WATER SOLUBLE FLAVONOIDS FROM *ARTEMISIA ANNUA* L.

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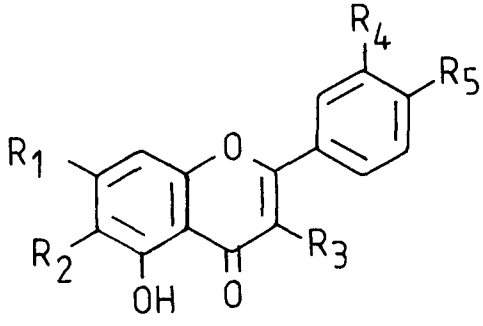
Artemisia annua L. has been used for about 1,500 years in traditional Chinese medicine for the treatment of liver diseases, malaria and as an anti-inflammatory (China Cooperative Research Group, 1982). The sesquiterpene lactone artemisinin which has been found to be active against chloroquine-resistant Plasmodium falciparum in the treatment of cerebral malaria was isolated from the n-hexane fractions (Jian et al, 1982) of A. annua together with 17 methoxylated flavonoids which were isolated from this fraction and the chloroform fractions (Yang et al, 1989). The major methoxylated flavonoids casticin, chrysoplenetin, chrysosplenol-D and circilineol at 10^{-6}M were found to enhance the antimalarial activity of artemisinin whilst at higher concentrations they had cytotoxic activity (10^{-5}M) (Liu et al 1989). However in traditional Chinese medicine aqueous decoctions are used and hence it was pertinent to investigate the constituents of the aqueous extracts. Plant material (19 kilos) extracted with methanol yielded 970 g of extract which was further partitioned between water and a sequence of solvents: a) n-hexane, b) chloroform, c) ethylacetate and d) butanol. The residue obtained from the butanol extract was 288 g and a number of flavones and their glycosides were isolated from the fraction using column chromatography of polyamide and purification on Sephadex LH-20. Compounds were identified by UV, MS ^{1}H-NMR and reference to the literature. Major constituents given in Fig. 1 were 1 luteolin-7-glucoside (2 mg), 2 quercetin-3'-glucoside (25 mg), 3 quercetin-3-glucoside (7 mg), 4 quercetin-7-glucoside (6 mg), 5 kempferol-3-glucoside (3 mg), 6 quercetagetin-3-methylether-3'-glucoside (8 mg) and 7 quercetagetin-4'-methylether-3-glucoside (3 mg).



1 R_1=OGlu; R_2=R_3=H; R_4=R_5=OH.
2 R_1=R_3=R_5=OH; R_2=H; R_4=OGlu
3 R_1=R_5=R_4=OH; R_2=H; R_3=OGlu
4 R_1=OGlu; R_2=H; R_3=R_4=R_5=OH
5 R_1=OH; R_2=R_4=H; R_3=OGlu; R_5=OH
6 R_1=R_2=OH; R_3=OCH_3; R_4=OGlu; R_5=OH
7 R_1=R_2=OH; R_3=OGlu; R_4=OH; R_5=OCH_3

Some flavonoids have been investigated for their anti-inflammatory action, particularly for their effects on the metabolism of phospholipids and arachidonic acid, whereas others have been shown to be beneficial in treatment of potential liver damage. Most interesting in these activities is the ability of flavonoids to scavenge free radicals and hence these constituents also have a role in the regulation of the immune response. In general flavonoid aglycones like kaempferol, luteolin and quercetin isolated from A. annua have been the most effective constituents (Cody et al, 1986). However whether or not these more polar flavonoids have a role in the antimalarial activity of A. annua has yet to be investigated.

China cooperative Research Group on Qinghaosu (1982) J. Trad. Chinese Med. 2: 3-8
Cody, V., Middleton, E., Harborne, J.G. eds. (1986) Progress in Clinical and Biological Research, Vol. 213 Plant Flavonoids in Biology and Medicine, Alan Liss Inc.
Jiang, J.B. (1982) Lancet II: 285-287
Liu K. C.-S. et al (1989) Planta Med. 55: 654-655
Yang, S.-L. et al (1989) Phytochemistry 28: 1509-1511