

Occupational contact dermatitis due to Croton (*Codiaeum variegatum* (L.) A. Juss var. *pictum* (Lodd.) Muell. Arg.)

Sensitization by plants of the Euphorbiaceae

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One of today's most decorative and popular ornamental potted plants is Croton. Handling this plant over a period of 6 months produced contact eczema of the hands in a nursery gardener. Patch tests with Croton leaves were positive. Control tests remained negative. Sensitization experiments in guinea pigs with a methanolic extract of the leaves were successful.

All results of the study indicate that:

- latex of croton produces no primary irritant reaction
- latex is able to induce a real contact allergy
- contact allergens are constituents of the milky sap.

Whether the di- and triesters of phorbol so far isolated as irritant and cocarcinogenic factors from the latex of various Euphorbiaceae species and sensitizers shall be investigated in further experiments.

Key words: Animal sensitization experiments - Croton allergy - occupational plant dermatitis - phorbol esters.

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For a long time it has been known that species of Euphorbiaceae produce a milky sap (latex) which causes irritation of the skin and eyes (Samochval & Krivak 1974, Smirnov & Efremov 1970, Safat et al. 1972, Sood et al. 1971). Furthermore it has been demonstrated that certain constituents of various Euphorbiaceae have a cocarcinogenic activity. These compounds have recently been isolated and investigated by Hecker and co-workers (Hecker 1975, Gschwendt & Hecker 1973, 1974, Hergenbahn et al. 1974).

It has been assumed that apart from these biological effects the latex may induce allergy of delayed type (Type IV) but this suspicion could not be confirmed by animal experiments (D'Acry 1974). Occupational allergy of Type I due to inhalation of pollen from *Euphoria fulgens* Karw. was first described by us in 1976 (Hausen et al. 1976).

Once of today's most decorative and popular ornamental potted plants is the Croton (*Codiaeum variegatum* (L.) A. Juss var. *pictum* (Lodd.) Muell. Arg.) of the

family Euphorbiaceae (synonym: *Croton variegatus* L.). It was brought to Europe more than 100 years ago from the Malaysian archipelago (Möhrling 1964, Parey's Blumengärtnerei 1958). Different species were often hybridized to produce the most decorative potted plants. Many hybrids are available today, the most common being Czar Alexander III, Baron de Rothschild, Albert Truffaut and Disraeli. Of all plants sold in the Federal Republic of Germany, Croton holds the fifth or sixth place in popularity. In 1976 more than 300,000 were sold.*

Recently we observed a patient with a dermatitis on both hands caused by this plant. He worked as a nursery gardener and had frequent contact with exotic plants such as Ficus, Croton and Philodendron. He was employed mainly in the cultivation of Croton hybrids like Philip Geduldig, Pucciana and Florida and he could not avoid contact of the hands with the milky sap of these plants. Six months after beginning this special job, the first eruption developed on his hands and later spread to the forearms. The condition cleared after he changed occupations. Patch tests were performed with our standard series as well as with plants and insecticides supplied by the patient. Positive skin reactions were found only with Croton hybrids (Table 1). Control tests with the same plants in 10 persons were negative.

To check the sensitizing capacity of Croton, latex sensitization experiments were carried out in guinea pigs using a methanol extract of the leaves. A total of 0.05 ml of a 10 % solution (methanol) was applied daily (except at weekends) for 3 weeks to the shaved skin of five animals.

* Market reports of NBV, UGA, Wiesmoor etc. For this information we thank Mr. W. Helfert of the editorial staff of TASPO, Braunschweig.

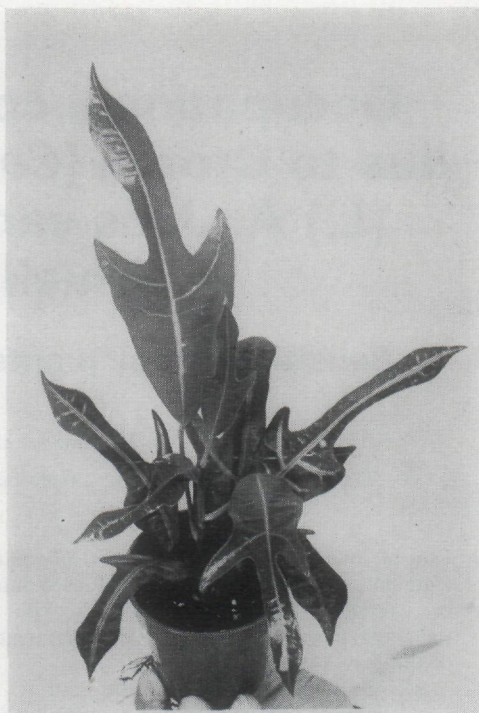


Fig. 1. Croton hybrid 'Florida'. *Codiaeum variegatum* (L.) A. JUSS var *pictum* (Lodd.) Muell. Arg.

There was no irritation during the first 3 days. On the fourth day slight erythema developed, which increased during the sensitization period. Two weeks after finishing this treatment, challenge was performed by application of 0.05 ml of 3 %, 1 %, 0.3 % and 0.1 % solutions. The animals showed positive reactions down to the 0.1 % dilution. The milky sap, exuding from a fresh cut leaf also produced a reaction in the sensitized animals after 24 and 48 h.

Application of the same materials (extract and latex) to the skin of normal guinea pigs not pretreated with Croton extracts was negative.

The results of these clinical and experimental studies indicate that

a) the latex of the investigated Croton

Table 1. Patch test results with different plants and Croton hybrids

		24 h	48 h
Ficus leaf	alc.	Ø	Ø
Croton leaf 'Philip Geduldig'	alc.	+	+
Croton leaf 'Pucciana'	alc.	++	++
Croton leaf 'Florida'	alc.	+	++
Philodendron leaf	alc.	Ø	Ø
Temik (insecticide)*	aq.	Ø	Ø
1:10			
Plant hormone	aq.	Ø	Ø

* 2-methyl-2 (methylthio)-propionaldehyde-O-(methyl-carbamoyl)-oxime (Aldicarb)

plant produces no primary irritant reaction on the skin after a single application

- b) some species of the family of Euphorbiaceae are able to induce a contact allergy; they have a sensitizing capacity
- c) the contact allergens are constituents of the milky sap.

Only a few cases of Croton dermatitis suspected to be due to a specific hypersensitivity have been described in the literature. Morton (1962) mentioned Croton as a plant which may cause dermatitis. Agrup (1969) observed a positive test reaction from Croton in a housewife with hand eczema. Lynne-Davies & Mitchell (1974) found no patch test reaction to the leaves of Croton in two normal persons. Tafelkruyer & van Ketel (1976) were the first to describe dermatitis in a flower grower who showed "an unmistakable allergic reaction" on patch testing with Croton. Their patient reacted to an aqueous but not to an alcoholic extract of the leaves.

Finally, Schmidt & Ølholm-Larsen (1977) examined four gardeners in Denmark observed since 1969 with an occupational dermatitis of the hands caused by Croton. After they had changed their jobs the skin lesions

cleared. All of them had a positive patch test to an aqueous extract, and two patients also reacted to an ether extract. No cross reactions could be obtained to another species of the Euphorbiaceae – *Croton tiglium* L. – which is known as the common Croton plant.

As mentioned above Hecker and co-workers have been successful in isolating the skin irritant and cocarcinogenic factors of some Euphorbiaceae species (Fig. 2). Chemically these compounds proved to be di- and triesters of the diterpene phorbol (esterification at the carbon atoms 12, 13 and 20). It is still not known whether these compounds also have a sensitizing action. The phorbol esters were found in the acetone-soluble part of a methanol extract. They could be identified on thin-layer chromatography plates by a vanillin-sulfuric acid reagent. Preliminary chemical investigations of our *Codiaeum* extracts showed several spots on the skin layers which gave a distinct colour reaction with this reagent. Further studies on the isolation and identification of the sensitizing agents of Croton latex are in progress.

Our further experimental studies in guinea pigs with the milky sap of the related species *Euphorbia fulgens* Karw. and

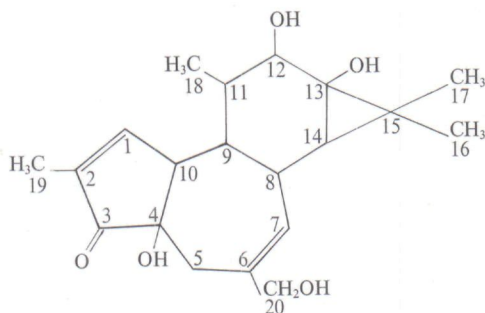


Fig. 2. Fundamental structure of cocarcinogenic and irritant factors of Euphorbiaceae (according to Hecker and co-workers). It is not known whether these compounds sensitize.

Euphorbia pulcherrima Willd. (Poinsettia, Christmas star) have also given evidence of sensitizing capacity in the latex of these species.

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