis

**Contraindications**

Severe liver or kidney disease. Metabolic or respiratory acidosis. Patients on sodium Restricted diet. Hypersensitivity to ammonium salt.

**Precautions**

Caution in children under two years (risk of mucus accumulation or choking). Use carefully in asthma or COPD-excessive secrets may worsen symptoms. Avoid overdose-higher doses may cause toxicity.

Monitor inpatient with electrolyte imbalances.

**Drug interaction**

May interact with urinary alkalinizes example sodium bicarbonate Use with alongside diuretics may affect electrolyte balance

No significant interactions in standard low dose expectorant use.

**Storage**

Store at room temperature 15 to 25 degrees Celsius Keep tightly close

**Clinical notes**

Always taken with blood to help thin mucus.

Commonly used in multi-ingredient cough syrups, often with antihistamines, bronchodilators, or decongestants. Not effective alone for chronic cough or severe mucus retention.

Avoid prolonged or unsupervised use, especially in young children.

**Summary table**

Parameters	Details
Drug class	Expectorant
Mechanism	Increase Bronchial secretion
Form	Syrup (often in combinations)
Pediatric use	Common in 2+ (years age-appropriate dosing)
Side effects	GI upset, nausea, rare CNS Symptoms
Use infants	Not recommended under 2 years
Pregnancy / Lactation	Caution advice L.T.D. data

**Clinical case example**

A 7-year-old child presents with a wet, chest cough for 4 days, no fever, normal appetite and activity chest is clear the doctor prescribes cough syrup containing ammonium chloride 5MG + diphenhydramine sodium citrate 5MG every 8 hours for five days along with the hydration saline nasal drops at follow up, the child shows reduced mucus thickness and cough frequency

**Case study**

Public Alert-Stop Use Notice

Stop Use Notice Regarding Coldrif Syrup (Batch No. SR-13) Due to Toxic Adulteration

The Food and Drugs Administration, Maharashtra, has been alerted to reports of the tragic deaths of children in Madhya Pradesh and Rajasthan, Coldrif Syrup (Phenylephrine Hydrochloride, Chlorpheniramine Maleate Syrup), Batch No. SR-13, Mfg. Dt. May-2025, Exp. Dt. April-2027, manufactured by Sresan Pharma, Sunguvarchathiram, Kancheepuram District, Tamil Nadu, which has been allegedly adulterated with Diethylene Glycol (DEG), a toxic substance.

In view of this, all the licensee and public hereby instructed to immediately stop sale/distribution/use of Coldrif Syrup, Batch No. SR-13, if anybody is in possession, and report it to the local Drugs Control Authorities without delay.



The public may also report possession of the said drug directly to the Food and Drugs Administration, Maharashtra, through the toll-free number 1800222365 or by email to [jchq.fda-mah@nic.in](mailto:jchq.fda-mah@nic.in) or ph.-9892832289

FDA Maharashtra officials are coordinating with the DCA authorities of Tamil Nadu, where the manufacturer Sresan Pharma is located, to track the distribution of the said product batch to Maharashtra.

All Drugs Inspectors and Assistant Commissioners have been instructed to immediately alert retailers, wholesalers, and hospitals to freeze any stocks of the said product batch if available in the market.



**Coldrif Cough Syrup Banned After Child Deaths** The Coldrif syrup (by Sresan Pharma) is banned after child deaths in MP C Rajasthan due to toxic chemical (DEG) contamination. States have recalled affected batches, and parents are warned not to give cough syrups to young children



<h2 style="color: red; margin: 0;">TOXIC SYRUP</h2>	
<p>➤ Six kids who died at GMCH-Nagpur had suffered renal failure due to toxicity of diethylene glycol, lab confirms</p>	
<p>➤ Earlier these deaths were assumed to be acute encephalitis syndrome (AES) cases</p>	
<p>➤ The samples were contaminated with <b>48.6%</b> of DEG</p>	
<p>➤ Of the 14 children, 3 are on ventilator while two in critical condition</p>	
<p>➤ No renal failure cases among children from Vidarbha districts have been reported so far</p>	
<h3 style="color: red; margin: 0;">What's DEG?</h3> <p>➤ Diethylene glycol (DEG) is a toxic industrial chemical used in production of unsaturated polyester resins, as a solvent for dyes and inks, and humectant in items like tobacco and glues</p> <p>➤ When consumed, DEG can cause severe damage to kidneys, liver, and nervous system</p>	

## Conclusion

Megabytes. Aspetar's. and bracer adaptors pay Crocuta roles in the management to cough, targeting deterrent aspects of rotatory condones, Mucolytics help equally and reduce the viscosity of mucus, expectorants promote mucus production and expulsion. while bronchodilators dilate the Aiwa's to improve breathing Combining these medications may be necessary to address specific underlying causes or symptoms of cough, but I should always be done under the supervision.

## Reference

1. Waner A, Salathe M, O'Riordan TG, Mucociliary clearance in the airways. Am J Respir Crit Care Med 1996; 154: 1868- 1902.
2. Rubin BK. The pharmacologic approach ta airway clearance: mucoactive agents. Respir Care 2002; 47: 818- 822.
3. King M, Rubin BK. Pharmacological
4. approaches to discovery and development of new mucolytic agents. Adv Drug Deliv Rev 2002; 54: 1475-1490.
5. Rogers DF, Barnes PJ. Treatment of airway mucus hypersecretion. Ann Med 2006; 38: 116-125
6. ~ Rubin BK, van der Schaans CP, eds. Therapy for Mucus Clearance Disorders. C. L'Enfant, executive editor. Biology of the Lung Series. New York, Marcel Dekker, 2004
7. Lopez-Vidrio MT. Airway mucus: production and composition. Chest 1981; 80: 799-804.
8. Kallner M, Marom Z, Paotow C, et al Human respiratory mucus. J Allergy Clair Immunol 1984; 73:318-323.
9. Braga PC, Zimin I, Allegra L
10. Classification of agents that act on bronchial mucus. In: Braga PC, Allegra L, eds. Drugs in Bronchial Mycology. New York, Raven Press, 1989, pp. 59-67
11. R Balsam, L Lanata, GC Egan European Respiratory Review 19(116)
12. Kristin Patzwaladt, Salvador Castaneda-Vega, Neural regeneration research 10(11),2.345-2346 2024.
13. Kick, Joss, F, W, shriven. C Beseechers, gusseting 3,536,713, October 27, 1970, assigned to Ingelheim G, m, b, H.
14. Yuta Baraniak JN; therapeutic approaches to mucus hypersecretion, cur allergy asthma rep 2005 may; 5(3);243-51.
15. Elisabetta pace, ISA Cervera, Donato laced onia, Gregorian Paone. Alessandro San dizi Zamparelli pharmaceutic 14(6), 1261,2022.
16. Hooper C, Calvert J; (carbonitride) in the management of chronic obstructive pulmonary diseases J corn obstruct pullman dis.2008 3(4); 659-69.

17. Tiruvannamalai R, Conrad CK, Bottiglieri T, et al. High-dose oral N-acetylcysteine, a glutathione prodrug, modulates inflammation in cystic fibrosis. *Proc Natl Accad Sci USA* 2006; 103: 4628-4633
18. Daulatabad N, Fischer P Aulbach B, et al. A phase II study on safety and efficacy of high- dose N- acetylcysteine in patients with cystic fibrosis. *Eury J Med Res* 2009; 14: 352-358.
19. Venhuizen PN. Antioxidant properties of N-acetylcysteine: their relevance in relation to chronic obstructive pulmonary disease. *Eury Respir J* 2004; 23: 629-636.
20. Reichenberger F, Tamm M. N- Acetylcysteine in der Therapie der chronischen Bronchitis. [N-acetylcysteine in the therapy of chronic bronchitis]. *Pneumology* 2002; 56: 793-797.
21. Gross NJ. Anticholinergic agents. In: Leff AR, ed. *Pulmonary and Critical Care Pharmacology and Therapeutics*. New York, McGraw-Hill, 1996; pp.535-552.
22. Arai N, Kondo M, Izumo T, et al. Inhibition of neutrophil elastase-induced goblet cell metaplasia by tiotropium in mice. *Eury Respir J* 2010; 35: 1164-1171.
23. Ramnarine Sly, Haddad EB, Khawaja AM, et al. On muscarinic control of neurogenic mucus secretion in ferret trachea. *J Physio* 1996; 494: 577-586.
24. Ishihara H, Shimura S, Satoh M, et al. Muscarinic receptor subtypes in feline tracheal submucosal gland secretion. *Am J Physio* 1992; 262: 223L-228L.
25. Olivier KN, Bennett WD, Honaker KW, et al. Acute safety and effects on mucociliary clearance of aerosolized uridine 5'-triphosphate +/- amiloride in normal human adults. *Am J Respir Crit Care Med* 1996; 154: 217-223.
26. Jai, A Hoar, James F Donohue Selwyn Sangeetha chronic obstructive pulmonary diseases journal of the COPD foundation 6(4), 341-51.
27. Kellerman D, Rossi Mospan A, Engels J, et al. Damfoos: a review of studies with inhaled P2Y2 agonists that led to phase 3. *Plum Pharmacol Ther* 2008; 21: 600-607.
28. Kellerman D, Rossi Mospan A, Engels J, et al. Damfoos: a review of studies with inhaled P2Y2 agonists that led to phase 3. *Plum Pharmacol Ther* 2008; 21: 600-607.
29. Rogers DF. Mucoactive drugs for asthma and COPD: any place in therapy? *Expert Opin Investing Drugs* 2002; 11: 15-35.
30. " Hafez R, Degand P, Roussel P, et al. Biochemical mechanism of action of cysteine derivatives on bronchial mucus. *Poupon Coeur* 1970; 26: 81-90.
31. Zheng JP, Kang J, Huang SG, et al. Effect of carbocysteine on acute exacerbation of chronic obstructive pulmonary disease (PEACE Study): a randomized placebo- controlled study. *Lancet* 2008; 371: 1813-1818.
32. Allegra L, Cordaro CI, Grassi C. Prevention of acute exacerbations of chronic obstructive bronchitis with carbocysteine lysine salt monohydrate: a multicenter, double-blind, placebo-controlled trial. *Respiration* 1996; 63: 174-180.
33. Yuta A, Baraniak JN. Therapeutic approaches to airway hypersecretion. *Curr Allergy Asthma Rep* 2005; 5: 243-251.
34. Zimin I. *Respiratory Pharmacology and Therapeutics*. Philadelphia, WB Saunders, 1988.
35. Donaldson SH, Bennett WD, Zeman KL, et al. Mucus clearance and lung in cystic fibrosis with hypertonic saline. *N Engl J Med* 2006; 354: 241-250.
36. Pucelle E, Girard F Polu JM, et al. Effect of the mucoregulator S-carboxy-methyl- cysteine in patients with chronic bronchitis. *Eura J Clin Pharmacol* 1978; 14: 177-184.
37. Colombo B, Tesconi P, Daffynition L, et al, Stimulation of Cl secretion by the mucoactive drug S-carboxy-methylcysteinelysine salt in the isolated rabbit trachea. *Eura Respir J* 1994; 7: 1622- 1628.
38. Asti C, Melillo G, Caselli GF, et al, Effectiveness of carbocysteine lysine salt monohydrate on models of airway inflammation and hyperresponsiveness *pharmacol Res* 1995; 31: 387-392.
39. Yeates DB, Cohen VR, Davis AL, et al. Effect of glyceryl guaiacolate on bronchial clearance in patients with chronic bronchitis. *Am Rev Respir Dis* 1977; 115: 182.
40. Sisson JH, Yonkers AJ, Waldman RH. Effects of guaifenesin on nasal mucociliary clearance and ciliary beat frequency in healthy volunteers. *Chest* 1995; 107: 747- 751.
41. Sisson JH, Yonkers AJ, Waldman RH. Effects of guaifenesin on nasal mucociliary clearance and ciliary beat frequency in healthy volunteers. *Chest* 1995; 107: 747- 751.
42. Fiocchi A Grasso U, Zuccotti G, et al. Diiodol treatment for bronchopulmonary diseases in the pediatric age group: a double-

blind controlled clinical trial versus placebo. J Int Med Res 1988; 16: 31-38.

43. Meltzer EO. Intranasal anticholinergic therapy of rhinorrhea. J Allergy Clin Immunol 1992; 90: 1055-1064.

44. Rahman I. Antioxidant therapeutic advances in COPD. Ther Adv Respir Dis 2008; 2: 351-74.

45. Pena LR, Hill DB, McClain CJ. Treatment with glutathione precursor decreases cytokine activity. JPEN J Parenteral Enteral Nutr 1999; 23:1-6.

46. Macio A, Mudede C, Panzone F, et al. Carbocysteine: clinical experience and new perspectives in the treatment of chronic inflammatory diseases. Expert Opin Pharmacotherapy 2009; 10: 693-703.

47. Petty TL. The national mucolytic study: results of a randomized, double blind, placebo-controlled study of iodinated glycerol in chronic obstructive bronchitis. Chest 1990; 98: 1309-1310.