

Hypericin- A Naphodianthrone from *Hypericum perforatum*

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Introduction

Hypericin is a substance isolated from a medicinal herb *Hypericum perforatum*, commonly known as St.John's Wort.¹ Hypericin belongs to group of compound known as naphodianthrone.² Hypericin is a secondary plant metabolite of St.John's Wort and the amount of Hypericin strongly depend upon the source of the plant material.^{3,4} Initially Hypericin was considered to be the antidepressant principle of *Hypericum perforatum*, but according to latest research Hyperforin has emerged as antidepressant principle of the herb.⁵ Hypericin is used as standard for identification of genuine plant material and thus has importance from quality control point of view. The standardization of *Hypericum perforatum* is now based on both hypericin and hyperforin content. The herb must contain 0.3% of hypericin.

Chemistry

Hypericin is a red dye that forms salt known as hypercinates with sodium and potassium. It is soluble in ethanol, methanol, pyridine, acetone, ethyl acetate, butanone, aqueous alkali solutions, but insoluble in water and methylene chloride.⁷ Hypericin produces singlet oxygen and other excited state intermediates that indicate it should be a very efficient phototoxic agent in the eye. It absorbs in the UV and visible range, which means it, can potentially damage both the lens and the retina. *Hypericum perforatum* is known to cause photosensitivity.⁸

Pharmacological activity

A. Antidepressant activity

In experiments, hypericin has shown weak monoamine oxidase inhibiting activity. It was found that hypericin in a dose of 0.35 mg has effects similar to imipramine.⁹ In other experiment hypericin in a dose of 9-28 mg/kg showed activity similar to bupropion.¹⁰ Hyperforin in comparison inhibits the neuronal uptake of serotonin, norepinephrine and dopamine antidepressants, but also inhibits GABA and L-glutamate uptake.¹¹ Research on hyperforin has been intensified and most of the published studies strongly indicate hyperforin to be the antidepressant constituent of *Hypericum perforatum*.^{12,13,14}

B. Anti viral activity

In animal models hypericin has shown to prevent replication of encapsulated viruses.¹⁵

C. Anti-inflammatory activity

Besides these activities, hypericin has shown anti-inflammatory activity also. It inhibits release of leukotrienes.¹⁶

D. Photosensitizing activity

Hypericin is known to cause phototoxicity. Lens alpha-crystallin, isolated from calf lenses, was irradiated in the

presence of hypericin and in the presence and absence of light. Hypericin-induced photosensitized photo-polymerization was assessed by sodium dodecylsulfate-polyacrylamide gel electrophoresis. Further analysis of the oxidative changes occurring in alpha-crystallin using mass spectrometry showed specific oxidation of methionine, tryptophan and histidine residues, which increased with irradiation time. Hypericin did not damage the lens protein in the dark. Damage to alpha-crystallin could undermine the integrity of the lens directly by protein denaturation and indirectly by disturbing chaperone function. From the study it was concluded that in the presence of light, hypericin could induce changes in lens protein that could lead to the formation of cataracts. Appropriate precautions should be taken to protect the eye from intense sunlight while the patient is on *Hypericum perforatum* therapy.

Pharmacokinetics

In a study, healthy volunteers were given hypericin orally in a dose of 900, 1800 and 3600 mg and blood samples were analyzed. The maximum plasma concentration was found after 6 hours.¹⁸

Standard

The hypericin content of *Hypericum perforatum* is determined by using spectroscopic method utilizing the visible absorption characteristics of hypericin in methyl alcohol.^{19, 20} In atypical chromatogram of standardized *Hypericum perforatum* extract, absorbance occurs at 588nm and the peak. The peak at 10.67 min is characteristic of Hypericin.

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