Short Communication

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# Functions of Epidermal Melanin: Possible Evolutionary Significance of Heavy Metal Chelation

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**ABSTRACT**

A topic that has attracted a great deal of attention in relation to human evolution is the pigmentation of the skin. In comparison to closely related species humans are relatively hairless but there are notable racial differences in the degree of epidermal melanisation. Viewed from the aspect of evolutionary selectivity the significance of the epidermal melanisation in man, it is suggested that one possible factor may be that the transcutaneous desquamation of melanin may have furnished a mechanism for excretion of metals, with particular reference to toxic heavy metals which are strongly bound to the pigment. This process may have been of importance in human evolution since the niche displacement of early humans resulted in profound changes of diet and the possibility that the new diet contained significant quantities of potentially toxic heavy metals. Such a hypothesis might cast some light on the racial changes in the degree of pigmentation which may reflect dietary alterations. The possibility that the degree of skin pigmentation affects iron homeostasis and may be a contributary factor in the susceptibility to anaemia is of current interest.

**Keywords:** Metal Chelation; Melanin; Heavy Metal Toxicity; Iron-Binding; Anaemia; Evolution; Selectivity

## Introduction

Melanin is the product of tyrosine oxidation and is widespread in nature. The initial oxidation product is dopachrome and this and related products form polymers which become attached to protein and distributed widely. In vertebrates melanin is synthesised in specialised intracellular organelles, known as melanosomes. This process takes place in melanocytes which are specialised dendritic cells embryonically derived from the neural crest which migrate to colonise the skin. In mammals the fully melanised melanosomes are generally transferred to surrounding epidermal cells by a process known as cytocrine transfer. In humans, as the epidermis is constantly renewed, this results in a turnover of melanin granules. It is known that melanin possesses several interesting physical characteristics which include those shown in Table 1.

**Table 1:** Characteristics of Melanin.

| | |
|---|---|
| 1 | Light Absorption |
| | Photoreceptor shielding |
| | Photoprotection |
| | Camouflage and display |
| 2 | Radiant heat loss |
| 3 | Free radical trap |
| 4 | Metal chelation |
| | Heavy metal detoxification |
| | Excretory pathway |

Of these major properties some may be regarded as more significant than others as factors influencing evolutionary selection.

### Light Absorption

In the case of human skin pigmentation, the absorption of UV radiation is often cited as an important factor in protecting against ultraviolet radiation induced genetic damage to skin cells especially in preventing the initiation of epidermal cancer. However, in evolutionary terms this effect may be insignificant because, as Haldane [1] pointed out many years ago, malignancies are of relatively late onset and are unlikely to exert any significant effect on procreation and therefore not relevant to natural selection.

### Radiant Heat Loss

The degree of epidermal melanisation and comparative hairlessness characteristic of early man appears to be consistent with the proposal that melanin-dependent radiant heat loss has an important influence on body temperature regulation as suggested by Detwiller [2]. In a humid environment, where heat loss from sweating is inefficient, the thermostatic advantage of infra-red heat emission from the skin might confer a significant survival advantage and it has been estimated that about two-thirds of the thermal losses in man (in the 10-mu wavelength range) occur through epidermal emissions. Some evidence favouring this evolutionary aspect of melanin pigmentation in man has been reviewed [3].

### Free Radical Trap

Much has been written about the significance of melanin as a free radical trap.

### Metal Chelation

However, one cannot avoid being impressed by the possibility of epidermal pigmentation acting as a detoxifying pathway. The skin is the largest organ of the body (about 2 sq meters in area in the adult) and the constant transfer of melanin to desquamating epidermal cells provides a large potential excretory pathway. Melanin constitutes a powerful ligand for cations and is able to bind heavy metals for which there is no other established excretory mechanism. The significance of this metal chelating property of epidermal melanin has been discussed in relation to early hominid evolution [4]. If one takes the view ascribed to Hardy (see Morgan [5]) that early humans evolved as a littoral animal as a result of niche displacement from an arborial habitat, they would have been exposed to a novel diet with a high heavy metal content, for it is known that molluscs have the ability to concentrate heavy metals [6]. Since these metals are known to be toxic to a number of human organ systems the existence of an excretory pathway in the form of an epidermal mechanism for desquamating chelated metals bound to melanin would be highly advantageous. High levels of transition metal binding to melanin have been demonstrated [7] and, of course, the use of pigmented hair samples for detecting heavy metals such as arsenic and lead is well-established in forensic pathology.

### Associated Phenomena

In association with the metal-binding hypothesis it is worth noting other instances where metal chelation by melanin may play a role. In vertebrate development the absence of melanin (in albinos) is associated with abnormalities that may be metal-related. Also, it is known that metals are implicated in pathological lesions of Parkinson's disease where neuromelanin defects occur. The possibility that metals chelation may explain the role of industrial melanisation in moths has also been explored [8].

### Iron Homeostasis

In relation to the relationship between the degree of human skin pigmentation and susceptibility to certain pathological conditions attention has been drawn to the possibility that the metal chelating action of melanin could have an impact on the metabolic iron turnover. The data of Green, et al. [9] indicate that transcutaneous iron loss is related to epidermal pigmentation, and this could be relevant to the susceptibility to iron-deficiency anaemia. Such a connection would be consistent with anaemia-related conditions such as Covid-19 related fatality and the ethnic link with maternal mortality [10,11].

## Conclusion

In summary, the principal evolutionary importance of epidermal melanin in human evolution may not lie in its action as a photoprotector or a result of its camouflage or display properties, but rather in its ability to act as a powerful chelating agent, enabling the excretion of metals through the skin [12].

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