Antiplasmodial Quinones from *Pentas longiflora* and *Pentas lanceolata*

Authors Milkyas Endale[1], John Patrick Alao[2], Hoseah M. Akala[3], Nelson K. Rono[1], Fredrick L. Eyase[3], Solomon Derese[1], Albert Ndakala[1], Martin Mbugua[1], Douglas S. Walsh[3], Per Sunnerhagen[2], Mate Erdelyi[4], Abiy Yenesew[1]

Affiliations The affiliations are listed at the end of the article

Key words
- *Pentas longiflora*
- *Pentas lanceolata*
- Rubiaceae
- anthraquinone
- 5,6-dihydroxydamnacanthol
- pyranonaphthoquinone
- malaria

Abstract

The dichloromethane/methanol (1:1) extracts of the roots of *Pentas longiflora* and *Pentas lanceolata* showed low micromolar (IC_{50} = 0.9–3 µg/mL) *in vitro* antiplasmodial activity against chloroquine-resistant (W2) and chloroquine-sensitive (D6) strains of *Plasmodium falciparum*. Chromatographic separation of the extract of *Pentas longiflora* led to the isolation of the pyranonaphthoquinones pentalongin (**1**) and psychorubrin (**2**) with IC_{50} values below 1 µg/mL and the naphthalene derivative mollugin (**3**), which showed marginal activity. Similar treatment of *Pentas lanceolata* led to the isolation of eight anthraquinones (**4**–**11**, IC_{50} = 5–31 µg/mL) of which one is new (5,6-dihydroxydamnacanthol, **11**), while three – nordamnacanthal (**7**), lucidin-ω-methyl ether (**9**), and damnacanthol (**10**) – are reported here for the first time from the genus *Pentas*. The compounds were identified by NMR and mass spectroscopic techniques.

Supporting information available online at http://www.thieme-connect.de/ejournals/toc/plantamedic

received February 19, 2011
revised July 21, 2011
accepted July 25, 2011

Bibliography
DOI http://dx.doi.org/10.1055/s-0031-1280179
Published online October 6, 2011
Planta Med 2012; 78: 31–35

ISSN 0032-0943

Correspondence
Abiy Yenesew
Department of Chemistry
University of Nairobi
Chiromo Road
30197-00100 Nairobi
Kenya
Phone: + 254 20 24 44 61 38
Fax: + 254 20 24 44 61 38
ayenesew@uonbi.ac.ke

Correspondence
Mate Erdelyi
Department of Chemistry
University of Gothenburg
Kemivägen 10
413 23 Gothenburg
Sweden
Phone: + 46 31 7 86 90 33
Fax: + 46 31 7 72 13 94
mate@chem.gu.se

Introduction

According to the estimates of the World Health Organization, almost one million deaths are caused by malaria each year in Africa alone, of which most are children under the age of five [1]. In addition, this mosquito-borne disease has a serious economic impact due to loss of commercial and labor outputs, predominantly in countries with tropical and subtropical climates. Over 300 000 000 people worldwide are infected, and each year nearly one-third of these exhibit acute manifestations of the disease [2]. While awaiting the development of a malaria vaccine, millions of lives are still dependent upon treatment with chemotherapeutic agents. Since most of the available drugs are becoming increasingly ineffective due to the rapid emergence of resistant *Plasmodium falciparum* strains [3], there is an urgent need for novel antimalarial agents. Because of the high cost of the few still effective antimalarial drugs [4], traditional medicine remains an important source of treatment in developing countries.

Pentas longiflora Oliver (Rubiaceae) is an important medicinal plant of Tropical East Africa [5]. In Kenya, a decoction of its roots mixed with milk is taken as a cure for malaria [6]. Although its leaves have previously been tested for *in vitro* antimalarial activity, no attempts were made to isolate and identify the antiplasmodial constituents [7]. *Pentas lanceolata* (Forsk.) is mostly found in the highlands of Kenya and was reported to exhibit micromolar *in vitro* antiplasmodial activity against *P. falciparum* [8]. Although extracts of these plants have been assayed against a range of diseases [8, 9], their constituents have not been investigated for antiplasmodial activity. Motivated by the traditional uses and the preliminary screening reports [7–9], we performed isolation, characterization, and an antiplasmodial investigation of naphthoquinones and anthraquinones found in the extracts of the roots of *P. longiflora* and *P. lanceolata*.

Materials and Methods

General experimental procedures

Column chromatography was performed on oxalic acid impregnated silica gel [the silica gel was deactivated by mixing 2 kg of silica gel 60 (70–230 mesh) with 3% oxalic acid (30 g in 1 L water) and allowed to stand for 30 min, filtered and dried in an oven (100 °C) for 45 min]. TLC was done using silica gel 60 F_{254} (Merck) precoated

This is a copy of the author's personal reprint

Phytochemistry Letters 4 (2011) 176–178

Contents lists available at ScienceDirect

Phytochemistry Letters

journal homepage: www.elsevier.com/locate/phytol

Terpurinflavone: An antiplasmodial flavone from the stem of *Tephrosia Purpurea*

Wanyama P. Juma [a], Hoseah M. Akala [b], Fredrick L. Eyase [b,c], Lois M. Muiva [a], Matthias Heydenreich [d], Faith A. Okalebo [e], Peter M. Gitu [a], Martin G. Peter [d], Douglas S. Walsh [b], Mabel Imbuga [c], Abiy Yenesew [a,*]

[a] Department of Chemistry, University of Nairobi, P.O. Box 30197-00100, Nairobi, Kenya
[b] United States Army Medical Research Unit-Kenya, MRU 64109, APO, AE 09831-4109, USA
[c] Department of Biochemistry, Jomo Kenyatta University of Agriculture and Technology, P.O. Box 62000, Nairobi, Kenya
[d] Institut für Chemie, Universität Potsdam, P.O. Box 60 15 53, D-14415 Potsdam, Germany
[e] School of Pharmacy, University of Nairobi, P. O. Box 30197-0011, Nairobi, Kenya

ARTICLE INFO

Article history:
Received 10 September 2010
Received in revised form 16 December 2010
Accepted 23 February 2011
Available online 29 March 2011

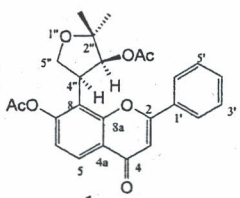
Keywords:
Tephrosia purpurea
Leguminosae
Stem
Flavone
Terpurinflavone
Antiplasmodial

ABSTRACT

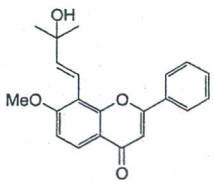
The stem extract of *Tephrosia purpurea* showed antiplasmodial activity against the D6 (chloroquine-sensitive) and W2 (chloroquine-resistant) strains of *Plasmodium falciparum* with IC_{50} values of 10.47 ± 2.22 μg/ml and 12.06 ± 2.54 μg/ml, respectively. A new prenylated flavone, named terpurinflavone, along with the known compounds lanceolatin A, (−)-semiglabrin and lanceolatin B have been isolated from this extract. The new compound, terpurinflavone, showed the highest antiplasmodial activity with IC_{50} values of 3.12 ± 0.28 μM (D6) and 6.26 ± 2.66 μM (W2). The structures were determined on the basis of spectroscopic evidence.

1. Introduction

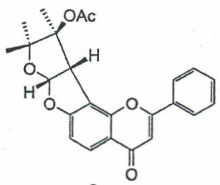
Tephrosia Pers (Leguminosae-Papilionoideae) is a large tropical and sub-tropical genus estimated to contain about three hundred species (Waterman and Khalid, 1980; Abou-Douh et al., 2005) out of which thirty species are found in Kenya (Tarus et al., 2002). The extracts of some *Tephrosia* species have shown various biological activities including antiplasmodial (Muiva et al., 2009), antibacterial (Abou-Douh et al., 2005) anticancer (Santram et al., 2006) and insecticidal activities (Delfel et al., 1970). The taxon *T. purpurea* is among the most widely used *Tephrosia* species in traditional medicine (Damre et al., 2003). Various biological activities including antibacterial (Hegazy et al., 2009; Chinniah et al., 2009), antidiabetic and antioxidant (Pavana et al., 2009), immunomodulatory (Damre et al., 2003), anti-inflammatory (Damre et al., 2003) and cancer chemopreventive activities (Chang et al., 2000) have been reported for extracts and pure compounds from this plant. *T. purpurea*. is rich in prenylated flavonoids including flavones (Hegazy et al., 2009; Pelter et al., 1981), flavanones (Pelter et al., 1981; Gupta et al., 1980), chalcones (Chang et al., 2000; Pelter et al., 1981) and rotenoids (Ahmad et al., 1999). In the search for compounds with antiplasmodial activity from Kenyan plants, the stem of *T. purpurea* has been investigated. This report is on the isolation and characterization of a new prenylated flavone, named terpurinflavone (**1**), with antiplasmodial activity along with three known flavonoids.



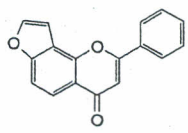
1



2



3



4

* Corresponding author. Tel.: +254 204 449 004x2170; fax: +254 204 446 138.
E-mail address: ayenesew@uonbi.ac.ke (A. Yenesew).

1874-3900/$ – see front matter © 2011 Phytochemical Society of Europe. Published by Elsevier B.V. All rights reserved.
doi:10.1016/j.phytol.2011.02.010

Phytochemistry Letters 5 (2012) 150–154

Contents lists available at SciencDirect

Phytochemistry Letters

journal homepage: www.elsevier.com/locate/phytol

Four isoflavanones from the stem bark of *Platycelphium voënse*

Ivan Gumula [a,b], Matthias Heydenreich [c], Solomon Derese [a], Isaiah O. Ndiege [b], Abiy Yenesew [a,*]

[a] Department of Chemistry, University of Nairobi, P.O. Box 30197-00100, Nairobi, Kenya
[b] Department of Chemistry, Kyambogo University, P.O. Box 1, Kyambogo, Kampala, Uganda
[c] Institut für Chemie, Universität Potsdam, P.O. Box 60 15 53, D-14415, Potsdam, Germany

ARTICLE INFO

Article history:
Received 29 October 2011
Received in revised form 26 November 2011
Accepted 28 November 2011
Available online 9 December 2011

Keywords:
Platycelphium voënse
Stem bark
Leguminosae
Isoflavanones
Platyisoflavanone
Mycobacterium tuberculosis

ABSTRACT

From the stem bark of *Platycelphium voënse* (Leguminosae) four new isoflavanones were isolated and characterized as (*S*)-5,7-dihydroxy-2′,4′-dimethoxy-3′-(3″-methylbut-2″-enyl)-isoflavanone (trivial name platyisoflavanone A), (±)-5,7,2′-trihydroxy-4′-methoxy-3′-(3″-methylbut-2″-enyl)-isoflavanone (platyisoflavanone B), 5,7-dihydroxy-4′-methoxy-2″-(2‴-hydroxyisopropyl)-dihydrofurano-[4″,5″:3′,2′]-isoflavanone (platyisoflavanone C) and 5,7,2′,3″-tetrahydroxy-2″,2″-dimethyldihydropyrano-[5″,6″:3′,4′]-isoflavanone (platyisoflavanone D). In addition, the known isoflavanones, sophoraisoflavanone A and glyasperin F; the isoflavone, formononetin; two flavones, kumatakenin and isokaempferide; as well as two triterpenes, betulin and β-amyrin were identified. The structures were elucidated on the basis of spectroscopic evidence. Platyisoflavanone A showed antibacterial activity against *Mycobacterium tuberculosis* in the microplate alamar blue assay (MABA) with MIC = 23.7 μM, but also showed cytotoxicity (IC_{50} = 21.1 μM) in the vero cell test.

1. Introduction

Platycelphium (family Leguminosae, sub-family Papilionoideae, tribe Sophoreae) is a monotypic genus that occurs in the drier parts of Eastern Africa, particularly in Kenya, Ethiopia, Somalia and Tanzania (Gillett et al., 1971). Sophoreae, containing genera of least specialization and diverse morphological features, has been described as "a tribe of convenience" (Gillett et al., 1971; Polhill, 1981). The tribe is considered to be transitional between the subfamilies Papilionoideae and Caesalpinoideae (Bentham, 1841) and DNA sequencing studies have shown that Sophoreae needs taxonomic realignment (Crisp et al., 2000; Doyle et al., 2000; Käss and Wink, 1995; Pennington et al., 2001). From morphological point of view the genus *Platycelphium* is closely related to the genera *Dicraeopetalum* and *Bolusanthus* all belonging to the Sophora group within the Sophoreae tribe (Polhill, 1994.). Whereas, there is some phytochemical information on the genus *Bolusanthus* (Asres et al., 1985; Bojase et al., 2001a,b), the information available on *Platycelphium voënse* (Asres et al., 1997b; Van Wyk et al., 1993) and *Dicraeopetalum* (Asres et al., 1997a; Van Wyk et al., 1993) is limited to the identification of quinolizidine alkaloids through GC–MS analysis of the leaves and twigs of plants from the two genera. Quinolizidine alkaloids have also been reported from *Bolusanthus* (Asres et al., 1986). With interest to see if phytochemical information supports the close association among these genera in the Sophora group within the Sophoreae tribe, the stem bark of *P. voënse* was investigated. This paper describes the isolation and characterization of four new prenylated isoflavanones along with seven known compounds (two isoflavanones, an isoflavone, two 3-methoxyflavones and two triterpenes).

2. Results and discussion

Column chromatography of the CH_2Cl_2–MeOH (1:1) extract of the stem bark of *P. voënse*, using n-hexane containing increasing amounts of ethyl acetate as the eluent and subsequent purification of the fractions, resulted in the isolation of eleven compounds including four new isoflavanones, **1–4** (Fig. 1).

Compound **1**, obtained as a white amorphous solid, showed a $[M]^+$ at *m/z* 384.1597 in the HREI-mass spectrum suggesting a molecular formula of $C_{22}H_{24}O_6$. The presence of an isoflavanone skeleton was deduced from UV (λ_{max} 288 nm), ^1H (δ 4.48, *dd*, *J* = −11.1, 11.2 Hz, H-2_{ax}; δ 4.66, *dd*, *J* = −11.1, 5.6 Hz, H-2_{eq}; δ 4.38, *dd*, *J* = 11.2, 5.6 Hz, H-3_{ax}) and ^{13}C (δ 71.6 for C-2; 45.9 for C-3 and 198.2 for C-4) NMR spectra. The ^1H NMR spectrum further revealed the presence of two methoxyl (δ 3.71 and 3.80), a chelated hydroxyl (δ 12.18) at C-5 as well as a 3-methylbut-2-enyl moiety (Table 1).

Two *meta*-coupled doublets at δ 5.95 and 5.97 (*J* = 2.0 Hz) were attributable to H-8 and H-6 implying that C-5 and C-7 of A-ring are oxygenated as expected from biogenetic point of view. In the

* Corresponding author. Tel.: +254 733 832576; fax: +254 204 446138.
E-mail address: ayenesew@uonbi.ac.ke (A. Yenesew).

1874-3900/$ – see front matter © 2011 Phytochemical Society of Europe. Published by Elsevier B.V. All rights reserved.
doi:10.1016/j.phytol.2011.11.012