

Review Article

A REVIEW ON PHYTOCHEMICAL CONSTITUENTS AND PHARMACOLOGICAL ACTIVITIES OF
CLINACANTHUS NUTANS

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ABSTRACT

Clinacanthus nutans commonly known as Belalai gajah (Malay), Phaya yo (Thai) is traditionally used medicinal plant. The plant is used in skin rashes, snake bites, lesions caused by herpes simplex virus, diabetic myelitis, fever, diuretics and green tea and served as fresh drink. The phytochemical constituents existing in the plant comprise lupeol, b-sitosterol, stigmasterol, Botulin, myricyl alcohol C-glycosyl flavones (vitexin, isovitexin, shaftoside, isomollupentin 7-O-b-glucopyranoside, orientin and isorientin), sulfur-containing glucosides, cerebrosides mixer, a monoacylmnogalactosylglycerol, 13-hydroxy-(13-S)-phaeophytin b, Pupurin-18-phytyl ester, phaeophorbide and chlorophyll derivatives. Pharmacological studies reported anti-Papillomavirus Infectivity, anti-viral activity on varicella-zoster virus, anti-inflammatory activity, anti-herpes Simplex virus type 1 and type 2 activity, anti-oxidant and protective effect against oxidative induced hemolysis.

Keywords: *Clinacanthus nutans*, Anti-viral, Anti-oxidant, Glycosides, Herpes Simplex Virus.

INTRODUCTION

Clinacanthus nutans (CN) have been used in traditional medicine in Thailand and Malaysia. Its therapeutic potential has not been explored completely. It is commonly known as Belalai gajah, Sabah Snake Grass in Malaysia [1], phaya yo or phaya plontong in Thailand [2] and Giro de flores, cocodrilo flor, e zui hua in chinese language [4]. *Clinacanthus nutans* (Burm. f.) Lindau is the accepted name of this species and *Clinacanthus nutans* var. *robinsonii* Benoist, *Clinacanthus burmanni* Nees, *Justicia nutans* Burm. f. are their synonyms[5]. It is distributed in Thailand, Indonesia, Malaysia, Vietnam and china (Guangdong, Guangxi, Hainan, Yunnan)[3].

Taxonomy [3]

Kingdom: Plantae (Plants)
Class: Equisetopsida C. Agardh
Subclass: Magnoliidae Novák ex Takht.
Superorder: Asteranae Takht.
Order: Lamiales Bromhead
Family: Acanthaceae Juss
Genus: *Clinacanthus* Nees

Traditional uses

In Malaysia, the fresh leaves are boiled with water and consumed as herbal tea. It is used for treating skin rashes and snake bites, lesions caused by herpes simplex virus, diabetic myelitis, fever and diuretics [6][7]. In Thailand, an alcoholic extract of fresh leaves is used externally for treatment of skin rashes, snake and insect bite, herpes simplex virus (HSV), and varicella-zoster virus (VZV) lesions. The leaves can be consumed as raw material or mixed with other juices such as apple juice, sugarcane or green tea and served as fresh drink [8].



Fig. 1: Leaves and Flower of *Clinacanthus nutans*

Table 1: Common names of *Clinacanthus nutans* all around the world [2-4]

Common names	Language
Belalai gajah	Malay
Sabah Snake Grass	
Twist of flowers	Chinese
Alligator flower	
e zui hua	
Phaya yo	Thai
Phaya plontong	

Table 2: Synonyms of *Clinacanthus nutans* [5]

<i>Clinacanthus nutans</i> (Burm. f.) lindau	Accepted name
<i>Clinacanthus nutans</i> var. <i>robinsonii</i> Benoist	Synonym
<i>Clinacanthus burmanni</i> Nees	Synonym
<i>Justicia nutans</i> Burm. f.	Synonym



Fig. 2: *Clinacanthus nutans*

Table 3: Traditioanal uses of *Clinacanthus nutans*

Country	Part use	Application
Malaysia	Fresh leaves	In Malaysia, the fresh leaves are boiled with water and consumed as herbal tea It is commonly used in traditional Malaysia for its nourishing and anti-oxidant property. It is also used economical in house regimens for cancer patient [6-7, 9]
Thailand	Leaves	It is used for treating skin rashes and snake bites, lesions caused by herpes simplex virus, diabetic myelitis, fever and diuretics[8]
Indonesia	Fresh leaves	In Thailand, an alcoholic extract of fresh leaves is used externally for treatment of skin rashes, snake and insect bite, herpes simplex virus (HSV), and varicella-zoster virus (VZV) lesions. The leaves can be consumed as raw material or mixed with other juice such as apple juice, sugarcane or green tea and served as fresh drink [8]

Phytochemistry

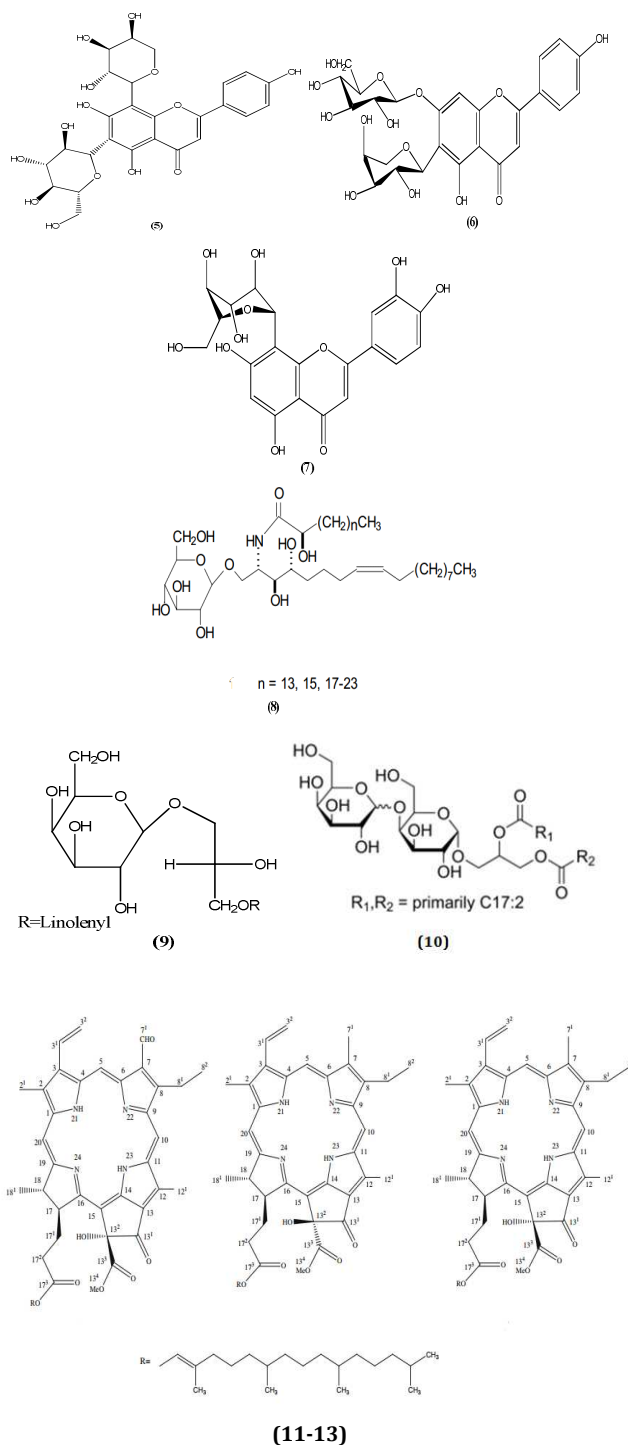
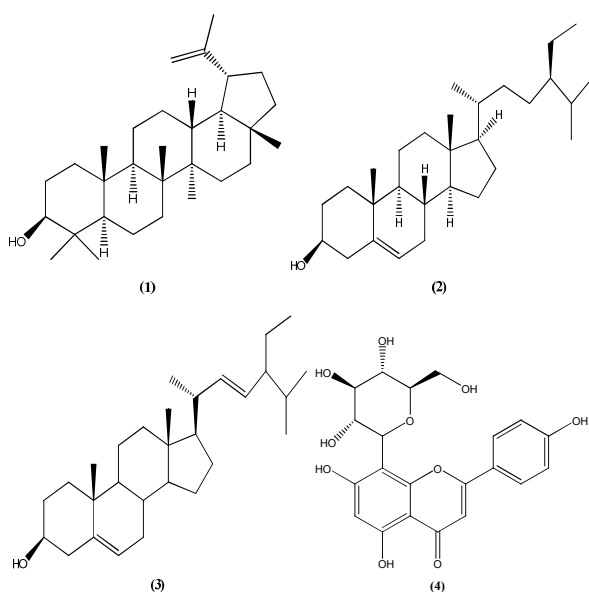
Clinacanthus nutans contains lupeol (1), β -sitosterol (2)[17], stigmasterol(3) [16] Botulin[18] and myricyl alcohol [10][11]. It also contain six known C-glycosyl flavones isolated from the n-BuOH- and water soluble portion of the methanolic extract of the stems and leaves of *C. nutans* collected in Thailand such as vitexin (4), isovitexin, shaftoside (5), isomollupentin 7-O- β -glucopyranoside (6), orientin (7) and isoorientin[12].

Five sulfur-containing glucosides were isolated from the n-BuOH-soluble portion of a methanolic extract of the stems and leaves of plant material [13]. A mixture of cerebrosides (8) and a monoacyl monogalactosyl glycerol[(2S)-1-O-linolenoyl-3-O- β -D-galactopyranosylglycerol](9) were isolated from the EtOAc-soluble fraction of the ethanolic extract of the fresh leaves of *C. nutans*,[14].

13-hydroxy- (13-S)-phaeophytin b, Pupurin-18-phytyl ester and Phaeophorbide a were isolated from leaves of hexane and chloroform extract of *C. nutans* [15]. Trigalactosyl and digalactosyl diglycerides(10) were isolated from the leave extract and possess anti-herpes simplex virus effect [19].

Hexane and chloroform leave extract of *C. nutans* contain, 132-hydroxy-(132-S) -chlorophyll-b, 132-hydroxy- (132-R)-chlorophyll-b,132-hydroxy-(132-S)- phaeophytin-b,132-hydroxy-(132-R)- phaeophytin-b, 132-hydroxy-(132-S)-phaeophytin-a,132-hydroxy-(132-R)-phaeophytin-a, purpurin-18- phytyl ester and phaeophorbide-a [20].

Three chlorophyll derivatives (phaeophytins) (11-13) were isolated from the chloroform extract of *Clinacanthus nutans* Lindau leaves. Three of these were known compounds with structures related to chlorophyll a and chlorophyll b namely 132-hydroxy- (132-R)-phaeophytin b, 132-hydroxy- (132-S)- phaeophytin-a and 132-hydroxy-(132-R) -phaeophytin [21].



Pharmacological activities reported

Fig. 3: Chemical structures of *Clinacanthus nutans*

Pharmacological activity	Part use	Extract/Fraction/Isolate	Dose tested/ route of administration	Animals/Cell line culture	Experimental model (In Vivo / In Vitro)	Results	Reference
Cholinergic modulation	L	Methanol	250 mg/kg, 500 mg/kg, 1 000 mg/kg bw	Male mice	In vivo	A	22
Cytotoxic Study	-----	Stock solution in DMSO	0.01,0.005,0.001, 0.0005, 0.0001 and 0.00001%	Koi Fin cell line (KFC)	In-vitro	B	23
Anti-Papillomavirus Infectivity	-----	Stock solution in DMSO	Different concentrations in different compounds	293FT cells	In-vitro	C	24
Anti-inflammatory activity	L	n-BuOH-soluble fraction	-----	-----	In-vitro	D	25
virucidal Activity	-----	ethanol extracts	-----	-----	In-vitro	E	26
Anti-viral Activity on varicella-zoster virus.	L	Crude extract	-----	-----	In-vitro	F	27
Dengue Virus Type 2 Infection	L	hexane and chloroform	34, 5, 20, 25 µg/ml	C6/36 cell line, A549 cell line	In-Vitro	G	28
Anti-herpes Simplex Virus type 1 Activity	L	Ethyl Acetate Extract	1.9,2, 4, 8, 19, 38, 76,152ug/ml	Vero cells	in vitro on the Vero cells by using plaque reduction assay	H	29
Acute toxicity Study	L	ethanolic	5.44g/Kg bw	rats	In vivo	I	30
Anti-herpes Simplex Virus type 2 Activity	L	-----	-----	Baby hamster kidney cell line	In-vitro	J	31
Anti-oxidant, protective effect against oxidative induced hemolysis	L	ethanolic	-----	-----	In-vitro	K	32

A= AChE activity was found highest in mice liver, followed by brain, kidney and heart

B= result was reported as 50% cytotoxicity concentration. *C. nutans* plant extract at 0.005% and 0.01% damaged KFC cells and had the cytotoxic effect to the cell in those concentrations.

C= This study demonstrates anti-HPV16 PsV infection of *C. nutans* compounds (136C and 136D) that inhibit the early step of infection by direct binding between HPV particles and host cell receptor and also prevent HPV16 PsVs internalization. These suggest the potential

role of the compounds on prevention of HPV infection.

D= It possess anti-inflammatory activity

E= virucidal against HSV-2 in vitro.

F= In a series of in vitro models a crude extract of the leaves showed significant inhibitory activity on VZV.

G=The results showed that out of four compounds, compound 2 could inhibit the production of viral RNA as well as viral protein when the DV2 infected cells were cultured in the compound. This novel property should be further investigated for action on DV infection in the molecular level. This compound may be developed for treatment of DV infection.

H= The results showed that the crude ethyl acetate extract of *C. nutans* exerted inhibitory effects on HSV-1 action

I= internal organ has No abnormalities

J= The result showed that extract inhibit plaque formation by HSV-2

K= The ethanolic extract of CN had an antioxidant activity and protective effect against free radical-

Induced hemolysis.

Clinical trials

Clinical trials have reported the successful use of a *C. nutans* preparation (cream) for treatment of genital herpes and varicella-zoster lesions in patients [33-36].

CONFLICT OF INTERESTS

Declared None

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