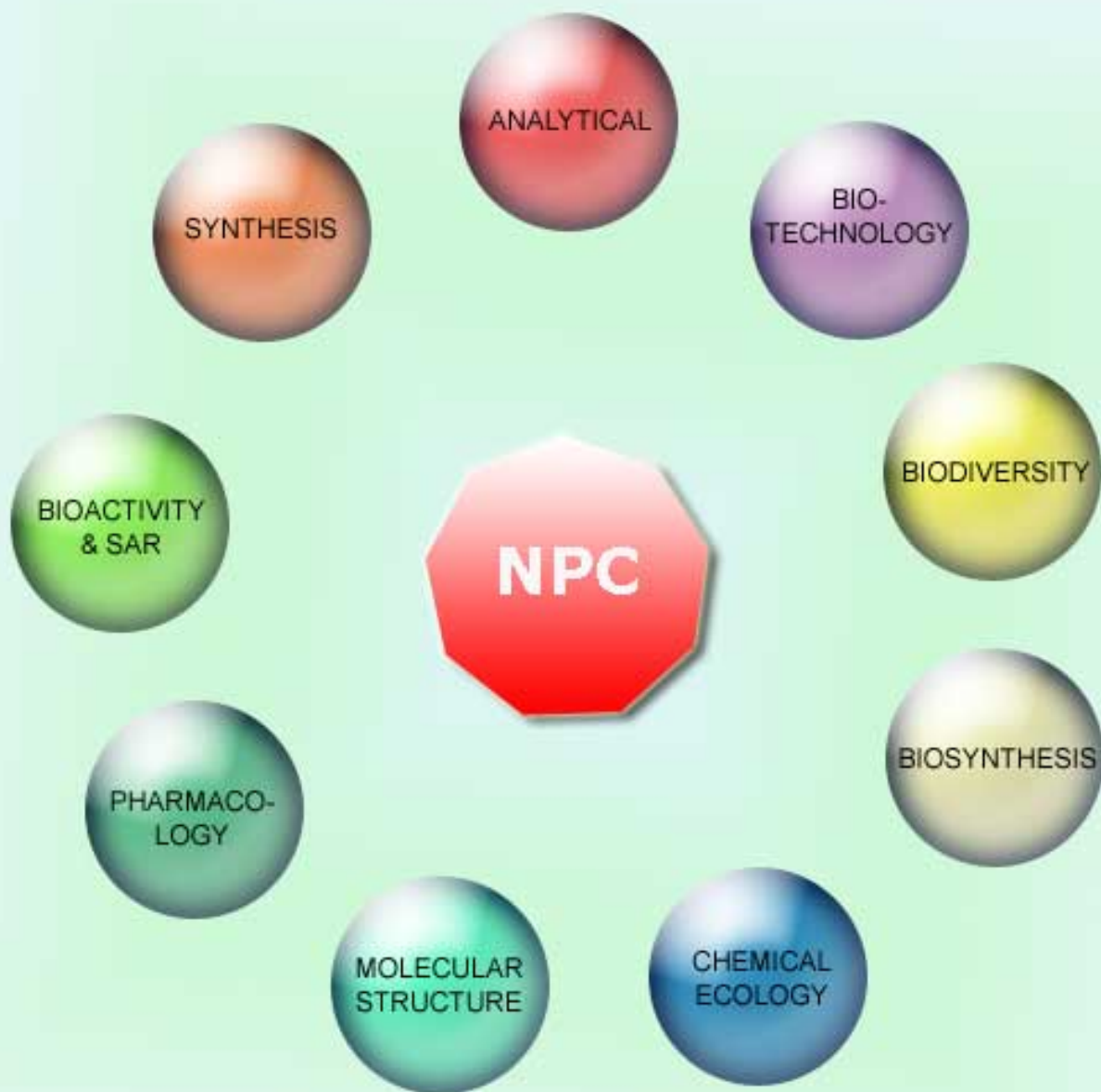


NATURAL PRODUCT COMMUNICATIONS

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



Volume 2. Issue 9. Pages 883-958. 2007
ISSN 1934-578X (printed); ISSN 1555-9475 (online)
www.naturalproduct.us

EDITOR-IN-CHIEF**DR. PAWAN K AGRAWAL**

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

EDITORS**PROFESSOR GERALD BLUNDEN**

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

PROFESSOR ALESSANDRA BRACA

Dipartimento di Chimica Bioorganica e Biofarmacia,
Universita di Pisa,
via Bonanno 33, 56126 Pisa, Italy
Email: 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 ERNST HASLINGER

Institute of Pharmaceutical Chemistry,
University of Graz,
A-8010 Graz, Austria
Ernst.Haslinger@uni-graz.at

PROFESSOR J. ALBERTO MARCO

Departamento de Química Organica,
Universidade 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
mimakiy@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 M. G. REINECKE

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

PROFESSOR YASUHIRO TEZUKA

Institute of Natural Medicine
Toyama Medical and Pharmaceutical University,
2630-Sugitani, Toyama 930-0194, Japon
tezuka@ms.toyama-mpu.ac.jp

ADVISORY BOARD

Prof. Oyvind Andersen
Bergen, Norway

Prof. Yoshinori Asakawa
Tokushima, Japan

Prof. Bruno Botta
Roma, Italy

Prof. Carlos Cerda-Garcia-Rojas
Mexico city, Mexico

Prof. Ioanna Chinou
Athens, Greece

Prof. Josep Coll
Barcelona, Spain

Prof. Geoffrey Cordell
Chicago, IL, USA

Prof. Samuel Danishefsky
New York, NY, USA

Dr. Biswanath Das
Hyderabad, India

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

Prof. Stephen Hanessian
Montreal, Canada

Prof. Michael Heinrich
London, UK

Prof. Kurt Hostettmann
Lausanne, Switzerland

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

Prof. Jerzy Jaroszewski
Copenhagen, Denmark

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. Chun-Nan Lin
Kaohsiung, china

Prof. Francisco Macias
Cadiz, Spain

Prof. Anita Marsaioli
Campinas, Brazil

Prof. Rachel Mata
Mexico D. F., Mexico

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. William Reynolds
Toronto, Canada

Prof. Raffaele Riccio
Salerno, Italy

Prof. Ricardo Riguera
Santiago de Compostela, Spain

Prof. Satyajit Sarker
Coleraine, UK

Prof. William N. Setzer
Huntsville, AL, USA

Prof. Monique Simmonds
Richmond, UK

Prof. Valentin Stonik
Vladivostok, Russia

Prof. Hermann Stuppner
Innsbruck, Austria

Prof. Apichart Suksamram
Bangkok, Thailand

Prof. Hiromitsu Takayama
Chiba, Japan

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. 2007 subscription price: US\$1,395 (Print, ISSN# 1934-578X); US\$1,095 (Web edition, ISSN# 1555-9475); US\$1,795 (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.

An *in-vivo* Study of the Immunomodulatory Activity of Coumarinolignoids from *Cleome viscosa*

Dyaneshwar U. Bawankule^a, Sunil K. Chattopadhyay^b, Anirban Pal^a, Kopal Saxena^a, Sachidanand Yadav^a, Narayan P. Yadav^a, Dayanandan Mani^a, Arun K. Tripathi^a, Salim U. Beg^a, Amit Srivastava^a, Anil K. Gupta^a and Suman Preet S Khanuja^{a*}

^aDivision of Genetic Resources and Biotechnology, CIMAP, Lucknow-15, India

^bDivision of Process and Product Development, CIMAP, Lucknow-15, India

khanujazy@yahoo.com

Received: May 13th, 2007; Accepted: June 18th, 2007

Cleome viscosa (Capparidaceae) is used in fever, inflammation and liver diseases. Systematic investigation of the seeds of this species has resulted in the isolation of three coumarinolignoids, cleomiscosin A, B and C. The present study was undertaken to determine the immunomodulatory activity of these coumarinolignoids using inbred female Swiss albino mice as an *in-vivo* study. Experimental animals were divided into six groups, each comprised of six mice. These received oral treatment for a period of 28 days. Body weight variation, and hematological, humoral and cell mediated immune response related parameters were studied in which coumarinolignoids at a dose of 10 mg/kg body weight enhanced the body immune function by significantly increasing the white blood cell count, hemagglutination antibody titer responses, and reducing delayed type hypersensitivity response towards rabbit red blood cells.

Keywords: Coumarinolignoids, *Cleome viscosa*, immunomodulation, humoral, cell-mediated, immunity.

The immune system plays a vital role as the main line of defense against infections and medicinal plants have been extensively used as a source of medicine in traditional systems of medicine to promote health and to maintain the body's resistance against infection by potentiating immunity [1]. Immunomodulation using either medicinal plant extracts or plant derived pure molecules can provide an alternative to conventional chemotherapy for a variety of diseases, especially when the host defense mechanism has to be activated under the conditions of impaired immune response.

Cleome viscosa (Capparidaceae) is an annual herb with yellow flowers and strong penetrating odor, which occurs as a weed in rain fed soils from north east to northern parts of India. In the Ayurvedic system of medicine, this plant is used in the treatment of fever, inflammation, liver diseases, bronchitis, diarrhea and infantile convulsions [2]. The seeds of this plant are widely said to be anthelmintic [3]. The rural people use the fresh juice of the crushed seed for the treatment of infantile convulsions and in mental disorders [4]. Systematic investigation of the

seeds of *C. viscosa* has resulted in the isolation of three coumarinolignoids, cleomiscosins A, B, and C [5]. *In-vivo* immunomodulatory activity of these coumarinolignoids is reported herein.

Body weight and hematological parameters: The effect of coumarinolignoids on the gain in body weights, along with hematological parameters (total RBCs and WBCs counts) were performed after 28 days oral administration of the test compounds in a dose-dependant manner. The rate of gain in body weight was found to be significantly higher in coumarinolignoids (30 and 100 mg/kg) and levamisole hydrochloride treated groups when compared with vehicle control. Significant difference was not observed in total RBC counts, but total WBC counts were significantly increased in the coumarinolignoids and levamisole hydrochloride treated groups and, conversely, significant decreases in total WBCs were observed in the cyclophosphamide monohydrate treated group when compared with vehicle control. The corresponding data are shown in Table 1.

Table 1: Effect of coumarinolignoids on rate of body weight gain and hematological parameters after 28 days oral administration.

Treatment	Humoral Immunity	Cell-mediated Immunity
	Antibody Titer (wells) (Mean±SE)	Foot Thickness (arbitrary unit) (Mean±SE)
Vehicle Control	3.71±0.57	0.028±0.003
Coumarinolignoids (10 mg/kg)	7.6±0.91*	0.023±0.007*
Coumarinolignoids (30 mg/kg)	7.14±0.57*	0.02±0.004*
Coumarinolignoids (100 mg/kg)	7.17±0.95*	0.018±0.005*
Levamisole (0.68 mg/kg)	7.17±0.47*	0.029±0.009*
Cyclophosphamide (200 mg/kg)	1±0.29 ^a	0.019±0.005*

n=06, P<0.05, using student's *t* test (Vehicle Control vs Treatment)* Significantly increased, ^aSignificantly decreased

Rabbit red blood corpuscles (RRBCs) isolated from New Zealand white rabbits were used as antigen. Blood was collected from the central artery of the ear and mixed with an anticoagulant, heparin. Blood was immediately centrifuged at 2000 rpm at 4°C for 10 minutes and the supernatant containing the plasma was discarded. The pellets containing the RRBCs were resuspended in an equal volume of Alsever's solution of the following composition, dextrose (2.05 g), sodium citrate (0.80 g), and sodium chloride (0.42 g) in 100 mL distilled water, and centrifuged again following the discarding of the supernatant. The process of washing was repeated 3 times before suspending the RRBCs in sterile normal saline to make it a 10% suspension.

Humoral Immune Response

Two schedules of immunization were used. In the first, mice were injected, ip, with 200µL (2×10^8 cells/mL) of RRBCs on the seventh day from the start of the experiment. A booster immunization was given 1 week later (day 14) and the animals were bled on day 28 to detect the presence of antibodies. About 0.5 mL blood was collected from the retro orbital plexus of the mice using hematocrit capillaries (HiMedia, India). The blood was allowed to clot at room temperature for one hour and then kept at 4°C for 60 minutes, followed by centrifugation at 2500 rpm for 10 minutes. The serum was collected and stored at -20°C till further use.

To quantify the antibodies, hemagglutination was performed. Briefly, this involved serial two-fold dilutions of serum samples in Alsever's solution, to which 100 µL of 10% RRBCs was added to 100 µL of the diluted test samples in U-bottom microtiter plates (Greiner, Germany). The plates were incubated for 1 to 2 hours at 25°C before RRBC setting patterns

were read. The HA titer was expressed as the reciprocal of the highest dilution of the serum showing definite positive pattern (flat sediment or shield formation) as compared to the negative pattern (smooth dot in the centre of the well). The respective antibody titer was expressed as the serial dilution of the serum per well, as per the method described [6].

Mice treated with coumarinolignoids and levamisole hydrochloride exhibited a significant increase in hemagglutinin antibody titer, and cyclophosphamide significantly decreased the antibody titer when compared with vehicle control. The data are depicted in Table 2.

Table 2: Effect of orally administered coumarinolignoids on humoral and cell mediated immune response in mice.

Treatment	Body wt. gain (g)	RBCs (Millions/mm ³)	WB C (Thousands/mm ³)
Vehicle Control	4.17±0.59	8.51±0.34	8.71±0.88
Coumarinolignoids (10mg/kg B.wt.)	4.25±0.69	8.58±0.28	11.46±0.37*
Coumarinolignoids (30mg/kg B.wt.)	5.00±0.93	7.69±0.29	12.02±1.23*
Coumarinolignoids (100mg/kg B.wt.)	5.50±0.45	8.74±0.26	10.89±2.34*
Levamisole (0.68mg/kg B.wt.)	4.75±0.6	8.42±0.14	10.77±0.84*
Cyclophosphamide (200mg/kg B.wt.)	0.83±0.27 ^a	6.17±0.33 ^a	3.94±0.49 ^a

n=06, P<0.05, using student's *t* test (Vehicle Control vs Treatment)* Significantly increased ;^a Significantly decreased

Cell Mediated Immune Response

Delayed type hypersensitivity test (DTH)/footpad thickness test in mice: The mice were immunized in the same way as that described for the humoral immune response, but in addition, on day 28 all mice were challenged with RRBCs (50 µL; 2×10^8 cells/mL) in the intra-plantar region of the hind right paw. The differences in the footpad thickness of the two paws were measured 24 hours later by the fluid displacement method using a phlethysmometer (Ugo Basile, Italy). The data are expressed in arbitrary units, as in the method described [7]. The footpad thickness of coumarinolignoid treated mice was significantly decreased in a dose dependent manner when compared with vehicle control. The data are depicted in Table 2.

Results of the present study demonstrate that coumarinolignoids produce a significant increase in the white blood cell count and hemagglutinin antibody titer when compared with the vehicle control mice. Previous reports [8] suggested that agents that increase white blood cell counts and

hemagglutinin antibody titers serve as immunostimulatory agents for the immune system. Immunostimulatory activity has been reported in a number of plants [9-12], including Indian Panax, *Panax heterophyllum*, *Tylophora indica*, *Ocimum gratissimum*, *O. sanctum* and *Picrorhiza kurroa* [13]. The foot pad thickness (local inflammation) induced by RRBCs was significantly reduced in coumarinolignoid treated mice when compared with the vehicle treated group. During the cell-mediated DTH response, the sensitized cells that are being challenged with the antigen secrete lymphokines [14]. Cutaneous DTH reactions are initiated when CD4 memory T cells are activated by antigen-presenting cells in the skin. The magnitude of the response to the antigen is measured as an increase in swelling at the site of challenge [15,16] Cutaneous DTH reactions induced by the antigen are a local inflammatory response [17,18] and so it may be hypothesized that the compounds could also be useful as a local anti-inflammatory agent.

This present study gives a clear indication that oral administration of cleomiscosins A, B, and C isolated from *C. viscosa* seeds enhance the body immune function by significantly increasing the white blood cell count, antibody responses and reducing the delayed type of hypersensitivity response towards rabbit red blood cells in female Swiss albino mice. Hence, the cleomiscosins have the potential to be used as an immunomodulatory agent.

Experimental

General: IR spectra were recorded on a PerkinElmer FTIR BX spectrophotometer. NMR spectra were recorded on a Bruker AVANCE 300 instrument. Mass spectra (electro spray ionization in positive mode) were recorded on an API 3000 (Applied Biosystem) spectrometer.

Seed material: The seeds were collected from the National Gene Bank for Medicinal and Aromatic Plants, CIMAP, Lucknow, India and the voucher specimens are available for authentication.

Isolation: Air dried pulverized seeds of *Cleome viscosa* (1 kg) were defatted with light petroleum (1L x 3) for 72 h. The defatted material was then exhaustively extracted with methanol (1L x 3) and

concentrated to a small volume (50 mL). It was adsorbed onto celite, dried at room temperature for 24 h and then packed in a cheese cloth and extracted with toluene, followed by ethyl acetate and methanol. The toluene and ethyl acetate fractions were mixed together, concentrated, and chromatographed over silica gel (60-120 mesh) using light petroleum. The column was eluted with mixtures of light petroleum–ethyl acetate in the ratio of 1:1 and 1:3, successively. From the above two eluants, on concentration, crystals precipitated, which were removed by filtration and washed with light petroleum–ethyl acetate (1:1) to give a mixture of cleomiscosins A, B and C in the ratio 21:25:4. From this mixture, by repeated column chromatography over silica gel (60-120 mesh) using light petroleum: ethyl acetate (1:1) as eluant, the three compounds were separated and characterized by comparison with reported spectral data (UV, IR, NMR, MS) [8].

Immunomodulatory studies: The *in-vivo* immunomodulatory study was approved by the Institute's Animal Ethical Committee and conformed to national guidelines on the care and use of laboratory animals. Female Swiss albino mice weighing 18-23 g were obtained from the laboratory animal house, CIMAP, Lucknow. These animals were used for the study and were maintained at a room temperature of 22±23°C with 50-70% relative humidity and cycles of 12:12 h of light and dark with *ad libitum* food and water. Animals were divided into six groups each comprising six animals. The first group served as vehicle control, fed with distilled water, the second to fourth groups served as tests, which were fed with the mixture of coumarinolignoids at doses of 1, 10 and 100 mg/kg body weight; the fifth group served as a positive control, which was given levamisole hydrochloride (Sigma-Aldrich, USA) as an immunopotentiating agent at a dose of 0.68 mg/kg body weight, and the sixth group served as a negative control, which was given cyclophosphamide monohydrate (Sigma-Aldrich, USA) as an immunosuppressive agent at 200 mg/kg body weight. These mice were treated orally for a period of 28 days by delivery directly into the stomach using flexible newborn-sized intragastric cannulae.

Acknowledgments – The authors are thankful to DBT, CSIR, New Delhi, for funding, and the

National Gene Bank of the Medicinal and Aromatic Plants, and to the Faculty, technical staff and students of the GRB Division, CIMAP, Lucknow, India for

providing seed material, and technical support during this work.

References

- [1] Hafeez B, Ahmad I, Haque R, Raisuddin S. (2001) Protective effect of *Cassia occidentalis* on cyclophosphamide-induced suppression of humoral immunity in mice. *Journal of Ethnopharmacology*, **75**, 13-18.
- [2] Chatterjee A, Pakrashi SC. (1991) *The Treatise on Indian Medicinal Plants*, PID, New Delhi: CSIR, India.
- [3] Asolkar LV, Kakkar KK, Chakre OJ. (1992) *Second Supplement to Glossary of Indian Medicinal Plants with Active Principles* part I (A-K), PID, KS Krishnan Marg, New Delhi, India, 217.
- [4] Nadkarni KM, Nadkarani AK. (1976) *Indian Materia Medica* (vol 1) Bombay, India, Prakashan, 498.
- [5] Chattopadhyay SK, Thakur RS, Patnaik GK, Shrimal RC. (1999) A process for the preparation of coumarinolignoids having liver protective activity from *Cleome viscosa*. *Indian patent*, no.182638.
- [6] Ray AB, Chattopadhyay SK, Kumar S, Konno C, Kiso Y, Hikino H. (1985) Structure of Cleomiscosin, coumarinolignoids of *Cleome viscosa* seeds. *Tetrahedron*, **41**, 209-214.
- [7] Mediratta PK, Sharma KK, Singh S. (2002) Evaluation of immunomodulatory potential of *Ocimum sanctum* seed oil and its possible mechanism of action. *Journal of Ethnopharmacology*, **80**, 15-20.
- [8] Ziauddin M, Phansalkar N, Patki P, Diwanay S, Patwardhan B. (1996) Studies on the immunomodulatory effects of Ashwagandha. *Journal of Ethnopharmacology*, **50**, 69-76.
- [9] Atal CK. (1985) Role of some important ayurvedic drugs in modulating the immune system in human body. *Indian Drug Manufacturers Association Bulletin*, **16**, 17.
- [10] Atal CK, Sharma ML, Kaul A, Khajuria A. (1986) Immunomodulatory agents of plant origin I: Preliminary screening. *Journal of Ethnopharmacology*, **18**, 133-141.
- [11] Godhwani S, Godhwani JL, Vyas DS. (1988) *Ocimum sanctum*: a preliminary study evaluating its immunoregulatory profile in albino rats. *Journal of Ethnopharmacology*, **24**, 193-198.
- [12] Dua PR, Shankar G, Srimal RC, Husian A. (1989) Adaptogenic activity of Indian *Panax pseudoginseng*. *Indian Journal of Experimental Biology*, **27**, 631-634.
- [13] Mungantiwar AA, Nair AM, Shinde UA, Dikshit VJ, Saraf MN, Thakur VS, Sainis, KB. (1999) Studies on the immunomodulatory effects of *Boerhaavia diffusa* alkaloidal fraction. *Journal of Ethnopharmacology*, **65**, 125-131.
- [14] Mustafa AS. (1992) *In vitro* correlates of cell-mediated immunity, *A Handbook of Practical and Clinical Immunology*. (2nd edition), Talwar GP, Gupta SK (Eds). CSB Publishers, pp 270-281.
- [15] Singh S, Majumdar DK. (1997) Evaluation of anti-inflammatory activity of fatty acids of *Ocimum sanctum* fixed oil. *Indian Journal of Experimental Biology*, **35**, 380-383.
- [16] Tizard I.R. (1996) Type IV hypersensitivity: Delayed hypersensitivity. *Veterinary Immunology: An Introduction* (5th edition) publisher WB. Saunders Company, Philadelphia, pp 381-401.
- [17] Savilahti E, Kirveskari J, Jarvinen A, Tervo T, Renkonen R. (2004) Monitoring leukocyte traffic *in vivo* into human delayed-type hypersensitivity reaction. *Journal of Immunological Methods*, **288**, 81-89.
- [18] Kunstfeld R, Hirakawa S, Hong YK, Schacht V, Lange-Asschenfeldt B, Velasco P, Lin C, Fiebiger E, Wei X, Wu Y, Hicklin D, Bohlen P, Detmar M. (2004) Induction of cutaneous delayed-type hypersensitivity reactions in VEGF-A transgenic mice results in chronic skin inflammation associated with persistent lymphatic hyperplasia. *Blood*, **104**, 1048-1057

Composition of the Leaf and Inflorescence Essential Oil of *Pogostemon benghalensis* Burm. F. from Kumaon

Chandan S. Chanotiya, Anju Yadav, Anil K. Singh and Chandra S. Mathela

941

Chemical Composition and Antibacterial Activity of *Cupressus dupreziana* A. Camus

Messaoud Ramdani, Oualida Rached, Hocine Laouer, Meriem El Koli and Takia Lograda

945

Review /Account

Genus *Chrysothamnus*: A Source of Bioactive Compounds

Mohamed-Elamir F. Hegazy, Abou El-Hamd H. Mohamed, Mohamed H. Abd El-Razek, Fayza M. Hammouda, Nahed M. Hassan, Usama A. Mahalel, Ali M. El-Halawany, Ahmed A. Mahmoud, Joe Karchesy, Toshifumi Hirata and Ahmed A. Ahmed

951

Natural Product Communications

2007

Volume 2, Number 9

Contents

Original paper

Page

- Reniformin, a Unique Diterpene Ester from the Roots of *Pelargonium reniforme***
Klaus Peter Lattè, Maki Kaloga and Herbert Kolodziej 883
- 3-O-(3'-Hydroxytetradecanoyl)lupeol from *Sorocea trophoides* Inhibits Cruzain**
Lori R. Richter, Bernhard Vogler, Ashley F. Penton, William N. Setzer, William A. Haber,
Conor R. Caffrey, Elizabeth Hansell and James H. McKerrow 887
- A New Triterpenoidal Saponin and a Flavone Glycoside from *Stachys parviflora***
Viqar Uddin Ahmad, Saima Arshad, Sadia Bader, Amir Ahmed, Shazia Iqbal, Afsar Khan,
Saleha Suleman Khan and Rasool Bakhsh Tareen 889
- Flavonoids and Triterpenoid Saponins from *Pimenta dioica* (Merr.) L.**
Fatma A. Moharram, Mona A Mohamed, Mohamed SA Marzouk and Elsayed A Aboutabl 895
- Two New Sulfated Sterols from the Marine Sponge *Lendenfeldia dendyi***
Mohamed M. Radwan, Susan P. Manly and Samir A. Ross 901
- Rufforone: a New Styrylpyrone from *Sanrafaelia ruffonammari***
John J. Makangara, Nobuhiro Hirai, Masahiro Inomata, Akira Murakami and Hajime Ohigashi 905
- Two New Flavonoid Glycosides from the Fern *Dryopteris villarii***
Filippo Imperato 909
- A Straight-Chain Alcohol Glycoside, with Smooth Muscle Relaxant Activity, from *Rubus idaeus* (Raspberry) Leaves**
Asmita V. Patel, Christopher G. Dacke, Gerald Blunden and Janne Rojas Vera 913
- Flavonoids from the Fern *Chingia sakayensis* (Zeiller) Holtt. and Evaluation of Their Cytotoxicity Against Murine Leukemia P-388 Cells**
Suyatno Sutoyo, Gunawan Indrayanto and Noor Cholies Zaini 917
- Spinocoumarin I, a New Coumarin Derivative from *Astragalus spinosus* Forssk.**
Mohamed M. Radwan, Nadia A. El-Sebakhy, Aya M. Asaad, Soad M. Toaima and David G. I. Kingston 919
- An *in-vivo* Study of the Immunomodulatory Activity of Coumarinolignoids from *Cleome viscosa***
Dyaneshwar U. Bawankule, Sunil K. Chattopadhyay, Anirban Pal, Kopal Saxena, Sachidanand Yadav,
Narayan P. Yadav, Dayanandan Mani, Arun K. Tripathi, Salim U. Beg, Amit Srivastava,
Anil K. Gupta and Suman Preet S Khanuja 923
- HPTLC Method for the Quantitative Determination of *ar*-Turmerone and Turmerone in Lipid Soluble Fraction from *Curcuma longa***
Vikas Jain, Vure Prasad, Satwayan Singh and Raghendra Pal 927
- 1-O-Alkylglycerol Ether Lipids in Two Holothurian Species: *Cucumaria japonica* and *C. okhotensis***
Viatcheslav Rybin, Konstantin Pavel and Dmitry Mitrofanov 933
- Furanosesquiterpenoids from *Lindera pulcherrima* (Nees.) Benth. ex Hook. f.**
Subhash C. Joshi, Rajendra C. Padalia, Dinesh S. Bisht and Chandra S. Mathela 937

Continued inside back cover