Luteolin in the Artemisia family

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The ethnobotanical use of this flavone includes applications in the treatment of cough, diarrhea, dysentery, diabetes, cancer and malaria.

The effects of a range of common dietary flavonoids on the growth of Plasmodium falciparum has been studied by A M Lehane et al., (BMC Res Notes, 1-26, 2008). Among the following molecules: kaempferol, myricetin, quercetin, isoquercitrin, acacetin, apigenin, baicalein, chrysin and luteolin, the latter was found to be the most active with IC50 values around 11 µM. Luteolin also was found to prevent the progression of parasite growth beyond the young trophozoite stage. The parasites are therefore unable to complete a full intra-erythrocytic cycle. A similar low IC50 had been found previously for luteolin extracted from S.parvifolia (V Van Baren et al., Z Naturforschung C. 61, 2006, 180-192). The IC50 values of luteolin 7-O-β-glucopyranoside displayed against Plasmodium falciparum was 2.9 µg/ml (H Kirmizibekmez et al., Phytother Res 142-6, 2011, 142-6). This strong antiplasmodial activity is eventually related to the inhibition of fatty acid biosynthesis by Plasmodium falciparum. These lipids are required for the detoxification by crystallization into hemozoin of heme resulting from hemoglobin digestion by the parasite. Apicomplexan parasites utilize a fatty acid synthesis pathway, independent of the human host and catalyzed by specific enzymes like FabG. These enzymes are a potential target of new antimalarials. Among 30 flavonoids studied (D Tazdemir et al., J Med Chem. 49, 2006, 3345-53) it was found that luteolin and quercetin had the lowest IC50 for the inhibition of these enzymes. In this same study these two flavonoids also showed in vitro activity in the submicromolar range against several strains of Plasmodium falciparum.

The flavonoid luteolin is found in all Artemisia species presenting an antimalarial activity. A. annua (JA Sanz et al., Pharmazie 45-5, 1990, 382-383), A. absinthium (O Craciunescu et al., Chem Central J. 6-97, 2012), A. herba alba (K Seddik et al., J Med Plant Res. 4-13 2010 1273-80), A. afra (A dube, Thesis Univ of Western Cape, 2008). This author also found that luteolin present at high concentrations in the herb specimen studied stays stable after several processing operations.

Salvia officinalis also contains luteolin. This plant has been known for its medicinal properties since ages (salvare, to heal, officinalis, medicinal). The University of Al Quds (M Akkawi et al., Malaria J. 2012. 11-Suppl P3) has demonstrated that Salvia officinalis is a potential antimalarial drug. It inhibits the formation of β-hematin. Other medicinal herbs rich in luteolin are chamomile, rooibos, thyme. lemongrass. A study of 13 medicinal plants in Pakistan shows that luteolin is present in all of

them, quercetin in 4, catechin in 3, kaempferol and rutin only in one (AM Khan et al., Pak J Bot 44:4, 2012, 1241-45).

The highest concentration of luteolin is found in hulls of peanuts (1071 µg/g), while it is absent in the kernels. (MM Win et al., Pak J Bot, 43-3, 2011, 1635-42). Some people mix Artemisia annua leaf powder with peanut butter for oral administration. It would eventually be beneficial to include some powder from the peanut hulls. Another abundant source of luteolin are the leaves of the oil palm tree (Elaeis guineensis).

Luteolin has anti-inflammatory properties at micromolar concentrations and reduces IL-6 production (S Jang et al., PNAS, 105-21, 2012, 7729-34) and TNF-α. A similar inhibition effect for IL-6 and IL-8 was seen (PM de Magalhaes et al., Food Chemistry, 28 Feb 2012) for Artemisia annua extract with low artemisinin content. Luteolin also has an excellent anti-oxidant properties (GB Sun et al., Toxicol Appl Pharmacol. 265, 2012, 229-40) by suppression of the NFκB pathway. When comparing the free radical scavenging activity of quercetin, rutin, luteolin and apigenin (K Horvathea, Neoplasma, 51-5, 2004, 395-9) it was found that luteolin and quercetin provided effective protection against oxidative attack. Apigenin had no protective effect and rutin was only marginal. The antioxidant potential of luteolin is twice stronger than that of Vitamin E.

Luteolin has some prophylactic activities against toxic substances causing renal lipidoperoxidation. Taking luteolin during 7 days before administering the toxic alleviates its toxicity, mainly by raising the glutathione level (S Sultana et al., Indian J Exp Biol. 47, 2009, 355-360).

Luteolin also has a hepatoprotective effect, 4 times higher than quercetin an 11 times higher than rosmarinic acid (CF Lima et al., University of Porto, Portugal).

It has well documented anti-tuberculosis properties (Dhiraj Kumar Singh et al., Conference paper March 2016, Keystone Colorado USA), (S Ntutela et al., Tuberculosis, 2009 Dec, 33-40).

Numerous papers describe the inhibitory effect of luteolin on tumors and cancer. It is not the purpose of the present document to review this important field of research.

Luteolin has strong antinociceptive (analgesic) properties, sometimes more active than well-known analgesic drugs, such as acetyl salicylic acid, acetaminophen, dipyrone, indomethacin (LC Block et al., J Ethnopharmacol. May 1998, 35-39). Topical application of wormwood extract is relatively equal to morphine. (M Shams, 2011 SHS Acta Horticulturae, IMAPS2010) The presence of luteolin may explain the antinociceptive properties in trials with mice and the antimalarial and antinociceptive effects noticed by Dr M Onimus during surgical interventions at Bangui (personal communication, available on request).

Luteolin is a potent hypoglycemic agent and improves insulin sensitivity and attenuates diabetes associated cognitive decline (Y Liu et al., Brain Res Bull. Feb 13 2013).

Luteolin has an inhibitory effect against rotavirus infection which leads to severe diarrhea (K Knipping et al., Virol J. 9:137, Jul 2012).

Intestinal absorption of luteolin from aqueous plant extracts is up to 5 times greater than for the pure luteolin (P Zhou et al., J Agric Food Chem. 9-56, 2008, 296-300). This was confirmed in another research work (JT Mukinda et al., J Ethnopharmacol 130-3, 2010, 439-49). The same effect has been observed for Artemisia annua extract versus pure artemisinin. As substances like luteolin or artemisinin are sparingly soluble in water it is recommended for therapeutic purposes to use dried herb powder (totum) rather than infusion.

No toxic effect was noticed for high doses of luteolin administered to rodents (JT Mukinda, Thesis, University of Western Cape)