[PA1-31] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Inhibition of Tissue Factor by Components from the Fruits of Chaenomeles Sinensis

Lee MingHong °, Han YongNam

Natural Products Research Institute, College of Pharmacy, Seoul National University,Seoul 110-460, Korea

Tissue factor (TF, tissue thromboplastin, or coagulation factor III) accelerates the blood clotting, activating both the "intrinsic" and "extrinsic" pathways to serve as a cofactor. In order to isolate TF inhibitor from the fruit of *Chaenomeles sinensis*, bioassay-guided purification was carried out to yield seven active compounds, 24-carboxyl-maslinic acid-28-glucopyranoside 2 (IC_{50}=6.0 μg/unit), its aglycone 2a (IC_{50}=2.7 μg/unit), luteolin-7-glucuronide 3 (IC_{50}=18.6 μg/unit), hyperin 4 (IC_{50}=16.6 μg/unit), hovetrichoside C 7 (IC_{50}=10.4 μg/unit), quercitrin 9 (IC_{50}=81.8 μg/unit) and avicularin 10 (IC_{50}=37.0 μg/unit), when evaluated by one stage clotting assay method. Another compounds such as trachelosperoside A-1 1, apigenin-7-glucuronide methyl ester 5, genistein-7-glucoside 6, luteolin-4'-glucoside 8, (-)-epicatechin 11, luteolin-3'-methoxy-4'-glucoside 12, luteolin-7-glucuronide methyl ester 13 and glucosyl-4'-hydroxy-ionylidene acetates 14 were inactive in the assay system used. Structures of these fifteen compounds were elucidated by the spectral analysis and chemical method. Compound 1, 7 , 14 were isolated for the first time from this plant and compound 2 is a new triterpene.

[PA1-32] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Arctigenin, a potent MKK1 inhibitor, suppresses lipopolysaccharide-induced AP-1 activity in murine macrophages: The role of AP-1 inhibition in the differential NO and TNF-α production

Cho Min Kyung°, Jang Young Pyo, Kim Young Choong, Kim Sang Geon

College of Pharmacy and Research Institute of Pharmaceutical Sciences, Seoul National University, Seoul 151-742, South Korea

A previous studies from this and other laboratories showed that arctigenin and demethyltraxillagenin, phenylpropanoid dibenzylbutyrolactone lignans with antioxidant and anti-inflammatory activities, inhibit the induction of nitric oxide synthase (iNOS) and tumor necrosis factor-α (TNF-α) by lipopolysaccharide (LPS) with suppression of NF-κB activation. In view of the fact that the regulatory regions of the inflammatory genes contain AP-1 response elements that play a critical role in the gene expression, we further studied the effect of arctigenin on LPS-inducible AP-1 activation and the signaling pathway of AP-1 inhibition in Raw264.7 cells. Activation of AP-1 was determined by gel mobility shift assay and immunoblot analysis. Activation of mitogen-activated protein (MAP) kinases was determined by immunoblot analyses. MKK1 activity was assayed *in vitro* using MAP kinase 2 as a substrate. Arctigenin (0.01-1 μM) inhibited LPS-inducible AP-1 activation, which accompanied the inhibition of ERK1/2 activation. Arctigenin potently inhibited the activity of MKK1 *in vitro* with the IC50 value being noted at 0.5 nM. These results demonstrated that arctigenin potently inhibited LPS-inducible AP-1 activation in murine macrophages through the inhibition of MKK1 and ERK1/2 activation. Inhibition of LPS-inducible NO and TNF-α production by arctigenin in macrophages may result from its inhibitory effect on MKK1 activity and ERK-mediated AP-1 activation as well as NF-κB activation.

[PA1-33] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

In vitro screening of several herbal medicines for antidiabetic activity

Kim SoYoung°, Kang HyoJoo, Park KyeongSoo, Chung SungHyun

College of Pharmacy, Kyunghee University, Seoul 130-701, Korea

Purpose: To establish reliable, repetitive and even fast screening tests for antidiabetic agents and determine

the correlation with in vivo hypoglycemic activity
Experimental methods: In vitro screening methods were established based on antidiabetic mechanisms dissected as follows, inhibition of intestine α-glycosidase, inhibition of hepatic Glucose 6-phosphatase (Glc6Pase) and/or phosphoenolpyruvate carboxykinase(PEPCK), stimulation of pancreatic β-cell and over- or downexpression of peroxisome proliferator activated receptor-γ(PPAR-γ) and resistin in adipocytes. All experiments were performed with aqueous extracts of thirteen herbs at dose of 1 mg/ml.
Results: There wasn't any herbal medicine that had markedly inhibitory effect on α-glycosidase. LR and MC had about 52% and 50% of inhibitory effects on Glc6Pase. PS had about 45% of inhibitory effects on PEPCK. CS and AP had stimulated the secretion of insulin in HIT-T15 cell by 4 times and 3 times. AR, AP, MC and CS increased expression of PPAR-γ.

[PA1-34] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Comparisons of antidiabetic activity between ethanol extract of white ginseng root and IH901 in streptozotocin-induced diabetic rats

Ko SungKwon°, Park SangHyun, Park JungMin, Chung SungHyun, Sung JongHwan

Korea Ginseng Institute, Chung-Ang University, Gyeonggi-do, Ansung-shi 456-756

Purpose: Antidiabetic activities between ethanol extract of white ginseng root (WGRE) and IH901, intestinal metabolite of ginsenoside Rb1, were compared in streptozotocin (STZ)-induced diabetic rats.
Experimental methods: WGRE or IH901 were coadministered with STZ on Day 1 at the dose of 100 and 300 mg or 10 and 30 mg, respectively, and continually administered for 16 days. STZ dissolved in citrate buffer was injected peritoneally at the dose of 20 mg/kg for 5 consecutive days. During the experiment, plasma glucose level and body weight were determined every 4th day. Food and water intakes were evaluated once a week and compared between groups.
Results: WGRE and IH901 both significantly reduced the plasma glucose levels on Day 16 as compared with the diabetic control group, but blood glucose lowering activities were not dose-dependent in both groups. In the meantime, food and water intakes in WGRE- and IH901-treated groups were significantly improved in dose dependent fashion as compared with the diabetic control group. Taken together, WGRE and IH901 showed the comparable antidiabetic activities at the corresponding doses we used in this experiment.

[PA1-35] [04/18/2002 (Thr) 14:00 - 17:00 / Hall E]

Renoprotective activity of water extract of Acanthopanax radix (ARWE) in streptozotocin-induced diabetic rats

Park KyeongSoo°, Kim SoYoung, Park JungMin, Chung SungHyun

School of Pharmacy, Kyung Hee University, Seoul 130-701, Korea

Purpose: Renoprotective activity of ARWE was examined in streptozotocin-induced diabetic nephropathic rats with regard to functional and immunohistochemical aspects.
Experimental methods: 20 mg/kg body weight of STZ in citrate buffer was injected intraperitoneally for 5 consecutive days. 20% of ARWE solution was given orally or subcutaneously for 2 weeks. STZ and ARWE were coadministrated for 5 days at the begin of study. Blood glucose and body weight were measured every 3 day. Urine glucose, albumin and creatinine clearance were determined at 2nd and 3rd week. Rats were sacrificed at 2nd and 3rd week of treatment, kidneys were removed. Then western blots for TGFβ1, ERK1, JNK2 and PAS staining of kidney tissue were also performed.
Results: A subcutaneous(SC) injection of ARWE prevented increase of blood glucose significantly. A SC injection of ARWE markedly prevented or delayed the development of diabetes induced by multiple low-dose STZ injection. A SC injection of ARWE also significantly lowered urine albumin and glucose. From the data we obtained, we may conclude ARWE has a renoprotective activity in STZ-induced nephropathic rats, and a discrepancy in renoprotective activity between oral and subcutaneous administration may be ascribed to dose administered.