ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Antimicrobial Activities of Selected Thai Medicinal Plants Bearing Quinonoids

Kitthisak Chansukh[a], Rawiwan Charoensup[b], Chanida Palanuvej[a,*], and Nijsiri Ruangrungsi[a,c]

[a]College of Public Health Sciences, Chulalongkorn University, Bangkok 10330, Thailand.
[b]School of Health Science, Mae Fah Luang University, Chiang Rai 57100, Thailand.
[c]Faculty of Pharmacy, Rangsit University, Patumthani 12000, Thailand.

ABSTRACT

Nine species of selected Thai medicinal plants bearing quinonoid compounds were investigated *in vitro* for their antimicrobial activities. The plant materials were sequentially extracted by maceration with petroleum ether and ethanol respectively. Thirteen tested pathogenic microorganisms included 5 gram positive bacteria, 6 gram negative bacteria and 2 fungi. The assays were performed by using agar well diffusion method for determination of inhibition zone and broth microdilution method for determination of minimum inhibitory concentrations (MIC) and minimum bactericidal concentration (MBC) or minimum fungicidal concentration (MFC) with two fold dilution. The results showed that most of the extracts and the quinone derivative compounds demonstrated a promising inhibitory effect against gram positive bacteria followed by fungi and gram negative bacteria. The ethanol extract of *Xyris indica* flowering heads and the petroleum ether extract of *Eleutherine americana* bulbs expressed broadest spectrum of antimicrobial activity. The petroleum ether extract of *Rhinacanthus nasutus* roots demonstrated lowest MIC and MBC on tested gram positive bacteria. The petroleum ether extract of *Morinda citrifolia* roots had promising antimicrobial potential against *Candida albicans*. This study revealed the antimicrobial potentials among selected Thai medicinal plants bearing quinonoid compounds which used as crude drugs in traditional Thai medicine.

Keywords: Quinonoid bearing plants, Antibacterial activity, Antifungal activity

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Quinones are natural coloured pigments from plants which can be divided into four groups including benzoquinones, anthraquinones, naphthoquinones and isoprenoid quinones. They are mainly found in bark, roots and tissues of plants. Quinone skeletons from simple 1,4-benzoquinone to triterpene quinone have been reported for their antimicrobial activities. 1,4-Benzoquinone was demonstrated to be essential compound for antibacterial activity in *Pyrus* spp. [1]. Heliotropinone A and B, the benzoquinones from the aerial parts of *Heliotropium ovalifolium* Forssk. (BORAGINACEAE) showed antibacterial activity against *Bacillus subtilis* and antifungal activities against *Cladosporium cucumerinum* and *Candida albicans* [2]. A diterpene quinone from the bark of *Cryptomeria japonica* (Thunb. ex L.f.) D. Don (TAXODIACEAE) showed moderate antifungal activities against *Alternaria alternata* and *Pyricularia oryzae* [3]. A triterpene quinone skeleton and groups in ring E were found to be structural requirements for antimicrobial activites in *Schaefferia cuneifolia* A. Gray and *Maytenus horrida* Reiss. (CELASTRACEAE) [4]. Chrysophanol has been reported as an antimicrobial anthraquinone from the root extract of *Colubrina greggii* S. Watson (RHAMNACEAE) [5]. A naphthoquinone–anthraquinone coupled pigment named newbouldiaquinone A from the roots of *Newbouldia laevis* Seem. (BIGNONIACEAE) demonstrated very pronounced antimicrobial activity against a wide range of microorganisms and moderate antimalarial activity against *Plasmodium falciparum* [6].

The medicinal plants which have been widely used in traditional Thai medicine for treatment of various infectious diseases are shown as plant containing quinone compounds as follows: Anthraquinone: *Xyris indica* Linn. (XYRIDACEAE) [7], *Cassia tora* Linn. (CAESALPINIACEAE) [8], *Morinda elliptica* Ridl. [9], *M. citrifolia* Linn. [10-12] and *M. coreia* Ham. (RUBIACEAE) [13]; Benzoquinone: *Ardisia elliptica* Thunb. (MYRSINACEAE) [14,15] and *Nigella sativa* Linn. (RANUNCULACEAE) [16]; Naphthoquinone: *Rhinacanthus nasutus* (L.) Kurz. (ACANTHACEAE) [17,18] and *Eleutherine americana* (Aubl.) Merr. (IRIDACEAE) [19]. This study aimed to evaluate the antimicrobial activities of these medicinal plants bearing quinonoids in Thailand.

MATERIALS AND METHODS

Plant materials

Thai medicinal plant materials bearing quinonoids were studied as follows: *X. indica* (flowering head) *C. tora* (seed), *M. elliptica* (root), *M. citrifolia* (root), *M. coreia* (root), *A. elliptica* (Fruit), *N. sativa* (seed), *R. nasutus* (root and aerial part) and *E. americana* (bulb). They were collected from traditional Thai drug stores, the local markets and various gardens in Thailand. All of the plants were authenticated by Associate Prof. Nijsiri Ruangrungsi, Ph.D. Voucher specimens were deposited at College of Public Health Sciences, Chulalongkorn University, Thailand.

Plant extraction

The plant materials were dried in hot air oven at 50°C and grounded to coarsely powder. Each dried powder was continuously macerated with petroleum ether and ethanol

at room temperature for 48 hours. The filtrate of each plant extract was further concentrated to dryness under reduced pressure at 50°C. The yields of the different extracts were weighed, recorded and dissolved in dimethyl sulfoxide (DMSO) to a concentration of 200 mg/ml. The samples were then stored at -20°C and further used for antimicrobial tests.

Microorganisms

Bacillus subtilis ATCC6633, *Staphylococcus aureus* ATCC6538P, *Escherichia coli* ATCC25922, *Pseudomonas aeruginosa* ATCC9027, *Candida albicans* ATCC10230 and *Saccharomyces cerevisiae* ATCC9763 were obtained from Department of Biochemistry and Microbiology, Faculty of Pharmaceutical Sciences, Chulalongkorn University; *Staphylococcus epidermidis* (Isolates), *Salmonella typhimurium* (Isolates) and *Shigella sp.* (Isolates) were from Department of Microbiology, Faculty of Science, Chulalongkorn University and *Basillus cereus* ATCC11778, *Micrococcus luteus* ATCC9341, *Salmonella typhi* (Isolates) and *Enterobacter aerogenes* ATCC13048 were from Department of Microbiology, Faculty of Sciences and Technology, Suan Sunandha Rajabhat University.

Determination of zone of inhibition

Bacterial and fungal strains were maintained on Muller-Hinton or Sabouraud agar respectively. They were inoculated at 37 °C, for 18-24 hrs for bacteria and 24-48 hrs for fungi. Four to five of isolated colonies from the overnight culture were suspended in normal saline. The turbidity of the suspension was adjusted to obtain the absorbance of 0.08-0.10 at 625 nm which comparable to 0.5 Mc Farland standards or approximately 1 x 10^8CFU/ml. One hundred microliters of the suspension was mixed with sterile seeded agar then poured on the sterile base agar. The plates were allowed to dry at room temperature. Agar wells were cut from seeded agar plates by a cork borer (6 mm.) and added with 20 µl of various plant extracts (200 mg/ml). DMSO was used as a negative control. Standard quinone derivatives: alizarin, juglone, lapachol, embelin and lawsone (10 mg/ml) and antibiotic drugs: ampicllin sodium and amikacin sulfate (10 mg/ml) were used as positive controls. The plates were incubated at 37 °C for 18 to 24 hrs and 24 to 48 hrs for bacterial and fungal strains respectively. The zones of inhibition were measured in millimeter and the experiment was carried out in triplicates.

Determination of minimum inhibitory concentration (MIC), minimum bactericidal concentration (MBC) and minimum fungicidal concentration (MFC)

A microbial suspension in broth was prepared by adding 10 µl of normal saline microbial suspensions to 1 ml of Muller-Hinton or Sabouraud broth. Into a sterile 96-well microplate, 50 µl of microbial suspended in broth was added to the wells containing 50 µl of plant extract (final concentrations: 3.9-2000 µg /ml with two-fold dilution), positive controls (final concentrations: 0.19-100 µg/ml with two-fold dilution) and negative control (DMSO). All of chemicals was prepared by diluting with broth to obtain final volume of 1 ml and incubated at 37°C, for 18 to 24 hrs for bacteria and 24 to 48 hrs for fungi.

The lowest concentration of each plant extract inhibiting the growth of the tested microorganisms detected by the lack of visual turbidity compared to the negative control

ISSN: 0975-8585

was defined as the MIC of the extracts. The broth from the wells with no turbidity were then streaked onto nutrient agar plates and incubated at 37 ^{o} C, for 18-24 hrs for bacteria and 24-48 hrs for fungi. The lowest concentration with no microbial growth observed on the plate was considered as the MBC or MFC values.

RESULTS AND DISCUSSION

Most of the extracts demonstrated antimicrobial activities against tested gram positive bacteria and fungi. Antimicrobial activity against gram negative bacteria was less potent (Table 1-2). The ethanol extract of *X. indica* flowering heads showed broadest antimicrobial spectrum followed by the petroleum ether extract of *E. Americana* bulbs. *Xyris* spp. were previously reported for their antifungal properties due to 1,8-dihydroxyanthraquinone derivatives [20]. Crude ethanolic extract from bulbs of *E. Americana* was formerly shown to be a good antimicrobial agent against foodborne gram-positive bacteria, certain gram-negative, and food spoilage organisms except *Candida albicans* [21]. The present study used higher dose of the extract and different agar diffusion technique (4 mg/well vs. 2.5 mg/disc) resulting in anti-candida potential of *E. Americana* bulbs.

Table 1: Zone of inhibition against gram positive bacteria

Plant extract[a] (4 mg/well)		**Zone of Inhibition (mm)[b]**				
		B. cereus	***B. subtilis***	***S. aureus***	***S. epidermidis***	***M. luteus***
X. indica (Flower)	P	7.3±0.6	7.3±0.6	NA	11.0±1.0	NA
	E	13.3±0.6	12.3±0.6	10.3±0.6	16.0±1.0	11.3±0.6
C. tora (Seed)	P	NA	8.3±1.5	NA	NA	NA
	E	NA	NA	NA	7.3±0.6	NA
R. nasutus (Root)	P	19.7±0.6	16.0±0.0	16.0±0.0	29.3±0.6	23.3±0.6
	E	NA	12.7±0.6	11.0±1.0	15.3±0.6	22.0±0.0
R. nasutus (Aerial part)	P	10.7±0.6	14.7±0.6	11.7±0.6	10.0±0.0	19.0±1.0
	E	12.7±0.6	13.0±1.0	11.3±0.6	13.0±0.0	16.3±0.6
M. elliptica (Root)	P	12.0±1.0	12.0±1.0	11.3±0.6	14.7±0.6	9.0±1.0
	E	10.3±0.6	11.0±1.0	11.0±0.0	10.7±0.6	12.0±1.0
M. citrifolia (Root)	P	15.3±0.6	14.3±0.6	11.7±0.6	16.3±0.6	15.0±0.0
	E	15.0±1.0	16.7±0.6	12.0±0.0	16.7±0.6	15.7±0.6
M. coreia (Root)	P	15.7±0.6	14.7±0.6	12.0±0.0	21.0±1.0	18.0±1.0
	E	9.7±0.6	12.7±0.6	10.3±0.6	11.3±0.6	11.0±0.0
A. elliptica (Fruit)	P	7.3±0.6	7.0±0.0	NA	7.0±0.0	9.7±0.6
	E	9.3±0.6	9.7±0.6	8.3±0.6	10.7±0.6	11.0±1.0
E. americana (Bulb)	P	24.3±0.6	17.7±0.6	21.0±0.0	32.7±0.6	20.0±0.0
	E	20.0±0.0	15.7±0.6	15.0±0.0	20.0±0.0	14.7±0.6
N. sativa (Seed)	P	18.3±0.6	12.0±0.0	10.7±0.6	15.3±0.6	15.0±0.0
	E	15.0±0.0	10.0±0.0	8.7±0.6	10.3±0.6	9.7±0.6
Drug control (0.2 mg/well)						
Alizarin		10.3±0.6	11.0±0.0	12.7±0.6	NA	NA
Juglone		NA	11.0±0.0	20.0±0.0	20.7±0.6	22.0±1.0
Lapachol		14.7±0.6	10.0±1.0	10.0±0.0	25.0±0.0	NA
Lawsone		15.3±0.6	25.7±1.2	20.0±0.0	22.7±0.6	15.0±0.0
Embelin		9.7±0.6	10.0±0.0	10.0±0.0	7.0±0.0	9.7±0.6
Ampicllin		40.3±0.6	19.3±0.6	50.3±0.6	30.7±0.6	46.0±1.0
Amikacin		32.0±0.0	29.3±0.6	30.0±0.0	31.3±0.6	30.0±0.0
DMSO		NA	NA	NA	NA	NA

[a]P = petroleum ether, E = ethanol; [b]means ± SD, NA = no activity, Ø 6 mm of well.
The tests were done in triplicate.

ISSN: 0975-8585

Table 2. Zone of inhibition against gram negative bacteria and fungi

Plant extract[a] (4 mg/well)		Zone of Inhibition (mm)[b]					
		Gram negative bacteria[c]				Fungi	
		E. coli	*E. aerogenes*	*S. typhimurium*	*Shigella* sp.	*C. albicans*	*S. cerevisiae*
X. indica (Flower)	P	NA	NA	NA	NA	NA	13.7±0.6
	E	9.7±0.6	8.7±0.6	11.0±1.0	12.7±0.6	9.7±0.6	11.0±0.0
C. tora (Seed)	P	9.0±1.0	NA	NA	NA	NA	NA
	E	NA	NA	NA	NA	NA	NA
R. nasutus (Root)	P	NA	NA	NA	NA	10.0±0.0	20.0±0.0
	E	10.3±0.6	NA	NA	12.0±0.0	NA	15.3±0.6
R. nasutus (Aerial part)	P	NA	NA	NA	NA	NA	11.0±0.0
	E	NA	NA	NA	NA	NA	16.7±0.6
M. elliptica (Root)	P	NA	NA	NA	NA	8.7±0.6	10.0±0.0
	E	NA	NA	NA	12.3±0.6	9.7±0.6	13.0±0.0
M. citrifolia (Root)	P	NA	NA	NA	NA	9.7±0.6	12.0±0.0
	E	NA	NA	NA	10.3±0.6	13.0±0.0	15.0±0.0
M. coreia (Root)	P	NA	NA	NA	NA	12.7±0.6	10.3±0.6
	E	NA	NA	NA	10.3±0.6	9.3±0.6	16.3±0.6
A. elliptica (Fruit)	P	NA	NA	NA	NA	NA	NA
	E	10.0±1.0	NA	NA	NA	7.7±0.6	14.3±0.6
E. americana (Bulb)	P	NA	8.7±0.6	11.0±0.0	17.3±0.6	14.0±0.0	14.0±0.0
	E	NA	NA	NA	13.0±0.0	10.0±0.0	17.7±0.6
N. sativa (Seed)	P	NA	NA	NA	NA	NA	NA
	E	NA	NA	NA	7.3±0.6	NA	NA
Drug control (0.2 mg/well)							
Alizarin		11.7±0.6	NA	NA	NA	9.7±0.6	NA
Juglone		13.3±0.6	NA	10.3±0.6	14.0±0.0	28.0±2.0	NA
Lapachol		NA	NA	NA	NA	NA	NA
Lawsone		19.3±0.6	NA	NA	14.7±0.6	10.7±2.1	10.0±0.0
Embelin		NA	NA	NA	NA	NA	NA
Ampicllin		32.0±0.0	18.7±0.6	40.0±0.0	33.0±0.0	NA	NA
Amikacin		21.0±0.0	23.3±0.6	30.0±0.0	41.0±1.0	NA	NA
DMSO		NA	NA	NA	NA	NA	NA

[a]P = petroleum ether, E = ethanol; [b]means ± SD, NA = no activity, Ø 6 mm of well;
[c]All extract showed no activity against *P. aeruginosa* and *S. typhi*. The tests were done in triplicate.

For antimicrobial potency, the petroleum ether extract of *R. nasutus* roots demonstrated lowest MIC and MBC on tested gram positive bacteria (< 20 μg/ml) which seemed to be more potent than quinone drugs such as alizarin, juglone, lapachol and lawsone (Table 3). The previous study also reported that hexane partition of *R. nasutus* roots inhibited gram positive bacteria more potently than chloroform and ethanol partitions. The roots had antibacterial potential than leaves and stems respectively [22]. The petroleum ether extract of *M. citrifolia* roots had promising antimicrobial potential against *Candida albicans* with MIC and MBC of 125 and 250 μg/ml respectively (Table 4). The phytochemical study of the chloroform soluble fraction of the methanol extract of *M. citrifolia* roots revealed at least 2 benzoquinones and at least 14 anthraquinones including alizarin [23]. The seed of *Cassia* spp. such as *C. fistula* Linn. was reported for the anticandida potential as well as anti gram positive and gram negative bacteria properties [24] whereas this study found that *C. tora* seeds possessed least spectrum of antimicrobial activity as well as least potency.

The mechanism of action on antimicrobial potential of quinonoids was associated with electron reduction of quinone to hydroquinone moiety. The hydroxyl groups could

ISSN: 0975-8585

covalently bonded with DNA to form DNA adduct resulting in mitotic blockage. The redox reaction of quinone compounds could also generate reactive oxygen species especially hydroxyl radicals which responsible to irreversibly complex formation with lipids and proteins in the microbial cell. These reactions might interfere to surface-exposed adhesins, cell-wall polypeptides, and membrane-bound enzymes of the microorganisms [25-27].

Table 3. MIC and MBC against gram positive bacteria

Plant extract[a] (µg/ml)		***B. cereus***		***B. subtilis***		***S. aureus***		***S. epidermidis***		***M. luteus***	
		MIC	**MBC**	**MIC**	**MBC**	**MIC**	**MBC**	**MIC**	**MBC**	**MIC**	**MBC**
X. indica (Flower)	P	250	2000	250	1000	NA	NA	**62.50**	>2000	NA	NA
	E	500	2000	500	2000	125	>2000	500	>2000	500	>2000
C. tora (Seed)	P	NA	NA	>2000	>2000	NA	NA	NA	NA	NA	NA
	E	NA	NA	NA	NA	NA	NA	2000	>2000	NA	NA
R. nasutus (Root)	P	**15.6**	**15.6**	**7.8**	**15.6**	**7.8**	>2000	**15.6**	>2000	**3.9**	**15.6**
	E	NA	NA	125	125	**62.5**	>2000	125	>2000	**62.5**	**62.5**
R. nasutus (Aerial part)	P	500	1000	250	250	500	>2000	>2000	>2000	500	2000
	E	500	1000	250	500	500	2000	>2000	>2000	500	2000
M. elliptica (Root)	P	250	500	250	250	125	>2000	250	>2000	250	1000
	E	500	2000	500	1000	250	>2000	500	>2000	500	>2000
M. citrifolia (Root)	P	125	250	125	125	125	>2000	250	1000	125	250
	E	500	1000	250	250	125	2000	500	>2000	125	2000
M. coreia (Root)	P	500	1000	250	250	125	>2000	250	1000	125	>2000
	E	500	2000	250	1000	125	>2000	1000	>2000	500	>2000
A. elliptica (Fruit)	P	**62.5**	**125**	**62.5**	**62.5**	NA	NA	125	500	125	125
	E	250	500	250	250	31.25	250	1000	2000	125	250
E. americana (Bulb)	P	**62.5**	125	125	125	**62.5**	500	125	>2000	125	500
	E	125	250	250	500	125	2000	500	>2000	2000	>2000
N. sativa (Seed)	P	250	250	125	125	250	500	2000	>2000	>2000	>2000
	E	2000	2000	2000	2000	500	>2000	>2000	>2000	>2000	>2000
Drug control (µg/ml)											
Alizarin		25	>100	25	>100	12.5	>100	NA	NA	NA	NA
Juglone		NA	NA	25	>100	12.5	>100	1.6	>100	6.2	>100
Lapachol		50	>100	100	>100	50	>100	25	>100	NA	NA
Lawsone		25	100	50	>100	12.5	>100	50	>100	50	>100
Embelin		6.2	6.2	6.2	6.2	6.2	12.5	12.5	50	6.2	12.5
Ampicllin		0.2	0.2	12.5	12.5	0.2	6.2	0.4	0.8	0.2	0.4
Amikacin		0.4	0.4	0.2	0.4	1.6	3.1	0.8	1.6	0.8	1.6
DMSO		NA	NA	NA	NA	NA	NA	NA	NA	NA	NA

[a]P = petroleum ether, E = ethanol; The tests were done in triplicate.

The potential of quinone antimicrobial effects is evidential. However, there are a range of antimicrobial efficacies. The difference in chemical structure affects both affinity of compound to target site and also compound solubility [25]. In addition, herbal medicines have more complicated mechanisms of action because of a variety of compounds. Synergistic or antagonistic interaction can occur and play an important role in efficacy of treatment.

ISSN: 0975-8585

Table 4. MIC against gram negative bacteria and fungi

Plant extract[a] (μg/ml)		MIC					
		Gram negative bacteria[b]				Fungi	
		E. coli	*E. aerogenes*	*S. typhimurium*	*Shigella* sp.	*C. albicans*	*S. cerevisiae*
X. indica (Flower)	P	NA	NA	NA	NA	NA	500
	E	2000	>2000	>2000	>2000	2000	250
C. tora (Seed)	P	>2000	NA	NA	NA	NA	NA
	E	NA	NA	NA	NA	NA	NA
R. nasutus (Root)	P	NA	NA	NA	NA	>2000	>2000
	E	>2000	NA	NA	>2000	NA	>2000
R. nasutus (Aerial part)	P	NA	NA	NA	NA	NA	>2000
	E	NA	NA	NA	NA	NA	>2000
M. elliptica (Root)	P	NA	NA	NA	NA	1000	500
	E	NA	NA	NA	>2000	2000	500
M. citrifolia (Root)	P	NA	NA	NA	NA	**125**[c]	250
	E	NA	NA	NA	500	250	500
M. coreia (Root)	P	NA	NA	NA	NA	250	500
	E	NA	NA	NA	1000	2000	2000
A. elliptica (Fruit)	P	NA	NA	NA	NA	NA	NA
	E	>2000	NA	NA	NA	250	2000
E. americana (Bulb)	P	NA	>2000	500	500	250	250
	E	NA	NA	NA	>2000	2000	250
N. sativa (Seed)	P	NA	NA	NA	NA	NA	NA
	E	NA	NA	NA	>2000	NA	NA
Drug control (μg/ml)							
Alizarin		25	NA	NA	NA	100	NA
Juglone		25	NA	100	100	100	NA
Lapachol		NA	NA	NA	NA	NA	NA
Lawsone		25	NA	NA	100	100	25
Embelin		NA	NA	NA	NA	NA	NA
Ampicllin		3.12	50	0.39	3.12	NA	NA
Amikacin		0.78	0.78	0.78	0.78	NA	NA
DMSO		NA	NA	NA	NA	NA	NA

[a]P = petroleum ether, E = ethanol; [b]All extract showed no activity against *P. aeruginosa* and *S. typhi*. [c]MBC = 250 μg/ml. The tests were done in triplicate.

ACKNOWLEDGEMENTS

The authors are thankful to the 90th Anniversary of Chulalongkorn University Fund (Ratchadaphiseksomphot Endowment Fund) and the Herbal Remedies and Alternative Medicine Task Force of STAR: Special Task Force for Activating Research under 100 Years Chulalongkorn University Fund. K.C. is gratitude to Suan Sunandha Rajabhat University for the scholarship and thankful to College of Public Health Sciences, Chulalongkorn University for providing facilities throughout the work.

REFERENCES

[1] Jin S, Sato N. Phytochem 2003; 62: 101–107.
[2] Guntern A, Ioset JR, Queiroz EF, Foggin CM, Hostettmann K. Phytochem 2001; 58: 631–635.
[3] Kofujita H, Ota M, Takahashi K, Kawai Y, Hayashi Y. Phytochem 2002; 61: 895–898.
[4] Moujir L, Gutierrez-Navarro AM, Gonzalez AG, Ravelo AG, Luis JG. Biochem Syst Ecol 1990; 18(1): 25-28.

[5] García-Sosa K, Villarreal-Alvarez N, Lübben P, Peña-Rodríguez LM. J Mex Chem Soc 2006; 50(2): 76-78.
[6] Eyong KO, Folefoc GN, Kuete V, Beng VP, Krohn K, Hussain H, Nkengfack AE, Saeftel M, Sarite SR, Hoerauf A. Phytochem 2006; 67: 605–609.
[7] Ruangrungsi N, Phadungcharoen T, Suriyagan S, Sekine T, Fujii Y, and Murakoshi I. Thai J Pharm Sci 1993; 17: 189-193.
[8] Choi JS, Lee HJ, Kang SS. Arch Pharm Res 1994; 17(6):462-6.
[9] Ismail NH, Ali AM, Aimi N, Kitajima M, Takayama H, Lajis NH. Phytochem 1997; 45(8): 1723-1725.
[10] Leistner E. Phytochem 1973; 12: 1669-1674.
[11] Inoue K, Nayeshiro H, Inouye H and Zenk M. Phytochem 1981; 20: 1693-1700.
[12] Ee GC, Wen YP, Sukari MA, Go R and Lee HL. Nat Prod Res 2009; 23: 1322-1329.
[13] Ruksilp T, Sichaem J, Khumkratok S, Siripong P, Tip-Pyang S. Chem Nat Compd 2013; 49(4): 746-748.
[14] Ogawa H and Natori S. Phytochem 1968; 7: 773-782.
[15] Shuayprom A, Povichit N, Bunjob M, Boonrod T, Bucha P, Suphaphon B. J Rajamangala Univ Technol Srivijaya 2010; 2(2): 69-77.
[16] Venkatachallam SKT, Pattekhan H, Divakar S, Kadimi US. J Food Sci Technol 2010; 47(6): 598-605.
[17] Wu TS, Tien HJ, Yeh MY, Lee KH. Phytochem 1988; 27(12): 3787-3788.
[18] Wu TS, Hsu HC, Wu PL, Teng CM, Wu YC. Phytochemi 1998: 49(7): 2001-2003.
[19] Mahabusarakam W, Hemtasin C, Chakthong S, Voravuthikunchai SP, Olawumi IB. Planta Med 2010; 76(4): 345-349.
[20] Barros Cota B, Braga de Oliveira A, Guilherme Guimaraes K, Pimentel Mendonca M, Dias de Souza Filho J, Castro Braga F. Biochem Syst Ecol 2004; 32(4): 391-397.
[21] Ifesan BOT, Ibrahim D, Voravuthikunchai SP. J Food Agr Environ 2010; 8(3-4): 1233-1236.
[22] Siripong P, Wongseri V, Piyaviriyakul S, Yahaufai J, Chanpai R, Kanokmedakul K. MU J Pharm 2006; 33(1-4): 15-22.
[23] Deng Y, Chin YW, Chai H, Keller WJ, Kinghorn AD. J Nat Prod 2007; 70(12): 2049-2052.
[24] Lachumy SJT, Zuraini Z, Sasidharan S. RJPBCS 2010; 1(4): 391-398.
[25] Lown JW. Mol Cell Biochem 1983; 55(1): 17-40.
[26] Saleem M, Nazir M, Ali MS, Hussain H, Lee YS, Riaz N and Jabbar A. Nat Prod Rep 2010; 27: 238-254.
[27] Kohanski MA, Dwyer DJ and Collins JJ. Nat Rev Microbiol 2010; 8(6): 423–435.