FLAVONOIDS FROM SUDANESE *ALBIZIA ZYGIA* (LEGUMINOSAE, SUBFAMILY MIMOSOIDEAE), A PLANT WITH ANTIMALARIAL POTENCY

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Abstract

Three flavonoids were isolated for the first time from the Sudanese medicinal plants *Albizia zygia.* Compounds **1**-**3** were identified by interpretation of ESI mass data, ^{1}H, ^{13}C and 2D NMR as well as by comparison with published data as 4',7-dihydroxyflavanone (**1**) 3',4',7-trihydroxyflavone (**2**), 3-*O*-methylfisetin (3',4',7-trihydroxy-3-methoxyflavone, **3**). All flavonoids were tested against *Plasmodium falciparum*, and only compound **2** showed high antimalarial activity (IC_{50} 0.078 μg/ml).

Keywords: *Albizia zygia*; Mimosoideae; flavonoids; antimalarial activity

Introduction

Albizia zygia (DC.) J.F. Macbr. (*Leguminosa*e subfamily *Mimosoideae)* is a gum producing tree widely found in West Africa (Hutchinson et al., 1972). In previous phytochemical studies of *A. zygia*, lupen-20(30)-en-3β-ol and its glycoside, stigmast-5-en-3β-ol, and 5α-stigmasta-7,22-dien-3β-ol were isolated (Schoppa and Pachaly, 1981) as well as albiziaprenol and phytol were reported (Pachaly et al., 1983). Also, the gum of the plant has been widely investigated for its chemical and physical properties (e.g. as thickening agent) in comparison with other mucilages (Ashton et al., 1975; Mital et al., 1979). In traditional medicine, the powdered bark of *A. zygia* is used alone or as a decoction in southern Sudan as an antimalarial and antiparasitic drug. The methanolic extract of the stem bark exhibited antiprotozoal activity (IC_{50} 1.0 μg/ml) against *Plasmodium falciparum* strain K1, the protozoa responsible for malaria, and *Trypanosoma brucei rhodesiense* (IC_{50} 0.2 μg/ml), which causes African trypanosomiasis (Ndjakou et al., 2007). It is interesting to note that lupeol, which was isolated previously from this plant has been found to inhibit the growth of *P. falciparum* by 45% at 25 μg/ml (De Almeida Alves et al., 1997), which could account at least in part for the antiprotozoal activity observed for the methanol extract of *A. zygia* (Ndjakou et al., 2007).

Material and Methods

The bark of *A. zygia* was collected from Shambat, Sudan, in June 2006. The plant material was authenticated by Mr. Wail El Saddig (National Research Centre, Sudan) based on comparison with voucher specimen deposited in the herbarium of the Institute of the Medicinal and Aromatic Plants, Khartoum, Sudan.

An air-dried sample (1.0 kg) of the bark of *A. zygia* was powdered and extracted (3×) with 50% CH_2Cl_2/MeOH. The extracts were pooled and evaporated under reduced pressure to give a dark brown residue (148.6 g). This extract was partitioned between ethyl acetate and water, which delivered 7.3 g of crude product after evaporation of the organic phase, and 139.5 g from the water phase. Fractionation of the organic extract was carried out using silica gel flash chromatography (230-400 mesh) with a cyclohexane/EtOAc gradient. According to the TLC profiles three major fractions were obtained. Fraction FI was further purified on Sephadex LH-20 (Lipophilic Sephadex, Amersham Biosciences Ltd.; purchased from Sigma-Aldrich Chemie, Steinheim, Germany) using CH_2Cl_2/MeOH (6:4) followed by gradient chromatography on LiChroprep RP-18 (Merck KGaA, Darmstadt, Germany) eluted with MeOH/H_2O (10:90 to 50:50), which afforded compound **1** (1.0 mg). Fraction FII was also separated on LiChroprep RP-18 eluted with MeOH/H_2O (10:90 to 50:50) to give compounds **2** (2.7 mg) and **3** (1.7 mg).

The gum from the water phase was triturated with MeOH and the soluble part, after evaporation to dryness, was subjected to gradient chromatography on silica gel eluted with EtOAc/MeOH. This afforded compound **4** (2.9 mg).

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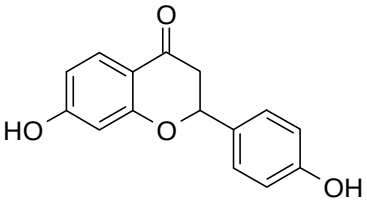
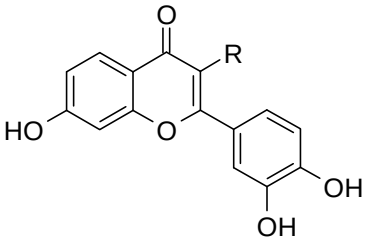
Results and Discussion

Compounds **1**-**4** were unambiguously identified by interpretation of ESI mass data, ^{1}H, ^{13}C and 2D NMR spectra as well as by comparison with published data as 4',7-dihydroxyflavanone (**1**) (Umehara et al., 2009), 3',4',7-trihydroxyflavone (**2**) (Wu et al., 2008), 3-*O*-methylfisetin (3',4',7-trihydroxy-3-methoxyflavone, **3**) (Wu et al., 2008), and lup-20(29)-en-3-ol (**4**) (Blair et al., 1970).

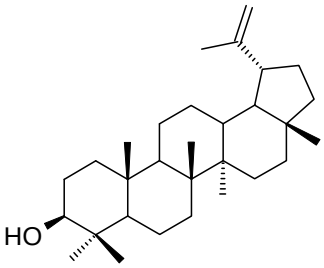
http://dx.doi.org/10.4314/ajtcam.v9i1.8



1



2: R = H
3: R = OCH_3



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The genus *Albizia* consists of over 150 species. The occurrence of albiziasaponins A, B, C (Pal, et al., 1995), macrocyclic alkaloids budmunchiamines L4, L5, and L6 (Ajay and Laxmi, 1997), and albizinin (Ma, 1997) have been reported from *Albizia lebbeck*. Kaempferol and quercetin were isolated from *A. julibrissin* (Lau et al., 2007) and *A. lebbeck* (El-Mousallamy, 1998). Prenylated flavonoids such as sophoflavescenol and kurarinone were also known from *A. lebbeck* (Jung et al., 2004). The unusual biflavonoids, eucaediflavone and albiproflavone were delivered from *A. procera* (Yadav and Bhadoria, 2004). Other flavonoids were reported from *A. amara* and *A. adianthifolia* (Arthur et al., 1978); however, this is the first report of flavonoids from the species *A. zygia*.

In our study compounds **1**-**3** were tested against *P. falciparum* K1: compound **2** exhibited high antimalarial activity (IC_{50} 0.078 μg/ml), but displayed unfortunately also cytotoxic effects (IC_{50} 0.405 μg/ml) against a cell line L6.

The results of this phytochemical study of the bark of *A. zygia* are in agreement with previous data reported for other *Albizia* species Arthur et al., 1978).

Acknowledgements

The authors would like to thank Dr. H. Frauendorf and Mr. R. Machinek for the mass and NMR spectra, F. Lissy and A. Kohl for technical assistance and Marcel Kaiser in Swiss Tropical Institute, Parasite Chemotherapy for determining the antimalarial activity. MAA thanks the German Academic Exchange Service (DAAD) for a Ph.D. grant.

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http://dx.doi.org/10.4314/ajtcam.v9i1.8