The Journal of Phytopharmacology 2014; 3(1): 57-76
Online at: www.phytopharmajournal.com

Review Article

ISSN 2230-480X
JPHYTO 2014; 3(1): 57-76
January- February

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Ethnobotany, phytochemistry, pharmacology and toxicology profiles of *Cassia siamea* Lam.

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Abstract

Cassia siamea is a shrub belonging to the Fabaceae family, native of Southeast Asia and better known in folklore medicine, feeding, agriculture and manifacture all over the world including Côte d'Ivoire. *C. siamea* has recently been shown to have antimicrobial, antimalarial, antidiabetic, anticancer, hypotensive, diuretic, antioxidant, laxative, anti-inflammatory, analgesic, antipyretic, anxiolytic, antidepressant, and sedative activities. Chromone (anhydrobarakol), Chromone alkaloids (barakol, cassiarin A-B), anthraquinones (chrysophanol, emodin), bianthraquinones (cassiamin A-B), flavonoids and phenolics compounds are the main constituents which are reported in this plant. Barakol was identified as the major constituents of *C. siamea* of leaves and flowers of the world. Due to the easy collection of the plant, it widespread and also remarkable biological activities, this plant has become a worldwide medicine. This review presents comprehensive analyzed information on the botanical, chemical, pharmacological and toxicological aspects of *C. siamea*. Web sites of Google Scholar, Pubmed and Hinari were searched for articles published. Some scientific data were collected through Scientific Units of Research and Formation (UFR) of the University Felix Houphouet-Boigny of Abidjan.

Keywords: *Cassia siamea - Ethnobotany - Chemistry – Pharmacology - Toxicology*.

Introduction

Cassia siamea (syn. *Senna siamea*) is an angiosperme native of Southeast Asia (Burma, Ceylon, India, Japan, Malaysia, Sri-Lanka and Thailand) and widely distributed in Africa (Cote d'Ivoire, Eritrea, Ethiopia, Ghana, Kenya, Malaysia, Nigeria, Sierra Leone, South of Africa, Tanzania, Togo, Uganda and Zambia), in Latin America (Cuba, Chile, Antigua and Barbuda, St Lucia, St Vincent and Grenadines and Trinidad and Tobago), and in Oceania (Australia and Fiji).[1-4] Firstly classified in Caesalpiniacae family, then in those of *Leguminoseae*, *C. siamea* is now classified among the *Fabaceae*.[5] This plant is a shrub which has a medium-size, 10-12 m tall, occasionally reaching 20 m.[6] The bole is short; crown dense and rounded at first, later becoming irregular and spreading. The young bark is grey and smooth, and later with longitudinal fissures. The leaves are alternate, 15-30 cm long, compound, with 6-14 leaflets each ending in a tiny bristle.[7] The flowers are bright yellow, in large, up to 60 cm long, upright, with pyramid-shaped panicles. The fruits are flat with indehiscent pod, 5-30 cm long, and constricted between the seeds. There are about 20 seeds per pod. The seeds are bean-shaped, greenish-brown, and 8-15 mm long (Figure 1).[1, 8]

1- Stem, 2- leaves, 3- flowering branch and flowers, 4- pods, 5- stem bark
From: Photography of the plant in Abobo (Côte d'Ivoire)

Figure 1: Different parts of *Cassia siamea*

For a long time, *C. siamea* is better known by the tropical populations for it various medicinal vertus.[9-11] It is also known for its various common uses in cattle rearing[12], agriculture, environment[13-14] and founiture[15]. Since review and systemic analysis of chemistry, pharmacology and clinical profiles of *C. siamea* have not been reported; we were prompted to provide current available information on traditional and local knowledge, ethnobiological and ethnomedicinal issues, and identification of pharmacologically important molecules, pharmacological and toxicological studies on this useful plant. This review aims at gathering the research work undertaken till to date upon this plant in order to provide sufficient baseline information for future works and commercial exploitation. The scientific information was collected through researcher's Floristic Center of Abidjan, and Units of Research and Formation (UFR) of Medicine, Pharmacy and Biology of Felix Houphouet Boigny university of Abidjan. Scientific-medical publications were also consulted in different databases (Sciencedirect, Pubmed, and Hinari) using key words such as *Cassia siamea*, *Senna siamea*, *Fabaceae*, *Leguminoseae*, *Caesalpiniaceae*, ethnobotany, chemistry, pharmacology, and toxicology.

Ethnobotany

Vernacular names

The diverse vernacular names of the plant through the different localities are given in table no. 1

Table 1: Vernacular names of *C. siamea*

Localities	Vernacular names	References
Benin	Kassia, cassiatin	16
Burkina Faso	Kasse tiiga	17
Côte d'Ivoire	Acassia gbêman, acassia oufoué	
Ethiopia	Yeferenji digita	
Ghana	Zangara tsi	18
Kenya	Ndek obino, Oyieko, Ndege owinu	19, 20
Malaysia	Sebusok, guah Hitam, juah, petai belalang, Johor	22
Nigeria	Bikini raskata, odan	
Tanzania, Uganda	Mjohoro	
Togo	Zangalati	24
France	Casse du siam, bois perdrix, de la casse	8
Creole isles	Kasia	
Spain	Flamboyan Amarillo	23
Cambodia	Ângkanh	
India:	Minjri, manjekonna, kassod, ponavari, vakai, simaiavari, kilek, Nela thangedu	21
Indonesia	Bujuk, dulang, johar,	21
Nepal	Criminal	21
Philippines	Robles	
Thailand	Kassod tree, yellow cassia, shower thailand, thai pod copper, iron wood, siamese senna, bombay blackwood, black cassia-wood, khilek or khilekluang, khilek-yai, chili phak, khi lek ban, sino-Tibetan	21
Vietnam	Humbo, c [aa] y mu [oof] ng den, mu [oof] ng [egg], mu [oof] ng xi [ee] m muoofng xieem.	21

Therapeutic uses

The leaves, stems, roots, flowers and seeds of *C. siamea* regardless the subspecies have been used for the treatment of several illnesses including mostly malaria, a tropical endemic disease with high morbimortality.[8, 15, 23-26] In this review, the preparation process of remedies was not clearly described and the dosages prescribed were approximative. Moreover, the treatments are supposed to be continued until recovery.[19] According to the ethnic differences of populations from localities, the plant is used alone or in combination with other plants or with natural substances for the preparation, especially in decoction. [19, 27] For the treatment, people mostly used the preparations by orale administration route.

Leaves uses

The leaves are the most used parts' the plant especially by African and Asian population in preparation of the herbal remedies. In Burkina Faso, fresh and dried leaves decoction (boiled for 20 min in 1L of water) is drunk with lemon juice or for body bath throughout the day to treat malaria and liver disorders.[17, 25, 28] In Côte d'Ivoire, the decoction of leaves is administered orally (0.5 L, twice daily) for treating cough, stomach pains[29] and malaria[2]. Also, in Sierra Leone and Togo, the leaves decoction is drunk against malaria[24, 30] and used as antimicrobial[31]. In Nigeria, the dried leaves are mixed with lemon's leaves (*Cymbopogon citratus*), pawpaw's leaves (*Carica papaya*), and the lime's leaves (*Citrus lemonum*) and are boiled within an hour. The "tea" of the mixture is drunk against malaria.[32] In Uganda, the leaves are picked, cleaned and chewed, and liquid swallowed to treat abdominal pains.[33] In India, the leaves are cleaned thoroughly and boiled. The decoction is filted in which is added honey. This preparation is drunk ¾ glass (150 mL), 3 times a day against anaemia and fever.[34] In Laos, fresh and dried leaves boiled at a ratio of 1:3 for 1 hour 2-3 times to reduce the bitterness, and then crushed to get a paste in which the pork bones are added. This dish called "chi om leck" is taken before breakfast as a vegetable which has sedative and euphorising effects.[35-36] In Thailand, dried leaves are sprayed to be regularly consumed in capsule form as vegetable for its laxative effect and as sleeping pill.[37-39] Other authors reported that *Cassia siamea* leaves decoction is drunk against constipation and hypertension and are inhaled in toothache.[30, 40]

Roots uses

In Benin, root decoction is used against fever, constipation, hypertension, and insomnia.[16] In Kenya, the infusion, decoction or maceration of mixture of the roots of *C. siamea* and those of *Zanthoxylum chalybeum* are used as antidote for snake bites.[20] In Southeast and Sub-Saharan Africa, and herbalists use the root decoction for the treatment of diabetes mellitus.[41] In these areas, the roots are crushed and mixed then the aqueous extract is drunk to treat sore throat.[33] In Côte d'Ivoire, small repeative doses of maceration or decoction roots' bark are drunk to treat angina and malaria, respectively.[2, 42]

Stems uses

In Burkina Faso, Ghana and Nigeria, the decoction of the whole stem or stem's bark is drunk or take for body bath against malaria and liver disorders.[18, 25, 33, 43-44] These same uses were reported in Malaysia.[22] Dried stems of *C siamea* mixed with the fruit of *Xylopia aethiopica* is pulverized and administered as laxative.[37] The decoction of the stem bark is drunk against diabetes. This decoction is used as a mild, pleasant, safe, and purgative in Japan. Also, Dalziel (1963) and Keharo (1974) indicated that its decoction is used against scabies, urogenital diseases, herpes, and rhinitis in Cambodia.[41]

Flowers and seeds uses

In Burkina Faso, flowers decoction is drunk or used in body bath against malaria and liver disorders. This decoction is also effective against insomnia and asthma.[25, 33]

The seeds are used to charm away intestinal worms[30] and as antidote for snake and scorpion bites[46]. The decoction of the mixture of *C. siamea* and *Ficus thonnigii* fruits' is drunk to prevent convulsions in children and to treat typhoid fever.[34] In Sri Lanka and Thailand, the flowers and young fruits are regularly consumed as vegetable and for treating curries. It provides laxative and sleeping-aid effect.[37] This dish is also anxiolitic and effective against dysuria.[38]

Whole plant uses

The decoction or the maceration of the mixture of different part of *C. siamea* is used for the management of diabetes[47] and used as laxative[48]. In China and Pakistan, the decoction of the leaves and the stems mixture is used as an aperitif, antirheumatic and against swellings.[49] In Congo,

this decoction is widely used in periodic fever and malaria.[30]

Chemistry

Qualitative analyse

Preliminary phytochemical screening of *C. siamea*, showed the presence of chromones and its derivatives (chromone alkaloids, chromones glycosides, dihydronaphthalenone compounds, bischromone), polyphenols (anthraquinones, bianthraquinones, anthrone, flavonoids, isoflavonoids, phenolics, tannins), alkaloids, saponins, steroids, carotenoids, antinutrients (oxalate, phytate), reducing sugars, vitamins, minerals and enzymes.[31, 49-56] Various bioactive compounds identified from *C. siamea* are shown in Table n°2. The structures of the main constituents are shown in figure n°2.

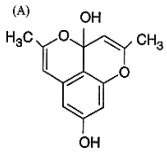
Table 2: Chemical composition of *Cassia siamea*

Plant part	Extract	Molecular groups	Molecules	Reference
Leaves	Chloroform	Chromone alkaloids	Barakol	61, 63, 64
	Methanol	Chromone	Anhydrobarakol ; 5-acetonyl-7-hydroxy-2-methylchromone; 5-acetonyl-7-hydroxy-5-acetonyl-7-hydroxy-2-hydroxymethylchromone	59, 60, 121
		Chromone alkaloids	cassiarin A, cassiarin B	66, 70
		Anthraquinones	Chrysophanol; emodin, physion, rhein, sennosides	3, 121
		Bianthraquinones	Cassiamin A, cassiamin B	60, 125
		Bischromones	Chrobisiamone A; resins	
	Ethanol	Triterpenoid	lupeol	58
		Flavonoid	D-pinitol, luteolin	58, 103
		Dihydronaphthalenone	4-(trans)-acetyl-3,6,8-trihydroxy-3-methyldihydronaphthalenone; 4-(cis)-acetyl-3,6,8-trihydroxy-3-methyldihydro-naphthalenone	58
	Hydroalcoholic	Steroids	β- and γ-sitosterol	59
		Carotenoids	Carotenes, xanthophylls	89
		Vitamin	Vitamin A,C,E	
	Aqueous	isoflavone glycoside	2',4',5,7-tetrahydroxy-8-C-glucosylisoflavone	85
	Hexane	Mineral	Iron , magnesium, manganese, potassium; calcium; sodium; copper; cadmium; lead; phosphorus	49
Stem bark	Methanol	Bianthraquinones	4-4'-bis(1,3-dihydroxy-2-methyl-6,8-dimethoxy-anthraquinone; 1,1'-bis(4,5-dihydsroxy-2-methyl-anthraquinone, cassiamin A, cassiamim B, cassiamin C; madagascarin	3, 80, 81
		Anthraquinones	Chrysophanol; emodin; physcion; chrysophanol-1-O-β-D-glucopyranoside; 1-[(β-D-glucopyranosyl-(1-6)-O-β-D-glucopyranosyl)-oxy]-8-hydroxy-3-methyl-9,10-anthraquinone; cycloart-25-en-3beta,24-diol	72, 77, 110

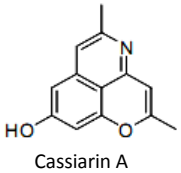
		Flavonoid	Piceatannol	72
		Triterpenoid glycoside	19α,24-dihydroxyurs-12-ene-28-oicacid-3-O-β-D-xylopyranoside	77
		Triterpenoid	Lupeol, friedelin	88, 110
		Mineral	Iron, magnesium, manganese, potassium; calcium; Sodium; copper; lead; chromium, nickel; zinc	51
	Chloroform	Triterpenoid	Betulinic acid	105
		Phenolic	Coumarin	
		Chromones	Siamchromones A-G	62
	n-butanol	Chromone glycosides	2-methyl-5-(2'(hydroxypropyl)-7-hydroxy-chromone-2'-O-β-D glucopyranoside; 2-methyl-5-propyl-7,12-dihydroxy-chromone-12-O-β-D-glucopyranoside	72, 73
		Favonoid	Kaempferol	83
Root bark	Methanol	Anthraquinones	Chrysophanol; emodin	76
		Bianthraquinones	1,1',3,8,8'-pentahydroxy-3',6-dimethyl[2,2'-bianthracene] 9,9',10,10'-tetrone; 7-chloro-1,1',6,8,8'-pentahydroxy-3,3'-dimethyl[2,2'-bianthracene]-9,9',10,10'-tetrone; cassiamin A, cassiamim B	79
Flowers	Chloroform	Chromone alkaloids	Barakol ;10, 11-dihydroanhydrobarakol, cassiarin C, D, E, and F	40, 63,64, 68, 69
	Methanol	Chromone alkaloids	Cassiadinine	71
		Phenolic acid	Gallic acid; protocatechuic; p-hydroxy benzoic acid; chorogenic acid; Vanilic acid; caffeic acid; syringic acid; p-coumaric acid; ferulic acid; sinapic acid	84
		Flavoniod	Rutin; Myricetin; Quercetin; Kaempferol	
Seeds	Hexane	Steroids	Cholesterol, stigmasterol, β-sitosterol	70
		Fatty acid	palmitic, stearic, oleic and linoleic acids	
	Aqueous	Anthraquinones	Aloe-emodin, sennosides A_1	74, 75
	NS	Vitamin	Vitamin B1, B2, B3, C, E	93
		Mineral	Calcium, phosphorus, sodium, magnesium, iron, zinc, copper	
		amino acids	Lysine, Valine, Leucine, Isoleucine, Threonine, Methionine, Cystine, Tyrosine, Histidine, Arginine, Aspartic acid, Serine, Glutamic acid, Proline, Glycine;Alanine	

NS, No specified

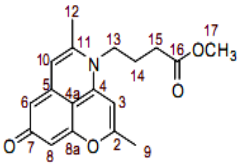
Chromone and derivatives



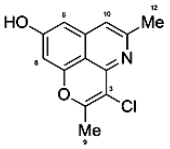
Barakol



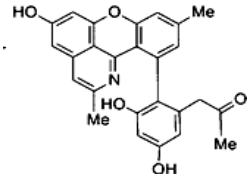
Cassiarin A



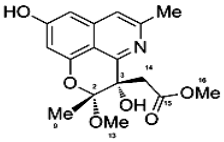
Cassiarin B



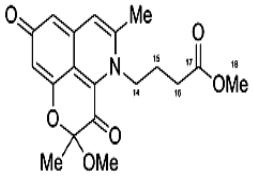
Cassiarin K



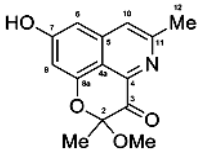
Cassiarin F



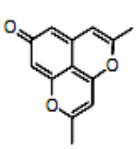
Cassiarin J



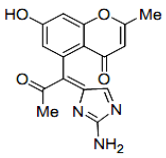
Cassiarin H



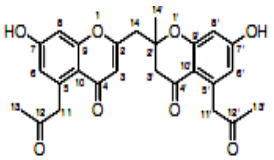
Cassiarin G



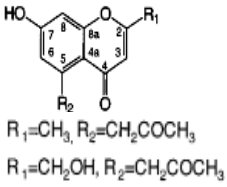
Anhydrobarakol



Cassiadinine



Chrobisiamone A

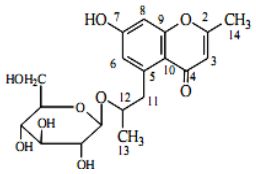


(5) R_1=CH_3, R_2=CH_2COCH_3

R_1=CH_2OH, R_2=CH_2COCH_3

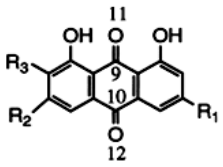
5-acetonyl-7-hydroxy-2-methylchromone

5-acetonyl-7-hydroxy-5-acetonyl-7-hydroxy-2-hydroxymethyl-

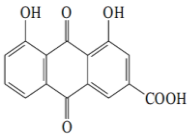


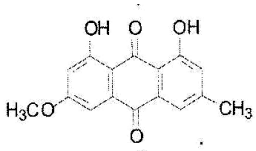
2-methyl-5-propyl-7,12-dihydroxy-chromone-12-O-β-D-glucopyranoside

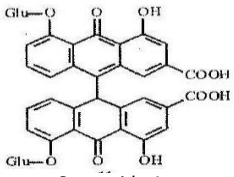
Anthraquinones



	R1	R2	R3
1	CH3	H	H
2	CH3	OH	H
3	CH2OH	H	H
4	CH3	OH	CL







Chrysophanol (**1**)

Aloe-émodin (**3**)

Emodin (**2**)

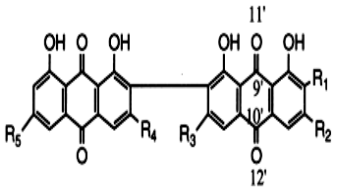
7-Chloroemodin (**4**)

Rhein

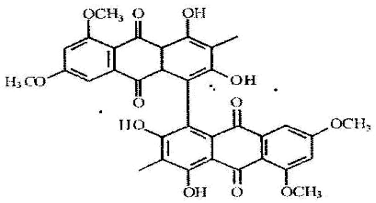
Physcion

Sennoside A

Bianthraquinones



	R1	R2	R3	R4	R5
5	H	OH	CH_3	CH_3	H
6	H	OH	CH_3	CH_3	OH
7	H	H	CH_3	CH_3	H
8	H	CH_3	OH	CH_3	OH
9	H	CH_3	OH	CH_3	H
10	CL	OH	CH_3	CH_3	H
11	H	H	CH_2OH	CH_2OH	H
12	H	CH_3	OH	CH_2OH	H



Cassiamin A (**5**)

Cassiamin C (**7**)

Cassiamin B (**6**)

Madagascarin (**8**)

4-4'-bis (1,3-dihydroxy-2-methyl-6,8-dimethoxyanthraquinone

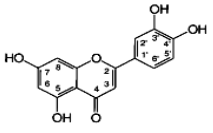
1,1',3,8,8'-pentahydroxy-3', 6-dimethy-l[2,2'-bianthracene]-9,9',10,10'-tetrone (**9**)

7-chloro-1,1',6,8,8'-pentahydroxy-3,3'-dimethyl[2,2'-bianthracene]-9,9,10,10'-tetrone(**10**)

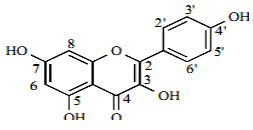
1,1',8,8'-tetrahydroxy-3,3'-dihydroxymethyl [2, 2'-bianthracene]-9, 9',10,10'-tetrone (**11**)

1,1',3,8,8'-pentahydroxy-3-hydro-xymethyl-6-methyl [2, 2'-bianthracene]-9, 9',10,10'-tetrone (**12**)

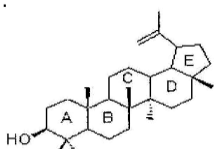
Flavonoids and triterpene



Luteolin(Flavonoid)



Kaempferol (Flavonoid)



Lupeol (Triterpenoid)

Figure 2: Strcuture of the phytoconstituents of *Cassia siamea*

Quantitative analyse

The contents of the most bioactive compounds are not known. Quantitative investigations of the leaves, stem bark and seeds of *C. siamea* showed vitamin, amino acid, elemental and proximate contents.[89, 92-93] Indeed, the oil from its seeds contains a high content of linoleic acid, stigmasterol and β-sitosterol.[90] The main compounds of the essential oils of *C. siamea* are (E)-geranyl acetone (5.8%), 1-octen-3-ol (5.8%), linalool (7.8%), iso-italicene (15.4%) and (E)-β-damascenone (11%).[91] In the seeds, the highest amounts of riboflavin, thiamine, niacin, ascorbic acid and tocopherol (mg/100g) are 0.13, 0.72, 2.08, 8.80 and 3.60, respectively. The elemental contents (mg/100g) of methanol extract / hexane extract of leaves are: Iron 6.74/112, magnesium 126/876, manganese 0.72/35, potassium 257/812; calcium 87.72/932; Sodium 350/612; copper 0.49/0.84; and lead 0.06/0.34, respectively.[49, 51] The elemental contents of methanolic extract of stem bark are (mg/100g): iron 5.51, magnesium 47.29, manganese 0.88, potassium 116.82, calcium 96.49; sodium 263.16; copper 069, lead 0.11, chromium 1.05, nickel 3.36, and zinc 17.99.[51] These results justify the traditional use of *C. siamea* in feeding.

Pharmacology

As *C. siamea* is a mixture of various groups of chemicals, it is of no surprise that it exhibits different modes of actions. Its major actions include (i) antimalarial, (ii) antidiabetic, (iii) antitumoral or anticancer, (iv) hypotensive, (v) diuretic, (vi) antioxidant, (vii) laxative, (viii) anti-inflammatory, (ix) analgesic, (x) antipyretic, (xi) anxiolytic, (xii) antidepressant, (xiii) sedative, and (xiv) antimicrobial activities.

Antimalarial effects

Various extracts of leaves, stem bark, and flowers of *C. siamea* were screened for its antimalarial activity.[98] Most of the activities described were determined in vitro on Plasmodium falciparum strains. Specified and bio-guided fractionation was also based on this antimalarial test. Activities were assessed on different strains, among which are chloroquine sensitive (3D7), chloroquine resistant (W2, FcM29-Cameroon) and multidrug resistant (K1) in order to find effective compounds against resistant malaria. In all studies, alkaloids fraction of the leaves exhibited better aniplasmodial activity than other extracts.[95] This alkaloids fraction, the chloroform and ethanol extracts of the leaves showed activity against 3D7 with IC_{50} value of 0.24, 2.41 and 7.06 µg/ml, respectively. Cassiarin A is the alkaloid compound which has more potential activities. Its activity is similar to that of chloroquine against 3D7 with IC_{50} value of 0.005 and 0.006 µg/mL, respectively.[96] The IC_{50} of this compound was IC_{50} 0.02 µg/mL against K1. Other compounds isolated from leaves such as cassiarin J (IC_{50} 0.3 µg/mL), cassiarin K (IC_{50} 1.4 µg/mL), chrobisiamone A (IC_{50} 2.6 - 5.6 µg/mL), 5-acetonyl-7-hydroxy-2-methylchromone (IC_{50} 4.5 - 19.4 µg/mL), anhydrobarakol (IC_{50} 7.8 µg/mL), cassiarin B (IC_{50} 22 µg/mL), cassiarin G (IC_{50} > 50 µg/mL), and cassiarin H (IC_{50} >50 µg/mL) showed moderate activity against 3D7, respectively.[60, 87, 97-99] Tested on W2, the chloroform, methanol, and hydroalcoholic extract of this plant part showed moderate activity with IC_{50} similar value up to 10 µg/mL; while the aqueous extract showed the lowest activity with IC_{50} value of 23.15 µg/mL.[25]

Among stem bark extracts, chloroform extract (IC_{50} 21±3 µg/mL) was the most interesting with promising antimalarial activity followed by ethanol extract (IC_{50} 31±5 µg/mL) and aqueous extract (IC_{50} > 100 µg/mL) on FcM2930. Against K1, Etyl acetate fraction of this part plant was active with IC_{50} 31±3 µg/mL and this activity was associated to emodin and lupeol which displayed similar IC_{50} value of 5 µg/mL.[87-88]

Phytochemical investigation of the flowers also afforded cassiarin C and 10,11-dihydroanhydrobarakol which possessed weak antiplasmodial activity with IC_{50} value of 24.2 µg/mL and 5.6 µg/mL against 3D7, respectively.[100-101] Three others alkaloids isolated from the flowers such as cassiarin D, E, and F with potent antimalarial activity were reported.[69, 100]

These in vitro studies were confirmed by in vivo studies. Indeed, the oral administration of *C. siamea*'s aqueous extract of leaves including alkaloids and quinines reduced parasitemia and hyperthermia in patients, significantly.[102] Alkaloid fraction (ED_{50} 0.47 mg/kg) exhibited most antimalaria activity than chloroform extract (ED_{50} 19.59 mg/kg) (po) and then ethanol extract (ED_{50} 34.7 mg/kg). The activity of cassiarin A (ED_{50} 0.17 mg/kg) was similar to that of chloroquine (ED_{50} 0.21 mg/kg) (ip). So, cassiarin A is a promising antimalarial drug.[96, 101] This compound reduces the cyto-adhesion via vasodilator action and promotes the lysis of *P. falcifarum*.[99, 103]

In addition, the effectiveness of *C. siamea* leaves' aqueous extract on mosquitoes larva was investigated against *Aedes aegypti* by determining the median lethal concentration (LC_{50}) within 24, 48, 72, and 96 hours. The results indicated that this extract exhibited 50 % inhibition of mosquito larvas at 419.65 mg/mL for 24 hours and at 218.43 mg/mL for 96 hours, respectively.[104] Also, in chronic administration within 21 days, chloroform extract of the stem bark including coumarin and betulinic exhibit 100 % and 90% of mortality on *Aedes aegypti*.[105] So, *C. siamea* could be used effectively as indigenous mosquito control agents alternatively to conventional chemical mosquito.

Antidiabetic and anti-lipemic effects

The potential effects of *C. siamea* (leaves, roots) on endocrinological system were evaluated by several methods. Ethanolic, ethyl acetate and hexane extracts of *C. siamea*'s leaves at doses 150 and 300 mg/kg were tested for antidiabetic activity in alloxan induced diabetes model and the plasma blood glucose levels were estimated by GOD-POD method at 0, 2, 4, 6, 8 and 12hr. So, ethyl acetate extract of *C. siamea*'s leaves at both different doses produced significant reduction when compared to ethanol and hexane extracts ($P<0.001$).[106] Ethanolic extract of leaves of *C. siamea* exhibits a hypoglycemic and antihyperglycemic effect in non-diabetic rats after induction of hyperglycemia with 2 g/kg/bw of glucose feeding within 1-5 hours. Indeed, this extract administrated orally at the doses of 500 and 750 mg/kg/bw significantly decreased blood glucose by 50.32 and 47.29 % per hour with glibenclamide (10 mg/kg/bw) as positive control ($P< 0.05$).[107] The aqueous extract of *C. siamea*'s root (1000 - 3000 mg/kg, orally) caused improvement blood glucose level and body weights within 24 hours in alloxan-induced hyperglyceamic rats, significantly ($P< 0.05$). We reported that sun-dried and freshly uprooted root have the same antidiabetic potential.[41] In addition, administrations of leaves' methanolic extract (250, 500 mg/kg, orally) within three week induced a significant decrease in streptozotocin (STZ) diabetic rats with high blood glucose levels. It also reduced their serum cholesterol and triglycerides and improved their HDL-cholesterol level ($P<0.01$).[108-109] Bioassay guided fractionation of the ethyl-acetate extract of *C. siamea* afforded 6 known compounds such as chrysophanol, physcion, emodin, cassiamin A, friedelin and cycloart-25-en-3β-24-diol. These compounds were further evaluated for pancreatic lipase inhibitory activity. Cassiamin A was found to be most active with IC_{50} value of 41.8 µM. Physcion and friedelin were found to be moderate enzyme inhibitors. The results indicate the antiobesity potential of *C. siamea* roots through pancreatic lipase inhibition.[110] Barakol seems to have no antidiabetic effects.[111] Overall; the results demonstrate significant antihyperglycemic, antidiabetic and anti-lipemic activities of *C. siamea* and justify the use of this plant in the treatment of diabetes. However, further investigations are therefore needed to go thoroughly into the molecular mechanisms and identify other bioactive molecules responsible for antidiabetic activity.

Antioxidant effects

An antioxidant is defined as any substance that when present at low concentrations compared to those of an oxidizable substrate, significantly delays or prevents oxidation of that substrate.[112] In this review, in vitro studies showed that various extracts of *C. siamea* possessed high antioxidant potential measuring using β-carotene bleaching method, 2,2'-azinobis(3-ethylbenzothiazoline-6-sulfonic acid) (ABTS) radical cation and superoxide anion radical scavenging assay.[56, 89, 113] Indeed, methanol and aqueous extract of barks (800 and 1000 µg/mL) inhibited 60.5% and 51.34% free radicals compared to those of rutin which exhibited 62.56% inhibition, respectively. While at 1000 µg/mL hexane, chloroform and ethyl acetate extracts of leaves showed moderate antioxidant activities, respectively.[113-114]

DPPH radical scavenging activity of flowers has been done. The results showed that the methanolic extract of flowers (250 µg/ml) neutralized 96% of DPPH radicals. This extract (500 µg/ml) scavenged 42.7%, 32.7% and 64.5% of the O_2•-, H_2O_2• and NO, respectively.[46] Also, methanol extract of leaves reduced hydroxyl radicals (OH•), peroxyl (ROO•) and superoxide (O_2•-) with IC_{50} value of 349.9 µg extract/mg DPPH.[115]

In vivo, ethanol extract of flowers (50-150 mg/kg; p.o) significantly protected against acute phase of hepatotoxicity and histopathological changes (necrosis, fatty degeneration) induced by a single intraperitoneal injection of carbon tetrachloride (CCl_4) in male Wistar rats. These results showed that *C. siamea* could afford significantly protection against oxidative damages to major biomolecules in the liver.[46, 84, 114]

Many antioxidant compounds such as barakol, vitamin C, Vitamin E, carotenoids, α-tocopherol, xanthophylls, tannins, flavonoid, phénolic acids, and diverse enzymes

(superoxide dismutase, catalase, and peroxidase) could be responsible for this activity.[53, 84, 116-117] So, barakol scavenged the DPPH radical 1.3 times higher than those of butylate hydroxytoluen (BHT) with EC_{50} value of 9.18 mg/mL.[118] Mechanisms of action of some of these identified natural antioxidants are known.[34]

Antitumor or anticancer effects

In research of natural or synthetic products as cancer chemopreventive agents, in vivo and in vitro antitumor activity studies were conducted with various extract of leaves and stem bark of *C. siamea*. In male wistar rats, feeding diet containing 4-5% of leaves of *C. siamea* for 2 weeks significantly reduced the activities of some hepatic P450 dependent monooxygenases such as aniline hydroxylase (ANH) and aminopyrine-N-demethylase (AMD) as well as the capacity to activate the mutagenicity of AFB1 towards Salmonella typhimurium TA100 is 31.73 % and 41 %. It increased the activities of glutathione S-transferase (GST) for 250% and UDP-glucuronyltransferase (UGT) for 220% which are phase II detoxification enzymes. It also decreased the multiplicity of mammary gland tumors as well as it slight delay of the onset of tumor development in female Sprague Dawley rats treated with carcinogenic agent such as 7,12-dimethylbenz[a]anthracene (DMBA). This activity may be partly due to its phase II enzyme inducing capacity as well as its phase I enzyme inhibitory ability in rat liver.[119-121] In addition; dietary *C. siamea*'s leaves did not induce micronucleus formation in mouse peripheral blood reticulocytes. Furthermore, it showed anticlastogenic potential against DMBA and cyclophosphamide-induced reticulocyte micronucleus formation.[122]

In vitro, clinical trials demonstrated that the plant aqueous extracts inhibited human recombinant hepatic cytochrome P450 such as CYP_2C_9 and GSTM1-1 with IC_{50} value of 346.5 mg/ml and 50 mg/ml, respectively. This inhibition of GSTs may be beneficial for cancer therapy.[123] Also, petroleum ether, dichloromethane, ethanol and aqueous extracts of leave showed cytotoxicity against human epidermoid carcinoma (KB) cell lines with IC_{50} value between 67 and 100 µg/ml.[124] However, methanol extract of leaves was inactive on human oral epidermal carcinoma (KB), breast adenocarcinoma (MCF-7) and small cell lung carcinoma's (NCI-H187) proliferation.[115]

The anticancer properties of C siamea could be due to anthraquinones (emodin and its derivatives) and bianthraquinones (cassiamin B and its derivatives).[121, 125-127] Indeed, twelve of these compounds have been tested for their inhibitory activities on EBV-EA activation induced by 12-O-tetradecanoylphorbol-13-acetate (TPA) in Raji cells using a short-term assay.[125] Then, inhibitory effects of emodin and cassiamin B on mouse two-stage skin carcinogenesis model using DMBA or NOR-1 as an initiator and TPA as a promoter were performed by skin rubbing. All the results indicated that anthraquinone monomers showed higher anticancer activity than bianthraquinones.[121, 125] The effects of these anti-tumor promoters' molecules were correlated to their standard redox potentials and their electronic properties using PM3 method with CAChe MOPAC program.[126-127]

Antihypertensive effects

Studies on antihypertensive activities of *C. siamea* (leaves) was undertaken to find the pharmacological basis for the ethnomedical use of the plant. In vitro, chloroform and methanol extract of leaves showed promising dose-dependent vasorelaxant action by measurement of vascular isometric force in endothelium-intact and -denuded mesenteric artery rings.[103] Two chromones alkaloids like cassiarin A and barakol were responsible for this activity. Indeed, acute pre-treatment with barakol (10 mg/kg, iv) reduced thebeating heart rate for 89% with significant fall of the systemic blood pressure in anesthetized rats for 86%128. Barakol also showed significant protective effects on aconitine-induced ventricular fibrillation and tachycardia in cats and rats. In contrast, vasorelaxant action of barakol was attenuated by its chronic administration ($p<0.05$).[129-130] The mechanisms of action of antihypertensive compounds were unclear and needed further investigations. Nevertheless, preclinical assay showed that cassiarin A vasorelaxant effect in wistar rats was partially mediated by endothelium-derived releasing factor (EDRF), nitric oxide (NO) and prostaglacycline (PGI2).[103, 129-131]

Laxative effects

C. siamea (leaves, flowers) is known for its laxative effect in Thailand. Several laxative compounds such as anhydrobarakol, barakol, aloe-emodin, rhein-8-monoglucoside, rhein, chrysophanic acid, anthrone, dianthrone, chrysophanol, sennoside A were identified in this plant.[57, 132-136] For example, sennoside A of *C. siamea* (20-30 mg/kg, po) in combination with other compounds (guanethidine, neostigmine, castor oil and intraluminal hypertonic glucose) induced a strong myoelectric inhibition of the colon about 10 hours after administration

which was followed by an abundant diarrhea in dog.[137] Barakol caused laxative effect on small intestine and colon via excitation of cholinergic motor neurons with EC_{50} 0.3 and 0.4 mM, respectively.[57] In this activity, barakol stimulated chloride secretion without affecting electrogenic sodium absorption in rat colonic epithelium. The mechanisms involved basolateral Na+-K+-2Cl- cotransporters and apical Cl- channels which were partly mediated by the release of cyclooxygenase metabolites. These results indicated that barakol and sennosides may produce a purgative action in small intestine which may be clinically important in patients with intestinal hypomotility disorders.[57, 132, 138]

Anti-inflammatory, analgesic and antipyretic effects

Nsonde-Ntandou *et al*., (2010) have shown that ethanol and aqueous extracts of *C. siamea*'s leaves and stem bark (100 – 400 mg/kg, po, for 4 hours) had significant dose-dependent anti-inflammatory, analgesic and antipyretic activities using experimental rat models ($p<0.01$). The results indicate that aqueous extracts had better anti-inflammatory potential than diclofenac (5 mg/kg, po) on paw oedema using hot plate test. The mechanisms of action involved inhibition of cyclooxygenase. The analgesic and antipyretic effects of these extracts were more important than paracetamol (50 mg/kg, po) and morphine (2 mg/kg, po) ($p <0.001$).[124] Recently, Monin *et al.* (2012) have been shown that leaves' ethanol extract exhibited high analgesic activity using acetic acid induced writhing test in mice. They found that leaves' ethanol extract (500 mg/kg) exhibit significant inhibition of writhing reflex by 61.98% while the diclofenac (25 mg/kg) Na inhibition was found to be 85.95% ($p<0.001$).[139] These results justify the traditional use of *C. siamea* in fever. However, the bioactive compounds of *C. siamea* responsible to these activities were not specified. According to the literature, four major families of compounds may explain these activities: triterpenes (lupeol, oleanolic acid, ursolic acid, friedelin, and betulin), flavonoids (apigenin, kaempferol, and luteolin), anthraquinones (emodin), phytosterols (stigmasterol, β-sitosterol).[124]

Anxiolitic, antidepressant and sedative effects

C. siamea (leaves, flowers) is active on central nervous system. Anxiolitic effect of aqueous extracts of leaves and flowers (10 - 120 mg/kg, po) were demonstrated using an elevated plus-maze (EPM) test in rats.[140] Also, clinical trials reported that leaves' alcoholic extracts used as syrup or tablet (10 mg/kg, po) caused drowsiness and improve sleep quality in insomniac patients.[141] Barakol was the only compound identified in these neuropharmacological activities. Indeed, barakol (10 mg/kg; ip) showed similar anxiolitic activity as diazepam (1 mg/kg, ip) in wistar rats.[140] But, it increased locomotor behavior contrary to diazepam.[40, 142] The mechanism of action involved inhibition of endogenous dopamine (DA) release and turnover in the rat striatum. This inhibition was antagonized by the dopamine D2 receptor antagonist eticlopride, suggesting that the anti-anxiety activity of barakol may be related to its agonistic action without a change in dopamine uptake.[143-144] However, the lowest dose of barakol showed no effect on exploratory behaviours using the holeboard test which indicates that 5HT mechanism and $5HT_{1A}$ receptor may not be involved in the anxiolytic effects.[145] Then, barakol (10 - 100 mg/kg, p.o.) had no anxiolytic effects in male wistar rats using an EPM test.[146-147] These constrast results suggest that anxiolitic effect of barakol was dose-dependent and required a peritoneal administration.

The antidepressant effect of barakol (5 - 30 mg/kg, po, for 7 days) was similar to that of imipramine (25 mg/kg, po). Also, barakol (5 - 25 mg/kg, ip) decreased the duration of immobility and increased struggling in isolated and stressed rats using the forced swimming test ($P<0.05$). In contrast, barakol (5 - 10 mg/kg ip) had not antidepressant effect in the socially reared rats.[140, 148] So, we must pay attention to experimental conditions because socially conditions of animal influence the antidepressive effect of *C. siamea*.

The sedative effect of barakol was assessed in mice behaviour using neurochemical tests. So, chronic administration of barakol (10 - 100 mg/kg, po; for 30 days.) reduced spontaneous locomotor activity, increased the duration of sleeping and prolonged the thiopental-induced sleeping duration in wistar rats. [146] Its sedative effect does not involve the GABA or glycine systems but may be via the chloride ion channel like barbiturates.[143, 149-150] Thus, these studies suggest that the acute barakol administration by intraperitoneal route exerts an anxiolytic effect while the long-term treatment by oral administration causes sedation. Therefore, it is essential to consider carefully when assessing the value of barakol as anxiolytic or sedative drugs.[150]

Antibacterial effects

C. siamea (leave) has been valued for its use in the treatment of infectious diseases. Recently, interest in *C. siamea* has focused on its antibacterial activity evaluated against various Gram positive and Gram negative bacteria species by using cylinder plate assay.[151]

The methanol leave extract showed strong antibacterial activity against *Bacillus cereus* and *Listeria monocytogenes* with IC_{50} 5.2 mg/mL and 20.8 mg/mL for 24 hours exposition at 37°C, respectively. In the same conditions, it had low activity against *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas fluorescens*, *Salmonella risen*, *Salmonella typhimurium*, *Staphilococcus aureus*, *Yersinia enterocolitica*, *Lactobacillus planetarium* with IC_{50} up to 166.7 mg/mL.[115] At 400 µg/disc hexane extract showed high activities on *Corynebacterium diptheriae*, *Salmonella typhi*, *Shigella sonii*, *Pseudomonas aeruginosa*, *Shigella boydii* at 37°C within 24 hours but it inactive on *Proteus mirabilis*, *Staphylococcus aureus* and *Staphylococcus pyogenes*. Alkaloids, phenolics and sterols could be responsible to this effects.[152]

The ethanol leave extracts (500 - 1000 µg/disc) showed more activities than ciprofloxacin (30µg/disc) on *Staphylococcus aureus*.[59] It showed moderate activity on *Bacillus subtilis* but it inactive on Escherichia coli and *Pseudomonas aeruginosa*. At 40 mg/mL concentration for 18 hours exposition, it showed highest activity on *Salmonella thyphi* with inhibition zone (iz.) value of 10 mm followed acetone and aqueous extracts with iz. 15, 8 and 3.5 mm, respectively. These effects were compared to those of ampicillin, chloramphenicol, cotrimoxazole and ciprofloxacin at 5 mg/mL which showed inhibition zone value of 8, 16, 14, and 30 mm, respectively.[153]

Aqueous leave extract is active against various bacteria Gram-. At 500 and 1000 µg/mL/disc, it inhibited *Pseudomonas aeruginosa* (iz. 16 mm, respectively). At 0.1mL/disc/37°C for 24 hours, it showed inhibition on *Staphylococcus aureus* (iz. 11.7 mm), *Bacillus cereus* (iz. 10 mm) and *Escherichia coli* (iz. 10.2 mm).[59, 143, 154] But, it was inactive against *Staphylococcus aureus*, *staphylococcus pyogens*, *E. coli*, *Salmonella typhi* and *Shigella disenteriae*. When this extract was mixed with the extract of the fleshy part of *Momordica charantia* Linn, the combination showed a powerful inhibitory action on *Bacillus cereus*, *Salmonella typhi* and *Staphylococcus aureus*. In addition, chloroform extract was found to be active against *Pseudomonas aeruginosa* (iz. 8 -14 mm).[155] These activities enumerated could be due to alkaloids (barakol), steroids, saponins, tannins, resins, glycosides and anthraquinones.[59, 153, 156] So, barakol (50 mg/kg, ip) was found to be associated with antibacterial activity against Gram+ (*Staphylococci aureus*, *Bacillus subtilis*) and Gram- (*Echeriachia coli*, *Salmonella thyphi*, *Salmonella dysenteriae* and *Pseudomonas aeruginosa*).[3]

These results indicate that *C. siamea* has very higher potential antibacterial. But, the mechanisms of action were not investigated and need further researches.

Antifungal effects

Various fungi species found to be sensitive to hexane, ethanol, methanol and aqueous extract of *C. siamea*. The ethanol and aqueous bark extract (100 mg/mL) was active on six strains of Candida (*C. albicans*, *C. glabrata*, *C. tropicalis*, *C. krusei*, *C. parapsilosis* and *C. guilliermondii*) and this activity was similar to fluconazole (25 µl/mL) for 24 hours exposition.[157] But, ethanol leave extract was inactive on *C. albicans* and *Aspergillus fumigatus*.[92] The methanol extracts of this plant (400 µg/mL/27°C for 7days) inhibited *Microsporum canis* (97.95%), *Trichophyton longifuses* (92.45%), *Fusarium solani* (84.53%), *Macrophomina phaseolina* (76.94%), *Trichophyton simii* (22.98%), *Pseudallescheria boydii* (9.91%) and *Trichophyton schoenleinii* (9.90%). This activity was associated to phenols. But, this extract was inactive on *Candida albicans*, *Trichophyton mentagrophyte*, *Rhizoctonia solani*, *Candida lipolytica*, *Hanseniaspora uvarum*, *Pichia membranaefaciens*, *Rhodotorula glutinis*, *Schizosaccharomyces pombe* and *Zygosaccharomyces rouxii*.[152]

Hexane extracts of leaves of *C. siamea* (400 µg/mL/27°C for 7days) inhibited *Pseudallescheria boydii*, *Aspergillus Niger*, *Microsporum canis*, *Fusarium solani*, and *Trichophyton schoenleinii*. Its inhibition capacity was similar to those of miconazole and ketoconazole and could be due to sterols and alkaloids-like barakol. This extract was inactive on *Trichophyton longifuses*, *Candida albicans*, *Trichophyton mentagrophytes*, *Trichophyton simii*, *Macrophomina phaseolina*, and *Rhizoctonia solani*.[31, 115, 152, 158] Through studies, we noted that *C. siamea* could be useful in candidose and against growth of fungi in agricultural products.

Toxicology

C. siamea seems less toxic justifying its wide use in folklore medicine.[70] Indeed, its stem bark's aqueous extract

(1600 mg/kg; po / 7 weeks) showed less sub-chronic toxicity in male wistar rats.[159] This extract and root's aqueous extracts were found to be relatively not toxic on blood, hepatic and renal cells in wistar rats at 400 mg/kg and 1500 mg/kg; p.o. for 4 weeks, respectively.[23, 124]

However, at a higher dose, diverse extracts of *C. siamea* showed acute toxicity in various experiemental animals' models. Indeed, its leaves' ethanol extracts caused mortality of experimental rats with an intraperitoneal LD_{50} of 9600 mg/kg within 24 h.[160] The root's aqueous extracts (8000 mg/kg, po, 24 hours) showed hypersensitivity reactions, cytotoxicity and increases aggressivity in rats.[40] Also, the chronic toxicity studies showed that aqueous extracts (2000 mg/kg; po / 2 weeks, respectively) led to hepatic and renal cell destruction in albinos' rats.[161] This toxicity involved a drastic reduction ($p<0.05$) in activities of alkaline phosphatase (ALP), aspartate transaminase (AST) and alanine transaminase (ALT) in the liver with a corresponding increase in the serum levels.[162] Authors reported that male rat appeared to be more susceptible to the toxic effect of *C. siamea* than female rats.[161] *In vitro*, ethanol and aqueous extracts of the leaves were absolutely devoid of toxicity against vero (African green monkey kidney) cells line with IC_{50} up to 100 µg/ml.[124]

In addition, clinical trials using *C. siamea* extracts were investigated. These studies indicate that the crude extract of the leaves in continual oral administration for six months decreased the number of humans' hematocrit and neutrophiles. The powder induced irritation of the nose, throat and eyes and it increased the rate of transaminase after oral administration.[163]

According to the literature, these toxic effects could be due to saponins, glycosides, alkaloids like barakol, anthraquinones and tannins.[160] In this review, barakol seems most responsible for C siamea toxicity. Indeed, in vivo, barakol showed an acute and subacute hepatotoxic effect with LD_{50} 2330 mg/kg in wistars rats[164] and subchronic toxicity effects on blood cells in rats fed with normal and high cholesterol diets[111]. Barakol produced acute toxicity and death in mice with LD_{50} 324.09 mg/kg by intraperitoneal injection. Also, barakol may disrupt liver function and an increase of bilirubin in the rats, especially at the dose 240 mg/kg.[148]

In vitro, cytotoxicity of barakol (5 mM) on hepatocytes of carp fish (*Cyprinus carpio*) was found after 72 hours of exposure.[165] Also, in clinical trials, barakol (40 mg/kg; p.o, 60 days) induced an acute hepatitis in 29-81 years old patients.[166] Barakol showed cytotoxic effects in dose and time-dependent manner with IC_{50} value of 0.68 mM within 96 hours of exposure on humans hepatoma cell line HepG2. Mechanisms involved lactate dehydrogenase leakage, which decreased GSH/GSSG ratio.[167] It was also showed that barakol-toxicity was mainly associated to the ROS generation, followed by the ambalance of the Bax/Bcl-2 ratio, and caspase-9 activation leading to apoptotic cell death168. Apart from barakol, sennosides of *C. siamea* showed very less hepatotoxicity with LD_{50} 5000 mg/kg in rat and mice.[132, 169] Continuous consumption of barakol might not be suitable for health. All toxicity studies showed that the toxic effects of *C. siamea* were reversible after stopping administration.

Conclusion

The objective of this article is to show the recent progress in the exploration of *C. siamea* as phytotherapy and to illustrate its potential as a therapeutic agent. With the current information, it is obvious that *C. siamea* has pharmacological functions including antimalaria, antidiabetic, antihypertensive, antioxidant, antitumor, anti-inflammatory, analgesic, antipyretic, anxiolytic, sedative, antibacterial, and antifungal activities. As the current information shows more ninety bioactive compounds were isolated from *C. siamea*. Pharmacological effects of most of these compounds are not yet known. Nevertheless, from the results of studies carried out, it is possible that chromone alkaloids (barakol, cassiarin A), antraquinones (emodin, chrysophanol), and biantraquinones (cassiamin A, cassiamin B) might be useful in the development of new drugs to treat various diseases. However, the present results suggest a possibility that these compounds can be further developed as a potential disease-curing remedy. It must be kept in mind that clinicians should remain cautious until more definitive studies demonstrate the quality and effectiveness of *C. siamea*. For these reasons, extensive pharmacological and chemical experiments, together with human metabolism will be a focus for future studies. Last but not the least, this review emphasizes the potential of *C. siamea* to be employed in new therapeutic drugs and provide the basis for future researches on the application of transitional medicinal plants.

Acknowledgment

The authors are thankful to the authorities of FHB University, for providing support to the study and other

necessary facility like internet surfing, library and other technical supports to write this review article.

References

1. Gutteridge R.C. *Senna siamea* (Lamk). Plant Resources of South-East Asia, 1997; 1: 232-236.

2. N'Guessan, K. Contribution à l'étude ethnobotanique en pays Krou (République de Côte d'Ivoire). Thèse de 3è Cycle, Université de Cocody-Abidjan, 1995, pp.156-157.

3. Singh V., Sharma J.P. Anthraquinones from heartwood of *Cassia siamea*. Phytochemistry1992; 31: 2176-2177.

4. Thongsaard W., Chainakul S., Bennett G.W. Determination of barakol extracted from *Cassia siamea* by HPLC with electrochemical detection. Journal of Pharmaceutical and Biomedical Analysis2001; 25: 853-859.

5. Veerachari U., Bopaiah A.K. Preliminary phyto-chemical evaluation of the leaf extract of five *Cassia* species. Journal of Chemical and Pharmaceutical Research 2011; 3: 574-583.

6. Jensen, M. Trees Commonly Cultivated in Southeast Asia - an illustrated field guid. FAO, Bangkok, Thailand, 1995, pp. 38-93,

7. Haba F.L., Kamelina A.B., Laberche J.C. Structure de la feuille et sa variabilité intraspécifique chez les plantes ligneuses tropicales: *Cassia siamea* Lamk. (Sempervirente) et *Cassia sieberiana* DC (Caducifoliee). Revue de Cytologie et de Biologie Végétales 2000; 23: 35-40.

8. Nacoulma, O.G. Plantes médicinales et pratiques médicales traditionnelles au Burkina Faso: cas du Plateau central. Thèsede Doctorat d'État. Université de Ouagadougou, Burkina Faso. Tome 1 et Il, 1996, p. 581.

9. Basco, K.L., Ruggeri C, Le Bras J. Molécules antipaludique: mécanisme d'action, mécanisme de résistance. 1ère éd, Paris, Masson, 1994, pp. 205-214.

10. Shivjeet S., Sandeep K.S., Ashutosh Y. Review on Cassia species: Pharmacological, Traditional and Medicinal Aspects in Various Countries. American Journal of Phytomedicine and Clinical Therapeutics 2013; 1: 291-312.

11. Tchaou, O. Recensement des travaux de recherche sur la valorisation de la pharmacopée traditionnelle africaine à l'université de Cocody-Abidjan 1994-1998. Thèse, Côte d'Ivoire, 1999: pp.1-13.

12. Sahni, K.C. Trees for the 21st century. In: Advances in Forest Genetics, (ed.) P.K.Khosla, Ambika publications, New Delhi, 1981, pp. 81- 100.

13. Hauser S. Effect of *Acioa barteri*, *Cassia siamea*, *Flemingia macrophylla* and *Gmelina arborea* leaves on germination and early development of maize and cassava. Agriculture, Ecosystems & Environment A 1993; 45: 263-273.

14. Rupal A.V., Savalia D.M., Narasimhacharya A.V. Plant extracts as biotermiticides. Electronic Journal of Environmental Sciences 2011; 4: 73-77.

15. Oyedunmade E.E., Olabiyi T.I. Carbofuran and golden shower (*Cassia siamea* L.) as controls of Meloidogyne incognita infection on soybean (*Glycine max* L.). Crop Research 2006; 32: 507-511.

16. Allabi AC.., Busia K., Ekanmian V., Bakiono F. The use of medicinal plants in self-care in the Agonlin region of Benin. Journal of Ethnopharmacology 2011; 133: 234–243.

17. Nadembega P., Boussim J.I., Nikiema J.B., Poli F., Antognoni F. Medicinal plants in Baskoure, Kourittenga Province, Burkina Faso: An ethnobotanical study. Journal of Ethnopharmacology 2011; 133: 378–395.

18. Asase A., Akwetey G.A., Achel D.G. Ethnopharmacological use of herbal remedies for the treatment of malaria in the Dangme West District of Ghana. Journal of Ethnopharmacology 2010; 129: 367–376.

19. Ejobi F., Mosha R.D., Ndeje S., and Kamoga D. Ethno-veterinary plants of the Lake Victoria: A bioprospection. Journal of Animal and Veterinary Advances 2007; 6: 257-261.

20. Owuor B.O., and Kisangau D.P. Kenyan medicinal plants used as antivenin: a comparison of plant usage. Journal of Ethnobiology and Ethnomedicine 2006; 2: 7.

21. Sravan P.M., Venkateshwara R.K., Shantosha D., Chaitanya R.S., and David B. Medicinal plant used by the Ethnic practitioners in Valgonda District, Andhara Pradhesh, India. International Journal of Research in Ayurveda & pharmacy 2010; 1: 493-496.

22. Al-Adhroey A.H., Nor Z.M., Al-Mekhlafi H.M., and Mahmud R. Ethnobotanical study on some Malaysian anti-malarial plants: A community based survey. Journal of Ethnopharmacology 2010; 132: 362–364.

23. Otimenyin S.O., Kolawole J.A., and Nwosu M. Pharmacological basis for the continual use of the root of *Senna siamea* in traditional medicine. International Journal of Pharmaceutical and Biological Sciences 2010; 1: 975-6299.

24. Koudouvo K., Karou D.S., Kokou K., Essien K., Aklikokou K., Glitho I.A., Simpore J., Sanogo R., Souza C., and Gbeassor M. An ethnobotanical study of antimalarial plants in Togo Maritime Region. Journal of Ethnopharmacology 2011; 134: 183–190.

25. Sanon S., Ollivier E., Azas N.C., Mahiou B.V., Gasquet M., Ouattara C.T., Nebie D.I., Traoré A.S., Esposito F., Balansard G., Timon-David C.P., and Fumoux F. Ethnobotanical survey and in vitro antiplasmodial activity of plants used in traditional medicine in Burkina Faso. Journal of Ethnopharmacology 2003; 86: 143–147.

26. Etkin, N.L., and Ross, P.J. Malaria, medicine, and meals: Plant use among the Hausa and its impact on disease. In Romanucci-Ross L, Moerman DE, Tancredi LR, ed. The Anthropology of Medicine: From Culture to Method, New York: Praeger, 1983; pp: 231-259.

27. Maurya R., Dongarwar N. Studies on the medicinal uses of wild trees of Nagpur District. International Journal of Life Science and Pharma Research 2012; 2: 21-24.

28. Fowler, D.G. Traditional Fever remedies: a list of Zambian plants, 2006; p. 38.

29. Koné W.M., Atindehou, K.K. Ethnobotanical inventory of medicinal plants used in traditional veterinary medicine in Northern Côte d'Ivoire (West Africa). South African Journal of Botany 2008; 74: 76–84.

30. Mbatchi S., Mbatchi B., Banzouzi J., Bansimba T., Nsonde N.G., Ouamba J., Berry A., and Benoit-Vical F. In vitro antiplasmodial activity of 18 plants used in Congo Brazzaville traditional medicine. Journal of Ethnopharmacology 2006; 104: 168-174.

31. Souza C., Koumaglo K., Gbeassor M., Evaluation des propriétés antimicrobiennes des extraits aqueux totaux de quelques plantes médicinales. Pharm Med Tra Afro 1995 :103-112.

32. Ogunkunle A.T., Ladejobi T.A. Ethnobotanical and phytochemical studies on some species of *Senna* in Nigeria. African Journal of Biotechnology 2006; 5: 2020-2023.

33. Kamatenesi M.M., Acipa A., Oryem-Origa H. Medicinal plants of Otwal and Ngai Sub counties in Oyam District, Northern Uganda. Journal of Ethnobiology and Ethnomedicine 2011; 7: 1-14.

34. Sati S.C., Sati N., Rawat U., Sati O.P. Medicinal plants as a source of Antioxydants. Rechearch Journal of Phytochemistry 2010; 4: 213-224.

35. Bhagya B. and Sridha K.R. Ethnobiology of Coastal sand dune legumes of Southwest coast of India. India Journal of Traditional Knowlelge 2009; 8: 611-620.

36. Grisanapan, W. Ethnomedicinal plants popularly used in Thailand as laxative drugs. In Debprasad Chattopadhyay (Editor). Ethnomedicine: a Source of Complementary Therapeutics, 2010; pp. 295-315.

37. Kiepe; P. Effect of *Cassia siamea* hedgerow barriers on soil physical properties. Geoderma 1995; 66: 113-120.

38. Ngamrojanavanich N., Manakit S., Pornpakakul S., Petsom A. Inhibitory effects of selected Thai medicinal plants on Na+/K+-ATPase. Fitoterapia 2006; 77: 481-483.

39. Tapsoba H., Deschamps J.P. Use of medicinal plants for the treatment of oral diseases in Burkina Faso. Journal of Ethnopharmacology 2006; 104: 68–78.

40. Thongsaard W., Deachapunya C., Pongsakorn S., Boyd E.A., Bennetts G.W., and Marsdens C.A. Barakol: a potential anxiolytic extracted from *Cassia siamea*. Pharmacology Biochemistry and Behavior 1996; 53: 753-758.

41. Odason E.E., Kolawole J. Anti-diabetic properties and brine shrimp toxicity of the aqueous extract of the root of *Cassia siamea* lam. (Ceasalpiniaceae). Nigerian Journal of Pharmaceutical Research 2007; 6: 66-69.

42. Swier, J. Sustainability of medicinal plant trade in southern Benin: an analysis of the sustainable harvest and trade of medicinal and magical barks, woods and roots in southern Benin. Minor thesis, Plant Biotechnology, 2012, pp. 25.

43. Adebayo J.O., Krettli A.U. Potential antimalarials from Nigerian plants: A Review. Journal of Ethnopharmacology 2011; 133: 289-302.

44. Odugbemi T.O., Akinsulire O.R., Aibinu I.E., Fabeku P.O. Medicinal plants useful for malaria therapy in okeigbo, ondo state, southwest Nigeria. African Journal of Traditional Complementary and Alternative Medicines 2007; 4: 191- 198.

45. Dalziel, J.M. The useful plants of West Tropical Africa – An appendix to the second edition of the flora of West Tropical Africa (Hutchinson, J and Dalziel, J.M) Great Britain Watcmangs Ltd., 1963, pp. 596-597.

46. Kaur G., Alam M., Jabbar Z., Javed K., Athar M. Evaluation of antioxidant activity of *Cassia siamea* flowers. Journal of Ethnopharmacology 2006; 108: 340-348.

47. Lawal I.O., Uzokwe NE., Igboanugo A.B., Adio A.F., Awosan E.A., Nwogwugwu J.O., Faloye B., Olatunji B.P.,

Adesoga A.A. Ethnomedicinal information on collation and identification of some medicinal plants in Research Institutes of South-west Nigeria. African Journal of Pharmacy and Pharmacology 2010; 4: 1-7.

48. Hu X.M., Zhang W.K., Zhu Q.S. An Encyclopaedia of Chinese Medical Herbs. Shanghai Scientific Technological Publishers 1999; 4: 3105.

49. Ali S. Determination of chemical composition of *Senna siamea* (Cassia leaves). Pakistan Journal of Nutrition 2009; 8: 119-121.

50. Kaur P., Arora S. Polyphenols of Caeselpiniaceae. Journal of Chinese Clinical Medicine 2010; 5: 282-290.

51. Mohammed A., Liman M.L., Atiku M.K. Chemical composition of the methanolic leaf and stem bark extracts of *Senna siamea* Lam. Journal of Pharmacognosy and Phytotherapy 2013; 5: 98-100.

52. Veerachari U., Bopaiah A.K. Phytochemical investigation of the ethanolic, methanolic and ethyl acetate extract of the leaves of six Cassia species. Journal of Pharmacognosy and Herbal Formulations 2012; 2: 36-46.

53. Parui S., Kumar A.M., Mandal S. Peroxidase isozyme profiles of immature and mature pollen of seven tropical plants from eastern India. Grana1998; 37: 228-232.

54. Subramanian D.P., Venugopal S. Comparative study of antioxidant activities of *Cassia auriculata* and *Cassia siamea* flowers. International Research Journal of Pharmacy 2011; 2: 208-212.

55. Ganapaty S., Thomas P.S., Ramana K.V., Vidyadhar K., Chakradhar V. A review of phytochemical studies of *Cassia* species. Journal of Natural Remedies 2002; 2: 102-120.

56. Xu R., Liu X.Q., Tie D.X., Zhao Y.H., Wan D.R. Study on pharmacognostic identifcation of *Cassia siamea*. Zhong Yao Cai 2008; 31: 974-977.

57. Deachapunya, Poonyachoti S., Thongsaard W., Krishnamra N. Barakol extracted from *Cassia siamea* stimulates chloride secretion in rat colon. Journal of Pharmacology and Experimental Therapeutics 2005; 314: 732-737.

58. Ingkaninan K., Ijzerman A., Verpoorte R. Luteolin, a compound with adenosine a (1) receptor-binding activity, and chromone and dihydronaphthalenone constituents from *Senna siamea*. Journal of natural products 2000; 63: 315-317.

59. Bukar A., Mukhtar M.D., Hassan A.S. Phytochemical screening and antibacterial activity of leaf extracts of *Senna siamea* (Lam) on *Pseudomonas aeruginosa*. Bayero Journal of Pure and Applied Sciences 2009; 2: 139-142.

60. Oshimi S., Tomizawa Y., Hirasawa Y., Honda T., Ekasari W., Widyawaruyanti A., Rudyanto M., Indrayanto G., Zaini N., Morita H. Chrobisiamone A, a new bischromone from Cassia siamea and a biomimetic transformation of 5-acetonyl-7-hydroxy-2-methylchromone into cassiarin A. Bioorganic & Medicinal Chemistry Letters 2008; 18: 3761-3763.

61. Padumanonda T., Gritsanapan W. Barakol contents in fresh and cooked *Senna siamea* leaves. Southeast Asian Journal of Tropical Medicine and Public Health 2006; 37: 388-393.

62. Hu Q.F., Zhou B., Gao X.M., Yang L.Y., Shu L.D., Shen Y., Li G.P., Che C.T., Yang G.Y. Antiviral Chromones from the Stem of *Cassia siamea*. Journal of Natural Products. 2012; 75:1909-1914.

63. Padumanonda T., Suntornsuk L., Gritsanapan W. A quantitative analysis of barakol content in *Senna siamea* leaves and flowers by CCM-densitometry. Medical Principles and Practice 2007; 16: 47-55.

64. Padumanonda T., Suntornsuk L., Gritsanapan W. A quantitative analysis of barakol content in *Senna siamea* leaves and flowers by TLC-densitometry. Medical Principles and Practice 2007; 16: 47–52.

65. Kanputhorn S., Petsom A., Thamyongkit P. Transformation of barakol into cassiarins A, B, and their derivatives. Tetrahedron 2010; 66: 7539-7543.

66. Morita H., Oshimi S., Hirasawa Y., Koyama K., Honda T., Ekasari W., Indrayanto G.C. Cassiarins A and B, novel antiplasmodial alkaloids from *Cassia siamea*. Organic letters 2007; 9: 3691-3693.

67. Rudyanto M., Tomizawa Y., Morita H., Honda T. First total synthesis of cassiarin A, a naturally occurring potent antiplasmodial alkaloid. Organic letters 2008; 10: 1921-1922.

68. Oshimi S., Deguchi J., Hirasawa Y., Ekasari W., Widyawaruyanti A., Wahyuni T., Zaini N., Shirota O., Morita H. Cassiarins C-E, antiplasmodial alkaloids from the flowers of *Cassia siamea*. Journal of natural products 2009; 72: 1899-1901.

69. Deguchi J., Hirahara T., Oshimi S., Hirasawa Y., Ekasari W., Shirota O., Honda T., and Morita H. Total Synthesis of A Novel Tetracyclic Alkaloid, Cassiarin F from the Flowers of *Cassia siamea*. Organic letters 2011; 13: 4344–4347.

70. Teangpook C., Paosangtong U., Titatarn Y., Onhem S., Puminat W. Production and Nutrition of Khi Lek (Siamese

cassia) Curry from Central Thailand. Kasetsart Journal: Natural Science 2011; 45: 510 – 520.

71. Shahriar K., Robin J.M. Chromone and Flavonoid Alkaloids: Occurrence and Bioactivity. Molecules 2012; 17: 191-206.

72. Lü T., Yi Y., Mao S., Zhou D., Xu Q., Tong H., Zhang S. Studies on the anthraquinones of *Cassia siamea*. Yao Xue Xue Bao 2001; 36: 547-548.

73. Lü T., Yi Y., Yuan H., Zhang Z., Liu W. A new chromone glycoside from *Cassia siamea* Lamk. Chinese Chemical Letters 2001; 12: 703-704, Yao Xue Xue Bao 2003; 38: 113-115.

74. Ahmed R., Nagori K., Kumar T., Singh M., Dewangan D. Phytochimical estimation of anthraquinones from *Cassia siamea*. International Journal of Research in Ayurveda and Pharmacy 2011; 2: 1320 – 1323.

75. Christ B., Poppinghaus T., Wirtz-Peitz F. Isolation and structural definition of a new sennosides from *Cassia senna*. Arzneimittelforschung 1978; 28: 225-231.

76. Dave H. and Ledwani L. A review on anthraquinones isolated from *Cassia* species and their applications. Indian Journal of Natural Products and Ressources 2012; 3: 291-319.

77. Hemlata S.J., Agrawal B. New triterpenoid glycoside and anthraquinones from *Cassia siamea*. International journal of pharmacognosy 1994; 32: 65-68.

78. Koyama J., Morita I., Tagahara K., Jameelah B.B., Aqil M. Capillary electrophoresis of anthraquinones from *Cassia siamea*. Notes Chemical and Pharmaceutical Bulletin 2002; 50: 1103-1105.

79. Koyama J., Morita I., Tagahara K., Aqil M. Bianthraquinones from *Cassia siamea*. Phytochemistry 2001; 56: 849-851.

80. Patil V.B., Ramarao A.V., Venkataraman K. Cassiamin A, B, C, three 2, 2-bianthraquinoyls in *Cassia siamea*. Indian Journal of Chemistry 1970; 8: 109-112.

81. Buckley D.G., Ritchie E., Taylor W.C., Young L.M. Madagascarin, a new pigment from the leaves of *Harungana madagascariensis*. Australian journal of chemistry 1972; 25: 843–855.

82. Lopez-Lazaro M. Distribution and biological activities of the Flavonoid Luteolin. Mini-Reviews in Medicinal Chemistry 2009; 9: 31-59.

83. Calderón-Montaño J.M., Burgos-Morón E., Pérez-Guerrero C., and López-Lázaro M. A review on the Dietary Flavonoid Kaempferol. Mini-Reviews in Medicinal Chemistry 2011; 11: 298-344.

84. Onanong K., Sirithon S., Natthida W., Naret M. Phenolic compounds and antioxidant activities of edible flowers from Thailand. Journal of Functional Foods 2011; 3: 88-99.

85. Shafiullah P.M., Kamil M. A new isoflavone C-glycoside from *Cassia siamea*. Fitoterapia 1995; 66: 439-441.

86. Bolanda G.M., and Donnelly M.X. Isoflavonoids and related compounds. Natural product reports 1998; 15: 241-260.

87. Ajaiyeoba E.O., Ashidi J.S. Antiplasmodial compounds from *Cassia siamea* stem bark extract. Phytotherapy research 2008; 22: 254-255.

88. Gallo B.C., and Sarachine J. Biological activities of lupeol. International Journal of biomedical and pharmaceutical sciences 2009; 3: 46-66.

89. Chanwitheesuk A., Teerawutgulrag A., and Rakariyatham N. Screening of antioxidant activity and antioxidant compounds of some edible plants of Thailand. Food Chemistry 2005; 92: 491–497.

90. Lalita L., and Shelley O. Fatty acids and sterols in the seeds of Cassia auriculata and *Cassia siamea*. Journal of the Indian Chemical Society A 2009; 86: 1224-1227.

91. Ogunwande I.A., Avoseh N.O., Flamini G., Hassan A.S., Ogunmoye A.O., Ogunsanwo A.O., Yusuf K.O., Kelechi A.O., Tiamiyu Z.A., and Tabowei G.O. Essential oils from the leaves of six medicinal plants of Nigeria. Natural Product Communications 2013; 8: 243-248.

92. Cheeptham N., and Towers G.H. Light-mediated activities of some Thai medicinal plant teas. Fitoterapia 2002; 73: 651–662.

93. Ingweye J.N., Kalio G.A., Ubua J.A., and Effiong G.S. The potentials of a lesser known *Nigerian legume*, *Senna siamea* seeds as a plant protein source. Australian Journal of Basic and Applied Sciences 2010; 4: 2222-2231.

94. Gbeassor M., Kossou Y., Amegbo K., Souza C., Koumaglo K., and Denke A. Antiplasmodial activity of eight Africans medicinales plants. Journal of Ethnopharmacology 1989; 25: 115-118.

95. Hussian H.S. Plant in Kano. Ethnomedecine: screening for antimicrobial activity and alkaloids. Journal of Pharmacology 1991; 29: 51-56.

96. Wiwied E., Aty W., and Cholies Z.N. Antimalarial activity of cassiarin A from the leaves of *Cassia siamea*. Heterocycles A 2009; 78: 1831-1836.

97. Bero J., Frederich M., and Quetin-Leclercq J., Antimalarial compounds isolated from plants used in traditional medicine. Journal of Pharmacy and Pharmacology 2009; 61: 1401-1433.

98. Jun D., Tomoe H., Yusuke H., Wiwied E., Aty W., Osamu S., Motoo S., and Hiroshi M. New tricyclic alkaloids, cassiarins G, H, J, and K from leaves of *Cassia siamea* Chemical and. Pharmacetical. Bulletin 2012; 60: 219-222.

99. Morita H., Tomizaw Y., Deguchi J., Ishikawa T., Arai H., and Zaima K. Synthesis and structure–activity relationships of cassiarin A as potential antimalarials with vasorelaxant activity. Bioorganic & Medicinal Chemistry 2009; 17: 8234–8282.

100. Nogueira C.R., and Lopes L.M. Antiplasmodial Natural Products. Molecules 2011; 16: 2146-2190.

101. Ronan B., Ademir J.S., and Alaíde B.O. Plant-Derived Antimalarial Agents: New Leads and Efficient Phytomedicines. Part II. Non-Alkaloidal Natural Products. Molecules 2009; 14: 3037-3072.

102. Nsonde-Ntandou G.F., Ndounga M., Ouamba J.M., Gbeassor M., Etou-Ossebi A., Ntoumi F., and Abena A.A. Enquête ethnobotanique: screening chimique et efficacité thérapeutique de quelques plantes utilisées contre le paludisme en médecine traditionnelle à Brazzaville. Plant and Soil 1993; 155 – 156: 325-328.

103. Matsumoto T., Kobayashi T., Ishida K., Hirasawa A., Morita B., Honda B., and Kamata K. Vasodilator effect of cassiarin A, a novel antiplasmodial alkaloid from, *Cassia siamea*, in rat isolated mesenteric artery. Biological & Pharmaceutical Bulletin 2010; 33: 844-848.

104. Pavananunda P., Jiraungkoorskul K, Kosai P., and Jiraungkoorskul W. Larvicidal properties of *Cassia siamea* leaf against Aedes aegypti larvae. International Journal of Modern Agriculture 2013; 2: 1-8.

105. Nsonde-Ntandoua G.F., Lucantoni L., Banzouzi JT, Ndounga M., Yerbanga S., Ouambaf J.M., Habluetzel A., Esposito F., and Abena A.A. Mosquitocidal and antifecundity effects of coumarin and betulinic acid isolated from *Cassia siamea* (Fabaceae) stem bark chloroform extract on female *Anopheles stephens* (*Dipteria cilicidae*). Abstract, actes du Symposium International, Bénin; 2010.

106. Luangpirom A., and Saenbuaphan N. Hypoglycemic effect of *Senna siamea* (Lam.) leaf extract in rats. Kku research journal 2006; 11: 77-83.

107. Ravi K.J., Ganga R.B., Lakshmi N.M., Mallikarjun R.T. Evaluation of antidiabetic activity of *Cassia siamea* leaves in alloxan induced diabetic rats. International Journal of Phytopharmacology 2013; 4: 237-40.

108. Kumar S., Kumar V., and Prakash O.M. Antidiabetic and anti-lipemic effects of *Cassia siamea* leaves extract in streptozotocin induced diabetic rats. Journal of Tropical Medicine 2010; 3: 871-873.

109. Patel D.K., Kumar R., Laloo D., and Hemalatha S. Natural medicines from plant source used for therapy of diabetes mellitus: An overview of its pharmacological aspects. Asian Pacific Journal of Tropical Disease 2012; 2: 239-250.

110. Kumar D., Karmase A., Jagtap S., Shekhar R ., and Bhutani K.K. Pancreatic lipase inhibitory activity of cassiamin A, a bianthraquinone from *Cassia siamea*. Natural Product Communications 2013; 8: 195-198.

111. Maniratanachote R., Kijsanayotin P., Phivthong-ngam L., Thongsaard W., Niwattisaiwong N., and Lawanprasert S. Subchronic effects of barakol on blood clinical biochemistry parameters in rats fed with normal and high cholesterol diets. Thai Journal of Pharmacology 2002; 24: 101-111.

112. Asgarpanah J. Review: Phytochemistry, pharmacology and medicinal properties of *Hypericum perforatum* L. African Journal of Pharmacy and Pharmacology 2012; 6: 1387-94.

113. Kaur P., Arora S. Superoxide anion radical scavenging activity of *Cassia siamea* and *Cassia javanica*. Medicinal chemistry research 2011; 20: 9-15.

114. Chanda S., Dave R. In vitro models for antioxidant activity evaluation and some medicinal plants possessing antioxidant properties: An overview. African Journal of Microbiology Research 2009; 3: 981-996.

115. Nanasombat S., Teckchuen N. Antimicrobial, antioxidant and anticancer activities of Thai local vegetables. Journal of Medicinal Plants Research 2009; 3: 443-449.

116. Indra M., Suganthi J.S., Muthuchelian K. Antioxidant activities of mother plant and tissues cultured plants of *Cassia siamea* (Fabacae). Journal of Biosciences Research 2011; 2: 171-175.

117. Suganthi J.S., Deva M., Indra M., Muthuchelian K. Enzymatic activities of mother plant and tissue cultured plants of *Cassia siamea* (Fabaceae). Journal of Biomedical Sciences and Research 2011; 2: 183-188.

118. Subhadhirasakul S., and Khumfang P. Screening of barakol from Cassia plants and some of its biological activities.

Songklanakarin Journal of Science and Technology 2000; 22: 429-434.

119. Tepsuwan A., Kupradinun P., Kusamran W.R. Effect of *Cassia siamese* leaves on the activities of chemical carcinogen metabolizing enzymes and on mammary gland carcinogenesis in the rat. Mutation Research 1999; 428: 363–373.

120. Koyama J., Tagahara K., Osakai T., Tsujino Y., Tsurumi S., Nishino H., and Tokuda H. Inhibitory effects on Epstein-Barr virus activation of anthraquinones: correlation with redox potentials. Cancer Letters 1997; 15: 179-183.

121. Koyama J., Morita I., Tagahara K., Nobukuni Y., Mukainaka T., Kuchide M., Tokuda H., and Nishino H. Chemopreventive effects of emodin and cassiamin B in mouse skin carcinogenesis. Cancer Letters 2002; 182: 135-139.

122. Kupradinun P., Tepsuwan A., and Kusamran W.R. Anticlastogenic potentials of neem flowers, *Cassia siamea* leaves and Thai bitter gourd fruits in erythrocyte micronucleus assay in the mouse. Asian Biomedicine 2011; 5: 669-673

123. Appiah-Opong R., Commandeur J.N.M., Axson C., and Vermeulen N.P.E. Interactions between cytochromes P450, glutathione s-transferases and Ghanaian medicinal plants. Food and Chemical Toxicology 2008; 46: 3598-3603.

124. Nsonde-Ntandou G.F., Banzouzi J.T, Mbatchi B, Elion-Itou RD, Etou-Ossibi AW, Ramos S, Benoit-Vical F, Abena AA and. Ouamba J.M. Analgesic and anti-inflammatory effects of *Cassia siamea* Lam. stem bark extracts. Journal of Ethnopharmacology 2010; 127: 108-111.

125. Koyama J., Morita I., Tagahara K., Ogata M., Mukainaka T., Tokuda H., Nishino H. Inhibitory effects of anthraquinones and bianthraquinones on Epstein - Barr virus activation. Cancer Letters 2001; 170: 15-18.

126. Koyama J., Morita I., Kobayashi N., Osakai T., Nishino H., and Tokuda H. Correlation between reduction potentials and inhibitory effects on Epstein–Barr virus activation of poly-substituted anthraquinones. Cancer Letters 2005; 225: 193–198.

127. Koyama J., Inoue M., Morita I., Kobayashi N., Osakai T., Nishino H., Tokuda H. Correlation between reduction potentials and inhibitory effects on Epstein–Barr virus activation by emodin derivatives. Cancer Letters 2006; 241: 263–267.

128. Chen F., Ito H, Okabe F., Momose Y., Yamamura S., Ridtitid W., Chaichantipyuth C., Leelasangaluk V., and Tongroach P. Effects of barakol on aconitine-induced cardiac arrhythmias. Pharmaceutical Biology 1999; 37: 105-108.

129. Nayak B.S., and Pereira L.M. Catharanthus roseus flower extract has wound-healing activity in Sprague Dawley rats. Alternative medicine 2006; 6: 4.

130. Sawanobori T., Hirano, Y., and Hiraoka M. Aconitine-induced delayed after depolarization in frog atrium and guinea pig papillary muscles in the presence of low concentrations of Ca+. Journal of Physiology 1987; 37: 59-79.

131. Busarakkumtragu P., Tep-Areenan P., Chainakul S., Wongsawakul O. Effets of barakol on vascular functions in rats. International Journal of Pharmacology 2010; 6: 257-263.

132. Morales M.A., Hernández D., Bustamante S., Bachiller I., Rojas A. Is Senna laxative use associated to cathartic colon, genotoxicity, or carcinogenicity ? Journal of Toxicology 2009; 2009: 1-8.

133. Pumpaisalcha W., Kaewichit S., Taesothikul T., Niwatananun W., and Sanichwankul K. The antidepressive effect of barakol in the forced-swimming test. Chiang Mai University Journal 2005; 4: 191-198.

134. Sakulpanich A., and Gritsanapan W. Laxative anthraquinone contents in fresh and cooked *Senna siamea* leaves. Southeast Asian Journal of Tropical Medicine and Public Health 2009; 40: 835-839.

135. Elujoba A.A., Ajulo O.O., and Iweibo G.O. Chemical and biological analyses of Nigerian *Cassia* species for laxative activity. Journal of Pharmaceutical & Biomedical Analysis 1989; 7: 1453-1457.

136. Leng-Peschlow E. Sennoside-induced secretion and its relevance for the laxative effect. Pharmacology 1993; 47: 14-21.

137. Fioramonti J., Staumont G., Garcia-Villar R., Bueno L. Effects of sennosides on colon motility in dogs. Pharmacology 1988; 36: 23-30.

138. Deachapunya C., Thongsaard W., and Poonyachoti S. Barakol suppress norepinephrine-induced inhibition of spontaneous longitudinal smooth muscle contractions in isolated rat small intestine. Journal of Ethnopharmacology 2005; 101: 227-232.

139. Momin A.M., Rana M.S., Khan M.R., Emran T.B. and Hosen S.M. Antimicrobial and peripherally acting analgesic activity of *Senna siamea*. Molecular & Clinical Pharmacology 2012; 3: 149-157.

140. Wongwitdecha N. Neuro-psychopharmacological studies the effects of barakol, a traditional Thai medicine. Srinagarind Medical Journal 2007; 22: 325-332.

141. Pooviboonsuk P., Tappayuthpijarn P., and Hincheeranund T. Hypnotic effect of shape modification herbal extract *Cassia siamea* in human subjects. Journal of the psychiatric association of Thailand 2000; 45: 251-259.

142. Zhang Z. Therapeutic effects of herbal extracts and constituents in animal models of psychiatric disorders. Life Sciences 2004; 75: 1659-1699.

143. Sukma M., Chaichantipyuth C., Murakami Y., Tohda M., Matsumoto K., and Watanabe H. CNS inhibitory effects of barakol, a constituent of *Cassia siamia* Lamk. Journal of Ethnopharmacology 2002; 83: 87-94.

144. Thongsaard W., Pongsakorn S., Sudsuang R., Bennett G.W., Kendall D.A. and Marsden C.A. Barakol, a natural anxiolytic, inhibits striatal dopamine release but not uptake in vitro. European Journal of Pharmacology 1997; 319: 157-164.

145. Saiyudthong S., Thongsaard W., and Marsden C.A. Acute effects of barakol and serotonergic drugs on exploratory behavior in rats. Journal of Medicine and Health Sciences 2005; 12: 77-84.

146. Deachapunya C., and Thongsaard W. Behavioral effects of acute and chronic oral administration of barakol in rats. Journal of the Medical Association of Thailand 2009; 92: 29-37.

147. Fiorino D.F., Treit D., Menard J., Termer L., and Phillips A.G. Is barakol anxiolytic? Behavioural pharmacology 1998; 9: 375-378.

148. Pumpaisalchai W., Kaewichit S., Taesothikul T., Niwatananun W., and Sanichwankul K. HPLC analysis method and pharmacokinetics of barakol. Chiang Mai University Journal 2005; 4: 49-58.

149. Arunlakshana O. Studies of indigenous drugs: Pharmacological actions of the leaves of *Cassia siamea*. Siriraj Hospital Gaz 1949; 1: 434-443.

150. Jantarayota P. Actions of barakol on the central nervous system. M.S. thesis, Faculty of Pharmacy, Chulalongkorn University, Bangkok, 1987, pp. 82.

151. Majji L.N., Battu G.R., Jangiti R.K., and Talluri M.R. Evaluation of in-vitro antibacterial activity of *Cassia siamea* leaves. International journal of pharmacy and pharmaceutical sciences 2013; 5: 263-265.

152. Ali M.S., Azhar I., Amtul Z., Ahmad V.U., and Smanghani K.U. Antimicrobial screening of some Caesalpiniaceae. Fitoterapia 1999; 70: 299-304.

153. Doughari J.H., and Okafor N.B. Antibacterial activity of Senna siamae leaf extracts on Salmonella typhi. African Journal of Microbiology Research 2008; 2: 42-46.

154. Krasaekoopt W., and Kongkarnchanatip A. Anti-microbial properties of Thai traditional flower vegetable extracts. Assumption University Journal of Technology 2005; 9: 71-74.

155. Nagadatta A., Julamanee B., Chaisawadi N., paksachadkul A., Archsiwanon M., Pewleang P., Chaisawadi S., and Thongbute D. Preliminary study of antimicrobial activities on Thai local bitter vegetables. University of Technology Thonburi, Bangkok 10140, Thailand, 2011, pp.1-3.

156. Takahashi N., Marushige S., and Otake N. The chemistry of physiologically active natural products, University Press, Tokyo, 1977, pp.167-246.

157. Prabhakar K., Kumar L.S., Rajendran S., Chandrasekaran M., Bhaskar K., and Sajit K.A.K. Antifungal activity of plant extracts against *Candida* species from oral lesions. India Journal of Pharmaceutical Sciences 2008; 70: 801-803.

158. Jones N.P., Arnason J.T., Abou-Zaid M., Akpagana K., Sanchez-Vindas P., and Smith M.L. Antifungal activity of extracts from medicinal plants used by First Nations Peoples of eastern Canada. Journal of Ethnopharmacology 2000; 73: 191–198.

159. Mohammed A., Mada S.B., Yakasai H.M. Sub-chronic study of aqueous stem bark extract of *Senna siamea* in rats. Asian Journal of Biological Sciences 2012; 5: 314-321.

160. Wiam I.M., Jacks T.W., and Zongoma Y.A. Acute toxicity and phytochemical studies of *Cassia siamea* extracts in rats. Pakistan Journal of Biological Sciences 2005; 8: 586-588.

161. Chavalittumrong P., Chivapat S., Rattanajarasroj S., Suyasootcharee B., Soonthornchareonnon N., and Punyamung S. Chronic toxicity of *Cassia siamea* Lam. leaves in rats. Journal of the Medical Sciences 2003; 45: 101-114.

162. Alli Y.R., Adanlawo I.G., Asaolu M.F., and Agbewole O.O. Effect of aqueous extract of *Senna siamea* (Cassia leaves) on the liver and kidney of albino rats. Asian Journal of Pharmaceutical and Health Sciences 2011; 1: 193-195.

163. Wiwanitkit V., Palaniswamy U.R., Gardner Z.E., and Craker L.E. *Cassia siamea* induced hepatitis, a case report of phytomedicine side effect. Traditional Medicine and Nutraceuticals 2005; 6: 191-194.

164. Pumpaisalchai W., Kaewvichit S., Siriaunkgul S., Taesothikul T., Niwatananun W., and Sanichwankul K. Toxicity

of barakol: hepatotoxicity and subacute toxicity. International Society for Horticultural Science 2001; 170: 15-18.

165. Sirimanapong W., Buranasinsup S., Toniti P., Laungkajornlert W., Soparkwijit W., and Chantong B. In vitro cytotoxicity of barakol in hepatocytes of carp fish (*Cyprinus carpio*). International Association for Aquatic Animal Medicine, Thailand, 2008, pp. 75-76.

166. Hongsirinirachorn M., Threeprasertsuk S., and Chutaputti A. Acute hepatitis associated with barakol. Journal of the Medical Association of Thailand 2003; 86: 484-489.

167. Lawanprasert S., Chaichantipyuth C., Unchern S., and lawanprasert Y. In vitro hepatotoxicity study of barakol using human hepatoma cell line HepG2. Thai Journal of Pharmaceutical Sciences 2001; 25: 149-159.

168. Wongtongtair S., Chanvorachote P., Hutamekalin P., Chaichantipyuth C., Lipipuna V., Tiensiwakul P., and Meksuriyen D. Barakol-induced apoptosis in P19 cells through generation of reactive oxygen species and activation of caspase-9. Journal of Ethnopharmacology 2011; 137: 971-978.

169. Mitchell J., Mengs U., and Mcpherson S. An oral carcinogenicity and toxicity study of senna (Tinnevelly senna fruits) in the rat. Archives of Toxicology 2006; 80: 34-44.