Asian Journal of Chemistry; Vol. 24, No. 11 (2012), 4843-4846

ASIAN JOURNAL OF CHEMISTRY

www.asianjournalofchemistry.co.in

MINI REVIEW

Various Botanical Sources of Betulinic Acid: A Review

M. GHAFFARI MOGHADDAM[1,*] and F.B.H. AHMAD[2]

[1]Department of Chemistry, University of Zabol, P.O. Box 98615-538, Zabol, Iran
[2]Department of Chemistry, Universiti Putra Malaysia, 43400 UPM Serdang, Selangor, Malaysia

*Corresponding author: E-mail: mansghaffari@gmail.com

(*Received*: 29 October 2011; *Accepted*: 21 May 2012) AJC-11509

Betulinic acid is a naturally occurring pentacyclic lupane-type triterpene. It shows a broad range of biological and medicinal properties. This review provides the various botanical sources of betulinic acid.

Key Words: Betulinic acid, Triterpene, Lupane, Medicinal plant.

INTRODUCTION

Betulinic acid (Fig. 1) (3β-hydroxy-lup-20(29)-en-28-oic acid), pentacyclic lupane triterpene, is a known natural product, which has gained considerable attention, since it exhibits a variety of biological and medicinal properties such as inhibition of human immunodeficiency virus (HIV)[1,2], antibacterial[3,4], antimalarial[5], antiinflammatory[6-9], anthelmintic[10], antinociceptive[11], anti-HSV-1[12,13] and anticancer activities[14-17]. Recently, betulinic acid has been reported to possess the ability to inhibit the growth of various cancerous cell lines *in vitro* without toxic side effects[18]. As far as toxicity of betulinic acid is concerned, no toxicity was observed on tumour-bearing mice at doses of 500 mg/kg body weight[14,17]. Betulinic acid is considered as a promising anticancer agent due to the selective cytotoxicity and favourable therapeutic index[19,20].

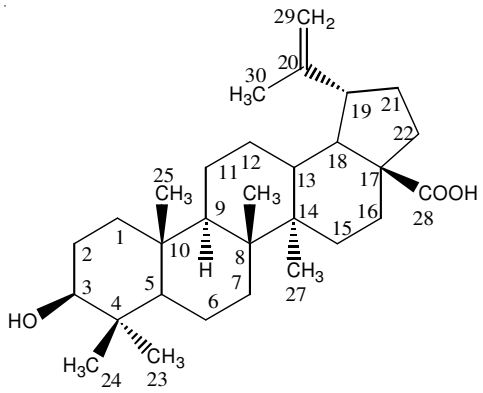

Fig. 1. Structure of betulinic acid

Betulinic acid is widely distributed throughout the plant kingdom[19]. The birch tree (*Betula* spp., Betulaceae) is one of the most widely reported sources of betulinic acid which can be obtained in considerable quantities[21-23]. Betulinic acid could also be isolated from various sources include *Ziziphus* spp. (Rhamnaceae)[4,17,24], *Syzygium* spp. (Myrtaceae)[1,25], *Diospyros* spp. (Ebenaceae)[26-28], *Triphyophyllum peltatum* and *Ancistrocladus heyneanus*[5], *Tovomita krukovii*[29], *Ipomoea pes-caprae* (L.) R. Br.[30], *Diospyros leucomelas*[28], *Guizhi Fuling* Capsula[31], *Rosa canina* L[32], *Rosmarinus officinalis* L[33] and *Paeonia* spp. (Paeoniaceae)[34]. We describe herein some recent isolation methods of betulinic acid and various botanical aspects of betulinic acid.

Procedures for isolation of betulinic acid from various botanical sources: Recently, betulinic acid was isolated from the leaves of the *Ligustrum lucidum* Ait., *Ligustrum pricei* Hayata and *Ligustrum sinensis* Lour plants[35] as follows: the dried leaves of the *Ligustrum* plants were extracted five times with methanol. The resultant extract was combined and concentrated under reduced pressure to obtain the methanol extract. The betulinic acid determination of the three *Ligustrum* spp. was carried out using high performance liquid chromatography (HPLC) with a photodiode array detector.

Guinda et al.[36] obtained betulinic acid from the fruit pulp of *Argania spinosa* by solid/liquid extraction with absolute ethanol according to the procedure described as follows: the whole fruits of *Argania spinosa* were washed with distiller water and air-dried for a week. Then, the whole organs were twice extracted by maceration with absolute ethanol.

Betulinic acid was isolated from the *Bacopa monniera* (L.)[37] as follows: the air-dried and powdered whole plant of the

TABLE- 1
SOME BOTANICAL SOURCES OF BETULINIC ACID

Plant (Binomial name)	Part of Plant	Reference
Syzrgium claviflorum	Leaves	[2]
Vitex negundo L	Leaves	[3]
Zizyphus joazeiro	Stem Bark	[4]
Berlina grandiflora	Stem Bark	[10]
Jacaranda mimosaefolia	Stem Bark	[44]
Ilex pubescens var. glabra.	Stem	[45]
Pneumatophores of *Avicennia marina* (Forssk.) Vierh	Aerial roots	[46]
Ficus lutea Vahl (Moraceae)	Woods	[47]
Dorstenia convexa.	Leaves	[48]
Rhaphidophora hongkongensis	Whole of plant	[49]
Gladiolus segetum (Iridaceae)	Aerial parts	[50]
Anemone tomentosa	Root	[51]
Hyptidendron canum	Stem	[52]
Eucalyptus globulus	Harvesting residues and bark generated by the pulp industry	[53]
Forsythia suspensa VAHL	Fruit	[54]
Peltophorum africanum	Stem Bark	[55]
betuale cortex, *Betula pendula roth*., *betulaceae*	Inner and external birch bark	[56]
Rosae pseudofructus cum/sine fructibus, *Rosa canina* L., Rosaceae	Rose hip with and without fruits	[57]
Platanus orientalis	Bark	[58]
Betula platyphylla suk.	Bark	[59]
Cratoxylum arborescens	Leaves and Twigs	[60]
Betulae cortex	Outer Bark	[61]
Avicennia officinalis	Bark	[62]
Eucalyptus globules	Fruits	[63]
Amoora cucullata	Stem Bark	[64]
Bischofia javanica	Bark	[65]
Nerium oleanderand	Leaves	[66]
Engelhardtia serrata	Stem Bark	[67]
Calophyllum brasiliense	Root	[68]
Clusia ellipticifolia	Stem Bark	[69]
Caesalpinia paraguariensis Burk.	Aerial	[70]
Quisqualis Fructus	Ground of the Plant	[71]
Coussarea paniculata	Twigs	[72]
Ilex macropoda	Twigs	[73]
Anemone raddeana	Roots	[74]
Eucalyptus globules	Inner and outer bark	[75]
Doliocarpus schottianus	Bark (top and bottom), wood and leaves	[76]
Orthosiphon stamineus	Aerial	[77]
Syncarpia glomulifera (Myrtaceae)	Bark	[78]
Eucalyptus camaldulensis var. *obtuse*	Leaves	[79]
Physocarpus intermedius	Stem Bark	[80]
Tetracentron sinense	Stem Bark	[81]
Combretum quadrangulare	Leaves	[82]
Uapaca nitida Müll-Arg. (Euphorbiaceæ)	Root Bark	[83]
Vochysia divergens	Stem Bark	[84]
Tetracera boiviniana	Twigs and Stem Bark	[85]
Malaysian Callistemon specious D. E	Leaves	[86]
Chaenomeles lagenaria	Fruit	[87]
Paeonia lactiflora	Aerial	[88]
Melaluca cajuputi	Seed	[89]
Paeonia japonica, Paeonia lactiflora and *Paeonia suffruticosa*	Callus tissues derived from the stem	[90]

B. monniera was defatted with petroleum ether. The defatted material was then extracted with methanol. The crude extract was evaporated in vacuum. The residue was then suspended in water and successively partitioned with chloroform, ethyl acetate and *n*-BuOH. The chloroform fraction was subjected to the column chromatography on silica gel to obtain betulinic acid.

Kumar *et al.*[38] isolated betulinic acid from the fruits of *Dillenia indica* L. according to the procedure described as follows: the dried fruits (calyx) of *Dillenia indica* L. were extracted with methanol. The extract was then filtered and the solvent was evaporated under vacuum. The methanol extract was suspended in water and partitioned successively with ethyl acetate and *n*-butanol. The ethyl acetate fraction was chromatographed on silica gel using increasing polarity of different solvents to isolate betulinic acid.

Betulinic acid was isolated from the leaves of *Pentalinon andrieuxii* (Apocynaceae)[39]. The dried leaves of *P. andrieuxii* were extracted with ethanol. The solvent was then evaporated. The crude extract was fractionated by successive liquid-liquid partition with hexane, ethyl acetate and butanol. The low polarity fraction was subjected to the column chromatography on silica gel to obtain pure betulinic acid.

Subramanyam *et al*.[40] isolated betulinic acid from the roots of *Tephrosia calophylla* according to the following procedure: betulinic acid was extracted into methanol from dried and powdered roots of *Tephrosia calophylla*. The total extract was concentrated in vacuum. The residue was suspended in water and then partitioned successively with chloroform and *n*-butanol. The chloroform part was subjected to the column chromatography on silica gel. The fractions were further purified by repeated silica gel column chromatography followed by column chromatography to give betulinic acid.

Choi *et al*.[41] isolated betulinic acid from the roots of *Saussurea lappa* C.B. Clarke using the following procedure: the dried roots of *S. Lappa* were extracted three times with MeOH at room temperature for seven days. The MeOH extract was suspended in water and partitioned with EtOAc. The EtOAc-soluble fraction was subjected to the silica gel chromatography to isolate the betulinic acid.

Betulinic acid was isolated from the stem barks of five *Uapaca species* (Euphorbiaceae) including *Uapaca acuminata, Uapaca guineensis, Uapaca heudolotti, Uapaca paludosa* and *Uapaca vandhoutei* by Nyasse *et al*.[42]. The dried bark pieces of *Uapaca* were extracted with ethyl acetate. The extracts were then evaporated to dryness. The crude extracts were stirred in cool methanol to participate significant amounts of betulinic acid which was recrystallized in methanol to afford substantial amounts of very pure betulinic acid.

De Melo *et al*.[43] isolated betulinic acid from the *Clusia nemorosa* L. (Clusiaceae). The dried and powdered roots of *Clusia nemorosa* were extracted with *n*-hexane and ethanol. The ethanol extract was concentrated to obtain a participate which was filtered and recrystallized with ethanol to yield the pure betulinic acid.

Botanical sources of betulinic acid: Some other sources of betulinic acid are presented in Table-1.

REFERENCES

1. Y. Kashiwada, H.K. Wang, T. Nagao, S. Kitanaka, I. Yasuda, T. Fujioka, T. Yamagishi, L.M. Cosentino, M. Kozuka, H. Okabe, Y. Ikeshiro, C.Q. Hu, E. Yeh and K.H. Lee, *J. Nat. Prod.*, **61**, 1090 (1998).
2. T. Fujioka, Y. Kashiwada, R.E. Kilkuskie, L.M. Cosentino, L.M. Ballas, J.B. Jiang, W.P. Janzen, I.S. Chen and K.H. Lee, *J. Nat. Prod.*, **57**, 243 (1994).
3. C. Chandramu, R.D. Manohar, D.G. Krupadanam and R.V. Dashavantha, *Phytother. Res.*, **17**, 129 (2003).
4. W. Schühly, J. Heilmann, I. Callis and O. Sticher, *Planta Med.*, **65**, 740 (1999).
5. G. Bringmann, W. Saeb, L.M. Assi, G. Francois, A.S.S. Narayanan, K. Peters and E.M. Peters, *Planta Med.*, **63**, 255 (1997).
6. S. Alakurtti, T. Mäkelä, S. Koskimies and Y.J. Kauhaluoma, *Eur. J. Pharm. Sci.*, **29**, 1 (2006).
7. P. Bernard, T. Scior, B. Didier, M. Hibert and J. Berthon, *Phytochemistry*, **58**, 865 (2001).
8. A.I. Huguet, M.D.C. Recio, S. Manez, R.M. Giner and J.L. Rios, *Eur. J. Pharmacol.*, **410**, 69 (2000).
9. P.K. Mukherjee, K. Saha, J. Das, M. Pal and B.P. Saha, *Planta Med.,* **63**, 367 (1997).
10. N.M. Enwerem, J.I. Okogun, C.O. Wambebe, D.A. Okorie and P.A. Akah, *Phytomedicine*, **8**, 112 (2001).
11. K. Kinoshita, M. Akiba, M. Saitoh, Y. Ye, K. Koyama, K. Takahashi, N. Kondo and H. Yuasa, *Pharm. Biol.*, **36**, 50 (1998).
12. S.Y. Ryu, C.K. Lee, J.W. Ahn, S.H. Lee and O.P. Zee, *Arch. Pharmacol. Res.*, **16**, 339 (1993).
13. S.Y. Ryu, C.K. Lee, C.O. Lee, H.S. Kim and O.P. Zee, *Arch. Pharmacol. Res.*, **15**, 242 (1992).
14. V. Zuco, R. Supino, S.C. Righetti, L. Cleris, E. Marchesi, C. Gambacorti-Passerini and F. Formelli, *Cancer Lett.*, **175**, 17 (2002).
15. S. Fulda and K.M. Debatin, *Med. Pediatr. Oncol.*, **35**, 616 (2000).
16. S. Fulda, I. Jeremias, H.H. Steiner, T. Pietsch and K.M. Debatin, *Int. J. Cancer*, **82**, 435 (1999).
17. E. Pisha, H. Chai, I.S. Lee, T.E. Chagwedera, N.R. Farnsworth, A.C. Cordell, C.W.W. Beecher, H.H.S. Fong, A.D. Kinghorn, D.M. Brown, M.C. Wani, M.E. Wall, T.J. Hieken, T.K. Das Gupta and J.M. Pezzuto, *Nat. Med.*, **1**, 1046 (1995).
18. J.S. Kessler, F.B. Mullauer, G.M. de Roo and J.P. Medema, *Cancer Lett.*, **25**, 132 (2007).
19. R.H. Cichewicz and S.A. Kouzi, *Med. Res. Rev.*, **24**, 90 (2004).
20. D.A. Eiznhamer and Z.-Q. Xu, *I. Drugs*, **7**, 359 (2004).
21. T. Galgon, D. Hoke and B. Drager, *Phytochem. Anal.*, **10**, 187 (1999).
22. B.J.W. Cole, M.D. Bentley and Y. Hua, *Holzforschung*, **45**, 265 (1991).
23. M.M. O'Connell, M.D. Bently, C.S. Campbell and B.J.W. Cole, *Phytochemistry*, **27**, 2175 (1998).
24. S.G. Jagadeesh, G.L.D. Krupadanam, G. Srimannarayana, S.S. Murthy, A. Kaur and S.S. Raja, *J. Agr. Food Chem.*, **46**, 2797 (1998).
25. C.W. Chang, T.S. Wu, Y.S Hsieh, S.C. Kuo and P.D.L. Chao, *J. Nat. Prod.*, **62**, 327 (1999).
26. M. Higa, K. Ogihara and S. Yogi, *Chem. Pharm. Bull*., **46**, 1189 (1998).
27. P. Singh and S. Sharma, *J. Indian Chem. Soc*., **74**, 504 (1997).
28. M.C. Recio, R.M. Giner, S. Manez, J. Gueho, H.R. Julien, K. Hostettmann and J.L. Rios, *Planta Med.*, **61**, 9 (1995).
29. Z. Zhang, H.N. Elsohly, M.R. Jacob, D.S. Pasco, L.A. Walker and A.M. Clark, *Planta Med.*, **68**, 49 (2002).
30. R. Krogh, R. Kroth, C. Berti, A.O. Madeira, M.M. Sourza, V. Cechinel-Felho, F. Delle-Monache and R.A. Yunes, *Pharmazie*, **54**, 464 (1999).
31. Wang, C. Li, J.-C. Li and W. Xiao, *Chin. Tradit. Herbal Drugs*, **42**, 856 (2011).
32. L. Saaby, L. Moesby, E.W. Hansen and S.B. Christensen, *Phytother. Res.*, **25**, 195 (2011).
33. J.P. Benincá, J.B. Dalmarco, M.G. Pizzolatti and T.S. Fröde, *Food Chem.*, **124**, 468 (2011).
34. H.C. Lin, H.Y. Ding and Y.C. Wu, *J. Nat. Prod.*, **61**, 343 (1998).
35. C.R. Wu, U.C. Hseu, J.C. Lien, L.W. Lin, Y.T. Lin and H. Ching, *Molecules*, **16**, 1 (2011).
36. A. Guinda, M. Rada, T. Delgado and J.M. Castellano, *J. Lipid Sci. Tech.*, **113**, 231 (2011).
37. V. Viji, B. Shobha, S.K. Kavitha, M. Ratheesh, K. Kripa and A. Helen, *Int. Immunopharmacol.*, **10**, 843 (2010).
38. D. Kumar, S. Mallick, J.R. Vedasiromoni and B.C. Pal, *Phytomedicine*, **17**, 431 (2010).
39. D.B. Domínguez-Carmona, F. Escalante-Erosa, K. García-Sosa, G. Ruiz-Pinell, D. Gutierrez-Yapu, M.J. Chan-Bacab, A. Giménez-Turba and M.L. Peña-Rodríguez, *Phytomedicine*, **17**, 379 (2010).
40. R. Subramanyam, A. Gollapudi, P. Bonigala, M. Chinnaboina and D.G. Amooru, *J. Photochem. Photobiol. B*, **94**, 8 (2009).
41. Y.J. Choi, M. Na, I.H. Hwang, S.H. Lee, E.Y. Bae, B.Y. Kim and J.S. Ahn, *Molecules*, **14**, 266 (2009).
42. B. Nyasse, J.J. Nono, Y. Nganso, I. Ngantchou and B. Schneider, *Fitoterapia*, **80**, 32 (2009).
43. C.L. De Melo, M.G.R. Queiroz, A.C.V. Arruda Filho, A.M. Rodrigues, D.F. De Sousa, J.G.L. Almeida, O.D.L. Pessoa, E.R Silveira, D.B. Menezes, T.S. Melo, F.A. Santos and A.V.S. Rao, *J. Agric. Food Chem.*, **57**, 8776 (2009).
44. A.M. Zaghloul, A.A. Gohar, M.M. Ahmad, H.N. Baraka and A.A. El-Bassuony, *Nat. Prod. Res.*, **25**, 68 (2011).
45. L.-P. Lin, W. Qu and J.-Y. Liang, *Chin. J. Nat. Med.*, **9**, 176 (2011).
46. S.A. Mahera, V.U. Ahmad, S.M. Saifullah, F.V. Mohammad and K. Ambreen, *Pak. J. Bot.*, **43**, 1417 (2011).
47. H.M.P. Poumale, V.V.B.S. Djoumessi, B. Ngameni, L.P. Sandjo, B.T. Ngadjui and Y. Shiono, *Acta Chim. Slov.*, **58**, 81 (2011).
48. H.M.P. Poumale, D. Amadou, Y. Shiono, G.D.W.F. Kapche and B.T. Ngadjui, *Asian J. Chem.*, **23**, 525 (2011).
49. X. Wu, R. Chen, D. Fang, Q. Huang, T. Huang, J. Chen and X. Chen, *Chin. J. Appl. Environ. Biol.*, **17**, 24 (2011).
50. D. Abdessemed, N. Alloui and A. Dibi, *Asian J. Chem.*, **23**, 609 (2011).
51. H.-B. Hu, X.-D. Zheng, J.-H. Zhu, Y. Li and X.-W. Zhang, *Chin. Pharm. J.*, **46**, 252 (2011).
52. G.D.F. Lemes, P.H. Ferri and M.N. Lopes, *Quim. Nova.*, **34**, 39 (2011).

53. R.M.A. Domingues, G.D.A. Sousa, C.S.R. Freire and A.J.D. Silvestre, *Ind. Crop. Prod.*, **31**, 65 (2010).
54. S.J. Shin, C.E. Park, N.I. Baek, I.C. Chung and C.H. Park, *Biotechnol. Bioproc. Eng.*, **14**, 140 (2009).
55. A. Theo, T. Masebe, Y. Suzuki, H. Kikuchi, S. Wada, C.L. Obi, P.O. Bessong, M. Usuzawa, Y. Oshima and T. Hattori, *Tohoku J. Exp. Med.*, **217**, 93 (2009).
56. E.E. Kovac-Bešovic, K. Duric, Z. Kalodera and E. Sofic, *Bosn. J. Basic Med. Sci.*, **9**, 31 (2009).
57. E.M. Wenzig, U. Widowitz, O. Kunert, S. Chrubasik, F. Bucar, E. Knauder and R. Bauer, *Phytomedicine*, **15**, 826 (2008).
58. D.Z.L. Bastos, I.C. Pimentel, D.A. De Jesus and B.H. De Oliveira, *Phytochemistry*, **68**, 834 (2007).
59. G. Zhao, W. Yan and D. Cao, *J. Pharm. Biomed. Anal.*, **43**, 959 (2007).
60. V. Reutrakul, W. Chanakul, M. Pohmakotr, T. Jaipetch, C. Yoosook, J. Kasisit, C. Napaswat, T. Santisuk, S. Prabpai and P. Kongsaeree, *Planta Med.*, **72**, 1433 (2006).
61. M. Laszczyk, S. Jäger, B. Simon-Haarhaus, A. Scheffler and C.M. Schempp, *Planta Med.*, **72**, 1389 (2006).
62. M.E. Haque, H.U. Shekhar, A.U. Mohamad, H. Rahman, A.K.M.M. Islam and M.S. Hossain, *J. Pharm. Sci.*, **3**, 53 (2006).
63. S.I. Pereira, C.S.R. Freire, C.P. Neto, A.J.D. Silvestre and A.M.S. Silva, *Phytochem. Anal.,* **16**, 364 (2005).
64. M.S. Rahman, R. Chowdhury, B. Begum, K.M. Rahman and M.A. Rashid, *J. Pharm. Sci.*, **4**, 73 (2005).
65. S.I. Wada and R. Tanaka, *Chem. Biodivers.*, **2**, 689 (2005).
66. L. Fu, S. Zhang, N. Li, J. Wang, M. Zhao, J. Sakai, T. Hasegawa, T. Mitsui, Kataoka, S. Oka, M. Kiuchi, K. Hirose and M. Ando, *J. Nat. Prod.*, **68**, 198 (2005).
67. H. Liu, S. Wang, B. Cai and X. Yao, *Physiol. Biochem.*, **42**, 475 (2004).
68. D.E.B. Isaias, R. Niero, V.F. Noldin, F. de Campos-Buzzi, R.A. Yunes, F. Delle-Monache and V. Cechinel-Filho, *Pharmazie*, **59**, 879 (2004).
69. A.M. Salama, S. Gamboa and G. Buitrago, *Cienc. Quim. Farm.*, **33**, 156 (2004).
70. G.M. Woldemichael, M.P. Singh, W.M. Maiese and B.N.Z. Timmermann, *Z. Naturforsch.*, **58c**, 70 (2003).
71. H.C. Kwon, Y.D. Min, K.R. Kim, E.J. Bang, C.S. Lee and K.R. Lee, *Arch. Pharm. Res.*, **26**, 275 (2003).
72. C.V.S. Prakash, J.K. Schilling, R.K. Johnson and D.G. Kingston, *J. Nat. Prod.*, **66**, 419 (2003).
73. D.K. Kim, I.Y. Nam, J.W. Kim, T.Y. Shin and J.P. Lim, *Arch. Pharm. Res.*, **25**, 617 (2002).
74. K. Yamashita, H. Lu, J. Lu, G. Chen, T. Yokoyama, Y. Sagara, M. Manabe and H. Kodama, *Clin. Chim. Acta*, **325**, 91 (2002).
75. C.S.R. Freire, A.J.D. Silvestre, C.P. Neto and J.A.S. Cavaleiro, *Holzforschung*, **56**, 372 (2002).
76. B.H. De Oliveira, C.A. Santos and A.P. Espindola, *Phytochem. Anal.*, **13**, 95 (2002).
77. Y. Tezuka, P. Stampoulis, A.H. Banskota, S. Awale, K.Q. Tran, I. Saiki and S. Kadota, *Chem. Pharm. Bull.*, **48**, 1711 (2000).
78. W.N. Setzer, M.C. Setzer, R.B. Bates and B.R. Jackes, *Planta Med.*, **66**, 176 (2000).
79. B.S. Siddiqui, I. Sultana and S. Begum, *Phytochemistry*, **54**, 861 (2000).
80. Y.K. Kim, S.K. Yoon and S.Y. Ryu, *Planta Med.*, **66**, 485 (2000).
81. J.H. Yi, G.L. Zhang, B.G. Li and Y.Z. Chen, *Phytochemistry*, **53**, 1001 (2000).
82. A.H. Banskota, Y. Tezuka, I.K. Adnyana, Q. Xiong, K. Hase, K.Q. Tran, K. Tanaka, I. Saiki and S. Kadota, *Biol. Pharm. Bull.*, **23**, 456 (2000).
83. J.C. Steele, D.C. Warhurst, G.C. Kirby and M.S. Simmonds, *Phytother. Res.*, **13**, 115 (1999).
84. S.C. Hess and F.D. Monache, *J. Braz. Chem. Soc.*, **10**, 104 (1999).
85. J. Ma, S.R. Starck and S.M. Hecht, *J. Nat. Prod.*, **62**, 1660 (1999).
86. F. Ahmad, J. Omar and A.M. Ali, *Ultra Science*, **11**, 357 (1999).
87. X. Guo, L. Zhang, S. Quan, Y. Hong, L. Sun and M. Liu, *Zhongguo Zhong Yao Za Zhi*, **23**, 546 (1998).
88. K. Kamiya, K. Yoshioka, Y. Saiki, A. Ikuta and T. Satake, *Phytochemistry*, **44**, 141 (1997).
89. F. Ahmad, V.U. Hassan, R. Zakaria and J. Ali, *Orient. J. Chem.*, **13**, 231 (1997).
90. A. Ikuta, K. Kamiya, T. Satake and Y. Saiki, *Phytochemistry*, **38**, 1203 (1995).