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A Review on Cough Syrup Related Tragedies

M.Sarishma Devi[1], Dr.Anusree.S[2], Dr.Kiran K.J[3], Dr.Prasobh G.R[4], Mrs.Divya S.Nair[5]

1.Student, Seventh Semester B.Pharm, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India – 695502
2.Associate professor,Department of pharmacology, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India – 695502
3. Professor and Head, Department of Pharmacology, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India 695502
4.Principal, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India – 695502
5.Assistant Professor, Department of Pharmacology, Sree Krishna College of Pharmacy and Research Centre, Parassala, Thiruvananthapuram, Kerala, India – 695502

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ABSTRACT: Cough syrups are widely used medicines for the management of dry and productive cough. Despite their therapeutic benefits, several tragic incidents worldwide have revealed serious risks associated with contaminated and irrationally formulated cough syrups. This review mainly focuses on major cough syrup tragedies reported between 2020 and 2025, including incidents in India, Gambia, Cameroon, Uzbekistan, and Indonesia. Most of these deaths were linked to contamination with toxic chemicals such as diethylene glycol (DEG) and ethylene glycol (EG), leading to acute kidney injury, multi-organ failure, and death in children. The review also briefly discusses cough classification, treatment approaches, and the importance of regulatory monitoring, quality control, and public awareness.

KEYWORDS: Cough syrup, DEG poisoning, Pediatric deaths, Cough syrup tragedy, Toxic contamination

I.INTRODUCTION:

Cough is one of the most common protective reflexes of the human body. It helps in clearing mucus, dust, microorganisms, and foreign particles from the respiratory tract. Cough may be classified as dry cough (non-productive) or wet cough (productive) depending on the presence of sputum. Although cough is a symptom rather than a disease, it is one of the leading causes for outpatient visits and self-medication worldwide.

Cough syrups are widely used medicines for the management of cough associated with common cold, respiratory infections, allergies, asthma, bronchitis, and other respiratory disorders. These syrups may contain antitussives, expectorants, antihistamines, mucolytics, bronchodilators, and herbal ingredients. Due to easy availability and frequent use in children, cough syrups have become one of the most commonly consumed over-the-counter medicines.

However, during the years 2020–2025, several tragic incidents involving contaminated cough syrups shocked the world. Many children died due to poisoning caused by toxic chemicals such as diethylene glycol (DEG) and ethylene glycol (EG). These substances are industrial solvents commonly used in antifreeze products and are extremely harmful to the kidneys, liver, brain, and other organs.

Mechanism of Cough

The cough reflex begins when cough receptors present in the throat, larynx, trachea, or bronchi are stimulated by irritants such as mucus, smoke, dust, allergens, or infectious agents. Signals travel through the vagus nerve to the cough center in the medulla of the brain. The brain then activates respiratory muscles, producing a forceful expulsion of air known as cough.

Treatment of Cough

Treatment depends on the type and cause of cough. Major classes of drugs include:

- Antitussives – suppress dry cough (e.g., dextromethorphan, codeine)
- Expectorants – help remove mucus (e.g., guaifenesin)
- Mucolytics – reduce mucus viscosity (e.g., bromhexine, acetylcysteine)
- Antihistamines – reduce allergy-related symptoms
- Bronchodilators – relieve bronchospasm
- Herbal medicines – tulsi, vasaka, liquorice, ginger, honey

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Although these medicines provide relief, misuse or irrational combinations can lead to adverse effects such as sedation, dizziness, respiratory depression, confusion, and toxicity.

EPIDEMIOLOGY OF COUGH:

Respiratory infections contribute significantly to the burden of cough. According to reports from India, respiratory infections caused millions of cases and several thousand deaths annually. Viral infections account for the majority of upper respiratory tract infections, while bacterial infections form a smaller proportion.

In India, cough is commonly associated with conditions such as common cold, bronchitis, pneumonia, asthma, chronic obstructive pulmonary disease (COPD), gastro-oesophageal reflux disease (GERD), and tuberculosis. Environmental factors like smoking, dust, pollution, and allergens also increase the occurrence of cough.

The COVID-19 pandemic further increased the prevalence of cough worldwide, as cough was one of the major symptoms of the infection. Due to its high frequency and multiple causes, cough remains an important public health concern and a common reason for medical consultation.Chronic cough = cough lasting >8 weeks or >3 months. It is a common global health problem Caused by interaction between host and environment.

Asia shows unique patterns due to:

- Rapid urbanization
- Industrialization
- Diverse lifestyle

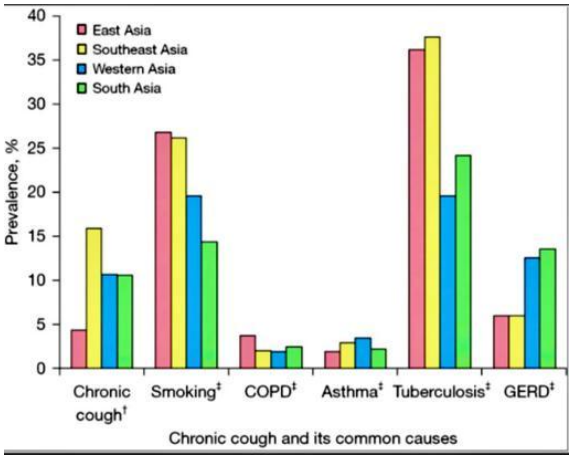

Fig 1: Diagrammatic representation of Prevalence of Chronic Cough and Its Common Causes Across Asian Region

II.COUGH SYRUP RELATED TRAGEDIES

1.COLDRIF COUGH SYRUP TRAGEDY: The deaths 20-24 Children—all under the age of 5—have shaken India following the report of their consumption of a cough syrup that was later discovered to be tainted.1–4 The affected Medicine is Coldrif syrup, Batch No: SR-13 (manufactured on May 2025, expiry on April 2027) of the company Sresan Pharmaceuticals, Kanchipuram, Tamilnadu. According to the laboratory samples, taken from Chennai as well as Bhopal, the syrup contains almost 48.6% diethylene Glycol (DEG) in Chennai and ~46.28% in Bhopal, both of which are highly alarming as the DEG is one of the toxic industrial chemicals. In many children the Death was linked to, acute kidney Failure which was characterized by a decrease in urine output, increase in creatinine and urea. But this is not a medical blunder.

Toxicity:

This tragedy reached a turning point when diethylene glycol was found in the Coldrif syrup. Laboratory testing indicated DEG levels were almost 500 times the safe limit. DEG is extremely poisonous and toxic and can lead to:

- Acute kidney failure
- Brain damage
- Multi-organ failure
- Death

2.**GAMBIA COUGH SYRUP DEATHS (2022)**:The Gambia cough syrup deaths are a mass poisoning incident involving the deaths of at least 70 Gambian children, predominantly under five years, from acute kidney injury due to the consumption of contaminated cough syrups from India.

Key facts:

- Date: July–October 2022
- Victims: About 70 children under age 5
- Cause: Diethylene glycol and ethylene glycol poisoning
- Manufacturer: Maiden Pharmaceuticals Ltd. (India)
- Importer: Atlantic Pharmaceuticals (The Gambia)
- WHO alert issued: October 5, 2022

Background and outbreak:

In mid-2022, Gambia hospitals began to see increased cases of acute kidney injury (AKI) in children.In mid-2022, Gambia hospitals began to see an increase in acute kidney injury (AKI) among young children. The Ministry of Health and the World Health Organization (WHO) conducted

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investigations and found that four syrups—Promethazine Oral Solution, Kofexmalin Baby Cough Syrup, Makoff Baby Cough Syrup and Magrip N Cold Syrup—were manufactured by Maiden Pharmaceuticals.
In the laboratory, lethal levels of two toxic chemicals, diethylene glycol (DEG) and ethylene glycol (EG) present in industrial antifreeze and brake fluid were discovered.This incident led to international alarm, legal action and, as in the case of pharmaceutical supply chains, renewed scrutiny of the global supply chain.

3.CAMEROON CONTAMINATED COUGH SYRUP INCIDENT(2023): These pediatric deaths were reported in 2023 in Cameroon for a cough syrup contaminated with the ingredient diethylene glycol (DEG) under the trade name Naturcold. The incident was part of a pattern of contaminants found to cause the deaths of children in several countries, which led to worldwide warnings and investigations of the quality and supply of medicines.
Key facts:

- Location: Fundong health district, North-West Region, Cameroon
- Period of alert: April-June 2023
- Suspected product: Naturcold pediatric cough syrup.
- Reported child deaths: At least 6–12 children under five years old.
- Main toxic contaminant: Diethylene glycol (DEG), at ~28.6% in some samples.

Background and incident:
In early 2023, the Ministry of Public Health in Cameroon issued an alert due to a number of children who had suddenly developed severe kidney disease and passed away shortly after taking Naturcold syrup for common respiratory ailments. The majority of cases occurred in the Fundong district and were also restricted to children less than five years old. An internal alert was issued in Cameroon and safety warnings were issued in other African countries, such as Nigeria and Ghana, saying that Naturcold was either substandard or contaminated and couldn't be legally sold in some markets. A later test by the World Health Organization (WHO) determined that diethylene glycol (DEG) was present in samples of Naturcold to much higher levels than normal (up to 28.6% against the limit of 0.1%). DEG is an industrial solvent that is used in antifreeze that ingested can cause vomiting, abdominal pain, acute kidney injury and death.

4.UZBEKISTAN COUGH SYRUP SCANDAL :The Uzbekistan cough syrup scandal (2022-2023 Dok-1 Max case) was a mass poisoning tragedy in which at least 68 children in Uzbekistan succumbed to cough syrups that were manufactured in India. The event revealed the defects in the pharmaceutical monitoring system and resulted in the successful holding of a large-scale criminal trial in Tashkent, which ended in 2024.
Key facts:

- Period: December 2022 – February 2024
- Deaths: At least 68 children
- Product involved: Dok-1 Max and Ambronol syrups
- Manufacturer: Marion Biotech
- Distributor: Quramax Medikal
- Main toxin: Diethylene glycol / ethylene glycol

Contamination/Initial response: Child deaths were initially blamed on the imported Dok-1 Max in late 2022 by Uzbek authorities. The amount of diethylene glycol and ethylene glycol were hundreds of times higher than safe levels in laboratory analysis. These industrial solvents are very poisonous, and persons that ingest them will experience kidney failure and death. In January 2023, the World Health Organization issued a global warning of the possibility of the same syrups circulating outside Uzbekistan.

5.INDONESIA ACUTE KIDNEY INJURY OUTBREAK: The acute kidney injury outbreak in August to October 2022 was an outbreak of acute kidney injury in children(primarily <5 years) was reported in hospitals across Indonesia, affecting the entire nation and caused by toxic chemicals in children's liquid medicines. There were hundreds of child cases of acute kidney failure, so drug withdrawals and import restrictions were implemented, and the government made changes to public health policy.
Key Facts:

- Location: Indonesia
- Period: Early–late 2022
- Cases: Over 320 children affected
- Deaths: More than 200 reported
- Presumed cause: Ethylene Glycol And Diethylene Glycol Contamination

Background: The outbreak came to the forefront when clusters were observed in several provinces, and the sale of all syrup based medicines was stopped while investigations were conducted.

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Causes Behind the Tragedies

1. Poor manufacturing practices
2. Use of contaminated raw materials
3. Failure to perform DEG/EG testing
4. Weak regulatory monitoring
5. Irrational fixed-dose combinations
6. Delay in identifying contaminated products
7. Lack of pharmacovigilance and reporting systems

Prevention and Safety Measures

To prevent future cough syrup tragedies, strict pharmaceutical quality control measures are essential. Manufacturers must ensure proper testing of raw materials and finished products. Regulatory authorities should strengthen inspections and enforce Good Manufacturing Practices (GMP).

Healthcare professionals should prescribe cough syrups carefully, especially in children. Public awareness about self-medication and overdose risks is also important. Rapid reporting systems and pharmacovigilance programs can help identify harmful medicines early and reduce mortality.

III.CLINICAL EFFECTS OF DIETHYLENE GLYCOL (DEG) POISONING

Diethylene glycol (DEG) poisoning is a serious toxic condition that has been responsible for several cough syrup-related tragedies worldwide. DEG is an industrial solvent that may accidentally contaminate pharmaceutical preparations. Following ingestion, it is metabolized into toxic compounds, particularly diglycolic acid (DGA), which causes damage to multiple organs, especially the kidneys, nervous system, liver, pancreas, and respiratory system.

Acute Kidney Injury (AKI) is the hallmark feature of DEG poisoning and is the major cause of morbidity and mortality. Toxic metabolites accumulate in proximal renal tubular cells, causing acute tubular necrosis, reduced glomerular filtration rate (GFR), oliguria, anuria, and renal failure. Many patients require hemodialysis for survival. Metabolic acidosis, particularly high anion-gap metabolic acidosis, frequently accompanies AKI due to the accumulation of acidic metabolites and impaired renal acid excretion.

Neurological manifestations range from headache, dizziness, and drowsiness to encephalopathy, seizures, coma, and respiratory failure. Delayed neurological complications such as facial nerve palsy, optic neuritis, hearing loss, peripheral neuropathy, quadriparesis, and ascending paralysis have also been reported. Some survivors experience permanent neurological deficits.

Gastrointestinal symptoms are often the earliest clinical manifestations and include nausea, vomiting, abdominal pain, abdominal cramps, diarrhea, and heartburn. In severe cases, patients may develop severe abdominal pain, back pain, and hematemesis. Respiratory complications such as tachypnea,

pulmonary edema, respiratory failure, and cardiorespiratory arrest may occur, particularly in severe poisoning.

Hepatic involvement is characterized by elevated liver enzymes, hepatomegaly, toxic hepatitis, and centrilobular hepatic necrosis. Pancreatic injury has also been reported, with increased serum amylase and lipase levels and cases of acute pancreatitis. These findings indicate the multi-organ toxic effects of DEG.

In conclusion, DEG poisoning is a life-threatening condition characterized by acute kidney injury, metabolic acidosis, neurological toxicity, respiratory failure, hepatotoxicity, pancreatitis, and gastrointestinal disturbances. Early diagnosis, prompt treatment with supportive care, fomepizole therapy, and hemodialysis are essential to improve patient outcomes and prevent fatalities associated with contaminated cough syrups.

IV.BANNDED COUGH SYRUP IN INDIA:

SL.No.	Syrup / Category	Reason
1.	Coldrif Syrup	DEG contamination
2.	Respifresh TR	Toxic contamination
3.	ReLife Syrup	DEG poisoning

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4.	Marion Biotech syrups (Dok-1 Max, Ambronol)	DEG contamination
5.	QP Pharmachem syrups (Punjab-based)	WHO flagged contamination
6.	Digital Vision Pharma syrups	Substandard quality
7.	Maiden Pharmaceuticals syrups (e.g., Promethazine Oral Solution, Kofexmaaby Cough Syrup)	DEG & Ethylene glycol contamination
8.	Ascoril Flu Drops	Sedation + heart effects due to antihistamine & decongestant
9.	Alex Syrup (Glenmark)	Multi-drug toxicity risk (FDC)
10.	T-Minic (Haleon)	CNS + respiratory + cardiac side effects

BANNED COMBINATIONS FOR COUGH SYRUP FORMULATION:

- Pholcodine + Promethazine
- Chlorpheniramine maleate + Dextromethorphan + Guaifenesin + Ammonium chloride + Menthol
- Chlorpheniramine maleate + Codeine (syrup)
- Ammonium chloride + Bromhexine + Dextromethorphan
- Bromhexine + Dextromethorphan + Ammonium chloride + Menthol
- Dextromethorphan + Chlorpheniramine + Guaifenesin + Ammonium chloride
- Paracetamol + Bromhexine + Phenylephrine + Chlorpheniramine + Guaifenesin
- Salbutamol + Bromhexine
- Chlorpheniramine + Codeine phosphate + Menthol (syrup)
- Ammonium chloride + Sodium citrate + Chlorpheniramine maleate + Menthol (syrup)
- Salbutamol + Hydroxyethyltheophylline (Etofylline) + Bromhexine

V.CONCLUSION

Cough syrups are very important in the treatment of cough but the safety of these cannot be neglected. The recent tragedy obviously demonstrates that even common medicines can be harmful if proper precautions are not taken.

To avoid such incidents there has to be strict quality control in the manufacturing, proper testing of raw material and strong regulatory monitoring. Cough syrups should be used judiciously, particularly in children and should not be used in inappropriate combinations of drugs.

Public awareness is also very crucial. Self-medication is not advised and dosage should always be correct. If there are any unusual symptoms after taking the cough syrup, they should be reported immediately.

To conclude, cough syrups can be very useful medicines but should be taken responsibly, safely, and with proper guidance to avoid the potential serious health risks and future tragedies.

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