

เอกสารอยู่ด้วยกันในใบ



นางณอมจิต สุภาวดี

## ศูนย์วิทยทรัพยากร

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปรัชญา เกษชศาสตรมหาบัณฑิต

ภาควิชา เกษชพุกศาสตร์

บัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย

พ.ศ. 2522

008884

ว 1541430

**ALKALOIDS OF *UNCARIA ATTENUATA* KORTH.**

**MRS. TANOMJIT SUPAVITA**

A Thesis Submitted in Partial Fulfillment of the Requirements

for the Degree of Master of Science in Pharmacy

Department of Pharmaceutical Botany

Graduate School

Chulalongkorn University

1979

Thesis Title Alkaloids of *Uncaria attenuata* Korth.

By Mrs. Tanomjit Supavita

Department Pharmaceutical Botany

Thesis Advisor Assistant Professor Dhavadee Ponglux, Ph.D.

---

Accepted by the Graduate School, Chulalongkorn University in  
partial fulfillment of the requirements for the Master's degree.

..... S. Bunnag ..... Dean of Graduate School

(Associate Professor Supradit Bunnag, Ph.D.)



Thesis Committee :

..... Vichiara Jirawongse ..... Chairman

(Professor Vichiara A. Jirawongse, Ph.D.)

..... Bamrung Tantisewie ..... Member

(Assistant Professor Bamrung Tantisewie, B.Sc. in Pharm.)

..... Laddawan Boonyaratanaakornkit ..... Member

(Assistant Professor Laddawan Boonyaratanaakornkit, M.Sc. in Pharm.)

..... Dhavadee Ponglux ..... Member

(Assistant Professor Dhavadee Ponglux, Ph.D.)

Thesis Title Alkaloids of *Uncaria attenuata* Korth.

By Mrs. Tanomjit Supavita

Department Pharmaceutical Botany

Thesis Advisor Assistant Professor Dhavadee Ponglux, Ph.D.

---

Accepted by the Graduate School, Chulalongkorn University in  
partial fulfillment of the requirements for the Master's degree.

..... S. Bunnag ..... Dean of Graduate School

(Associate Professor Supradit Bunnag, Ph.D.)

Thesis Committee :

..... Vichiara Jirawongse ..... Chairman  
(Professor Vichiara A. Jirawongse, Ph.D.)

..... Bamrung Tantisewie ..... Member  
(Assistant Professor Bamrung Tantisewie, B.Sc. in Pharm.)

..... Laddawan Boonyaratankornkit ..... Member  
(Assistant Professor Laddawan Boonyaratankornkit, M.Sc. in Pharm.)

..... Dhavadee Ponglux ..... Member  
(Assistant Professor Dhavadee Ponglux, Ph.D.)

หัวข้อวิทยานิพนธ์ ชลกาลอยด์จากใบโงบ

ชื่อผู้สืบทอด นางวนิดา สุภาวดี

อาจารย์ที่ปรึกษา ผู้ช่วยศาสตราจารย์ ดร.ชาวดี ผ่องสกษณ์

ภาควิชา เกษตรพุกศาสตร์

ปีการศึกษา 2522



จากการใช้สมุนไพรงำเน่ สามารถแยกชลกาลอยด์จากใบโงบ (*Uncaria attenuata* Korth., Rubiaceae) ได้ 2 ประเภท คือ heteroyohimbines และ oxindoles, heteroyohimbines ที่ได้ ศิว tetrahydroalstonine และ rauniticine ชลกาลอยด์ชนิดหลังนี้ ยังไม่เคยมีรายงานว่าพบในพืชสกุล *Uncaria* ได้ศึกษาคุณสมบัติทางกายภาพ รวมทั้ง คุณสมบัติและปฏิกิริยาทางเคมีของชลกาลอยด์ทั้งสอง นอกเหนือไป ยังแยกได้ heteroyohimbine ใหม่ ที่ยังไม่เคยมีรายงานมาก่อน เลยทั้งในธรรมชาติและโดยการสังเคราะห์ ได้ทำการศึกษา คุณสมบัติทางกายภาพและเคมี และกำหนดว่าเป็น 14-hydroxy-3-isorauniticine พร้อม ทั้งบรรยายการกำหนดสูตรโครงสร้างอย่างละเอียด ส่วน oxindoles ที่แยกได้ 2 ชนิดมีปริมาณ น้อยมาก รวมทั้งได้พบร่องรอยของ oxindole อีก 1 ชนิด ทึ้งได้อธิบายเกี่ยวกับชลกาลอยด์ ทั้งหมดที่มีรายงานว่าพบในพืชสกุล *Uncaria*

Thesis Title Alkaloids of *Uncaria attenuata* Korth.

Name Mrs. Tanomjit Supavita

Thesis Advisor Assistant Professor Dhavadee Ponglux, Ph.D.

Department Pharmaceutical Botany

Academic Year 1979

#### ABSTRACT

Heteroyohimbine and oxindole alkaloids have been isolated from the leaves of *Uncaria attenuata* Korth. (Rubiaceae) by means of column chromatography. The isolated heteroyohimbines are tetrahydroalstonine, and rauniticine which has never been reported as being present in this genus before. Physical and chemical properties including chemical transformations of these two alkaloids are studied. One novel heteroyohimbine, not previously been reported elsewhere either naturally or synthetically, has been obtained. From the physical and chemical properties being studied, it is assigned as 14-hydroxy-3-isorauniticine. A detailed discussion on the elucidation of chemical structure is included. Only small quantities of two oxindoles have been obtained and traces of another oxindole is revealed. A discussion of the so far reported alkaloidal content of the genus *Uncaria* is presented.



## ACKNOWLEDGEMENTS

The author must first of all, express her sincere gratitude and thanks to her advisor, Assistant Professor Dr. Dhavadee Ponglux of the Department of Pharmacognosy, Chulalongkorn University Faculty of Pharmaceutical Sciences for her supervision of the research, ideas, keen interest, kindness, continual encouragement and understanding during the course of this study and editing of the dissertation.

The author wishes to express her appreciation to Associate Professor Dr. Payom Tantivatana, Head of the Department of Pharmaceutical Botany, Chulalongkorn University Faculty of Pharmaceutical Sciences, for her kindness to accept her to study in the Department of Pharmaceutical Botany.

The author would also like to express her appreciation to Professor Dr. Vichiara A. Jirawongse and Assistant Professor Bamrung Tantisewie, the former and the present Head of the Department of Pharmacognosy respectively, Chulalongkorn University Faculty of Pharmaceutical Sciences, and also to Assistant Professor Laddawan Boonyaratankornkit of the Department of Pharmaceutical Botany, Chulalongkorn University Faculty of Pharmaceutical Sciences, for their very useful suggestions.

The author wishes to express her thanks to Dr. C.E. Ridsdale of the Rijksherbarium, Leiden, The Netherlands for his kindness in identifying the plant material.

The author is heartfully grateful to Dr. J.D. Phillipson, Reader of the Department of Pharmacognosy, The School of Pharmacy, University of London, London, England for his kindness in determining the ultraviolet, infrared, nuclear magnetic resonance and mass spectra, and also for his invaluable discussions on the characterisation and identification of the isolated alkaloids.

Finally, the author's grateful thanks are due to Chulalongkorn University Graduate School for granting her partial financial support (of eight thousand and three hundred Baht) for conducting this investigation.

ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย

CONTENTS

	page
ABSTRACT (Thai) ... . . . . .	iv
ABSTRACT (English) ... . . . . .	v
ACKNOWLEDGEMENTS ... . . . . .	vi
CHAPTER I INTRODUCTION ... . . . . .	1
CHAPTER II HISTORICAL ... . . . . .	11
1. Alkaloids isolated from species of <i>Uncaria</i> ... . . . . .	11
2. <i>Uncaria</i> alkaloids isolated from other botanical sources	62
2.1 Heteroyohimbine alkaloids ... . . . . .	62
2.1.1 Closed E ring heteroyohimbine alkaloids	62
2.1.2 Open E ring heteroyohimbine alkaloids	67
2.2 Oxindole alkaloids ... . . . . .	70
2.2.1 Closed E ring oxindole alkaloids	70
2.2.2 Open E ring oxindole alkaloids	74
2.3 Pyridino-indolo-quinoxolidinone alkaloids ... . . . . .	81
2.4 $\beta$ -Carboline alkaloids ... . . . . .	84
2.5 Yohimbine alkaloids ... . . . . .	85
3. Chemistry of the alkaloids ... . . . . .	89
3.1 Heteroyohimbine and oxindole alkaloids ... . . . . .	89
3.1.1 Basic structures ... . . . . .	89
3.1.2 Configuration of heteroyohimbine and oxindole alkaloids ... . . . . .	91

<b>3.1.3 Preferred conformations</b>	...	...	...	98
<b>Heteroyohimbine alkaloids</b>	...	...	...	98
<b>Closed E ring</b>	...	...	...	98
<b>Open E ring</b>	...	...	...	100
<b>Oxindole alkaloids</b>	...	...	...	102
<b>Closed E ring</b>	...	...	...	102
<b>Open E ring</b>	...	...	...	105
<b>3.1.4 Alkaloid N-oxides</b>	...	...	...	108
<b>3.2 Other indole alkaloids isolated from species of Uncaria</b>	114			
<b>3.2.1 Pyridino-indolo-quinolizidinone alkaloids</b>	...	...	114	
<b>3.2.2 Roxburghines A, B, C, D and E</b>	...	...	114	
<b>3.2.3 B-Carboline alkaloids</b>	...	...	...	115
<b>3.2.4 Yohimbine and its isomers</b>	...	...	...	116
<b>3.2.5 Orouparine, gambirtannines and related alkaloids</b>	117			
<b>3.2.6 Geissoschizine methyl ether</b>	...	...	...	118
<b>3.2.7 Yohimbine oxindole alkaloids</b>	...	...	...	118
<b>3.2.8 Tetracyclic pseudoindoxyl alkaloids</b>	...	...	...	119
<b>3.2.9 Africanine and hanadamine</b>	...	...	...	120
<b>3.2.10 Mitaversine</b>	...	...	...	120
<b>4. Chemical Transformations</b>	...	...	...	120
<b>4.1 In vitro</b>	...	...	...	121
<b>4.1.1 Isomerisation of heteroyohimbine alkaloids</b>	...	...	121	
<b>4.1.2 Isomerisation of oxindole alkaloids</b>	...	...	123	
<b>4.1.3 Conversion of heteroyohimbine alkaloids             to oxindole alkaloids</b>	...	...	...	126

4.1.4 Conversion of oxindoles to heteroyohimbine alkaloids ... ... ...	130
4.2 <i>In vivo</i> ... ... ...	132
5. N-oxidation of heteroyohimbine and oxindole alkaloids ...	134
6. Biogenesis ... ... ...	136
6.1 Heteroyohimbine alkaloids ... ... ...	136
6.2 Oxindole alkaloids ... ... ...	147
6.3 Biogenesis of other indole alkaloids ... ...	149
6.3.1 Pyridino-indolo-quinolizidinone alkaloids ...	149
6.3.2 Roxburghines A, B, C, D and E ... ...	150
6.3.3 $\beta$ -Carboline alkaloids ... ... ...	150
6.3.4 Yohimbine alkaloids ... ... ...	151
6.3.5 Geissoschizine methyl ether ... ...	151
6.4 Biogenesis of the <i>Uncaria</i> alkaloids ... ...	152
CHAPTER III EXPERIMENTAL ... ... ...	156
1. Source and authentication of plant material ... ...	156
2. General techniques ... ... ...	156
2.1 Extraction of alkaloids ... ... ...	156
2.2 Purification of crude alkaloidal extract ... ...	157
2.3 Thin layer chromatography ... ... ...	157
2.3.1 Analytical ... ... ...	157
2.3.2 Preparative ... ... ...	158
2.4 Column chromatography ... ... ...	159
2.5 Melting point ... ... ...	159
2.6 Ultraviolet absorption spectra ... ... ...	159

2.7 Infrared absorption spectra ... ... ... ...	159
2.8 Nuclear magnetic resonance spectra ... ... ...	160
2.9 Mass spectra ... ... ... ...	160
<b>3. Isolation of individual alkaloids</b> ... ... ...	160
<b>3.1 Extraction of alkaloids from the leaves of         <i>Uncaria attenuata</i> Korth.</b> ... ... ...	160
<b>3.2 Separation of alkaloids by column chromatography</b> ...	161
<b>3.3 Isolation of alkaloids from the fraction T<sub>d</sub></b> ...	162
<b>3.4 Examination of alkaloids fraction T<sub>a</sub></b> ... ...	163
<b>4. Isomerisation of the isolated alkaloids</b> ... ...	164
<b>4.1 Isomerisation of 3-isorauniticine from rauniticine</b> ..	164
<b>4.2 Isomerisation of akuammigine from tetrahydroalstonine</b>	165
<b>5. Identification and characterisation</b> ... ... ...	165
<b>5.1 Identification of the isolated alkaloids and         the isomerisation products</b> ... ... ...	165
<b>5.1.1 Identification of TS<sub>1</sub> as tetrahydroalstonine</b>	166
<b>5.1.2 Identification of TS<sub>7</sub> as akuammigine</b> ...	167
<b>5.1.3 Identification of TS<sub>2</sub> as rauniticine</b> ...	168
<b>5.1.4 Identification of TS<sub>6</sub> as 3-isorauniticine</b> ...	169
<b>5.2 Characterisation</b> ... ... ... ...	170
<b>Characterisation of TS<sub>3</sub> as 14-hydroxy-3-isorauniticine</b>	170
<b>CHAPTER IV DISCUSSION</b> ... ... ... ...	173
<b>1. The alkaloidal content of <i>Uncaria</i> species</b> ... ...	173
<b>2. The structure of the new naturally occurring         heteroyohimbine alkaloid</b> ... ... ...	182

CHAPTER V CONCLUSION AND RECOMMENDATION ...	...	...	...	186
REFERENCES ...	...	...	...	188
APPENDIX ...	...	...	...	207
Dragendorff's spray reagent	...	...	...	208
Key to the Fig, XIX - L	...	...	...	209
Thin layer chromatograms	...	...	...	212
Spectra ...	...	...	...	231
VITA ...	...	...	...	245

ศูนย์วิทยทรัพยากร  
จุฬาลงกรณ์มหาวิทยาลัย