Photo Chemotherapy

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INTRODUCTION

Ultraviolet (UV) light is widely used by dermatologists for skin conditions. The choice of UV over other forms of treatment depends on things such as a patient's age, disease, skin type, previous treatments and current medication. Photochemotherapy, or PUVA therapy, has received much attention recently, for it is one of the more promising advances in dermatologic therapy. Photochemotherapy (PUVA) is the treatment method in which radiation of appropriate wavelength is used to induce a therapeutic response in the presence of a photosensitizing drug. The radiation must be absorbed by a target molecule—a chromophore, which is an exogenous drug in PUVA. Ultraviolet and visible radiation are used therapeutically in dermatology; UVC—100–290 nm is absorbed by the ozone layer, UVB—292–320 nm for phototherapy, UVA—320–400 nm for PUVA (Psoralens plus UVA) and visible light - 400 to 800 nm for photodynamic therapy. The purpose of the psoralen is to make the skin more reactive to light. PUVA is useful for patients with various skin disorders, including psoriasis, oral lichen planus, polymorphic light eruption, graft versus host disease and mycosis fungoides. A wide range of diverse field for its possible utility provides an alternative armamentarium in many immunological disorders for dermatologist and also for oral diagnostician.

Key words: Psoralens, Photochemotherapy, Ultraviolet Radiation.

Abstract: Ultraviolet (UV) radiation has been used for decades with great success and at a constantly increasing rate in the management of skin diseases and has thereby become an essential part of modern dermatological therapy. The combination of medication and UV light therapy is called photochemotherapy. UVA rays alone are not an effective form of treatment. The effective agent in PUVA treatment is psoralen, a light-sensitizing medication that is taken orally or applied topically. It is used because some medications make your skin more reactive to light. PUVA is useful for patients with various skin disorders, including psoriasis, oral lichen planus, polymorphic light eruption, graft versus host disease and mycosis fungoides. A wide range of diverse field for its possible utility provides an alternative armamentarium in many immunological disorders for dermatologist and also for oral diagnostician.

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Starting from historical date up to modern era the safe and useful modes of PUVA has been documented in many immunological disorders. It is used in various skin disorders, including psoriasis, oral lichen planus, polymorphic light eruption, graft versus host disease and mycosis fungoides. Oral PUVA consists of administering UV rays in special irradiation chambers an hour or two after ingesting the drug psoralen. PUVA treatments are given once every two or more days, two to three times a week. Patients treated with PUVA need to be careful to avoid natural UV exposure (including exposure through window, glass and cloud) throughout the course. It should be avoided in patients with a history of skin cancer or those, who require a higher maintaining dose. This review is concerned with molecular mechanisms considered accountable for the photochemotherapeutic effects, the development of new chemical structures aimed at improving the effectiveness and/or overcoming some undesired side effects will also be reported.

HISTORY

The first report of the use of 'phototherapy' in the treatment of skin disorders dates from 1400 BC from India when patients with vitiligo were given certain plant extracts (whose active ingredients included psoralens) and then exposed to the sun. The real interest in the use of ultraviolet (UV) irradiation in the treatment of various skin diseases started in the 19th century when Niels Finsen received the Nobel Prize (1903) for his therapeutic results with UV irradiation in lupus vulgaris, the only dermatologist ever to be awarded one. In 1974, Parrish et al., reported successful treatment of severe psoriasis with 8-MOP (p) with UV and coined by acronym PUVA. In the 1980s narrowband UVB (nbUVB) (311 nm) treatment was developed and found to be more effective than broadband UVB in the treatment of many dermatological diseases.

PHOTOCHEMOTHERAPY CHEMISTRY

Psoralens belong to the furocoumarin class of compounds, which are derived from fusion of furan with a coumarin found naturally in certain plant species or synthesized in vitro. It occurs naturally in many plants including limes, lemons, and parsnips. Among the three psoralens, the trimethyl derivative is only synthesized in vitro, 8-MOPs (methoxysalens), 5-MOPs (Bergapten), and 4,5,8 TMPs (trioxsalen); the trimethyl derivative is not found naturally and is synthesized in vitro. The structure of psoralens was originally deduced using its degradation reactions. It exhibits the normal reactions of the
lactone of coumarin, such as ring opening by alkali to give a coumarinic acid or coumaric acid derivative. Potassium permanganate causes oxidation of the furan ring, whereas other methods of oxidation produce furan-2,3-carboxylic acid. IUPAC name for psoralens is 7 H-furo [3,2-g] chromen-7-one.9

**PSORALEN DERIVATIVES**

One isomer of psoralens is angelicin and most furocoumarins can be regarded as derivatives of psoralsen or angelicin. Some important psoralsen derivatives are xanthotoxin, bergapten, andnodekenetin. Another important feature of this class of compounds is its ability in generating singlet oxygen.10

**PHARMACOKINETIC**

The psoralens are absorbed rapidly after oral administration. Absorption of psoralsen is dependent upon many factors namely the formulation of drug, coexistent food intake, first pass effect in liver, and individual differences in absorption of drug but this accounts partly for the rare cases, which not gives respond expectedly to PUVA therapy in the usual dose. After absorption, psoralens get distributed to all tissues and are excreted in the urine within an average of 12 hours. Peak levels of psoralens in the blood after oral intake are seen within 1-8 hours with a mean of 2 hours. This forms the basis for giving UV radiation after 2 hours of oral intake in PUVA therapy. Following oral administration of 8-MOP, absorption and resulting plasma concentrations show considerable variation between subjects, but UV A exposure is given usually 2 h after ingestion at the average time of peak plasma concentration.11 PUVA may also be given using topical psoralen, either painted onto the skin surface or, more frequently, using a bath delivery system in which the patient soaks for 15 min in a weak psoralen solution. Significant concentrations of psoralen in plasma are not achieved with topical psoralen.12

**MECHANISM OF ACTION**

The action spectrum for oral PUVA is between 320 and 400 nm. Two types of reaction are involved in causing photosensitivity after PUVA. (a) an anoxic reaction that affects cellular deoxyribonucleic acid (DNA) with formation of photo adducts that may inhibit the proliferation of epidermal cells and induce apoptosis, and (b) an oxygen dependent reaction that give rise to free radicals and reactive oxygen that may damage membrane by lipid per oxidation. PUVA promotes melanogenesis in normal skin, increased pigmentation results from the transfer of melanosomes from melanocytes to epidermal cells, however, there is no change in the size of melanosomes or in their distribution. In vitiligo, a stimulatory effect on melanocytes secondary to action on c-AMP pathway is postulated.13 There is an effect on DNA synthesis, proliferation of cells, immunological alternation and on the biosynthesis of prostaglandin in the skin. Psoralsen act much more on cells that are actively dividing than on resting cells. This explains why they are effective only in the active stage of scleroderma and not in the fibrotic stage. Action on actively dividing or activated immune cells especially on T cell, explain their action in immune mediated disease like psoriasis, lichen planus, graft versus host disease.14

**DOSAGE**

Psoralen can be taken as a tablet (two hours before treatment with UV A), or applied externally to the skin as a gel or cream (30 minutes before treatment with UV A). Another option is to add the psoralen to bath water and soak in the bath for 10-15 minutes.

**DURATION**

The time of exposure and number of treatments required to obtain satisfactory results vary based on a number of factors including whether the psoralen is taken orally or applied topically, the skin type of the patient, the type of UVA unit being used, and the severity of the condition.15

**INDICATIONS**

It is widely used in the treatment of psoriasis, vitiligo, lichen planus, atopic dermatitis, Eczema, cutaneous t-cell lymphoma, acute graft-versus-host disease (GVHD), chronic graft-versus-host disease (GVHD), alopecia areata, chronic palmoplantar pustulosis, mycosis fungoides, granuloma annulare, morphea and localized skin lesions associated with scleroderma, photodermatoses, pityriasis lichenoides, severe refractory atopic dermatitis/eczema, severe urticaria pigmentosa, Eosinophilic folliculitis and other pruritic eruptions of human immunodeficiency virus (HIV) infection. PUVA can induce melanocyte pigmentation in vitiligo, resulting in cosmetic pigmentation.16

**CONTRAINDICATIONS**

1. History of arsenic exposure
2. History of ionizing radiation exposure
3. History or presence of melanoma or other skin cancer
4. Pregnancy or breast feeding
5. Persons suffering from some sun sensitive diseases like porphyria, lupus or xeroderma pigmentosum

**APPLICATIONS**

**Psoriasis**

Approximately 80% of people with psoriasis notice an improvement in their skin after they have been in the sunshine. The use of the sun's rays has been used to treat psoriasis for over a century, however, of the ultraviolet rays emitted by the sun, only UVA and UVB is of benefit to people with psoriasis. UV light helps to power chemical reactions that affect the function of skin cells. PUVA can be more successful on thicker plaques of psoriasis than UVB, as the UVA is absorbed much deeper in the skin. Hand and foot PUVA machines are also used to treat palmar-plantar pustular psoriasis.17

**Oral Lichen Planus**

Photchemotherapy may be useful for severe forms of erosive OLP that do not respond to conventional treatment. Photchemotherapy with 8-methoxypsoralen and long wave ultraviolet light (PUVA) has been used successfully in the treatment of skin lesions and cutaneous lichen planus.

**Vitiligo**

Narrowband UVB and PUVA can both induce repigmentation. Up to 70% of patients with vitiligo benefit if they are treated continuously for a year or more. Those with trichrome pattern vitiligo, that is, those with areas of reduced pigment as well as areas of normal skin and of complete pigment loss, tend to respond better.

**Polymorphic light eruption**

Mild PLE is usually managed with advice on behavioral, clothing, and topical sunscreen photo protection measures. However, when it is more severe and impairing life quality, prophylactic PUVA or UVB phototherapy administered in spring is beneficial. Narrowband UVB is as effective as PUVA, and
CONCLUSION

The present overviews regarding PUVA provide a sound idea in over all aspects from historical age to modern era as one of the alternative effective therapy for many immunological disorder and systematic disease. To be on a safer side, steps should be taken to lower the dose of PUVA by changing the dose schedule, reducing the unnecessary maintaining dose and by adding a psoralens, or oral retinoids to the regimen. PUVA therapy is best avoided in patients with a history of skin cancer or those, who require a higher maintaining dose.

REFERENCES


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