Lubrizol

TECHNICAL DATA SHEET

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Toxicity of Carbopol® Polymers As A Class

The Carbopol® polymers, like other high molecular weight polymers, demonstrate a low toxic and irritation potential based on their physical and chemical properties. Accordingly, such cross-linked, high molecular weight acrylic polymers have been found safe for use in a wide variety of cosmetics, detergents and pharmaceuticals by appropriate regulatory and nonregulatory bodies concerned with such products.

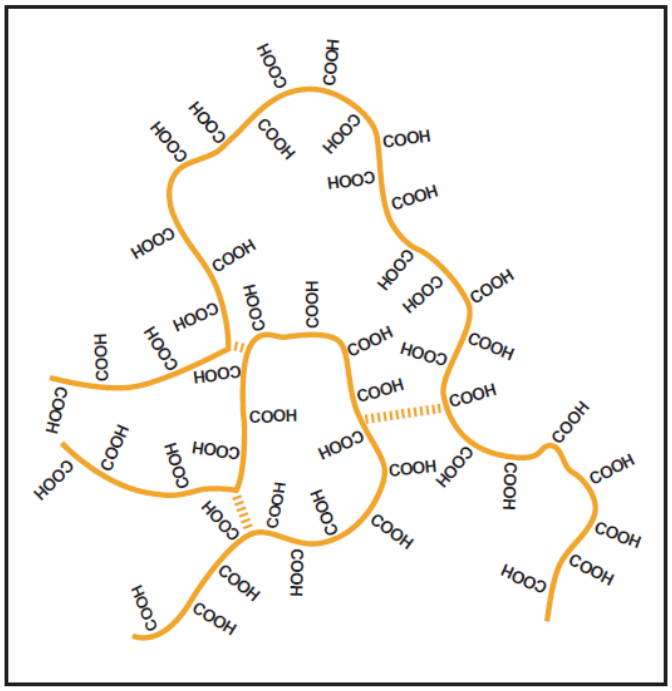
he chemical composition and the chemical and physical properties of the Carbopol polymers suggest that similar toxicological properties are to be expected with these polymers. The Carbopol polymers are cross-linked homopolymers of acrylic acid or cross-linked copolymers of acrylic acid with a minor acrylic comonomer.

The molecular weight range of these polymers is estimated to be from 740,000 to 4-5 million. There are no methods available to measure the actual molecular weight of a cross-linked (i.e. 3-dimen-sional) polymer of this type. The backbone of the homopolymer Carbopol is the same (see Figure 1). The main difference is related to cross-link density and molecular weight, rather than the cross-linker used. With very minor adjustments in the cross-linker density, one can produce a large number of Carbopol type products similar in gross molecular structure but varying in application properties, for example, viscosity. Cross-link density can be varied by minor shifts in position of the cross-linker on the acrylic backbone (Figure 1).

Because the actual cross-linker itself has little, if any, effect on the biological properties of a particular Carbopol polymer, the Cosmetic, Toiletries and Fragrance Association (CTFA) has adapted a family monograph, "carbomer," for the Carbopol homo-polymer polymers.

The three-dimensional nature of these polymers confers some unique characteristics, such as biological inertness, not found in similar linear polymers. The Carbopol polymers are hydrophilic substances that are not soluble in water. Rather, these so-called "water soluble" polymers swell when dispersed in water forming a colloidal, mucilage-like dispersion.

Figure 1
Schematic drawing of a molecular segment of a cross-linked polyacrylic acid polymer



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Many of the Carbopol polymers have found diverse applications in the cosmetic, detergent and pharmaceutical industries. Due to their physical properties, inertness and low toxicity, the Carbopol polymers have been used in such preparations as suspending, flow control, thickening and emulsion stabilizing agents.

Another family member, Carbopol 934P, has a National Formulary (USP-NF) monograph, carbomer 934-P, pertaining to its use as a drug ingredient. Due to the use of Carbopol 934-P in a wide variety of internal and external pharmaceuticals, an extensive drug master file (DMF #153) is maintained with the Food and Drug Administration.

Carbomer is the generic (i.e. nonproprietary) name adopted by USP-NF, United States Adopted Names Council (USAN) and CTFA for various Carbopol polymers. The Cosmetic Ingredient Review (CIR) Expert Panel in their assessment* of the safety of the carbomers for cosmetic ingredients summarized the toxicity of the carbomers as follows:

Acute oral studies with rats, guinea pigs, mice, and dogs showed that carbomers 910, -934, -940 and -941 have low toxicities when ingested. The inhalation LC_{50} of carbomer 910 in albino rats was 1.71 mg/l. The dermal LD_{50} of rats exposed to carbomer 910 was greater than 3.0 g/kg. No mortalities occurred in rabbits injected intravenously with 1%, 2% or 3% carbomer 934 in aqueous solution at a dose of 5 ml/kg. Rabbits showed minimal skin irritation when tested with 100% carbomer 910 or -934, and zero to moderate eye irritation when tested with carbomers 910, -934, -934P, -940, -941, and/or their various salts at concentrations of 0.20-100%.

Subchronic feeding of rats with doses up to 5.0 g/kg/day carbomer 934 (49 days) and of rats and dogs with up to 5.0% carbomer 934P in the diet (21 and/or 90 days) resulted in lower than normal body weights. In rats fed carbomer 934P at dietary levels of 5.0% for 90 days, absolute liver weights and liver to body and brain weight ratios were reduced, but no pathological changes were observed.

When dogs were chronically fed up to 1.0 g/kg/day carbomer 934 (32 months) or -934P (six and one-half months), and when rats chronically received less than 4.0% carbomer 934P in their diet (six and one-half months), there was no significant effect on body weight, food consumption, mortality, behavior, or blood chemistries. Hematology, gross pathology, histology, and urinalyses of treated animals were comparable to those of controls.

Rats fed carbomer 934P at dietary levels of 0.1%, 0.5%, or 5.0% for six and one-half months exhibited various organ weight changes. Dogs fed 0.5 or 1.0 g/kg/day carbomer 934P for six and one-half months manifested gastrointestinal irritation and marked pigment deposition within Kupffer cells of the liver.

Clinical studies with carbomer 934 and its various salts showed that these polymers have low potential for skin irritation and sensitization at concentrations of 0.5%, 5.0%, 10.0%, and 100%. When tested on humans at 1.0% concentration, carbomers 940, -941, and their various salts also demonstrated low potential for skin irritation and sensitization. Further, formulations containing up to 0.25% carbomer 934 demonstrated low potential for human skin irritation, sensitization, phototoxicity, and photo-contact allergenicity.

Clinical data for assessing the skin irritation and sensitization potential of carbomer 940 and -941 were limited to studies in which concentrations of only 1.0% were tested. Clinical data for assessing phototoxicity and photo-contact allergenicity were limited to formulation studies in which concentrations of only 0.25% carbomer 934 were tested.

The CIR Expert Panel called attention to the presence of benzene as an impurity in the carbomers and recommended efforts to reduce it to the lowest possible level.

In pursuit of this goal, Lubrizol Advanced Materials, Inc. has developed new Carbopol polymers which use alternate polymerization solvent systems (e.g. ethyl acetate, cyclohexane, etc.). These Carbopol polymers are chemically identical to the benzene polymerized Carbopol polymers and are therefore listed on the U.S. Environmental Protection Agency's TSCA inventory as acrylic acid polymers or acrylic acid copolymers.

Preliminary toxicity test results on the ethyl acetate polymerized polymers are essentially similar to the previous products. They are not primary irritants or sensitizers in human repeated patch tests. The dermal LD_{50} was greater than 2000 mg/kg of body weight in the rabbit. Likewise it was minimally irritating to rabbit eyes. An acute oral LD_{50} could not be obtained since intubation of enough polymer was not possible.

* "Final Assessment Report of the Safety of Carbomers -934, -910, -934P, -940, -941, and -962" Journal of the American College of Toxicology, Vol. 1, No. 2, 1982, pp. 109-141.

Results on a Carbopol copolymer polymer made in ethyl acetate were consistent with the results expected for these polymers. That is, it was not an irritant to rabbit skin; undiluted polymer was a mild to moderate irritant to the rabbit eyes, while a 1% solution (neutralized and unneutralized) were not eye irritants; application to human skin did not cause any skin irritation or sensitization. The LD_{50} in rats is greater than 5,000 mg/kg and the dermal LD_{50} in rabbits is greater than 2,000 mg/kg.