

Although methotrexate (MTX) has been in clinic for decades, its side effects limit its usefulness in cancer chemotherapy. Efforts to reduce such unfavorable effect include structural modifications on pteridine nucleus and 1,4-disubstituted benzene moiety of MTX. In addition to such modifications, a new model was introduced as a nonclassical antifolate which does not retain glutamic acid moiety in MTX. Recently, a combination of two strategies resulted in trimetrexate (Neutrexin) and piritrexin (PTX) which showed promising results in clinical trials. The anticancer activity of the latter two stems from the inhibition of thymidylate synthase in nucleotide synthesis while that of MTX comes from the inhibition of dihydrofolate reductase. We herein describe the design, synthesis and biological activities of 7H-pyrazolo[3,4-d]pyrimidine-based antifolate as potential antitumor agents.

[PD1-9] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Synthesis of [1,2,5]thiadiazole-1,1-dioxides and their cytotoxicities

Kim IH, Kim JM, Jung SH

College of Pharmacy, Chungnam National University, Daejeon 305-764

Arylsulfonylimidazolidinones **1** have been reported to be potential antitumor agents. According to the study of the structure activity relationship of these compounds, 4-phenyl-1-phenylsulfonylimidazolidinone moiety has been identified as a pharmacophore. However the necessity of planar ureido moiety for their activity has not been fully tested. Therefore, a tetrahedral sulfamide in place of ureido group of **1** was introduced to vary the stereochemistry of their position. Accordingly compounds **2** and **3** were synthesized and tested against human cancer cell lines.

[PD1-10] [10/20/2000 (Fri) 11:30 - 12:30 / [Hall B]]

Optimal Synthesis Condition of Magnesium Trisilicate

Park IH*, Shin WW

College of Pharmacy, Wonkang University

Magnesium trisilicate was prepared by reacting Magnesium chloride solution with Sodium silicate solution in this study. The optimum synthesis conditions base on the yield of the product were established by applying Box-Wilson experimental design. It was found that the optimum synthesis condition of Magnesium trisilicate were as follows; Reacting temperature: 57~90°C Concentration