

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 carbazolepyranocoumarin 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 IC₅₀ 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,

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 ¹H 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 $\delta_{\rm H}$ 9.75 (1H, s, 3-CHO) and 3 aromatic singlet protons at $\delta_{\rm H}$ 7.88 (1H, s, H-4), 7.41 (1H, s, H-5), and 6.97 (1H,

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Position	$\delta_{\rm H}$ multiplet/J values	δ _C (ppm)	HMBC
1a	-	145.3	
1	-	108.9	
2	-	156.7	
3	-	114.8	
4	7.88 (s, 1H)	123.7	C-1a, C-2, C-4a, -CHO
4a	-	116.8	
ōa	-	116.2	
5	7.41 (s, 1H)	117.2	C-6", C-7, C-8a
6	-	124.1	
7	-	153.8	
3	6.97 (s, 1H)	97.2	C-5a, C-6, C-7, C-8a
За	-	140.9	
l'	3.54 (d, J = 6.8 Hz, 2H)	21.6	C-1, C-1a, C-2, C-2', C-3'
2'	5.30 (d, J = 6.8 Hz, 1H)	121.2	
3'	-	132.0	
Ba'	1.68 (s, 3H)	23.6	C-2', C-3', C-3b'
зь'	1.83 (s, 3H)	16.8	C-2', C-3', C-3a'
3-CHO	9.75 (s, 1H)	195.8	
2"	-	162.6	
3"	6.00 (d, J = 9.6 Hz, 1H)	107.2	C-2", C-4a"
t	8.04 (d, J = 9.6 Hz, 1H)	140.8	C-2", C-5"
ła"	-	103.9	
5"	-	152.6	
5a"	-	109.8	
5"	4.76 (dd, <i>J</i> = 8.0, 10.0 Hz, 1H)	29.5	C-5, C-6, C-5a", C-7"
7"	2.05 (dd, <i>J</i> = 10.0, 13.6 Hz, 1H) 2.31 (dd, <i>J</i> = 8.0, 13.6 Hz, 1H)	40.8	C-5", C-8", C-8a", C-8b"
3"	-	76.4	
Ba"	1.34 (s, 3H)	22.3	C-7", C-8", C-8b"
3Ь"	1.41 (s, 3H)	27.4	C-7', C-8', C-8a"
)a"	-	159.5	
0"	-	114.8	
0a"	-	158.6	
	-	40.9	
a'''	1.72 (s, 3H)	28.9	C-1", C-1b", C-2", C-10"
Ъ'''	1.72 (s, 3H)	28.9	C-1", C-1a", C-2", C-10"
2'''	6.35 (dd, <i>J</i> = 10.7, 17.4 Hz, 1H)	150.8	C-1''', C-3'''
3a''' 3b'''	4.93 (dd, <i>J</i> = 1.2, 10.7 Hz, 1H) 4.85 (dd, <i>J</i> = 1.2, 17.4 Hz, 1H)	106.6	C-1", C-2"

Table 1. ¹H (600 MHz), ¹³C (151 MHz) NMR and HMBC Spectral Data of 1 in CDCl₂.

s, H-8). The 3-isomethyl prenyl group attached to the ring A of carbazole alkaloid was signified by 2 peaks at $\delta_{\rm H}$ 3.54 (2H, d, J = 6.8 Hz, H-1'), $\delta_{\rm H}$ 5.30 (1H, d, J = 6.8 Hz, H-2') and 2 isomethyl groups signals at $\delta_{\rm H}$ 1.68 (3H, s, H-3a'), $\delta_{\rm H}$ 1.83 (3H, s, H-3b'), respectively. Moreover, the existence of pyranocoumarin unit was revealed by 2 pairs of doublet protons at $\delta_{\rm H}$ 6.00 (1H, d, J = 9.6 Hz, H-3") and $\delta_{\rm H}$ 8.04 (1H, d, J = 9.6 Hz, H-4"), pyran ring at $\delta_{\rm H}$ 4.76 (1H, dd, J = 8.0, 10.0 Hz, H-6"), 2 anisotropic protons at $\delta_{\rm H}$ 2.05 (1H, dd, J = 10.0, 13.6 Hz, H-7"), $\delta_{\rm H}$ 2.31 (1H, dd, J = 8.0, 13.6 Hz, H-7"), and gemdimethyl at $\delta_{\rm H}$ 1.34 (3H,s, H-8a"),

 $δ_{\rm H}$ 1.41 (3H,s, H-8b"). In addition, the characteristic of prenyl group attached to C-10 position of core coumarin has shown signals at $δ_{\rm H}$ 6.35 (1H, dd, J = 17.4, 10.7 Hz, H-2"), 4.93 (1H, dd, J = 10.5, 1.2 Hz, H-3a"), 4.85 (1H, dd, J = 17.4, 1.2 Hz, H-3b"'), and 2 methyl groups at $δ_{\rm H}$ 1.72 (6H, s, H-1a" and -1b"'). The ¹³C-NMR (Nuclear Magnetic resonance) and DEPT (Distortionless Enhancement by Polarization Transfer) (90, 135) spectra of **1** indicated the presence of 1 aldehyde carbon $δ_c$ 195.8, 1 cyclic lactone carbonyl carbon $δ_c$ 162.6, 16 sp² quaternary carbons ($δ_c$

159.5, 158.6, 156.7, 153.8, 152.6, 145.3, 140.9, 132.0, 124.1, 116.8, 116.2, 2×114.8 , 109.8, 108.9, 103.9), 2 sp³ quaternary carbons (δ_c 76.4, 40.9), 7 sp² methine carbons (δ_c 150.8, 140.8, 123.7, 121.2, 117.2, 97.2), sp³ methine (δ_c 29.5), 1 exomethylene carbon (δ_c 106.6), 2 methylene carbons (δ_c 40.8, 21.6), and 6 methyl carbons (δ_c 2 × 28.9, 27.4, 23.6, 21.6, 16.8) (Table 1; Supplemental Figure S2). The data presented above, also DQF-COSY (Double Quantum Filtered- ¹H-¹H correlated spectroscopy), and HSQC (Heteronuclear Single Quantum Correlation) data indicate that 1 is the binary of carbazole-pyranocoumarin conjugate (Supplemental Figures S3 and S4). There are several correlations pointed out by the ¹H-¹³C long range coupling of HMBC (Heteronuclear Multiple Bond Correlation) spectrum of 1, which are between H-4/C-1a, C-2, C-4a, and -CHO. The location of H-4 proton and the group of aldehyde were confirmed to be attached to C-3 carbon of ring-A in carbazole unit. Another correlation was that a group of prenyl was attached to C-1 position of carbazole and it was revealed by H-1' to C-1, C-1a, C-2, C-2', and C-3'. Its pattern is also similar to heptaphylline. Moreover, the singlet proton, H-5 on ring-C of carbazole, gave correlation to C-6", C-7, C-8a, and again, H-6" of pyranocoumarin to C-5, C-6, C-5a", C-7" proved that 2 units are connected at C-6 of carbazole and C-6" of pyranocoumarin. The existence of typical pyranocoumarin lactone carbon was showing correlation H-2", H-3" to C-2", C-4a", and C-5". The attachment of prenyl group to C-10" of pyranocoumarin was confirmed by the cross peaks of H-1a" to C-1", C-1b", C-2", and C-10" by HMBC spectrum (Table 1; Figure 1 and Supplemental Figure S5). The spectrum of NOESY owned by 1 showed the cross-peaks of H-4 with H-5, 3-CHO, and another cross-peaks displayed H-5 to H-7", H-4 (Figure 1 and Supplemental Figure S6). This type of binary compounds previously has been reported from C. *excavata* as carbazomarin- A^{10} and carbazomarin-B.¹¹ The spectral data of **1** in pyranocoumarin unit are the same as the previously reported compounds. However, the carbazole unit is different from **1**. The spectral data of **1** revealed that the carbazole unit is similar to 7-hydroxyheptaphylline. In addition, the previously reported binary compounds explained that the coumarin unit was substituted at ring A of carbazole, whereas **1** was substituted at ring C. Hence, the structure of **1** was assigned to be (*S*)-2,7-dihydroxy-6-(5-hydroxy-8,8-dimethyl-10-(2-methylbut-3-en-2-y1) - 2 - 0 x 0 - 7, 8 - d i h y d r 0 - 2 H, 6 H - p y r a n 0 [3, 2 - g] chromen-6-yl)-1-(3-methylbut-2-en-1-yl)-9H-carbazole-3-carbaldehyde (Figure 2). It was named as carbazomarin-C.

Careful analyses were carried out to determine the physicochemical properties and spectroscopic data. Later on, a comparison step was carried out with the previously reported literatures where 2 known compounds were identified as mukonine^{2,6} and xanthoxyletin^{3,12} as shown in Figure 2. All of the isolated compounds were then undergone examination to measure antidiabetic activity. The examination was done by using yeast α-glucosidase inhibitory assay. Meanwhile, in order to measure the antioxidant activity, DPPH assay (Table 2) was carried out. There was a potent inhibition demonstrated by the isolated compounds 1 and 3 against yeast α -glucosidase with IC₅₀ values 0.22 and 4.81 mM. Both 1 and 3 have stronger inhibition activity than standard acarbose (IC50 value 4.89 mM). Especially the new compound, carbazomarin-C (1), which has inhibitory effect exhibited the highest values. Unfortunately, there were no inhibition on antioxidant activity presented by all of the isolated compounds. Referring to the newest studies, the isolated components from the root of C. excavata possess the potentials to act as natural *a*-glucosidase inhibitors. More

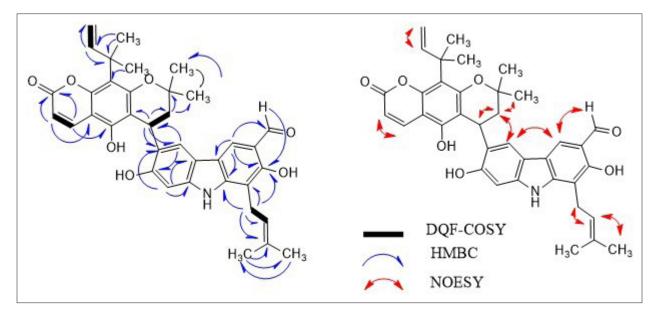


Figure 1. COSY (black bold), key HMBC (blue), and NOESY (red) correlation of 1.

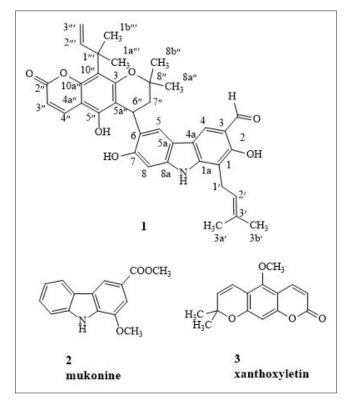


Figure 2. The structure of *Clausena excavata's* isolated compounds.

researches on maltase and sucrase α -glucosidase inhibition activity are strongly recommended.

Experimental

Plant Material

The collection of *C. excavata* was done in Myanmar, precisely on Pyin Ma Nar Township. The plants' substantial (voucher specimen MU-22032018) were collected on October 2016 under the authentication of Prof. Soe Myint Aye. Prof. Aye works as a botanist in the Botany Department of Mandalay University in Myanmar.⁴

Extraction and Isolation

The roots sample of *C. excavata* (3.6 kg) was air-dried before finally being extracted with 95% EtOH (12.0 L) for 14 days under ambient temperature. After removing the solvent, 156 g of extract was obtained. Afterward, as much as 100 g of the extract was partitioned by liquid-liquid extraction. It was successfully done 3 times by using the solvent of *n-hexane* and MeOH with the ratio of 1:1 in volumes. Furthermore, a vacuum liquid chromatography (VLC) was exposed to as much as 80.4 g of methanol portion over silica gel which was eluted with different mixtures of *n*-hexane and ethylacetate. It was done by slowly intensifying the gradient polarity until 7 combined fractions (MF-1 to -7) were acquired. Fraction MF-3.2 was exposed to silica gel column

Table 2.	α-Glucosidase	Inhibitory	and the	Isolated	Compounds'
(1-3) Rad	ical Scavenging	Activities.			

()		
Compound	α-Glucosidase, yeast IC ₅₀ (mM)	DPPH IC ₅₀ (mM)
1	0.22	NI
2	NI	NI
3	4.81	NI
Acarbose	4.89	-
Ascorbic acid	-	0.01

NI, no inhibition.

chromatography. There were 3 different solvent systems precisely the mixture between *n*-hexane, CHCl₃, and EtOAc with the ratio 100:5:20. As a result, there were 300 fractions gained and produced 6.8 mg of compound (**2**) and 15.3 mg of compound (**3**). A total of 25.6 g of fraction MF-6 was exposed to VLC with the mixtures *n-hexane*:EtOAc (EtOAc, 10%-100%) with gradient polarity. The outcome produced 23 subfractions, and after combining the same component fractions, it created MF-6.1 to -6.7. Silica gel column chromatography was exposed to Fraction MF-6.2.1.3 with various solvents (CHCl₃:MeOH/MeOH 5%) which produced a total of 99 fractions. After the recrystallization of fraction 82 to 88, a new compound (**1**, 10.6 mg) was obtained.

Carbazomarin-C, yellowish solid, mp. 251°C-252°C; UV (MeOH), λ_{max} (log ε) 335 (1.23), 279 (2.08), 228 (1.53). ¹H NMR (Methanol- d_4 , 600 MHz), δ 9.75 (1H, s), 8.04 (1H, d, J = 9.6 Hz), 7.88 (1H, s), 7.41 (1H, s), 6.97 (1H, s), 6.35 (1H, dd, J = 17.4, 10.6 Hz), 6.00 (1H, d, J = 9.6 Hz), 5.41-5.24 (2H, m), 4.93 (2H, dd, J = 17.4, 1.2 Hz), 4.85 (2H, dd, J = 10.6, 1.2 Hz), 4.78-4.73 (3H, m), 3.54 (3H, d, J = 6.8 Hz), 3.35 (1H, s), 2.31 (2H, dd, J = 13.8, 7.8 Hz), 2.04 (3H, dd, J = 13.8, 10.1 Hz), 1.90 (0H, s), 1.83 (4H, s), 1.72 (6H, s), 1.68 (3H, s), 1.68 (3H, s), 1.41 (3H, s), 1.34 (3H, s) and ¹³C NMR (151 MHz, Methanol- d_4) δ 195.78, 162.58, 159.54, 158.62, 156.75, 153.87, 150.76, 145.26, 144.77, 140.83, 132.02, 124.08, 123.68, 121.22, 117.73, 116.80, 114.78, 110.12, 109.76, 108.93, 107.65, 106.63, 103.99, 97.20, 76.47, 42.78, 41.66, 40.88, 40.52, 29.41, 28.91, 28.15, 24.49, 24.49, 23.75, 23.03, 22.33, 16.66.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Supplemental Material

Supplemental material for this article is available online.

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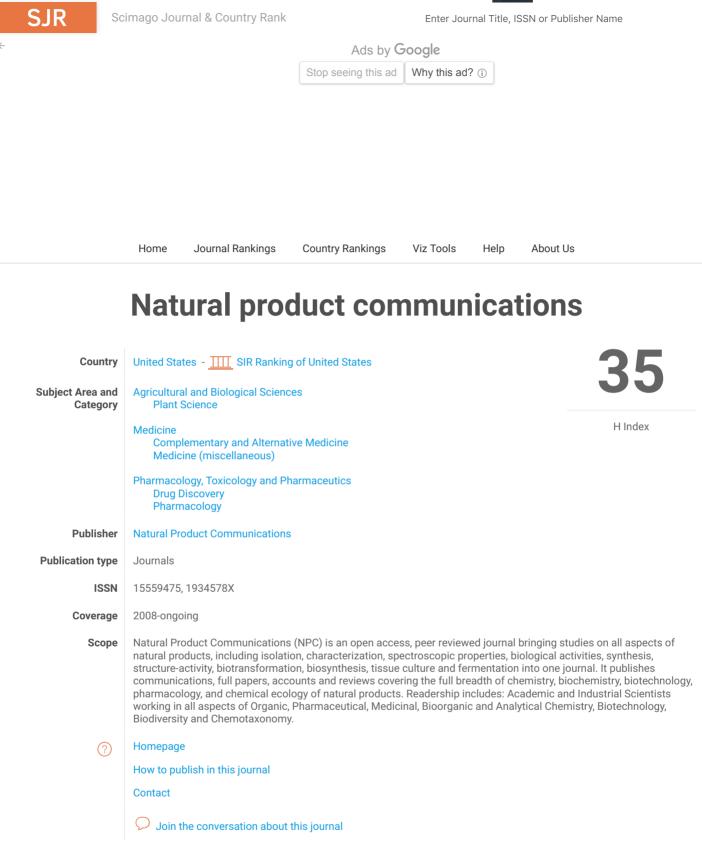
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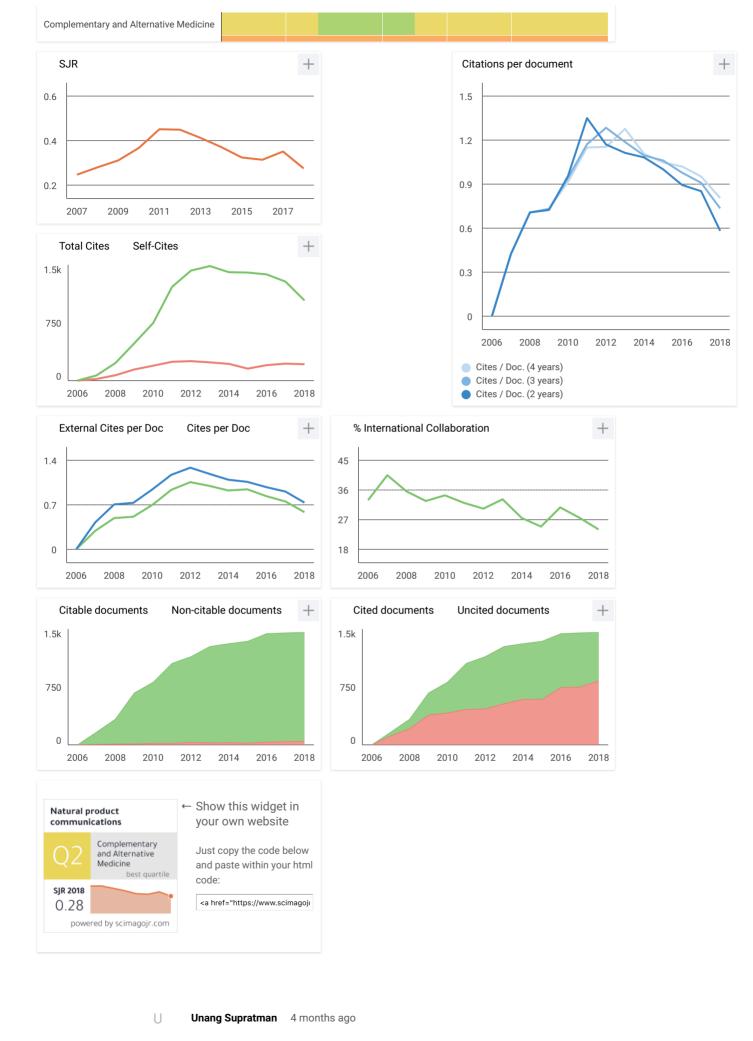
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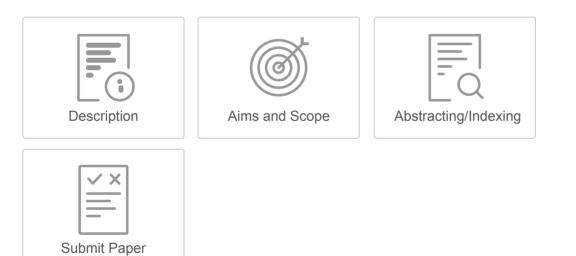
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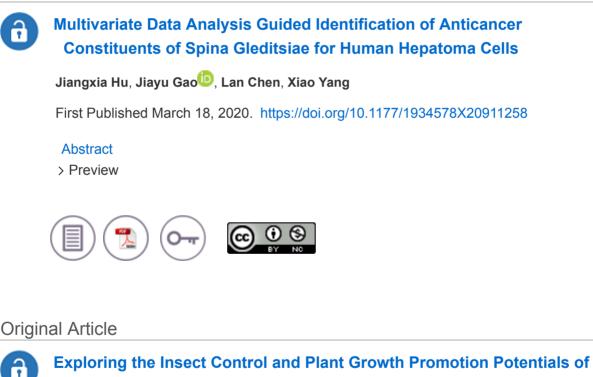


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Abstract

> Preview



Terpenoids and Related Compounds – Structure, Synthesis, and Biological Activity

Original Article

1

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

Nanik S. Aminah^(D), Tin M. Thant, Alfinda N. Kristanti, Rico Ramadhan, Hnin T. Aung, Yoshiaki Takaya

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A

Advances in Pharmacological Activities of Terpenoids

Wenqiang Yang, Xu Chen, Yanli Li, Shaofen Guo, Zhen Wang, Xiuling Yu ២

First Published March 16, 2020. https://doi.org/10.1177/1934578X20903555

Abstract

> Preview



Original Article

A Pair of Novel Sulfonyl-Containing *N*-Acetyldopamine Dimeric Enantiomers From *Aspongopus chinensis*

Li Liao, Yong-Ming Yan⁽¹⁰⁾, Te Xu, Hou-Lin Xia, Yong-Xian Cheng

First Published March 16, 2020. https://doi.org/10.1177/1934578X20911270

Abstract

> Preview



Flavonoids and Related Compounds as Natural Products Original Article



Epigallocatechin-3-Gallate Protects Neuro-2a Cells From Sodium Fluoride-Induced Oxidative Damage In Vitro

Na Li, Dongdong Xin, Hongbo Li^D, Yanyan Zhao, Wei Zhou, Hao Zhang, Liangbin Hu, Yaming Ge, Haizhen Mo

First Published March 16, 2020. https://doi.org/10.1177/1934578X20911476

Abstract

> Preview



Short Communication



Size-Tunable Paclitaxel Nanoparticles Stabilized by Anionic Phospholipids for Transdermal Delivery Applications

Noriyuki Uchida^(D), Masayoshi Yanagi, Hiroki Hamada^(D)

First Published March 12, 2020. https://doi.org/10.1177/1934578X19900684

Abstract

> Preview



Original Article

Schisantherin A Improves the Learning and Memory by Reducing the Phosphorylation of Tau Protein of the Hippocampus in AD Mice

Shu Jing, Cong Liu, Huijiao Lin, Xinyun Zhang, Fei Wang, Jiaqi Gao, Jinghui Sun, Jianguang Chen, Chunmei Wang, He Li

First Published March 12, 2020. https://doi.org/10.1177/1934578X19900687

Abstract

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Original Article



A New Chlorinated Phenolic Compound From the Antarctic Lichen, Pertusaria dactylina

Man H. Koo, Min J. Kim, Jae E. Seo, Ji H. Kim, Se J. Han, II C. Kim, Jun H. Lee, Ui J. Youn Ð

First Published March 12, 2020. https://doi.org/10.1177/1934578X20902886

Abstract

> Preview



Terpenoids and Related Compounds – Structure, Synthesis, and Biological Activity

Review



Original Article

1

Protective Effect of Curcumin on Acrylamide-Induced Hepatic and Renal Impairment in Rats: Involvement of CYP2E1

Rui Sun, Wenhui Chen, Xiaolu Cao, Jie Guo, Jun Wang

First Published March 12, 2020. https://doi.org/10.1177/1934578X20910548

Abstract

> Preview



Original Article



Separation and Purification of Zizyphusine, Spinosin, and 6"-Feruloylspinosin From Zizyphi Spinosi Semen

Jiong Ran Wang^(b), Yan Zhou Hu, Xiao Han, Ke Ding^(b)

First Published March 12, 2020. https://doi.org/10.1177/1934578X20910556

Abstract

> Preview



Original Article



Exploring Chemical Structures From Cortex Lycii, Based on Manual and Automatic Analysis of the HPLC-Q-TOF-MS Data

Zhi-Bo Jiang¹⁰, Yong-Xin Chen, Jing-Zhi Chen, Xing Lu, Xin Guo, Bing-Zhen Ma, Chong-Long Li, Xuan Fang, Yong-Hong Tang, Xiao-Li Ma

First Published March 12, 2020. https://doi.org/10.1177/1934578X20911255

Abstract

> Preview



Original Article

Prenylated Flavonoids as Antioxidant and Melanin Inhibitors From Stingless Bee (*Wallacetrigona incisa*) Propolis

Enos Tangke Arung¹⁰, Syafrizal , Whicliffe Fiernaleonardo Pasedan, Nataniel Tandirogang, Sukemi , Ahmed E. Allam, Yhiya Amen¹⁰, Kuniyoshi Shimizu, Hiroya Ishikawa

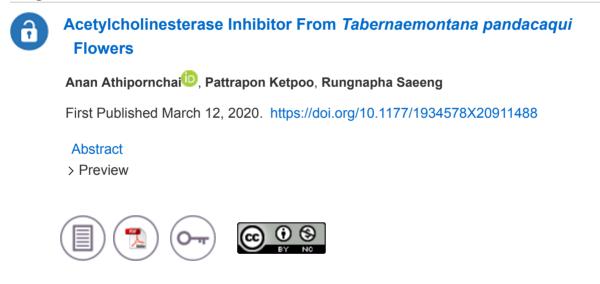
First Published March 12, 2020. https://doi.org/10.1177/1934578X20911272



> Preview



Flavonoids and Related Compounds as Natural Products Original Article



Special Collection in honor of Professor Dr. Gerald Blunden's 80th Birthday Original Article 1

Stereoselective Reduction of Bisdemethoxycurcumin to (*R*)-Hexahydrobisdemethoxycurcumin by Cultured *Morus bombycis* Plant Cells

Kei Shimoda, Naoji Kubota, Hiroki Hamada^(D), Kouki Kawakami, Noriyuki Nakayama, Hatsuyuki Hamada

First Published March 5, 2020. https://doi.org/10.1177/1934578X20902555

Abstract

> Preview



Original Article



One New Terphenyl Glycoside From a Sponge-Derived Fungus *Trichoderma reesei* (HN-2016-018)

Saif Ur Rehman, Jing-Shuai Wu, Lu-Jia Yang, Shi Ting, Chang-Lun Shao, Chang-Yun Wang

First Published March 5, 2020. https://doi.org/10.1177/1934578X20907753

Abstract > Preview



Original Article

Transformation of Mangiferin to Norathyriol by Human Fecal Matrix in Anaerobic Conditions: Comprehensive NMR of the Xanthone Metabolites, Antioxidant Capacity, and Comparative Cytotoxicity Against Cancer Cell Lines

José R. R. Souza, Maria Teresa Salles Trevisan, Judith P. A. Feitosa, Nágila M. P. S. Ricardo, William E. Hull, Gerhard Erben, Gerd Würtele, Andrea Breuer, Eva Frei, Cornelia M. Ulrich, Robert W. Owen

First Published March 5, 2020. https://doi.org/10.1177/1934578X20910286

Abstract

> Preview



Original Article



Bibenzyl Derivatives From Leaves of Dendrobium officinale

Gang Ren⁽¹⁰⁾, Wen-Zan Deng, Yan-Fei Xie, Chun-Hua Wu, Wen-Yan Li, Chuan-Yun Xiao, Yun-Long Chen

First Published February 28, 2020. https://doi.org/10.1177/1934578X20908678

Abstract

> Preview



Review



Na Zhao¹⁰, Xiaoming Su, Yueyang Wang, Jianguang Chen, Wenyue Zhuang

First Published February 27, 2020. https://doi.org/10.1177/1934578X20905148

Abstract

> Preview







Natural Product Communications Manuscript ID - NPX-19-0232

1 message

Natural Product Communications <onbehalfof@manuscriptcentral.com>

Tue, Sep 3, 2019 at 11:10 AM

Reply-To: npx@sagepub.com To: tin.myo.thant-2017@fst.unair.ac.id, nanik-s-a@fst.unair.ac.id, alfinda-n-k@fsaintek.unair.ac.id, rico.ramadhan@fst.unair.ac.id, hninthandaaung07@gmail.com, ytakaya@meijo-u.ac.jp

03-Sep-2019

Dear Dr. Aminah:

Your manuscript entitled "Carbazomarin: A potent new α -glucosidase inhibitor from Clausena excavata roots" has been successfully submitted online and is presently being given full consideration for publication in Natural Product Communications.

Your manuscript ID is NPX-19-0232.

Please mention the above manuscript ID in all future correspondence or when calling the office for questions. If there are any changes in your street address or e-mail address, please log in to ScholarOne Manuscripts at https://mc.manuscriptcentral.com/npx and edit your user information as appropriate.

You can also view the status of your manuscript at any time by checking your Author Center after logging in to https://mc.manuscriptcentral.com/npx.

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Thank you for submitting your manuscript to Natural Product Communications.

Sincerely, Shivani Barthwal Natural Product Communications npx@sagepub.com



Natural Product Communications NPX-19-0232.R1

1 message

Natural Product Communications <onbehalfof@manuscriptcentral.com> Reply-To: npx@sagepub.com Thu, Oct 17, 2019 at 1:27 AM

To: nanik-s-a@fst.unair.ac.id, tin.myo.thant-2017@fst.unair.ac.id, alfinda-n-k@fsaintek.unair.ac.id, rico.ramadhan@fst.unair.ac.id, hninthandaaung07@gmail.com, ytakaya@meijo-u.ac.jp

16-Oct-2019

Dear Dr. Aminah:

Your revised manuscript entitled "Carbazomarin: A new Potential of α -glucosidase inhibitor from Clausena excavata roots" has been successfully submitted online and is presently being given full consideration for publication in Natural Product Communications.

Your manuscript ID is NPX-19-0232.R1.

You have listed the following individuals as authors of this manuscript: Aminah, Nanik; Thant, Tin; Kristanti, Alfinda; Ramadhan, Rico; Aung, Hnin; Takaya, Yoshiaki

Please mention the above manuscript ID in all future correspondence or when calling the office for questions. If there are any changes in your street address or e-mail address, please log in to ScholarOne Manuscripts at https://mc.manuscriptcentral.com/npx and edit your user information as appropriate.

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Thank you for submitting your manuscript to Natural Product Communications.

Sincerely, Shivani Barthwal Natural Product Communications npx@sagepub.com



Natural Product Communications: Final files required for production

12 messages

Natural Product Communications <onbehalfof@manuscriptcentral.com> Reply-To: Shivani.Barthwal@sagepub.in To: nanik-s-a@fst.unair.ac.id Thu, Nov 7, 2019 at 1:04 PM

07-Nov-2019

NPX-19-0232.R1 - Carbazomarin: A new Potential of α -glucosidase inhibitor from Clausena excavata roots

Dear Dr. Aminah:

Hope you are doing well.

I am glad to let you know that the final files are required to be sent for production.

Please provide the below required files for production.

(1) Accepted clean accepted manuscript in MS Word document format.

(2) Please provide separate figure files in (JPG/JPEG/PNG) formats) and tables in excel or word format.

(3) Please provide supplementary file in MS Word document format with all the supplementary figures and tables cited in the main document.

Look forward to receiving the final files for production.

Sincerely, Ms. Shivani Barthwal Natural Product Communications

nanik siti aminah <nanik-s-a@fst.unair.ac.id> To: Shivani.Barthwal@sagepub.in

Dear Ms. Shivani Barthwal Natural Product Communications

I am happy to receive your email.

Attach files, I send your request :

(1) Manuscript in MS Word document format.

(2) figure files in (JPG/JPEG/PNG) formats) and tables in excel or word format.

(3) Supplementary file in MS Word document format with all the supplementary figures and tables cited in the main document.

I hope you receive well all files, If you have any other requests please don't hesitate to contact me.

With best regard,

[Quoted text hidden]

Dr. Nanik Siti Aminah

Assoc. Professor on Natural Product Chemistry Dept. of Chemistry Fac. of Science and Technology Universitas Airlangga

https://mail.google.com/mail/u/0?ik=c623abfa38&view=pt&search=all&permthid=thread-f%3A1649521890420185688&simpl=msg-f%3A1649521890420185... 1/5

Thu, Nov 7, 2019 at 9:32 PM

Vice Dean on Research and Partnership Faculty of Science and Technology Universitas Airlangga Komplek Kampu C UNAIR JI. Ir. Soekarno Surabaya-East Java Indonesia email address : nanik-s-a@fst.unair.ac.id

4 attachments

Draft_NPC_NANIK_main-2019-FOR PUBLISH.docx
 Draft_NPC_NANIK_figure_2019_FOR PUBLISH.docx
 Draft_NPC_NANIK_table_2019_FOR PUBLISH.docx
 Draft_NPC_NANIK_Suppli_2019_FOR PUBLISH.docx
 10338K

Shivani Barthwal <Shivani.Barthwal@sagepub.in> To: nanik siti aminah <nanik-s-a@fst.unair.ac.id> Thu, Nov 14, 2019 at 6:09 PM

Dear Dr. Aminah,

Thank you for your email.

While checking the manuscript, the below points were observed.

(1) All the supplementary figures are not cited in the manuscript.

(2) Please provide separate figures as figure 2 was not present in the document. The format should be JPG/JPEG/PNG only.

Look forward to your earliest reply.

Regards

Shivani

From: nanik siti aminah <nanik-s-a@fst.unair.ac.id>
Sent: Thursday, November 7, 2019 8:03 PM
To: Shivani Barthwal <Shivani.Barthwal@sagepub.in>
Subject: Re: Natural Product Communications: Final files required for production

[EXTERNAL]

[Quoted text hidden]

Shivani Barthwal <Shivani.Barthwal@sagepub.in> To: nanik siti aminah <nanik-s-a@fst.unair.ac.id> Thu, Nov 14, 2019 at 6:12 PM

Dear Dr. Aminah,

Please ensure that the supplementary figures should also be in JPG/JPEG/PNG format.

Regards

Shivani

[Quoted text hidden]

nanik siti aminah <nanik-s-a@fst.unair.ac.id> Thu, Nov 14, 2019 at 6:21 PM To: Tin Myo Thant <kotinkoko.kse@gmail.com>, tin myo <tin.myo.thant-2017@fst.unair.ac.id>

------ Forwarded message ------From: **Shivani Barthwal** <<u>Shivani.Barthwal@sagepub.in</u>> Date: Thu, 14 Nov 2019, 18:09 Subject: RE: Natural Product Communications: Final files required for production To: nanik siti aminah <<u>nanik-s-a@fst.unair.ac.id</u>>

[Quoted text hidden]

nanik siti aminah <nanik-s-a@fst.unair.ac.id> Thu, Nov 14 To: tin myo <tin.myo.thant-2017@fst.unair.ac.id>, Tin Myo Thant <kotinkoko.kse@gmail.com>

Thu, Nov 14, 2019 at 8:30 PM

------ Forwarded message ------From: **nanik siti aminah** <nanik-s-a@fst.unair.ac.id> Date: Thu, Nov 7, 2019 at 9:32 PM Subject: Re: Natural Product Communications: Final files required for production To: <Shivani.Barthwal@sagepub.in> [Quoted text hidden] [Quoted text hidden]

Draft_NPC_NANIK_Suppli_2019_FOR PUBLISH.docx 10338K

tin myo <tin.myo.thant-2017@fst.unair.ac.id> To: nanik siti aminah <nanik-s-a@fst.unair.ac.id> Fri, Nov 15, 2019 at 7:39 AM

Selamat pagi ibu, I revised the manuscript as they requested and attached to you. Corrected words were high light
with yellow color and figure was changed to JGPEG format. If you have any problems please let me know.
Best regards,
Tin
[Quoted text hidden]

4 attachments



Shivani Barthwal <Shivani.Barthwal@sagepub.in> To: nanik siti aminah <nanik-s-a@fst.unair.ac.id> Tue, Nov 19, 2019 at 12:18 PM

Dear Dr. Aminah,

Hope you are doing well.

This is a gentle reminder to provide the below required files for production.

Regards

Shivani

From: Shivani Barthwal
Sent: Thursday, November 14, 2019 4:43 PM
To: 'nanik siti aminah' <nanik-s-a@fst.unair.ac.id>
Subject: RE: Natural Product Communications: Final files required for production

Dear Dr. Aminah,

Please ensure that the supplementary figures should also be in JPG/JPEG/PNG format.

Regards

Shivani

From: Shivani Barthwal Sent: Thursday, November 14, 2019 4:40 PM To: nanik siti aminah <nanik-s-a@fst.unair.ac.id>

[Quoted text hidden]

[Quoted text hidden]

nanik siti aminah <nanik-s-a@fst.unair.ac.id>Wed, Nov 20, 2019 at 3:06 PMTo: Shivani Barthwal <Shivani.Barthwal@sagepub.in>, tin myo <tin.myo.thant-2017@fst.unair.ac.id>

Dear Dr. Shivani Barthwal

Attach files, I send the data of :

(1) All the supplementary figures are cited in the manuscript (please see the yellow color in the manuscript).

(2) All of the figures in the format of JPG.

Thank you for your kind help and cooperation.

With best regard,

[Quoted text hidden]

5 attachments	
Draft _NPC_NANIK_main-2019 133K	-FOR PUBLISH-rev.doc
Draft_NPC_NANIK_table_2019 23K	9_FOR PUBLISH-rev.doc
FIGURE 1-2.jpg.zip 65K 65K 65K	
figures_S1-6 fornpc.zip 289K	
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Shivani Barthwal <Shivani.Barthwal@sagepub.in> Thu, Nov 21, 2019 at 12:47 PM To: nanik siti aminah <nanik-s-a@fst.unair.ac.id>, tin myo <tin.myo.thant-2017@fst.unair.ac.id>

Dear Dr. Aminah,

Thank you for your email.

I have uploaded all the files on your behalf and the manuscript has been sent to production.

[Quoted text hidden]

nanik siti aminah <nanik-s-a@fst.unair.ac.id> To: Shivani Barthwal <Shivani.Barthwal@sagepub.in>

Dear Dr. Shivani Barthwal

Thank you for your nice information [Quoted text hidden]

Shivani Barthwal <Shivani.Barthwal@sagepub.in> To: nanik siti aminah <nanik-s-a@fst.unair.ac.id>

Dear Dr. Aminah,

Thank you for your email and wish you all the best.

[Quoted text hidden]

Thu, Nov 21, 2019 at 1:45 PM

Thu, Nov 21, 2019 at 1:47 PM



Natural Product Communications - Next steps for your article

2 messages

Natural Product Communications <onbehalfof@manuscriptcentral.com> Reply-To: natalie.gerson@sagepub.com Thu, Nov 21, 2019 at 12:54 PM

To: nanik-s-a@fst.unair.ac.id, tin.myo.thant-2017@fst.unair.ac.id, alfinda-n-k@fsaintek.unair.ac.id, rico.ramadhan@fst.unair.ac.id, hninthandaaung07@gmail.com, ytakaya@meijo-u.ac.jp

21-Nov-2019

Dear Dr. Aminah:

Congratulations on the acceptance of your manuscript, NPX-19-0232.R1, entitled "Carbazomarin: A new Potential of α -glucosidase inhibitor from Clausena excavata roots" to Natural Product Communications. This email is to let you know what you can expect next.

In 6-10 days, you will receive an email from our Production system with the proofs of your article for you to review. The email will come from this email address: SageEdit.journalproofs@exeterpremedia.com.

Please make sure that you whitelist this email address, as it does sometimes go to spam. If you do not receive this email within 10 days, please check your spam folder before contacting the Editorial office.

If you do not receive this email after 10 days, and it is not in your spam folder, you may email me at that time.

Sincerely, Natalie Gerson, Publishing Editor Natural Product Communications Natalie.gerson@sagepub.com

nanik siti aminah <nanik-s-a@fst.unair.ac.id> To: natalie.gerson@sagepub.com Thu, Nov 21, 2019 at 1:50 PM

Dear Natalie Gerson, Publishing Editor Natural Product Communications

Thank you for your kind information. We will be patient to wait the email from SageEdit.journalproofs@exeterpremedia.com.

Best regard, [Quoted text hidden]

Dr. Nanik Siti Aminah

Assoc. Professor on Natural Product Chemistry Dept. of Chemistry Fac. of Science and Technology Universitas Airlangga

Vice Dean on Research and Partnership Faculty of Science and Technology Universitas Airlangga Komplek Kampu C UNAIR JI. Ir. Soekarno Surabaya-East Java Indonesia email address : nanik-s-a@fst.unair.ac.id