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Miscellanea

Experimental Studies on Skin Hazard with *Cycloocta-1,5-diene* and *Cyclododeca-1,5,9-triene*

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The two oligomers, *cycloocta-1,5-diene* (COD) and *cyclododeca-1,5,9-triene* (CDT), are very reactive chemicals and have applications as intermediates in the plastics industry, in the manufacture of synthetic lubricants, and in numerous other industrial and laboratory reactions.

No published information has been found on the toxicity of these chemicals, and the experimental studies reported here were designed to give guidance on the dermal aspect of safe handling.

Experimental

The samples of COD and CDT were obtained from Shell Chemicals U.K. Company Ltd. The COD sample contained 98% w/w of the *cis, cis*-isomer with 0.02% w/w 2,6-diterbutyl-4-methylphenol to inhibit the formation of peroxides. The CDT sample contained at least 90% w/w of the *cis, trans, trans*-isomer with 0.1% of the same preservative. The physical properties of these compounds are shown in Table I and their structures in Figures 1 and 2.



FIG. 1

Cycloocta-1,5-diene (COD)



FIG. 2

Cyclododeca-1,5,9-triene (CDT)

Dermal toxicity was assessed in guinea-pigs, hairless mice, and rabbits by means of tests for the determination of skin irritation and sensitization that have been reported elsewhere (Hunter, Brown, and Ferrigan, 1966; Brown, Ferrigan, and Stevenson, 1967; Brown,

1967). Tests for the determination of eye irritancy were made on rabbits (United States Federal Register, 1964; U.S. Department of Health, Education and Welfare, 1964).

Results

Skin Irritation Studies In the covered test in rabbits, the irritation caused by both materials was very severe. Epidermal sloughing was particularly apparent after the application of COD. The use of sulpham blue showed the skin to be grossly injured. Histopathological examination of skin taken from the rabbits *post mortem* revealed necrosis of the epidermis and ulceration and marked inflammation of the dermis with COD, and following CDT application there were acanthosis and a proliferative epidermal reaction.

COD, in the uncovered application tests in rabbits, guinea-pigs, and 'hairless' mice, produced an immediate erythematous reaction after only one application. A severe acute contact dermatitis followed with epidermal sloughing. With the same tests, CDT was highly irritant and produced a very

TABLE I

SOME PHYSICAL PROPERTIES OF *Cycloocta-1,5-DIENE* AND *Cyclododeca-1,5,9-TRIENE*

	<i>Cycloocta-1,5-diene</i>	<i>Cyclododeca-1,5,9-triene</i>
Molecular weight	108.2	162.3
Boiling point (760 mm.Hg) (°C.)	150.9	—
Boiling point (11 mm.Hg) (°C.)	—	100.00
Freezing point (°C.)	-69.5	-18.00
Refractive index n_D^{20}	1.4905	1.5072
Density (20°C.) (g./cc.)	0.8833	0.8906

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severe contact dermatitis in all species. Ulceration was observed in the skin of one 'hairless' mouse on histopathological examination. With both compounds, hair growth was suppressed around the shorn sites of application in the rabbits and guinea-pigs.

Because of the severity and nature of the reaction, a group of guinea-pigs was treated as above but not killed until three weeks after the last application of test material. Histological examination of the skins from these animals showed that epidermal thickening and considerable acanthosis were still present.

Skin Sensitization Studies Both COD and CDT were found to be potent skin sensitizers in the two tests performed on each compound (Table II).

TABLE II
SENSITIZATION REACTIONS OBSERVED IN GUINEA-PIGS

Material under Test as 0.1% w/v Solution in Light Liquid Paraffin	No. of Guinea-pigs showing Positive Sensitive Reaction			
	Topical Test		Intradermal Test	
	24 hours	48 hours	24 hours	48 hours
COD	10/10	10/10	9/10	9/10
CDT	10/10	10/10	10/10	10/10

Eye Tests in Rabbits Both oligomers were immediately irritant to the eyes but produced only a mild conjunctivitis which faded within 48 hours. The main effect was associated with the eyelids, which became red and swollen and exuded a purulent discharge. The blepharitis caused by

COD took a few days to heal; blepharitis was still apparent one week after the application of CDT.

Discussion and Conclusions

COD and CDT were shown to be capable of causing severe contact dermatitis, and even trace amounts produced a sensitization reaction. This sensitization reaction to cyclic aliphatic compounds is not unprecedented, as cyclopentadiene was shown to give positive sensitization reactions in man (Malten and Zielhuis, 1964) although only a very faint sensitization reaction was observed in guinea-pigs with cycloheptatriene (Brown *et al.*, 1967).

It is unlikely that accidental splashing of these two oligomers into the eye will cause permanent damage but pain and discomfort will be apparent. The eyelids in particular may be painfully involved. Nevertheless, immediate first aid is essential.

Strict precautions should be taken to avoid skin contact with either COD or CDT.

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