Acanthoside-D, one of major components of Acanthopanacis Cortex, is known as a ginseng-like substance. it has been known to possess diverse biological effects. Acanthoside-D has a furofuran lignan structure and the synthesis of which poses interesting and often unsolved proplems of stereocontrol. Although a few interesting syntheses providing this natural product have been reported, an intermolecular McMurry coupling - intramolecular Mitsunobu cyclization route has not yet been explored. We report here a short and efficient synthetic pathway to the total synthesis of Acanthoside-D from aryl aldehydes and methyl acrylates via Baylis-Hillman reaction, intermolecular McMurry coupling and intramolecular Mitsunobu cyclization as key reactions.

**[PD1-50] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]**

## Synthesis and biological activity of novel substituted pyridines and purines containing 2,4-thiazolidinedione

Bok Young Kim, Joong Bok Ahn, Hong Woo Lee°, Joon Kyum Kim, Jae Soo Shin, Sung Kwon Kang, Jung Hwa Lee, Soon Kil Ahn, Sang Jun Lee, Chung Il Hong, Seung Soo Yoon
*Chong Kun Dang Pharm*

Type 2 diabetes is characterized by high level of blood glucose and insulin and impaired action. In recent years, the treatment of type 2 diabetes has been revolutionized with the advent of thiazolidinedione (TZD) class of molecules that ameliorate insulin resistance and thereby normalize elevated blood glucose levels. These TZDs are synthetic, high-affinity ligands of peroxisome proliferator activated receptor-gamma (PPARγ); a member of the nuclear receptor family that controls the expression of genes in the target tissues of insulin action. Shortly after the launch of the TZDs, several reports of treatment-related toxicity have been published. Rosiglitazone, the second launched TZD is a potent ligand of PPARγ and shows efficient insulin sensitization in type 2 diabetes patients. Even though, rosiglitazone has been associated with liver, cardiovascular and hematological toxicity. In order to synthesize novel TZDs with better safety and efficacy, we designed and prepared a series of novel TZD compound containing substituted pyridines and purines group using LUDI program and molecular modeling study. Based on these results, we modified the substituted pyridines and purines with TZD moiety (Entry No. 6a-d, 12a-e, 18a-d, 23a-c). We evaluated their effect on triglyceride accumulation in 3T3-L1 cells and their hypoglycemic activity in genetically diabetic $KKA_y$ mice in vivo. On the basis of their biological activities, 5-(4-{2-[N-methyl-(5-phenyl-pyridin-2-yl)amino}ethoxy]benzyl}thiazolidine-2,4-dione (6d) was selected for further evaluation and is presently under further pharmacological studies.

**[PD1-51] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]**

## Synthesis and Anti-cancer Activity of Indirubin Derivatives as the CDK Inhibitors

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The cyclin-dependent kinases (CDKs), a group of serine/threonine kinases that form active heterodimeric complexes binding to cyclins, are key regulators of the cell cycle. The role of cyclin dependent kinases(CDKs) in cell cycle regulation has stimulated an interest in them as potential targets for proliferative diseases such as cancer, psoriasis, and chemotherapeutic agent-induced alopecia. Indirubin, an active ingredient of a traditional Chinese recipe Danggui Longhui Wan, are potent CDK inhibitors competing with ATP for binding to the catalytic site of the CDKs. In this study, we synthesized several indirubin analogs and evaluated them for their inhibitory activities. Among the induribin derivatives tested in cytotoxic activities against several human cancer cell lines compared to Ellipticine, AGM 011 displayed equally high cytotoxic activity with an $IC_{50}$ value of 1.2 mM against human stomach cancer cell line.

**[PD1-52] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]**

## Synthesis and Biological Evaluation of Allylamine Type Antimycotics

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Structure-activity relationship studies of allylamine type of antimycotics were carried out to evaluate the effect of naphthyl and methyl portion of naftifine. Compounds with 4-fluorphenyl, 2-fluorophenyl, 2,4-dichlorophenyl, 2,6-dichlorophenyl, 4-nitrophenyl, and 2,3-dihydro-benzo[1,4]dioxin-6-yl instead of naphthyl group with hydrogen, methyl, and ethyl in the place of methyl in naftifine were synthesized and tested their in vitro anti-fungal activity against five different fungi. Eight compounds showed significant antifungal activity against T. mentagrophytes. (E)-N-ethyl-(3-phenyl-2-propenyl)-4-nitro-benzenemethaneamine displayed moderate antifungal activity against all five different fungi.

**[PD1-53] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]**

## Total Synthesis of New Apicidin Derivatives as Potent Antitumor Agents

**hyungkyo kim**°
*Cheng Hua Jin, Jeong Whan Han, Hyang Woo Lee, Yin Won Lee, Ok Pyo Zee, Young Hoon Jung*

The antiparasitic agent apicidin, which was recently isolated from cultures of Fusarium Pallidoroseum, belongs to a rare group of cyclictetrapeptide fungal metabolites. Apicidin inhibits protozoal HDAC and is orally active against Plasmodium berghei malaria in mice. The biological activity of apicidin appears to be attributable to inhibition of apicomplexan HDAC at low nanomolar concentrations. In the present, we have worked about the synthesis of new apicidin derivatives and discovered that apicidin and some derivatives have mild antitumor activity. They caused the change of tumor cells to normal ones in morphology. As part of our program toward the development of new antitumor agents, we designed and synthesized several cyclictetrapeptide compounds, especially the side chain moiety of Apicidin. A key step in this synthesis is the coupling reaction of ethylvinyl ketone and iodide, prepared from the appropriately protected L-serine.In this presentation, we will report the total synthesis of these Apicidin analogues.

**[PD1-54] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]**

## Synthesis and $BK_{Ca}$-channel Opening Activity of Substituted 10-H-Benzo[4-5]furo[3,2-b]indole-carboxylic acids

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Large-conductance $Ca^{2+}$ activated potassium channels ($BK_{Ca}$) are widely distributed and play key roles in various cell functions. In nerve cells, $BK_{Ca}$ channels shorten the duration of action potentials and block $Ca^{2+}$ entry thereby repolarizing excitable cells after excitation. $BK_{Ca}$ channel opening has been postulated to confer neuroprotection during stroke and has attracted attention as a means for therapeutic intervention in asthma, hypertension, convulsion, and traumatic brain injury. Several novel benzofuroindole derivatives are prepared and evaluated as openers of the cloned $BK_{Ca}$ channel macroscopic and single channel level rSlo channels expressed in Xenopus laevis oocytes by utilizing electrophysiological methods. From this study a potent $BK_{Ca}$ channel opener (LDD 108) was identified as an effective opener in heterogeneous expression system.

**[PD1-55] [ 2003-10-10 14:00 - 17:30 / Grand Ballroom Pre-function ]**

## Synthesis of Novel 3-(H or aralkyl)-1-phenyl-5-(p-H or halo)phenyl-2-thiohydantoins as Selective COX-2 Inhibitors

**Park Hae-Sun**°, Kim Nan-Young, Choi Hee-Jeon, Park Eun-Hee, park Myung-Sook, Lee Myung-Sook, Shin Hea-Soon, Kwon Soon-Kyoung
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Nonsteriodal antiinflammatory drugs(NSAIDs) are widely used to treat pain, fever, and inflammatory conditions