Shin HS, CHoi HJ, Kwon SK, Park MS

College of Pharmacy, Duksung Women's University, Seoul, Korea

The ability of non-steroidal anti-inflammatory drugs(NSAIDs) to inhibit cyclooxygenase-2(COX-2) may well explain their therapeutic efficacy as anti-inflammatory drugs by blocking prostaglandins formation, whereas inhibition of cyclooxygenase-1(COX-1) may well explain their unwanted the gastric and renal side effects. In this study, a series of analogues were prepared to develope new useful COX-2 inhibitors. Novel 7-bromo-1,2-benzothiazine derivatives, which could exhibit potential anti-inflammtory activity, were synthesized through 1,2-benzothiazine and 4-bromotoluene over the sulfonation, amination and oxidation, by Gabriel-Colman rearrangement. These compounds were evaluated for their ability of inhibiting cyclooxygenase-2 in murine macropharge RAW 264.7 cell line. To investigate the structure-activity relationship of 7-bromo-1,2-benzothiazine derivatives, accumulation of prostaglandins by the selective expression of COX-2, which was expressed by the lipopolysaccharide-stimulated macropharges, were screened.

[PD1-33] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

6-(1-Alkoxyiminoalkyl)-5,8-Dimethoxy-1,4-Naphthoquinones : Synthesis, Evaluation of Cytotoxic Activity and Antitumor Activity

You YJ°, Kim Y, Ahn BZ

College of Pharmacy, Chungnam National University

2-Acyl-1,4,5,8-Tetramethoxynaphthalene (TN) derivatives were treated with hydroxylamine to produce 2-(1-hydroxyiminoalkyl)-TN derivatives. These were oxidatively demethylated to 6-(1-hydroxyiminoalkyl)-5,8-dimethoxy
-1,4-naphthoquinone (DMNQ) derivatives. These DMNQ derivatives were tested for cytotoxic activity against L1210 cells and anitumor activity using S-180 fluid tumor. Their ED50 values on L1210 cells ranged over 0.1~0.3mg/ml. They generally exhibited a potent anitumor activity. It was found that the activity was dependent on size of the side chains with longer chain being more potent. Among the compounds tested, nine exhibited a higher T/C value than 300 %.

[PD1-34] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Synthesis of New Allyl Sulfonate Analogues as Potential Antitumor Agents

Jin cheng hua°, Lee MJ, Kang HO, Kim DK*, Moon HI, Lee KR, Chung KH, Zee OP, Jung YH

College of pharmacy Sungkyunkwan University, Woosuk University*

Much attention has been focused on developing new chemotherapeutic agents for a treatment of cancer from natural products. As parts of a program, aimed at developing new antitumor agents, a monoterpenoid compound (10-isobutyloxy-8,9-epoxythymol isobutyrate) isolated from *Carpesium divaricatum* S. *et* Z. and its derivatives have been synthesized and their structure-activity relationships have been investigated. At this time, to study the effect of *p*-methoxy substituent on biological activity, we designed and synthesized *p*-methoxy epoxythymol. And we modified ester bond to relatively stable sulfonyl ester bond because the ester bond is easily hydrolyzed by esterase in the body. Furthermore, modification of aromatic moiety in thymol skeleton with intact allyl sulfonate has been carried out. The in vitro cytotoxic activities of the synthetic compound against human cancer cell lines were evaluated.

[PD1-35] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Phytochemical Constituents of Hylomecon vernale

Kim MJ[O], Hwang BY 1[X], Kang SJ2[X], Choi WH, Hong SS, Ro JS, Lee KS

College of Pharmacy, Chungbuk National University, 1[X] Korea Research Institute of Bioscience and Biotechnology, 2[X]Korea Food and Drug Administration

The constituents of *Hylomecon vernale* Max. (Papaveraceae) were studied phytochemically in order to investigate medicinal resources. This plant is perennial herb grown on damp shady regions in Korea. According to the ancient Chinese herbal literature, it is effective for the treatment of arthritis, edema and dysfunction of blood circulation. The chemical constituents of the genus *Hylomecon* were reported as benzophenanthridine alkaloids (chelerythrine, chelidonine, chelilutine, chelirubine, protopine, sanguinarine) and protoberberine alkaloids (coptisine, cryptopine, allocrytopine, berberine, tetrahydroberberine). However, only a few chemical investigations of *Hylomecon vernale* have been studied and its biological activities have not been reported. In the course of studies on chemical constituents, three compounds were isolated from the aerial parts of this plants by repeated silica gel column chromatograpy. The structure were identified on the basis of their physicochemical and spectroscopic data (UV, mass, 1^{X}H-NMR and 13^{X}C-NMR).

[PD1-36] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Benzophenanthridine Alkaloids from Hylomecon hylomecoides

Jo YS[O], Kim W, Bae KH, Kim YH

College of Pharmacy, Chungnam National University

Hylomecon hylomecoides (Papaveraceae) is an indigeneous plant and distributed in southern part of Korea. Phytochemical studies were carried out from the alkaloid fraction of the root of H. hylomecoides. Four benzophenanthridine alkaloids were isolated from the repeated silicagel column chromatography. On the basis of spectral data, their structures were identified as 8-methoxydihydrosanguinaline, dihydrosanguinarine, 8-hydroxymethyldihydrosanguinarine and 8-acetonyl dihydrosanguinaline.

[PD1-37] [04/21/2000 (Fri) 14:50 - 15:50 / [1st Fl, Bldg 3]]

Aldose Reductase Inhibition of Magnesium Lithospermate B isolated from the Root of Salvia Miltiorhiza

Jung M[O], Lee HC, Park HJ, Choi SH, Ham JY, Kim H, Ahn CW, Lee GT

Department of Chemistry and Division of Endocrinology, Department of Internal Medicine, Yonsei University

Magnesium Lithospermate B was isolated from an aq. MeOH extract of Salvia Miltiorhiza (Dan-Shen, 丹蔘), and its subsequent purification by normal silica gel column chromatography with polar-eluent (Yield: 1g from Dan-Shen 100g). The in vitro effect of magnesium lithospermate B on rat mesangial cell line was assessed by spectrophotometry. We evaluated the activity of aldose reductase, which is considered to be a major enzyme of the signal transduction in the pathogenesis of not only diabetic neuropathy but also diabetic nephropathy. There was a tendency to decreased activity of aldose reductase in accordance with the increasing dosage of magnesium lithospermate B. The magnesium lithospermate B showed significant dose dependent effect on aldose reductase activity