

Anti-Viral

1. Modified nucleosides as anti-viral agents

Lieven, S. J. and Chung, C. K.

Pharmasset, Ltd.; University of Georgia Research Foundation, Inc., USA

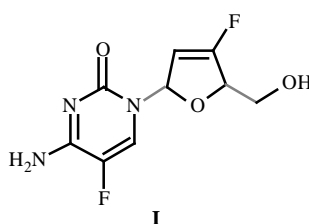
PCT Int. Appl. WO 2004, 43, 402 (Cl. A61K), 27 May 2004 US Appl. PV425, 534, 12 Nov. 2002; 49 pp; C.A. **141**(1): 1201h

Abstract: Compound **I** exhibited significant anti-HBV activity in Hep AD38 cells. Other compounds dealing generally with anti-viral infections and particularly HBV/HIV treated 3-substituted-2,3-didehydro-2,3-dideoxy-*-L-*-nucleosides, their salts and their prodrugs are also described.

Activity: Anti-viral

Bioassay: Hep AD38 cells

Origin: Synthetic



Web URL: <http://www.worldcatlibraries.org/wcpa/ow>

2. Synthesis and antiviral evaluation of some 3-fluoro bicyclic nucleoside analogs

Christopher, M., Antonella, C., Robert, S., Graciela, A., Erik, D.C. and Jan, B.

Welsh School of Pharmacy, Cardiff University, Cardiff, UK

Nucleosides, Nucleotides & Nucleic Acids 2004, **23**(1 & 2), 1-5; C.A. **141**(2): 23840t

Abstract: 3-OH of most of the anti-VZV furanopyrimidine deoxynucleosides (BCNAs) on replacement with 3-fluoro resulted in decreased antiviral activity, suggesting the significance of 3'-OH presence to enhance antiviral activity. Preparation of these 3-fluoro derivatives (for both alkyl and alkyl phenol series) is described along with their biological activities on Herpes virus

Web URL: <http://www.worldcatlibraries.org/wcpa/ow>

3. Synthesis and anti-viral activity of novel fluorinated 2,3-dideoxynucleosides

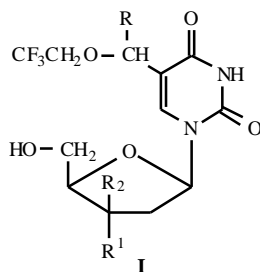
Piyush, K., Kazue, O., Jan, B., Erik, D. E. C., Koh-ichi, S. and Leonared, W. I.

Faculty of Pharmacy and Pharmaceutical Sciences, University of Alberta, Edmonton, AB Canada

Nucleosides, Nucleotides & Nucleic Acids 2004, **23**(1 & 2), 7-29; C.A. **141**(2): 23841u

Abstract: Fluorinated 2,3-dideoxynucleosides were prepared and their biological activities studied. A series of 5-(trifluoroethoxymethyl)-2,3-dideoxyuridines and 5-[bis(trifluoroethoxy)-methyl]-2,3-dideoxyuridines were synthesized. These compounds were tested against a variety of viruses.

Activity and bioassay: Anti-viral and weakly cytotoxic. Some activity against anti-HIV-1 and anti-HIV-2 assays was observed by compounds **I** (R = H or OCH₂CF₃; R¹ = N₃ or F; R² = H or F).



Web URL: <http://www.wiley-vch.de/publish/en/journals/>

4. Synthesis and antimalarial activity of trioxaquine derivatives

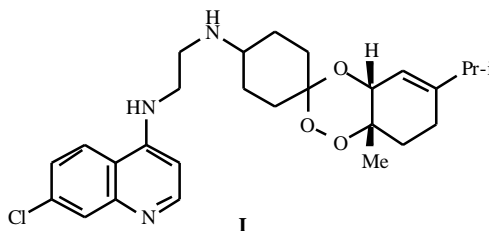
Odile, D. C., Franocise, B.-V., Christophe, L., Anne, R., Heinz, G., Anne, B., Henri, V., Jean-Francois, M., Jean-Paul, S. and Bernard, M.

Labratoire de Chimie de Coordination du CNRS, 31077 Toulouse, France

Chemistry – A European Journal 2004, **10**(7), 1625-1636; *C.A.* **141**(3): 38591m

Abstract: A series *cis*-trioxaquine (DU1302c) (**I**) derivatives were synthesized. These derivatives exhibited strong antimalarial activity.

Activity and bioassay: Antimalarial **I** displayed ($IC_{50} = 5-19$ nM) activity against strains of *Plasmodium falciparum* *in vitro*.



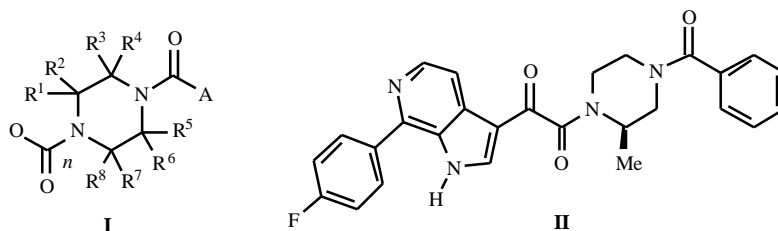
5. Composition and antiviral activity of substituted azaindoleoxoacetic piperazine derivative

Tao, W., Zhongxing, Z., Nicholas, M. A., John, K. F., Zniwei, Y., May, X. Q., Alicai, R.-R., John, M. D. and Yastsugu, U.

U.S. Pat. Appl. Publ. US 2004 110,785 (Cl. 514-300 C07D471/02), 10 Jun 2004, US Appl. 214,982, 7Aug 2002; 350 pp. cont-in-part of U.S. Pat. Appl. 2003 207,910; *C.A.* **141**(3): 38633b

Abstract: Compounds **I** [$n = 1$ or 2 ; Q = (un)substituted azaindole heterocycle; A = alkoxy, (un)substituted aryl or heteroaryl] were synthesized and studied for biological activity. Compound **II** was subjected to luciferase expression inhibition.

Activity and Bioassay: These compounds were found to be excellent antiviral compounds used alone or combined with other antivirals anti-infectives, immuno-modulators or HIV entry inhibitors.



6. Preparation of substituted aryl thioureas as inhibitors of viral replication

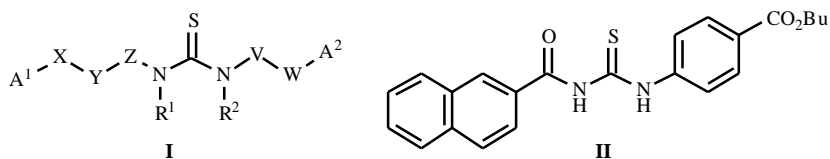
Dqwei, C., Milind, D., Andrew, T., Avinash, P., Xiangzhu, W., Yiping, S., Cuixian, I., Jesse, Q., Junko, O. and Shouming, L.

Achillion Pharmaceuticals, Inc., USA

PCT Int. Appl. WO 2004 46,095 (Cl. C07C335/26), 3 Jun 2004, US Appl. PV 427,634, 19 Nov 2002; 218 pp; C.A. **141**(2): 23305x

Abstract: Synthesis, formulations and antiviral activity of compounds **I** [A^1 = (un)substituted aryl, 5-6 membered heteroaryl; etc A^2 = (un)substituted Ph, 2-pyridyl, 5-pyrimidinyl, etc.; X, W = O, S, NR, absent (wherein R = H, alkyl, arylalkyl); V = alkyl, alkenyl, cycloalkyl, absent; Y = alkyl, cycloalkyl, alkenyl, etc.; when V is absent, W is absent; Z = carbonyl, thiocarbonyl, imino, alkylimino; R^1 , R^2 = substituted alkyl, alkenyl, alkynyl; or R^1 and R^2 are joined to form (un)substituted 5-7 membered saturated or mono-unsaturated rings containing one additional heteroatom, N, S or O] are described.

Activity and Bioassay: $EC_{50} < 30 \mu M$ was displayed by **II**, suggesting it to be a potent inhibitor of HCV replication of the HCV replicon. Detailed studies of compound **I** revealed this to be excellent and selective inhibitors of hepatitis C virus replication.



Web URL: <http://sciencedirect.com>

7. Inhibitors of hepatitis C virus NS3.4A protease. Part 3: P₂ proline variants

Robert, P. B., Lue, F. J., Kevin, G. M., John, C. J., Lawrence, C. F., David, D. D., Cynthia, G. A., Scott, H. L., Joseph, K. L., Chao, L., Kai, L., Yu-Ping, L., John, M. P., Murcko, P. M. A., Janos, L., Govinda, R. B., Wayne, S. C., Roger, T. D., John, V. D. H., Keith, W. and John, T. A.

Vertex Pharmaceuticals Inc.; Cambridge, MA 02139, USA

Bioorganic & Medicinal Chemistry Letters 2004, **14**(8), 1939-1942; C.A. **141**(1): 40r

Abstract: Improved anti- HIV activity of 3-substituted proline analogues as compared to previously reported 4-hydroxyproline derivatives was observed and attributed to the 3-alkyl-substituted prolines in P₂, possessing relatively small size.

Activity: Anti-viral

Origin: Synthetic

8. Thiadiazolyl quinazolones as potential antiviral and antihypertensive agents

Pandey, V. K., Sarah, T., Zehra, T., Raghubir, R., Dixit, M., Joshi, M. N. and Bajpai, S. K.

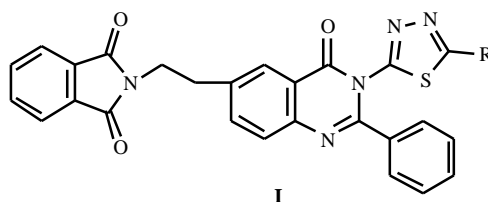
Chemistry Department, University of Lucknow, Lucknow 226007, India

Indian Journal of Chemistry, Section B: Organic Chemistry Including Medicinal Chemistry 2004, **43B**(1), 180-183; C.A. **141**(1): 388n

Abstract: The manuscript describes the preparation of 6-(*N*-ethylphthalimido)-3-[2-(5-*aralkyl*-1,3,4-thiadiazolyl)]-2-phenyl-4-oxo-(3H)-quinazolines. The antiviral and antihypertensive activities of these compounds with respect to their structures are also discussed.

Activity and bioassay: Compound **I** (wherein R = Ph or *n*-Pr) exhibited activity against the Japanese encephalitis virus and herpes simplex virus; whereas compound **I**, with R = Me, Et, *o*-hydroxyphenyl, *p*-chlorophenyl, exhibited no anti-viral activity, but showed noticeable antihypertensive activity.

Origin: Synthetic



Web URL: pubs.acs.org/journals/jnprdf/index.htm

9. Dimeric flavonol glycoside and galloylated *C*-glucosylchromones from *Kunzea ambigua*

Hideyuki, I., Naoki, K., Harukuni, T., Hoyoku, N., Takashi, Y.

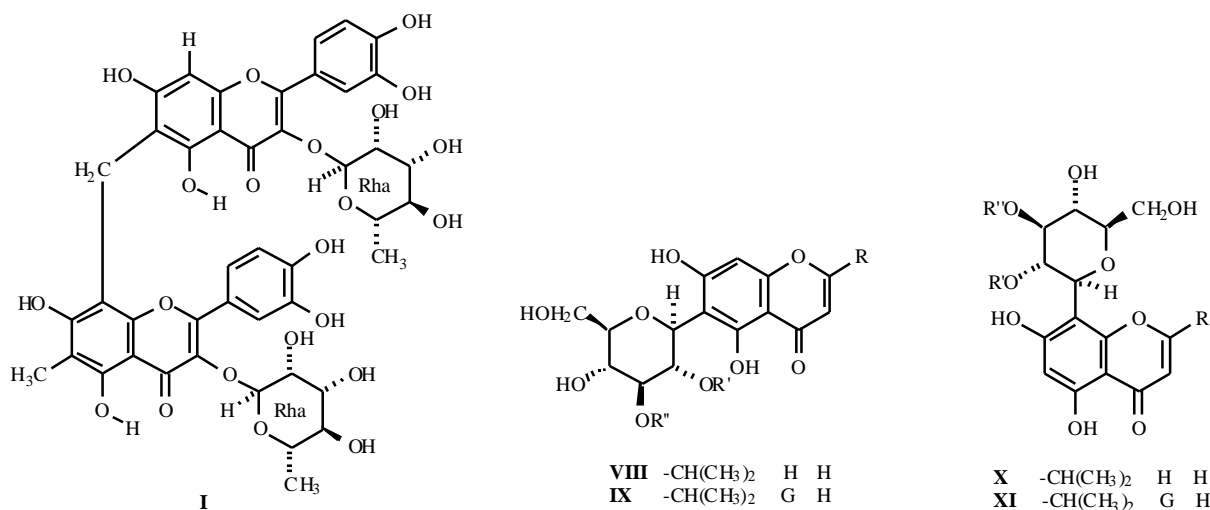
Faculty of Pharmaceutical Sciences, Okayama University, Tsushima, Okayama, Japan 700-8530

Journal of Natural Products 2004, **67**(3), 411-415; *C.A.* **141**(1): 4120s

Abstract: From the leaf extract of *Kunzea ambigua*, a novel dimeric flavonol glycoside, had been isolated namely kunzeagin A (**I**), alongwith six new chromone *C*-glucosides, kunzeachromones A-F (**II-VII**) and seven known compounds. **I** and 6-*C*- and 8-*C*-glucosylchromones and their monogallates showed significant inhibitory effects on activation of Epstein-Barr virus early antigen (EBV-EA) induced by 12-*O*-tetradecanoylphorbol. SAR of these compounds are also provided.

Activity and bioassay: In *in vitro* preliminary screening test for searching possible anti-tumor-promoting agent EBV-EA using Raji cells. **I**, **VIII** and **X** remarkably inhibited 67-76% of EBV-EA activation induced by 12-*O*-tetradecanoylphorbol 13-acetate (ATP) at a concentration of 500 mol ratio/TPA without exhibiting cytotoxicity. These results are comparable to that of 65.1% inhibition of EGCG.

Origin: Natural product



Web URL: <http://cpb.pharm.or.jp>

10. The anti-HBsAg (human type B hepatitis, surface antigen) and anti-HBeAg (human type B hepatitis, e antigen) C₁₈ dibenzocyclooctadiene lignans from *Kadsura matsudai* and *Schizandra arisanensis*

Ming-der, W., Ray-ling, H., Li-ming, K. Y., Chia-cheng, H., Chi-Wi, O. and Yao-haur, K.

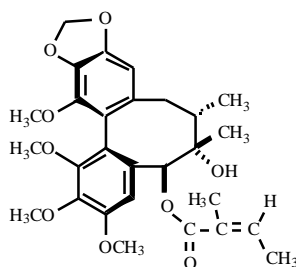
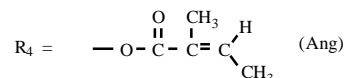
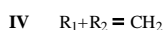
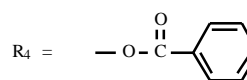
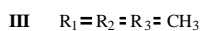
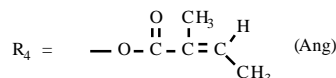
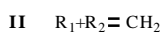
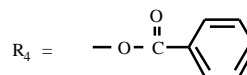
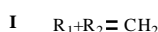
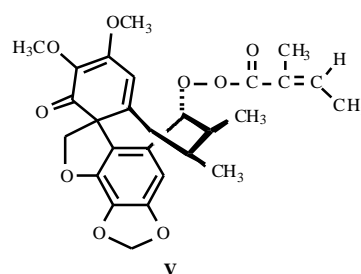
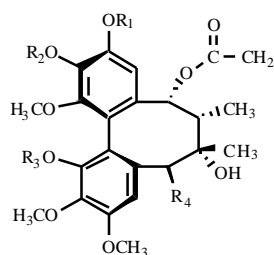
Department of Chemistry, National Sun Yat-Sen University, Kaohsiung, Taiwan 804

Chemical & Pharmaceutical Bulletin 2003, **51**(11), 1233-1236; *C.A.* **141**(1): 4101m

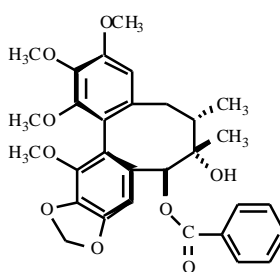
Abstract: Bioassay-guided purification of ethyl acetate extracts of *Kadsura matsudai* and *Schizandra arisanensis* led to the isolation of bioactive natural products, and their anti-HbeAg (human type B hepatitis, e antigen) and anti-HbsAg (human type B hepatitis, surface antigen) effects were measured. These findings included three novel C₁₈ dibenzocyclooctadiene lignans, schizanrin F (**I**), G (**II**), H (**III**), along with the known kadsurarin (**IV**) from *K. matsudai*, whereas phytochemical investigation on *S. arisanensis* furnished new C₁₉ homolignan schiarisanrin E (**V**), together with the known C₁₈ lignans, gomisin B (**VI**), G (**VII**) and (+)-gomisin K3 (**VIII**). Detailed spectral data and SAR studies are also provided.

Activity and bioassay: Compound **I-VIII** were evaluated for anti-HbsAg anti-HbeAg. Compounds **I-V** were inactive. These exhibited inhibition % < 25% at concentration of 50 and 100 µg/ml. High activity in anti-HbsAg assay test was found to be 74.1, 76.3 and 76.3% inhibition by **VI**, **VII** and **VIII** respectively, at concentrations of 100 and 50 µg/ml. These compounds **VI-VIII** also showed strong activity at 50 µg/ml concentration.

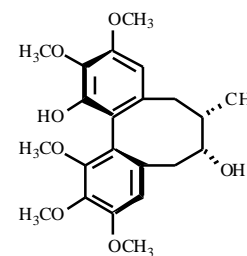
Origin: Natural product



VI



VII



VIII