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ScienceDirect
Phytochemistry 68 (2007) 2096–2100
PHYTOCHEMISTRY
www.elsevier.com/locate/phytochem

α-Glucosidase inhibitory constituents from stem bark of *Terminalia superba* (Combretaceae)

Jean Duplex Wansi [a,*], Marie-Christine Lallemand [d], David Daco Chiozem [b], Flavien Aristide A. Toze [a], Luc Meva'a Mbaze [a], Shamsun Naharkhan [c], Muhammad Choudhary Iqbal [c], François Tillequin [d], Jean Wandji [b], Zacharias Tanee Fomum [b]

[a] *Department of Chemistry, University of Douala, Faculty of Science, P.O. Box 24157, Douala, Cameroon*
[b] *Department of Organic Chemistry, University of Yaoundé I, Faculty of Science, P.O. Box 812, Yaoundé, Cameroon*
[c] *H.E.J Research Institute of Chemistry, University of Karachi, Karachi 75270, Pakistan*
[d] *Laboratoire de Pharmacognosie, UMR-8638, Université René Descartes, Faculté des Sciences Pharmaceutiques et Biologiques, 4-Avenue de l'Observatoire, 75006 Paris, France*

Received 17 September 2006; received in revised form 13 February 2007
Available online 16 April 2007

Abstract

The CH_2Cl_2/CH_3OH (1/1) extract of the dried stem bark of *Terminalia superba* afforded two compounds, (7*S*,8*R*,7′*R*,8′*S*)-4′-hydroxy-4-methoxy-7,7′-epoxylignan and *meso*-(*rel* 7*S*,8*R*,7′*R*,8′*S*)-4,4′-dimethoxy-7,7′-epoxylignan along with 11 known compounds. The structures of the compounds were established by analysing the spectroscopic data and also comparing it with the data of previously known analogues. All the isolated compounds were evaluated for their glycosidase inhibition activities. Gallic acid and methyl gallate showed significant α-glucosidase inhibition activity.

Keywords: *Terminalia superba*; Combretaceae; Stem bark; Lignans; Gallic acid; α-Glucosidase activity

1. Introduction

Terminalia superba Engl. and Diels (Combretaceae) is a plant used by traditional healers as a remedy for diabetes mellitus in Africa. The Sotho people of Southern Senegal take the powdered stem bark of this plant against diabetes. In Niger and in Mali this plant is used to treat hepatitis (Ajanohoun et al., 1979, 1980). *Terminalia superba* is a big tree, up to 50 m in height and 120 cm in stem diameter, with deciduous leaves. It is widely distributed in the dense humid forests, semi-deciduous forests and also in easily flooded and secondary forests (Burkill, 1985). Both the methanol and methylene chloride extracts of the stem bark of *Terminalia superba* were previously reported to have anti-diabetic activity (Kamtchouing et al., 2006). The methanol extract of *Terminalia superba* also induces endothelium-independent relaxation of rat thoracic aorta (Dimo et al., 2006). The widespread use of *Terminalia superba* in indigenous medicine for different ailments, as well as the significant anti-diabetic activity and vasorelaxant effects exhibited by extracts obtained from *Terminalia superba*, justified further attempts to isolate and identify active compounds. In this paper, we report the isolation and the structural elucidation of two new lignans, and the α-glucosidase inhibition study of some isolated compounds.

2. Results and discussion

The stem bark of *T. superba* was extracted with a mixture of CH_2Cl_2/MeOH (1/1). The extract which showed

* Corresponding author. Tel.: +237 781 77 31.
E-mail address: jdwansi@yahoo.fr (J.D. Wansi).

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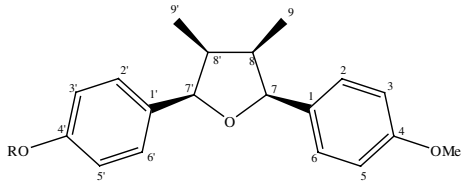
doi:10.1016/j.phytochem.2007.02.020

considerable α-glucosidase inhibitory activity, was separated using repeated column chromatography and preparative TLC (PTLC) to afford two new compounds and eleven known compounds identified as ellagic acid, ellagic acid 3,3′-dimethyl ether, ellagic acid-4-*O*-β-D-xylopyranoside-3,3′-dimethyl ether, gallic acid, methyl gallate, oleanolic acid, betulinic acid, lupeol, β-amyrin, stigmasterol and β-sitosterol respectively, by comparison of their spectroscopic data with those of authentic samples or values reported in the literature (Atta-ur-Rahman et al., 2002; Khac et al., 1990; Tanaka et al., 1998).



1 R = H

2 R = Me

Compound **1**, $[\alpha]_D^{25} = +35.0°$, was obtained as a white powder. Its molecular formula $C_{19}H_{22}O_3$ was deduced from the CIMS, EIMS and HR EIMS ($[M]^+$, *m/z* found 298.1527, calc. 298.1560). The UV spectrum showed two maxima at 277 and 227 nm, suggesting the presence of a tetrahydrofuran lignan (Urzua et al., 1987). The ^1H NMR spectrum (Table 1), showed characteristic signals arising from the tetrasubstituted tetrahydrofuran ring system comprising of two secondary methyl groups at δ 0.55 and 0.57 (*d*, *J* = 5.7 Hz), a two-proton multiplet at δ 2.68 (*ddq*, *J* = 5.8; 5.7; 3.1 Hz) due to the H-8 and H-8′ methine protons, and a two proton doublet at δ 5.10 (*d*, *J* = 5.8 Hz) due to the two oxymethine protons, H-7 and H-7′. The ^1H NMR spectrum of **1**, showed one additional methoxyl at δ 3.80 (*s*) and two AA′BB′ systems for aromatic protons at δ 6.81 (*d*, *J* = 8.5 Hz, H-3 and H-5), 6.88 (*d*, *J* = 8.8 Hz, H-3′ and H-5′), 7.27 (*d*, *J* = 8.4 Hz, H-2 and H-6) and 7.31 (*d*, *J* = 8.6 Hz, H-2′ and H-6′) implying that each aromatic ring has a 1,4-disubstitution pattern. The presence of tetrahydrofuran lignan was confirmed by the observation of two methyl groups, twelve methine groups and four quaternary carbon resonances in the ^{13}CNMR spectrum (Table 1). Complete assignment of the proton spin systems in **1** was achieved by COSY ^1H–^1H and 2D-NOESY, while carbons were assigned from HMQC and HMBC spectra. The analysis of the HMBC spectrum permitted the attribution of aromatic hydroxyl and the *O*-methyl signals. The relative configuration at C-7, C-7′, C-8 and C-8′ was assigned by a combination of NOE data and analysis of the chemical shifts H-7/H-7′, the methyl protons (Me-9/Me-9′) and C-7/C-7′ (Rimando et al., 1994). Me-9 showed a NOE correlation with the Me-9′ proton resonance and with the *ortho* proton of the phenolic ring, Me-9′ showed NOEs with Me-9, and the *ortho*-proton of the methoxy-bearing aromatic ring. This finding clearly establish the *cis*-relation of the two methyl groups, as well as the *cis*-relation between the two methyl groups and their vicinal aryl substituents. This was confirmed by the chemical shift of the methyl groups (δ 0.55, Me-9; δ 0.57, Me-9′), which are clearly shielded by the neighbouring aromatic rings, and gave evidence for the *cis*-relation, compared with those of (7*S*,8*S*,7′*S*,8′*S*)-3,3′,4′-trihydroxy-4-methoxy-7,7′-epoxylignan (Abou-Gazar et al., 2004), and *rel*- (7*S*,8*S*,7′*R*,8′*R*)-3,3′,4,4′,5,5′-hexamethoxy-7.0.7′,8, 8′-lignan (Conserva et al., 1990). The coupling constants between the H-7 and H-8 and H-7′ and H-8′ (*J* = 5.8 Hz) indicated a 7,8-*cis*-7′,8′-*cis* relationship. All these informations are in agreement with the proposed structure **1** (or enantiomer). The absolute configuration of **1** was assigned by a combination of analysis of the CD spectrum and comparison of optical rotation data ($[\alpha]_D^{25} = +35.0°$ (*c* = 0.007 in MeOH)) data with those of 7,7′-epoxylignans (Urzua et al., 1987; Minh Giang et al., 2006; Prasad et al., 1998). The CD spectrum showed negative cotton effects in both the 240–250 and

Table 1
^1H (500 MHz) and ^{13}C (125 MHz) assignments for **1** and **2** in $CDCl_3$

Attribution	**1**		**2**	
	^{13}C	^1H	^{13}C	^1H
1	132.6	–	133.0	–
2/6	127.5	7.27 (*d*, *J* = 8.4)	128.0	7.30 (*d*, *J* = 8.6)
3/5	113.4	6.81 (*d*, *J* = 8.5)	112.4	6.74 (*d*, *J* = 8.6)
4	154.3	–	155.3	–
7/7′	82.6	5.10 (*d*, *J* = 5.8)	83.5	5.12 (*d*, *J* = 6.1)
8/8′	41.5	2.68 (*ddq*, *J* = 5.8; 5.7; 3.1)	42.9	2.62 (*m*)
1′	132.9	–	133.0	–
2′/6′	127.7	7.31 (*d*, *J* = 8.6)	128.2	7.30 (*d*, *J* = 8.6)
3′/5′	114.8	6.88 (*d*, *J* = 8.6)	115.3	6.74 (*d*, *J* = 8.6)
4′	158.5	–	159.5	–
OH	–	4.69 (*s*)	–	4.75 (*s*)
Me-9	11.8	0.55 (*d*, *J* = 5.7)	12.0	0.57 (*d*, *J* = 5.8)
Me-9′	11.8	0.57 (*d*, *J* = 5.7)	12.0	0.57 (*d*, *J* = 5.8)
MeO	55.2	3.80 (*s*)	56.0	3.83 (*s*)

Assignments were based on HMQC, HMBC and NOESY experiments.