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Letter to Editor

Unlocking Youthful Skin: Liquorice's Role in Combating Oxidative Stress and Inflammation

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Skin aging and many chronic skin conditions stem from two interrelated biological processes: (a) Oxidative stress, which damages structural proteins and disrupts redox balance, and (b) Chronic inflammation, often initiated by cellular stress signals—particularly the molecule high-mobility group box 1 (HMGB1) protein [1,2]. Normally located in the nucleus, HMGB1 is released into the extracellular space by skin or immune cells in response to UV exposure, mechanical injury, infection, or aging. Exposure to ultraviolet rays (UV) emanating from the sun, is the most significant factor in aging of skin [Figure 1]. Ultraviolet radiation has a higher frequency (shorter wavelength) than violet light, and is divided into three bands: UVA, UVB, and UVC [Figure 2]. UVA is long-wave UV, penetrates deeper into the skin, and is associated with tanning and photoaging. UVB is medium-wave UV, is mostly absorbed by the ozone layer of atmosphere, and is primarily associated with sunburn and skin damage.

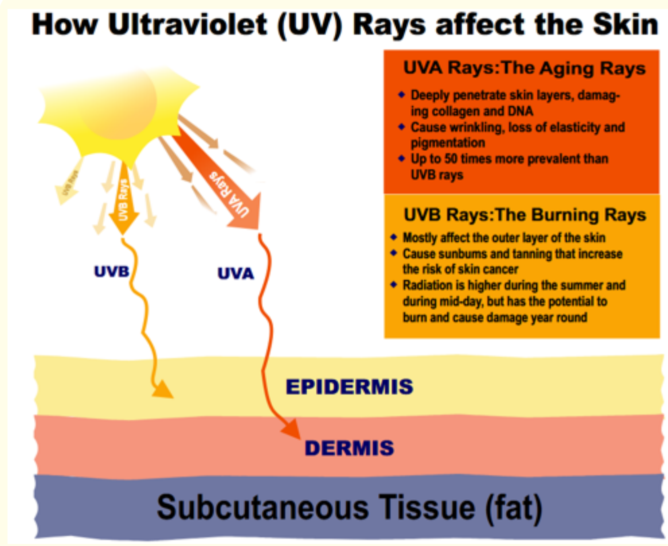

Figure 1: UVA is most damaging for skin, and stimulates the cutaneous cells to secrete HMGB1 protein, which causes aging changes to skin.

On being released into the extracellular space by UV exposure and other factors mentioned above, the HMGB1 protein acts as a damage-associated molecular pattern (DAMP), which activates receptors such as RAGE (receptor for advanced glycation end products) and TLR4, thereby amplifying inflammatory signalling pathways (e.g., NF-κB, IRF3), attracting neutrophils, and driving cytokine-mediated skin diseases such as psoriasis, atopic dermatitis, lupus, and photo-aging. Persistent extracellular

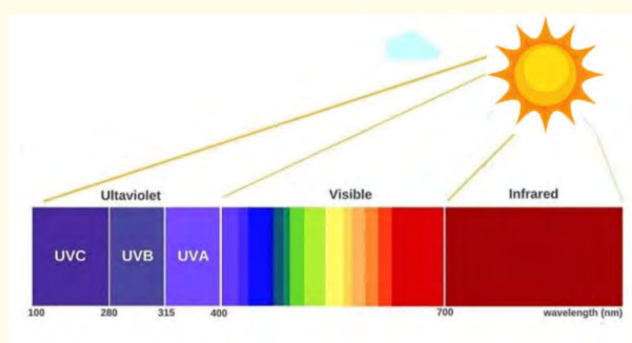

Figure 2: The spectrum of light radiation.

HMGB1 also hampers wound healing and promotes neutrophil extracellular trap (NET) formation, which may contribute to tumorigenesis in chronically inflamed skin [3-5]. Thus, targeting both oxidative stress and extracellular HMGB1 represents a promising therapeutic strategy in dermatology.

Figure a

The root of Liquorice (*Glycyrrhiza glabra*) contains glycyrrhizin—a bioactive saponin—along with flavonoids like glabridin, liquiritin, licochalcone A, isoliquiritigenin, and dehydroglyasperins [6]. These compounds scavenge reactive oxygen species, enhance endogenous antioxidant systems (SOD, CAT, GSH-Px), and inhibit key enzymes that degrade skin matrix components—such as MMP-1/3, elastase, and hyaluronidase—by over 90% in laboratory settings [7]. A particularly valuable property of glycyrrhizin is its moderate affinity for HMGB1, allowing it to bind selectively to the A and B box domains of HMGB1 without disrupting its nuclear functions [8]. The formation of this glycyrrhizin-HMGB1 complex prevents HMGB1 from binding to RAGE and TLR4, effectively dampening downstream inflammatory responses (Figure 3).

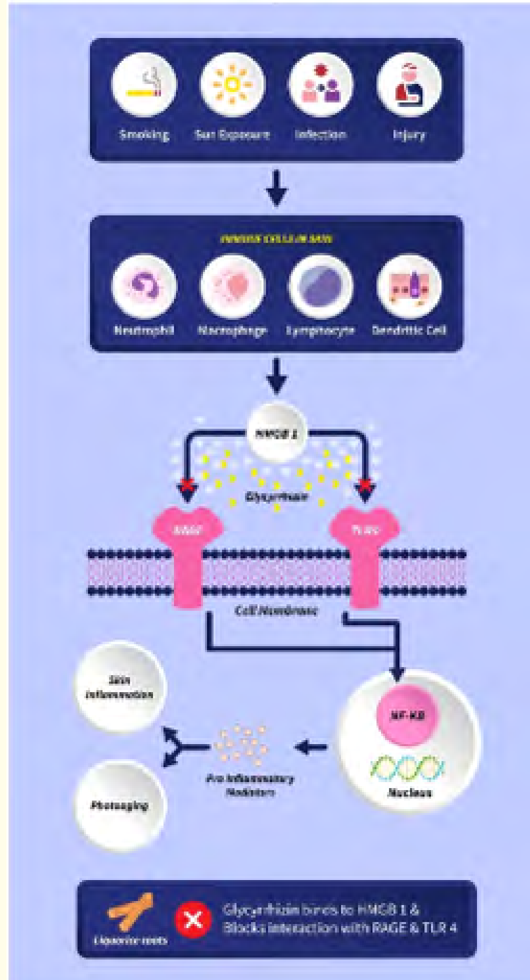

Figure 3: Shows binding of Glycyrrhizin to HMBG1, thus blocking the interaction of HMGB1 with RAGE and TLR4 receptors. The white triangular molecules represent HMGB1, while the yellow lunate shaped molecules are of Glycyrrhizin.

Glycyrrhizin has also been suggested to inhibit HMGB1 release, resulting in inhibition of the pro inflammatory cytokine-like activity of this protein. Hu., *et al*. demonstrated that administration of glycyrrhizin reduced the expression of HMGB1, TLR4 and RAGE in an animal model [9]. In UV-exposed mouse skin, 18β-glycyrrhetinic acid (a metabolite of glycyrrhizin) has been shown to restore collagen, reduce wrinkles, and suppress inflammatory cytokines like IL-6 and TNF-α [10]. Fermented or heat-treated liquorice extracts possess even stronger antioxidant properties due to enhanced polyphenol content [11]. Thus, Liquorice offers dual antioxidant and anti-inflammatory benefits, making it particularly effective for managing skin disorders, and preventing the effects of aging, resulting in youthful skin even in old age [12].

Liquorice root, known as mulethi in India, can be consumed in a variety of ways. It is widely used as a flavouring agent in various confectionary products, including candies and sweets. Liquorice is approximately 30-50 times sweeter than sucrose, which is why it is called Yastimadhu (sweeter than honey) in Sanskrit. This natural sweetness makes it an ideal ingredient for use in custards, cakes and puddings. Adding a pinch of powdered liquorice to most sweetmeats (mithai) can enhance their flavour while providing health benefits. In traditional remedies, small pieces of raw mulethi sticks are slowly sucked to provide relief from sore throat and coughs. This practice can also be employed with benefit for protecting the skin.

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