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Carbazomarin: A New Potential of α-Glucosidase Inhibitor From *Clausena excavata* Roots

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Abstract

Continuing our exploration for dual functions antidiabetic and antioxidant agents from Myanmar medicinal plant, a new carbazole-pyranocoumarin conjugate, carbazomarin-C (**1**) along with a known carbazole alkaloid, mukonine (**2**) and a pyranocoumarin, xanthoxyletin (**3**), was isolated from the roots of *Clausena excavata*. The chemical structures of these compounds were identified using a combination of spectroscopic methods. Among isolates, there was a strong inhibition of compounds (**1**) and (**3**) on yeast α-glucosidase in a dose-dependent manner. It was shown when *p*-nitrophenyl-α-D-glucopyranoside was used as a substrate in vitro with IC_{50} values 0.22 and 4.81 mM, respectively. However, all isolated compounds displayed no inhibition against DPPH (2,2-diphenyl-1-picrylhydrazyl) radicals.

Keywords

Clausena excavata, coumarin, carbazole alkaloid, carbazomarin-C, α-glycosidase, DPPH

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Clausena excavata Burm. f. is commonly found in the tropical and subtropical regions such as India, China, and Southeast Asia countries. The plants are a member of *Rutaceae* family and they are in a form of wild shrubs. They are known to have medicinal properties since its leaves, twigs, and roots are widely used for the traditional treatment of cold, fever, wound, abdominal pain, snake-bite, a preliminary stage of AIDS, and skin diseases.[1] Previous phytochemical analyses found that *C. excavata* possesses an abundant amount of coumarins,[2-4] carbazole alkaloids,[5] and a few limonoids.[6] The coumarins isolated from this plant raised the writers' attention due to its bioactive properties. For instance, clauslactones A to J which were isolated from the leaves exhibited tumor promotion inhibitory effects. Nordentatin showed antibacterial and antioxidant properties, while pyranocoumarin and clausenidin which were isolated from roots displayed an anti-HIV-1 activity.[4,7]

Diabetes mellitus (DM) is one of the complex chronic illness which demands constant medical checkup. As a consequence, many strategies are already developed in order to reduce the multifactorial risk through glycemic control.[8] Elevated plasma glucose causes overproduction of free radicals and other reactive oxygen species that destroy cells through oxidative stress, which supports the goal of developing antidiabetic drugs with radical scavenging. Dual function agents which have both antidiabetic (α-glucosidase inhibitor) and radical scavenging capacities are particularly relevant for the treatment of T2DM (Type 2 Diabetes Mellitus) and its complications. In this study, we searched for an antidiabetic and antioxidant agent having a dual mechanism from a medicinal plant.[9] Here, we have been isolated 1 new carbazomarin-C (**1**) along with carbazole alkaloid, mukonine, and pyranocoumarin, xanthoxyletin. Cabarzomarin-C (**1**) was obtained as a solid with yellowish color with a melting point of 251°C to 252°C. The absorption maxima shown by the UV spectrum were at 335, 278, and 227 nm due to 7-oxygenated coumarin. The ^{1}H NMR (Nuclear Magnetic Resonance) spectrum (Table 1; Supplemental Figure S1) displayed the presence of 2,7-dihydroxy-1,3,6-tri-substituted carbazole skeleton by 1 aldehydic proton δ_H 9.75 (1H, s, 3-CHO) and 3 aromatic singlet protons at δ_H 7.88 (1H, s, H-4), 7.41 (1H, s, H-5), and 6.97 (1H,

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