Journal of Asian Natural Products Research

Country United Kingdom - SIR Ranking of United Kingdom

Subject Area and Category

Biochemistry, Genetics and Molecular Biology
- Molecular Medicine

Chemistry
- Analytical Chemistry
- Organic Chemistry

Medicine
- Complementary and Alternative Medicine
- Medicine (miscellaneous)

Pharmacology, Toxicology and Pharmaceutics
- Drug Discovery
- Pharmaceutical Science
- Pharmacology

35

H Index

Publisher Taylor & Francis

Publication type Journals

ISSN 10286020, 14772213

Coverage 1998-ongoing

Scope The Journal of Asian Natural Products Research (JANPR) publishes chemical and pharmaceutical studies in the English language in the field of natural product research on Asian ethnic medicine. The journal publishes work from scientists in Asian countries, e.g. China, Japan, Korea and India, including contributions from other countries concerning natural products of Asia. The journal is chemistry-orientated. Major fields covered are: isolation and structural elucidation of natural constituents (including those for non-medical uses), synthesis and transformation (including biosynthesis and biotransformation) of natural products, pharmacognosy, and allied topics. Biological evaluation of crude extracts are acceptable only as supporting data for pure isolates with well-characterized structures. All published research articles in this journal have undergone rigorous peer review, based on initial editor screening and anonymized refereeing by at least two expert referees.

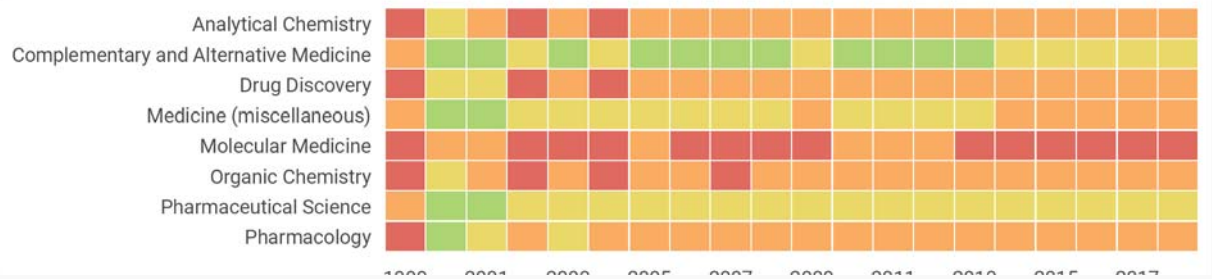
Homepage

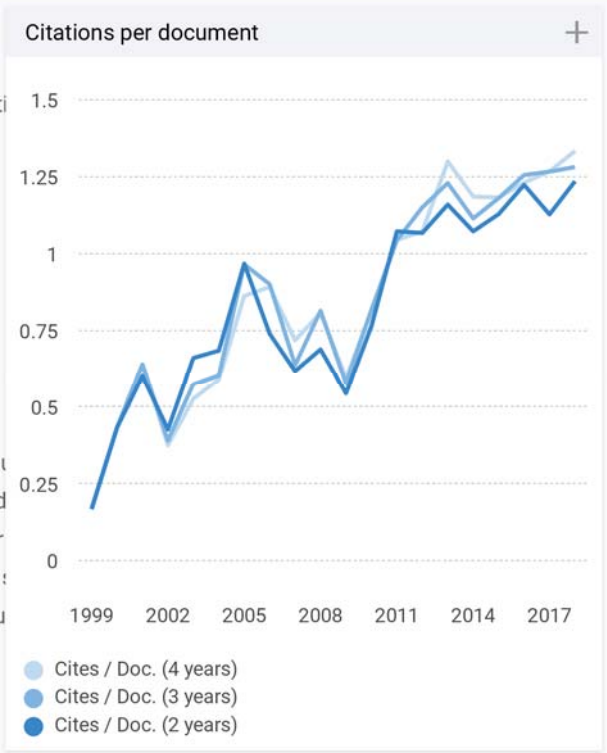
How to publish in this journal

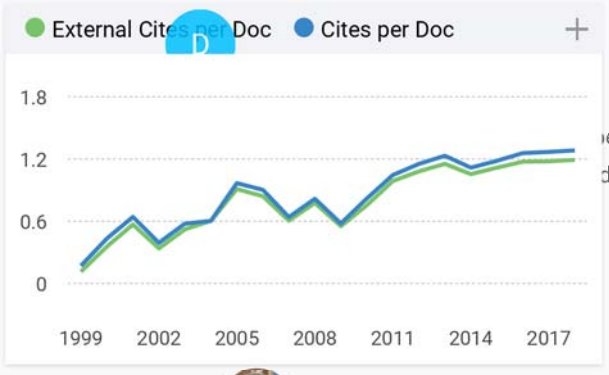
Contact

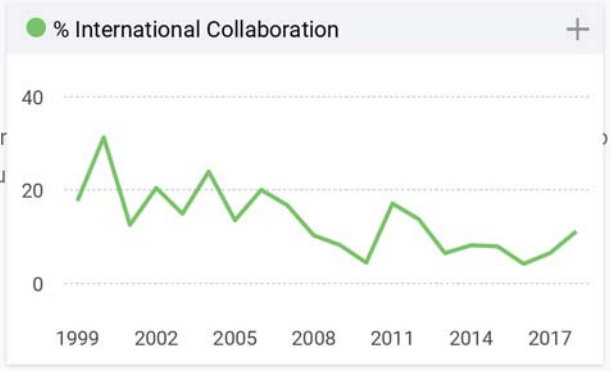
Join the conversation about this journal

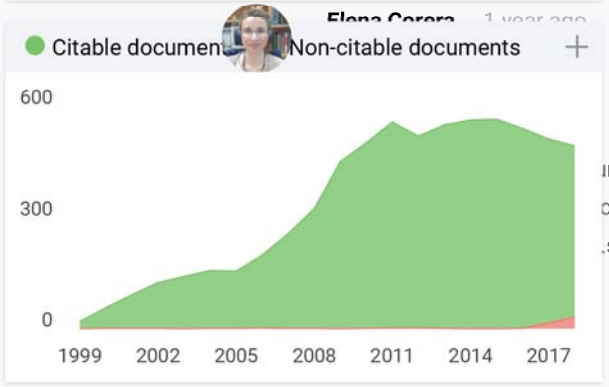
Quartiles

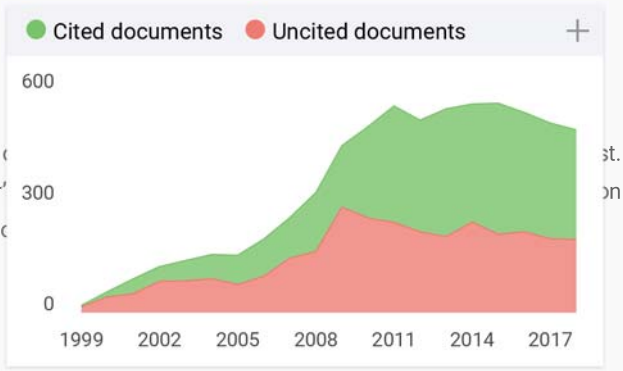












← Show this widget in your own website

Just copy the code below and paste within your html code:

<a href="https://www.scim

I'm not a robot

reCAPTCHA
Privacy - Terms

Submit

The users of Scimago Journal & Country Rank have the possibility to dialogue through comments linked to a specific journal. The purpose is to have a forum in which general doubts about the processes of publication in the journal, experiences and other issues derived from the publication of papers are resolved. For topics on particular articles, maintain the dialogue through the usual channels with your editor.

Journal of Asian Natural Products Research

Journal news

2016 Impact Factor: 1.071, ©2017 Thomson Reuters, 2017 Journal Citation Reports®

Browse our exclusive editor's choice collection for free!

Latest articles

Article
A new highly oxygenated pregnane and two new 5-hydroxymethylfurfural derivatives from the water decoction of *Poria cocos* ›
Chen et al.
Published online: 9 Oct 2017

Article
Furanone derivative and sesquiterpene from Antarctic marine-derived fungus *Penicillium* sp. S-1-18 ›
Zhou et al.
Published online: 9 Oct 2017

Article
Two new 2-(2-Hydroxy-2-phenylethyl)chromens from agarwood originating from *Aquilaria crassna* ›
Wang et al.
Published online: 6 Oct 2017

Article
A new single-stage method for obtaining of betulin phenylcarbamates ›
Mamaeva et al.
Published online: 5 Oct 2017

View more ›

See all volumes and issues

‹ | **Volume 11**, 2009 | Vol 10, 2008 | Vol 9, 2007 | Vol 8, 2006 ›

‹ | Issue 12 | Issue 11 | Issue 10 | Issue 9 | Iss 8 ›

Original Articles

Article

Five new compounds from *Dendrobium crystallinum* ›

Lei Wang , Chao-Feng Zhang , Zheng-Tao Wang , Mian Zhang & Luo-Shan Xu

Pages: 903-911

Published online: 04 Nov 2009

Article

Two new compounds from the broth of the marine fungus *Penicillium griseofulvum* Y19-07 ›

Ya-Nan Wang , Li Tian , Hui-Ming Hua , Xuan Lu , Sha Sun , Hong-Hua Wu & Yue-Hu Pei

Pages: 912-917

Published online: 04 Nov 2009

Article

Autophagic and apoptotic mechanisms of curcumin-induced death in K562 cells ›

Yan-Li Jia , Jun Li , Zheng-Hong Qin & Zhong-Qin Liang

Pages: 918-928

Published online: 04 Nov 2009

Article

Macagigantin, a farnesylated flavonol from *Macaranga gigantea* ›

Mulyadi Tanjung , Euis H. Hakim , Didin Mujahidin , Muhammad Hanafi & Yana M. Syah

Pages: 929-932

Published online: 04 Nov 2009

Article

Kinetics studies on the lignan class of natural compounds that inhibits α-chymotrypsin ›

M.A. Abbasi , M.A. Lodhi , V.U. Ahmad & M.I. Choudhary

Pages: 933-939

Published online: 04 Nov 2009

Article

Explore

Most read articles | Most cited articles

Article
Two new compounds from an endophytic fungus *Pestalotiopsis heterocornis* ›
Xing et al.
Published online: 25 Nov 2011
Views: 3036

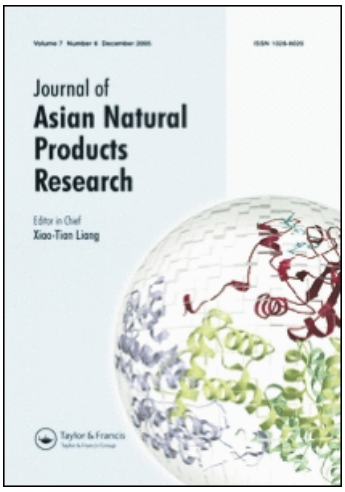
Article
Natural products – antifungal agents derived from plants ›
Arif et al.
Published online: 3 Jul 2009
Views: 1872

Article
Coumarins from *Daphne feddei* and their potential anti-inflammatory activities ›
Liang et al.
Published online: 25 Nov 2011
Views: 1813

Article
Isolation and characterization of secondary metabolites from *Plumeria obtusa* ›
Saleem et al.
Published online: 25 Nov 2011
Views: 1605

View more›

Editorial board



Journal of Asian Natural Products Research
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713454007

Macagigantin, a farnesylated flavonol from Macaranga gigantea

Mulyadi Tanjung [a]; Euis H. Hakim [a]; Didin Mujahidin [a]; Muhammad Hanafi [b]; Yana M. Syah [a]
[a] Natural Products Chemistry Research Group, Organic Chemistry Division, Institut Teknologi Bandung, Bandung, Indonesia [b] Indonesian Institute of Science, Research Center for Chemistry, Tangerang, Indonesia

Online Publication Date: 01 November 2009

To cite this Article Tanjung, Mulyadi, Hakim, Euis H., Mujahidin, Didin, Hanafi, Muhammad and Syah, Yana M.(2009)'Macagigantin, a farnesylated flavonol from Macaranga gigantea',Journal of Asian Natural Products Research,11:11,929 — 932
To link to this Article: DOI: 10.1080/10286020903302315
URL: http://dx.doi.org/10.1080/10286020903302315

Journal of Asian Natural Products Research
Vol. 11, No. 11, November 2009, 929–932

Macagigantin, a farnesylated flavonol from *Macaranga gigantea*

Mulyadi Tanjung[a], Euis H. Hakim[a], Didin Mujahidin[a], Muhammad Hanafi[b] and Yana M. Syah[a]*

[a]*Natural Products Chemistry Research Group, Organic Chemistry Division, Institut Teknologi Bandung, Jalan Ganesha 10, Bandung 40132, Indonesia;* [b]*Indonesian Institute of Science, Research Center for Chemistry, Serpong, 15310 Tangerang, Indonesia*

(*Received 29 April 2009; final version received 1 September 2009*)

A new farnesylated flavonol derivative, macagigantin (**1**), together with two known flavonoids, glyasperin A (**2**) and apigenin (**3**), had been isolated from the acetone extract of the leaves of *Macaranga gigantea*. The structure of the new compound was elucidated as 6-farnesylkaempferol based on its spectroscopic data, including UV, IR, 1D and 2D NMR, and HR-EI-MS spectra. Compounds **1**–**3** were evaluated for their cytotoxic properties against P-388 cells, their IC_{50} values being 11.3, 6.0, and 5.1 μM, respectively.

Keywords: macagigantin; farnesylated flavonol; *Macaranga gigantea*; Euphorbiaceae; cytotoxicity; P-388 cells

1. Introduction

The genus *Macaranga* (Euphorbiaceae) contains about 250 species distributed very widely from Africa and Madagascar in the west to tropical Asia, North Australia, and Pacific Islands in the east [1]. This genus has been shown to produce a number of phenolic compounds, particularly flavonoids and stilbenoids [2]. Recently, we have reported the first dihydrochalcone derivatives, along with flavanones, from an endemic *Macaranga* species in Indonesia, *Macaranga trichocarpa* [3]. In continuation of our phytochemical work on Indonesian tropical plants aiming to find new cytotoxic compounds [4–9], we had examined another *Macaranga* species, *Macaranga gigantea* (Reichb.f. & Zoll.) Müll. Arg. In this paper, we report the isolation of a farnesylated flavonol, 6-farnesylkaempferol (**1**), together with two known compounds **2** and **3** (Figure 1), from the acetone extract of the title plant leaves. The cytotoxic properties of compounds **1**–**3** against murine leukemia P-388 cells are also briefly described.

2. Results and discussion

Compound **1** was isolated as a yellow solid and the molecular formula $C_{30}H_{34}O_6$ was deduced from its HR-EI-MS data. The UV spectrum of **1** exhibited maxima typical for a flavonol structure (λ_{max} 271, 348, and 283 nm), and showed bathochromic shifts on addition of $AlCl_3$ and NaOAc [10]. The IR spectrum indicated absorptions for hydroxyl (3419 cm^{-1}), conjugated carbonyl (1649 cm^{-1}), and aromatic (1608 and 1560 cm^{-1}) groups. In the ^{13}C NMR spectrum (APT experiment; Table 1), 28 carbon signals representing 30 carbon atoms were observed. Two of them,

*Corresponding author. Email: yana@chem.itb.ac.id

ISSN 1028-6020 print/ISSN 1477-2213 online

DOI: 10.1080/10286020903302315
http://www.informaworld.com

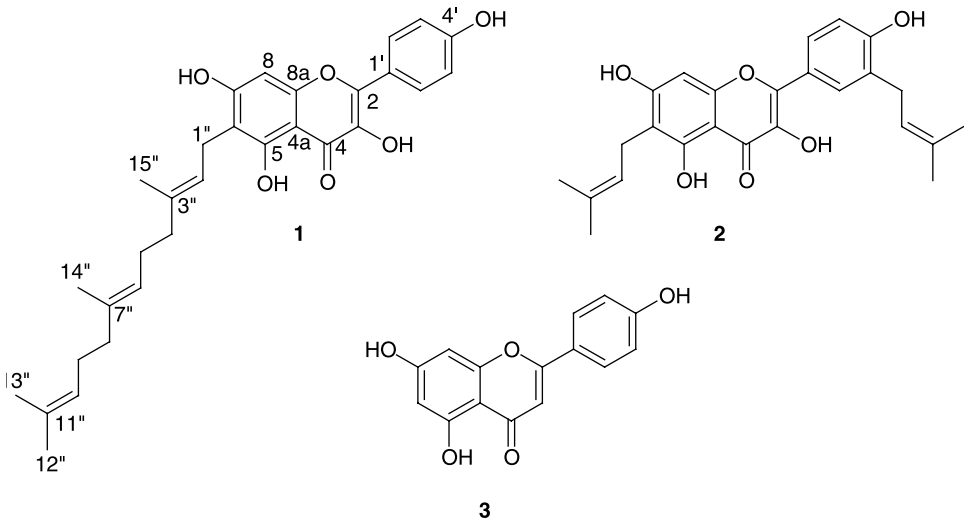


Figure 1. Structures of flavonoids **1**–**3**.

namely the signals at δ_C 136.5 and 176.5, are characteristic for C-3 and C-4 of a flavonol structure [11,12]. These spectroscopic data, therefore, suggested that **1** is a flavonol containing a C-15 side chain. Moreover, the presence of other five oxyaryl signals (δ_C 146.6, 155.6, 158.1, 160.0, and 162.6) indicated that the flavonol is a derivative of kaempferol.

The side chain was deduced to be a farnesyl group from the observation in the ^{1}H NMR spectrum (Table 1) of four methyl singlets at δ_H 1.51, 1.54, 1.57, and 1.79, five methylene signals at δ_H 1.8–3.5, and three methine vinyl signals of three substituted alkenes at δ_H 5.00, 5.06, and 5.29. The presence of the proton signals of a pair of doublets ($J = 9.0$ Hz) in the aromatic region at δ_H 7.00 and 8.12 (each 2H), assignable to the signals of a *p*-hydroxyphenyl group, and a singlet at δ_H 6.59, suggested that the farnesyl group is either at C-6 or C-8 of the kaempferol structure. The presence of long-range correlations in the HMBC spectrum of **1** between the proton signal of a chelated —OH group at δ_H 12.41 and three quaternary carbon signals at δ_C 104.0 (C-4), 158.1 (C-5), and 111.7 (C-6) unambiguously placed the farnesyl group at C-6. Therefore, compound **1**, trivially named macagigantin, was elucidated as 6-farnesylkaempferol or 6-[(2*E*,6*E*)-3″,7″,11″-trimethyldodeca-2″,6″,10″-trienyl]-kaempferol. Other HMBC correlations consistent with structure **1** are shown in Table 1. Further support for structure **1** was also obtained from the comparison of the NMR spectral data with those reported for 6-geranylkaempferol (macarangin) [11,12]. To our knowledge, compound **1** was the first example of flavonoid in the genus *Macaranga* with a farnesyl side chain.

On cytotoxic evaluation against P-388 cells, compounds **1**–**3** exhibited IC_{50} values of 11.3 ± 0.4, 6.0 ± 0.9, and 5.1 ± 0.7 μM, respectively (artonin E as a positive control, IC_{50} 1.38 ± 0.2). These cytotoxic data suggested that the presence of a terpenoid (farnesyl) substituent at C-6 (ring A) of the kaempferol structure reduces cytotoxic properties, while a similar substituent (isoprenyl) in the ring B enhances cytotoxicity.

3. Experimental

3.1 General experimental procedures

UV and IR spectra were measured with a Varian 100 Conc and an FT-IR Spectrum

Table 1. The NMR spectral data (d_6-acetone) of compound **1**.

No.	δ_H (multiplicity, J in Hz)	δ_C	HMBC (H ⇔ C)
2	–	146.6	–
3	–	136.5	–
4	–	176.5	–
4a	–	104.0	–
5	–	158.1	–
6	–	111.7	–
7	–	162.6	–
8	6.59 (s)	93.8	C-4, C-4a, C-6, C-7, C-8a
8a	–	155.6	–
1′	–	123.4	–
2′/6′	8.12 (d, 9.0)	130.3	C-2, C-4′, C-6′/2′
3′/5′	7.00 (d, 9.0)	116.2	C-4′, C-1′, C-5′/3′
4′	–	160.0	–
1″	3.37 (d, 6.7)	21.9	C-5, C-6, C-7, C-2″, C-3″
2″	5.29 (tm, 6.7)	123.2	C-1″, C-4″, C-15″
3″	–	135.1	–
4″	1.97 (t, 7.3)	40.4	C-2″, C-5″, C-3″, C-6″, C-15″
5″	2.06 (br q, 7.3)	27.0	C-4″, C-6″, C-7″
6″	5.06 (br t, 7.3)	124.8	C-5″, C-8″, C-14″
7″	–	135.4	–
8″	1.85 (br t, 7.3)	40.4	C-6″, C-7″, C-9″, C-10″, C-14″
9″	1.93 (br q, 7.3)	27.3	C-8″, C-10″, C-11″
10″	5.00 (br t, 7.3)	125.0	C-9″, C-12″, C-13″
11″	–	131.5	–
12″	1.57 (br s)	25.8	C-10″, C-11″, C-13″
13″	1.51 (br s)	17.6	C-10″, C-11″, C-12″
14″	1.54 (br s)	16.2[a]	C-6″, C-7″, C-8″
15″	1.79 (br s)	16.1[a]	C-2″, C-3″, C-4″
5-OH	12.41 (s)		C-4a, C-5, C-6

[a]Assignments could be interchanged.

One Perkin-Elmer instrument, respectively. ^{1}H and ^{13}C NMR spectra were recorded with a JEOL ECA500 spectrometer operating at 500 (^{1}H) and 125 (^{13}C) MHz, using residual and deuterated solvent peaks (δ_H 2.04 and δ_C 29.8, respectively) as reference standards. Mass spectra were obtained with a VG Autospec mass spectrometer (EI mode). Vacuum liquid chromatography (VLC) and radial chromatography were carried out using Si gel 60 G (article no. 1.07731.1000, Merck KgaA, 64271 Darmstadt, Germany) and Si gel 60 PF_{254} (article no. 1.07749.1000, Merck KgaA, 64271), respectively, and for TLC analysis, precoated Si gel 60 F_{254} plates (article no. 1.05554.0001, Merck KgaA, 64271) were used. Solvents used for extraction and separation were of technical grades that were distilled before use.

3.2 Plant material

The leaves of *M. gigantea* were collected in November 2007 from Lungkut Layang Village, District Kapuas, Kalimantan, Indonesia. The specimen was identified by Mr Ismail, Herbarium Bogoriense, Center of Biological Research and Development, National Institute of Science, Bogor, Indonesia, and the voucher specimen has been deposited at the herbarium.

3.3 Extraction and isolation

The dried and powdered leaves of *M. gigantea* (1.2 kg) were macerated in

acetone at room temprature (3×, 7.5 liters), and the acetone extract was evaporated under reduced pressure to give a crude acetone extract (50 g). The extract was fractionated by VLC on silica gel eluted with *n*-hexane–EtOAc mixtures [17:3 (4×) and 4:1 (4×)] to give five major fractions A–E. On TLC analysis, fraction D (1 g) showed two major spots (R_f 0.71 and 0.43, eluent $CHCl_3$–EtOAc = 9:1) and on purification of this fraction using centrifugal planar chromatography eluted with *n*-hexane–$CHCl_3$ (7:3 → 1:9), $CHCl_3$, and $CHCl_3$–EtOAc (9:1) afforded macagigantin (**1**) (23 mg) and glyasperin A (**2**) (64 mg) [13]. The same procedure was applied to fraction E (330 mg) to give apigenin (**3**) (25 mg) [14].

3.3.1 *Macagigantin (**1**)*

A yellow solid. UV (MeOH) λ_{max} (log ε): 204 (4.58), 271 (4.20), 333 (4.13), 368 (4.18) nm, (MeOH+NaOH) 210 (4.90), 240 (sh, 4.32), 279 (4.22), 322 (4.09), 417 (4.27) nm, (MeOH+$AlCl_3$) 203 (4.59), 273 (4.27), 347 (3.85), 431 (4.25) nm, (MeOH+$AlCl_3$/HCl) 203 (4.58), 272 (4.26), 348 (3.86), 431 (4.24) nm; (MeOH+NaOAc) 203 (4.85), 272 (4.21), 333 (4.07), 368 (4.06) nm; IR (KBr) ν_{max}: 3419 (OH), 2922, 2852 (CH-alkyl), 1649 (conj. C=O), 1608, 1560 (C=C aromatic) cm^{-1}; ^1H NMR (500 MHz) spectral data, see Table 1; ^{13}C NMR (125 MHz) spectral data, see Table 1; HR-EI-MS *m/z*: 490.2357 $[M]^+$ (calcd for $C_{30}H_{34}O_6$, 490.2355); EI-MS *m/z* (% rel.): 490 (17), 421 (24), 353 (56), 337 (15), 311 (12), 299 (100), 121 (10), 69 (25).

3.4 *Cytotoxic evaluation*

Cytotoxic properties of the isolated compounds **1**–**3** against murine leukemia P-388 cells were evaluated according to the method of MTT assay as described previously [15].

Acknowledgements

The authors are grateful for the financial support from the office of the Ministry of National Education, Republic of Indonesia (Hibah Pasca Grant VII 2009). We also thank Associate Prof. E.L. Ghisalberti, the University of Western Australia, for mass spectra measurements.

References

[1] F.R. Blattner, K. Weising, G. Banfer, U. Maschwitz, and B. Fiala, *Mol. Phyl. Evol.* **19**, 331 (2001).
[2] B.J. Yoder, S. Cao, A. Norris, J.S. Miller, F. Ratooson, J. Razafitsalama, R. Andriantsiferana, V.E. Rasamison, and D.G.I. Kingston, *J. Nat. Prod.* **70**, 342 (2007).
[3] Y.M. Syah, E.H. Hakim, S.A. Achmad, M. Hanafi, and E.L. Ghisalberti, *Nat. Prod. Commun.* **4**, 63 (2009).
[4] E.H. Hakim, S.A. Achmad, L.D. Juliawaty, L. Makmur, Y.M. Syah, N. Aimi, M. Kitajima, H. Hiromitsu, and E.L. Ghisalberti, *J. Nat. Med.* **60**, 161 (2006).
[5] Y.M. Syah, L.D. Juliawaty, E.H. Hakim, S.A. Achmad, and E.L. Ghisalberti, *J. Nat. Med.* **60**, 308 (2006).
[6] Muhtadi, E.H. Hakim, L.D. Juliawaty, Y.M. Syah, S.A. Achmad, J. Latif, and E.L. Ghisalberti, *Fitoterapia* **77**, 550 (2006).
[7] H. Saroyobudiono, L.D. Juliawaty, Y.M. Syah, S.A. Achmad, and E.H. Hakim, *J. Nat. Med.* **62**, 195 (2008).
[8] Ferlinahayati, E.H. Hakim, Y.M. Syah, L.D. Juliawaty, H. Takayama, I.M. Said, and J. Latip, *Z. Naturforsch.* **63c**, 35 (2008).
[9] I. Musthapa, L.D. Juliawaty, Y.M. Syah, E.H. Hakim, J. Latip, and E.L. Ghisalberti, *Arch. Pharm. Res.* **32**, 191 (2009).
[10] T.J. Mabry, K.R. Markham, and M.B. Thomas, *The Systematic Identification of Flavonoids* (Springer-Verlag, New York, 1970), pp. 41–164.
[11] E. Hnawia, O. Thoison, F. Gueritte-Voegelein, D. Bourret, and T. Sevenet, *Phytochemistry* **29**, 2367 (1990).
[12] S. Sutthivaiyakit, S. Unganont, and P. Sutthivaiyakit, *Tetrahedron* **58**, 3619 (2002).
[13] L. Zeng, T. Fukai, T. Nomura, R.Y. Zhang, and Z.C. Lou, *Heterocycles* **34**, 575 (1992).
[14] T.J. Batterham and R.J. Highet, *Aust. J. Chem.* **17**, 428 (1964).
[15] Sahidin, E.H. Hakim, L.D. Juliawaty, Y.M. Syah, L.B. Din, E.L. Ghisalberti, J. Latip, I.M. Said, and S.A. Achmad, *Z. Naturforsch.* **60c**, 723 (2005).