



Skin Contact: Irritancy, Sensitization, and Penetration of Glutaraldehyde

Glutaraldehyde can cause irritation if in contact with the skin, and in a small percentage of exposed individuals, skin sensitization has been reported. Glutaraldehyde at concentrations of 10 percent and less is not known to be absorbed across the skin in harmful amounts.

Skin Irritation

Skin irritation from exposure to glutaraldehyde is affected by a number of factors. These include the site of contact on the body, concentration of glutaraldehyde, duration of contact, and whether the contact site is open to the air or covered. Concentrations up to five percent may not induce an irritant effect if only briefly applied to bare skin, but may be an irritant if the skin is occluded, such as seepage of glutaraldehyde under protective clothing or gloves. In general, by sustained contact for several hours under occlusive conditions on sensitive skin, the threshold for inducing primary skin irritation is 0.2 percent glutaraldehyde, or 2000 ppm active.

Concentrations of glutaraldehyde below 1000 ppm, typical of industrial applications, have not demonstrated skin irritation. At 2000 ppm, less than three percent of tested human volunteers had marginal erythematous reaction. Low concentrations of glutaraldehyde, e.g., two to four percent, may cause minor irritation with local itching and possible slight local redness. Prolonged contact and concentrations higher than five percent cause mild-to-moderate local redness and swelling. Aqueous glutaraldehyde solutions containing 45 percent and greater may be corrosive to the skin.

Skin Sensitization

Several reports of observations on humans indicate that glutaraldehyde has a potential to produce allergic contact dermatitis⁽¹⁾. The number of reports relative to the widespread and diverse usage of glutaraldehyde, as well as controlled studies involving human volunteers⁽²⁾, suggest a low incidence (less than a few percent) of skin sensitization. This is confirmed by the comparatively few cases of skin sensitization to glutaraldehyde described in reports documenting the deliberate use of glutaraldehyde to treat various dermatological disorders. There is no cross-sensitization to aliphatic monoaldehydes (e.g., formaldehyde).

Skin Penetration

Laboratory studies and observations on humans provide no evidence that glutaraldehyde can be absorbed across the skin in harmful amounts. *In vitro*⁽³⁾ skin penetration studies showed that human skin had a permeability about that of rat skin, but was significantly less permeable to glutaraldehyde than the skin of mouse, rabbit, or guinea pig. Glutaraldehyde is a protein-crosslinking agent, and its reactivity with skin proteins is a major factor in limiting percutaneous absorption. Studies applying up to 7.5 percent radio-labeled glutaraldehyde to the skin showed the largest proportion remained in the skin at the site of application.

The low potential for systemic toxicity by absorption of glutaraldehyde across the skin has been confirmed by *in vivo* material balance and pharmacokinetic studies, which have shown that percutaneous absorption is limited; that there is relatively rapid elimination of glutaraldehyde and metabolites from the body; and that there is no selective accumulation of glutaraldehyde (or metabolites) in any tissue or organ. Thus, in practice, it is unlikely that substantial amounts of glutaraldehyde will be absorbed across the skin, particularly if skin is rinsed immediately after contamination.

To determine the potential for cumulative local and systemic toxicity by repeated application to the skin, an extensively monitored study was conducted in the rat (which has skin permeability characteristics similar

to that of the human). Twenty applications of up to 7.5 percent aqueous glutaraldehyde each for six hours were made over a 28-day period. There was only one minor and intermittent local erythema, and no evidence of any percutaneous systemic target organ or tissue toxicity.

Precautions

- Immediately remove contaminated clothing, or protective gloves, if glutaraldehyde seeps into glove.
- Rinse skin immediately with plenty of water for 15-20 minutes.
- Obtain medical attention if irritation persists.
- Wash contaminated clothing before reuse. Discard if disposable. If contaminated shoes or clothing cannot be thoroughly washed, discard.

Glutaraldehyde is an irritant to mucosal surfaces, and if introduced into body cavities it can lead to inflammatory reactions. This has occurred with medical instruments that have been inadequately rinsed after high level disinfection with glutaraldehyde solutions. It has been most frequently reported with residual glutaraldehyde in lower bowel endoscopes, such as colonoscopes, leading to colitis or proctocolitis. Other less frequently described complications include laryngotracheitis with poorly washed endotracheal tubes, and synovitis with arthroscopes. These cases clearly indicate the need to ensure that endoscopes and other surgical instruments are completely decontaminated of the disinfectant. This should be accomplished by manually rinsing with fresh water multiple times (consult with the sterilant manufacturer to determine how many rinses are necessary) or, preferably, with automatic reprocessors equipped with a full rinse cycle.

Footnotes

1. Allergic contact dermatitis is a reaction elicited by the immune system when it recognizes a material as biologically "foreign," and may occur in response to exposure to a chemical substance. It differs from simple irritation in that prior exposure to the substance, or in some cases a closely related substance, is required to induce the allergic state (*i.e.*, sensitize) in susceptible individuals. In the sensitized individual, the concentration needed to produce allergic contact dermatitis is lower than that needed to produce a primary irritant effect. Furthermore, the variability in susceptibility between individuals of a population tends to be greater for sensitization than for many other types of toxic effects. Thus, the proportion of a population that may develop sensitization to a given material is as important as the severity of the effects produced.
2. Ballantyne, B. and Berman, B. (1984). "Dermal sensitizing potential of glutaraldehyde: a review and recent observations." *J. Toxicol. - Cut. and Ocular Toxicol.*, 3, 251-262, and Marzulli, F.N. and Maibach, H.I. (1974). "The use of graded concentrations in studying skin sensitizers: Experimental contact sensitization in man." *Food Cosmetic Toxicol.*, 12, 219-227, and Weaver, J.E. and Maibach, H.I. (1974). "Dose response relationships in allergic contact dermatitis: Glutaraldehyde-containing fabric softener." *Contact Dermat.*, 3, 65-68.
3. *In vivo* means in the living tissues of a plant or animal, as opposed to *in vitro*, which is outside the living body and in an artificial environment. Hence, *in vivo* studies are carried out in living organisms, and *in vitro* studies in culture media.

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