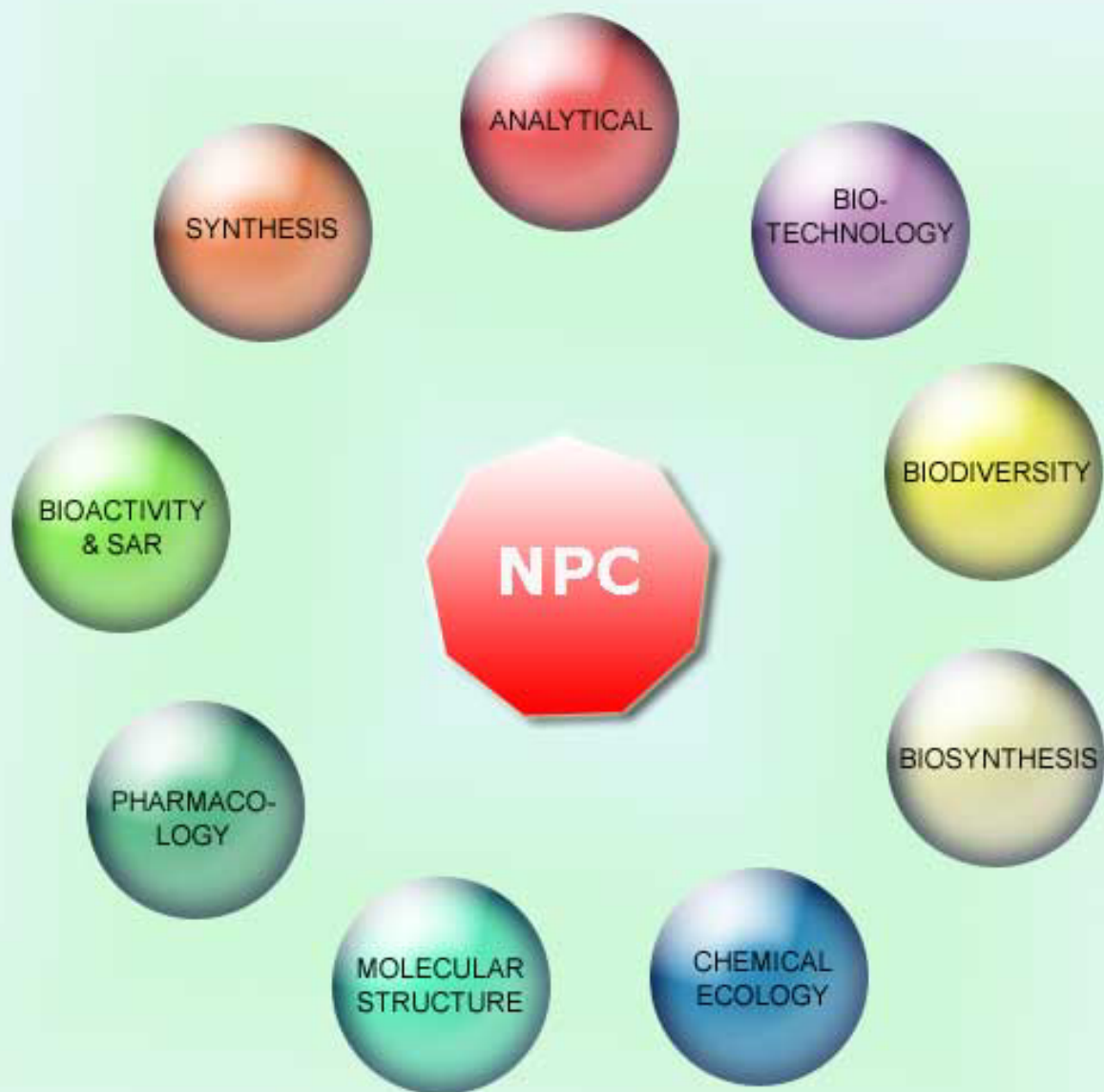


# NATURAL PRODUCT COMMUNICATIONS

An International Journal for Communications and Reviews Covering all  
Aspects of Natural Products Research



Volume 4. Issue 6. Pages 749-888. 2009  
ISSN 1934-578X (printed); ISSN 1555-9475 (online)  
[www.naturalproduct.us](http://www.naturalproduct.us)

# NPC

# Natural Product Communications

## EDITOR-IN-CHIEF

### DR. PAWAN K AGRAWAL

Natural Product Inc.  
7963, Anderson Park Lane,  
Westerville, Ohio 43081, USA  
agrawal@naturalproduct.us

## EDITORS

### PROFESSOR ALESSANDRA BRACA

Dipartimento di Chimica Bioorganica e Biofarmacia,  
Università di Pisa,  
via Bonanno 33, 56126 Pisa, Italy  
braca@farm.unipi.it

### PROFESSOR DEAN GUO

State Key Laboratory of Natural and Biomimetic Drugs,  
School of Pharmaceutical Sciences,  
Peking University,  
Beijing 100083, China  
gda5958@163.com

### PROFESSOR J. ALBERTO MARCO

Departamento de Química Orgánica,  
Universidad de Valencia,  
E-46100 Burjassot, Valencia, Spain  
alberto.marco@uv.es

### PROFESSOR YOSHIHIRO MIMAKI

School of Pharmacy,  
Tokyo University of Pharmacy and Life Sciences,  
Horinouchi 1432-1, Hachioji, Tokyo 192-0392, Japan  
mimaki@ps.toyaku.ac.jp

### PROFESSOR STEPHEN G. PYNE

Department of Chemistry  
University of Wollongong  
Wollongong, New South Wales, 2522, Australia  
spyne@uow.edu.au

### PROFESSOR MANFRED G. REINECKE

Department of Chemistry,  
Texas Christian University,  
Forts Worth, TX 76129, USA  
m.reinecke@tcu.edu

### PROFESSOR WILLIAM N. SETZER

Department of Chemistry  
The University of Alabama in Huntsville  
Huntsville, AL 35809, USA  
wsetzer@chemistry.uah.edu

### PROFESSOR YASUHIRO TEZUKA

Institute of Natural Medicine  
Institute of Natural Medicine, University of Toyama,  
2630-Sugitani, Toyama 930-0194, Japan  
tezuka@innm.u-toyama.ac.jp

### PROFESSOR DAVID E. THURSTON

Department of Pharmaceutical and Biological Chemistry,  
The School of Pharmacy,  
University of London, 29-39 Brunswick Square,  
London WC1N 1AX, UK  
david.thurston@pharmacy.ac.uk

## HONORARY EDITOR

### PROFESSOR GERALD BLUNDEN

The School of Pharmacy & Biomedical Sciences,  
University of Portsmouth,  
Portsmouth, PO1 2DT U.K.  
axuf64@dsl.pipex.com

## ADVISORY BOARD

Prof. Berhanu M. Abegaz  
Gaborone, Botswana

Prof. Viqar Uddin Ahmad  
Karachi, Pakistan

Prof. Øyvind M. Andersen  
Bergen, Norway

Prof. Giovanni Appendino  
Novara, Italy

Prof. Yoshinori Asakawa  
Tokushima, Japan

Prof. Lee Banting  
Portsmouth, U.K.

Prof. Anna R. Bilia  
Florence, Italy

Prof. Maurizio Bruno  
Palermo, Italy

Prof. Josep Coll  
Barcelona, Spain

Prof. Geoffrey Cordell  
Chicago, IL, USA

Prof. Samuel Danishefsky  
New York, NY, USA

Prof. Duvvuru Gunasekar  
Tirupati, India

Prof. A.A. Leslie Gunatilaka  
Tucson, AZ, USA

Prof. Stephen Hanessian  
Montreal, Canada

Prof. Kurt Hostettmann  
Lausanne, Switzerland

Prof. Martin A. Iglesias Arteaga  
Mexico, D. F., Mexico

Prof. Jerzy Jaroszewski  
Copenhagen, Denmark

Prof. Leopold Jirovetz  
Vienna, Austria

Prof. Teodoro Kaufman  
Rosario, Argentina

Prof. Norbert De Kimpe  
Gent, Belgium

Prof. Hartmut Laatsch  
Gottingen, Germany

Prof. Marie Lacaille-Dubois  
Dijon, France

Prof. Shoen-Sheng Lee  
Taipei, Taiwan

Prof. Francisco Macias  
Cadiz, Spain

Prof. Anita Marsaioli  
Campinas, Brazil

Prof. Imre Mathe  
Szeged, Hungary

Prof. Joseph Michael  
Johannesburg, South Africa

Prof. Ermino Murano  
Trieste, Italy

Prof. Virinder Parmar  
Delhi, India

Prof. Luc Pieters  
Antwerp, Belgium

Prof. Om Prakash  
Manhattan, KS, USA

Prof. Peter Proksch  
Düsseldorf, Germany

Prof. Satyajit Sarker  
Wolverhampton, UK

Prof. Raffaele Riccio  
Salerno, Italy

Prof. Monique Simmonds  
Richmond, UK

Prof. Valentin Stonik  
Vladivostok, Russia

Prof. Hiromitsu Takayama  
Chiba, Japan

Prof. Karen Valant-Vetschera  
Vienna, Austria

Prof. Peter G. Waterman  
Lismore, Australia

Prof. Paul Wender  
Stanford, USA

## INFORMATION FOR AUTHORS

Full details of how to submit a manuscript for publication in Natural Product Communications are given in Information for Authors on our Web site <http://www.naturalproduct.us>.

Authors may reproduce/republish portions of their published contribution without seeking permission from NPC, provided that any such republication is accompanied by an acknowledgment (original citation)-Reproduced by permission of Natural Product Communications. Any unauthorized reproduction, transmission or storage may result in either civil or criminal liability.

The publication of each of the articles contained herein is protected by copyright. Except as allowed under national "fair use" laws, copying is not permitted by any means or for any purpose, such as for distribution to any third party (whether by sale, loan, gift, or otherwise); as agent (express or implied) of any third party; for purposes of advertising or promotion; or to create collective or derivative works. Such permission requests, or other inquiries, should be addressed to the Natural Product Inc. (NPI). A photocopy license is available from the NPI for institutional subscribers that need to make multiple copies of single articles for internal study or research purposes.

**To Subscribe:** Natural Product Communications is a journal published monthly. 2009 subscription price: US\$1,695 (Print, ISSN# 1934-578X); US\$1,395 (Web edition, ISSN# 1555-9475); US\$2,095 (Print + single site online). Orders should be addressed to Subscription Department, Natural Product Communications, Natural Product Inc., 7963 Anderson Park Lane, Westerville, Ohio 43081, USA. Subscriptions are renewed on an annual basis. Claims for nonreceipt of issues will be honored if made within three months of publication of the issue. All issues are dispatched by airmail throughout the world, excluding the USA and Canada.

## Cytotoxic Action of Triterpene Glycosides from Sea Cucumbers from the genus *Cucumaria* on Mouse Spleen Lymphocytes. Inhibition of Nonspecific Esterase

Dmitry L. Aminin<sup>a</sup>, Alexandra S. Silchenko<sup>a</sup>, Sergey A. Avilov<sup>a</sup>, Vadim G. Stepanov<sup>b</sup> and Vladimir I. Kalinin<sup>a,\*</sup>

<sup>a</sup>Pacific Institute of Bioorganic Chemistry, Vladivostok, 690022, Russian Federation

<sup>b</sup>Kamchatka Department of the Pacific Institute of Geography, Petropavlovsk-Kamchatsky, 683000, Russian Federation

kalininv@piboc.dvo.ru

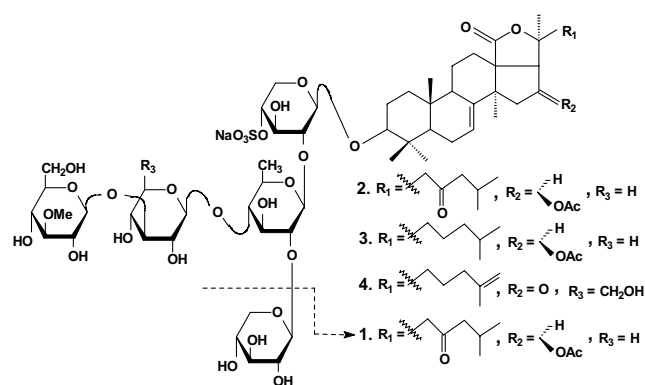
Received: February 25<sup>th</sup>, 2009; Accepted: March 22<sup>nd</sup>, 2009

Four triterpene glycosides from sea cucumbers belonging to the genus *Cucumaria*, okhotoside A<sub>1</sub>-1 (**1**), cucumarioside A<sub>0</sub>-1 (**2**), frondoside A (**3**) and cucumarioside A<sub>2</sub>-2 (**4**) inhibit the activity of nonspecific esterase of mouse spleen lymphocytes. The dependence of the inhibitory activity of the glycosides on their structure is similar to that for hemolytic activity. The absence of inhibitory activity for the preparation Cumaside, which is a complex of cucumarioside A<sub>2</sub>-2 and related compounds with cholesterol, shows a cholesterol-dependent character of the inhibitory action of the glycosides. The effective inhibitory concentrations of frondoside A and cucumarioside A<sub>2</sub>-2 are significantly higher than the immunomodulatory doses of these glycosides.

**Keywords:** Lymphocytes, cytotoxicity, triterpene glycosides, sea cucumber, *Cucumaria*, nonspecific esterase.

Triterpene glycosides from sea cucumbers (Holothurioidea, Echinodermata) possess a wide spectrum of biological activities caused by their ability to form complexes with cholesterol and other 5,6-unsaturated sterols followed by formation of single ion channels and large pores in cell membranes, depending on concentration. Most of these substances are strong membranolytic agents and have, for example, antifungal and hemolytic activities, are ichthyotoxic, and are cytotoxic to tumor cells [1]. The different kinds of biological activities caused by membranolytic action similarly depend on glycoside structure [1–5]. This dependence may be relatively easily predicted [6].

Recently, biological activities of sea cucumber triterpene glycosides in sub-toxic doses that may not be caused by their interaction with cholesterol have attracted considerable attention. The specific interest is in the action of the glycosides as modulators of cell-immunity. Indeed sub-toxic dosages of cucumarioside A<sub>2</sub>-2 and other



**Figure 1:** Chemical structures of : **1** – okhotoside A<sub>1</sub>-1 from *Cucumaria okhotensis* [14]; **2** – cucumarioside A<sub>0</sub>-1 from *C. okhotensis* [14]; **3** – frondoside A from *C. okhotensis* [16]; **4** – cucumarioside A<sub>2</sub>-2 from *C. japonica* [17].

monosulfated glycosides from the Far Eastern sea cucumber *Cucumaria japonica* increased lysosomal activity of mouse peritoneal macrophages both *in vivo* and *in vitro* [7,8]. Frondoside A from *C. frondosa* also increased lysosomal activity of

macrophages, and stimulated macrophage phagocytosis and ROS formation in the macrophages [9]. Moreover, the compound increased lymphocyte formation in mouse spleen [9]. The preparation Cumaside, which is a complex of cucumarioside A<sub>2</sub>-2 and other monosulfated glycosides with cholesterol, increases lysosomal activity of macrophages and stimulates phagocytosis and ROS formation in macrophages [10]. Cumaside in doses of 0.1–1 µg/mL may restore the level of CD3, CD4 and CD8-antigenes of human blood lymphocytes decreased by pre-incubation of these lymphocytes with the immunodepressant, hydrocortisone [10].

Hence it is of interest to obtain information about the character of the cytotoxic action of glycosides from the sea cucumbers of the genus *Cucumaria* against lymphocytes. To study cytotoxic activity we have chosen hydrolysis of fluorescein diacetate (FDA) with nonspecific esterase, which produces the easily measured fluorescein. This procedure is a simple and convenient method to estimate viability i.e. general level of metabolic activity for different kinds of cells [11], including lymphocytes [12].

The series of monosulfated glycosides isolated from sea cucumbers of the genus *Cucumaria*, having similar structures distinguished only by small differences in the carbohydrate chains and aglycones, was chosen for studying the character of the cytotoxic activity (Figure 1).

Using the procedure of lysosome staining with a molecular probe followed by quantitative analysis of cell fluorescence it was shown that glycosides **1–4** inhibit the activity of nonspecific esterase in mouse spleen lymphocytes. However, Cumaside, which has immunomodulatory action comparable to that of glycoside **4**, showed no nonspecific esterase inhibition in doses of 50 µg/mL (Table 1).

The effective immunomodulatory doses *in vitro* for frondoside A (**3**), cucumarioside A<sub>2</sub>-2 (**4**), and preparation Cumaside do not exceed 0.1–1 µg/mL [7–10]. The obtained results showed that the cytotoxic activity of the glycosides having evident immunomodulatory activity against immune cells occurred in concentrations significantly higher than the immunomodulatory doses. An immunomodulatory preparation, Cumaside showed no cytotoxic activity at a concentration of 50 µg/mL. This indicates a cholesterol-dependent cytotoxic action of these glycosides against immune cells.

**Table 1:** Influence of triterpene glycosides on activity of nonspecific esterase of mouse spleen lymphocytes.

Substance	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>	Cumaside
EC <sub>50</sub> (µg/mL)	2.4	4.1	5.0	8.0	No activity

The monosulfated tetraoside, okhotoside A<sub>1</sub>-1 (**1**) differs from the monosulfated pentaoside, cucumarioside A<sub>0</sub>-1 (**2**) only by the absence of a terminal xylose residue attached to a quinovose residue. Studies of hemolytic activity have shown that ED<sub>50</sub> values for linear tetraosides are three times less than those for glycosides having an additional xylose residue attached to the second monosaccharide residue, quinovose [4]. Hence the stronger cytotoxic action of glycoside **1** against lymphocytes in comparison with glycoside **2** correlates very well with the data on hemolytic activity.

Cucumarioside A<sub>0</sub>-1 (**2**) is very similar to frondoside A (**3**) in structure, but differs by the presence of a keto-group at C-23 of the aglycone. Nevertheless, even such a small difference causes higher cytotoxic activity of glycoside **2** against lymphocytes than that of glycoside **3**. This indicates some contribution of the 23-keto-group in cytotoxic activity.

Frondoside A (**3**) differs from cucumarioside A<sub>2</sub>-2 (**4**) by the presence of an acetate group at C-16 instead of a keto-group. Moreover, the aglycone of cucumarioside A<sub>2</sub>-2 has a 25(26)-terminal double bond in the side chain and glucose instead of xylose as the third monosaccharide residue. Frondoside A has about three times higher hemolytic activity (three times lesser ED<sub>50</sub>) than cucumarioside A<sub>2</sub>-2. [4,5]. Hence the stronger cytotoxic action of frondoside A against lymphocytes compared with that of cucumarioside A<sub>2</sub>-2 correlates very well with the data on hemolytic activity.

The hemolytic activity (ED<sub>50</sub>) of cucumarioside A<sub>2</sub>-2 (**4**) is about 2.5 µg/mL, but the corresponding activity for Cumaside is about 50 µg/mL [10]. There also is some correlation between cytotoxic activity against lymphocytes and hemolytic activity.

Hence the cytotoxic activity of these substances against lymphocytes occurs at doses significantly higher than their immunomodulatory doses (about 50–100 times). The dependence of inhibition of nonspecific esterase on glycoside structure is similar to that for the hemolytic activity of these substances

and their structure. This observation and the cholesterol-dependent nature of inhibition of nonspecific esterase of lymphocytes by glycosides in cytotoxic concentrations indicate that the action of sea cucumber glycosides against lymphocytes in cytotoxic doses has the common membranolytic mode for this class of substances. The results confirm that data on dependence of activity of sea cucumber glycosides on their structure obtained for one kind of cells (for example, erythrocytes, fungal, tumor, sea urchin eggs) may be used to predict their cytotoxic action against other kinds of cells if sterol-dependent membranolytic activity is involved [6].

### Experimental

**Triterpene glycosides:** Okhotosides A<sub>1</sub>-1 (**1**) and cucumarioside A<sub>0</sub>-1 (**2**), previously reported for *C. japonica* [13], were isolated from *C. okhotensis* [14]. Frondoside A, reported for *C. frondosa* [15], was isolated from *C. okhotensis* [16]. Cucumarioside A<sub>2</sub>-2 (**4**) was isolated from *C. japonica* [17]. All the glycosides were individual compounds, as shown by HPLC data and <sup>13</sup>C NMR spectra. The glycoside structures are presented in Figure 1. Cumaside, a complex of monosulfated glycosides from *C. japonica* and cholesterol (1:2 molar ratio) was produced by a published method [10]. The glycoside / cholesterol molar ratio was checked by the ratio of the signals of methyl groups of cholesterol and aglycones in the <sup>1</sup>H NMR spectrum of Cumaside in C<sub>5</sub>D<sub>5</sub>N.

**Lymphocytes:** The total fraction of mouse lymphocytes (spleenocytes) was isolated from the spleen of BALB/C line mice. The spleen was

homogenized in PSB solution (pH 7.4) and the cell suspension filtered through nylon voile (280 mesh). The suspension of spleenocytes was washed three times with PSB (pH 7.4) and centrifuged (1500 rpm for 5 min) to remove debris and re-suspended in PSB to make the final cell concentration 2–5×10<sup>6</sup> cells/mL.

### Determination of activity of nonspecific esterase:

The test substance solution (10 µL) and 100 µL of cell suspension was placed in each of a 96-hole plate, which was incubated in a thermostat at 37°C for 1 h. A stock solution of probe fluorescein diacetate (FDA, Sigma) in DMSO (1 mg/mL) was prepared. After incubation of the cells with the test compound, 10 µL FDA solution (50 µg/mL) was added into each hole and the plate was incubated in a thermostat at 37°C for 15 min. Fluorescence was measured with a plate reader (Fluoroskan Ascent) at λ<sub>ex</sub> = 485 nm and λ<sub>em</sub> = 518 nm. All experiments were repeated in triplicate. The means and standard errors for each treatment were calculated and EC<sub>50</sub> values were estimated from dose-response plots using SigmaPlot 3.02 software (Jandel Scientific, San Rafael, CA).

**Acknowledgments** – The authors acknowledge the financial support of a Grant of Presidium of the Russian Academy of Science “Basic Researches for Medicine” and Grant of the President of the Russian Federation for support of scientific schools No. NSH-2813.2008.4. The authors very much appreciate the help of Professor J.M. Lawrence, University of South Florida (Tampa, FL) for correction of the manuscript.

### References

- [1] Kalinin VI, Aminin DL, Avilov SA, Silchenko AS, Stonik VA. (2008) Triterpene glycosides from sea cucumbers (Holothurioidea, Echinodermata), biological activities and functions. In: *Studies in Natural Product Chemistry (Bioactive Natural Products)*, Vol. 35, Atta-ur-Rahman (Ed.). Elsevier Science Publisher, Amsterdam, 135–196.
- [2] Maltsev II, Stekhova SI, Schentsova EB, Anisimov MM, Stonik VA. (1985) Antimicrobial activities of the glycosides from sea cucumbers belonging to family Stichopodidae. *Khimiko-Pharmaceuticheskiy Zhurnal*, **19**, 54–56.
- [3] Kitagawa I. (1988) Research of biologically active marine natural products. *Yakugaku Zasshi*, **108**, 398–416.
- [4] Kalinin VI, Volkova OV, Likhatskaya GN, Prokofieva NG, Agafonova IG, Anisimov MM, Kalinovskiy AI, Avilov SA, Stonik VA. (1992) Hemolytic activity of triterpene glycosides from Cucumariidae family holothurians and evolution of this group of toxins. *Journal of Natural Toxins*, **1**, 17–30.
- [5] Kalinin VI, Prokofieva NG, Likhatskaya GN, Schentsova EB, Agafonova IG, Avilov SA, Drozdova OA. (1996) Hemolytic activities of triterpene glycosides from the holothurian order Dendrochirotrida: Some trends in the evolution of this group of toxins. *Toxicon*, **34**, 475–483.
- [6] Kalinin VI. (2000) System-theoretical (holistic) approach to the modelling of structural-functional relationships of biomolecules and their evolution: an example of triterpene glycosides from sea cucumbers (Echinodermata, Holothurioidea). *Journal of Theoretical Biology*, **206**, 151–168.

- [7] Aminin DL, Agafonova IG, Berdyshev EV, Isachenko EG, Avilov SA, Stonik VA. (2001) Immunomodulatory properties of cucumariosides from the edible Far-Eastern holothurian *Cucumaria japonica*. *Journal of Medicinal Food*, **4**, 127–135.
- [8] Agafonova IG, Aminin DL, Avilov SA, Stonik VA. (2003) Influence of cucumariosides upon intracellular  $[Ca^{2+}]_i$  and lysosomal activity of macrophages. *Journal of Agricultural and Food Chemistry*, **51**, 6982–6986.
- [9] Aminin DL, Agafonova IG, Kalinin VI, Silchenko AS, Avilov SA, Stonik VA, Colin PD, Woodward C. (2008) Immunomodulatory properties of frondoside A, a major triterpene glycoside from the North Atlantic commercially harvested sea cucumber *Cucumaria frondosa*. *Journal of Medicinal Food*, **11**, 443–453.
- [10] Aminin DL, Pinegin BV, Pichugina LV, Zaporozhets TS, Agafonova IG, Boguslavsky VM, Silchenko AS, Avilov SA, Stonik VA. (2006) Immunomodulatory properties of Cumaside. *International Immunopharmacology*, **6**, 1070–1082.
- [11] Chrzanowski TH, Crotty RD, Hubbard JG, Welch RP. (2005) Applicability of the fluorescein diacetate method of detecting active bacteria in freshwater. *Microbial Ecology*, **10**, 179–185.
- [12] Afrimzon E, Deutsch A, Shafran Y, Zurgil N, Sandbank J, Pappo I, Deutsch M. (2008) Intracellular esterase activity in living cells may distinguish between metastatic and tumor-free lymph nodes. *Clinical and Experimental Metastasis*, **25**, 213–224.
- [13] Drozdova OA, Avilov SA, Kalinovskiy AI, Stonik VA, Milgrom YM, Rashkes JW. (1993) New glycosides from the sea cucumber *Cucumaria japonica*. *Khimiya Prirodnih Soedinenii*, **2**, 242–248.
- [14] Silchenko AS, Avilov SA, Kalinin VI, Stonik VA, Kalinovskiy AI, Dmitrenok PS, Stepanov VG. (2007) Monosulfated triterpene glycosides from *Cucumaria okhotensis* Levin et Stepanov – new species of sea cucumbers from the Sea of Okhotsk. *Bioorganicheskaya Khimiya*, **33**, 81–90.
- [15] Girard M, Belanger J, ApSimon JW, Garneau F-X, Harvey C, Brisson J-R. (1990) Frondoside A. A novel triterpene glycoside from the holothurian *Cucumaria frondosa*. *Canadian Journal of Chemistry*, **68**, 11–18.
- [16] Silchenko AS, Avilov SA, Kalinin VI, Kalinovskiy AI, Dmitrenok PS, Fedorov SN, Stepanov VG, Dong Z, Stonik VA. (2008) Constituents of the sea cucumber *Cucumaria okhotensis*. Structures of okhotosides B<sub>1</sub>–B<sub>3</sub> and cytotoxic activities of some glycosides from this species. *Journal of Natural Products*, **71**, 351–356.
- [17] Avilov SA, Stonik VA, Kalinovskiy AI. (1990) Structure of four new triterpene glycosides from the sea cucumber *Cucumaria japonica*. *Khimiya Prirodnih Soedinenii*, **6**, 787–792.

<b>Simultaneous Quantification of Eight Major Bioactive Phenolic Compounds in Chinese Propolis by High-Performance Liquid Chromatography</b> Na Sha, Hui-Lian Huang, Jin-Qiang Zhang, Guang-Tong Chen, Si-Jia Tao, Min Yang, Xing-Nuo Li, Ping Li and De-An Guo	813
<b>Total Phenolic Content and Antioxidant Activity of Myrtle (<i>Myrtus communis</i>) Extracts</b> MahassineAmensour, Esther Sendra, Jamal Abrini, Samira Bouhdid, José Angel Pérez-Alvarez and Juana Fernández-López	819
<b>Simultaneous Determination of Oxyresveratrol and Resveratrol in Rat Bile and Urine by HPLC after Oral Administration of <i>Smilax china</i> Extract</b> Hui-lian Huang, Jin-qiang Zhang, Guang-tong Chen, Zhi-qiang Lu, Na Sha and De-an Guo	825
<b>Composition of Essential Oils from Leaves and Flowers of <i>Stachys germanica</i> subsp. <i>salviifolia</i> (Ten.) Gams (Labiatae) and Related Secretory Structures</b> Claudia Giuliani, Roberto Maria Pellegrino, Bruno Tirillini and Laura Maleci Bini	831
<b>Volatile Constituents of <i>Trifolium pratense</i> and <i>T. repens</i> from N.E. Italian Alpine Pastures</b> Aldo Tava, Daniele Ramella, Maris Grecchi, Paolo Aceto, Renato Paoletti and Efisio Piano	835
<b>Seasonal Variation and Bioactivity in the Leaf Oil of <i>Liriodendron tulipifera</i> Growing in Huntsville, Alabama</b> Sarah L. Miller, Heather E. Villanueva, Maria C. Palazzo, Brenda S. Wright and William N. Setzer	839
<b>Composition and Seasonal Variation of the Essential Oil from <i>Abies sachalinensis</i> from Hokkaido, Japan</b> Tadaaki Satou, Mariko Matsuura, Shio Murakami, Shinichiro Hayashi and Kazuo Koike	845
<b>Compositional Variation of the Essential Oils of <i>Artemisia afra</i> Jacq. from three Provinces in South Africa - A Case Study of its Safety</b> Adebola O. Oyedeki, Anthony J. Afolayan and Anne Hutchings	849
<b>Chemical Variability of Essential Oils of <i>Lippia alba</i> (Miller) N. E. Brown Growing in Costa Rica and Argentina</b> Gabriela Ricciardi, José F. Cicció, Rafael Ocampo, Daniel Lorenzo, Armando Ricciardi, Arnaldo Bandoni and Eduardo Dellacassa	853
<b>Composition and Antibacterial Activity of Essential Oils from Leaf, Stem and Root of <i>Chrysanthemum parthenium</i> (L.) Bernh. from Iran</b> Ali Shafaghat, Hajar Sadeghi and Khodamali Oji	859
<b>Antibacterial Activity and Composition of Essential Oils from Flower, Leaf and Stem of <i>Chaerophyllum macropodum</i> Boiss. from Iran</b> Ali Shafaghat	861
<b>Composition and Antimicrobial Activity of the Leaf Essential Oil of <i>Litsea nakaii</i> from Taiwan</b> Chen-Lung Ho, Eugene I-Chen Wang, Pei-Yeh Lee and Yu-Chang Su	865
<b>Chemical Composition and Antimicrobial Activity of <i>Clausena indica</i> (Dalz) Oliv. (Rutaceae) Essential Oil from Vietnam</b> Pham Thi Minh Diep, Agata Maria Pawlowska, Pier Luigi Cioni, Chau Van Minh, Le Mai Huong and Alessandra Braca	869
<b>Acetylcholinesterase Inhibition and Antioxidant Activity of Essential Oils from <i>Schinus areira</i> L. and <i>Schinus longifolia</i> (Lindl.) Speg.</b> Ana P. Murray, María S. Vela Gurovic, Silvana A. Rodriguez, María G. Murray and Adriana A. Ferrero	873
<b>Potential Anti-dementia Agents in Traditional Chinese Medicine</b> Xue-Juan Li and Hong-Yu Zhang	877

# Natural Product Communications

## 2009

Volume 4, Number 6

### Contents

<b><u>Original Paper</u></b>	<b><u>Page</u></b>
<b>Thymol-evoked Ca<sup>2+</sup> Mobilization and Ion Currents in Pituitary GH<sub>3</sub> Cells</b> Ai-Yu Shen, Mei-Han Huang, Trey-Shy Wang, Hui-Ming Wu, Ya-Fei Kang and Chi-Lan Chen	749
<b>Iridoids from <i>Spathodea campanulata</i> P. Beauvais Leaves</b> Yaser G. Gouda	753
<b>A New Longipinene Diester from <i>Stevia monardifolia</i> Kunth</b> Rodrigo E. Rojas-Pérez, Ernestina Cedillo-Portugal, Pedro Joseph-Nathan and Eleuterio Burgueño-Tapia	757
<b>A New Sesquiterpene from the Roots of <i>Vladimiria souliei</i></b> Jing Xu, Xiaojun Zhao, Yuanqiang Guo, Wenyan Gao and Shuzhong Zhang	763
<b>Asiatic Acid Derivatives Protect Primary Cultures of Rat Hepatocytes against Carbon Tetrachloride-Induced Injury via the Cellular Antioxidant System</b> Mi Kyeong Lee, Seung Hyun Kim, Hyekyung Yang, Doo-Yeon Lim, Je-Ho Ryu, Eung Seok Lee, Sang-Sup Jew, Hyeung-Guen Park, Sang Hyun Sung and Young Choong Kim	765
<b>A Minor, Sweet Cucurbitane Glycoside from <i>Siraitia grosvenorii</i></b> Zhonghua Jia and Xiaogen Yang	769
<b>Cytotoxic Action of Triterpene Glycosides from Sea Cucumbers from the genus <i>Cucumaria</i> on Mouse Spleen Lymphocytes. Inhibition of Nonspecific Esterase</b> Dmitry L. Aminin, Alexandra S. Silchenko, Sergey A. Avilov, Vadim G. Stepanov and Vladimir I. Kalinin	773
<b>Inhibition of Mast Cell Degranulation by Saponins from <i>Gleditsia sinensis</i>- Structure-activity Relationships</b> Wang Chong, Xia Yu Feng, Gao Zheng Zhen, Lu Dan and Dai Yue	777
<b>Molecular Modeling, NOESY NMR, and the Structure of Nicandrenone Isolated from <i>Nicandra physalodes</i> (Solanaceae)</b> Patrick F. Jonas and Geoffrey A. Cordell	783
<b>Analysis of <i>Salvia coccinea</i> from Jamaican Populations</b> Glenroy D. A. Martin, William F. Reynolds and Paul B. Reese	789
<b>Antimicrobial, Antiparasitic and Cytotoxic Spermine Alkaloids from <i>Albizia schimperiana</i></b> Volodymyr Samoylenko, Melissa R. Jacob, Shabana I. Khan, Jianping Zhao, Babu L. Tekwani, Jacob O. Midiwo, Larry A. Walker and Ilias Muhammad	791
<b>DMD Mediated Formal Synthesis of (±)-Coerulescine</b> Oscar R. Suárez-Castillo, Myriam Meléndez-Rodríguez, Yaneth M. A. Contreras-Martínez, Alejandro Álvarez-Hernández, Martha S. Morales-Ríos and Pedro Joseph-Nathan	797
<b>Globulixanthone F, a New Polyoxygenated Xanthone with an Isoprenoid group and two Antimicrobial Biflavonoids from the Stem Bark of <i>Symphonia globulifera</i></b> Pierre Mkounga, Zacharias T. Fomum, Michèle Meyer, Bernard Bodo and Augustin E. Nkengfack	803
<b>Cytotoxic Effect on Cancer Cells and Structural Identification of Phenols from <i>Spatholobi caulis</i> by HPLC-ESI-MS<sup>n</sup></b> Dan Lu, Hua He, Bin Wu and Shanjing Yao	809

Continued inside back cover