[*Planta Medica*, **67**, 705-708 (2001)] [Lab. of Hygienics]

Inhibitory Effect of Magnolol and Honokiol from *Magnolia obovata* on Human Fibrosarcoma HT-1080 Invasiveness *in vitro*.

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We investigated the inhibitory effect of *Magnolia obovata* Thunb. bark ethanol extracts on human fibrosarcoma HT-1080 cells invasion of a reconstituted basement membrane [Matrigel (MG)]. We found that the effective components of the bark ethanol extracts were magnolol and honokiol, two biphenyl compounds. The extracts, magnolol and honokiol, did not affect HT-1080 cells adhesion to MG, but did inhibit HT-1080 cells migration at a high concentration (100μM). HT-1080 cells secrete matrix metalloproteinase (MMP)-9, which degrades the extracellular matrix as a part of the invasive process. Magnolol and honokiol inhibited the activity of MMP-9, which may have been responsible, in part, for the inhibition of tumor cell invasiveness.

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Suppressive Effect of Aspirin on Chromosome Aberration Induced by Mitomycin C in Mice

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Chromosome aberrations induced by mitomycin C (MMC) were suppressed by aspirin in a mouse micronucleus test with peripheral blood and bone marrow cells. Aspirin at doses of 0.5, 5, and 50 mg/kg was injected intraperitoneally or per administered orally 0.5, 6, or 24 h after administration of MMC, and then peripheral blood and/or bone marrow cells were sampled 48 h after administration of MMC. The suppressive effect of aspirin was more pronounced in the aspirin-treated groups 24 h than 0.5 and 6 h after administration of MMC. In the aspirin-treated group at 24 h, the frequency of polychromatic erythrocytes with micronuclei was decreased by about 60-80% after intraperitoneal injection and by about 40-70% after oral administration. It is suggested that aspirin may directly act on MMC metabolites, but not on MMC itself.

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Tumor Autocrine Motility Factor is an Angiogenic Factor that Stimulates Endotherial Cell Motility.

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Autocrine motility factor (AMF) is a type of tumor-secreted cytokine which primarily stimulates tumor cell motility via receptor-mediated signaling pathways, and is thought to be connected to tumor progression and metastasis. Using *in vivo* models, we showed that critical neovascularization responded to a biological amount of AMF. This angiogenic activity was fixed by specific inhibitors against AMF. AMF stimulated *in vitro* motility of human umbilical vein endothelial cells (HUVECs), inducing the expression of cell surface AMF receptor localizing a single predominant perinuclear pattern closely correlated with its motile ability. AMF also elicited the formation of tube-like structures mimicking angiogenesis when HUVECs were grown in three-dimensional type I collagen gels. We further immunohistochemically detected AMF receptors on the surrounding sites of newborn microvessels. These findings suggest that AMF is a possible tumor progressive angiogenic factor which may act in a paracrine manner for the endothelial cells in the clinical neoplasm, and it will be a new target for anti-angiogenic treatment.

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Analysis of Benzphetamine and Its Metabolites in Rat Urine by Liquid Chromatography-Electrospray Ionization Mass Spectrometry.

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An analytical method to identify and determine benzphetamine (BMA) and its five metabolites, N-benzylamphetamine, p-hydroxybenzphetamine (p-HBMA), p-hydroxy-N-benzylamphetamine, methamphetamine and amphetamine in urine was developed by liquid chromatography-electrospray ionization mass spectrometry (LC-ESI-MS) using the solid-phase extraction column Bond Elut SCX. Deuterium-labeled compounds, used as internal standards, were separated chromatographically from each corresponding unlabeled compound in the alkaline mobile phase with an alkaline-resistant ODS column. This method was applied to the identification and determination on BMA and its metabolites in rat urine collected after oral administration of BMA. This analytical method for p-HBMA, structurally closer to the unchanged drug of all the metabolites, was very sensitive, making this a viable metabolite for discriminating the ingestion of BMA longer than the parent drug or other metabolites in rat.