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

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

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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.

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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

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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.

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In vitro screening of several herbal medicines for antidiabetic activity

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