Hypericin

Hypericin is a naphthodianthrone, a red-colored anthraquinone-derivative, which, together with hyperforin, is one of the principal active constituents of Hypericum (Saint John's wort).

Hypericin is believed to act as an antibiotic, antiviral and non-specific kinase inhibitor. Hypericin may inhibit the action of the enzyme dopamine β-hydroxylase, leading to increased dopamine levels, although thus possibly decreasing norepinephrine and epinephrine.

It was initially believed that the anti-depressant pharmacological activity of hypericin was due to inhibition of monoamine oxidase enzyme. The crude extract of Hypericum is a weak inhibitor of MAO-A and MAO-B. Isolated hypericin does not display this activity, but does have some affinity for NMDA receptors. This points in the direction that other constituents are responsible for the MAOI effect. The current belief is that the mechanism of antidepressant activity is due to the inhibition of reuptake of certain neurotransmitters.

The large chromophore system in the molecule means that it can cause photosensitivity when ingested beyond threshold amounts.

Photosensitivity is often seen in animals that have been allowed to graze on St. John's Wort. Because hypericin accumulates preferentially in cancerous tissues, it is also used as an indicator of cancerous cells. In addition, hypericin is under research as an agent in photodynamic therapy, whereby a biochemical is absorbed by an organism to be later activated with spectrum-specific light from specialized lamps or laser sources, for therapeutic purposes. The antibacterial and antiviral effects of hypericin are also believed to arise from its ability for photo-oxidation of cells and viral particles.

Hypericin derives from polyketides cyclisation.

The biosynthesis of hypericins is in the polyketide pathway where an octaketide chain goes through processes of cylizations and decarboxylations form emodin anthrone which are believed to be the precursors of hypericin. Oxidization reactions yield protoforms which then are converted into hypericin and pseudohypericin. Theses reactions are photosensitive and take place under exposure to light and using the enzyme Hyp-1.

Senders et al., systematically review all clinically tested fluorescent agents for application in fluorescence guided surgery (FGS) for glioma and all preclinically tested agents with the potential for FGS for glioma.

They searched the PubMed and Embase databases for all potentially relevant studies through March 2016.

They assessed fluorescent agents by the following outcomes: rate of gross total resection (GTR), overall and progression free survival, sensitivity and specificity in discriminating tumor and healthy brain tissue, tumor-to-normal ratio of fluorescent signal, and incidence of adverse events.

The search strategy resulted in 2155 articles that were screened by titles and abstracts. After full-text screening, 105 articles fulfilled the inclusion criteria evaluating the following fluorescent agents: 5 aminolevulinic acid (5-ALA) (44 studies, including three randomized control trials), fluorescein (11), indocyanine green (five), hypericin (two), 5-aminofluorescein-human serum albumin (one),

endogenous fluorophores (nine) and fluorescent agents in a pre-clinical testing phase (30). Three meta-analyses were also identified.

5-ALA is the only fluorescent agent that has been tested in a randomized controlled trial and results in an improvement of GTR and progression-free survival in high-grade gliomas. Observational cohort studies and case series suggest similar outcomes for FGS using fluorescein. Molecular targeting agents (e.g., fluorophore/nanoparticle labeled with anti-EGFR antibodies) are still in the pre-clinical phase, but offer promising results and may be valuable future alternatives. [1].

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Senders JT, Muskens IS, Schnoor R, Karhade AV, Cote DJ, Smith TR, Broekman ML. Agents for fluorescence-guided glioma surgery: a systematic review of preclinical and clinical results. Acta Neurochir (Wien). 2017 Jan;159(1):151-167. doi: 10.1007/s00701-016-3028-5. Review. PubMed PMID: 27878374; PubMed Central PMCID: PMC5177668.