CHEMICAL MODIFICATION OF FOREIGN COMPOUNDS BY RED CLOVER (*TRIFOLIUM PRATENSE*)

Akiko OGIWARA

Department of Toxicology,
Faculty of Veterinary Medicine,
Hokkaido University, Sapporo 060, Japan

The effect of a plant extract on metabolism, *in vivo* toxicity and mutagenesis of xenobiotics was investigated. The metabolic activity of the extract prepared from red clover (*Trifolium pratense*) was investigated using imipramine as a substrate. Imipramine metabolites were quantified by high performance liquid chromatography. The effect of possible metabolic activity of the extract on oral acute toxicity was tested using fenitrothion, an organophosphorous insecticide, as a model toxic agent. The effect of the plant extract on mutagenicity in the Ames' *Salmonella*/mammalian microsomes mutagenicity test was also investigated using benzo(a)pyrene and furylfuramide(AF–2) as mutagens.

Imipramine was N-demethylated by the plant extract containing green pigments in the absence of NADPH or NADH. The reaction occurred in the presence of SKF–525A, a cytochrome P–450 inhibitor or after heat treatment (60°C, 30min) of the plant extract. It was suggested that imipramine N-demethylation may be catalyzed by a plant component other than P–450, such as chlorophyll, for instance, which showed the ability to N-demethylate imipramine in a separate experiment. The effect of the plant extract on *in vivo* oral acute toxicity was not clear from this study. But the chlorophyll-containing plant extract markedly reduced the mutagenicity of benzo(a)pyrene, which requires metabolic activation for its mutagenicity, while no effect was observed on the mutagenicity of AF–2, a direct mutagen.

It was concluded that the extract of *Trifolium pratense* has the ability to metabolize and chemically modify drugs and mutagens, and that this effect most likely depends on chlorophyll, which requires further investigation.