

# Possible role of psoralen-induced phototoxicity in the development of vitiligo



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## INTRODUCTION

Vitiligo is a complicated, multifaceted pigmentation disorder affecting approximately 0.5% to 2% of the global population.<sup>1</sup> While the mechanism responsible for the development of vitiligo remains undetermined, the condition can be triggered by oxidative stress to melanocytes. Triggers include severe sunburn, mechanical trauma, chemical exposures, or other phototoxic reactions. This damage can ultimately lead to a response that targets melanocytes, resulting in progressive skin depigmentation.

## CASE REPORT

A 60-year-old woman presented to our dermatology clinic with multiple depigmented lesions located symmetrically on her arms, legs, and trunk. The patient stated that the lesions appeared following a severe, blistering sunburn acquired during a beach vacation approximately 1 year prior to her current evaluation. On the day the patient obtained the burn, the weather was sunny with a temperature of approximately 15.5 °C. Her sun exposure was limited to 3 hours while wearing sunscreen with a sun protection factor of 30. The patient was joined by her biologic sister, who did not display any signs of sun damage or photosensitivity. A review of social history revealed that the patient had been on a “celery juice cleanse” prior to the vacation. She gained the inspiration from a health blogger’s social media campaign endorsing the unregulated, unmeasured consumption of celery juice. The patient explained that she consumed a minimum of 4 glasses of celery juice per week for 6 months prior to the trip.

The patient denied any previous medical conditions, including diabetes, thyroid disorders,

### Abbreviations used:

PUVA: psoralen plus ultraviolet A  
UV-A: ultraviolet A

pernicious anemia, psoriasis, or alopecia areata. Additionally, she denied any previous observation of similar lesions or any personal or familial history of pigmentation disorders. However, she recalled experiencing a slight tingling sensation in her extremities leading up to the incidence of the sunburn that seemed to correlate with sun exposure, suggestive of photosensitivity.<sup>2</sup>

A previous consultation with a dermatologist 3 months after her initial burn confirmed a provisional diagnosis of photosensitivity reaction with no treatment or follow up advised. In seeking a second opinion, the patient was seen in our clinic, and the attending physician diagnosed vitiligo due to the presence of several well-demarcated, depigmented lesions located bilaterally and symmetrically on the arms, legs, and trunk present for more than 1 year (Fig 1). The patient also had a halo nevus located on the right shin. Serum values for thyroid-stimulating hormone, free T<sub>4</sub>, T<sub>3</sub>, and vitamin D were within the normal ranges. Furthermore, the patient denied any history of dermatitis or any other skin conditions that would lead to postinflammatory hypopigmentation.

## DISCUSSION

Celery is a common household vegetable known to contain furocoumarins. Furocoumarins, including psoralens, are a group of substances derived from plants with mutagenic and cytotoxic properties upon

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**Fig 1.** Images of depigmented lesions in the lower extremities (A) and shoulder regions (B, C).

UV radiation exposure.<sup>3</sup> Ingested sources of psoralens are detected in plasma within 15 minutes of consumption and remain throughout circulation to organs for another 3 hours.<sup>4</sup> The predilection for psoralens to accumulate near the epidermis becomes hazardous when combined with UV exposure, leading to the development of dermatitis, blisters, severe sunburns, age spots, and even skin cancer.<sup>5</sup> Ultraviolet activation of psoralens induces oxidative stress, or DNA damage resulting from oxidation-reduction reactions that produce chemically reactive oxygen species.<sup>6</sup>

The major theories regarding the mechanism of vitiligo include autoimmune destruction of melanocytes, genetic predisposition to defective melanocytes, and deficient defenses against exogenous environmental stressors, such as DNA damage from oxidative stress.<sup>7</sup> In each theory, however, an environmental trigger, such as severe sunburns from excessive UV radiation, can produce sufficient amounts of oxidative stress within melanocytes necessary to overwhelm the body's protective antioxidant system.<sup>8,9</sup> Supporting this theory of mechanism, the enzyme responsible for attenuating the response toward reactive oxygen species, catalase, has been shown to be decreased in the melanocytes of patients with vitiligo. The accumulation of reactive oxygen species in the melanocytes can result in melanocyte degeneration and subsequent loss of pigmentation.<sup>7</sup> Moreover, the appearance of new cutaneous lesions on previously unaffected skin following a traumatic event, or the Koebner phenomenon, has been associated with vitiligo presentation.<sup>7</sup>

Although a plethora of research regarding vitiligo exists, many unknown variables exist with regard to the prevention, detection, and treatment of vitiligo. A literature search produced few reports suggesting a correlation between overconsumption of celery and phototoxicity. One source detailed a patient that consumed approximately 45 mg furocoumarins followed by UV exposure, which resulted in the development of a generalized phototoxic reaction with severe burns, blistering, and edema.<sup>9</sup> Although the identified source proposes psoralen-induced phototoxicity, there is still a deficit of data pertaining to the relationship between psoralen-induced photosensitivity and the clinical development of lesions suggestive of vitiligo secondary to oxidative stress. This deficit highlights the potential for additional research to provide further insight into this relationship.

Research into various treatment options may be warranted upon investigation into this hypothesized association. Specifically, photochemotherapy treatment combining 8-methoxypsoralen and high-intensity long-wave ultraviolet light (referred to as psoralen plus UV-A "PUVA") is a current treatment indicated for vitiligo cases. While usually an efficacious treatment, there are documented case reports of paradoxical skin depigmentation, which could prompt the idea that photochemotherapy may in fact cause damage to melanocytes, contrary to previous findings.<sup>10</sup> Additionally, there are citations of patients undergoing higher-dose PUVA therapy developing severe sunburn-like reactions, as well as skin cancers, following exposure.<sup>5</sup> These incidences pose the relationship that exists between unregulated,

excessive use of psoralens and/or UV-A exposure and exacerbated symptoms of photosensitivity.

We hypothesize that the overconsumption of celery juice may have precipitated the development of vitiligo in the patient described in this case. Previous evidence supporting the role of psoralen-induced phototoxicity in the accumulation of oxidative stress and the associations between the oxidative stress and the development of vitiligo, in conjunction with clinical anecdotes warrants further investigation into the direct correlation between psoralen-induced vitiligo. As diet trends remain persistent throughout modern history, community awareness regarding the potentially detrimental side effects of these dietary modifications is paramount. As information continues to unveil the links between diet and phototoxicity, it is imperative that the medical community is knowledgeable of the possible adverse reactions arising from exposure to psoralens, both unintentionally and intentionally.

#### Conflicts of interest

None disclosed.

#### REFERENCES

1. Bergqvist C, Ezzedine K. Vitiligo: a review. *Dermatology*. 2020; 236(6):571-592. <https://doi.org/10.1159/000506103>
2. Stoner JG, Rasmussen JE. Plant dermatitis. *J Am Acad Dermatol*. 1983;9(1):1-15. [https://doi.org/10.1016/s0190-9622\(83\)70104-0](https://doi.org/10.1016/s0190-9622(83)70104-0)
3. Ljunggren B. Severe phototoxic burn following celery ingestion. *Arch Dermatol*. 1990;126(10):1334-1336.
4. Melough MM, Vance TM, Lee SG, et al. Furocoumarin kinetics in plasma and urine of healthy adults following consumption of grapefruit (citrus paradisi macf.) and grapefruit juice. *J Agric Food Chem*. 2017;65(14):3006-3012. <https://doi.org/10.1021/acs.jafc.7b00317>
5. Sun W, Rice MS, Park MK, et al. Intake of furocoumarins and risk of skin cancer in 2 prospective US cohort studies. *J Nutr*. 2020;150(6):1535-1544. <https://doi.org/10.1093/jn/nxaa062>
6. Berakha GJ, Lefkovits G. Psoralen phototherapy and phototoxicity. *Ann Plast Surg*. 1985;14(5):458-461. <https://doi.org/10.1097/00000637-198505000-00010>
7. Rychik K, Cohen J, Glass A. Localized vitiligo occurring in an old biopsy scar: a case report. *JAAD Case Rep*. 2020;6(4):326-328. <https://doi.org/10.1016/j.jdc.2020.02.003>
8. Schallreuter KU, Wood JM, Berger J. Low catalase levels in the epidermis of patients with vitiligo. *J Invest Dermatol*. 1991; 97(6):1081-1085. <https://doi.org/10.1111/1523-1747.ep12492612>
9. Deo SS, Bhagat AR, Shah RN. Study of oxidative stress in peripheral blood of Indian vitiligo patients. *Indian Dermatol Online J*. 2013;4(4):279-282. <https://doi.org/10.4103/2229-5178.120637>
10. Todes-Taylor N, Abel EA, Cox AJ. The occurrence of vitiligo after psoralens and ultraviolet a therapy. *J Am Acad Dermatol*. 1983;9(4):526-532. [https://doi.org/10.1016/s0190-9622\(83\)70164-7](https://doi.org/10.1016/s0190-9622(83)70164-7)