P54 Effect of Byakangelicin from *Angelica dahurica* and its Semi-synthetic Derivatives on Aldose Reductase, Galactosemic Cataracts, the Polyol Contents and Na^+, K^+-ATPase activity in Sciatic Nerves of Streptozotocin-induced Diabetic Rats.

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Aldose reductase(AR), a rate-limiting enzyme in the polyol pathway, has been demonstrated to cause the intracellular accumulation of sorbitol or galactitol and hence to play key roles not only in the cataract formation in the lens but also in the pathogenesis of diabetic complications such as neuropathy, retinopathy and nephropathy, etc.

In a series of investigations to evaluate potential AR inhibitors from medicinal plants , we have shown that some hot water extracts exhibited a significant inhibition of a significant inhibition of bovine lens AR *in vitro*. Among active plants, the roots of *Angelica dahuria* (Umbelliferae) were shown to have relatively potent AR inhibitory activity.

Systematic fractionation of the ether soluble fraction monitored by bioassay led to isolation of two furanocoumarins, byakangelicin(I) and ter-O-methyl byakangelicin(Ⅱ), were identified as potential AR inhibitors, their IC_{50} values being 6.2 M and 2.8 M, respectively.

Byakangelicin(I), a main furanocoumarin constituent, was evaluated to be effective in the treatment of galactosemic cataract and diabetic complications in rats. Galactosemic cataract formation and galactitol accumulation in the lenses of rats fed a 30% galactose diet were significantly prevented by intragastric(i.g.) administration of byakangelicin(I) at a dose of 100mg/kg for 14 days. Administration of the drug for 18 days was found to suppress sorbitol accumulation and cause a significant reversal of depleted myo-inositol contents as well as Na^+, K^+-ATPase activity in the sciatic nerves of streptozotocin-induced diabetic rats.

The two semi-synthetic derivatives of byakangelicin such as 2',3'-dihydro-byakangelicin(III) and 2', 3', 3, 4-tetrahydrobyakangelicin(IV) synthesized by reductive reaction were found to possess weaker AR inhibitory potency than byakangelicin.