

# Efficacy of Anti-Melanogenic and Anti-Ageing Properties of Glutathione with Additional UV Protection and Skin Whitening Benefits Led by the Combination of Oral Polypodium as Whitevit Plus

Rana Neha \*, Mathur Shabla \*\*, Dr. Babbar Sandeep \*\*

\* Pharmacist, Pure Natural Products Pvt. Ltd., Faridabad, India

\*\* Researcher, Pure Natural Products Pvt. Ltd., Faridabad, India

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**Abstract-** Widespread concerns regarding the rise in prevalence of skin cancer and the adverse effects of both acute and chronic photo-damage due to exposure to UV rays, has led to various modes of treatment. The latest development in this regard is the findings about Glutathione and Polypodium dry extract as potential treatment components for skin conditions. Glutathione plays pivotal role in protecting cells against oxidative stress-induced cellular damage and in detoxifying Xenobiotics and drug metabolism. The added photo-protective effects of oral Polypodium with its antioxidant, immunoregulatory and anti-inflammatory properties aid also in prevention of chronic skin damage, photoaging, and skin cancer led by UV exposure. Its decreased levels are associated with the common features of aging as well as of a wide range of pathological conditions, including neurodegenerative disorders.

**Index Terms-** skin whitening, anti-melanogenic, tyrosinase enzyme inhibitor, anti-aging, melanogenesis, oxidized glutathione, topical glutathione, Polypodium , alpha lenoic acid , psoriasis,

## I. GLUTATHIONE FUNCTION AND CELL DEATH

Notably, Glutathione depletion and/or alterations in its metabolism appear to be crucial in the onset of Parkinson's disease. Despite the fact that it is required for cell survival, the molecular mechanism that links Glutathione depletion to cell death remains poorly understood. Recently, considerable attention has been focused on a newly defined type of cell death: iron-dependent cell death, also referred to as "ferroptosis".<sup>1</sup> The iron chelator deferoxamine nearly abolishes ferroptosis induced by inhibiting Glutathione synthesis or Cystine uptake by the xCT transporter. Deferoxamine preferentially abrogates the intralysosomal accumulation of iron and inhibits oxidative stress-induced lysosomal membrane permeabilization and cell death. The use of Glutathione and a prodrug derived from it can be useful, since the dysfunction of the Glutathione redox system appears to cause a variety of diseases including neurodegenerative disorders. We also review trials that have been designed to cope with this difficulty; e.g. the use of

precursors such as N-acetyl cysteine and chemical modification such as methylation.<sup>1</sup>

## II. GLUTATHIONE INHIBITS TYROSINASE ENZYME FUNCTION

Glutathione is present intracellularly in its reduced form and plays an important role in various physiological functions. Its skin-lightening effects result from direct as well as indirect inhibition of the tyrosinase enzyme and switching from eumelanin to phaeomelanin production. It is available in oral, parenteral and topical forms.<sup>2</sup>

The tyrosinase enzyme is involved in the oxidation and reduction process in the epidermis. These chemical reactions that the enzyme catalyzes are of principal importance in the melanogenesis process. The overproduction of melanin, come up by the action of the tyrosinase, can cause different disorders in the skin related to the hyperpigmentation.<sup>3</sup>

## III. EFFICACY OF ORAL POLYPODIUM IN COMBINATION WITH ALPHA LIPOIC ACID

Taken orally, Alpha Lipoic Acid (ALA), an antioxidant is capable of regenerating other antioxidants, such as vitamin C and E. It's clear from the research that ALA is a potent antioxidant, but it isn't the only one; there are lots of great antioxidants for skin like Polypodium.<sup>4</sup> The extract of Polypodium is an oral photo-protectant with strong anti-oxidative properties. Recent studies to determine its chemical composition have shown 4-hydroxycinnamic acid (p-coumaric), 3 methoxy-4-hydroxycinnamic acid (ferulic), 3, 4-dihydroxycinnamic acid (caffeic), 3-methoxy-4-hydroxybenzoic acid (vanillic) and 3-caffeoquinic acid (chlorogenic) to be among its major phenolic components, of which ferulic and caffeic are the most powerful antioxidants. These phenolic compounds contribute to the health benefits afforded by this oral photo-protectant.<sup>4</sup>

Thus, the combination of Oral Polypodium and Alpha Lipoic Acid with its anti-oxidative properties can be very protective for the skin against UV impact and thereby the issues arising from it.

#### **Box 1: Important physiological functions of glutathione**

- Maintenance of the sulphydryl groups of proteins and other molecules
- Catalysis of exchange reactions
- Scavenging of free radicals, most importantly hydrogen peroxide
- Translocation of amino acids across cell membranes
- Detoxification of xenobiotics
- Participation as a coenzyme in certain important processes of cellular metabolism

#### **IV. EFFICACY OF GLUTATHIONE WITH VITAMIN C**

Glutathione helps maintain the C vitamin and lower the required intake by recycling it. The recycling occurs after the C vitamin has neutralized a free radical by giving up an electron to the free radical. GSH in turn gives up an electron to the C molecule, returning it to work as an antioxidant.

One human trial led by C.S. Johnston at the Arizona State University and published in the American Journal of Clinical Nutrition in 1993 showed that vitamin C was able to elevate glutathione levels in red blood cells by nearly 50% compared to baseline after daily supplementation with 500 mg for 2 weeks. Individual results among the participants of this study ranged from modest 8% to significant 84%. It is important to note that a high dose group that took 2,000 mg of vitamin C a day did not exhibit better results than a 500 mg group.<sup>5</sup>

#### **V. POLYPODIUM ON PSORIASIS**

The fern Polypodium, has a clinically documented use in the treatment of psoriasis.<sup>6</sup> One of the inflammatory mediators isolated in abnormally high quantities in the psoriatic skin is leukotriene B4 (LTB4). It was tested in an in vitro model using human leukocytes for its ability to inhibit the LTB4 formation. The inhibition was found to be caused by the polyunsaturated fatty acids (PUFAs) linoleic, linolenic and arachidonic acid. IC<sub>50</sub> values were determined for the isolated acids and compared to a group of closely related acids also commonly found in nature. The IC<sub>50</sub> values for most acids tested were of the same magnitude (20-60 microM) except for arachidonic acid which showed stimulatory activity and 8(R) hydroxylinoleic acid which gave 30% inhibition with the highest dose tested (120 microM). The amounts of PUFAs in different Polypodium extracts were quantitatively analysed and it is concluded that the fatty acid constituents of Polypodium may contribute to the clinical effects of the extract.<sup>6</sup>

#### **VI. TOPICAL GLUTATHIONE FOR SKIN WHITENING**

Glutathione is a tripeptide consisting of cysteine, glycine, and glutamate and functions as a major antioxidant. It is synthesized endogenously in humans. Glutathione protects thiol protein groups from oxidation and is involved in cellular

detoxification for maintenance of the cell environment.<sup>5</sup> Reduced glutathione (GSH) has a skin-whitening effect in humans through its tyrosinase inhibitory activity and topical oxidized glutathione GSSG is safe and effectively whitens the skin and improves skin condition in healthy women.<sup>4</sup>

An experiment was carried to determine skin-whitening and skin-condition effects of topical GSSG in healthy women.<sup>5</sup> It was found that the skin melanin index was significantly lower with GSSG treatment than with placebo from the early weeks after the start of the trial through to the end of the study period (at 10 weeks,  $P<0.001$ ). In addition, in the latter half of the study period GSSG-treated sites had significant increases in moisture content of the stratum corneum, suppression of wrinkle formation, and improvement in skin smoothness. There were no marked adverse effects from GSSG application.<sup>5</sup>

#### **VII. POLYPODIUM ON POLYMORPHIC LIGHT ERUPTION**

Oral Polypodium treatment is beneficial for the prevention of Polymorphic light eruption (PLE).<sup>7</sup> A total of 35 patients with long-standing PLE were included in an open, uncontrolled bicenter study. PLE was induced by photo-provocation with artificial UVB and UVA light, thereafter oral treatment with PL was initiated. Two weeks later a second photo-provocation was performed while the patients were still taking PL. Thirty patients developed PLE lesions after repeated irradiation with UVA. Of these, 18 patients also responded to UVB. After PL treatment, 9 (30%) and 5 (28%) patients, respectively, were unresponsive to repeated UVA and UVB exposure. In the remaining patients, the mean number of UVA and UVB irradiations required to elicit PLE increased significantly.<sup>7</sup>

#### **VIII. DOSAGE:**

Orally administered Polypodium extract decreases UV-mediated oxidative damage to DNA by enhancing the activity of endogenous antioxidant systems responsible for blocking the formation of reactive oxygen species. Its beneficial effects have been attributed to the phenolic components of Polypodium extract including chlorogenic acid, coumaric acid, vanillic acid, and especially the potent oxidation inhibitors caffeic and ferulic.<sup>8</sup> Our group reported that oral GSH administration (500 mg/d) resulted in lightening of skin color, when given for 4 weeks.

#### **IX. CONCLUSION**

We demonstrated that GSSG application to the face whitened the skin and improved skin condition in healthy women. Further studies are needed in future to clarify the mechanisms by which topical GSSG produces these skin benefits<sup>9</sup> and *Polypodium dry* extract 240mg with alpha lipoic acid 50 mg taken twice daily for 60 days is safe and effective means for reducing the damaging effects of ultraviolet radiation. These agents which can be taken orally and has not been noted to have serious adverse reactions, offers unique advantages in that they can be given orally, thus avoiding patient resistance to topically applied sunscreens.

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## AUTHORS

**First Author** – Neha Rana, Pharmacist at & Production Executive Purenatural Products Pvt. Ltd., Faridabad and neha@purenaturals.life  
**Second Author** – Shabla Mathur, Content-Researcher at Purenatural Products Pvt. Ltd., Faridabad and shabla@purenaturals.life

**Correspondence Author** – Dr. Sandeep Babbar- 9810317213, drsandeepbabbar@gmail.com  
Dr. Indu Taneja 9818590029 , drindu.taneja@gmail.com  
Dr. Evita Taneja- 7024141251, Evita.taneja@gmail.com