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Hawthorn berry extract lowers kynurenic acid and anthranilic acid formation

Berthold Kepplinger[1], Halina Baran[1,2]*, Carina Kronsteiner[1,3] and **Mirosław Więcek[4]**
[1]Karl Landsteiner Research Institute Mauer, Austria
[2]Veterinary Medical University Vienna, Austria
[3]Germany; 4Friends of Nature Society IWA, Poland

Background: *Hawthorn* berry "haws" are used to make wine, jelly and flavor brandy and this plant has been used as a remedy for heart problems and also to treat Alzheimer's disease. Since elevated kynurenine metabolism has been documented in patients with cardiovascular problems and also in several brain pathologies including dementia we searched the biochemical properties of *Hawthorn* extract with respect to kynurenic acid (KYNA) and anthranilic acid (ANA) formation. KYNA is an endogenous metabolite of tryptophan degradation and is an antagonist of the glutamate ionotropic EAA and of the nicotine cholinergic receptors. KYNA and ANA, both influence the mitochondria respiratory parameters. We questioned whether *Hawthorn* drink has an ability to influence KYNA and ANA formation in the rat tissues, in an *in vitro* study as we have observed with other anti-dementia drugs.

Methods: The activities of the KYNA synthesising enzyme kynurenine aminotransferase II (KAT II) and ANA synthesising enzyme kynureninase in rat liver homogenates were analysed in the presence of different amount of *Hawthorn* drink (N= 5) and in respectively controls (N=5). Formed KYNA and ANA were measured using a HPLC and enzymatic method in the presence of 100 µM L-kynurenine, 70 µM pyridoxal 5'-phosphate and 150 mM Tris-acetate buffer, pH 7.4. The blanks were obtained by using tissue which has been heat inactivated for 30 min in a boiling water bath. As a comparison drug to block KAT II activity we used D-cycloserine in the assay, too (Eur Neuropsychopharmacol. 2014 24(4): 639-44).

Results: *Hawthorn* drink dose-dependently and significantly reduced KAT II activity of rat liver homogenate. Furthermore, *Hawthorn* drink exerted a dose-dependent inhibition of rat kynureninase activities, too. The inhibitory effect of *Hawthorn* drink was more pronounced for KAT II than for kynureninase under assay conditions. Under used assay conditions *Hawthorn* extract and D-cycloserine exerted similar dose-dependent inhibitory effect on KYNA synthesis.

Discussion: This study for the first time demonstrates the ability of *Hawthorn* berry to lower KYNA and ANA formation in rat liver homogenate. Components of *Hawthorn* berry extract are able to affect pyridoxal-5-phosphate complex causing a lowering of KYNA and ANA formation. It is to assume that the inhibitory effect can be seen in other tissue homogenates, as well. We propose *Hawthorn* extract as a drink susceptible of therapeutic exploitation in disorders associated with enhanced KYNA and ANA synthesis in the periphery and in the CNS particularly in diseases with cardiovascular problem and/or with memory impairment and dementia. We believe that frequent use of this berry extract can prevent the development of pathological condition with mostly significant advantage of use such as a lack of side effects. This study suggests anti-dementia action for *Hawthorn* berry due to lowering of KYNA formation.

halina.baran@neuro-lab.eu

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