



## Selenium Supplementation in Psoriasis Patients

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Psoriasis is an autoimmune skin disease known for inflammation and hyper-proliferation of epidermal keratinocytes (Luo *et al.*, 2020). 2-3% of the population suffer from psoriasis (Parisi *et al.*, 2013). Emotional distress in psoriasis patients impairs quality of their life. Moreover, they suffer from the burden of comorbidities like obesity, diabetes mellitus, metabolic syndrome (Armstrong *et al.*, 2013b), and hypertension (Armstrong *et al.*, 2013a) through the increase in psoriasis severity. The pathogenesis of psoriasis is not well understood yet. It is concluded from the interactions between genetic predisposition and the environmental risk factors, such as diet, alcohol consumption, stress, obesity, and smoking (Ricketts *et al.*, 2010). One pathogenesis of psoriasis is amplifying T-cells and dendritic cells from the immune system, which releases various pro-inflammatory cytokines and chemokines with simultaneous activation of growth factors (Al-Harbi *et al.*, 2020). Moreover, oxidative stress and

reactive oxygen species (ROS) production causes inflammation (Wacewicz *et al.*, 2017). High free radicals have harmful effects through structural changes on proteins, lipids, and nucleic acids. The increase in oxidants leads to active antioxidant defense mechanisms (Lobo *et al.*, 2010). Enzymatic antioxidant defense mainly includes glutathione peroxidase (containing selenium), superoxide dismutase (including copper and zinc as cofactors), and catalase (Armstrong *et al.*, 2011). Trace elements also play an essential role in immunologic and inflammatory reactions. Zinc and selenium influence the antioxidant structure of the human body. However, these vital elements act based on the normal physiological response of those enzymes elaborated in the antioxidant defense system (Fernández-Lázaro *et al.*, 2020). Selenium and selenoproteins regulate inflammation by changing eicosanoid production to anti-inflammation eicosanoid (Avery and Hoffmann, 2018). Although keratinization and melanin

formation are enzyme-dependent processes increased in patients with psoriasis (Chen *et al.*, 2019), the trace element deficiency in human body can decline the activity of the selenium-dependent enzyme in patients (Ricketts *et al.*, 2010). Furthermore, decreasing antioxidant blockade in the skin, and increasing free oxygen radicals create psoriatic plaques or lesions (Yildirim *et al.*, 2003). The treatment of psoriasis with mineral supplements (Ricketts *et al.*, 2010) and medicated shampoo containing selenium could prove beneficial (Verardino *et al.*, 2012).

The dietary habits among psoriasis patients were imbalanced. Previous epidemiological studies indicated a higher intake of saturated fatty acid (SFA), simple sugar, and alcohol; and a lower intake of proteins, fiber, and unsaturated fatty acids which exacerbate psoriasis, while the others such as low-calorie diet, gluten-free diet, vitamin D, vitamin B12, Omega-3-PUFAs, dietary fibers, selenium, or probiotic supplements ameliorate psoriasis (Ricketts *et al.*, 2010, Zuccotti *et al.*, 2018). There are contradictory findings about serum levels of trace elements and total antioxidant status in psoriasis patients. Studies demonstrated serum selenium level was lower among psoriasis patients compared with those in the control group (Kirit *et al.*, 2020, Waciewicz *et al.*, 2017); this indicates pro-antioxidant's imbalance among psoriasis. However, a meta-analysis showed some trace element (zinc, copper, not selenium) levels in a homeostatic imbalance in psoriasis patients compared with the control group (Chen *et al.*, 2019). The duration and severity of psoriasis could affect serum selenium concentration (Serwin *et al.*, 2003). Selenium deficiency can be considered a risk factor resulting in susceptibility to inflammatory skin diseases (Rayman, 2000). Selenium deficiency and overload could lead to cell injury (Rayman, 2000). Serum selenium level is related to plasma osteopontin level as an atherosclerosis predictor marker among psoriasis patients (Toossi *et al.*, 2015). Overexpression of osteopontin and low plasma levels of selenium are predictable factors for the incidence of psoriasis. The effect of selenium supplements has been investigated in some

randomized clinical trials. Fairris *et al.* studied 600  $\mu\text{g/day}$  selenium as selenium-enriched yeast for 12 weeks in comparison with 600  $\mu\text{g/day}$  selenium plus 600 IU vitamin E-enriched yeast and placebo group (Fairris *et al.*, 1989). In addition, Serwin *et al.* examined 200  $\mu\text{g/day}$  for 4 weeks with narrowband ultraviolet B therapy (Serwin *et al.*, 2006). However, these studies did not show significant improvement in Psoriasis Area and Severity Index (PASI). PASI is a typical score to measure severity in psoriasis patients. Oral administration of selenium (400  $\mu\text{g/day}$ ) did not indicate a significant change in proteins (P53, Fax, Bax, and Bcl-2) or a protective effect against skin damage by ultraviolet (DeSilva *et al.*, 2007). Although a double-blind placebo-controlled clinical study assessing 58 psoriasis patients revealed therapeutic effects of combined antioxidants, selenium (48  $\mu\text{g/day}$  for 30 – 35 day), vitamin E, and coenzyme Q10 showed a significant improvement in PASI and marker of oxidative stress (Kharaeva *et al.*, 2009). Selenium is a vital component of cellular antioxidant defenses, and it has protective effects against ultraviolet radiation-induced damage to skin cells (McKenzie, 2000) and ultraviolet B radiation-induced skin cancer in a murine model (Rafferty *et al.*, 2002). There is a need for better-designed studies with a proper dose of selenium and in combination with other antioxidants to assess the efficacy of selenium supplements in psoriasis patients. Selenium is a cofactor for thioredoxin reductase (Wadhvani *et al.*, 2016). It is also involved in 25 selenoprotein genes in the human genome, affecting immunomodulation, sperm motility, and preventing the risk of miscarriage (Rayman, 2000). Current evidence showed selenium nanoparticles (SeNPs) inhibit epidermal hyperplasia through anti-proliferative and anti-inflammatory activities. SeNPs have been identified as an anti-cancer agent (Pi *et al.*, 2013). In the animal model, SeNPs acted as an effective treatment in inflammation-driven disorders like arthritis, liver fibrosis, and nephropathy. Moreover, the anti-inflammatory activity of SeNPs and the reduction of inflammatory cytokines levels are known as the primary mechanisms of it (Yazdi *et al.*, 2015).

SeNPs as biological inertness may be the ideal therapy in psoriasis patients.

In summary, genetics and diet could play a critical role in prevention, improvement, treatment, and incidence of psoriasis. This inflammatory skin disease needs more trace elements which act in the antioxidant defense system; however, an overload of these trace elements could be harmful. A safe and appropriate dose of selenium in a patient with selenium deficiency could help to control the disease. Selenium deficiency is related to the severity and length of suffering from this disease. Long-term usage of comprehensive available treatment options in psoriasis patients could produce adverse effects. SeNPs, as safe nanomedicine, may have beneficial effects in the treatment of psoriasis patients. Further studies among psoriasis patients could provide more insights.

#### Authors' contributions

Gerami H, Khorasani AS and Lesani A drafted the manuscript. A.L critically revised the manuscript and agree to be fully accountable for ensuring the integrity and accuracy of the work. All authors read and approved the final manuscript.

#### Conflict of interest

The authors of the study declared no conflict of interest.

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