

Letter to the Editor: Toothpastes with diethylene glycol

Dear Editor,

On the 5th July of last year, the Ministry of Health and Consumer Affairs issued a health alert on the petition of the Spanish Drugs Agency due to the possible distribution of “suspicious” tubes of toothpaste in Spain. The adoption of this precautionary measure had its origin in the United States where, one month earlier, the Health Authorities found that some toothpastes imported from China contained up to 4% of a toxic substance called diethylene glycol (DEG) (1). In the analyses performed by the Centre for Research and Quality Control, of the Ministry of Health, DEG was detected in tubes of toothpaste included in washing bags that, paradoxically, had been provided to the patients of 6 public hospitals in the Valencian Community. A few days after issuing the health alert, about 180,000 “suspicious” packets of toothpaste had been seized in our country, from outlets in Andalusia, Asturias, Canary Islands, Castille-La Mancha, Castille and Leon, Catalunya, Ceuta, the Valencian Community, Extremadura, Galicia, the Basque Country, Rioja, Madrid, and Murcia. It was demonstrated that these toothpastes were not contaminated with DEG and that the “irregularities” to which the Ministry of Health referred were formal defects of labelling. Based on the results of this research, the Spanish Health Authorities minimised the importance of this episode, arguing that “the risk to health that the presence of DEG represents in toothpaste is minimal, as the paste is not swallowed in the quantities that would be necessary to cause toxicity”. Although this is probably a prudent attitude to take in order to avoid social alarm, we, as health professionals, are obliged to reflect more profoundly on this event.

DEG is an organic solvent discovered in 1869, and used in industry as antifreeze, a glycerine substitute, for the production of theatrical fog, and for the production of resins and explosives. The ingestion of DEG is a serious medical emergency, as its toxic potential can cause death in less than 48 hours; although the most common manifestation of acute poisoning is severe renal failure, it can also give rise to serious neurological alterations, cardiopulmonary disease, hepatitis and pancreatitis (2). The lethal dose in humans may be as low as 0.014 milligrams of DEG per kilogram body weight.

DEG was first used as a vehicle for the manufacture of drugs in 1937, specifically for the marketing of a sulfamide (sulfanilamide) in the form of a suspension, indicated for the treatment of streptococcal infections; its administration caused the death of 105 patients, and the rapid intervention of the FDA (Food and Drug Administration) was estimated to have avoided around 4000 victims (3). This dramatic episode was of particular relevance, as it served to push through legislation to protect citizens from

the dangers inherent to the premature distribution of new drugs; this legislation came into force in 1938 under the title of the “Federal Food, Drug and Cosmetic Act” (4). The greatest demonstration of its utility probably occurred almost 25 years later, on finding that virtually no embryopathies secondary to the administration of thalidomide had been detected in the United States, compared to the epidemic scale of those malformation in Europe. During the late seventies, sporadic episodes of DEG poisoning have been reported after the administration of drugs that contain this solvent, leading inexorably to a significant number of deaths (5-13) (Table 1). The majority of cases have occurred in developing countries and the drug in which the DEG was most often detected was Paracetamol in suspension, this being the probable reason for the predominance of children among the affected patients.

Some of the tubes of toothpaste withdrawn from the Valencian hospitals contained up to 8% of DEG, which is a potentially toxic concentration. DEG is rapidly absorbed from the digestive and respiratory tracts, and also through prolonged contact with the skin; in 1987, 5 patients admitted to a Burns Unit in Spain died due to acute poisoning with DEG after the topical application of a silver sulfadiazine cream that contained this toxin as an excipient (14). At the present time, the rate of absorption of DEG through the oral mucosa and the risks inherent to chronic exposure are unknown. The Ministry of Health and Consumer Affairs catalogues toothpastes under “cosmetics and products for personal hygiene”, and this permits their marketing under more permissive regulations that those that apply to medicaments. However, alerts have already been published in the literature concerning the occasional inclusion into toothpastes of products with potential systemic repercussions (15), and there are many references to undesirable effects such as allergic stomatitis (16), plasma cell gingivitis (17), or the development of leucoplakia (18,19). In summary, we should consider this episode as a further argument for the Health Authorities to analyse rigorously the innocuousness of “cosmetics and products for personal hygiene”, or even reconsider whether products that come into direct contact with the oral mucosa, such as toothpastes and mouth rinses, should be included in this category. For their part, dentists must gather specific information on the use of these products when taking a clinical history, and must take them into account when establishing a diagnostic suspicion.

Table 1. Episodes of acute diethylene glycol poisoning due to the administration of drugs contaminated with this solvent.

YEAR (reference)	COUNTRY	NUMBER of DEATHS	CONTAMINATED DRUG
1937 (3)	United States	105	Sulfanilamide in suspension
1969 (5)	South Africa	7	Antipyretics and sedatives in suspension
1986 (6)	India	14	Glycerine
1990 (7)	Nigeria	47	Paracetamol in suspension
1990-1992 (8)	Bangladesh	185	Paracetamol in suspension
1995-1996 (9)	Haiti	88	Paracetamol in suspension
1998 (10)	India	33	Expectorant syrup
2005 (11)	Argentina	15	Propolis syrup
2006 (12)	Panama	40	Antitussive syrup
2006 (13)	India	11	Paracetamol in suspension

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