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Glycidyl Methacrylate as Probably Carcinogenic to Humans

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Abstract

Glycidyl methacrylate (GMA) is a monomer widely used in the production of dyes, paper, beverages, epoxy polymers, and others. It is a genotoxic substance with occupational exposure that can reach the general population by inhalation and skin contact. This agent may produce a large spectrum of DNA damage, evidenced by various carcinogenicity studies conducted on animals, and strong evidence of being carcinogenic in primary human cells. There is a deficit/absence of studies related to and no threshold limit value for GMA, however, due to the principles of similarity and precaution, it should be classified as a human carcinogen, and collective and personal control measures should be implemented or reviewed. This study provides an alert of GMA human exposure and its genotoxic and carcinogenic potential.

Keywords: Glycidyl methacrylate • Carcinogenicity • Occupational exposure

Description

Glycidyl methacrylate (GMA, CAS nº106-91-2), an ester of methacrylic acid, is a chemical monomer used for the manufacture of epoxy polymers, acrylic and vinyl resins, dental resins and sealants, polymer coatings, adhesives, dyes, paper, beverages, and wastewater treatment [1-4]. Exposure to this agent may occur in various occupational settings as in the general population [3]. However, polymers can release monomers and co-monomers into the bloodstream, reaching all organs [5].

The most common occupational route of carcinogenic agent's absorption is inhalation, followed by the skin. Many substances are known to be genotoxic with the potential to cause genetic changes in the target tissue. Such alterations, if they occur in proto-oncogenes and tumor suppressor genes involved in the control of cell growth or differentiation, can lead to cancer initiation in target organs [6]. GMA is a genotoxic substance and therefore has this property.

The genotoxicity of methacrylate-monomers has special significance due to potential and severe phenotypic consequences such as cell death, mutations, cancer, and long latency period [5]. Furthermore, GMA induces an increase in the G2/M cell population, accompanied by a marked decrease in the S-phase cells and an increase in G0/G1 cell population [7]. Due to the broad spectrum of GMA genotoxicity, its use should be accompanied by precautions, reducing the chance of its release into the bloodstream and the possibility to induce adverse biological effects.

Poplawski et al. [5] suggest that methacrylate may start a broad spectrum of DNA damage, which may be the cause of mutagenicity, and potential carcinogenicity. There is strong evidence that GMA exhibits key characteristics of carcinogens to primary human cells. Moreover, there has been sufficient evidence in experimental animals to demonstrate the carcinogenicity of GMA. Studies revealed an increased incidence of malignant neoplasms in both sexes of two species exposed by inhalation. GMA induced nasal cavity haemangiosarcoma in both male and female mice, bronchioloalveolar carcinoma and uterine histiocytic sarcoma in female mice, nasal cavity squamous cell carcinoma in both males and female rats, and peritoneal mesothelioma in male rats [4].

An IARC Monographs Working Group reviewed epidemiological evidence, animal bioassays, and mechanistic evidence to reach conclusions such as the carcinogenic hazard to humans of exposure to GMA [3]. Figure 1 shows the level of certainty that a substance

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causes câncer [3]. Corroborating with these data, the European Trade Union Institute [8] published a list of potential carcinogens (or groups of carcinogens) to which GMA should incorporate in the Carcinogens and Mutagens Directive 2004/37/EC (CMD). The last published evidence makes us believe that GMA probably will be classified as carcinogenic to humans (Group 2A).

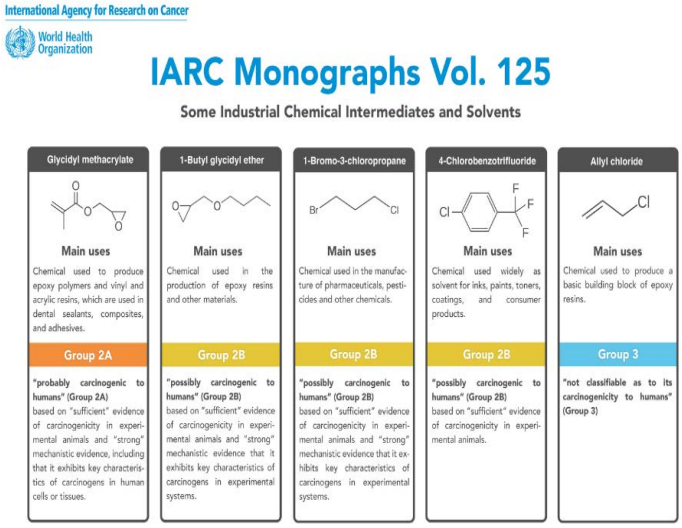

Figure 1. Level of certainty that a substance causes cancer [3].

There is no TLV-TWA (Threshold Limit Values-Time Weighted Average) for GMA [9,10]. The American Conference of Governmental Industrial Hygienists (ACGIH) provides the community with an indication of where chemical substances and other questions under study (TLV-CS Committee) fall in the development process. GMA is a substance that may move forward as a Notice of Intended Changes (NIC) or Notice of Intent to Establish (NIE) proposal in 2022, based on their status in the development process [11].

Therefore, based on the deficit or inexistence of GMA studies and the principles of similarity and precaution, we suggest classifying GMA as a probable human carcinogen. Collective and personal control measures should be reviewed, including, if possible, items related to workers' health surveillance. According to the Organization for Economic Co-operation and Development [10], there is a need to limit the exposure risk to GMA. The reclassification of GMA toxicological risk should evaluate health risks such as high eye irritation, skin sensitization, and genotoxic potential. It is important to emphasize that the analysis of a single substance does not reflect real-life exposures because individuals are exposed to mixtures of substances. So other risks can act in a cumulative or antagonistic fashion or even contain unknown components.

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Declaration of Conflicting Interests

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