










## Drug-induced Photosensitivity: Photoallergic, Phototoxic and Adverse Drug Reactions

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### Abstract

**Background:** Drug-induced photosensitivity refers to skin reactions caused by exposure to ultraviolet light following the use of certain medications, which can be administered topically or orally. When ultraviolet radiation interacts with a chemical present in adequate concentrations within the skin, it may trigger various reactions, particularly in susceptible individuals. The most common responses are photoallergic and phototoxic reactions.

**Methods:** In this paper, we discussed about drug-induced photosensitivity: Photoallergic, phototoxic and adverse drug reactions, and some of those medication that leads to these conditions.

**Results:** Photosensitive drug eruptions are cutaneous adverse events due to exposure to a medication and either ultraviolet or visible radiation.

**Conclusion:** Photosensitive drugs (PSDs) represent an important research area and more investigations would be helpful to better predict drug photosensitizing potential, prevent and manage cutaneous adverse events and find the most appropriate alternative therapeutic strategy. As well as, various medications, particularly antibiotics and analgesics, can induce both photoallergic and phototoxic reactions, there are significant differences between the two, including their onset timing, requirement for prior exposure, underlying mechanisms, clinical presentation, and histopathological features.

**Keywords:** drug-induced photosensitivity, photoallergic, phototoxic, adverse drug reactions, medications

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### Introduction

Drug-induced photosensitivity refers to a cutaneous condition that either develops or worsens due to ultraviolet (UV) exposure in combination with a chemical agent. Such exposure may occur through systemic or topical medications capable of penetrating the skin. Drug-induced photosensitivity is a relatively common phenomenon in clinical practice, accounting for approximately 8% of reported drug-related adverse skin reactions. [1] Photoallergic reactions are immunologically driven, requiring prior sensitization, and typically present similarly to allergic contact dermatitis. In contrast, phototoxic reactions do not necessitate prior sensitization and manifest as an exaggerated sunburn-like response. [2]

Both oral and topical medications can trigger photosensitive skin reactions when exposed to ultraviolet (UV) light. In predisposed individuals, photoallergy and phototoxicity arise when UV radiation interacts with chemicals concentrated in the skin. Although the current literature primarily comprises case reports and series, suggesting these occurrences are largely anecdotal, drug-induced photosensitivity remains a significant subset of drug-related cutaneous reactions, contributing to up to 8% of medication-associated adverse effects. [3] Although photoallergic and phototoxic reactions share some clinical features, they are distinguishable based on several key aspects.

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Characteristics of photoallergic reactions include: (i) they are less prevalent than phototoxic responses; (ii) their occurrence is independent of medication dose or radiant energy; (iii) minimal exposure to the photosensitizing drug is sufficient; (iv) they develop at least 24 hours following initial exposure; (v) prior sensitization is essential; (vi) they present as eczematous dermatitis, often extending beyond UV-exposed areas; (vii) histopathological findings demonstrate epidermal spongiosis rather than necrosis; (viii) they are mediated by immune mechanisms; and (ix) they may be triggered by cross-reacting drugs with structural similarities. [2]

## Material and Methods

### Effects of ultra violet A and B (UVA and UVB)

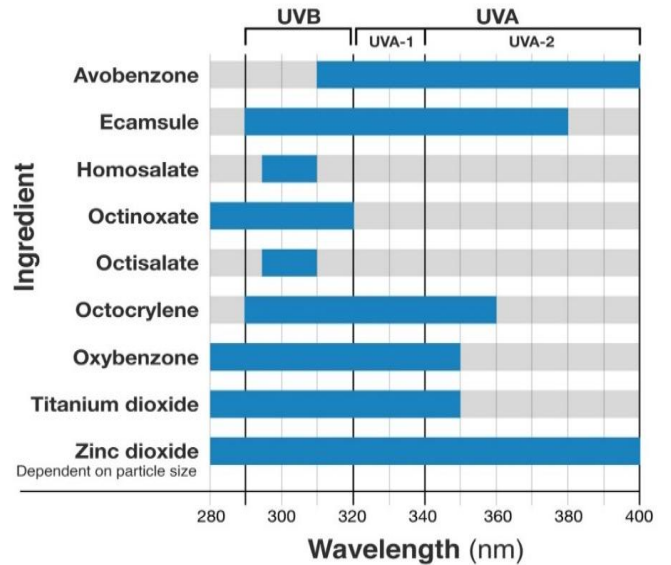
The primary distinction between UVA and UVB rays lies in their wavelength and energy:

- UVA rays have longer wavelengths with lower energy, enabling them to penetrate deeper into the skin.
- UVB rays have shorter wavelengths with higher energy, but they penetrate the skin more superficially. [4]

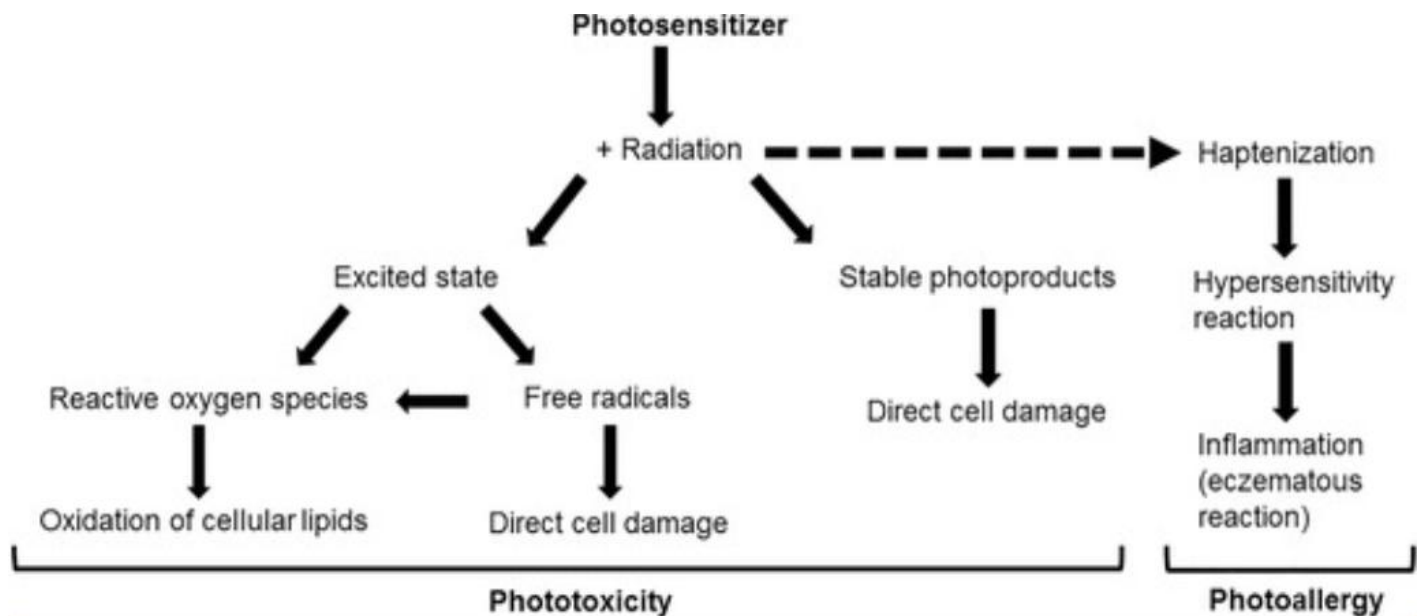
Both UVA and UVB rays contribute to skin damage and skin cancer, but each causes distinct types of harm, necessitating protection from both. Sunscreen application is one of the most effective methods for shielding the skin against UV radiation. It is crucial to choose a sunscreen offering protection against both UVA and UVB rays. Historically, sunscreens primarily protected against UVB radiation due to the earlier understanding of its effects, but it is now widely recognized that UVA rays also pose a significant risk. Ultra violet B protection is quantified by the SPF (Sun Protection Factor) rating

indicated on sunscreen labels. Although there is no standardized system to measure UVA protection, many modern sunscreens incorporate ingredients to counter UVA radiation as well. Such sunscreens are commonly labeled as “broad-spectrum” or “UVA/UVB protection”, signifying their efficacy against both types of UV rays. [Figure-1] However, as there is currently no universal standard defining the degree of UVA protection, these terms may lack precise meaning. [5]

**Figure-1 Effectiveness of sunscreen ingredients depends on their ability to protect against ultraviolet radiation [6]**



**Figure-2 Schematic illustration of the major mechanisms of phototoxic and photoallergic tissue damage [3]**



## Adverse drug reactions (ADRs)

Adverse drug reactions (ADRs) represent a major public health concern, contributing to increased mortality, morbidity, and healthcare expenditures, including higher hospital admission rates and extended hospital stays. [7] Healthcare professionals (HCPs)—including physicians, pharmacists, dentists, and nurses—play a pivotal role in pharmacovigilance programs. However, under-reporting of ADRs remains widespread, especially in low- and middle-income countries (LMICs). [8]

## Photosensitivity skin reactions with some class of medications

Photosensitivity skin reactions are often triggered by drugs (photosensitizers) administered either systemically or topically. Drug classes with high photosensitizing potential include antibiotics, diuretics, and nonsteroidal anti-inflammatory drugs (NSAIDs). Photosensitizers act as chromophores, typically possessing a planar, tricyclic, or polycyclic structure and a low molecular weight of 200–500 Da. [2]

These molecules are usually activated by ultraviolet (UV) light—most commonly UVA light (320–400 nm), which penetrates deeply into the dermis—or, less frequently, visible light. During this process, photosensitizers absorb radiant energy in the form of photons and enter an excited state, triggering photochemical reactions with other molecules in the epidermal and/or dermal tissues. These molecular interactions form the basis of photosensitivity reactions in the skin.

Based on the underlying pathophysiologic mechanisms, photosensitivity drug reactions are classified as either phototoxic or photoallergic. Phototoxic reactions are more common, can occur in any individual, and depend solely on the dose of the photosensitizer and the level of exposure to activating light wavelengths. In contrast, photoallergic reactions are rare, require prior sensitization, and occur independently of the photosensitizer dose. Many oral medications have been implicated in causing phototoxic skin eruptions, and some of these can also induce photoallergic responses. Notably, tetracyclines and quinolones are frequent causes of drug-induced phototoxicity. [2]

## Incidence of Drug- Induced Phototoxic and Photoallergic Reactions

Data on drug-induced photosensitivity are primarily derived from national reporting systems, such as the US Food and Drug Administration (FDA) and the UK's Committee on Safety of Medicines, with less frequent input from international sources like the WHO Program for International Drug Monitoring. Since reporting is typically voluntary, the data are often biased, incomplete, and disproportionately focused on newly marketed drugs. Despite these limitations, drug-induced photosensitivity is recognized as a relatively common event, accounting for up to 8% of all adverse drug reactions as shown in **Table-1 and 2** [9]

Phototoxic reactions can affect patients of any age, though they are more commonly observed in women. These reactions typically resemble severe sunburn and are confined to areas exposed to

**Table-1 Systemic medications causing phototoxicity and their action spectrum, selected [10]**

Class of drugs	Name of the drugs	Action of the spectrum
Antimicrobials	Doxycycline	UVA
	Minocycline	UVA
	Ciprofloxacin	UVA
	Levofloxacin	UVA
	Voriconazole	Unknown
Diuretics	Furosemide	Unknown
	hydrochlorothiazide	UVA
NSAIDs	Ketoprofen	UVA
	Naproxen	UVA
Others	Quinidine	UVA
	Psoralens	UVA
	Retinoids	UVA, UVB
	Calcium channel blockers	UVA

**Table 2. Topical medications causing photoallergy and their action spectrum, selected [10]**

Class of drugs	Name of the drugs	Action of the spectrum
NSAIDs	Ketoprofen	UVA
	Benzophenone	UVA
	Meloxicam	UVA
	Piroxicam	UV
Others	Acyclovir	UVA
	Hydrocortisone	UVA

**Table-3 Systemic medications causing photoallergy and their action spectrum, selected [10]**

Class of drugs	Name of the drugs	Action of the spectrum
Sulphur- containing drugs	Hydrochlorothiazide	UVA
	Sulfadiazine	UVB
	Sulfonamides	UVB
	Sulfonylureas	UVA
Antimicrobials	Chloramphenicol	Unknown
	Lomefloxacin	UVA, UVB
NSAIDs	Ketoprofen	UVA
	Naproxen	UVA
Phenothiazines	Chlorpromazine	UVA
Others	Dapsone	Unknown
	Amantadine	UVA
	Ranitidine	UVA

**Table-4 Oral medications capable of causing phototoxicity [11]**

Phototoxic	Name of the drugs	Action of the spectrum
Antimicrobials	Doxycycline	UVA
	Lymecycline	UVA
	Minocycline	UVA
	Tetracycline	UVA
	Demeclocycline	UVA
	Ciprofloxacin	UVA
	Enoxacin	UVA

Continue...

	Fleroxacin	UVA
	Levofloxacin	UVA
	Lomefloxacin	UVA and UVB
	Nalidixic acid	UVA
	Pefloxacin	UVA
	Sparfloxacin	UVA
	Griseofulvin	UVA
Sulfur-containing medications	Hydrochlorothiazide	UVA
	Sulfonamides	UVB
	UVA	UVA
NSAIDs	Ketoprofen	UVA
	Naproxen	UVA
	Suprofen	UVA and UVB
	Tiaprofenic acid	UVA
	Benzophenone	UVA
	Carprofen	UVA
Others	Atorvastatin	UVB
	Calcium-channel blockers	UVA
	Chlorpromazine	UVA
	Calcium channel blockers	UVA

sunlight. The hallmark symptoms include erythema and edema, which appear within minutes to a few hours after UV exposure. Vesiculation and blistering are rare. Persistent hyperpigmentation may occur, and skin damage can persist for years, even after the removal of the triggering drug. [12]

In contrast, photoallergic dermatitis occurs more frequently in men and usually develops 24 to 72 hours post-exposure and shown in **Table-3**. It commonly affects sun-exposed areas such as the face, neck, upper chest, and hands, though lesions may spread to non-exposed regions. This condition presents with

symptoms similar to contact dermatitis, including desquamation and prolonged hyperpigmentation, which can persist for over a year. The predominant feature of photoallergic dermatitis is eczematous dermatitis. [12]

### Diagnosis of photoallergy and phototoxicity

Drug-induced photoallergy and phototoxicity are diagnosed by correlating a history of photosensitizing drug use with the presence of sun-exposed skin eruptions. Differentiation between these conditions typically requires photo patch testing, minimal erythema dose (MED) testing, and, in some cases, skin biopsies. Photo patch testing involves applying suspected photoallergens to the skin in duplicate: one area is exposed to UVA light, while the other remains shielded. A plate glass barrier is used to block UVB contamination. Skin reactions are evaluated at 24, 48, and 72–96 hours post-exposure; a reaction confined to the UVA-exposed area confirms photoallergy. For suspected phototoxicity, skin areas not directly exposed to sunlight are irradiated with gradually increasing doses of both UVA and UVB to determine the Minimal Erythema Dose (MED). The MED represents the lowest dose of radiation required to induce visible skin redness. A response of erythema at a lower-than-expected MED indicates drug-induced phototoxicity. The MED typically returns to normal levels upon re-testing after two weeks. Skin biopsy can also be useful for differentiating between photoallergy and phototoxicity as shown in **Table-4**. Histopathological findings show that photoallergic reactions resemble allergic contact dermatitis, while phototoxic reactions mimic sunburn-like changes. [13]

### Management of photoallergy and phototoxicity

Patients should be advised to limit excessive exposure to sunlight when prescribed medications with photosensitizing potential. Using broad-spectrum sunscreens that provide protection against both UVA and UVB rays can help reduce the risk of photosensitive reactions. If photosensitivity occurs, management typically involves symptomatic relief, such as the use of cool compresses, soothing lotions, topical corticosteroids, and systemic antipruritic agents. The most definitive approach is to discontinue the causative medication; however, it is important to note that photosensitivity may persist for several months or even years after stopping the drug. [2]

## Conclusion

Photosensitive drugs (PSDs) are a crucial area of research, and further studies are needed to improve the prediction of their photosensitizing potential, prevent and manage skin-related adverse effects, and identify suitable alternative treatment options. Additionally, while various medications—especially antibiotics and analgesics—can cause both photoallergic and phototoxic reactions, these two conditions differ significantly in terms of onset time, the need for prior exposure, underlying mechanisms, clinical manifestations, and histopathological characteristics.

### Conflict of Interest – None

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## Authors' Contributions

**BOS** – Study design and data collection, **NMAM** – Study design, concepts, data collection, **BOS, NMAM** – Data collection and analysis, **BOS, SBS** – Data collection, Manuscript writing, **DAM** – Manuscript writing, and **BOS, NMAM, SBS, DAM, SJR** and **FAS** – All authors were wrote the manuscript, reading and checking all the aspects and approved by all authors.

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