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**Review Article** 

# Health Threat in the Tanning Trend

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## Abstract

Self enhancement products have become increasingly popular options to achieve tanning in the pursuit of darker complexion. This practice is relatively popular among both men and women for aesthetic purposes.

Melanotan-I and melanotan-II are synthetic alpha-melanocyte stimulating hormone ( $\alpha$ -MSH) analogues that stimulate tanning, which are available in two forms, injectable and nasal spray, and can be purchased via online portals and media outlets. The health consequences of these products range from minor to acute and chronic clinical outcomes. Sunless tanning products are alternatively, perceived as "healthy alternatives" to sunbathing, however, no consistent data on their safety is standardized.

**Keywords:** self-tanning; sunbed; tanning nasal spray; tanning injections; melanotan I; melanotan II; dysplastic naevi; melanoma

## Introduction

Appearance of tanned skin is currently perceived as a symbol of beauty and wellbeing.

In recent years, self-tanners have gained publicity, especially when similar outcomes can be achieved, avoiding the side effects of ultraviolet exposure [1], thus self-tanners in multiple forms are used as an alternative to sun tanning and tanning beds. Majority of self-tanning products contain dihydroxyacetone (DHA), a plant-based sugar molecule which reacts with keratin proteins in the stratum corneum [1].

Melanocortin hormones are involved in several biological functions including pigmentation, energy homeostasis, sexual function, immunomodulation, exocrine secretion, and steroidogenesis. The main melanocytic receptor in the skin is melanocortin-1 receptor (MCR-1) that when interact with a-MSH, modulate the process of pigmentation [2,3].

Synthetic melanocortin analogues like Melanotan I and Melanotan II are synthetic peptides that have a prolonged action, are enzymatically resistant, stable, and up to 1000 times more potent than  $\alpha$ -MSH, and increase the expression of eumelanin, via the activation of melanocortin type 1 receptors (MC1R) of melanocytes [4]. Melanotan I and Melanotan II are unregulated, non-licenced products sold in two forms: powder for injection and as a nasal spray. Afamelanotide (formerly known as Melanotan I) is the first synthesised  $\alpha$ -MSH analogue, that stimulates melanogenesis, and prevents phototoxicity in adult patients with Erythropoietic protoporphyria (EPP) for which it is approved [5, 6].

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Bremelanotide is the third available analogue of  $\alpha$ -MSH approved in the USA for the management of premenopausal women with acquired, generalized hypoactive sexual desire disorder [7].

The aim of this article is to pinpoint some reported outcomes and health consequences of tanning products in different forms.

## Discussion

#### Ultraviolet tanning beds and booths

Ultraviolet tanning offered by (tanning beds and booths) is mostly used by adolescents and young adults, which can limit the dosage of UVB light and the likelihood of sunburn, although more sessions are needed to offer tan, which can consequently increase the total dose of UVA radiation. One indoor tanning session increased the risk of developing melanoma by 20 percent [8]. There is significant evidence that younger people may be more susceptible to the carcinogenic effects of artificial ultraviolet (UV) radiation [9]. Other detrimental consequences of skin UV irradiation have been proven, including premature aging, photodamage, rhytids, solar elastosis, and lentigo spots [10].

#### Fake tan

Self-tanners are popular as these are less harmful than tanning beds or sunbathing. They are also often cheaper and more convenient; however, their application can result in a fake change in the appearance of a

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pigmented lesion that can affect monitoring in a skin cancer clinic or impact teledermatology image assessments [11]. Another emerging problem is that these tanners can induce contact allergic dermatitis in susceptible individuals [12].

#### Melanotan

The development of synthetic  $\alpha$ -MSH analogues such as afamelanotide has enhanced the study of melanocyte biological mechanisms and has prospective therapeutic purposes [13]. However, two other non-regulated forms of melanotan (nasal sprays and injectable powders) are sold via non authorised portals and are self-administered by the user [14]. They mimic the action of melanocortin on the MC-1 receptors of melanocytes, leading to eumelanin over-expression and thus skin tanning, due to the less selective nature of other physiological actions, such as enhancing sexual desire and decreasing appetite, which has been promoted by vendors as desirable effects [14]. However, they also elicit side effects [1, 4].

Warnings have been issued by the British Medicines and Healthcare Products Regulatory Agency (MHRA) [15], the US Food and Drug Administration (FDA) [16], the Irish Medicines Board and Several European national health authorities against the use of subcutaneous injections labelled as Melanotan after the upsurge in tan injections that has been noticed in recent years [17].

A PubMed search was performed to search for the terms Melanotan I and II, and a range of clinically undesirable outcomes were reported and will be stated in this review. Like any non-regulated medicine, there are general risks from non-sterile administration [11], moreover, high levels of impurities were detected in random samples purchased online, which may pose a hazard [18].

The acute adverse reactions associated with the administration of Melanotan II reported in phase I and II clinical studies include spontaneous erections, facial flushing, nausea, and vomiting [19,20].

Among the cutaneous complications that have been reported, are melanocytic changes and darkening of existing naevi and eruption of new naevi with dysplastic changes [21,22], [26-28], [31-33,35] and melanoma were reported from  $\alpha$ -MSH analogue in its two forms Melanotan I and II [23,25,30,34]. (table 1). There is a sequential relationship between the event of injecting Melanotan products followed by the appearance of clinically and histologically atypical naevi and melanoma, which can highlight the carcinogenic potential of Melanotan, although the causal relationship was not suggested by the authors.

Authors	Case report
Cardones and Grichnik (2009) <sup>21</sup>	multiple new naevi and dysplastic naevi in male aged 40
Cousen et al. (2009) <sup>22</sup>	eruption of new naevi and darkening of existing naevi, female
	19 years old
Ellis et al. $(2009)^{23}$	Melanoma in situ in male aged 23
Langan et al. (2009) <sup>24</sup>	dysplastic nevi developed in existing moles, 2 females aged 38
	and 48
Paurobally et al. (2011) <sup>25</sup>	Melanoma, female 42
Ferrandiz et al. (2011) <sup>26</sup>	dysplastic nevi developed in existing moles; male 63 years old
Thestrup et al. (2011) <sup>27</sup>	Emergence of new naevi and darkening of existing naevi, male
_	25
Sivyer (2012) <sup>28</sup>	Growth and darkening of existing naevi, female
Mang et al. (2012) <sup>29</sup>	Pigmented Spitz naevus, male 24
Ong and Bowling $(2012)^{30}$	melanoma in situ, Female 23
Burian and Burian (2013) <sup>31</sup>	Eruptive naevi, 2 females
Reid et al. (2013) <sup>32</sup>	Emergence of new naevi and darkening of existing naevi,
	female 33 years old
Schulze et al. (2014) <sup>33</sup>	Eruptive naevi
Hjuler and Lorentzen (2014) <sup>34</sup>	Melanoma, female 20 years old
Al Abadie and Sharara (2024) <sup>35</sup>	Eruptive naevi, new dysplastic naevi, female 28 years old

**Table 1:** Reports of eruptive naevi and Melanoma in relation to Melanotan use

 $\alpha$ -MSH and its analogues are mitogenic for human melanocytes, with direct stimulatory and immunoregulatory activities on melanocytes [36].

Other noncutaneous side effects have been reported, including neurological outcomes during the use of Melanotan II, sympathomimetic toxidrome, renal dysfunction, and rhabdomyolysis after using Melanotan for sexual stimulation [37,38]. Moreover, a male developed posterior reversible encephalopathy syndrome one week after using Melanotan [39].

## Conclusion

There is great public perception about the hazards of ultraviolet exposure. Artificial tan has been identified as a safe alternative to sun-tanning practices, although it has been found to hinder the accurate diagnosis of suspicious skin lesions.

Further clinical research is needed to investigate the incidence and health outcomes among melanotan users. Unexplained tan and rapidly pigmenting naevi provide clues about the use of recreational, unregulated products that can cause diagnostic confusion via distortion of the appearance of pigmented moles. Dermatologists play a significant role in highlighting these risks.

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