PIGMENTOGENIC EFFECTS OF PSORALENS

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INTRODUCTION

Cumulative exaggerated exposure to the sun produces damage to the skin leading to premature aging and ultimately to the development of skin cancer in a significant percentage of the caucasian population.

The skin responds to the UVR exposure with the promotion of two defensive systems. The first barrier developed is a thickening of the stratum corneum which is very effective. The second barrier is the elaboration of a melanin filter in the cell of the epidermis: the presence of melanin particles in the keratinocytes protects the nuclear DNA from harmful UVR alterations. It has been assumed and accepted, that this pigmentation induced by exposure to sunlight is protective against immediate and also delayed adverse effects of sunlight, although the initial exposure, prior to tanning, can lead to damage as expressed by the degree of erythema produced.

Melanin pigmentation of the human skin results from close interaction between the epidermal melanocytes producing melanosomes and the keratinocytes that acquire the melanosomes and transport them towards the horny layer.

MECHANISM OF PIGMENTOGENIC EFFECTS OF PSORALENS

The augmentation of melanin pigmentation in normal skin by topical or oral administration of psoralens and exposure to ultraviolet radiation (320-400 nm) involves also the close interaction of melanocytes and keratinocytes (1 & 2). During this process, five major events have been observed (3):

1 - Increasing number of functional melanocytes as the result of proliferation and/or activation of melanocytes.
2 - Increasing number of melanosomes in melanocytes as the result of increased synthesis of melanosomes in melanocytes.
3 - Increasing activity of tyrosinase.
4 - Increasing transfer of melanosomes as the result of more rapid turnover of keratinocytes.
5 - Modification of the pattern of melanosome distribution in caucasoid skin, possibly as a result of increase in the size of melanosomes.

Experimental data suggest that enhanced cutaneous hyperpigmentation following exposure of skin to psoralens plus sunlight is at least partly due to a direct effect on the pigment cells (4). Psoralen plus light appears to enhance the cellular enzymic machinery for pigment production by affecting the cell cycle (DNA photoadducts) and prolong the availability of MSH receptors (5).
EXPERIMENTAL EVIDENCE

It has been known for a long time that oral ingestion or topical application of psoralens makes individuals susceptible to significant pigmentation on exposure to either solar radiation or to UVA (1, 2 & 3).

More than fifteen years ago the first suntan product containing natural oil of bergamot, with standardized amounts of bergapten were introduced to the market in Europe. These products, in different vehicles also contained sunscreens and were used and sold to promote both tanning and protection from UVB. Because of the phototumerogenic potential of psoralens on animal, extensive studies have been conducted with the commercial formulations. Recent results demonstrate that these formulations did not show photomutagenic potential (Ames test, 6). Young et al. (7) have shown that when the products containing both natural bergamot oil and sunscreens are combined the phototumerogenicity is essentially or nearly completely blocked in albino mice.

Several studies were run using the sun preparations containing natural bergapten to establish their ability to tan.

The significant studies were those conducted by Tronnier and Agache (8), and by R. Sigafoues both of whom used commercially available products which were evaluated in normal volunteers under conditions which approximated conditions of use of the products.

More recently, a double-blind dose response study of lotion formulations of a sun product containing two levels of sunscreen with varying amounts of natural bergamot oil containing bergapten was conducted in 45 young adults with skin type I and II under natural sun exposure (San Diego, Ca).

The result clearly demonstrate that skin type I individuals, normally considered to be people who rarely can show any pigmentation when exposed to natural sunlight, could be significantly pigmented by the use of such preparations.

This study shows that 90% of a population of skin type I and skin type II individuals (42 out of 47) developed tans under the influence of natural bergapten and UVA, while only 20% developed a tan when no bergapten was present, which they can not do when they use a sunscreen or are exposed to the sun without bergapten present (9 out of 47).

PROTECTIVE VALUE OF PSORALEN INDUCED PIGMENTATION

According to Fitzpatrick (13), from the two types of melanins deriving from tyrosine in mammalians (eumelanins and pheomelanins) "only eumelanin is contained in human epidermis". Exposure of melanin to UVR generates free radicals, but paradoxally melanin is also able to quench singlet oxygen generated by UVR exposure in the skin.

Recent studies conducted on miniature pigs (10) or in human conditions (11) using topical sunscreen-bergapten product (5% ethyl hexyl cinnamate + bergapten 30 ppm) were tested. Test sites were challenge-irradiated, after induced pigmentation and erythema production, sunburn cell formation,