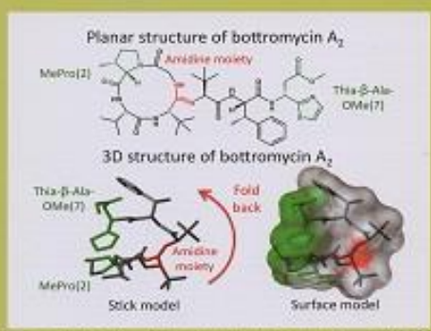
Chemical and Pharmaceutical Bulletin

February 2012

Vol. 60 No. 2

CPBTAL 60 (2) 169–284 (2012)



The Pharmaceutical Society of Japan

http://cpb.pharm.or.jp

Editorial Board

The ***Chemical and Pharmaceutical Bulletin***(Chem. Pharm. Bull.) publishes Reviews, Current Topics, Communications, Regular Articles, and Notes monthly in print and online. Chem. Pharm. Bull. is devoted to the publication of original reports on cutting-edge research including creative approaches and novel ideas for sharing the urgent and valuable results with all readers of this journal. Chem. Pharm. Bull. covers various topics of current interest in all of chemistry and interfacing areas of pharmaceutical sciences. The main targeted subjects of Chem. Pharm. Bull. are as follows: Organic Chemistry, Medicinal Chemistry, Chemical Biology, In Silico Science, Analytical Chemistry, Physical Chemistry, Inorganic Chemistry, Physical Pharmacy, Pharmaceutical Engineering, Pharmacognosy, and Natural Product Chemistry.

Pharmaceutical University

Yoshihito Nakatani
Editor
Faculty of Pharmaceutical Sciences, Teikyo Heisei University

Makiya Nishikawa
Editor
Faculty of Pharmaceutical Sciences, Tokyo University of Science

Yukihiro Ohno
Editor
Osaka Medical and Pharmaceutical University

Yoshiro Saito
Editor
National Institute of Health Sciences

Kumiko Sakai-Kato
Editor
School of Pharmacy, Kitasato University

Shigeki Shimba
Editor
Scoolo of Pharmacy, Nihon University

Michiru D. Sugawa
Editor
Charit? Universit?tsmedizin Berlin, Germany

Takayoshi Suzuki
Editor
The Institute of Scientific and Industrial Research, Osaka University

Yoshiyuki Tanabe
Editor
Faculty of Pharmaceutical Sciences, Yokohama University of Pharmacy

Futoshi Taura
Editor
Faculty of Pharmaceutical Sciences, University of Toyama

Kenichiro Todoroki
Editor
School of Pharmaceutical

Motohiro Nishida
Editor
Graduate School of Pharmaceutical Sciences, Kyushu University

Yasuko Obata
Editor
Faculty of Pharmaceutical Sciences, Hoshi University

Tomofumi Okuno
Editor
Faculty of Pharmaceutical Sciences, Setsunan University

Nozomi Saito
Editor
Meiji Pharmaceutical University

Kenji Sakamoto
Editor
Faculty of Pharma-Sciences, Teikyo University

Tomoya Shiro
Editor
Drug Research Division, Sumitomo Dainippon Pharma Co., Ltd.

Changquan Calvin Sun
Editor
University of Minnesota, U.S.A.

Sayo Suzuki
Editor
Keio University Faculty of Pharmacy

Ryo Suzuki
Editor
Faculty of Pharma-Science, Teikyo University

Hikaru Tanaka
Editor
Faculty of Pharmaceutical Sciences, Toho University

Takaki Toda
Editor
Faculty of Pharmaceutical Sciences, Hokkaido University of Science

Kiyofumi Ninomiya
Editor
Faculty of Pharmacy, Shujitsu University

Kohji Noguchi
Editor
Faculty of Pharmaceutical Sciences, Tokyo University of Science

Shinya Oishi
Editor
Kyoto Pharmaceutical University

Kei-ichi Ozaki
Editor
Faculty of Pharmaceutical Sciences, Doshisha Women's College of Liberal Arts

Yasuo Sato
Editor
Yokohama University of Pharmacy

Chisato Shimanoe
Editor
Department of Pharmacy, Saga University Hospital

Nobukazu Shitan
Editor
Faculty of Pharmaceutical Sciences, Kobe Pharmaceutical University

Toyofumi Suzuki
Editor
School of Pharmacy, Nihon University

Tsutomu Takahashi
Editor
School of Pharmacy, Tokyo University of Pharmacy and Life Sciences

Hiroyuki Tanaka
Editor
Faculty of Pharmaceutical Sciences, Sanyo-Onoda City University

Chihiro Tohda
Editor
Institute of Natural Medicine,

Subject Area

Physics
Chemistry
Biology, Life Sciences and Basic Medicine
Agriculture and Food Sciences
Pharmaceutical Sciences
Environmental Sciences

Other relevant information

Title
Chemical and Pharmaceutical Bulletin

Publisher
The Pharmaceutical Society of Japan

Address
2-12-15, Shibuya, Shibuya-ku,Tokyo 150-0002,Japan

Contact email address
(Please change "(at)" into "@".)
ronb(at)pharm.or.jp

URL
https://www.pharm.or.jp/eng/

Chemical and Pharmaceutical Bulletin

Online ISSN : 1347-5223
Print ISSN : 0009-2363
ISSN-L : 0009-2363

Volume 60 , Issue 2

Showing 1-20 articles out of 20 articles from the selected issue

Communication to the Editor

Three-Dimensional Solution Structure of Bottromycin A_2: A Potent Antibiotic Active against Methicillin-Resistant *Staphylococcus aureus* and Vancomycin-Resistant *Enterococci*

Hiroaki Gouda, Yutaka Kobayashi, Takeshi Yamada, Tetsuya Ideguchi, Aki ...

Type: Communication to the Editor
2012 Volume 60 Issue 2 Pages 169-171
Published: February 01, 2012
Released: February 01, 2012

DOI https://doi.org/10.1248/cpb.60.169

JOURNALS FREE ACCESS

SUPPLEMENTARY MATERIAL

Show abstract

Download PDF (1386K)

Regular Articles

Development and Evaluation of a Monolithic Floating Drug Delivery System for Acyclovir

Naser Tavakoli, Jaleh Varshosaz, Farid Dorkoosh, Sedigheh Motaghi, Lan ...

Type: Regular Article
2012 Volume 60 Issue 2 Pages 172-177
Published: February 01, 2012
Released: February 01, 2012

DOI https://doi.org/10.1248/cpb.60.172

JOURNALS FREE ACCESS

Download PDF (1060K)

Constituents from the Roots of *Taraxacum platycarpum* and Their Effect on Proliferation of Human Skin Fibroblasts

Tsutomu Warashina, Kaoru Umehara, Toshio Miyase

Type: Regular Article
2012 Volume 60 Issue 2 Pages 205-212
Published: February 01, 2012
Released: February 01, 2012

DOI https://doi.org/10.1248/cpb.60.205

JOURNALS FREE ACCESS

Show abstract

Download PDF (1157K)

Rupestines F—M, New Guaipyridine Sesquiterpene Alkaloids from *Artemisia rupestris*

Fei He, Alfarius Eko Nugroho, Chin Piow Wong, Yusuke Hirasawa, Osamu S ...

Type: Regular Article
2012 Volume 60 Issue 2 Pages 213-218
Published: February 01, 2012
Released: February 01, 2012

DOI https://doi.org/10.1248/cpb.60.213

JOURNALS FREE ACCESS

Show abstract

Download PDF (788K)

New Tricyclic Alkaloids, Cassiarins G, H, J, and K from Leaves of *Cassia siamea*

Jun Deguchi, Tomoe Hirahara, Yusuke Hirasawa, Wiwied Ekasari, Aty Widy ...

Type: Regular Article
2012 Volume 60 Issue 2 Pages 219-222
Published: February 01, 2012
Released: February 01, 2012

DOI https://doi.org/10.1248/cpb.60.219

JOURNALS FREE ACCESS

Show abstract

Download PDF (580K)

Synthesis and Pharmacological Evaluation of 2-(1-Alkylpiperidin-4-yl)-*N*-[(1*R*)-1-(4-fluorophenyl)-2-methylpropyl]acetamide Derivatives as Novel Antihypertensive Agents

New Tricyclic Alkaloids, Cassiarins G, H, J, and K from Leaves of *Cassia siamea*

Jun Deguchi,[a] Tomoe Hirahara,[a] Yusuke Hirasawa,[a] Wiwied Ekasari,[b] Aty Widyawaruyanti,[b] Osamu Shirota,[c] Motoo Shiro,[d] and Hiroshi Morita*[,a]

[a] *Faculty of Pharmaceutical Sciences, Hoshi University; 2–4–41 Ebara, Shinagawa, Tokyo 142–8501, Japan:* [b] *Faculty of Pharmacy, Airlangga University; Jalan Dharmawangsa Dalam, Surabaya 60286, Indonesia:* [c] *Faculty of Pharmaceutical Sciences at Kagawa Campus, Tokushima Bunri University; 1314–1 Shido, Sanuki, Kagawa 769–2193, Japan: and* [d] *X-Ray Research Laboratory, Rigaku Corporation; Akishima, Tokyo 196–8666, Japan.*
Received October 24, 2011; accepted November 28, 2011; published online December 5, 2011

Four new alkaloids, cassiarins G, H, J, and K (1—4) which showed moderate antiplasmodial activity against *Plasmodium falciparum* 3D7, were isolated from the leaves of *Cassia siamea* (Leguminosae) and the structures of 1—4 were elucidated by 1D- and 2D-NMR analysis and X-ray crystallographic analysis.

Key words alkaloid; *Cassia siamea*; cassiarin; antiplasmodial activity; *Plasmodium falciparum* 3D7

Cassia siamea Lam. (Leguminosae), has been widely used in traditional medicine, particularly for the treatment of periodic fever and malaria in Indonesia.[1,2] Cassiarin A,[3] an unprecedented tricyclic alkaloid exhibiting potent antimalarial activity against *P. falciparum in vitro* as well as *P. berghei in vivo*,[4] was isolated from the leaves of *C. siamea* and has attracted the attention of synthetic organic chemists[5—7] as well as pharmacologists.[8] Recently, we have also reported the synthesis of a series of a hydroxyl and a nitrogen-substituted derivatives of cassiarins A and B and their antimalarial activity against *P. falciparum in vitro* as well as a vasorelaxation activity.[9] Furthermore, we isolated a novel biaryl tetracyclic alkaloid, cassirin F and achieved its total synthesis.[10] In our continuing investigation of the pharmacologically and structurally unique alkaloids from this plant, we have isolated four new alkaloids possessing tricyclic skeleton. We herein report the structure elucidation of these alkaloids and antiplasmodial activity against *P. falciparum* 3D7.

The crude basic fraction obtained by a conventional procedure from the MeOH extract of the leaves of *C. siamea*, was purified by repeated chromatography to afford new alkaloids, cassiarins G (**1**; 0.0064%), H (**2**; 0.00008%), J (**3**; 0.0022%), and K (**4**; 0.0012%), along with cassiarins A and B[3] and 5-acetonyl-7-hydroxy-2-methylchromone.[11]

Cassiarin G (**1**) was obtained as yellowish needles (mp 213—218°C) and showed the molecular formula, $C_{14}H_{13}NO_4$, which was determined by high resolution-electrospray ionization-time-of-flight-mass spectrometry (HR-ESI-TOF-MS) [*m/z* 260.0921, $(M+H)^+$, −0.2 mmu]. IR absorptions implied the presence of hydroxy and/or amino (3116 cm^{-1}) and carbonyl (1673 cm^{-1}) functionalities. ^{1}H- and ^{13}C-NMR data are presented in Table 1. The ^{13}C-NMR spectrum revealed 14 carbon signals due to one carbonyl carbon, six sp^2 and one sp^3 quaternary carbons, three sp^2 methines, and three methyl groups. Among them, four sp^2 quaternary carbons (δ_C 144.0, 152.0, 155.4, 168.9), one sp^3 quaternary carbon (δ_C 106.8), and one sp^3 methyl carbon (δ_C 50.5) were ascribed to those bearing a nitrogen or an oxygen atom.

A partial structure, C-10 to C-12 was deduced from analysis of the ^{1}H–^{1}H correlation spectroscopy (COSY) spectrum including a long range coupling from H_3-12 to H-10. The heteronuclear multiple bond connectivity (HMBC) correlations for H-10 of C-4a (δ_C 110.2) and C-5 (δ_C 142.0), H-6 of C-10 (δ_C 121.7), and H-8 of C-4a, C-6 (δ_C 103.0), and C-7 (δ_C 168.9) gave rise to 3-methylisoquinolin-6-ol core, which is the same as the partial structure of cassiarin A. The other partial structure was assigned by HMBC correlations for H_3-9 and H_3-13 of C-2 and H_3-9 of C-3 (δ_C 189.0) and the downfield chemical shifts of C-2 (δ_C 106.8) and C-8a (δ_C 155.4) suggested the presence of an ether linkage between C-2 and C-8a to form a 2-methyl-2-methoxy-3-carbonylpyran ring. Thus, cassiarin G (**1**) was assigned to be a 2-methoxycassiarin A-3-one (Fig. 1). The proposed structure inferred by spectroscopic analysis was confirmed by X-ray crystallographic analysis (Fig. 2). **1** was found as a racemic form base on X-ray crystallographic information.

Cassiarin H (**2**) showed the molecular formula, $C_{19}H_{21}NO_6$, which was determined by HR-ESI-TOF-MS [*m/z* 360.1441, $(M+H)^+$, −0.6 mmu]. IR absorptions implied the presence of carbonyl (1726, 1683 cm^{-1}) functionality. The gross structure of **2** was elucidated by analyses of 2D-NMR data including ^{1}H–^{1}H COSY, heteronuclear multiple quantum coherence

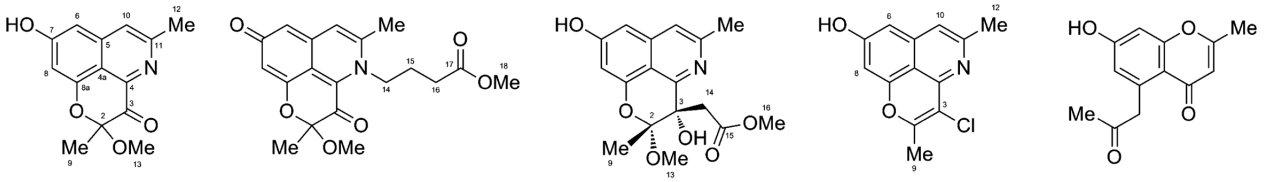


Chart 1

* To whom correspondence should be addressed. e-mail: moritah@hoshi.ac.jp

Table 1. ^{1}H-NMR Data [δ_H (J, Hz)] and ^{13}C-NMR Data [δ_C] of Cassiarins G, H, J, and K (**1**—**4**) in Methanol-d_4 at 300 K[a)]

	1		**2**		**3**		**4**	
Position	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C	δ_H	δ_C
2		106.8		102.2		107.1		157.4
3		189.0		187.0		76.1		113.7
4		152.0		137.5		156.9		148.4
4a		110.2		115.9		111.0		112.8
5		142.0		141.4		141.0		139.9
6	6.88 (1H, brs)	103.0	6.33 (1H, d, 1.8)	106.5	6.83 (1H, brs)	103.1	6.57 (1H, brs)	102.5
7		168.9		183.5		167.9		163.0
8	6.79 (1H, brs)	107.6	6.58 (1H, d, 1.8)	116.6	6.74 (1H, brs)	107.3	6.54 (1H, brs)	100.5
8a		155.4		153.2		154.4		155.2
9	1.71 (3H, s)	14.9	1.79 (3H, s)	17.4	1.76 (3H, s)	15.5	2.41 (3H, s)	18.2
10	7.70 (1H, s)	121.7	7.40 (1H, s)	121.8	7.57 (1H, s)	120.3	6.91 (1H, s)	115.3
11		144.0		145.1		141.0		153.8
12	2.73 (3H, s)	19.7	2.72 (3H, s)	20.1	2.65 (3H, s)	20.3	2.45 (3H, s)	23.9
13	3.25 (3H, s)	50.5	3.42 (3H, s)	51.3	3.20 (3H, s)	50.6		
14a			4.40 (2H, t, 8.5)	49.9	2.87 (1H, d, 13.2)	43.6		
14b					3.00 (1H, d, 13.2)			
15a			1.90 (1H, m)	27.0		170.7		
15b			2.14 (1H, m)					
16			2.51 (2H, m)	31.2	3.40 (3H, s)	52.4		
17				174.5				
18			3.69 (3H, s)	52.3				

a) δ in ppm.

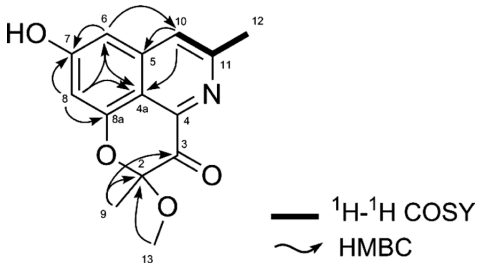


Fig. 1. Selected 2D-NMR Correlations for Cassiarin G (**1**)

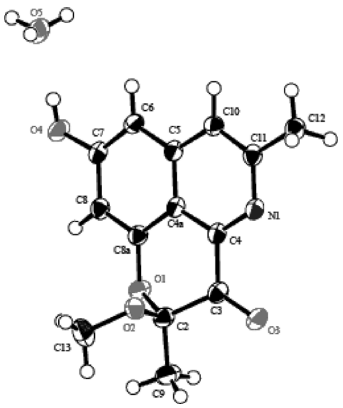


Fig. 2. An ORTEP Drawing for Cassiarin G (**1**)

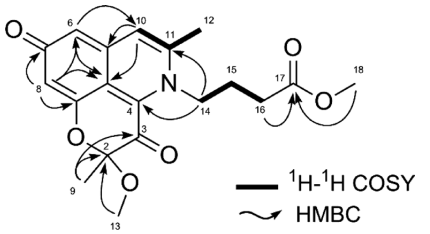


Fig. 3. Selected 2D-NMR Correlations for Cassiarin H (**2**)

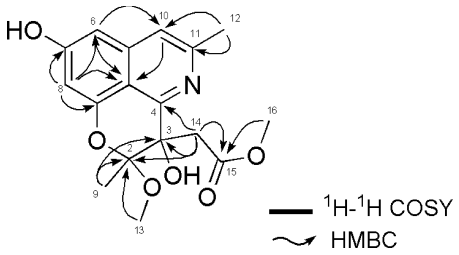


Fig. 4. Selected 2D-NMR Correlations for Cassiarin J (**3**)

(HMQC), and HMBC spectra in methanol-d_4 (Fig. 3). The ^{1}H- and ^{13}C-NMR (Table 1) spectra of **2**, which is like a combination of those of cassiarins B and G, indicated that **2** was concluded to be a 2-methoxycassiarin B-3-one. Due to the no optical rotation and Cotton effects, **2** might be racemic form.

Cassiarin J (**3**) showed the molecular formula, $C_{17}H_{19}NO_6$, which was determined by HR-ESI-TOF-MS [m/z 332.1107, $(M-H)^-$, −2.0 mmu]. IR absorptions implied the presence of hydroxy and/or amino (3370 cm^{-1}) and carbonyl (1632 cm^{-1}) functionalities. ^{1}H- and ^{13}C-NMR spectra are presented in Table 1. The gross structure of **3** was elucidated by analyses of 2D-NMR data including ^{1}H–^{1}H COSY, HMQC, and HMBC spectra in methanol-d_4 (Fig. 4). The structure of **3** resembled those of **1** except for the chemical shift and a moiety of C-3 (δ_C 76.1). The presence of a methylacetate and hydroxyl moiety at C-3 was supported by HMBC correlations for H_2-14 of C-2 (δ_C 107.1), C-3, C-4 (δ_C 156.9), and C-15 (δ_C 170.7) and H_3-16 of C-15. Thus, cassiarin J (**3**) was concluded to be methyl 3-hydroxy-2-methoxy-3-cassiarin A-acetate. The relative configuration of **3** was elucidated by rotating frame Overhauser

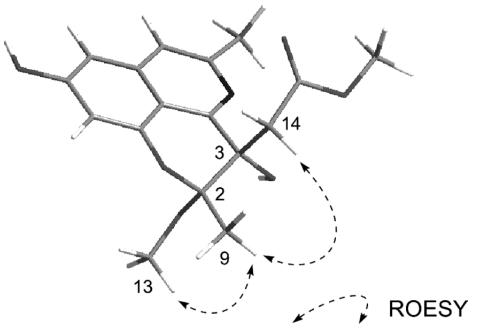


Fig. 5. Most Stable Conformation of Cassiarin J (**3**) by Monte Carlo Conformational Search and the Selected ROESY Correlations

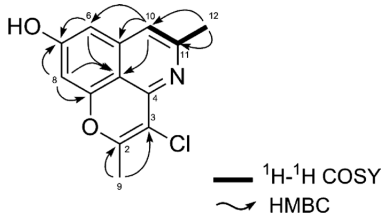


Fig. 6. Selected 2D-NMR Correlations for Cassiarin K (**4**)

enhancement spectroscopy (ROESY) correlations as depicted in the computer-generated three-dimensional drawing (Fig. 5). The ROESY correlations for H_3-9/H_3-13 and H_2-14 suggested the methyl at C-2 and the hydroxy at C-3 took equatorial orientations as in Fig. 5. The energetically most stable conformation of **3** found in the Monte Carlo conformational search[12] satisfied with the above-mentioned ROESY correlations. No optical rotation and Cotton effects indicated **3** might be racemic form.

Cassiarin K (**4**) showed the molecular formula, $C_{13}H_{10}NO_2Cl$, which was determined by HR-ESI-TOF-MS [*m/z* 248.0474, $(M+H)^+$, −0.4 mmu]. IR absorption implied the presence of hydroxy and/or amino (3420 cm^{-1}) functionality. The gross structure of **4** was elucidated by analyses of 2D-NMR data including ^{1}H–^{1}H COSY, HMQC, and HMBC spectra in methanol-d_4 (Fig. 6). The ^{1}H- and ^{13}C-NMR (Table 1) spectra of **4** are similar to those of cassiarin A except for the absence of H-3. The C-3 resonance of **4** was observed as a quaternary carbon at δ 113.7 as expected for a chlorine-bearing carbon resonance. Cassiarin K (**4**) is the first halogenated cassiarin analogue, has a structure in which H-3 of cassiarin A is substituted by a chlorine atom.

Biogenetically, cassiarins G, H and J (**1**—**3**) could be derived through oxidation of 5-acetonyl-7-hydroxy-2-methylchromone.

Cassiarin J (**3**) showed moderate *in vitro* antiplasmodial activity against *P. falciparum* 3D7 (IC_{50} **3**: 0.3 μM). Whereas cassiarins G, H, and K (IC_{50} **1**: >50 μM; **2**: >50 μM; **4**: 1.4 μM) were less active than cassiarin J (**3**), although they contained the similar cassiarin A-type skeleton.

Experimental

General Experimental Procedures 1D- and 2D-NMR spectra were recorded on a Bruker AV 400, Inova500, and Bruker AVANCE 700 spectrometers and chemical shifts were referenced to the residual solvent peaks (δ_H 3.31 and δ_C 49.0 for methanol-d_4). Standard pulse sequences were employed for the 2D-NMR experiments. ^{1}H–^{1}H COSY and ROESY spectra were measured with spectral widths of both dimensions of 4800 Hz, and 32 scans with two dummy scans were accumulated into 1 K data points for each of 256 t_1 increments. ROESY spectra in the phase sensitive mode were measured with a mixing time of 800 ms. For HMQC spectra in the phase sensitive mode and HMBC spectra, a total of 256 increments of 1 K data points were collected. For HMBC spectra with *Z*-axis PFG, a 50 ms delay time was used for long-range C–H coupling. Zero-filling to 1 K for F_1 and multiplication with squared cosine-bell windows shifted in both dimensions were performed prior to 2D Fourier transformation.

Material Leaves of *C. siamea* were collected at Purwodadi Botanical Garden in 2007. The botanical identification was made by Ms. Sri Wuryanti, Purwodadi Botanical Garden, Indonesia. A voucher specimen has been deposited at Purwodadi Botanical Garden, Pasuruan, Indonesia.

Extraction and Isolation The leaves of *C. siamea* (0.5 kg) were extracted with MeOH, and the extract was partitioned between EtOAc and 3% tartaric acid. The aqueous layer was adjusted at pH 9 with saturated Na_2CO_3 aq. and extracted with $CHCl_3$. $CHCl_3$-soluble alkaloidal materials were roughly separated by silica gel column chromatography ($CHCl_3$/MeOH, 1 : 0→0 : 1) to give seven fractions (1—7). The fraction 4 was rechromatogaphed over SiO_2 ($CHCl_3$/MeOH, 1 : 0→0 : 1), ODS (MeOH/H_2O, 40 : 60→100 : 0), and then purified by ODS HPLC (MeOH/0.1% TFA aq, 40 : 60) to afford cassiarin G (**1**, 0.0064%), cassiarin H (**2**, 0.00008%), cassiarin J (**3**, 0.0022%), and cassiarin K (**4**, 0.0012%) together with cassiarin A and 5-acetonyl-7-hydroxy-2-methylchromone.

Cassiarin G (**1**): Yellowish needles (mp 213—218°C) crystal solid; IR (KBr) ν_{max} 3116, 2316, and 1673 cm^{-1}; UV (MeOH) λ_{max} 213 (ε 16300), 243 (19600), 269 (10900), and 325 (2100) nm; ^{1}H- and ^{13}C-NMR, see Table 1; ESI-MS *m/z* 260 $(M+H)^+$; HR-ESI-TOF-MS *m/z* 260.0921 [$(M+H)^+$], (Calcd for $C_{14}H_{14}NO_4$, 260.0923).

Cassiarin H (**2**): Yellow amorphous solid; IR (film) ν_{max} 1726 and 1683 cm^{-1}; UV (MeOH) λ_{max} 215 (ε 2135), 238 (1978), 312 (1424), 387 (443), and 496 (310) nm; ^{1}H- and ^{13}C-NMR, see Table 1); ESI-MS *m/z* 360 $(M+H)^+$; HR-ESI-TOF-MS *m/z* 360.1441 [$(M+H)^+$], (Calcd for $C_{19}H_{22}NO_6$, 360.1447).

Cassiarin J (**3**): Yellow amorphous solid; IR (film) ν_{max} 3370 and 1632 cm^{-1};UV (MeOH) λ_{max} 242 (ε 16100), 289 (2600), and 327 (sh, 1600) nm;^{1}H- and ^{13}C-NMR, see Table 1); ESI-MS *m/z* 334 $(M+H)^+$; HR-ESI-TOF-MS *m/z* 332.1127 [$(M-H)^-$], (Calcd for $C_{17}H_{18}NO_6$, 332.1107).

Cassiarin K (**4**): Yellow amorphous solid; IR (KBr) ν_{max} 3420 cm^{-1}; UV (MeOH) λ_{max} 201 (ε sh, 5500), 219 (7300), and 336 (1500) nm; ^{1}H- and ^{13}C-NMR, see Table 1; ESI-MS *m/z* 248 $(M+H)^+$; HR-ESI-TOF-MS *m/z* 248.0474 [$(M+H)^+$], (Calcd for $C_{13}H_{11}NO_2Cl$, 248.0478).

Antiplasmodial Activity Human malaria parasites were cultured according to the method of Trager and Jensen.[13] The antimalarial activity of the isolated compounds was determined by the procedure described by Budimulya *et al.*[14] In brief, stock solutions of the samples were prepared in dimethyl sulfoxide (DMSO) (final DMSO concentrations of <0.5%) and were diluted to the required concentration with complete medium (RPMI 1640 supplemented with 10% human plasma, 25 mM *N*-(2-hydroxyethyl)piperazine-*N*′-2-ethanesulfonic acid (HEPES) and 25 mM $NaHCO_3$) until the final concentrations of

samples in culture plate wells were 10; 1; 0.1; 0.01; 0.001 μg/mL. The malarial parasite *P. falciparum* 3D7 clone was propagated in a 24-well culture plates. Growth of the parasite was monitored by making a blood smear fixed with MeOH and stained with Geimsa stain. The antimalarial activity of each compound was expressed as an IC_{50} value, defined as the concentration of the compound causing 50% inhibition of parasite growth relative to an untreated control. The percentage of growth inhibition was expressed according to following equation: growth inhibition %=100−[(test parasitaemia/control parasitemia)×100. Chloroqine: IC_{50} 0.011 μM.

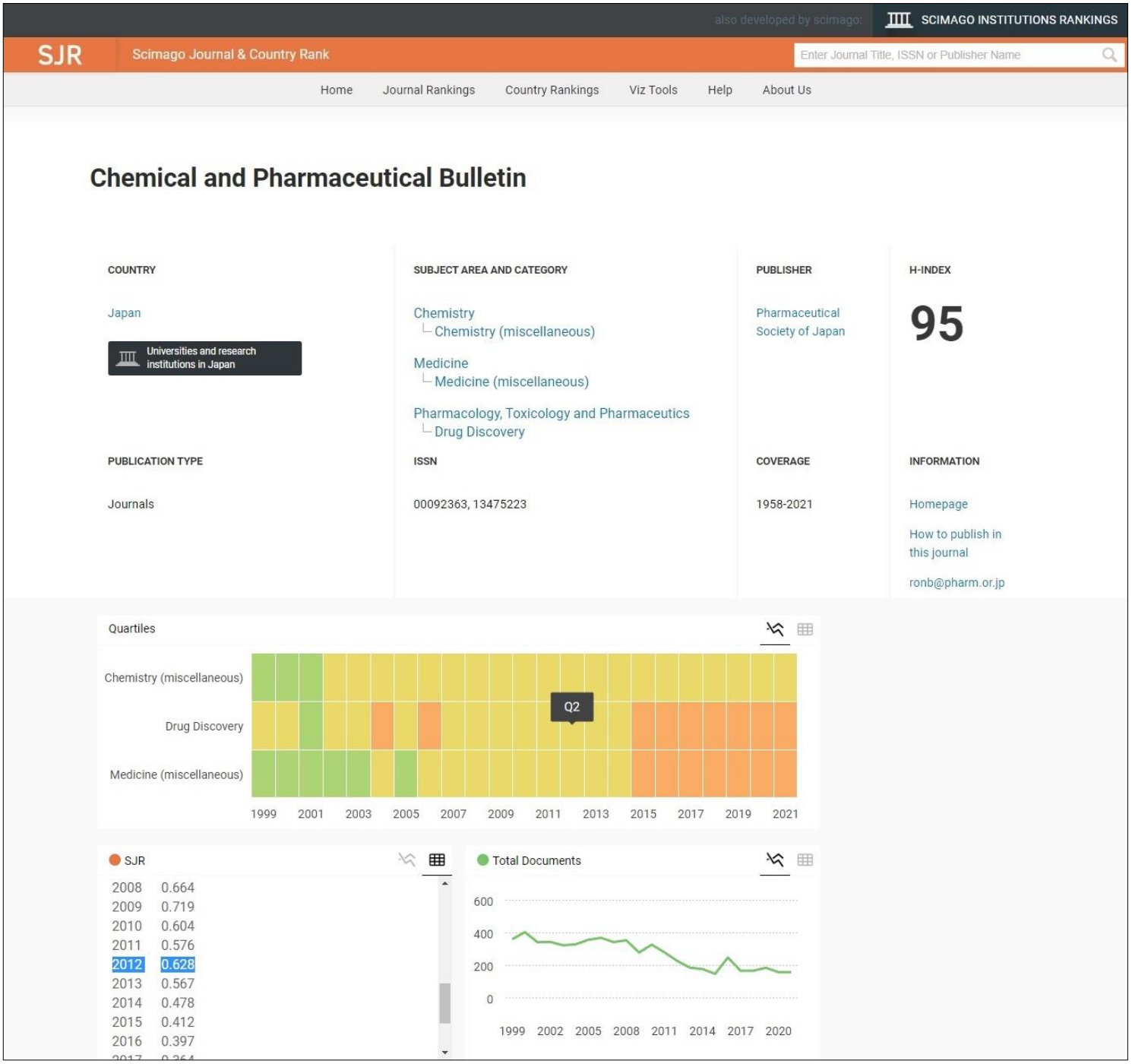
X-Ray Crystallography Measurement was made on a Rigaku RAXIS RAPID imaging plate area detector with graphite monochromated Cu$K\alpha$ radiation. Crystal data of cassiarin G: A yellow, block, triclinic, $C_{14}H_{15}NO_5$, M=277.28, crystal dimensions 0.12×0.12×0.05 mm, space group P-1 (#2), a=7.22313(13) Å, b=9.79354(18) Å, c=10.3279(7) Å, V=629.94(5) Å^3, Z=2, D_{calc}=1.462 g/cm^3. Of the 21093 reflections that were obtained, 2292 were unique (R_{int}=0.026). The structure was solved by direct methods. $R1$=0.0371 ($I>2.00\sigma(I)$). All calculations were performed using the CrystalStructure crystallographic software package except for refinement, which was performed using SHELXL-97. The refined fractional atomic coordinates, bond lengths, bond angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). CCDC 848465 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/deposit, or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (Fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgment. This work was partly supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan, and a Grant from the Open Research Center Project. We also acknowledge the financial support provided by Faculty of Pharmacy, Airlangga University for antimalarial activity.

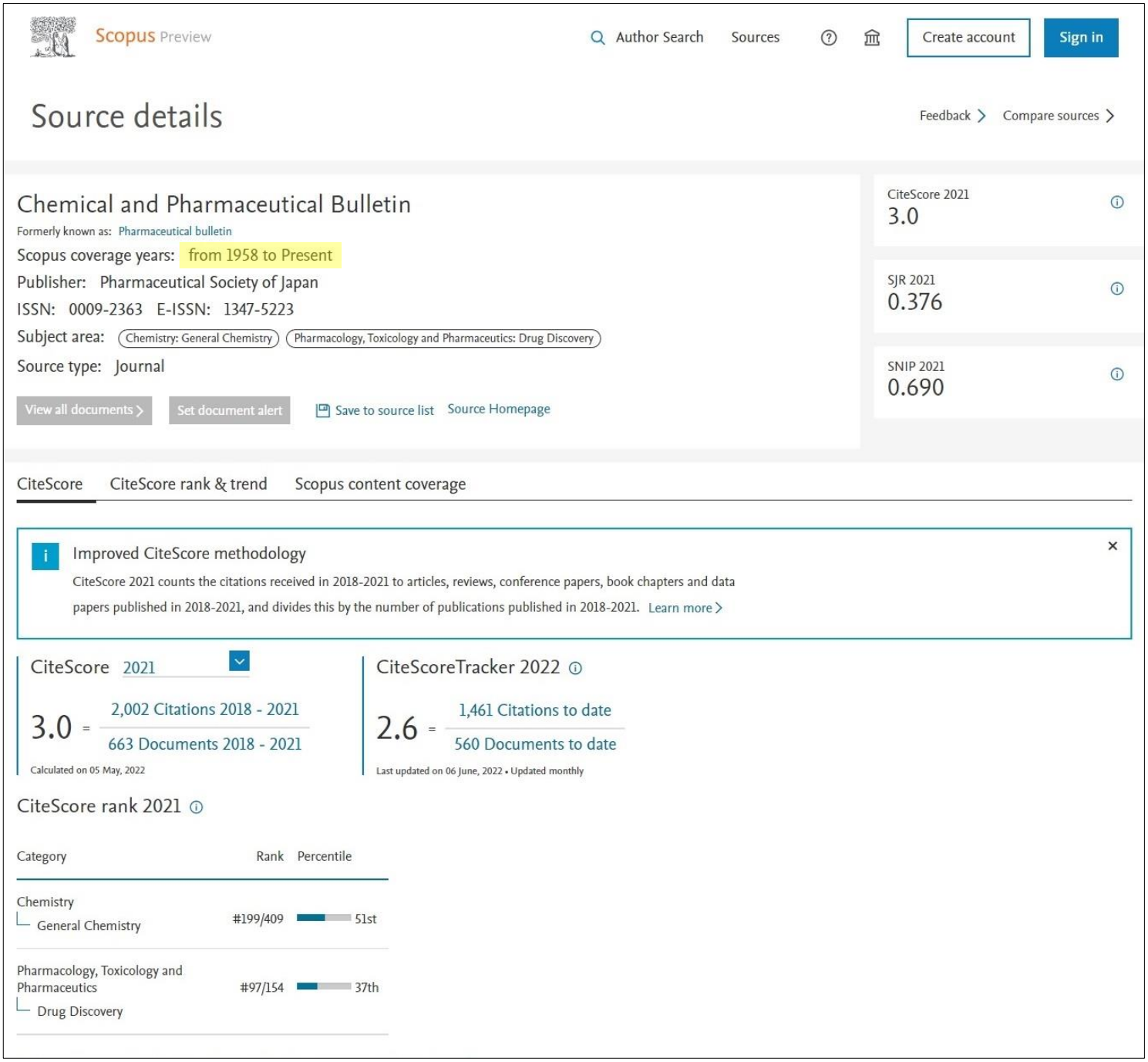
References

1) Mbatchi S. F., Mbatchi B., Banzouzi J. T., Bansimba T., Nsonde Ntandou G. F., Ouamba J. M., Berry A., Benoit-Vical F., *J. Ethnopharmacol.*, **104**, 168—174 (2006).
2) Sanon S., Ollivier E., Azas N., Mahiou V., Gasquet M., Ouattara C. T., Nebie I., Traore A. S., Esposito F., Balansard G., Timon-David P., Fumoux F., *J. Ethnopharmacol.*, **86**, 143—147 (2003).
3) Morita H., Oshimi S., Hirasawa Y., Koyama K., Honda T., Ekasari W., Indrayanto G., Zaini N. C., *Org. Lett.*, **9**, 3691—3693 (2007).
4) Ekasari W., Indrayanto G., Zaini N. C., Syafruddin D., Honda T., Morita H., *Heterocycles*, **78**, 1831—1836 (2009).
5) Rudyanto M., Tomizawa Y., Morita H., Honda T., *Org. Lett.*, **10**, 1921—1922 (2008).
6) Yao Y. S., Yao Z. J., *J. Org. Chem.*, **73**, 5221—5225 (2008).
7) Kanputhorn S., Petsom A., Thamyongkit P., *Tetrahedron*, **66**, 7539—7543 (2010).
8) Matsumoto T., Kobayashi T., Ishida K., Hirasawa Y., Morita H., Honda T., Kamata K., *Biol. Pharm. Bull.*, **33**, 844—848 (2010).
9) Morita H., Tomizawa Y., Deguchi J., Ishikawa T., Arai H., Zaima K., Hosoya T., Hirasawa Y., Matsumoto T., Kamata K., Ekasari W., Widyawaruyanti A., Wahyuni T. S., Zaini N. C., Honda T., *Bioorg. Med. Chem.*, **17**, 8234—8240 (2009).
10) Deguchi J., Hirahara T., Oshimi S., Hirasawa Y., Ekasari W., Shirota O., Honda T., Morita H., *Org. Lett.*, **13**, 4344—4347 (2011).
11) Arora S., Deymann H., Tiwri R. D., Winterfeldt E., *Tetrahedron*, **27**, 981—984 (1971).
12) Mohamadi F., Richards N. G. J., Guida W. C., Liskamp R., Lipton M., Caulfield C., Chang G., Hendrickson T., Still W. C., *J. Comput. Chem.*, **11**, 440—467 (1990).
13) Trager W., Jensen J. B., *Science*, **193**, 673—675 (1976).
14) Budimulya A. S., Syafruddin T. P., Wilariat P., Marzuki S., *Mol. Biochem. Parasitol.*, **84**, 137—141 (1997).

Bukti – Subject Area and Category, Quartile dan SJR Tahun Terbit (2012)



Bukti – Scopus Coverage, Publisher dan ISSN



Scopus Preview

Author Search Sources Create account Sign in

Source details

Feedback > Compare sources >

Chemical and Pharmaceutical Bulletin

Formerly known as: Pharmaceutical bulletin

Scopus coverage years: from 1958 to Present

Publisher: Pharmaceutical Society of Japan

ISSN: 0009-2363 E-ISSN: 1347-5223

Subject area: Chemistry: General Chemistry | Pharmacology, Toxicology and Pharmaceutics: Drug Discovery

Source type: Journal

View all documents > | Set document alert | Save to source list | Source Homepage

CiteScore 2021
3.0

SJR 2021
0.376

SNIP 2021
0.690

CiteScore | CiteScore rank & trend | Scopus content coverage

Improved CiteScore methodology

CiteScore 2021 counts the citations received in 2018-2021 to articles, reviews, conference papers, book chapters and data papers published in 2018-2021, and divides this by the number of publications published in 2018-2021. Learn more >

CiteScore 2021

3.0 = 2,002 Citations 2018 - 2021 / 663 Documents 2018 - 2021

Calculated on 05 May, 2022

CiteScoreTracker 2022

2.6 = 1,461 Citations to date / 560 Documents to date

Last updated on 06 June, 2022 • Updated monthly

CiteScore rank 2021

Category	Rank	Percentile
Chemistry General Chemistry	#199/409	51st
Pharmacology, Toxicology and Pharmaceutics Drug Discovery	#97/154	37th