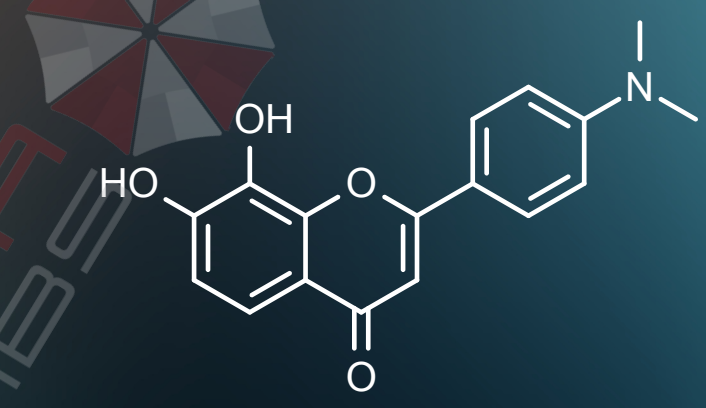
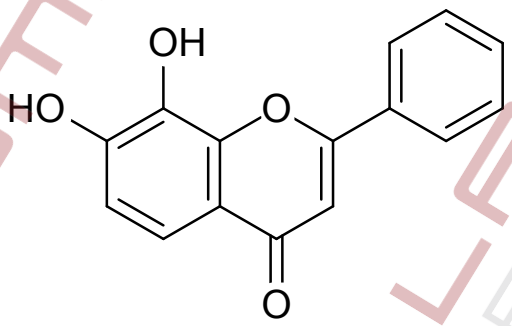


Eutropoflavin (4'-DMA-7,8-DHF): Pharmacological Properties, Mechanism of Action, and Preclinical Studies

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History

Eutropoflavin (also known as 4'-Dimethylamino-7,8-dihydroxyflavon) has first been described in 2010 as a promoter of neurogenesis with antidepressant effect , together with a series of similar molecules.1 All of these molecules are based on the general 7,8-dihydroxyflavone (also called Tropoflavin) structure.



7,8-Dihydroxyflavone

Flavones are a subclass of flavonoids, which are naturally occurring polyphenolic compounds widely distributed in plants, especially in fruits, vegetables, herbs, and medicinal plants. They contribute to the pigmentation, growth, and defence mechanisms of plants, while in humans they exhibit diverse biological activities such as antioxidant, anti-inflammatory, anticancer, antimicrobial, and antidiabetic effects. Due to their ability to modulate key enzymes and signaling pathways, flavones are one of the most pharmacologically interesting. Eutropoflavin is a fully synthetic flavone, meaning it is not known to be produced in any plant and has fully been made by chemical synthesis.

The chemical synthesis of eutropoflavin has also been described in the original publication.[1]

Further chemical optimizations to increase to potency of the flavones have been reported by the same researches who reported eutropoflavin.[2],[3]

Mechanism of Action

Eutropoflavin acts as agonist of TrkB (tropomyosin receptor kinase B), the main receptor of brain-derived neurotrophic factor (BDNF), meaning that eutropoflavin can mimic the effect of BDNF, which stimulates the survival of existing neurons and promoting the growth of new neurons and synapses. Relative to the basic 7,8- dihydroxyflavone, Eutropoflavin has higher potency at TrkB.

Pharmacokinetics

In mice, which were supplied orally with 1 mg/kg, rough estimations found peak concentrations in the brain after 4 hours, which declined slightly after 8 hours.[1]

Theoretical and in vivo studies which compared eutropoflavin and tropoflavin, found that

eutropoflavin is more potent, but does also have lower stability compared to tropoflavin. Maximum brain concentrations were also lower with eutropoflavin (8 ng/mlvs 48 ng/ml).[4]

Preclinical Trials

In mice, antidepressant-like effects were found in the initial study, those effects were linked directly to the agonism of eutropoflavin at TrkB. They also showed that eutropoflavin increased the growth of neurons in a long term treatment group (21 days) in mice.[1]

Eutropoflavin and tropoflavin both significantly improved motor deficits, ameliorated brain atrophy and extended survival in mice with artificial Huntington's disease, a chronic neurodegenerative genetic disorder.[5]

Conclusion

There are only three experimental trials describing the properties and effects of eutropoflavin, hence the data about it is very limited. One of those studies shows are relatively high potency, but a lower stability compared to the parent compound of the class. The identified properties of eutropoflavin are highly interesting for clinical research but also to increase cognitive abilities in healthy individuals. However, it is not clear if the effects of eutropoflavin in mice can be translated to humans.

Multiple attempts have been made to increase the potency and properties of tropoflavin. It is likely that more optimization can yield a derivative with more suitable pharmacological properties compared to eutropoflavin.

No toxicological data is available, but it is unlikely that eutropoflavin has a high in vivo toxicity based on animal experiments and previous experiments with flavones, which are known to be a safe group of compounds.

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