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### **Research Letter**

# Photoprotective, Immunomodulatory and Eco-Friendly: On the road to the Holy Grail of Sunscreen Development

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Phototherapy, utilizing Narrow band UVB, PUVA, UVA-1 or natural sunlight has long been used by dermatologists in the management of a range of dermatological conditions but is accompanied by the potential hazards associated with ultraviolet light exposure to the skin. A therapeutic sunscreen, a preparation which offers ultraviolet light protection, whilst permissive of the benefits of ultraviolet light therapy without the need for expensive medical equipment is an attractive concept.

Such a preparation should contain a substrate which both absorbs photons in ultraviolet spectrum thereby providing photoprotection, and in which absorption of the photon mediates a chemical reaction generating a pharmacological active compound. Excipients should extend the photoprotective spectrum and favour the generation of the active compound. Potential candidates for the inclusion in such a preparation would be the aromatic amino acid L-tryptophan, photo-oxidation of which generates 6-formylindolo[3,2-b] carbazole (FICZ), a potent endogenous ligand of the Aryl Hydrocarbon Receptor (AHR) [1]. L-tryptophan is also metabolized to nicotinamide via the Kynurenine Pathway (KP), several of the metabolic intermediates being active at the AHR, which plays an important role in cutaneous pathology [2]. Tapinarof, an AHR agonist currently available for atopic dermatitis [3] and psoriasis [4] demonstrates the benefit of AHR manipulation. Lecithin-based Multilamellar Liposomes (MLLs) have recently been reported to offer equivalent photo-protection to 50+ SPF sunscreens [5] and would be another potential component.

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Findings utilizing a preparation of 2% L tryptophan, 30% Sunflower lecithin, 3% Polyvinyl alcohol, 20% ethanol, pH 5.8 were presented at the Australasian college of Dermatologists 55th Annual Scientific Meeting [6]. This preparation demonstrated statistically significant activity at the AHR following graduated sun exposure as assessed by a quantitative assessment of Cytochrome P450 1A2 immunohistochemistry.

The Sun Protection Factor (SPF) was not formally determined although no erythema was noted following 20J of sun exposure. Participant Fitzpatrick skin types were one to three. Ethanol was included in the preparation to promote the aggregation of the phosphatidylcholine component of lecithin as phosphatidylcholine is more soluble in ethanol [7], and sterically was considered to favour the generation of FICZ from L tryptophan.

Secondary endpoints of the study included an assessment of EASI and PASI scores in patients treated with this preparation combined with 20J of sunlight exposure ascertained by a UV-SPEEDRE UV Integrator and comparison to a subgroup treated with Narrowband UVB. A total of 32 participants were enrolled with 22 completing the trial. 17 of these suffered from either psoriasis or atopic dermatitis. Losses were due principally to COVID restrictions. The results are outlined in the following table 1.

NBUVB PASI		Trial agent PASI	
Initial	Final	Initial	Final
6	0	10.8	3.5
4.8	0		
17.6	7.2		
12.4	0		
7.2	3.2		
NBUVB EASI		Trial agent EASI	
8.4	3.6	8.4	3.2
5.4	2	10.8	0
3.2	2.8	6.6	0
26	7.2	39.6	26
2.8	3.6	9.6	0.6
13.1	3.4		

Table 1: Significant improvements in both the NBUVB and Trial agent groups.

Statistically significant improvements are seen in both the NBU-VB (Mann Whitney z-score 2.69227, p-value 0 .00714) and Trial agent groups (Mann Whitney z-score is 2.0016, p-value .0455). Although this is a small study it supports the concept that lecithin-based sunscreens inclusive of L tryptophan may form the basis of a potential therapeutic sunscreen and further investigations are warranted. These preparations also offer the benefits of water resistance and as they are fully biodegradable, are considered environmentally friendly.

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