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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

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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

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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]]