

ผลกึ่งเจียบพลันของสารสกัดหญ้าปักกิ่งด้วยเอทานอลต่อเอนไซม์ไซโตโครม พี450 ในตับ และ
ค่าเคมีคลินิกในเลือดของหนูขาว



นางสาวอัจฉรา ฉัตรสุภาวงศ์

ศูนย์วิทยทรัพยากร

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาเภสัชศาสตรมหาบัณฑิต

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SUBACUTE EFFECTS OF *MURDANNIA LORIFORMIS* ETHANOLIC EXTRACT ON
HEPATIC CYTOCHROME P450 AND CLINICAL BLOOD CHEMISTRY IN RATS

Miss Achara Chatsupang

ศูนย์วิทยทรัพยากร

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อัจฉรา ฉัตรสุมาวงศ์ : ผลกึ่งเฉียบพลันของสารสกัดหนุ้าปักกิ่งด้วยเอทานอลต่อเอนไซม์ไซโตโครมพี450 ในตับ และค่าเคมีคลินิกในเลือดของหนูขาว. (SUBACUTE EFFECTS OF *MURDANNIA LORIFORMIS* ETHANOLIC EXTRACT ON HEPATIC CYTOCHROME P450 AND CLINICAL BLOOD CHEMISTRY IN RATS) อ. ที่ปรึกษา : [ผศ. พ.ต.ท.หญิง ดร. สมทรง ลาวัณย์ประเสริฐ], อ. ที่ปรึกษาร่วม : [ผศ. ดร. ลัดดาวัลย์ นีวทองงาม] 116 หน้า. ISBN 974-17-4449-8.

หนุ้าปักกิ่ง มีชื่อทางพฤกษศาสตร์ว่า *Murdannia loriformis* (Hassk.) Rolla Rao et Kammathy เป็นสมุนไพรพื้นบ้านที่นิยมใช้เพื่อรักษาและบรรเทาอาการจากโรคมะเร็งหลายชนิด การศึกษานี้มุ่งศึกษาผลกึ่งเฉียบพลันของสารสกัดหนุ้าปักกิ่งด้วยเอทานอลต่อการทำงานของเอนไซม์ในเฟสหนึ่ง คือเอนไซม์ไซโตโครมพี 450 (cytochrome P450, CYP) นอกจากนี้ยังได้ศึกษาผลของสารสกัดนี้ต่อค่าเคมีคลินิกและโลหิตวิทยาในเลือดของหนูขาวด้วย การทดลองใช้หนูขาวเพศผู้พันธุ์สตาร์จำนวน 30 ตัว โดยแบ่งหนูขาวแบบสุ่มเป็น 3 กลุ่ม กลุ่มละ 10 ตัว กลุ่มแรกเป็นกลุ่มควบคุมได้รับน้ำกลั่น ขนาด 1 มิลลิลิตร/กิโลกรัม/วัน กลุ่มที่สองและสามเป็นกลุ่มที่ได้รับสารสกัดหนุ้าปักกิ่งด้วยเอทานอลในขนาด 0.1 และ 1 กรัม/กิโลกรัม/วัน ตามลำดับ หนูแต่ละกลุ่มจะได้รับการป้อนเป็นเวลา 30 วัน ระหว่างทำการทดลอง บันทึกน้ำหนักตัวทุก 7 วัน เมื่อครบระยะเวลา ทำให้นุ้หมดความรู้สึก เก็บตัวอย่างเลือดจากหัวใจเพื่อตรวจค่าโลหิตวิทยา และแยกซีรัมเพื่อตรวจค่าเคมีคลินิก นำตัวมาเตรียมไมโครโซม เพื่อใช้ตรวจวิเคราะห์ความเข้มข้นของ total CYP, สมรรถนะของ CYP 1A1, 1A2, 2B1/2, 2E1 และ 3A ผลการทดลองพบว่าสารสกัดหนุ้าปักกิ่งด้วยเอทานอลทั้งสองขนาด ไม่มีผลต่อน้ำหนักตัว น้ำหนักสัมพัทธ์ของตับ อีกทั้งไม่มีผลต่อความเข้มข้นของ total CYP, สมรรถนะของ CYP 1A1, 1A2, 2B1/2, 2E1 และ 3A สารสกัดหนุ้าปักกิ่งด้วยเอทานอลทั้งสองขนาดไม่มีผลต่อค่าเคมีคลินิกและโลหิตวิทยา ต่าง ๆ ต่อไปนี้คือ AST, ALT, ALP, total bilirubin, direct bilirubin, BUN, SCr, total cholesterol, TG, LDL-C, HDL-C, glucose, sodium, potassium, chloride, hemoglobin, hematocrit, platelet count, WBC count, % differential WBCs, RBC indices (mean corpuscular volume, MCV; mean corpuscular hemoglobin, MCH; mean corpuscular hemoglobin concentration, MCHC) และ RBC morphology จากผลการทดลองนี้แสดงให้เห็นว่าสารสกัดหนุ้าปักกิ่งด้วยเอทานอลไม่มีผลเปลี่ยนแปลงสมรรถนะของเอนไซม์ส่วนใหญ่ในเฟสหนึ่งที่มีบทบาทสำคัญในการกระตุ้นฤทธิ์ของสารก่อมะเร็ง/สารก่อการกลายพันธุ์ นอกจากนี้สารสกัดหนุ้าปักกิ่งด้วยเอทานอล ยังไม่มีผลต่อการทำงานของอวัยวะหรือระบบของร่างกายที่สำคัญ เช่น ตับ ไต ระบบเลือด อิเล็กโตรไลต์ รวมทั้งเมแทบอลิซึมของไขมันและคาร์โบไฮเดรต

ภาควิชาเภสัชวิทยา

ลายมือชื่อนิสิต..... อัจฉรา ฉัตรสุมาวงศ์.....

สาขาวิชาเภสัชวิทยา

ลายมือชื่ออาจารย์ที่ปรึกษา..... นกน (ค) อัจฉรา ฉัตรสุมาวงศ์.....

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ลายมือชื่ออาจารย์ที่ปรึกษาร่วม..... อัจฉรา ฉัตรสุมาวงศ์.....

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Murdannia loriformis (Hassk). Rolla Rao et Kammathy is commonly called in Thai as "Ya Pak King". *M. loriformis* has been used traditionally as a remedy for many kinds of cancers. This study examined subacute effects of *M. loriformis* ethanolic extract on phase I hepatic cytochrome P450 (CYP) in rats. In addition, effects of this extract on clinical blood chemistry and hematology were also determined. Thirty male Wistar rats were randomly divided into three treatment groups, ten in each group. Rats in the first group were given distilled water 1 ml/kg/day serving as a control group. The other two groups of rats were given *M. loriformis* ethanolic extract at dosages of 0.1 and 1 g/kg/day. Each group were administered orally for 30 consecutive days. During the treatment period, body weight was recorded every week. At the end of the treatment period, rats were anesthetized. Blood samples were collected by heart puncture and serum samples were prepared for measuring hematology and clinical blood chemistry, respectively. Microsomes were prepared from livers and being used for determining concentrations of total CYP as well as activities of CYP 1A1, 1A2, 2B1/2, 2E1 and 3A. The results showed that *M. loriformis* ethanolic extract at both dosages given in this study did not affect body weight, relative liver weight, hepatic total CYP concentrations and the activities of CYP 1A1, 1A2, 2B1/2, 2E1 and 3A. Rats received both dosage regimens of *M. loriformis* ethanolic extract demonstrated no changes of the following clinical blood chemistry and hematology: AST, ALT, ALP, total bilirubin, direct bilirubin, BUN, Scr, total cholesterol, TG, LDL-C, HDL-C, glucose, sodium, potassium, chloride, hemoglobin, hematocrit, platelet count, WBC count, % differential WBCs, RBC indices (MCV, MCH, MCHC), and RBC morphology. These results suggested that *M. loriformis* ethanolic extract did not modulate the activities of the most phase I hepatic CYPs involving in carcinogenic/mutagenic bioactivation. Furthermore, no effects of this extract were shown on several important organs/systems such as liver, kidney, blood system, electrolytes as well as carbohydrate and lipid metabolism.

Department Pharmacology

Student's signature..... Achara Chatsupang

Field of study Pharmacology

Advisor's signature..... Pol. Lt. Col. Somsong Lawanprasert

Academic year 2003

Co-advisor's signature..... L. Phivthong-NGAM

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LIST OF ABBREVIATIONS

| | |
|------------------|-------------------------------------|
| AFB ₁ | = alfatoxin B ₁ |
| ALP | = alkaline phosphatase |
| ALT | = alanine aminotransferase |
| ANOVA | = a one way analysis of variance |
| AST | = aspartate aminotransferase |
| B(a)P | = benzo(a)pyrene |
| BR | = benzyloxyresorufin |
| BROD | = benzyloxyresorufin O-dealkylase |
| BSA | = bovine serum albumin |
| BUN | = blood urea nitrogen |
| BW | = body weight |
| CD | = cluster of differentiation |
| cm | = centimeter |
| CYP | = cytochrome P450 |
| dL | = deciliter |
| DMSO | = dimethyl sulfoxide |
| DNA | = deoxyribonucleic acid |
| ED ₅₀ | = median effective dose |
| e.g. | = exempli gratia |
| ER | = ethoxyresorufin |
| EROD | = ethoxyresorufin O-dealkylase |
| et al. | = et alii (and other) |
| fL | = femtoliter |
| g | = gram |
| G6P | = glucose 6-phosphate |
| G6PD | = glucose 6-phosphate dehydrogenase |
| GST | = glutathione S-transferase |
| Hb | = hemoglobin |
| Hct | = hematocrit |

LIST OF ABBREVIATIONS (*continued*)

| | |
|------------------|--|
| HDL-C | = high density lipoprotein cholesterol |
| i.p. | = intraperitoneal |
| kg | = kilogram |
| L | = liter |
| LD ₅₀ | = median lethal dose |
| LDL-C | = low density lipoprotein cholesterol |
| M | = molar (mole per liter) |
| MCH | = mean corpuscular hemoglobin |
| MCHC | = mean corpuscular hemoglobin concentration |
| MCV | = mean corpuscular volume |
| mEq | = milliequivalent |
| min | = minute |
| mg | = milligram |
| ml | = milliliter |
| mm | = millimeter |
| mM | = millimolar (millimole per liter) |
| mmol | = millimole |
| MR | = methoxyresorufin |
| mRNA | = messenger ribonucleic acid |
| MROD | = methoxyresorufin O-dealkylase |
| MW | = molecular weight |
| NADP | = nicotinamide adenine dinucleotide phosphate |
| NADPH | = nicotinamide adenine dinucleotide phosphate (reduced form) |
| nm | = nanometer |
| nM | = nanomolar (nanomole per liter) |
| nmol | = nanomole |
| PAH | = polycyclic aromatic hydrocarbon |
| PBMC | = peripheral blood mononuclear cell |
| pg | = picogram |

LIST OF ABBREVIATIONS (*continued*)

| | |
|--------|--|
| pmol | = picomole |
| PR | = pentoxyresorufin |
| PROD | = pentoxyresorufin O-dealkylase |
| RBC | = red blood cell |
| r.p.m. | = revolution per minute |
| SCr | = serum creatinine |
| SEM | = standard error of mean |
| SER | = smooth endoplasmic reticulum |
| sec | = second |
| TCA | = trichloroacetic acid |
| TCDD | = 2,3,7,8-tetrachlorodibenzo- <i>p</i> -dioxin |
| TG | = triglyceride |
| TLC | = thin layer chromatography |
| Tris | = Tris (hydroxymethyl) aminomethane |
| U | = unit |
| UDP-GT | = uridine diphosphoglucuronosyltransferase |
| WBC | = white blood cell |
| w/v | = weight by volume |
| v/v | = volume by volume |
| XRE | = xenobiotic response element |
| °C | = degree celsius |
| β | = beta |
| γ | = gamma |
| α | = alpha |
| μg | = microgram |
| μl | = microliter |
| μM | = micromolar (micromole per liter) |