Drug-Induced Photosensitivity

Robert S. Dawe, MBChB, MD, FRCPE*, Sally H. Ibbotson, MBChB, MD, FRCPE

KEYWORDS

• Drug • Xenobiotic • Photosensitivity • Phototoxicity • Photoallergy

KEY POINTS

- Drug-induced photosensitivity is common.
- The principal mechanism of systemic drug photosensitivity is phototoxicity and the principal mechanism of topical drug photosensitivity is photoallergy.
- Photopatch testing is helpful to determine suspected topical agent photoallergies (eg, from ultraviolet filters in sunscreens) but generally not helpful in detecting systemic drug photosensitivity.
- Drug-induced photosensitivity is usually best managed by stopping the suspected drug.
- Other measures, including phototherapy using wavelengths that do not elicit the response, are sometimes necessary.

INTRODUCTION

Drug-induced photosensitivity usually occurs through the mechanisms of phototoxicity and photoallergy.[1] Phototoxicity is non–immunologically mediated, whereas photoallergy requires immune sensitization. Most systemic drug photosensitivity is through a phototoxic mechanism, whereas photoallergy is more relevant to topical agent photosensitivity (such as from ultraviolet filters in sunscreens). Topical drugs, such as topically applied psoralens (whether therapeutically applied or from exposure to psoralen-containing plants), can also cause photosensitivity through a phototoxic mechanism.

Drug-induced photosensitivity can cause severe problems; therefore, diagnosis and management are important. Certain drugs that cause phototoxicity can also cause photocarcinogenesis[2–4]; this is best illustrated with the use of psoralens to cause phototoxicity as part of psoralen-ultraviolet A photochemotherapy (PUVA),[5,6] but may be an issue with some other drug groups.[7,8] It has recently become clear that increased risk of both melanoma and nonmelanoma skin cancers is an important issue with the photosensitizing antifungal voriconazole.[9] Vemurafenib, an inhibitor of mutated *BRAF*, shows promise as a treatment for metastatic malignant melanoma but is also associated with drug-induced phototoxicity and a greatly increased risk of squamous cell carcinoma of the skin.[10] It is plausible that the increased worldwide incidence of various skin cancers may be partly from the increased use of certain phototoxic drugs.

Phototoxicity will theoretically occur in any individual with exposure to enough phototoxin and appropriate irradiation, although idiosyncratic factors likely render some subjects more or less susceptible. Some drugs, such as psoralens and most fluoroquinolone antibiotics, can be expected to cause phototoxicity in anyone given a sufficiently high dose. However, the phototoxin is not always the parent drug: it may be a metabolite. It is likely that at least part of the reason why systemic drug phototoxicity can seem idiosyncratic, with only some individuals affected even if very high doses are administered, is because of individual differences in drug bioavailability and metabolism.

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Photobiology Unit, Department of Dermatology, Ninewells Hospital and Medical School, University of Dundee, Dundee DD1 9SY, Scotland, UK
* Corresponding author. Photobiology Unit, Level 8, Ninewells Hospital and Medical School, Dundee, Tayside DD1 9SY, Great Britain.
E-mail address: r.s.dawe@dundee.ac.uk

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Even with drugs such as ciprofloxacin,[11] which frequently cause phototoxicity, marked variation is seen between individuals in the degree of photosensitivity produced by a given dose of drug (**Fig. 1**). Different patterns of phototoxic reactions occur in the skin, including an almost immediate prickling/burning sensation, urticaria, sunburn-like reactions, and skin fragility states (**Table 1**).

Photoallergy is usually associated with exposure to topical agents, such as ultraviolet filters and topical nonsteroidal anti-inflammatory drugs.[12] In some parts of the world, certain antiseptics may still be relevant.[13]

EPIDEMIOLOGY

Although reported as the third most common cutaneous drug reaction in a recent Tunisian series,[14] drug-induced photosensitivity is frequently underdiagnosed. In tertiary referral populations seen at photodermatology centers, between 2% and 15% of patients were affected,[15–18] and 4% of those seen in the Dundee Photobiology Unit. Drug-induced phototoxicity is especially common in some populations, such as people with cystic fibrosis taking ciprofloxacin.[19] However, most who develop sunburn-like phototoxicity during a course of antibiotic therapy are likely to simply stop the drug and not seek a formal diagnosis. The prevalence of different types of drug photosensitivity will vary geographically, not only because of differing patterns of exposure to causative drugs and patterns of ultraviolet and visible light exposure, but also because of variations in an individual's endogenous photoprotection and differences in drug metabolism between populations.

PATHOGENESIS

The absorption of optical radiation by a photosensitizing drug or drug metabolite within the skin is an essential first step in both phototoxicity and photoallergy. Drug-induced photosensitivity can involve ultraviolet B (UVB) wavelengths, ultraviolet A (UVA) wavelengths, and visible wavelengths, depending on the absorption characteristics of the drug or drug metabolite. As a general rule, drug-induced photosensitivity is primarily a UVA phenomenon.

Once the energy is absorbed, photosensitizing radicals are produced through various mechanisms that can directly lead, again through a variety of mechanisms, to phototoxic effects. Alternatively, drug phototoxicity may be produced more indirectly by the altered chemicals, leading to alterations in endogenous porphyrin levels or triggering a lupus erythematosus–type reaction.

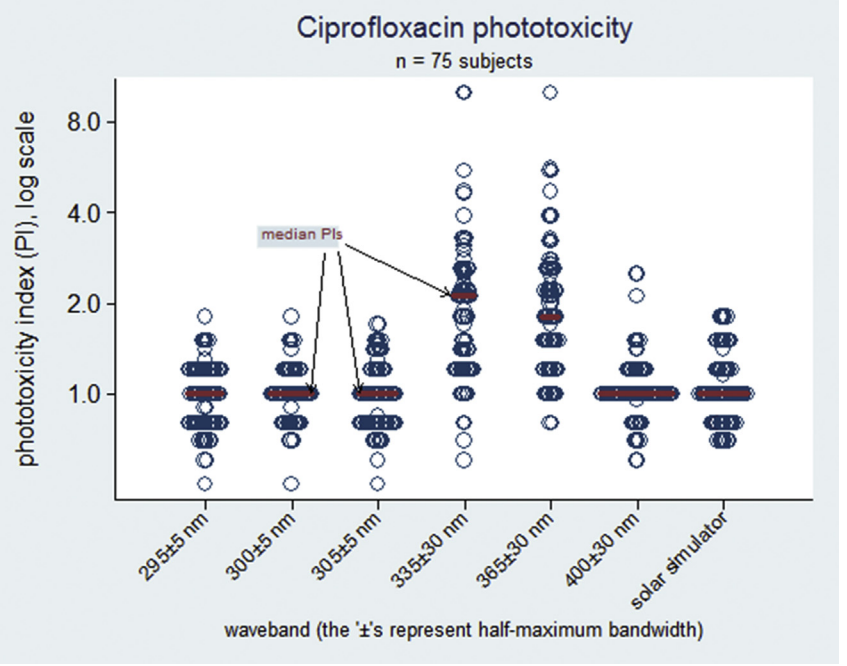

Fig. 1. Figure, taken from the results of several phototoxicity studies that included ciprofloxacin at a standard dose as a positive control drug, showing (1) the variability between individuals and (2) the wavelength dependency of phototoxicity with this particular drug. Note that at the 335 ± 30 nm waveband, the median phototoxic index (PI) is 2, indicating erythema with half the dose of this waveband that caused erythema without ciprofloxacin, but 2 individuals were severely photosensitive, with phototoxic indices greater than 8.