

Phytophotodermatitis

An experimental study using the chamber method

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Experimental phytophotodermatitis was produced using crushed leaves from the gas plant, *Dictamnus albus*. The tests were made using the chamber method and irradiated with ordinary black light tubes.

An occlusion time of not less than 30 min was needed to give a phototoxic reaction in all test subjects. An occlusion time 30-120 min gave the optimal results, but contact for 24 h produced only weak and inconsistent reactions.

The phototoxic substance was readily absorbed into the skin within 10-15 min. The phototoxic tendency already began to disappear within 30 min after the tests were removed.

UVA energy of 0.3 J/cm² was enough to evoke a phytophotoreaction in all of the test subjects when other conditions were optimal.

The reactions were enhanced by adding water to the test sites.

Deep-freezing of the plant material did not destroy the phototoxicity within a 4-month period.

Key words: Contact dermatitis - *Dictamnus albus* - light - phototoxicity - phytophotodermatitis.

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Certain plants may induce a form of photosensitivity reaction (van Dijk 1963, van Dijk & Berrens 1964, Kuske 1940, Pathak et al. 1962). The first report in the literature dates back to 1926, when Oppenheim called this phenomenon "dermatitis bullosa striata pratensis" (van Dijk 1963). Klaber (1942) used the name "phytophotodermatitis".

Most reactions of this type are caused by plants belonging to the Umbelliferae and Rutaceae families (van Dijk 1963, van Dijk & Berrens 1964, Pathak et al. 1962).

The requirements for this acute, blistering skin reaction are contact with one of these plants and exposure to sunlight. Moist skin has been regarded as a prerequisite for the reaction (van Dijk 1963, Ippen 1973, Sommer & Jillson 1967).

The reaction is phototoxic in character

and is caused by psoralens and UVA (Kuske 1940).

The photosensitizing properties of various plants have been investigated mostly using alcoholic extracts of the plants (van Dijk 1963, van Dijk & Berrens 1964, Kuske 1940). The more natural method, using a actual plant, is less widely used in research work.

The aim of this study is to examine the conditions under which phototoxic reactions can be elicited using a phototoxic plant itself.

Material and Methods

The leaves of the gas plant (*Dictamnus albus*) were crushed in a mortar. Epicutaneous tests were made with homogenates either freshly prepared each day or deep-

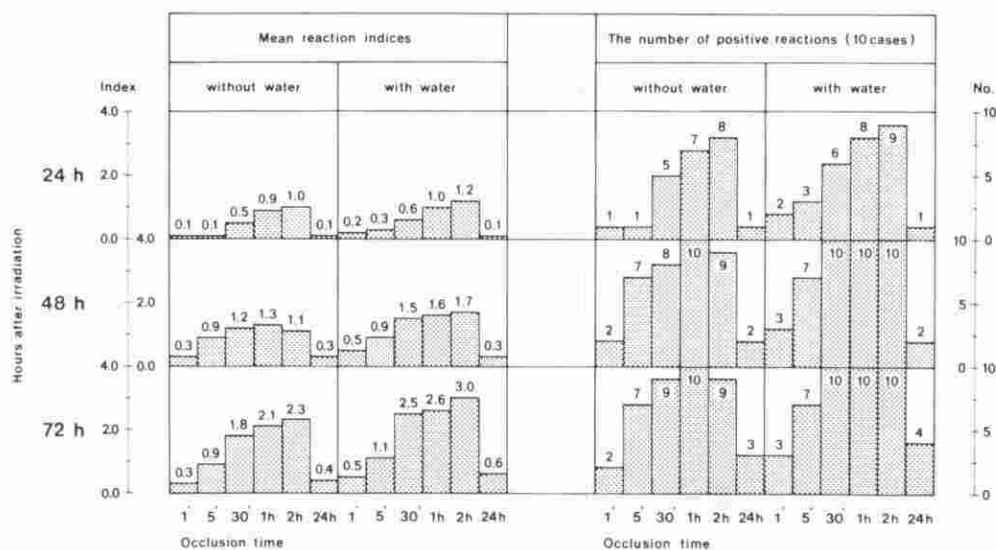


Fig. 1. Mean reaction indices and the number of positive reactions with graded occlusion times with and without water added to the chambers. The reactions were evaluated at 24, 48 and 72 h after irradiation. The irradiation time was 15 min. There were 10 test subjects. All dark controls were negative.

frozen using the chamber method (Finn Chamber, Epitest Ltd Oy, Helsinki 10) (Pirilä 1975, Suhonen et al. 1976).

Fresh material was used in parts 1–3 and deep-frozen leaves in parts 4 and 5 of the study. The aluminium chambers were filled to approximately half of their volume and fixed to the skin on the backs of the test subjects with porous adhesive tape (Scanpor®, Norgesplaster A/S, Oslo 2). No filter paper discs were used in the chambers. The tests were irradiated with a UVA source consisting of six Philips TL 20W/08 black light tubes as described earlier (Suhonen et al. 1976).

The test subjects were 45 volunteers, mostly dermatological patients without photosensitivity skin reactions. All patients with potentially photosensitizing medication were excluded.

The following aspects were studied: 1) influence of plant contact time, 2) influence

of moisture, 3) influence of the amount of UVA energy, 4) influence of the interval between the removal of the material and irradiation, and 5) influence of deep-freezing on the phototoxicity of the plant.

1. To examine the influence of the plant contact time, tests were removed after 1 min, 5 min, 30 min, 1 h, 2 h and 24 h. The test sites were irradiated for 15 min immediately after removal of the tests.

2. To examine the influence of moisture, water was added to each chamber, exceeding its volume. The occlusion time and irradiation time were the same as in the first part of the study, and both test series were carried out simultaneously on the same 10 patients (Fig. 1).

3. The irradiation time was graded (30 sec, 1 min, 5 min, 10 min and 15 min) while the occlusion time was a constant 30 min (Fig. 2). There were 10 test subjects.

4. In this part of the study the influence

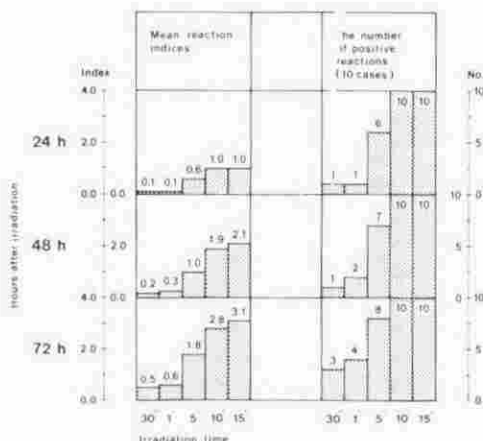


Fig. 2. Mean reaction indices and the number of positive reactions with graded irradiation times. The occlusion time was 30 min. Irradiation was performed immediately after the tests were removed. There were 10 test subjects. All dark controls were negative.

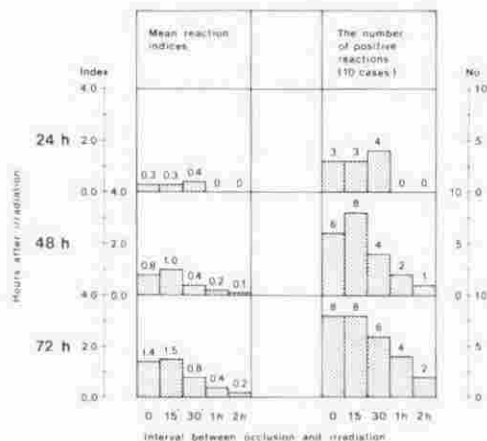


Fig. 4. Mean reaction indices and the number of positive reactions with graded intervals between removal of the tests and irradiation. The occlusion time was 1 min. There were 10 test subjects. All dark controls were negative.

of the interval between removal of the tests and irradiation was studied. Two different occlusion times were used, 1 min and 30 min. The intervals were 0, 15, 30, 60, 120

min and 0, 30, 60, 120 min and 24 h. The irradiation time for both test series was 15 min. There were 10 test subjects in both series (Figs. 3 and 4).

5. Plant material was stored at -50°C for 1, 2 and 4 months. The phototoxicity of the frozen material was tested using an occlusion time of 30 min, an irradiation time of 15 min and the addition of water to each chamber. There were five test subjects.

The results were evaluated 24, 48 and 72 h after irradiation on a scale 0-4. In this scale 0 means no reaction, 1 erythema, 2 erythema with moderate oedema, 3 erythema with beginning vesiculation and 4 a uniform bulla. All the reactions were scored on this scale to calculate the mean reaction indices (0-4). The test results were evaluated also on the basis of the number of positive reactions.

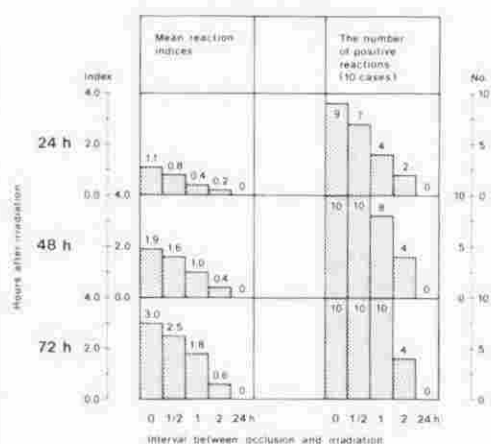


Fig. 3. Mean reaction indices and the number of positive reactions with graded intervals between removal of the tests and irradiation. The occlusion time was 30 min. There were 10 test subjects. All dark controls were negative.

Results

An occlusion time of 1 min was sufficient

to evoke a photosensitivity reaction in 2 out of 10 patients (Fig. 1). The number of positive reactions was highest with a 1-h contact, but the difference was not marked from 30 min to 2 h. Two hours' occlusion gave the highest reaction indices. Both the reaction indices and the number of positive reactions were at their highest 72 h after irradiation (Fig. 1).

The addition of water increased both the reaction indices and the number of positive reactions (Fig. 1).

Ten minutes' irradiation gave a positive reaction in all 10 patients; the mean reaction index was 2.8 (Fig. 2). An additional 5 min increased the mean reaction index to 3.1. The irradiation time of 30 sec evoked a reaction in only 3 out of 10 cases (Fig. 2).

In the tests with an occlusion time of 30 min and using graded intervals between the end of plant contact and light exposure, irradiation immediately after removing the tests produced the strongest reactions (Fig. 3). A 30-min wait made the mean reaction index fall, but the tests were still positive on all 10 subjects up to an interval of 1 h. Six out of 10 patients failed to react after an interval of 2 h and a 24-h wait before irradiation abolished all signs of photosensitivity (Fig. 3).

In the tests with an occlusion of 1 min, waiting 15 min potentiated reactions (Fig. 4). Two out of 10 patients reacted even after an interval of 24 h. These tests were performed with the plant sample from late summer, which may have been more phototoxic than the one used in previous series.

Crushed plants reserved their phototoxicity for at least 4 months when kept at -50°C .

In all the tests both the reaction indices and the number of positive reactions reached their maximums at 72 h.

Dark controls were negative in all the tests.

Discussion

Phytophotodermatitis is caused by psoralen derivatives (furocoumarins) of some plants together with sunlight (van Dijk 1963, Kuske 1940, Pathak et al. 1962). Although several different furocoumarins have been found in plants, only a few of them are strongly phototoxic (Pathak et al. 1967). Gas plant, *Dic-tamnus albus*, contains 5-methoxypsoralen, bergapten, which is definitely phototoxic (Berrens & van Dijk 1964).

Jensen & Hansen (1939) and Kuske (1940) have proved that the action maximum for phytophotodermatitis lies in the UVA range (320–400 nm).

The results of this study show that the length of plant contact time plays an important role in the experimental production of phytophotodermatitis. An occlusion time of at least 1 h was needed in order to reach the optimal reaction rate. The continuation of plant contact until next day strongly diminished signs of skin photosensitivity. Birmingham et al. (1961) noticed the same phenomenon in their experiments with celery. Some authors have used an open application for up to 10 min with alcoholic extracts of plants without a definite occlusion and irradiated the skin after waiting 15 min to 1 h (van Dijk 1963, Kuske 1940, Pathak et al. 1960).

The addition of water increased both the strength of the reactions and the number of positive results. Harber & Baer (1965) and Levine & Harber (1969) have shown that an increase in relative humidity increases the phototoxic response of topical 8-methoxypsoralen but not to the drug when administered systemically. They concluded that increased humidity enhances the penetration of the phototoxic substance. In addition, the potentiating effect of water in phytophotodermatitis may be due partly to the better availability of furocoumarin acids or glycosides in phototoxic plants, which are water-

soluble contrary to bergapten (van Dijk 1963).

The UVA source used in this study was found to be effective enough in a previous study on photoepicutaneous testing with 8-methoxypsoralen (Suhonen et al. 1976), so it was probable that it would be suitable also for testing with furocoumarin-containing plant material. In fact, Camm et al. (1976) used the light source of the same type in studying phytophotodermatitis due to *Heracleum mantegazzianum*.

The UVA exposure was graded from 30 sec to 15 min. In this part of the work the contact time was only 30 min in order to avoid the strongest, unacceptable reactions. A 100 % reaction rate was already obtained with an irradiation time of 10 min (Fig. 2).

The results show that there exists a direct relationship between the strength of the phytophotoreaction and the UVA dose used for irradiation. With the light source used in this study it was not possible to study the proportional significance of the UVA intensity or of the length of the exposure in determining the strength of the reactions.

It is not easy to get reliable measurements on UVA energy generated in an equipment with a large irradiating area as the UVA source used in the present study (Alsins 1976, Stratigos & Magnus 1968). We measured a dose of 0.51 J/cm² with an irradiation time of 15 min. The lack of measurements on UVA energy derived from the sun at Finland's latitude made it impossible to compare the UVA energy used in this study with that of the sun. Birmingham et al. (1961) found that celery containing bergapten produced phytophotodermatitis even with an exposure of 30 sec of summer sunlight in Michigan.

The results of previous studies with alcoholic extracts of phototoxic plants (van Dijk 1963, Kuske 1940, Pathak et al. 1960) and the present findings support the conception that a relatively short contact time

— only about 1 min — is often sufficient to produce a phototoxic reaction. Penetration is fast and is enhanced by moisturizing the skin.

The chamber method giving standard occlusion has been found to be well suited for photoepicutaneous testing (Suhonen et al. 1976). The concave shape of the chamber allows its ready use for testing with crushed plant material.

Deep-frozen material can also be used in studies on plant phototoxicity. This increases the potential for examining the phototoxicity of various plants *per se* during winter time as well.

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