Phototoxic Plant Interactions: Unraveling the Complexities of Phytophotodermatitis in Unani system of Medicine

Aatika Hussain[1], Nawalur Rehman Khan[1*], Mohammad Mohsin[2], Malik Nuzhat Fatima[2] Ataullah Fahad[3] Mohammad Anas[4]

[1] PG Scholar, D/O Amraz-e-Jild wa Zohrawiya, AKTC, AMU, Aligarh
[2] Associate Professor D/O Amraz-e-Jild wa Zohrawiya, AKTC, AMU, Aligarh
[3] Assistant Professor D/O Ilmulm Amraz, AKTC, AMU, Aligarh
[4]Assistant professor Department of ilmul Atfal, AMU, Aligarh

***Corresponding Author:** Nawalur Rehman Khan
***Email:** nawalstylo@gmail.com

Abstract
Phytophotodermatitis named from the terms 'phyto' means plant, 'photo' means light, and 'dermatitis' means skin inflammation, is a type of Contact dermatitis (*Iltihab-e-Jild Ittesali*). Phytophotodermatitis is the eruption that occurs after contact with photosensitizing compounds in plants (like, furanocoumarins) and exposure to sunlight (especially UV-A, 320-400 nm range of the spectrum). Furanocoumarins, present in some plants (e.g., parsley, celery, carrots, and limes), react using their parent compound, psoralen, with the UV radiation, which forms the eruptions on the skin. These Plants may cause allergic contact, irritant contact, and phototoxic dermatitis. Most phototoxic plants are in the families Umbelliferae, Rutaceae, Compositae, and Moraceae. Phytophotodermatitis a rare phenomenon seen in Indian settings, may sometimes get misdiagnosed as fungal skin infection, allergic contact dermatitis or cellulitis. The present study helps in unraveling the interactions, pathophysiology and complications of phytophotodermatitis.

Key words: Phytophotodermatitis, Phototoxic dermatitis, Furanocoumarins, *Iltihab-e-jild Ittesali*

Introduction

'Dermatitis' denotes an inflammatory condition of the skin and is thus a broader term in contrast to eczema, which is only one of numerous different forms of skin inflammation. Eczema is a Greek word (Ec indicates out, and Zeo indicates boil).[1] Whereas in modern textbooks, eczema (*Nar farsi*) is defined as an inflammatory reaction of the skin to various stimuli marked by erythema, swelling, vesicle formation, crusting, oozing as well as lichenification.[2] Furthermore, it can be described as an inflammatory skin condition marked by spongiosis in histology.[3] In Unani Medicine, eczema is also called by variety of other names like *Chajan*, *Akota*, *Nar farsi*.[4] Kabiruddin, a notable Unani physician, defines eczema as a skin ailment with burning sensations on lesions, resembling fire.[5] Another famous scholar of Unani medicine, *Ghulam Jilani* also characterized *Nar farsi* as a skin condition with a burning sensation on the affected body part.[6] Ahmad Al Hasam Jurjani, in "Zakhira Khwarzam Shahi," defined Nar Farsi as a dermatological condition with fluid-filled vesicles, severe burning, and itching.[7] According to *Hakim Akbar Arzani*, a famous Scholar of Unani Medicine explained *Nar farsi* as a sickness characterized by lesions filled with water, as well as burning and itching.[8] Thus, Dermatitis refers to skin inflammation and is thus a broader term than eczema, which is merely one of several different kinds of skin inflammation.[9] Phytophotodermatitis, uncommon in India, necessitates careful evaluation to avoid misdiagnosis. It's a form of contact dermatitis, linked to plants and light-induced skin inflammation.[10] Phytophotodermatitis is a non-immunologic inflammatory skin reaction which develops following cutaneous contact with photoactive compounds in certain plants called furocoumarins in conjunction with sunlight exposure.[11] Phototoxic plants like agrimony, angelica, and parsley, found in Umbelliferae, Rutaceae, Compositae, and Moraceae, can cause phytophotodermatitis. Occupational risks include exposure to Sclerotinia sclerotiorum in celery farming, and disease-resistant celery may pose risks for grocery workers due to furocoumarins.[12] Phytophotodermatitis, a cutaneous phototoxic reaction, results from contact with furanocoumarins in plants like parsley, celery, carrots, and limes, activated by UV-A radiation. Psoralen, a particle in furanocoumarins, contributes to skin eruptions in a direct, immune-independent reaction.[13] Phytophotodermatitis a rare phenomenon seen in Indian settings may sometimes get misdiagnosed as fungal skin infection, allergic contact dermatitis or cellulitis.[14] Phytophotodermatitis symptoms appear 24 hours post-exposure, peaking at 48–72 hours, with blistering, itching, redness, inflammation, pain, and crusted patches. Healing takes 7-14 days, leaving hyperpigmentation or post-inflammatory pigmentation, lasting weeks or months. Mild reactions may be realized only through subsequent hyperpigmentation.[15] The most common location for phytophotodermatitis is the dorsum of the hand, as it is a body surface with both psoralen contact and sun exposure. [16] Many plants, mainly from Rutaceae, Moraceae, and Umbelliferae families, contribute to phytophotodermatitis. Principal causative plants are listed below. [17]

Common Phototoxic Plants[17]

Sr. No.	Common Name	Scientific Name	Family
1.	Fig Tree (*Anjeer*)	*Ficus Carica*	Moraceae
2.	Burning bush	*Dictamnus albus*	Rutaceae
3.	Bitter orange	*Citrus aurantium*	Rutaceae
4.	Graper fruit	*Citrus paradissi*	Rutaceae
5.	Lime	*Citrus aurantifolia*	Rutaceae
6.	Lemon	*Citrous lemon*	Rutaceae
7.	Bergamot lime	*Citrus beyamia*	Rutaceae
8.	Sweet orange	*Citrus sinenrit*	Rutaceae
9.	Rue	*Ruta graueolens*	Rutaceae
10.	Mokihana	*Pelea anisate*	Rutaceae
11.	Parsley	*Petroselinum crispum*	Umbelliferae
12.	Celery	*Apium graveolens*	Umbelliferae
13.	False Bishop's weed (*Atrilal*)	*Ammi majus*	Umbelliferae
14.	Carrot	*Daucus carota*	Umbelliferae
15.	Parsnip (*Zardak*)	*Pastinaca sativa*	Umbelliferae
16.	Cow parsley	*Heracleum sphondylium*	Umbelliferae
17.	Angelica	*Angelica archangelica*	Umbelliferae
18.	Fennel (*Badiyan*)	*Foeniculum vulgare*	Umbelliferae
19.	Cow parsley, chervil	*Anthricus sylvestris*	Umbelliferae
20.	Giant hogweed	*Heracleum mantegazzianum*	Umbelliferae
21.	Cow parsnip	*Heracleum lanatum*	Umbelliferae

Images of Some Common Phytotoxic Plants

Hossain MA, Al Touby S :(2020)

Figure 1: False Bishop's weeds (*Ammi majus*)[18]

Luoma MO: 2019

Figure 2: Cow Parsley (*Anthricus sylvestris*)[19]

Chawla A, et *al*: 2012[20]

Figure 3: Fig Tree (*Ficus carica*)

Historical Background of the Phytophotodermatitis

The phenomenon of phytophotodermatitis has been known for more than 3,000 years, dating back to the ancient Egyptians. The Ebers Papyrus, one of the oldest and most important medical papyri (the ancient equivalent of Annals), described a condition thought to be vitiligo.[15] Patients with vitiligo in China, Egypt, and India had certain plant extracts applied to the affected areas and were then instructed to lie in the sun.[21] In 1834, Kalbrunner isolated bergapten (5-methoxypsoralen) from Citrus bergamia. Earlier, in 1916, Freund described hyperpigmented skin lesions resulting from exposure to bergamot oil in perfume and the sun, a condition currently known as berloque dermatitis.[22] Oppenheim, in 1934, coined the term dermatitis bullosa striata pratensis to describe an erythematous, bullous eruption in a bizarre configuration appearing on sunbathers who had been lying in grass.[23] It was in 1942 that Klaber introduced the term phytophotodermatitis to elucidate the role of plants (phyto) and light (photo) in the manifestation of dermatitis.[22] The work of Kuske established the relationship between the chemical components of certain plant tissues and the development of phytophotodermatitis.[24]

Pathophysiology of phytophotodermatitis

Cutaneous inflammation resulting from plant exposure encompasses various conditions, including urticarial dermatitis, irritant contact dermatitis, allergic contact dermatitis, and the distinct phytophotodermatitis. Unlike immune-dependent reactions, phytophotodermatitis, characterized by erythema, blistering, and epidermal necrosis, occurs without prior sensitization. This condition arises from the interaction of furocoumarins, such as psoralens, with ultraviolet (UV) radiation, specifically UV-A. Natural sunlight, spanning 270-5000 nm, contains photons capable of triggering photochemical reactions. UV-A, predominant in phytophotodermatitis induction, exhibits peak activity at 335 nm. When UV-A interacts with furocoumarins, it elevates these compounds to a triple excited state, releasing energy during their return to the ground state. Phytophotodermatitis involves two independent photochemical reactions: Type I, occurring without oxygen, and Type II, in its presence. These reactions lead to cell membrane and DNA damage, including interstrand cross-linking between psoralen furan rings and DNA bases. Oxygen-independent reactions attach RNA and nuclear DNA to UV-activated furocoumarins, while oxygen-dependent reactions cause cell membrane damage and edema. Clinically, phytophotodermatitis manifests as erythema, blistering, and eventual desquamation.[13] According to the Unani Medicine, this condition occurs due to increase in *Hiddat* of *Khilt-e-Dam* (Sanguineous humour).[25] In the Unani Medicine perspective, influenced by Ibn Sina, phytophotodermatitis disrupts the Mizaj (Temperament) of the exposed body part, accumulating Khilt-e-Safra and causing Iltihab-e-Jild (Dermatitis) due to imbalances in the humours—Dam, Balgham, Safra, and Sauda. This holistic approach provides a unique insight into the interconnectedness of dermatological conditions with bodily humours in unani system of medicine.[26] In case of phytophotodermatitis the pathogens and UV rays affects the *Mizaj* (Temperament) of the exposed part of body and causes accumulation of *Khilt-e-Safra* (Bilious humour), this viscid and acrid humour causes itching and irritation at the site and thereafter leads to *Iltihab-e-Jild* (Dermatitis).

Sign and Symptom of Phytophotodermatitis

After sun exposure, a burning erythema emerges, followed by edema, vesicle, or bullae formation. Persistent hyperpigmentation may last for weeks. The initial mild phototoxic reaction might not be recalled despite notable hyperpigmentation. Fragrance products with bergapten from oil of bergamot induce this. If applied before sun exposure, berloque dermatitis arises, marked by hyperpigmentation on the neck and face. Dermatitis bullosa striata pratensis, linked to yellow-flowered meadow parsnip, causes streaks, vesicles, and bullae, healing with hyperpigmentation. Sunbathing in fields with phototoxic plants is a common cause. This summarizes the dermatological reactions to phototoxic substances and plants.[12]

Treatment

Most cases of phytophotodermatitis clear up with minimal intervention. However, treatment is available to reduce pain and shorten the duration of symptoms. Treatment options include: Avoiding re-exposure: It is important to take steps to avoid the plant that caused the skin reaction. For many individuals, this may be enough to alleviate the symptoms.

Avoiding other s kin irritants: It may be helpful to wear cotton clothing and avoid the use of harsh detergents, soaps, and personal care products that may make the symptoms worse. Cold compresses: Placing a cool washcloth on the affected area provides relief. Topical creams: Applying soothing ointments, lotions, and creams to the skin may reduce swelling and itching. Corticosteroids: Topical steroidal creams will reduce inflammation and itching. Over-the-counter nonsteroidal anti-inflammatory drugs (NSAIDs): NSAIDs include aspirin and ibuprofen, and they may help reduce pain and swelling. Prescribed medications: A doctor may prescribe oral corticosteroids or antihistamines for severe symptoms. Reducing sun exposure: Spending less time in the sun, especially when UV rays are at their strongest, may help prevent hyperpigmentation from becoming even darker. Also, a person should always wear sunscreen when they cannot avoid sun exposure.[15] After a short treatment with topical steroids (triamcinolone 0.1% cream twice daily), the lesions in our patient healed. Four weeks after the initial clinical presentation, very slight hyperpigmentation over the affected areas remained.[27]

Unani Treatment

Izala-e-Sabab: Treat and expel the cause which is responsible for the disease.[4] Tanqiya-e-Mawad (for evacuation of morbid humour): For this purpose Joshanda of Sana makki (Cassia angustifolia) 5gm, Saqmooniya (Convolvulus scammonia) 5gm, Haleela kabuli (Terminalia chebula) 5gm, Aaloo Bukhara (Prunus domestica) 5gm can be given to the patient before taking Musaffiyat-e-Dam.[26,28] Use of Musaffiyat-e-Dam (blood purifiers): Mufrad advia (Single drugs): Shahtra (Fumaria indica Pugsley), Sarphoka (Tephrosia purpurea Linn.), Gul-e-Mundi (Sphaeranthus indicus Linn.), Chiraita (Swertia chirayita Roxb.) etc.[4] Murakkab advia (Compound formulations): Itreefal Shahatra, Habb-e-Musaffi-e-Khoon, Majoon Ushba, Sharbat-e-Musaffi Murakkab, Sharbat-e-Neelofar, Sharbat-e-Unnab etc.[4] Use of Mohallilat (Resolvents), Mudammilat (Cicatrizant/healing agents) and Murakhkhiyat (Relaxants): Ibn Sina and other Unani physicians emphasized the use of medications with the aforementioned properties locally Roghan Gul (Oil of Rosa damascene), Roghan Kameela (Oil of Mallotus Phillippinensis), Roghan zaitoon (Oil of Olea europea)[28]. Musakkin-e-Jild (Sedative to skin) and Mann-e-Ufoonat-e-Jild (Anti-infective)- Application of Rasot mixed with Roghan-e-Gul, local application of Marham-e-Safedah Kafoori, local application of Sandal, Murdarsang, and Kafoor after mixing in Arq-e-Gulab.[4, 28]

Prevention

It may be possible to prevent the inflammatory skin reaction associated with phytophotodermatitis by Identifying the plants that may cause a skin reaction and taking steps to avoid contact with them Washing the skin, especially the hands, within 1-2 hours of cooking, spending time outdoors, or coming into contact with plants to remove the plant chemicals from it Covering up the skin with suitable clothing when outdoors and in woodland areas Wearing gloves when gardening, cooking, or slicing fruits or vegetables using sunscreen before exposing the skin to the sun.[29]

Conclusion

Phytophotodermatitis is a condition that happens after a person's skin comes into contact with chemicals from a plant. The chemicals then react when the person goes out in the sun, and a blistering skin reaction occurs. This condition is usually mild and resolves on its own, but on rare occasions, it can be severe. People can avoid the condition by identifying the plant to which they are sensitive and avoiding contact with it, as well as limiting their exposure to sunlight. The treatment options to relieve symptoms include creams, corticosteroids, and pain-relieving medications. Phytophotodermatitis a rare phenomenon seen in Indian settings may sometimes get misdiagnosed as fungal skin infection, allergic contact dermatitis or cellulitis.

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