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## Toxicological Profile of Diethylene Glycol and Its Implications in Pediatric Cough Syrup Poisonings

*Soham Ravindra Parthe\*, lokesh vyas, Sonali uppalwar*

### ABSTRACT:

When ingested, ethylene glycol (EG), which is frequently present in goods like antifreeze, can result in potentially fatal poisoning. While children are frequently exposed through unintentional drinking from unlabeled containers, adults may purposefully consume it or use it as an alcohol substitute. EG is not very toxic in and of itself, but the body quickly transforms it into toxic acids that harm the kidneys, heart, brain, and lungs. Kidney failure may result from severe acidosis and calcium oxalate crystals caused by these toxic byproducts. A number of fatal cases demonstrate how rapidly symptoms can worsen in the absence of prompt diagnosis and treatment. In low- and middle-income nations, tainted children's cough syrups containing EG or diethylene glycol (DEG) have recently led to poisoning outbreaks and tragic deaths.

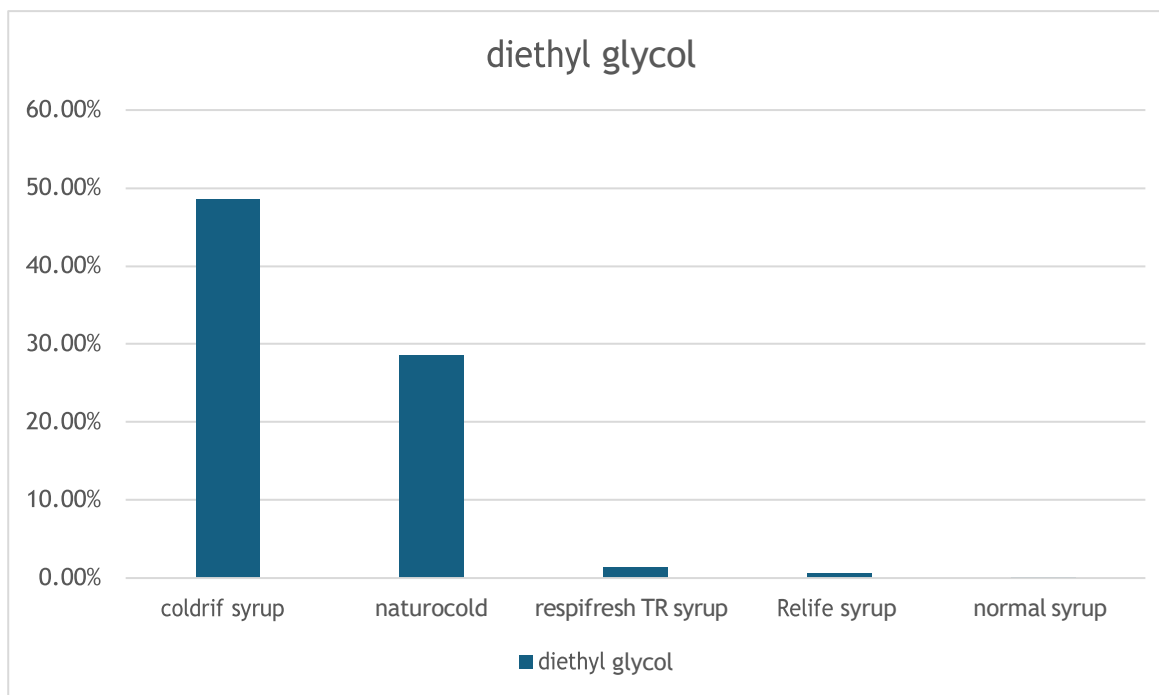
### INTRODUCTION

Glycerol and safe, pharmaceutical-grade PG are used in medicinal syrups to add thickness and sweetness. Because they can cause serious organ damage and even death, hazardous industrial chemicals like DEG and EG should never be used.[1] The enzymes alcohol dehydrogenase and aldehyde dehydrogenase break down alcohol to produce these harmful metabolites.[1,2] Because DEG and EG are much less expensive than pharmaceutical-grade propylene glycol (PG) and glycerol, medical products may become contaminated with them if barrels are inadvertently or purposely mislabelled. Although glycerol and PG of industrial grade are less expensive, they should never be utilised in pharmaceutical products.[3] Glycolic acid and oxalic acid, the breakdown products of ethylene glycol, are toxic to the body and contribute significantly to severe metabolic acidosis.[4,5] Elixir Sulfanilamide, an antibiotic, was the subject of the first documented case of poisoning from tainted medication in the United States in 1937.[6] Products like antifreeze contain ethylene glycol, a sweet-tasting, odourless liquid. It absorbs quickly when swallowed and can cause dangerous poisoning within hours.[7] The breakdown

products of ethylene glycol are toxic to cells. They prevent the body from producing energy normally, which can result in symptoms like sleepiness or unconsciousness and ultimately lead to heart, lung, and kidney failure.[8,9] The slowest step in breaking down ethylene glycol is converting glycolic acid into glyoxylic acid. Glycolic acid accumulates in the bloodstream due to the slow pace of this process. The excess glycolic acid leads to severe acidosis, and oxalate crystals can form when it combines with calcium, causing deposits in the kidneys and other tissues[10,11] In October 2025, reports linked a serious outbreak to contaminated medicine containing diethylene glycol, causing the deaths of about 20–23 children in Madhya Pradesh and nearby regions—a heartbreaking public health tragedy.[12] During sample testing, the authorities banned the entire batch and detained the company's leaders.[13,14] These most recent occurrences come after other worldwide incidents, such as The Gambia in 2022, where Indian-made syrups were connected to DEG/EG pollution and child fatalities, leading governments and the WHO to issue warnings following scores of infant deaths.[15,16,17]

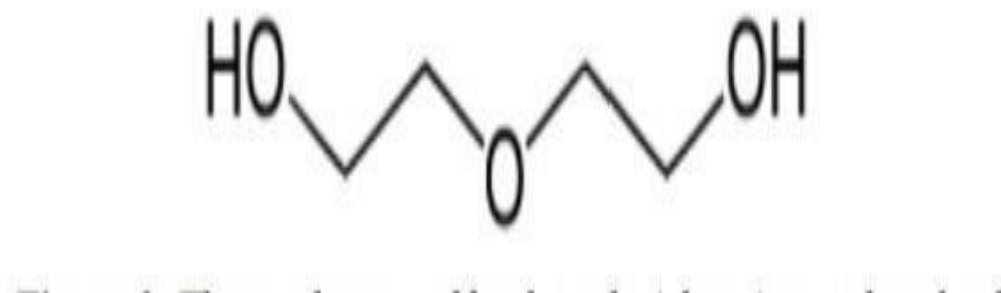
### TOXICOLOGY AND MECHANISM OF INJURY

Diethylene glycol (DEG) and ethylene glycol (EG), two tiny, sweet-tasting solvents, are used illegally by some manufacturers as low-cost alternatives to safe pharmaceutical components like glycerine and propylene glycol.[18] Once ingested, these chemicals are broken down in the body into hazardous metabolites, such as oxalic and glycolic acids. These can damage the kidneys, alter the body's acid balance, and depress the central nervous system.[19,20] Due to their smaller stature and impaired renal function, children are particularly at risk. The sickness frequently begins with symptoms affecting the brain and digestive system, and over 24 to 72 hours, it can escalate to acute kidney injury. If not treated, it can be fatal.[21]

**TABLE :1** syrup and diethylene glycol percentages

### Diethylene Glycol Pathophysiology

Human pharmacokinetic data for DEG were not collected directly. This is mainly because DEG metabolites are highly hazardous, and cases of DEG poisoning are generally discovered late, making it difficult to obtain correct data. For this reason, preclinical studies are a vital tool for understanding how DEG generates toxicity and its effects on the body [22] Although DEG is constituted of two ethylene glycol molecules, it creates distinct metabolites. DEG does not produce kidney-damaging calcium oxalate crystals like EG does.[23,24] ADH and ALDH convert 50–70% of DEG in rat studies into HEAA, which is mostly eliminated by the kidneys and results in organ damage and metabolic acidosis in DEG overdose.[25,26] Kidney damage from DEG poisoning occurs because DGA induces tubular cell death, edoema, and obstructions, which limit urine flow and can lead to anuria and uraemia.[27]

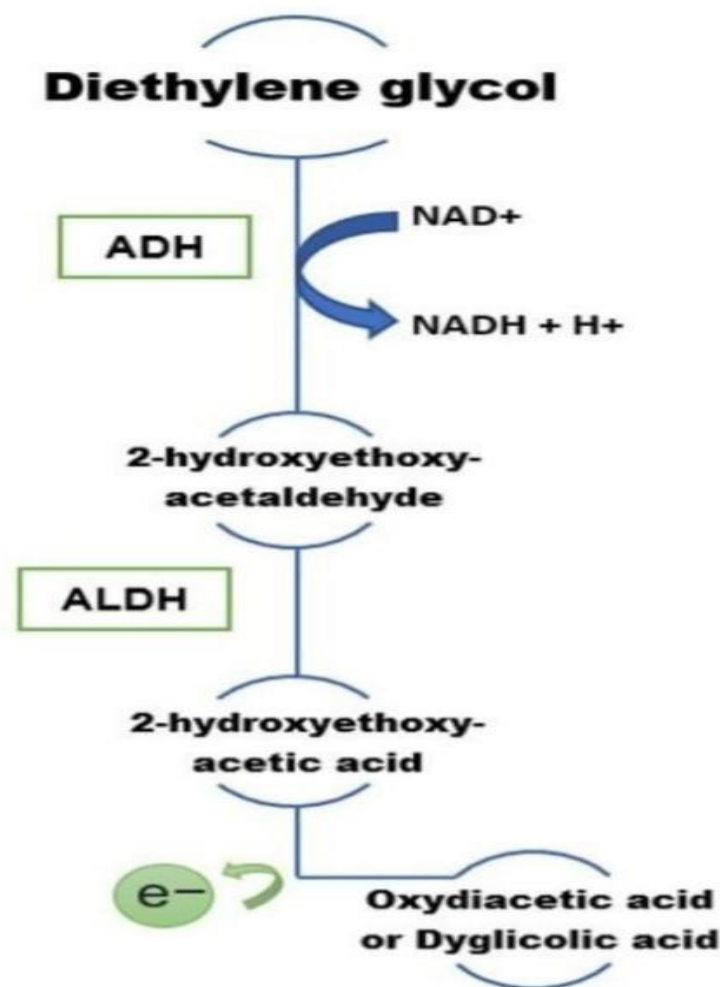
**Figure: 1** Diethyl Glycol

### Manufacturing, supply-chain and regulatory failures patterns and lessons

Financial strains or inadequate supplier inspections frequently cause outbreaks, which are exacerbated by inadequate testing of raw materials and finished goods and result in the hazardous replacement of medicinal components with industrial glycols.[28,29,30] Failures in detection and enforcement occurs because laboratory resources are distributed too thin and regulatory monitoring is insufficient.[31] India's regulatory agency, DCGI, has tightened regulations in the wake of the October 2025 incident, demanding quick sample testing and DEG/EG testing of raw materials and completed goods. These regulations are in line with WHO guidelines but must be strictly enforced.[32] Immediate measures include collecting stockpiles, banning items, conducting targeted tests on new lots and manufacturers, and, when appropriate, holding responsible company executives accountable, including possible arrests.[33,34] As declared by DCGI and backed by international agencies, stricter regulations include centralised reporting, increased lab capacity, and DEG/EG testing in excipients and final goods.[35,32,33] All glycerine/propylene glycol batches and completed children's oral liquids must be tested for DEG/EG as required by regulators. Manufacturers must follow suppliers, retain certificates of analysis, and guarantee these documents are available for regulatory examinations.[32,36]

### Principles of management

First, make sure the patient's respiration, circulation, airway, seizures, and fluids are all under control. Fomepizole is the principal antidote for toxic alcohol poisoning; if unavailable, ethanol can be used instead [37] Public health teams work to identify and remove contaminated products or areas. They actively search for new cases and make sure to inform both the public and healthcare professionals prompted [38,39]



**Figure:2** Diethylene glycol is initially metabolized by alcohol dehydrogenase to 2- hydroxyethoxy acetaldehyde. This is then further metabolized by aldehyde dehydrogenase into 2-hydroxyethoxy acetic acid, also known as HEAA, which is the causative agent for metabolic acidosis and organ damage. DEG toxicity does not involve calcium oxalate crystals, in contrast to certain other poisonings.

Adapted from: Kraut, J. A., C Kurtz, I. (2008). Toxic Alcohol Ingestions: Clinical Features, Diagnosis, and Management. Clinical Journal of the American Society of Nephrology, 3(1), 208–225. Doi:10.2215/cjn.03220807

### DIAGNOSIS

The patient's history, symptoms, and the clinician's degree of suspicion are typically taken into consideration while starting treatment. Although gas chromatography can be used to confirm exposure, these tests are not widely available.[40] You may also find higher-than- normal levels of liver enzymes and amylase in the Blood [41,42] The osmolal gap frequently increases—sometimes exceeding 20 mOsm/L—in the initial hours following poisoning, indicating the presence of a tiny, unknown chemical in the body.[41] Clinical warning signs to watch for in children who have recently taken cough syrup include vomiting, unusual tiredness or low energy, peeing much less than normal (or not at all), quick breathing to compensate for metabolic acidosis, and high creatinine values that may imply kidney problems.[19] Lab findings may demonstrate growing azotaemia, an increased osmolar gap, and a high–anion-gap metabolic acidosis. When available, toxicological tests can detect the presence of DEG or EG.[43]

### TREATMENT

Even though there isn't much evidence available, treatment for DEG poisoning normally comprises supportive care, washing the gastrointestinal tract, treating any acid–base imbalances, and in certain cases employing hemodialysis [44 ] To inhibit alcohol dehydrogenase and stop DEG from being metabolised, some experts

advise using ethanol or fomepizole. When it comes to binding to this enzyme, fomepizole is roughly 500 times more powerful than ethanol, and even at much lower blood concentrations, it can completely inhibit its action.[45,46] Fomepizole treats methanol and ethylene glycol toxicity but is pricey and hard to obtain. Ethanol is more affordable and readily available. For DEG poisoning, fomepizole is used off-label and given intravenous pH.[47,48]

Hemodialysis may also be required to help eliminate DEG and its metabolites from the body and to address serious metabolic issues.[44,49,50]

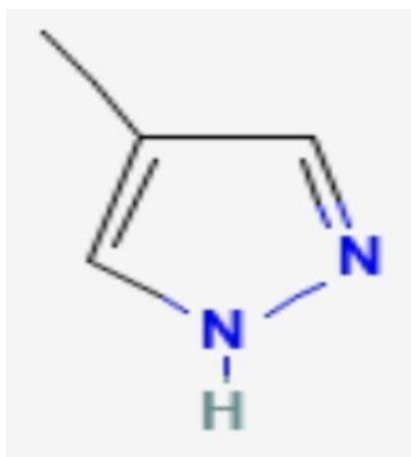


Figure :3 Fomepizole

## Conclusion:

Diethylene glycol is extremely toxic, causing serious damage to the kidneys, brain, and metabolism. Paediatric cough syrup poisonings highlight regulatory gaps and stress the need for stringent quality control, early clinical recognition, and preventive measures to avoid fatal outcomes.

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