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Toxic Exposure in Coldrif Cough Syrup: A Review of the 2025 Pediatric Drug Safety Crisis in India

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ABSTRACT

In the year 2025, India experienced two distressing public health emergencies involving pediatric cough syrups that resulted in numerous child fatalities and hospitalizations. The first incident involved a cough syrup called "Coldrif", which was produced by Sresan Pharmaceuticals and was contaminated with toxic diethylene glycol (DEG). As a result, approximately 11 child deaths were confirmed in Madhya Pradesh. These incidents highlighted serious regulatory failures compounded by poor manufacturing and pharmacovigilance practices; they also emphasized the acute need for reform to improve drug safety in India, focusing specifically on pediatric formulations. This review presents available evidence, regulatory responses, toxicological observations, and lessons learned to strengthen drug regulation, manufacturing oversight, and public health policy in India.

Keywords: Paediatric, Drug safety, Pharmacovigilance.

1. Introduction

Pediatric cough syrups are a common choice throughout India, either prescribed from a healthcare provider or purchased over-the-counter, for common cold symptoms in children. The precaution of using cough syrup, however, is chiefly dependent on the manufacturing process, regulations of oversight, and physicians' prescribing practices. In 2025, India experienced a tragic event regarding the deaths of children consuming contaminated cough syrup: Coldrif, which was contaminated with diethylene glycol (DEG) and contained the active ingredient dextromethorphan hydrobromide.

These incidents are reminiscent of earlier mass poisonings occurring in The Gambia and Uzbekistan in 2022 and 2023, where Indian-made syrups resulted in dozens of deaths, due to DEG contamination. While there is considerable concern globally, it is likely that domestic regulatory safeties were insufficient. The purpose of this review is to document and analyze the Coldrif tragedy and to highlight systemic deficiencies associated with drug manufacturing, toxicological oversight, and the safety of pediatric medication.

Fig. 1 - Cough syrup containing Dextromethorphan Hydrobromide. *(Photo: Getty Images)*

2. Overview of the Coldrif Cough Syrup Incident tting of Mathematical Components

2.1 Background

In the middle of 2025, several children in the Chhindwara district of Madhya Pradesh began showing signs of acute renal failure and quickly worsened after taking a cough syrup known as Coldrif. The cough syrup was produced by Sresan Pharmaceuticals, located in Tamil Nadu.

2.2 Laboratory Findings

After securing a probable cause, the Tamil Nadu Drugs Control Department tested a carton of Coldrif syrup (Batch SR-13, Mfg. May 2025). The results were disturbing- a 48.6% diethylene glycol (DEG) content was detected in the syrup. DEG is a solvent that is highly toxic and is commonly used as an industrial antifreeze and brake fluid. DEG ingestion is strictly prohibited from being used and utilized in pharmaceuticals. Ingesting DEG can produce acute kidney injury, metabolic acidosis, neurological sequelae, and death, especially in children.

2.3 Clinical Outcomes

Health officials in Madhya Pradesh have confirmed that at least 11 child fatalities occurred. More than a dozen other children were hospitalized for symptoms consistent with DEG poisoning. Reportedly, children displayed symptoms of vomiting, altered mental status, and oliguria leading to multi-organ failure.

2.4 Regulatory and Legal Action

After the contamination was confirmed, the following occurred:

- Coldrif syrup was prohibited in Madhya Pradesh and several other states around India such as Tamil Nadu, Punjab, and Maharashtra.
- A joint inspection of the manufacturer revealed >350 GMP violations including, rusted equipment, unclean conditions, no batch validation, and no proper quality control.
- The IMA (Indian Medical Association) filed a police complaint, which resulted in arrests including at least one physician that allegedly distributed the syrup.
- India’s Central Drugs Standard Control Organization (CDSCO) issued alerts and launched a nationwide inspection on poor quality drug manufacturing.
- In Chhattisgarh, after child deaths were reported due to contamination in neighbouring Madhya Pradesh, the state government mandated audits and examinations in pharmacies. The sale of pediatric syrup without prescription was also temporarily prohibited, and syrup including Coldrif (batch SR-13) were randomly sampled for testing.

- The Chhattisgarh Chemist and Druggists Association was instructed to stop the sale of Coldrif and similar syrups until further testing and guidance was performed.

3. Toxicological Analysis

3.1 Diethylene Glycol (DEG) Toxicity

Diethylene glycol (DEG) is a colorless, odorless, hygroscopic liquid used in industry for antifreeze, solvents, and brake fluids. Although it was not designed for pharmaceuticals, it has been used in the past as a cheap adulterant or by virtue of contamination from low-quality excipients such as glycerin or propylene glycol.

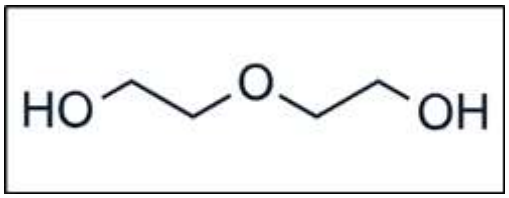

Fig. 2 - Chemical Structure of Diethylene Glycol

Ingestion of DEG leads to:

- Acute kidney injury

- Metabolic acidosis

- CNS depression

- Hepatic failure

- Multi-organ failure

In children, the lethal dose is estimated to be 0.14 mL/kg, though lower doses can be fatal depending on age and hydration status. Symptoms of DEG poisoning may not be immediate, with symptoms beginning 24–72 hours after ingestion

3.2 Dextromethorphan Pharmacology

Dextromethorphan Hydrobromide (DXM) is a non-opioid NMDA antagonist that is an antitussive used to relieve coughing. At low doses, DXM suppresses cough reflexes; at higher doses it can cause:

- Drowsiness, dizziness
- Nausea, vomiting
- Dissociative hallucinations
- Respiratory depression
- CNS toxicity

While generally safe under therapeutic doses, children under 4-6 years old are more sensitive, particularly if dosing errors are made. With Coldrif, any actual contribution of DXM toxicity is secondary to the DEG poisoning.

3.3 Contamination and Drug-Excipient Interaction

The Coldrif syrup's toxicity did not arise from a Dextromethorphan overdose; it resulted from contamination with DEG, likely introduced during the manufacturing process due to contaminated solvents or a deliberate substitute. The substitution of pharmaceutical-grade glycerin with industrial-grade solvent is a common problem in poorly regulated manufacturing settings.

4. Regulatory and Manufacturing Failures

4.1 GMP Violations at Sresan Pharmaceuticals

The Drug Control Department of Tamil Nadu inspected the manufacturing facility and observed more than 350 violations of Good Manufacturing Practices (GMP). Some examples are:

- Unsterilized and corroded equipment being used
- Absence of any validation for testing protocols
- No documented records verifying the raw materials used in manufacturing
- Inadequate batch release records
- No standard operating procedures (SOPs) were in place.

These findings are indicative of systemic operational failure, and strongly suggest that while contamination may have occurred, it would have likely been prevented if routine quality checks were performed.

4.2 Failures in Regulatory Oversight

Although Coldrif syrup was distributed across different states in India, no batch testing conducted at a central location indicated contamination prior to the adverse incident. This indicates:

- A breakdown of robust inter-state coordination across state and central drug authorities

- Missing an important process of mandatory testing for toxicity before batch release

- Delay in pharmacovigilance, including no warnings or recalls ahead of the report

India's Central Drugs Standard Control Organization, CDSCO, issued notice only after children's deaths were reported, indicating a regulatory focus on the reporting of adverse events rather than proactiveness to testing and batch release practice.

5. Public Health Impact

5.1 Pediatric Mortality and Morbidity

As August 2025, consumption of Coldrif syrup in Madhya Pradesh was linked to at least 11 reported child deaths. Additional children were hospitalized with renal and neurological illnesses.

As there is little access to toxicology treatment in rural areas, unreported or undiagnosed cases likely vastly outnumber those reported.

Because of limited toxicology access in rural areas, there may be significantly more undiagnosed or unreported cases than what is formally reported.

5.2 Public Distrust and Panic

The event ignited panic among parents and caregivers, particularly in states where Coldrif was distributed, and the public expressed backlash toward health professionals, undermining trust in government-distributed pediatric medication.

The fact that a doctor and nurse ingested the syrup to observe that it would be safe and subsequently became ill only fueled the public's heightened alarm and media scrutiny.

5.3 International Implications

India has been previously scrutinized globally in 2022 regarding deaths associated with DEG in The Gambia and in 2023 regarding Uzbekistan. The Coldrif case raises further reputation concerns relating to pharmaceutical exports, but this specific incident has only occurred in the Indian domestic market.

International health organizations, including the WHO and UNICEF, have repeatedly called for greater oversight of Indian pharmaceutical production.

6. Discussion

The Coldrif event is simply another instance of the same breakdown of failure of the Indian pharmaceutical manufacturing and regulation system — reminiscent of the earlier DEG tragedies of Haryana (1998), Bangalore (1973). There are similar root causes:

- Substandard ingredients
- Lax enforcement of GMP
- Regulatory leniency toward small-scale manufacturers

The over-burdened and under-resourced drug regulatory system in India, especially at the state level, is not prepared to address these risks, especially for pediatric formulations that require stricter safety margins.

Furthermore, India lacks a real-time, high-quality pharmacovigilance system with the capacity for recall. In addition, there is no pre-distribution toxicity screening, nor the use of a barcode tracking system, contributing to unsafe drugs remaining on the marketplace under the radar.

7. Discussion

The 2025 Coldrif syrup tragedy highlights the potential for inadequate pharmaceutical oversight to allow a life-saving medicine to become a poison that kills. The lack of past experience with DEG has left India’s regulatory and manufacturing environments at risk of failure once again. The most vulnerable population, children, have bore the worst consequences.

This review urges a need for urgent and systemic reform - not only to enhance standards of drug manufacturing, but also to restore trust in India's health system. If done in good faith, the recommendations in this paper could avert similar, avoidable tragedies in the future.

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