THESIS TITLE : HEPATOPROTECTIVE EFFECTS OF THE EXTRACT FROM MEDICINAL HERB " LIN - RADD " (Tetracera loureiri) AGAINST CHEMICAL TOXICANTS

AUTHOR : MR. TAWEESAK JANYACHAROEN

THESIS ADVISORY COMMITTEE :

Veerapol Kukongviriyapan .....Chairman

(Associate Professor Dr. Veerapol Kukongviriyapan)

P. Pannangpetch .....Member

(Assistant Professor Dr. Patchareewan Pannangpetch)

Wichittra Tassaneeyakul .....Member

(Assistant Professor Dr. Wichittra Tassaneeyakul)

## ABSTRACT

Toxic substances from environment can induced damage to several tissue , especially the liver , since liver is the prime organ to metabolize endogenous and exogenous (xenobiotics) chemicals. Biotransformation by liver enzymes , eventhough is usually resulted in detoxification of chemicals , can also activate an innocuous chemical to some noxious species , for instance carbon tetrachloride , chloroform and paracetamol. Moreover apart from chemical - induced liver injuries , viral hepatitis infection is one of the major causes of liver injuries in Thailand. Treatment of liver injuries is usually symptomatic. Although some specific antidotes are available , they are only useful for limited types of liver injuries.

The objective of this study is to examine protective effects of Lin - Radd (Tetracera loureiri (Fin.&Gagnep.) Pierre ex Craib , Dillenniaceae.) , a medicinal herb used by Thai traditional doctors in the treatment of liver ailments , on animal models of chemical - induced liver injuries. The model employed isolated rat hepatocyte suspensions and known chemical hepatotoxicants ,

included paracetamol , bromobenzene and tertiary butyl hydroperoxide to induced cell damage. Degree of cell injury was assessed by assays of leakage of the enzyme lactate dehydrogenase , alanine aminotransferase and percent cell viability. In order to investigate mechanisms of protective actions of the plant extracts , degree of oxidative injury was estimated by assays of glutathione and lipid peroxidation. The herb was collected , dried , powdered and extracted initially with 50% ethanol in water. Crude extract was then concentrated and freezed dry. After initial studies , crude extract was further purified by partition the extract with hexane and ethyl acetate. Initial crude extract , hexane and ethyl acetate and the residue fraction left from hexane and ethyl acetate extraction , were tested for hepatoprotective activity. Extracts were dissolved in suitable solvents and added into hepatocyte suspensions before challenged with chemical hepatotoxicants. It was found that crude extract and the residue fraction possessed higher activities than other fractions.

The indicators of cytotoxicity were well correlated. Leakage of LDH and percentage of cell viability was highly correlated and more sensitive than leakage of ALT. Hepatoprotective effect of the extract was dose - dependent and cytotoxicity was completely abolished at the high dose (5 mg/ml) of the extract. The extract confered the maximum cytoprotection when it was added before the challenge with toxicants. Cytoprotective effect was diminished when the extract was added 30 minutes or 1 hour after toxicants. Glutathione levels and ratio of GSH/GSSG were sharply declined within 30 minutes after the addition of toxicants , while leakage of enzymes and formation of thiobarbituric reacting substance were linearly increased with time and cell viability was linearly declined with time. Experiments in rats revealed that alcoholic extract at dose of 1 g/kg body weight given by oral route almost completely protected liver damage induced by paracetamol (800 mg/kg , I.P.)

This study forms a basis for further study in vivo for testing drug properties and search for important medicinal herbs that be able to attenuate inflammation or injury of the liver after intoxication by chemical hepatotoxicants.