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A TANNIN ANTI-CANCER PROMOTOR FROM *TERMINALIA ARJUNA*

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Key Word Index—*Terminalia arjuna*; Combretaceae: leaves; ellagitannins.

Abstract—A new ellagitannin named, arjunin, four known tannins and two phenolic acids were isolated from *Terminalia arjuna*. The structures were elucidated by spectroscopic analyses. © 1998 Published by Elsevier Science Ltd. All rights reserved

INTRODUCTION

Terminalia arjuna is a large tree found on canal and road sides, and has economic importance for its timber and tannins. Extracts of some species of *Terminalia* showed antiviral activity and strong anti-HSV-1 activity [1]. Water and methanol extracts of stem bark of *T. arjuna* were subjected to screening for their inhibitory effect on human immunodeficiency virus (HIV-1) and were found to inhibit the HIV-1 activity by more than 70% at 0.2 mg ml^{-1} [2]. The genus *Terminalia* is chemically characterized by the presence of tannins and related compounds [3–7]. The heartwood of *T. arjuna* was found to contain β-sitosterol, oleanolic acid, a trihydroxy triterpene carboxylic acid and arjunolic acid, besides ellagic acid [8–9].

RESULTS AND DISCUSSION

The leaves of *Terminalia arjuna* afforded a new ellagitannin identified as 3-*O*-galloyl-4,6-gallagyl-α,β-glucopyranose, named arjunin (**1**), in addition to the known tannins, punicalin (**1a**) [7], 1,2,3,4,6-pentagalloyl glucose (**2**) [7], 2,3,4,6-tetragalloyl glucose (**3**) [10], 2,3:4,6-*bis*-hexahydroxydiphenyl-1-galloyl-β-glucose (**4**) [10] and the phenolic acids, gallic and ellagic.

The ^1H NMR of (**1**) showed two one-proton singlet signals at δ 6.51 and 6.63, beside one two-protons singlet signal at δ 7.01. The latter signal suggested the presence of one galloyl group. The observation of aliphatic proton signals at δ 5.2 *t*, 4.22 (*dd*, $J = 2.13$ Hz), 4.8 (*dd*, $J = 2.13$ Hz) indicated the presence of hexapyranose core, with acylation of positions 3 and 6, respectively. The duplication of signals was due to the lack of substitution at the anomeric hydroxyl centre. When hydrolyzed in 1N sulfuric acid, a hydrolysate (**1a**) was obtained together with gallic acid. Compound (**1a**) was identified as punicalin by comparison of its ^1H and ^{13}C NMR with previously recorded data [3]. The structure of (**1**) was finally proved by ^{13}C NMR, which showed four carbonyl signals at δ 157.9, 158.2, 167.0 and 168.2, due to the gallagyl group and the carbonyl signal at δ 168.6 due to the galloyl group. The spectrum showed the α,β C-1 of the glucose signals at δ 91.2 and 95.0, respectively. Other signals appeared at positions corresponding with those for punicalin, except that for H-3 of the glucose moiety which appeared at δ 79.1.

The biological activity examination of the ethanolic extract of the leaves of *T. arjuna* and the isolated compound **1** showed that they have moderate cytotoxic activity against BT-20 human breast carcinoma cells. The Ic_{50} of the extract and the compound were 2.5 and 6.5 μg ml^{-1}, respectively. The growth inhibition effect of **1** was higher than that of the extract.

EXPERIMENTAL

Leaves of *T. arjuna* Bedd. were collected in August 1996 and identified by Dr M. El-Gibali, Herbarium, NRC. Dried powdered leaves were extracted with 80% EtOH in H_2O. The concd extract was defatted and subjected to a Sephadex L-H-20 CC using EtOH, 20% EtOH, 50% EtOH and EtOH–H_2O–Me_2CO (1:1:2) as eluents. Examination of the obtained frs by PC using BAW (4:1:5) and 15% HOAc led to the isolation of arjunin (**1**), in addition to the known com-

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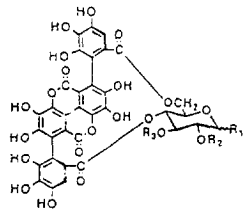
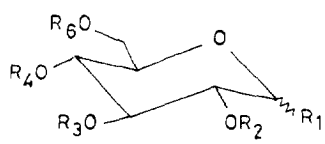




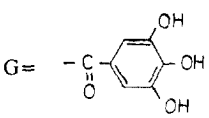
1 R_1= R_2= H, R_3= G

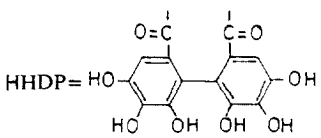
1_a, R_1= R_2= R_3= H

2, R_1= R_2= R_3= R_4= R_6= G

3, R_1= H, R_2= R_3= R_4= R_6= G

4, R_1= G, R_2-R_3= R_4- R_6= HHDP

G= 

HHDP= 

Scheme 1.

pounds, 1,2,3,4,6-pentagalloyl glucose 2,3,4,6-tetragalloyl glucose 2,3 : 4,6-*bis*-hexahydroxydiphenyl-1-galloyl-β-glucose, punicalin, gallic and ellagic acids.

Arjunin (**1**)

UV (MeOH): λ_{max} 279 nm. ^{1}H NMR (500 MHz): δ 2.17 (1H, *m*, H-5), 4.22 (1H, *dd*, *J* = 13 Hz, H-6), 4.80 (1H, *dd*, *J* = 2, 10 Hz, H-6), 5.2 (1H, *t*, *J* = 10 Hz, H-3), 6.51, 6.63, 7.01 (each singlet, aromatic protons). ^{13}C NMR (125 MHz): δ 168.6, 168.2, 167.0 (COO), 158.2, 157.9 (γ-lactone), 95.0 (C-1-β-glucose), 9.12 (C-1-α-glucose), 60.0–79.1 (C-2, 3, 4, 5, 6-α,β-glucose).

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