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Proceeding Paper

Isolation and Structural Elucidation of Flavonol and a Flavonol Glycoside from the Butanol Fraction of *Globimetula oreophila* a Mistletoe on *Azadirachta indica* A. Juss (Melliacea) †

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Abstract: *Globimetula oreophila*, is a hemiparasitic shrub in the Loranthaceae family, known for growing on dicotyledonous trees like neem, rubber, citrus, cocoa, and kola nut. It is used in traditional medicine for malaria, diarrhea, headaches, and insomnia. Traditionally valued for remedying malaria, diarrhea, headaches, and insomnia, this research targets uncovering bioactive compounds within the plant's butanol fraction. Employing extraction methods and chromatographic techniques, the study successfully isolates quercetin and quercetin rhamnoside, previously unexplored within this species. These discoveries not only expand the plant's chemical taxonomy but also hint at potential pharmacological applications, offering a glimpse into the intricate biochemistry of this botanical entity.

Keywords: quercetin; flavonol glycoside; *Globimetula oreophila*; malaria; spectroscopy

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1. Introduction

Traditional medicine, rooted in the use of plant-derived compounds, serves as the primary healthcare system for a significant portion of the global population, as acknowledged by the World Health Organization [1]. Natural compounds found in plants offer therapeutic benefits with minimal toxicity, contrasting synthetic pharmaceuticals [2]. Plant secondary metabolites, such as tannins, steroids, phenolic compounds, and alkaloids, house medicinal potential, exemplified by compounds like morphine and quinine [3,4]. Recent research has intensified exploration into medicinal plants, revealing their diverse properties including anti-inflammatory, antioxidant, and antimicrobial capacities [5,6].

Globimetula oreophila, commonly known as mistletoe, is a hemiparasitic plant from the Loranthaceae family, utilizing dicotyledonous trees as hosts across tropical Africa [4,7]. Its chemical composition and biological activities, influenced by host plants, have been traditionally harnessed to treat various ailments, notably malaria [6,8,9].

Studies have unveiled a spectrum of secondary metabolites within the genus Globimetula, including flavonoids with antimalarial potential [4,6,10]. This study embarks on isolating and characterizing secondary metabolites from *Globimetula oreophila* growing on *Azadirachta indica*, employing column chromatography and spectroscopic analyses to elucidate their structures, contributing to the plant's chemical taxonomy and potential pharmacological utility.

2. Methods

2.1. Extraction and Fractionation

The study commenced with the maceration of 900 g of powdered plant material in 8 L of 70% ethanol for 3 days, resulting in 74.55 g (8.28%) of a dark green semi-solid mass known as the crude ethanol extract (CEE). This extract was sequentially partitioned with n-hexane, chloroform, ethyl acetate, and n-butanol, yielding distinct fractions: n-hexane (HF), chloroform (CF), ethyl acetate (EF), and n-butanol (nBF). Subsequent column chromatographic analysis was performed on the ethyl acetate, n-hexane, and n-butanol fractions, marking a pivotal step in the extraction and characterization of bioactive compounds from the plant material [11] (Figure 1).

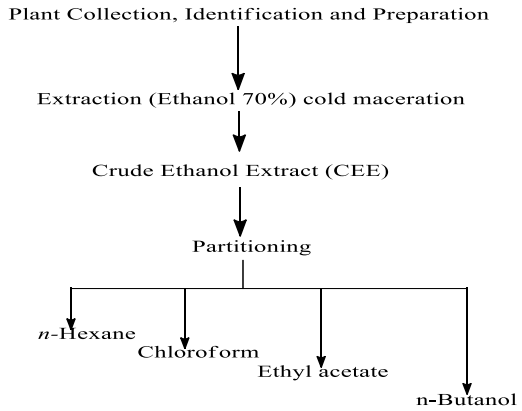


Figure 1. Extraction and partitioning processes conducted on Globimetula oreophila leaves.

2.2. Isolation of Compounds DG1 and DG5 from G. oreophila

Column Chromatographic Separation of n-Butanol Fraction (n-BF)

In the study, the n-butanol fraction (10 g) underwent adsorption onto silica gel (10 g) and was subsequently subjected to chromatography in a column packed with 400 g of silica gel. A gradient elution method was employed, starting with 100% ethyl acetate and gradually transitioning to ethyl acetate: methanol mixtures of increasing polarity until a ratio of 65:35 was reached, followed by a final wash with 100% methanol. The eluate was fractionated into 45 collections, which were consolidated based on similar thin-layer chromatography (TLC) profiles to yield 9 significant fractions labeled BF1-BF9. Further purification of fraction BF7 through gel filtration over Sephadex LH-20 with methanol as the eluting solvent led to the isolation of compounds DG1 (10 mg) and DG5 (12 mg) (Figure 2).

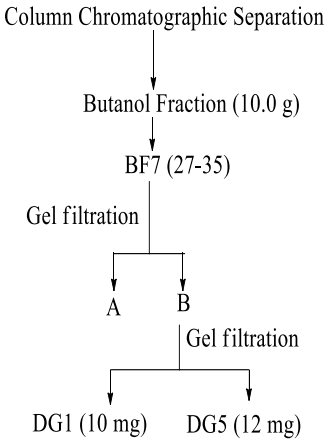


Figure 2. Column Chromatographic Studies on *G. oreophila* Fractions.

2.3. Characterization of Compounds

All the isolated compounds were individually subjected to physical and chemical tests, FTIR, UV-visible spectroscopy, 1D, and 2D NMR analysis to elucidate the structures of the compounds.

3. Results

Structural Elucidation of Isolated Compounds (DG1 and DG5)

The ethanol crude extract obtained via the cold maceration method was successively partitioned sequentially with various solvents to give *n*-hexane, chloroform, ethyl acetate, and *n*-butanol fractions. The *n*-butanol fraction was separated via column chromatography (CC) and Sephadex LH-20 to provide quercetrin (DG1) and quercetin (DG5). Based on the nuclear magnetic resonance spectroscopy of DG1 and DG5 (Figures S1–S5), the presence of two compounds is suggested (Tables 1 and 2) due to the elution of some compounds in the chromatographic analysis of *n*-butanol fraction.

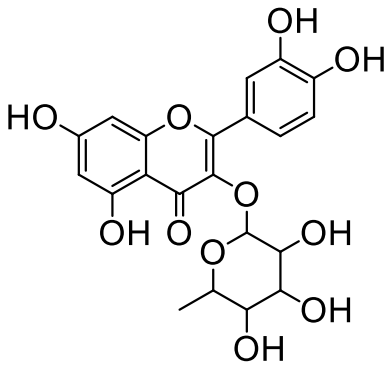
Table 1. Summary of 1D and 2D spectral data for compound DG1 (MeOD, 400 MHz).

Position	δ_H DG1 (*J* in Hz, MeOD)	δ_C (ppm)	COSY	HMBC
2	-	158.83	-	-
3	-	136.52	-	-
4	-	179.95	-	-
5	-	163.54	-	-
6	6.19 (1H, d, *J* = 4.0 Hz)	100.10	H-8	C-8, 9, 10
7	-	166.20	-	-
8	6.37 (1H, d, *J* = 4.0 Hz)	94.99	H-6	C-5, 6, 10
9	-	159.61	-	-
10	-	106.18	-	-
1′	-	123.44	-	-
2′	7.29 (1H, d, *J* = 4.0 Hz)	116.65	H-6′	C-2, 2′, 3′
3′	-	146.60	-	-
4′	-	150.12	-	-
5′	6.90 (1H, d, *J* = 8.0, 8.0 Hz)	117.20	H-6′	C-1′, 3′
6′	7.33 (1H, t, *J* = 4.0, 8.0 Hz)	123.14	H-5′, H-2′	C-2, 1′, 3′, 6′
1″	5.30(1H, brs)	103.84	H-2″	C-1″, 3, 4
2″	4.17 (1H, d, *J* = 4.0 Hz)	72.39	H-1″, 3″	C-1″, 3″
3″	3.71 (1H)	72.34	H-2″, 4″	C-2″, C-4″
4″	3.69 (1H)	73.53	H-3″	C-4″

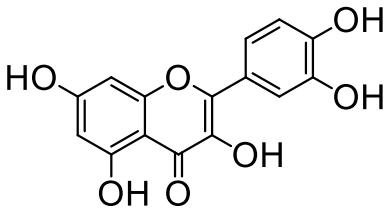
5″	3.37 (1H)	72.20	H-6″	C-6″
6″	0.90 (3H, brs)	17.96	H-5″	-

Table 2. Summary of 1D spectral data for compound DG5 (MeOD, 400 MHz).

Position	δ_H DG5 (*J* in Hz, MeOD)	δ_C DG5 (ppm)	DEPT
2	-	149.42	
3	-	137.88	
4	-	177.99	
5	-	163.16	
6	6.18 (1H, d, *J* = 2.04 Hz)	99.88	CH
7	-	166.26	
8	6.39 (1H, d, *J* = 2.04 Hz)	95.05	CH
9	-	158.88	
10	-	105.15	
1′	-	124.79	
2′	7.73 (1H, d, *J* = 2.08 Hz)	122.31	CH
3′	-	146.87	
4′	-	148.64	
5′	6.88 (1H, d, *J* = 8.52 Hz)	116.86	CH
6′	7.63 (1H, dd, *J* = 2.08, 8.48 Hz)	116.63	CH



DG_1 (quercetrin)



DG_5 (Quercetin)

Supplementary Materials: The following supporting information can be downloaded at: www.mdpi.com/xxx/s1, Figure S1: Proton (^{1}H) NMR Spectroscopy of Compound DG1 isolated from BF fraction of *Globimetula oreophila* leaf extracts; Figure S2: Proton (^{1}H) NMR Spectroscopy Expanded Aromatic Region (7.5–5.8 ppm) of Compound DG1 isolated from BF fraction of *Globimetula oreophila* leaf extracts; Figure S3: Proton (^{1}H) NMR Spectroscopy Expanded Sugar Region (5.6–0.4 ppm) of Compound DG1 isolated from BF fraction of *Globimetula oreophila* leaf extracts; Figure S4: Carbon 13 (^{13}C) NMR Spectroscopy of Compound DG1 isolated from BF fraction of *Globimetula oreophila* leaf extracts; Figure S5: Proton (^{1}H) NMR Spectroscopy of Compound DG5 isolated from BF fraction of *Globimetula oreophila* leaf extracts, Figure S6: Proton (^{1}H) NMR Spectroscopy Expanded of Compound DG5 isolated from BF fraction of *Globimetula oreophila* leaf extracts, Figure S7: Carbon 13 (^{13}C) NMR Spectroscopy of Compound DG5 isolated from HF fraction of *Globimetula oreophila* leaf extracts.

Author Contributions: Conceptualization, D.G., Y.M.S., M.G.M. and H.H.S.; methodology, D.G., Y.M.S., M.G.M. and H.H.S.; software, D.G., B.H.A. and B.B.; validation, D.G., A.S., M.G.M., Y.M.S. and H.H.S.; formal analysis, D.G., B.H.A., A.M.M., M.I.A., M.G.M. and Y.M.S.; investigation, D.G., Y.M.S., M.G.M., M.I.A. and H.H.S.; resources, D.G., A.S., B.B., M.G.M. and B.H.A.; writing—original draft preparation, D.G., Y.M.S., M.G.M. and H.H.S.; writing—review and editing, D.G., Y.M.S., M.G.M., H.H.S. and A.M.M.; supervision, Y.M.S., M.G.M. and H.H.S.; project administration, Y.M.S., M.G.M., H.H.S. and D.G. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare no conflicts of interest.

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