

อัลคาลอยด์ของใบบัวบกนำ



นางสาว นารา ปิตาลัย

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญา เกษตรศาสตรมหาบัณฑิต

ภาควิชาเกษตรเวท

บัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย

พ.ศ. 2530

ISBN 974-567-409-5

ลิขสิทธิ์ของบัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย

012375

๑๐๒๙๒๘๖๗

ALKALOID(S) OF ANNONA SQUAMOSA LINN. LEAVES

MISS NARA PETASAI

A Thesis Submitted in Partial Fulfillment of the Requirements  
for the Degree of Master of Science in Pharmacy

Department of Pharmacognosy

Graduate School

Chulalongkorn University

1987

Thesis Title                            Alkaloid (s) of *Annona squamosa* Linn. Leaves  
By                                        Miss Nara Petasai  
Department                             Pharmacognosy  
Thesis Advisors                        Associate Professor Kalaya Pharadai  
    Associate Professor Bamrung Tantisewie

---



Accepted by the Graduate School, Chulalongkorn University, in  
Partial Fulfillment of the Requirements for the Master's Degree.

*Thavorn Vajrabhaya* ..... Dean of Graduate School  
(Professor Thavorn Vajrabhaya, Ph.D.)

Thesis Committee

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

*M.L.Pranod Xumsaeng* ..... Member  
(Professor M. L. Pranod Xumsaeng, B.Sc. in Pharm.)

*Kalaya Pharadai* ..... Member  
(Associate Professor Kalaya Pharadai, M.Eng.)

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

หัวข้อวิทยานิพนธ์

อัลคาลอยด์ของใบบอนบอน

ชื่อนิสิต

นางสาว นารา พีดาลัย

อาจารย์ที่ปรึกษา

รองศาสตราจารย์ กัลยา ภราไชย

รองศาสตราจารย์ บำรุง ตันติเสวี

ภาควิชา

เภสัชเวท

ปีการศึกษา

2529



บทคัดย่อ

โดยการใช้กรรมวิธีทางสุ่มภรังคเลช ทำให้สามารถแยกอัลคาloyd Lanuginosine ซึ่งเป็น oxoaporphine alkaloid ได้จากสิ่งสกัดจากใบของต้นบอนบอน (Annona squamosa Linn.) ทั้งได้ทำการศึกษาคุณสมบัติทางกายภาพและเคมีของสารประกอบนี้ด้วย

Thesis Title                    Alkaloid(s) of *Annona squamosa* Linn. Leaves  
Name                            Miss Nara Petasai  
Thesis Advisors                Associate Professor Kalaya Pharadai  
                                  Associate Professor Bamrung Tantisewie  
Department                     Pharmacognosy  
Academic year                1986

#### ABSTRACT

By means of column chromatography, an oxoaporphine alkaloid "Lanuginosine" was isolated from the leaves extract of *Annona squamosa* Linn. Its physical and chemical properties were studied.



#### ACKNOWLEDGEMENTS

The author wishes to express her deepest appreciation and grateful thanks to her advisors, Associate Professor Kalaya Pharadai, the Head Department of Pharmacognosy and Associate Professor Bamrung Tantisewie, the former Head Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, Chulalongkorn University for their inspiration, invaluable guidance as well as useful suggestions throughout the course of practical work.

The author was indebted to Professor Maurice Shamma and Dr. Alejandro Urzua of the Department of Chemistry, the Pennsylvania State University, U.S.A. for their assistance in determining and interpreting the UV, IR, NMR and Mass spectra.

Particularly to Mrs. Mataya Puntukanon, the author extends her heartfelt thanks to her dearest friend for her continuing concern and cordial contribution.

A special word of thanks is due to Miss. Srunya Vajrodaya, who has kindly drawn out botanical figure of *Annona squamosa* Linn.

A sincere gratitude is also extended to all the staff members and colleagues of the Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, Chulalongkorn University for their encouragements and helps.

Eventually, the author thanks the Graduate School, Chulalongkorn University for granting her partial financial support (Thirteen thousand and one hundred baht) to conduct this study.



## CONTENTS

	Page
ABSTRACT (Thai) .....	iv
ABSTRACT (English) .....	v
ACKNOWLEDGEMENTS .....	vi
CHAPTER I INTRODUCTION .....	1
CHAPTER II HISTORICAL REVIEW	
Alkaloids Distribution in Genus <i>Annona</i> .....	15
Chemistry of <i>Annona</i> alkaloids .....	22
1 Simple Tetrahydroisoquinolines .....	22
2 Benzylisoquinolines .....	23
3 Protoberberines .....	25
4 Proaporphines .....	29
5 Aporphines .....	31
6 Oxoaporphines .....	33
7 Phenanthrenes .....	35
8 Non-isoquinoline Alkaloids .....	36
8.1 Purine .....	36
8.2 Pyrimidine- $\beta$ -carbolines .....	37
Biosynthesis .....	38
Biological and Pharmacological Activity of <i>Annona</i> Alkaloids .....	49

	Page
CHAPTER III EXPERIMENTAL .....	54
I Source of Plant Materials .....	54
II General Techniques .....	54
a) Thin Layer Chromatography .....	54
b) Column Chromatography .....	55
c) Physical Constant .....	56
d) Spectroscopy .....	57
III Extraction and Isolation of Alkaloids from the Leaves of <i>Annona squamosa</i> Linn.	
a) Extraction of Crude Alkaloids .....	57
b) Isolation of Alkaloids .....	59
c) Identification of Alkaloid N <sub>1</sub> as Lanuginosine .....	60
CHAPTER IV DISCUSSION .....	63
CHAPTER V CONCLUSION AND RECOMMENDATION .....	66
REFERENCES .....	68
APPENDIX .....	79
Thin Layer Chromatography .....	80
Spectra .....	87
VITA .....	92



## CHAPTER I

### INTRODUCTION

*Annona squamosa* Linn. (Synonym : *A. biflora* Sessé, *A. cinerea* Dunal, *A. forskahlii* DC. (1a) Thai name : Noi-Naa, English names : Sugar Apple, Sweet Sop, Anon, Custard Apple) is notable countrywide in Thailand for its sweet, juicy and very agreeable flavor fruit. It is cultivated throughout Thailand. Not only a tasty fruit it is, but it is also used in folk medicine.

There are numerous phytochemical reports in many aspects on *Annona squamosa* Linn. such as in alkaloidal contents (1b-9) etc. In addition, biological and pharmacological activities, for example antitumor (10), uterotonic (11), and insecticide (12-14) have been reported.

As a matter of fact that, the quantity and proportions of alkaloids in plants are to some extent under genetic control, and greatly affected by many factors. The first factor is fluctuations of the environment e.g. light intensity (15), the second is variation in growth conditions arising from seasonal, climatic, geographical and soil differences, and the last one is maturation (16).

Moreover, none of those phytochemical studies were undertaken in Thailand, which prompted the author to re-investigate the alkaloids in *Annona squamosa* Linn. growing in Thailand.

## Botanical Features of *Annona* Species

### 1. Distribution and Origin

According to Willis (17), *Annona* is one of the chief genera in Annonaceae. The genus *Annona* is native of tropical America and Africa. Some members of this genus were carried to the East in very early times, and have been cultivated there still. It is naturalized in the Old World (18, 19).

### 2. Classification

Up till now, the genus *Annona* comprises 207 species.

Following are an alphabetical list of valid species of the genus *Annona* (20-36) .

*Annona acuminata* Saff.

A. *acutiflora* Mart.

A. *acutifolia* Saff. ex R.E. Fries

A. *africana* Linn.

A. *amambayensis* Hassler

A. *amara* Raeusch.

A. *amazonica* R.E. Fries

A. *ambotay* Aubl.

A. *amplexicaulis* Lam.

A. *angustifolia* Huber

A. *antioquensis* Linden

A. *asiatica* Linn.

A. *asplundiana* R.E. Fries

A. *atabapensis* H.B. & K.

A. *aurantiaca* Barb.

A. *australis* St. Hil.

*Annona axilliflora* DC.

A. *barteri* Benth.

A. *bicolor* Urb.

A. *biflora* Sessé see A. *squamosa* Linn.

A. *billbergii* R.E. Fries

A. *bullata* A. Rich.

A. *burchellii* R.E. Fries

A. *cacans* Warm.

A. *calophylla* R.E. Fries

A. *campestris* R.E. Fries

A. *cancellata* Mart.

A. *cascarilloides* Griseb.

A. *cauliflora* Mart.

A. *cearaensis* Barb.

A. *cercocarpa* Saff.

A. *cherimolia* Mill. Cherimoyer, Cherimoya

A. *cherimolioides* Triana & Planch.

A. *cheriquensis* Linden

A. *chrysopetala* Steud.

A. *chrysophylla* Boj.

A. *cinerea* Dunal see A. *squamosa* Linn.

A. *colorata* Vell.

A. *conica* Ruiz & Pav.

A. *conifera* Ruiz ex R.E. Fries

A. *conophylla* Triana & Planch.

A. *coriacea* Mart.

*Annona cornifolia* St. Hil.

A. *crassiflora* Mart.

A. *crassifolia* Mart.

A. *crassivenia* Saff.

A. *cristalensis*

A. *crotonifolia* Mart.

A. *cubensis* R.E. Fries

A. *cuyabaensis* Barb.

A. *deminuta* R.E. Fries

A. *densicoma* Mart.

A. *depressa* Baill.

A. *divica* St. Hil.

A. *diversifolia* Saff.

A. *dolichophylla* R.E. Fries

A. *domingensis* R.E. Fries

A. *duckei* Diels

A. *dumetorum* R.E. Fries

A. *echinata* Dunal

A. *ecuadorensis* R.E. Fries

A. *ekmanii* R.E. Fries

A. *elliptica* R.E. Fries

A. *excellens* R.E. Fries

A. *excelsa* H.B. & K.

A. *fagifolia* St. Hil. & Tul.

A. *falsifolia* Glaz.

A. *foetida* Mart.

*Annona forskahlii* DC. see *A. squamosa* Linn.

*A. friesii* Robyns & Ghesquière

*A. frutescens* R.E. Fries

*A. fruticosa* Sessé & Moc.

*A. furfuracea* St. Hil.

*A. gardneri* R.E. Fries

*A. geraensis* Barb.

*A. glabra* Linn. Pond Apple

*A. glauca* Schum. & Thonn.

*A. glaucophylla* R.E. Fries

*A. globiflora* Schlecht.

*A. gracilis* R.E. Fries

*A. grandiflora* Lam.

*A. grandifolia* St. Hil. & Tul.

*A. guaricensis* Pittier

*A. haematantha* Miq.

*A. haitiensis* R.E. Fries

*A. havanensis* R.E. Fries

*A. hayisii* Saff.

*A. heinsenii* Engl. & Diels

*A. holosericea* Saff.

*A. hostmanni* Steud.

*A. humboldtii* Dunal

*A. humilis* Benth.

*A. hypoglauca* Mart.

*A. imbitibana* Glaz.

*Annona impressivenia* Saff. ex. R.E. Fries

A. *incana* Bartram

A. *inconformis* Pittier

A. *insignis* R.E. Fries

A. *involucrata* Baill.

A. *ionophylla* Triana & Planch.

A. *iquitensis* R.E. Fries

A. *jahnii* Saff.

A. *jamaicensis* Sprague

A. *jenmanii* Saff.

A. *klainii* Pierre ex Engl. & Diels.

A. *laevigata* Mart.

A. *laevis* H.B. & K.

A. *lasiocalyx* Mart.

A. *latifolia* S. Elliot

A. *laurentii* Engl. & Diels.

A. *laurifolia* Dunal see A. *glabra* Linn.

A. *lepidota* Miq.

A. *liebmanniana* Baill.

A. *longepetiolata* (R.E. Fries) Robyns & Ghesquiere

A. *longiflora* S. Wats. Wild Cherimoya of Jalisco

A. *longifolia* Sessé & Moc. see A. *reticulata* Linn.

A. *longipes* Saff.

A. *lutescens* Saff.

A. *macrocalyx* R.E. Fries

A. *macrocarpa* Barb.

*Annona macrophyllata* Donn. Smith

A. *malmeana* R. Fries

A. *manabiensis* Saff. ex. R.E. Fries

A. *maniote* H.B. & K.

A. *mannii* Oliver

A. *maregravii* Mart.

A. *membranacea* R.E. Fries

A. *mexicana* Lodd. ex. G. Don.

A. *micrantha* Bert. ex. Spreng.

A. *microcarpa* Ruiz & Pav.

A. *minensis* Glaz.

A. *moagensis* Leon & Alain

A. *montana* Macfad. Mountain Soursop

A. *monticola* Mart.

A. *muricata* Linn. Soursop

A. *nana* Exell

A. *nano-fruticosa* Herzog

A. *neglecta* R.E. Fries

A. *nipensis* Alain

A. *nitida* Mart.

A. *nutans* R.E. Fries

A. *oblongifolia* R.E. Fries

A. *oligocarpa* R.E. Fries

A. *palmeri* Saff.

A. *paludosa* Aubl.

A. *palustris* Linn. see A. *glabra* Linn.

- Annona paraensis* R.E. Fries  
*A. paraguayensis* R.E. Fries  
*A. parviflora* Ruiz & Pav.  
*A. pavonii* G. Don  
*A. peduncularis* Steud.  
*A. phaeoclados* Mart.  
*A. pisonis* Mart.  
*A. pittieri* Donn. Sm.  
*A. polycarpa* DC.  
*A. praetermissa* Rendle  
*A. prestoei* Hemsl.  
*A. primigenia* Standley & Steyermark.  
*A. punctata* Aubl.  
*A. punicifolia* Triana & Planch.  
*A. purpurea* Moc. & Sessé ex Dunal Soncoya  
*A. pyriformis* Boj.  
*A. quinduensis* H.B. & K.  
*A. reticulata* Linn. Bullock's Heart, Custard-Apple  
*A. rhizantha* Eichl.  
*A. rhombipetala* Ruiz & Pav.  
*A. rigida* R.E. Fries  
*A. riparia* H.B. & K.  
*A. rodriguesii* Barb.  
*A. rosei* Saff.  
*A. rufa* Presl  
*A. saffordiana* R.E. Fries

*Annona salzmanni* A. DC.

*A. salicifolia* Ekman & R.E. Fries

*A. sanctae-crucis* S. Moore

*A. sariffa* Roxb. ex Henschel

*A. scandens* Diels ex Pilg.

*A. scleroderma* Saff.

*A. sclerophylla* Saff.

*A. senegalensis* Pers.

*A. sericea* Dunal ex Sprague

*A. sessiliflora* Benth.

*A. sinensis* Raeusch.

*A. sphaerocarpa* Splitg.

*A. spinescens* Mart.

*A. spraguei* Saff.

*A. squamosa* Linn. Sugar Apple, Sweet Sop, Custard Apple,  
Anon

*A. stenophylla* Engl. & Diels

*A. sulcata* Urb.

*A. surriffa* Roxb.

*A. symphyocarpa* Sandwith

*A. tenuiflora* Mart.

*A. tenuifolia* A. DC.

*A. tenuipes* R.E. Fries

*A. tessmannii* Diels

*A. testudinea* Saff.

*A. tomentosa* R.E. Fries

*A. trinitensis* Saff.



*Annona trunciflora* R.E. Fries  
*A. tuberosa* Noronha  
*A. ulei* R.E. Fries  
*A. uliginosa* H.B. & K.  
*A. urbaniana* R.E. Fries  
*A. velutina* St. Hil. & Tul.  
*A. vepreronum* Mart.  
*A. volubilis* Lundell  
*A. walkeri* S. Moore  
*A. xylopiifolia* St. Hil. & Tul.  
*A. zenkeri* Engl. & Diels

In Thailand, only four species of *Annona* are cultivated (37).

They are:

- *Annona cherimolia* Mill. น้อยหน้าอสเตรเลีย *Noinaa ostrelia* (General); Cherimoya
- *Annona muricata* Linn. ทุเรียนแขก *Thurian khack*, ทุเรียนเทศ *Thurian thet* (Central); มะทุเรียน *Ma thurian* (Northern); Sour Sop, Guanabana, Durian Belanda
- *Annona reticulata* Linn. น้อยหนัง *Noinang* (Peninsular); น้อยโภนง *Noinong* (Central); มะดาอก *Madaak* (Phrae); มะเนียงแข้ง *Maniang haeng*; มะโภนง *Manong* (Northern); เร็งนา *Reng-naa* (Karen-Kanchanaburi); หนองล้าว *Nonlaao* (Ubon Ratchathani); หมากอ้อ *Maak-o* (Shan-Mae Hong Son); Custard Apple, Bullock's Heart

- *Annona squamosa* Linn. ເຕີບ Tiap (Khmer); ນ້ອຍທຳ Noinaa (Central); ນ້ອຍແນ້ Noinae (Peninsular); ມະນອແນ້ Manonae; ມະແນ້ Manae; ນອແນ້ Nonae (Northern); ມະອຈ້າ, ມະໄອຈ້າ Ma-o-chaa (Shan-Northern); ລາກນັງ Laa nang (Pattani); ກົມເກລົກະແຊ No-kloh-sae (Shan-Mae Hong Son); ທັນເຂົ້າບ Mak khiap (Northeastern); Custard Apple, Sugar Apple, Sweet Sop (38) .

### 3. Botanical Characteristic of *Annona*

On the basis of morphology and habitat, the genus *Annona* composes of very homogenous plants.

They are trees or shrubs. Flowers solitary or fascicled, terminal or leaf-opposed. Sepals 3, small, valvate. Petals 3-6, valvate in two series, or the inner series wanting, outer triquetrous, base concave. Stamens numerous, anther-cells narrow, dorsal, contiguous, top of connective ovoid. Ovaries many, subconnate, style oblong, ovule 1, erect. Ripe carpels confluent into a many-celled ovoid or globose many-seeded fruit. Fruits aggregate, often very large, made up of the individual berries, sunk in and united with the fleshy receptacle (17,18). Seeds are large, often arillate, with copious and markedly ruminated endosperm and minute embryo.

Oil sacs occur throughout in the parenchyma, even in the parts of the flowers (39, 40).

Annona squamosa Linn.

1. Botanical Features

The origin of *Annona squamosa* Linn. is in Middle or South America. In Thailand it is mostly cultivated in the Central and North-Eastern regions.

It is characterized as a small tree, 3-5 m. in height, leaves simple, alternate, 5-7.6 by 1.9-3.8 cm., membranous, oblong, glaucous beneath, pubescent when young; apex obtuse or acuminate; base acute.

Flowers solitary, 2.5 cm. long; pubescent. Petals 3, narrow-oblong. The fruit is large and heart-shaped, fleshy, areolate, tubercled. The ovaries become united with each other and the floral axis to form a fleshy mass in which the seeds are embedded (18, 40, 41, 46).

2. Ethnomedical Use

Various parts of *Annona squamosa* Linn. are used in Thai's folk medicine as follows:-

- Leaves: antiinflammatory, antifungal, anthelmintic, antipediculosis
- Bark: astringent
- Fruit: anthelmintic, antifungal
- Seed: antipediculosis, antiinflammatory, vermicidal
- Root: laxative

*Annona squamosa* Linn. has been used in folk medicine not only in Thailand, but also in various parts of the world.

The details are as demonstrated in Table 1.

Table 1 Summary of Ethnomedical Use of *Annona squamosa* Linn.

	Use	Part Used	Reference
1	Antitumor	Leaves, Fruits	45, 46
2	Fever	Leaves	45
3	Uterine Stimulant (abortifient, relieve prolong labor)	Leaves, Seeds	19, 45-47
4	Ecbolic & Emmenagogue	not mentioned	46
5	Dyspepsia	Leaves	19, 46
6	Vermicide & Insecticide	Leaves, Seeds, Fruits	19, 46, 47
7	Anthelmintics	Fruits, Leaves	44, 45
8	Scabies & Skin diseases of children	Leaves	19
9	Astringent	Fruits, Roots, Barks	19, 45-47
10	Antipediculosis (Anti-lice)	Seeds	19, 46, 47
11	Drastic purgative	Roots	19, 46
12	Laxative	Fruits	45

The only pharmacological study of *Annona squamosa* Linn. seeds & leaves was carried out in Thailand on anti-pediculosis action by Oranuth Puapattanakul, 1980 (48). The result provided that blended seeds crushed with coconut oil in the concentration ratio of 1:2 was the best way to destroy 98% of lice (*Pediculus humanus* var. *capitis* Linn.) (49).