STUDIES ON THE CUTANEOUS SENSITIZATION REACTION OF GUINEA PIGS TO PURIFIED AROMATIC CHEMICALS

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Abstract. The sensitization reactions to purified cinnamic aldehyde and its chemically related substances were investigated using the maximization test on guinea pigs. Mutual cross-sensitivities were also examined. Cinnamic aldehyde was found to be the most potent sensitizer in this series, and a strong cross-sensitizer. From the chemical structures of these substances, the following speculations were made. There was a tendency that as the number of hydrocarbons of alkyl groups replacing the e-hydrogen in the molecule increased, the rate of sensitization reaction declined. The conjugated system of double bonds was suspected to be a determinant factor in relation to the sensitization ability of the substances in this series.

Key words: Sensitization; Maximization test; Cinnamic aldehyde and related substances; Molecular structure; Chemical bond

It is well known that cinnamic aldehyde is a chemical substance used as flavouring material and perfume compound. As it has often been suspected to be a sensitizer causing allergic contact dermatitis (1, 2, 3, 11), much attention has been paid to this chemical (9, 10, 11).

The present study deals with the maximization test (8) in order to establish, in terms of molecular structure and hypersensitivity, the relationship between cinnamic aldehyde and related substances, all chemically purified.

MATERIALS AND METHODS

Cinnamic aldehyde (CALD) and the chemically related substances α-methyl-cinnamic aldehyde (AMCALD), α-amyl-cinnamic aldehyde (AACALD), β-methyl-cinnamic aldehyde (BMCALD), dihydrocinnamic aldehyde (DHCAALD), cinnamic alcohol (CALC) and styrene (STYRN) were used in the present investigation. The chemical structure of each substance is illustrated in Fig. 1. All these chemicals were estimated for purity by gas chromatography before use.

Ten male albino guinea pigs, weighing 350-400 g, were used for each group of the test substances. The maximization test was used according to Magnusson & Kligman (8).

The concentration of each chemical for induction by both the intradermal injection and topical patch application was chosen according to the maximization test results shown in Table 1.

![Fig. 1. Molecular structures of cinnamic aldehyde and related substances.](image-url)

The abbreviations of each chemical name are given in brackets.
The results of the sensitization reactions appear in Table 1. The two cross-sensitization reactions between CALD and AMCALD, and between CALD and BMCALD were recorded. Whereas animals induced by CALD reacted to the challenge of CALC, those induced by CALC without sensitization failed to respond to CALD challenge. It was recognized that CALD was the most potent sensitizer, and a strong cross-sensitizer in this series. Occasionally, as shown in Fig. 2, animals sensitized by this chemical showed intense redness and even erosion in the challenged area. Fig. 3 shows the histological findings from one of the animals sensitized by CALD.

Figs. 4, 5 and 6 demonstrate the sensitization reaction induced by BMCALD and the cross-sensitization reactions between CALD and BMCALD, and between AMCALD and CALD, respectively. Among the cinnamic aldehyde derivatives, the degree of sensitization was observed with the following sequence: CALC > AMCALD = BMCALD > AACALD.
DISCUSSION

The relationship between molecular structure and hypersensitivity is an interesting topic in the study of allergic reactions. Pioneering work has been performed by Landsteiner and his co-workers (4, 5, 6, 7), who put forward several significant ideas in this field.

Some speculations on the mechanism of cinnamic aldehyde sensitization and quenching effects have been made regarding its molecular structure (9, 10, 11), but conclusive explanation has never been established.

Cinnamic aldehyde (CALD) was considered to have three different kinds of chemically characteristic parts to the molecule: the carbonyl group (aldehyde group), the conjugated double bond, and the benzene nucleus. They are all included in a system of elongated conjugated double bonds.

All substances tested in this series have a benzene ring as common structure. Therefore, it was assumed that the different degrees of sensitization might be attributable to the form of chemical bond attached to the benzene ring.

Dihydrocinnamic aldehyde (DHCALD) and cinnamic alcohol (CALC), both having such functional groups at the terminal of the main chains as a carbonyl group and a hydroxyl group, showed no sensitization reaction. While styrene (STYRN), which had no functional group in the molecule, elicited mild sensitization.

From the results obtained, the conjugated system of double bonds or the participation of \( \pi \)-electrons...
Fig. 6. Cross-reaction observed at the challenged site of the guinea pig: induction; AMCALD, challenge; CALD.

included in this system was considered to be conceivably connected with sensitization.

As to the \( \alpha \)-derivatives, the larger was the number of hydrocarbons of alkyl groups replacing the \( \alpha \)-hydrogen in the molecule, the more mild was the degree of sensitization reaction.

It is well recognized in the field of physical organic chemistry that the conjugated compounds are so very reactive because they possess delocalized \( \pi \)-electrons. This peculiar fact may be associated with the allergic reactions seen in the present study. The substitute alkyl groups on the \( \alpha \)-carbon may play an important role in weakening the response at some stage in the allergic procedure.

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REFERENCES