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ENANTIOMER OF MICRANTHOSIDE

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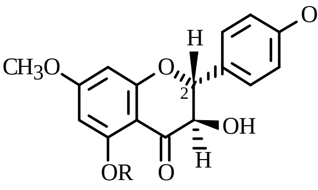
A dihydroflavonol glycoside called neomicranthoside was isolated from Eupatorium micranthum *introduced into Georgia. It was established using chemical and spectral data that it was an enantiomer of micranthoside, the structure of which has been previously established. Both glycosides are enantiomers of a* trans-*type dihydroflavonol glucoside with 2*R*,3*R*- and 2*S*,3*S*-configurations, respectively.*

Key words: *Eupatorium micranthum,* Asteraceae, dihydroflavonol glycoside, micranthoside, neomicranthoside, enantiomer.

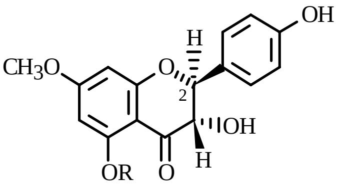
Eupatorium micranthum (syn. *E. ligustrinum* DC.) (Asteraceae) introduced from Mexico to Sukhumi and Batumi Botanical Gardens is a perennial evergreen bush 1.5-5 m in height [1].

We have previously reported the composition of the nonpolar and polar fractions of the aqueous alcohol extract from aerial parts of *E. micranthum* introduced into Sukhumi Botanical Garden [2-5]. The flavonoids included 7-methylaromadendrin, rhamnocitrin 5-*O*-*β*-D-glucopyranoside, and the new dihydroflavonol glycoside micranthoside (7-methylaromadendrin 5-*O*-*β*-D-glucopyranoside) (**1**) [2], detected later as a minor component only in leaves of a hybrid *Podocarpus nivalis* [6].



1

R = D-glucose



2

The content of **1** in leaves, stems, and flowers of introduced *E. micranthum* was 4.82, 4.69, and 5.20%, respectively.

The aqueous alcohol extract of *E. micranthum* leaves afforded a crystalline powder in 2% yield. The crystals were a conglomerate mixture of **1** (98%) and its stereoisomer (**2**), which we called neomicranthoside (2%). Conglomerates are known to be capable of self-induced decomposition. which was first described by us for dihydroflavonols. Because enantiomers have identical properties, in contrast with diasteromers, a pair of enantiomers cannot be separated directly by distillation, crystallization, or ordinary adsorption methods [7]. After selecting crystals from the conglomerate, we obtained **1** (mp 239°C) as white and **2** (mp 146-148°C, after melting, crystals that melt at 239-241°C formed) as golden yellow crystals.

The UV, IR, and NMR spectra of **1** and **2** were identical. The UV spectra (EtOH, λ_{max}, nm) gave peaks at 230 and 282 (log ε 4.47 and 4.27). The IR spectra had absorption bands characteristic of OH (3417 cm^{-1}), dihydro-*γ*-pyrone C=O (1666), an aromatic ring (1612, 1574, and 1520), a CH_3O (2931, 2885), and others. Assignments for peaks in NMR spectra recorded in DMSO-d_6 enabled the compound to be classified as a dihydroflavonol monoside. Compound **2** had signals for protons of D-glucose (6H, 4.52-5.03 ppm) and an anomeric proton (5.29, d, SSCC 4.3 Hz), consistent with a *β*-glycoside bond. The weak-field part of the spectrum exhibited signals (AA′BB′ system) for protons 2′,6′ and 3′,5′ with SSCC 8.1 Hz at 7.30 and 6.78 ppm, respectively, and 1H doublets with *m*-SSCC 1.7 Hz for H-8 and H-6 at 6.49 ppm and 6.24 ppm, respectively. Protons H-2 and H-3 resonated at 5.03 and 4.36 ppm and appeared as signals typical of an AB system. This was confirmed by double resonance. The SSCC of 11.1 Hz was consistent with the *trans*-conformation [7-10]. The lack of a signal at 11-14 ppm confirmed that the C-5 hydroxyl of D-glucose was substituted [10]. The methoxy signal appeared at 3.79 ppm.

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Compounds **1** and **2** differ from each other mainly in the color of the crystals and the sign of the rotation of the polarization plane at 589, 436, 405, and 365 nm. This led to a conclusion about their absolute configurations and identified **1** as the (+)(2*R*,3*R*) dihydroflavanol glycoside; **2**, (-)(2*S*,3*S*). It was taken into account that glycosylation of (+)(2*R*,3*R*) *trans*-dihydroflavonols at the C-5 OH changes the sign of the rotation to the opposite direction at 589 nm [6]. The obtained compounds are unique flavonoids, (+)(2*R*,3*R*) and (-)(2*S*,3*S*) enantiomers of a glycosylated *trans*-dihydroflavonol, namely 7-methylaromadendrin 5-*O*-*β*-D-glucopyranoside.

Natural dihydroflavonols with a positive optical rotation are usually *trans*-isomers with the 2*R*,3*R* configuration. The *cis*-isomers are mainly prepared synthetically. The number of their natural isomers is limited so that their detection always requires careful proof [11]. At present, in addition to the known folerogenin (7-methoxyaromadendrin) from leaves of *Glycyrrhiza glabra* L., the following natural *cis*-isomers have been isolated and identified: hovenitin II (2*R*,3*S*-5,7,4′,5′-tetrahydroxy-3′-methoxydihydroflavonol) and hovenitin III (2*R*,3*S*-3′,5,7,4′,5′-pentahydroxydihydroflavonol) from seeds and fruit of *Hovenia dulcis* Thunb. [12]; 2*R*,3*S*-3′,5-dihydroxy-4′,7-dimethoxydihdyroflavonol from stem bark of *Lannea coromandelica* L. [13]; isoastilbin (2*R*,3*R*-taxifolin 3-*α*-L-rhamnoside) and neoisoastilbin (2*R*,3*S*-taxifolin 3-*α*-L-rhamnoside) from leaves of *Engelhardtia chrysolepis* Hanse [14]; and 2*S*,3*R*-taxifolin 3-xylopyranoside and 2*R*,3*S*-taxifolin 3-xylopyranoside from leaves of *Thujopsis dolobrata* Zieb. et Zucc. [15]. The last two in addition to *cis*-isomers contain the *trans*-isomers with the 2*R*,3*R* and 2*S*,3*S* configurations [14, 15]. (2*S*,3*S*)-5,7,3′,4′-Tetrahydroxyflavon-3-*O*-*β*-D-glucopyranosyl-(1→3)-*α*-L-rhamnopyranoside was also isolated from *E. chrysolepis* [16]. (-)-Fustin (2*S*,3*S*-7-hydroxydihydroflavonol) from *Platymiscium praecox* Mart. [17], sophoronol from *Sophora tomentosa*, the flavonlignan silychristin from *Silybum marianum* (L.) Gaertn. [8], and (-)-taxifolin from *L. coromandelica* L. [13] also have this configuration.

EXPERIMENTAL

IR spectra were recorded on a Termo Nicolet Avatar 370 spectrometer in KBr; UV spectra, on a Spectromom 204 (Hungary) in EtOH; and NMR spectra, on a Bruker AC-300 spectrometer at resonance frequency 300.13 MHz for ^{1}H in DMSO-d_6 with TMS internal standard on the δ scale. Rotation angles were determined on a Digipol-781 digital polarimeter. Melting points were measured on a Kofler block.

Isolation of Dihydroflavonol Enantiomers. Air-dried ground leaves of *E. micranthum* (0.3 kg) at room temperature were extracted with ethanol (80%). The alcohol was evaporated from the aqueous alcohol extract. The aqueous liquid was purified with $CHCl_3$. A conglomerate (6.0 g) of two types of white and golden yellow crystals crystallized from the aqueous part. The crystals were separated to afford 5.78 and 0.12 g, respectively.

Micranthoside (1) formed white needle-like crystals, mp 239-241°C, UV spectrum (λ_{max}, nm) 230 and 282 (log ε 4.47 and 4.27). IR spectrum (ν, cm^{-1}): 3417 (OH), 1666 (dihydro-γ-pyrone), 1612, 1574, 1520 (aromatic ring), 2931, 2885 (CH_3O), etc. PMR spectrum (δ, ppm, J/Hz): 7.31 (2H, d, J = 8.5, H-2′,6′), 6.78 (2H, d, J = 8.5, H-3′,5′), 6.49 (1H, d, J = 2.1, H-8), 6.25 (1H, d, J = 2.1, H-6), 5.03 (1H, d, J = 11.1, H-2), 4.37 (1H, d, J = 11.1, H-3), 3.79 (3H, s, OCH_3), 5.33 (1H, d, J = 4.3, H′), 4.57-5.03 (m, sugar protons). Rotation angle: $[\alpha]_D^{23}$ -14.25°, $[\alpha]_{577}^{23}$ -4.98°, $[\alpha]_{546}^{23}$ -16.14°, $[\alpha]_{436}^{23}$ -50.51°, $[\alpha]_{405}^{23}$ +7.20° (*c* 0.04, EtOH:H_2O, 1:1).

Neomicranthoside (2) formed golden yellow needle-like crystals, mp 146-148°C, after melting of which crystals that melted at 239-241°C were formed, in agreement with the mp of **1**. UV spectrum (λ_{max}, nm) 230 and 282 (log ε 4.47 and 4.27). IR spectrum (ν, cm^{-1}): 3417 (OH), 1666 (dihydro-γ-pyrone), 1612, 1574, 1520 (aromatic ring), 2931, 2885 (CH_3O) etc. PMR spectrum (δ, ppm, J/Hz): 7.30 (2H, d, J = 8.1, H-2′,6′), 6.78 (2H, d, J = 8.1, H-3′,5′), 6.49 (1H, d, J = 1.7, H-8), 6.24 (1H, d, J = 1.7, H-6), 5.03 (1H, d, J = 11.1, H-2), 4.36 (1H, d, J = 11.1, H-3), 3.79 (3H, s, OCH_3), 5.29 (1H, d, J = 4.3, H′), 4.52-5.03 (m, sugar protons). Rotation angle: $[\alpha]_D^{23}$ +50.94°, $[\alpha]_{577}^{23}$ -71.62°, $[\alpha]_{546}^{23}$ -1.25°, $[\alpha]_{436}^{23}$ +6.02°, $[\alpha]_{405}^{23}$ -21.81° (*c* 0.04, EtOH:H_2O, 1:1).

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