

Screening of Natural Products for Endothelial and Renal Nitric Oxide Production

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Natural products, which have been used for the treatment of hypertension, diuresis and nephritis in traditional oriental medicine, were selected for the screening of nitric oxide (NO) production in endothelial cells and kidney tissues *in vitro* as well as *in vivo* by measuring the conversion of [¹⁴C]-L-arginine to [¹⁴C]-L-citrulline, a coproduct of the enzyme reaction with NO. Confluent monolayer of endothelial cells were used for the screening of 16 natural products. Among the natural products, *Zizyphus jujuba* and *Codonopsis pilosula* stimulated endothelial NO synthase activity. Thus, both confluent monolayer of endothelial cells and kidney homogenates (glomeruli, cortical tubules, medullae) were treated with *Zizyphus jujuba* and *Codonopsis pilosula* (final concentration 10 μ g/ml) and NO releases were compared with those by receptor - dependent agonists, bradykinin and ADP and receptor - independent calcium ionophore A23187 *in vitro*. In rat experimnt, NO releases in glomeruli, cortical tubules and medullae and plasma renin activity were assessed after intraperitoneal injection of *Zizyphus jujuba* and *Codonopsis pilosula* (10 mg/kg/day for 4 days). As a result, both *Zizyphus jujuba* and *Codonopsis pilosula* significantly increased NO releases in cultured endothelial cells, kidney tissues *in vitro* as well as *in vivo*. Stimulation of NO releases by *Zizyphus jujuba* and *Codonopsis pilosula* was similar to those by receptor - dependent agonists, bradykinin and ADP and receptor - independent calcium ionophore A23187 in cultured endothelial cells. However, plama renin activity was not influenced by these two natural products. In conclusion, stimulatory effects of *Zizyphus jujuba* and *Codonopsis pilosula* on NO release in kidney may contribute thier hypotensive effects and antinephritic action possibly by increasing renal blood flow.