Pharmaceutical Biology

ISSN: 1388-0209 (Print) 1744-5116 (Online) Journal homepage: informahealthcare.com/journals/iphb20

Potent antihypertensive activity of Thai-Lanna medicinal plants and recipes from "MANOSROI III" database

Aranya Manosroi, Warangkana Lohcharoenkal, Parirat Khonsung, Worapaka Manosroi & Jiradej Manosroi

To cite this article: Aranya Manosroi, Warangkana Lohcharoenkal, Parirat Khonsung, Worapaka Manosroi & Jiradej Manosroi (2013) Potent antihypertensive activity of Thai-Lanna medicinal plants and recipes from "MANOSROI III" database, Pharmaceutical Biology, 51:11, 1426-1434, DOI: 10.3109/13880209.2013.796391

To link to this article: https://doi.org/10.3109/13880209.2013.796391

Published online: 22 Jul 2013.

Submit your article to this journal

Article views: 1979

View related articles

Citing articles: 1 View citing articles

Full Terms & Conditions of access and use can be found at
https://informahealthcare.com/action/journalInformation?journalCode=iphb20

Pharmaceutical Biology

http://informahealthcare.com/phb
ISSN 1388-0209 print/ISSN 1744-5116 online
Editor-in-Chief: John M. Pezzuto
Pharm Biol, 2013; 51(11): 1426–1434
© 2013 Informa Healthcare USA, Inc.
DOI: 10.3109/13880209.2013.796391

informa
healthcare

ORIGINAL ARTICLE

Potent antihypertensive activity of Thai-Lanna medicinal plants and recipes from ‘‘MANOSROI III’’ database

Aranya Manosroi[1,2], Warangkana Lohcharoenkal[1], Parirat Khonsung[3], Worapaka Manosroi[4], and Jiradej Manosroi[1,2]

[1]Faculty of Pharmacy, [2]Natural Product Research and Development Center (NPRDC), Science and Technology Research Institute (STRI), [3]Department of Pharmacology, Faculty of Medicine, and [4]Department of Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

Abstract

Context: Traditional medicines have long been used by Thai practitioners for the treatment of many diseases including hypertension. The antihypertensive recipes and plants were searched and selected by a computer program from Thai/Lanna medicinal plant recipe database ‘‘MANOSROI III’’ using hypertensive symptoms as keywords.
Objectives: To evaluate the antihypertensive potential of 30 recipes and 10 Thai-Lanna medicinal plants selected from ‘‘MANOSROI III’’ database using L-NAME induced hypertensive rat model.
Materials and methods: Extracts from the selected recipes and plants were prepared according to the traditional indications. Antihypertensive activities including the decrease of the mean arterial blood pressure (MABP) and heart rate (HR) of the extracts as well as duration of action were investigated by intra-arterial assessment technique. All extracts were screened for phytochemicals including anthraquinone, glycoside, xanthone, tannin, carotenoid, flavones and alkaloids using standard methods.
Results and conclusions: All 12 of the 30 selected recipes (40%) demonstrated antihypertensive activity with the maximum decrease of MABP at 27.17 ± 3.17% that was 2.41-fold of prazosin hydrochloride. Most recipes exhibiting antihypertensive activity contained plants in the families of Zingiberaceae and Piperaceae. The top five antihypertensive recipes showed the presence of glycosides, xanthones and alkaloids. Ten single plants from these recipes were extracted and evaluated for antihypertensive activity. The cassumunar ginger extract exhibited the maximum decrease of MABP at 39.83 ± 3.92%, which was 3.54-times that of prazosin hydrochloride. This study demonstrated the potent antihypertensive activity of Thai medicinal plants and recipes that can be further developed as antihypertensive agents.

Keywords

Arterial blood pressure, heart rate, L-NAME-induced hypertensive rats, Thai medicinal plants

History

Received 22 November 2012
Revised 3 February 2013
Accepted 26 March 2013
Published online 22 July 2013

Introduction

High blood pressure is a prevalent risk factor for cardiovascular disease. It affects over 72 million people in the United State and over 1 billion people worldwide (Patel et al., 2010; Rosamond et al., 2007). The burden of hypertension increases with age. Among individuals aged 60 and above, hypertension prevalence is 65.5%. Also, hypertension is associated with many chronic conditions such as insulin resistance, obesity, carbohydrate tolerance, concomitance, haemaglutinin, hyperuricacidemia, atherosclerosis and cardiovascular diseases (Zhu, 1997). The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC7) recommends the blood pressure treatment goal of <140/90 mmHg for most patients and <130/80 mmHg for patients with diabetes mellitus (DM) or kidney disease (Cheng, 2008). Also known as the ‘‘silent killer,’’ hypertension is estimated to cause 4.5% of the current global disease burden and is as prevalent in many developing countries as in the developed world (Whitworth, 2003). Since the proportion of the hypertensive patients will increase dramatically worldwide, the prevention, detection, treatment and control of this condition should be a top priority (Kearney, 2005). However, most people in the developing countries have poor access to modern health care in using of the antihypertensive drugs and their combinations.

Antihypertensive drugs can be divided into six categories, including diuretic, β-blocking agents, calcium antagonists, angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists and α-receptor blocking agents (Ke, 2004; Wang, 2004). The efficacy of these drugs is only 40–60% and usually two or more antihypertensive drugs from different categories are needed to be combined to achieve the optimal results. However, side effects from these medications are an important concern (Du & Chen, 2005). Recently, attention has been focused on herbal and mineral preparations that have been traditionally used in the prevention and management of cardiovascular diseases as the potential

Correspondence: Jiradej Manosroi, Faculty of Pharmacy, Chiang Mai University, Chiang Mai 50200, Thailand. Tel: +66 53 894806. Fax: +66 53 894169. E-mail: pmpti006@chiangmai.ac.th

Copyright Informa Healthcare 2013
Not for Sale or Commercial Distribution

source for the new therapeutic agent development (Bhatt et al., 1998). In fact, medicinal plants are used to treat several diseases based on the folklore traditional wisdoms that have been perpetuated along several generations. It has been estimated that approximately 25% of all the prescribed medications today are of natural plant sources (Gamaniel, 2000).

The Natural Product Research and Development Center (NPRDC) at Chiang Mai University in Thailand by Prof. Dr. Jiradej Manosroi has developed the Thai medicinal plant recipe database ''MANOSROI III'' since 1993. This database contained the recipes collected from all over Thailand including institutes, temples and folklore doctors (Manosroi et al., 2006). At present, 658 Thai medicinal plant textbooks with over 200 000 recipes, with different local names of 7994 diseases and 3735 medicinal plants have been collected and about 62 000 recipes were translated, interpreted and put in the ''MANOSROI III'' database. Interestingly, a large number of antihypertensive medicinal plant recipes have been found in this database to treat hypertension symptoms such as persistent high blood pressure, dizziness, headache, blurred vision, palpitation, tinnitus and nose bleeding. In this study, 30 antihypertensive medicinal plant recipes selected from the 100 antihypertensive recipes in the ''MANOSROI III'' database and the ten single plants selected from the selected recipes were examined for antihypertensive activity using the *N*-(G)-nitro-L-arginine methyl ester (L-NAME)-induced rat model in order to evaluate their potential to develop as an antihypertensive agent.

Materials and methods

Recipe selection

One hundred antihypertensive medicinal plant recipes were collected in the ''MANOSROI III'' database. The associated symptoms of hypertension including flushing, dizziness, headache, blurred vision, palpitation, tinnitus and nose bleeding with no apparent reasons were the keywords for the selection of these recipes. All medicinal plants in these 100 recipes were scored and ranked by the frequency of the medicinal plants appeared in the recipes. Then, thirty recipes with the highest total scores of the medicinal plants were selected for the experiment.

Preparation of the recipe crude extracts

Parts of plants as indicated in the recipes were collected from the medicinal plant garden at Faculty of Pharmacy, Chiang Mai University in Thailand from October to November in 2010. The voucher specimens of each plant (Manosroi 0029-0172) were kept at the NPRDC herbarium. The recipe extracts were prepared according to the instructions of the recipes. Briefly, the plant materials were dried in an oven at 50–60 °C for 72 h and ground into powder with a grinding mill (HiPlan Associated, Thailand). Each plant powder was separately kept in an air tight container and stored in a dry cool place. An amount of each plant powder indicated in the recipe were mixed with the total of 40 g and placed in a beaker. The mixture was boiled in 800 ml of the distilled water for 2 h and filtered through Whatman® paper No.1 (Whatman®, Kent, England). The filtrate was concentrated and dried under vacuum with a freeze-dryer (Alpha 1-2 LD Model Christ, Osterode am Harz, Germany). The dried extracts were kept in a tight container at 4 °C until use.

Plant selection

All medicinal plants in the 12 recipes which showed antihypertensive activity were scored and ranked by the total frequency of the medicinal plants appearing in the recipes. Ten single plants with the highest total scores were selected for the study.

Preparation of the single plant crude extracts

Parts of the selected plants as indicated in the recipes were collected. The voucher specimens of the ten plants (Manosroi 0029, 0030, 0032, 0036, 0037, 0039, 0051, 0060, 0067, 0083) were kept at the NPRDC herbarium. The plant extracts were prepared according to the instructions of the recipes. Briefly, the plant materials were dried in an oven at 50–60 °C and ground into powder. The plant powder was kept in an air-tight container and stored in the dry cool place. The plant powder (40 g) was boiled in 800 ml of the distilled water for 2 h and filtered through Whatman® filter paper No.1 (Whatman®, Kent, England). The filtrate was concentrated and dried under vacuum by a freeze-dryer (Alpha 1-2 LD Model Christ, Osterode am Harz, Germany). The dried extract was kept in a tight container at 4 °C until use.

Extract fractionation

The top three plant crude extracts which indicated the highest antihypertensive activity were fractionated by solvent partition. The crude extract (1 g) was dissolved in 200 ml of distilled water and transferred to a separatory funnel. Ethyl acetate and butanol fractions were obtained by partitioning 3-times with 200 ml of ethyl acetate or butanol. The fractions were dried using a rotary evaporator (R-124 Buchi, Switzerland) and the percentage yields of each fraction were calculated. The dried fractions were kept in an air-tight container at 4 °C until use.

Phytochemical assays

All crude extracts and fractions were analysed for phytochemicals including anthraquinone, glycoside, xanthone, tannin, carotenoid, flavones and alkaloid using the standard methods. For anthraquinones, about 0.05 g of the sample were placed into a dry test tube and 2 ml of chloroform was added and shaken for 5 min. The extract was filtered and the filtrate was mixed and shaken with an equal volume of 10% ammonia solution. A pink violet or red color in the ammoniacal layer (lower layer) indicated the presence of anthraquinone (Odebiyi & Sofowora, 1978). For glycosides, a few mg of the sample were dissolved in 4 ml of distilled water and filtered. The filtrate was resolved on TLC plate coated with silica gel 60. The mobile phase was butanol/acetic acid/diethyl ether/water (9:6:1:3). The spot was detected by spraying with 10% H_2SO_4 and heated. Sucrose, glucose and fructose were used as standards (Vadivu & Lakshmi, 2008). For xanthones, an amount of 0.05 g of the sample was heated

in 2 ml of methanol for 10 min and centrifuged. The clear solution was reacted with 100 µl of 5% KOH solution. The positive result was indicated by the yellow precipitate (Sofowora, 1982). For tannin, the sample was treated with 15% ferric chloride test solution. The blue color indicated the presence of hydrolysable tannin (Odebiyi & Sofowora, 1978). For carotenoids, an amount of 0.05 g of the sample was extracted with 2 ml of chloroform and centrifuged. The clear solution was reacted with 100 µl of sulfuric acid. A positive result was indicated by blue or blue-green solution (Banso & Ngbede, 2006). For flavones, an amount of 0.05 g of the sample was heated in 2 ml of methanol for 10 min and centrifuged. Magnesium wire was added into the clear solution. Then, 100 µl of hydrochloric acid were added. Dark red or yellow color of the solution indicated the presence of flavanone or flavones (Williamson et al., 1996). For alkaloids, an amount of 0.05 g of the sample was boiled in 2 ml of 1.5% v/v hydrochloric acid and filtered. Dragendorff's reagent (100 µl) was added into 2 ml of the filtrate. Formation of the orange-brown precipitate indicated the presence of alkaloids (Swarup & Umadevi, 1998).

Effects of the recipe, plant crude extracts and fractions on blood pressure and heart rate in the L-NAME-induced hypertensive rat model

Animals

Male Sprague-Dawley rats (National Laboratory Animal Centre, Mahidol University, Salaya, Nakhon Pathom, Thailand) weighing between 300 and 350 g were used. The rats were maintained in the animal house at the Faculty of Pharmacy, Chiang Mai University in Chiang Mai, Thailand, fed and allowed access to clean water *ad libitum*. All animal experiments were conducted in accordance with the directive 2010/63/EU and the guidelines for the care and use of laboratory animals of Chiang Mai University, Thailand.

Experimental

The rats were anaesthetized by an intraperitoneal injection of pentobarbital sodium (40 mg/kg). The experiment was performed as previously described with some modification (Magos & Vidrio, 1991). The anaesthetized rats were fixed on the supine position on a dissecting table. A longitudinal midtracheal incision, approximately 2 cm long, was made in order to expose the trachea, right jugular vein and both common carotid arteries. The trachea was cannulated with a polyethylene tube (2.75 mm diameter) to maintain the free air way. For the administration of the extracts and the isotonic saline solution, the right jugular vein was cannulated with a saline filled polyethylene tube (1 mm diameter). The exposed surface of the cannulation was covered with the cotton wool moist with warm saline. Systemic blood pressure was recorded from the left carotid arterial cannula that was connected to a physiological pressure transducer (Statham P23 AC Strain Gauge Transducer, Laboratories, Inc. Hato Rey, Puerto Rico) and displayed on the Grass 7D Polygraph (Grass Instrument Co., Quincy, MA). The cannulation of the carotid artery was the same as of the jugular vein using the polyethylene tube (1 mm diameter) filled with heparin sodium in saline solution. Blood pressure (BP) and heart rate (HR) were monitored until the steady baseline levels were obtained. L-NAME at 3 mg/kg BW was administered via venous cannula for hypertension induction. After the BP was stabilized as indicated by steady blood pressure for at least 20 min, the crude extracts (10 mg/kg BW) were injected through the jugular vein cannula. For the fractions, the doses of each fraction were calculated from the percentage yields of each fraction and the administration dose of the crude extract (10 mg/kg BW) as follows:

$$\text{Dose (mg/kg BW)} = (10 \times \% \text{ yield of the fractions})/100$$

The changes in BP were determined as the difference between the steady-state value before and after injection at the lowest reading. The mean arterial blood pressure (MABP) was calculated as the diastolic BP plus one-third pulse width.

$$\text{MABP} = \text{Pd} + 1/3(\text{Ps} - \text{Pd}) \text{ mmHg}$$

where Pd = diastolic blood pressure and Ps = systolic blood pressure

Prazosin hydrochloride at 2 mg/kg BW was used as the standard antihypertensive drug.

Statistical analysis

All data were expressed as means ± SEM ($n = 6$). The means of the different groups were compared using one-way analysis of variance ($p < 0.05$).

Results and discussions

Recipe selection and extraction

Compositions, percentage yields and physical characteristics of the 30 crude extracts of the antihypertensive recipes selected from the Manosroi III database are shown in Table 1. Most recipes contained plants from the Piperaceae (24/30) and Zingiberaceae (22/30) families. The numbers of the plant species in each recipe were ranging from 3 to 40 species. Yields (%) and physical characteristics of the recipe extracts are demonstrated in Table 1. The yields of the extracts were in the range of 8.46–32.20%. The colors of the extracts were either yellow or brown. All extracts were soluble in water.

Plant selection and extraction

The 10 single plants with the highest frequency appeared in the 12 antihypertensive recipes including ginger (*Zingiber officinale* Roscoe [Zingiberaceae]), garlic (*Allium Sativum* Linn. [Amaryllidaceae]), galangal (*Alpinia galanga* Linn. [Zingiberaceae]), szechwan lovage rhizome (*Ligusticum chuanxiong* Hort. [Umbelliferae]), Indian long pepper (*Piper chaba* Trel & Yunck [Piperaceae]), pepper (*Piper nigrum* Linn. [Piperaceae]), cassumunar ginger (*Zingiber cassumunar* Roxb. [Zingiberaceae]), golden shower (*Cassia fistula* Linn. [Fabaceae]), myrtle grass (*Acorus calamus* Linn. [Acoraceae]) and myrobalan wood (*Terminalia chebula* Retz. [Combretaceae]) were selected. Most of these selected plants are routinely used as spices or seasoning in Thai culinary. The yields (%) of the plant extracts in the range of

Table 1. Compositions, percentage yields (%) and physical characteristics of the 30 antihypertensive recipes selected from the ''MANOSROI III'' database.

Recipe	Example of plants	Percentage yield (%)	Color of the extracts	Solubility in water
HT001	*Cassia fistula, Cyperus rotundus, Lawsonia inermis, Nigella sativa, Asclepias curassavica, Anethum graveolens, Cassia siamea, Eugenia aromatic, Diospyros decandra, Dracaena loureiri, Glycyrrhiza glabra, Mimusops elengi, Zingiber officinale, Zingiber cassumunar*	17.12	Brown	Soluble
HT002	*Aegle marmelos, Plumbago zeylanica, Zingiber officinale, Piper ribesioides, Piper longum*	20.26	Dark brown	Soluble
HT003	*Plumbago zeylanica, Piper longum, Coriandrum sativum, Mesua ferrea*	16.89	Brown	Soluble
HT004	*Allium sativum, Piper nigrum, Piper longum, Kaempferia galangal*	21.39	Brown	Soluble
HT005	*Allium sativum, Piper nigrum, Zingiber officinale, Piper longum*	27.87	Brown	Soluble
HT006	*Kaempferia galangal, Phyllanthus emblica, Chrysopogon zizanioides, Nelumbo nucifera, Terminalia chebula, Zingiber officinale*	21.98	Brown	Soluble
HT007	*Piper nigrum, Piper longum, Kaempferia roscoeana, Acorus calamus*	21.43	Brown	Soluble
HT008	*Alpinia galanga, Piper nigrum, Piper longum, Kaempferia roscoeana*	16.08	Brown	Soluble
HT009	*Lawsonia inermis, Zingiber officinale, Piper nigrum, Piper longum*	15.29	Light brown	Soluble
HT010	*Piper longum, Cyperus rotundus, Coriandrum sativum, Acorus calamus*	22.90	Brown	Soluble
HT011	*Piper nigrum, Piper longum, Zingiber officinale*	32.20	Creamy white	Soluble
HT012	*Alpinia galangal, Zingiber officinale, Piper longum, Piper ribesioides*	16.32	Brown	Soluble
HT013	*Zingiber officinale, Piper longum, Cyperus rotundus, Glycyrrhiza glabra*	24.42	Brown	Soluble
HT014	*Piper nigrum, Zingiber officinale*	25.82	Red brown	Soluble
HT015	*Piper ribesioides, Solanum trilobatum, Citrus aurantifolia*	9.68	Red brown	Soluble
HT016	*Allium sativum, Cassia fistula, Zingiber officinale, Capsicum frutescens, Blumea balsamifera, Alpinia officinarum*	20.54	Brown	Soluble
HT017	*Piper longum, Piper nigrum*	11.53	Red brown	Soluble
HT018	*Combertum extensum, Piper ribesioides, Citrus aurantifolia, Solanum trilobatum*	10.67	Red brown	Soluble
HT019	*Allium sativum, Piper longum, Piper nigrum, Cyperus rotundus*	25.29	Brown	Soluble
HT020	*Zingiber officinale, Piper longum, Eugenia aromatica*	25.04	Yellowish brown	Soluble
HT021	*Zingiber officinale, Piper nigrum, Saccharum officinarum*	22.97	Light brown	Soluble
HT022	*Boesenbergia rotunda, Allium sativum, Alpinia galangal, Zingiber officinale*	29.12	Dark brown	Soluble
HT023	*Azima sarmentosa, Diospyros decandra, Citrus aurantifolia, Nelumbo nucifera, Zingiber cassumunar*	11.89	Red brown	Soluble
HT024	*Plumbago zeylanica, Piper nigrum, Cyperus rotundus, Vitex tritolia, Moringa oleifera*	22.26	Dark brown	Soluble
HT025	*Plumbago zeylanica, Piper nigrum, Zingiber officinale, Oryza sativa, Croton crassifolius*	18.67	Brown	Soluble
HT026	*Tiliacora triandra, Harrisonia perforate, Tinospora crispa, Cassia siamea, Nelumbo nucifera, Ficus racemosa, Artocarpus heterophyllus, Mesua ferrea, Mimusops elengi, Capparis micracantha*	13.59	Red brown	Soluble
HT027	*Diospyros decandra, Dracaena loureiri*	8.46	Yellow	Soluble
HT028	*Alpinia galangal, Zingiber officinale*	15.67	Dark brown	Soluble
HT029	*Piper longum, Citrus aurantifolia, Allium sativum*	27.97	Dark brown	Soluble
HT030	*Spondias mombin, Zingiber cassumunar, Saccharum officinarum*	20.72	Light brown	Soluble

7.29–65.17% are shown in Table 1. All extracts were soluble in water.

Effects of the extracts on blood pressure and heart rate

In Table 2, 12 recipe extracts demonstrated antihypertensive activity with the decrease percentage changes of MABP in the range of 8.33–27.17%. A total of 9 of the 12 recipe extracts exhibited higher MABP than the standard drug (prazosin hydrochloride). The highest percentage decrease of MABP at $27.17 \pm 3.17\%$ was observed in recipe HT016 that was 2.41-times more potent than standard drug. On the contrary, 18 of the 30 recipe extracts demonstrated the increase MABP in the range of 4.75 to 35.00 with the highest activity at $35.00 \pm 13.53\%$ found in recipe HT018. This may be due to the recipe selection process since the keywords of the symptoms were used, but the symptoms indicated in the recipes recorded by the practitioners may be confusing to imply for treatment or to cause the symptoms. It appeared that 50% of the recipes were increasing and decreasing blood pressure equally. For the effect on heart rate, extract of recipe HT010 showed the highest percentage changes of HR from the baseline at $19.50 \pm 23.33\%$. Recipe HT016 gave the highest decrease percentage changes of MABP and decreased heart rate by 8.17%, while the standard drug gave the decrease % MABP of 11.25 ± 1.72 and an increase of heart rate at $3.10 \pm 5.05\%$. In all, 12 and 18 recipe extracts of the 30 recipes showed an increase and decrease in percentage change of heart rates, respectively. Also, no specific relationship between the MABP and HR was observed. This may be due to the different compositions of the mixed plants in

Table 2. Percentage changes of the mean arterial blood pressure (MABP), heart rate (%) and duration of action of the aqueous extracts of 30 selected recipes evaluated with the L-NAME-induced hypertensive rat model in comparison with the standard drug, prazosin hydrochloride.

		Intra-arterial BP (mm Hg)		Percentage changes of MABP (%)			Heart rate (bpm)		Percentage changes of the heart rate (%)		
				Decrease							
Recipes	Doses (mg/kg)	Before extract administration	After extract administration	Percentage changes	Folds of prazosin	Increase	Before extract administration	After extract administration	Decrease	Increase	Duration of action (s)
HT001[a]	7.10	122.83 ± 4.01	94.17 ± 4.87	**23.33 ± 2.94**	**2.07**	–	226.67 ± 5.58	266.67 ± 13.33	–	**1.57 ± 3.32**	**749.17 ± 138.28**
HT002	8.40	133.47 ± 5.05	174.84 ± 8.28	–	–	31.00 ± 13.98	246.88 ± 10.89	234.54 ± 17.76	5.00 ± 2.92	–	249.00 ± 208.08
HT003	7.00	127.78 ± 3.77	142.15 ± 5.34	–	–	11.25 ± 6.34	255.43 ± 12.25	237.55 ± 9.05	7.00 ± 4.24	–	103.75 ± 45.34
HT004	8.90	139.83 ± 7.64	124.50 ± 7.90	9.17 ± 1.72	0.82	–	267.50 ± 20.23	251.33 ± 16.76	10.17 ± 1.19	–	203.00 ± 87.94
HT005	11.50	135.83 ± 8.06	117.50 ± 7.31	13.50 ± 1.89	1.20	–	265.00 ± 11.18	252.50 ± 15.10	6.00 ± 1.84	–	384.17 ± 185.42
HT006	9.20	124.90 ± 2.45	151.13 ± 6.76	–	–	21.00 ± 5.00	267.98 ± 19.73	289.42 ± 16.90	–	8.00 ± 1.73	260.00 ± 183.30
HT007	8.90	137.55 ± 6.54	159.56 ± 5.10	–	–	16.00 ± 7.90	233.12 ± 13.75	241.98 ± 12.09	–	3.80 ± 2.80	1641.00 ± 3173.38
HT008	6.70	141.33 ± 2.36	123.17 ± 2.83	13.33 ± 1.33	1.18	–	253.33 ± 22.12	235.00 ± 19.79	7.00 ± 1.29	–	332.50 ± 129.87
HT009	6.40	134.67 ± 4.22	123.33 ± 4.56	8.33 ± 1.02	0.74	–	278.33 ± 24.82	258.33 ± 20.40	6.50 ± 1.71	–	147.00 ± 80.33
HT010	9.50	138.67 ± 5.09	169.16 ± 2.12	–	–	15.50 ± 0.71	247.89 ± 8.87	199.55 ± 8.13	19.50 ± 23.33	–	90.00 ± 42.43
HT011	13.40	126.75 ± 1.99	145.34 ± 4.82	–	–	14.67 ± 7.57	288.67 ± 6.48	307.92 ± 21.77	–	6.67 ± 4.62	203.33 ± 150.44
HT012	6.80	141.32 ± 2.13	167.46 ± 3.98	–	–	18.50 ± 7.55	254.90 ± 15.44	220.49 ± 11.45	13.50 ± 6.56	–	153.75 ± 178.48
HT013	10.20	127.81 ± 4.47	146.72 ± 7.17	–	–	14.80 ± 7.92	277.14 ± 13.22	241.11 ± 13.34	13.00 ± 3.67	–	96 ± 116.96
HT014	10.80	140.77 ± 4.86	169.98 ± 4.80	–	–	20.75 ± 16.68	229.27 ± 9.87	118.00 ± 7.44	18.00 ± 19.44	–	97.50 ± 45.00
HT015	4.00	132.89 ± 3.59	151.49 ± 3.87	–	–	14.00 ± 4.97	263.21 ± 11.35	239.52 ± 14.98	9.00 ± 2.00	–	97.50 ± 15.00
HT016[a]	8.60	134.17 ± 5.56	97.00 ± 3.34	**27.17 ± 3.17**	**2.42**	–	280.00 ± 8.56	256.67 ± 7.15	**8.17 ± 1.58**	–	**335.00 ± 136.91**
HT017	4.80	139.79 ± 6.98	153.77 ± 5.74	–	–	10.00 ± 7.81	237.87 ± 17.57	226.76 ± 10.17	4.67 ± 4.04	–	135.00 ± 25.98
HT018	4.40	142.54 ± 2.11	192.43 ± 1.63	–	–	35.00 ± 13.53	291.11 ± 21.63	318.27 ± 15.87	–	9.33 ± 9.24	325.00 ± 251.15
HT019	10.50	129.76 ± 4.87	145.98 ± 5.00	–	–	12.50 ± 4.20	282.31 ± 17.54	290.78 ± 13.76	–	3.00 ± 2.00	285.00 ± 185.74
HT020	10.40	133.83 ± 2.50	114.50 ± 4.10	14.50 ± 2.42	**1.29**	–	298.33 ± 9.46	292.50 ± 13.89	7.50 ± 1.18	–	64.67 ± 23.87
HT021	9.60	133.47 ± 7.55	157.93 ± 6.41	–	–	18.33 ± 2.52	269.59 ± 11.44	289.35 ± 12.55	–	7.33 ± 1.15	80.00 ± 48.22
HT022	12.10	129.88 ± 5.91	157.15 ± 3.66	–	–	21.00 ± 4.36	247.98 ± 12.24	267.00 ± 12.88	–	7.67 ± 5.13	193.33 ± 41.63
HT023[a]	5.00	137.67 ± 4.66	104.00 ± 3.37	**24.00 ± 1.75**	**2.13**	–	290.00 ± 3.42	290.83 ± 6.64	–	**6.00 ± 1.24**	**509.27 ± 207.91**
HT024	9.30	136.91 ± 4.79	157.99 ± 3.75	–	–	15.40 ± 8.08	266.88 ± 16.67	278.96 ± 4.91	–	4.60 ± 1.52	215.00 ± 165.38
HT025	7.80	137.67 ± 3.33	122.33 ± 4.59	8.00 ± 1.53	0.71	–	255.00 ± 17.65	231.67 ± 17.40	9.00 ± 0.93	–	83.33 ± 55.61
HT026	5.70	132.53 ± 8.52	147.90 ± 2.31	–	–	11.60 ± 6.35	283.75 ± 4.84	260.48 ± 16.33	8.20 ± 6.57	–	387.00 ± 194.54
HT027	3.50	147.17 ± 3.41	127.17 ± 5.24	13.66 ± 2.16	1.21	–	265.00 ± 8.06	266.67 ± 7.15	–	5.67 ± 0.76	131.67 ± 94.00
HT028	6.50	144.86 ± 4.57	151.74 ± 8.32	–	–	4.75 ± 2.22	230.85 ± 18.45	218.15 ± 9.60	5.50 ± 3.11	–	266.25 ± 236.34
HT029[a]	11.70	143.00 ± 2.52	119.50 ± 1.45	**16.50 ± 0.99**	**1.47**	–	292.50 ± 12.37	296.67 ± 8.03	–	**6.33 ± 0.76**	**50.17 ± 14.30**
HT030[a]	8.60	123.50 ± 3.55	99.67 ± 3.46	**19.33 ± 1.78**	**1.72**	–	255.00 ± 15.86	228.33 ± 14.00	**10.00 ± 2.80**	–	**250.83 ± 101.89**
Prazosin hydrochloride	2.00	128.66 ± 2.38	114.18 ± 2.15	11.25 ± 1.72	–	–	241.95 ± 10.01	249.45 ± 11.52	–	3.10 ± 5.05	>1 hr

[a]Significant difference in comparing to prazosin hydrochloride ($p < 0.05$).

The administration doses of each recipe extract was calculated based on the traditional use of the recipes as a pill according to the following equation: Dose $(\mathrm{mg/kg}) = \frac{\%\ \text{yield of the extract (g/100 g)}}{60(\text{average human BW, Kg})} \times 25$ where, the weight of 1 pill is about 1 g. Dose translation factor from human to rat calculated from the Km factor, body weight (kg) divided by body surface (m^2) is 25 (Reagan-Shaw et al., 2008). The bioavailability of the oral administration was approximately equal to 10% according to the reported average oral bioavailability of water-soluble biologically active constituents in plants (Bhattacharya & Ghosh, 2009; Manach et al., 2004).

Table 3. Percentage yield, percentage decrease of the mean arterial blood pressure (MABP), heart rate change and duration of action of the aqueous extracts of the 10 selected plants evaluated with the L-NAME-induced hypertensive rat model in comparison with the standard antihypertensive drug, prazosin hydrochloride.

No.	Extract	Percentage yield (%)	Decrease of MABP (%)		HR change (%)[b]	Duration of action (second, s)
			% decrease	Folds of prazosin hydrochloride		
1	Cassumunar ginger (*Zingiber cassumunar*)	29.19	39.83 ± 3.92[a]	3.54	$(+)11.50 \pm 4.33$	180.00 ± 88.99
2	Garlic (*Allium Sativum*)	65.17	35.83 ± 3.79[a]	3.18	$(-)8.00 \pm 1.03$	362.50 ± 117.37
3	Ginger (*Zingiber officinale*)	26.94	21.00 ± 2.56[a]	1.87	$(+)8.33 \pm 1.17$	490.00 ± 118.66
4	Galangal (*Alpinia galanga*)	21.35	17.67 ± 3.38	1.57	$(+)9.50 \pm 2.74$	287.50 ± 114.46
5	Indian long pepper (*Piper chaba*)	16.25	17.17 ± 1.35	1.53	$(-)8.83 \pm 3.04$	316.67 ± 96.63
6	Pepper (*Piper nigrum*)	8.01	16.33 ± 1.52	1.45	$(-)7.83 \pm 1.70$	183.33 ± 90.36
7	Myrobalan wood (*Terminalia chebula*)	17.68	16.17 ± 2.94	1.44	$(+)7.83 \pm 2.12$	220.83 ± 119.95
8	Szechwan lovage rhizome (*Ligusticum chuanxiong*)	40.05	13.33 ± 1.77	1.84	$(-)4.17 \pm 2.06$	84.17 ± 55.35
9	Golden shower (*Cassia fistula*)	7.29	10.17 ± 1.28	0.90	$(-)9.17 \pm 2.99$	25.83 ± 4.36
10	Myrtle grass (*Acrous calamus*)	18.35	10.00 ± 1.06	0.89	$(-)8.50 \pm 0.92$	24.17 ± 3.75
11	Prazosin hydrochloride (2 mg/kg)	–	11.25 ± 1.72	1	$(+)3.10 \pm 5.05$	>1 h

[a] = significant difference from the standard drug ($p < 0.05$), [b](+) = increase, (−) = decrease.

the recipes. All recipes exhibited short duration of MABP and HR in the range of 50.17 to 749.17 sec with the highest duration of 749.17 sec observed in recipe no. HT001 which also gave the high decrease of the % MABP at 23.33 ± 2.94 (2.07-fold more potent than the standard drug) and a slightly increase of the % HR of only 1.57 ± 3.32. Recipe HT001 appeared to be the best recipe with the superior % MABP and HR, but a duration of about 5-times shorter than prazosin hydrochloride. The mechanisms of these recipe extracts to cause the change of % MABP and HR were still not clear. According to the BP induction in this study, the sustained elevation of the BP after administration of L-NAME [a nitric oxide synthase (NOS) inhibitor] was from the increase of the peripheral vascular resistance in NO-deficient rats resulting in systemic vasoconstriction, endothelial dysfunction and finally hypertension. Thus, the MABP reduction effects of the recipe extracts may be from the decrease of the total peripheral resistance (Loeb & Longnecker, 1992; Noll et al., 1997; Pechanova et al., 1999). However, the increase blood flow may be from some compounds or plants in the recipes, for example, *Piper longum.* In addition, the very short duration of action of the recipe extracts may be due to the instability of the antihypertensive active compounds that are susceptible to the degradation in the blood circulation environment (Srivastava et al., 2011). In fact, this problem can be solved by formulation development strategies of the extracts. Most recipe extracts (12 recipes) which gave the antihypertensive effects are composed of plants in the Zingiberaceae and Piperaceae families. Several plants in the Zingiberaceae family are reported to lower the BP, such as *Aframomum melegueta* and *Zingiber cassumunar*. The precise mechanism is not known, but some mechanisms have been proposed. The peptides from the pepsin hydrolysis of the protein from the rhizome extract of some Zingiberaceae plants have been shown angiotensin-I converting enzyme inhibitor (ACEI) activity (Lawal et al., 2007). Also, the hypotensive activity in rats of amide mixture isolated from *Piper tuberculatum* Jacq (Piperaceae) has been reported (Duarte et al., 2004). Therefore, plants in the recipes belonging to these two families may be responsible for the antihypertensive activities.

For the 10 selected plant extracts, the administration dose of each plant extract at 10 mg/kg BW was used. Interestingly, all extracts from the selected plants demonstrated antihypertensive activity with the highest decrease of MABP at $39.83 \pm 3.92\%$ observed in the cassumunar ginger extract (Table 3), which was 3.54-times significantly more active than the standard antihypertensive drug (prazosin hydrochloride). Garlic and ginger also showed a significant BP lowering effect of 3.18- and 1.87-times more potent than the standard drug, respectively. In fact, the lowering of arterial blood pressure in the anesthetized rats of ginger and galangal at the given doses from 0.3 to 20 mg/kg BW has been reported (Ghayur & Gilani, 2005). Surprisingly, these three plants were in the compositions of the recipes including recipe nos. HT 001, 016, 023, 029 and 030 which exhibited high antihypertensive effects (Table 1). This result can also confirm the suitability of the plant selection criteria from the antihypertensive recipes in the ''MANOSROI III'' database. These plants have been demonstrated to have effects on the vascular smooth muscle relaxation and the blockade of the voltage-dependent calcium channels causing the BP lowering activity (Ghayur & Gilani, 2005). The peptides from the pepsin hydrolysis of the protein from the rhizomes extract of cassumunar ginger have been reported to be a potent source for angiotensin I-converting enzyme inhibitor (ACEI) bioactive compounds (Yodjun et al., 2012) which were related to the antihypertensive effects. According to the mechanisms of high blood pressure induction by L-NAME mentioned previously, these plant extracts may reduce total vascular resistance (Loeb & Longnecker, 1992; Noll et al., 1997; Pechanova et al., 1999). All plant extracts gave the percentage changes of HR from the baseline in the range of −8.83 to 11.50%, while the standard drug gave 3.10%. The highest increase HR of 11.50% was found in the cassumunar ginger extract that gave the highest BP lowering activity. Fifty percentage of the selected plants gave an increase and decease HR, equally. The mechanisms of the heart rate alleviation by ginger, galangal, cassumunar ginger and myrobalan wood extracts might be

Table 4. Percentage yield (%), dose (mg/kg), percentage decrease of the mean arterial blood pressure (MABP), heart rate change (%) and duration of action of the extracted fractions of cassumunar ginger (*Zingiber cassumunar*), garlic (*Allium Sativum*) and ginger (*Zingiber officinale*) in the L-NAME-induced hypertensive rat model.

				Decrease of MABP (%)			
Extract	Fraction	Percentage yield (%)	Dose (mg/kg)	% decrease	Folds of prazosin hydrochloride	% HR change[b]	Duration of action (second, s)
Cassumunar ginger (*Zingiber cassumunar*)	Water (F1)	43.20	4.32	10.83 ± 0.87	0.92	(−)4.67 ± 0.82	22.76 ± 3.33
	Butanol (F2)	21.12	2.11	17.67 ± 3.16[a]	1.57	(+)5.83 ± 1.38	80.00 ± 26.46
	Ethyl acetate (F3)	10.59	1.06	12.67 ± 1.83	1.13	(−)1.50 ± 0.67	31.67 ± 6.54
Garlic (*Allium sativum*)	Water (F4)	62.55	6.26	27.17 ± 1.83[a]	2.42	(−)7.00 ± 1.30	232.50 ± 74.87
	Butanol (F5)	3.275	0.33	13.83 ± 2.34	1.23	(−)3.33 ± 0.56	132.50 ± 48.13
	Ethyl acetate (F6)	2.67	0.27	20.33 ± 1.69[a]	1.81	(+)0.50 ± 0.50	107.50 ± 62.74
Ginger (*Zingiber officinale*)	Water (F7)	62.31	6.23	12.33 ± 1.38	1.09	(+)2.17 ± 2.17	108.33 ± 86.43
	Butanol (F8)	6.49	0.65	18.00 ± 1.63[a]	1.60	(+)4.67 ± 0.84	127.50 ± 44.12
	Ethyl acetate (F9)	4.18	0.42	15.67 ± 1.11	1.39	(+)3.00 ± 1.03	36.67 ± 5.87
Prazosin hydrochloride	–	–	2	11.25±1.72	1	(+)3.10 ± 5.05	>1 h

[a] = significant difference from the standard drug ($p < 0.05$), [b](+) = increase, (−) = decrease.

Doses of each extract were calculated from the amount of the recipes administration as the traditional bolus dose as follows: Dose (mg/kg) = [% yield of the extract (g/100 g)/60 (average human BW, Kg)] × 25, where, the weight of 1 pill is about 1 g. The tolerance in rats was equal to 25-times of human. The bioavailability of the oral administration was approximately equal to 10%.

Table 5. Phytochemical constituents of the top 5 aqueous recipes extracts selected from the ''MANOSROI III'' database.

	Phytochemical constituents[a]									
				Glycoside						
Recipes	Triterpene	Alkaloid	Anthraquinone	F	G	S	Flavonoid	Carotenoid	Tannin	Xanthone
HT 001	−	−	−	+	−	+	−	−	−	+
HT 016	−	+	−	+	−	+	−	−	−	−
HT 023	−	−	−	+	−	+	−	−	−	+
HT 029	−	+	−	+	−	+	−	−	−	−
HT 030	−	+	−	+	−	+	−	−	−	+

[a] + = presence, − = absence.

from the baroreceptor reflex, one of the body's homeostatic mechanisms for maintaining blood pressure, which provided the negative feedback loop in order to raise the BP (Berne & Levy, 2001). In contrast, some extracts demonstrated negative chronotropic effects indicated by a decrease of HR (Patel et al., 2010). All plant extracts indicated shorter antihypertensive activity than the standand drug. The longest duration of the antihypertensive action of the extracts at 490.00 ± 118.66 sec was found in the ginger extract that was 7.34-times shorter than the standard drug. Again, this might be due to the instability of the antihypertensive bioactive compounds in the plant extracts that may be degraded in the blood circulation environment (Srivastava et al., 2011).

Cassumunar ginger, garlic and ginger extracts which demonstrated the highest antihypertensive activity, were selected for fractionation and tested for antihypertensive activity. Cassumunar ginger, garlic and ginger are popular spices considered as essential components of the kitchen pharmacy. These medicinal plants have been used since ancient times as food additives to impart its taste and smell and also for its therapeutic value in a wide variety of diseases, especially in gastrointestinal disorders such as constipation, diarrhea and dyspepsia. The yields (%) of the water, butanol (BuOH) and ethyl acetate (EtOAc) fractions of the selected three plant crude extracts are shown in Table 4. The water fractions of all crude extracts gave high yield in the range of 43.2 to 65.5%, while the low yield was from the ethyl acetate fraction of 2.67 to 10.59%, since all fractions were from the aqueous crude extracts. The effects of the fractions on BP and HR in the L-NAME-induced hypertensive rat model were evaluated (Table 5). All fractions demonstrated antihypertensive activity with the highest decrease of MABP at 27.17 ± 1.83% found in the water fraction of the garlic crude extract followed by the ethyl acetate fraction of garlic (20.33 ± 1.69%), the butanol fraction of ginger (18.00 ± 1.63%) and the butanol fraction of cassumunar ginger (17.67 ± 3.16%), which were significantly ($p < 0.05$) more potent than the standard drug and similar to those obtained from their crude extracts. The antihypertensive effects of different solvent fractions from different crude extracts may be due to the different antihypertensive bioactive compounds that were soluble in different polarity solvents. The changes of the HR from the baseline of all fractions were in the range of 0.50 ± 0.50 to 7.00 ± 1.30%, similar to the standard drug, with less severe heart rate side effect than their crude extracts. This may imply that after fractionation, some compounds which cause the HR changes may be removed resulting in the lesser effect on the HR. In addition, all

Table 6. Phytochemical constituents of the 10 selected single plant extracts from the 12 antihypertensive medicinal plant recipes.

	Phytochemical constituents[a]									
				Sugar[b]						
Extract	Triterpene	Alkaloid	Anthraquinone	F	G	S	Flavonoid	Carotenoid	Tannin	Xanthone
Cassumunar ginger (*Zingiber cassumunar*)	−	+	−	−	−	−	++	−	−	−
Garlic (*Allium Sativum*)	−	+	−	−	−	−	−	−	−	−
Ginger (*Zingiber officinale*)	++	+++	−	−	−	−	+	+	−	−
Galangal (*Alpinia galanga*)	+	−	−	−	−	+	++	−	+	−
Indian long pepper (*Piper chaba*)	+	+	−	−	−	+	++	+	+	−
Pepper (*Piper nigrum*)	++	+	−	−	−	−	++	+	−	−
Myrobalan wood (*Terminalia chebula*)	−	++	−	−	−	++	+++	−	++	+++
Szechwan lovage rhizome (*Ligusticum chuanxiong*)	−	+++	−	−	−	+++	++	−	+	+
Golden shower (*Cassia fistula*)	+++	−	++	−	−	−	+++	−	+++	++
Myrtle grass (*Acrous calamus*)	−	++	−	−	−	−	++	−	−	−

[a]+ = presence, − = absence.
[b]F = fructose, G = glucose and S = sucrose.

fractions gave a HR effect similar to their corresponding crude extracts. For example, all fractions from ginger extract tended to increase HR, whereas most of the fraction from the garlic extract decreased HR in the same trend as their crude extracts. For the duration of action, all fractions gave shorter duration than their crude extracts and the recipe extracts where they were containing. The longest duration at 232.50 ± 74.87 s was obtained from the water fraction of the garlic crude extract, but was still shorter than its crude extract and recipe. The active antihypertensive constituents in the environment of the plant mixture in the recipe or the compound mixture in the crude extracts may be more chemically stable than when they were semi-purified as fractions. In addition, the effects on the changes of HR appeared to be decreased when the plant crude extracts were semi-purified by fractionation. Also, this study indicates that the compounds in each fraction may contribute to the total antihypertensive activity and the duration of action of its crude extract.

Phytochemical screening

The five aqueous recipe extracts which gave the highest antihypertensive activity including HT016, HT023, HT001, HT030 and HT029 with the decrease of MABP at 27.17 ± 3.17, 24.00 ± 1.75, 23.33 ± 2.94, 19.33 ± 1.78 and $16.50 \pm 0.99\%$, respectively, were selected to test for phytochemical constituents (Table 5). All extracts contained glycosides which are molecules with a sugar bound to a non-carbohydrate moiety. Xanthones and alkaloids were also found in some recipe extracts. In fact, the ACEI inhibitory effect of several glycosides, such as acteoside from *Syringa vulgaris* Linn. (Oleaceae) and procyanidin glycoside from *Rhamnus lycioides* Linn. (Rhamnaceae) has been reported (Ahmad et al., 1995; Terencio et al., 1991). Furthermore, the extraction of acteoside from various plants in *Piper* genus, which was the component in recipes HT016, HT023, HT001 and HT030 has been indicated (Watanabe et al., 2007). In addition, alkaloids such as reserpine from *Rauwolfia serpentina* and alkaloid fraction from *Moringa oleifera,* one of the component in recipe no. HT029, were widely used in the traditional medicine for antihypertensive activity (Dangi et al., 2002). Several xanthone derivatives have also been reported to exhibit effective hypotensive activity in anesthetized rats from the vasodilating properties of these compounds via calcium channels and the beta adrenergic blocking pathway (Wang et al., 2002)

The phytochemical constituents of the selected plant extracts are shown in Table 6. Alkaloids and flavonoids were presented in most extracts. Flavonoids such as total flavonoid extract from the seed of *Astragalus complanatus* has been reported to reduce BP in both renal hypertensive rats (RHR) and spontaneously hypertensive rats (SHR) by plasma angiotensin II decreasing effect resulting in the decrease of the total peripheral resistance (TPR) (Li et al., 2005). Thus, glycosides, alkaloids, flavonoids, and xanthones might be responsible for the antihypertensive activities of these selected plant extracts.

Conclusions

Potent antihypertensive effects of the traditional antihypertensive medicinal plants and recipes selected from the ''MANOSROI III'' database are described. A total of 12 of the 30 (40%) recipes showed antihypertensive activity with the highest percentage reduction of MABP at $27.17 \pm 3.17\%$ observed in recipe HT016 which was 2.41 folds higher, but 10.75-times shorter duration, in comparison to the standard drug (prazosin hydrochloride). Plants in the Zingiberaceae and Piperaceae families were found in most active recipes. The phytochemical constituents found in the recipes were glycosides, xanthones and alkaloids. Ten Thai medicinal plants appearing frequently in the 12 active recipes were selected to test for anti-hypertensive activities. All selected aqueous plant extracts demonstrated antihypertensive activity with the highest decrease of MABP at $39.83 \pm 3.92\%$ in the cassumunar ginger extract which was 3.54-fold of the standard drug, whereas garlic and ginger extracts gave the percentage decrease of MABP at 35.83 ± 3.79 and $21.00 \pm 2.56\%$, respectively. All plant extracts demonstrated changes of HR from the baseline in the range of 4.17 ± 2.06 to $11.50 \pm 4.33\%$. For the phytochemical test, alkaloids and flavonoids were observed in most plant extracts. For the duration of action, the selected recipe extracts gave shorter action than the standard drug. All three plant crude extracts (cassumunar ginger, garlic and ginger) demonstrated

antihypertensive activity. When they were fractionated into water, butanol and ethyl acetate fractions, all fractions demonstrated antihypertensive activity with the highest decrease of MABP at $27.17 \pm 1.83\%$ found in the garlic water fraction. The plant crude extracts appeared to give higher antihypertensive effects with lesser effects on HR changes than their corresponding recipe extracts. However, the selected plant fractions gave lower antihypertensive activity with lesser effect on HR changes than their corresponding plant crude extracts. In addition, both the plant crude extracts and their fractions exhibited shorter duration of action than their corresponding recipes and plant crude extracts, respectively. The results from this study have not only confirmed the folklore wisdom of the Thai traditional antihypertensive medicinal plants and recipes selected from the ''MANOSROI III'' database, but also the potential of these plants and recipes to be developed as modern antihypertensive drugs as well.

Acknowledgements

This work was supported by Science and Technology Research Institute (STRI), Chiang Mai University, Department for Development of Thai Traditional and Alternative Medicine (DTAM), Ministry of Public Health, and Natural Product Research and Development Center (NPRDC), Chiang Mai University, Thailand.

Declaration of interest

The authors report no declarations of interest.

References

Ahmad M, Rizwani GH, Aftab K, et al. (1995). Acteoside: A new antihypertensive drug. *Phytother Res* 9:525–7.

Banso A, Ngbede JE. (2006). Phytochemical screening and *in vitro* antifungal properties of *Fagara zanthoxyloides*. *J Food Agric Environ* 4:8–9.

Berne RM, Levy MN. (2001). *Cardiovascular Physiology.* 8th ed. MO, USA: Mosby, 115–53.

Bhatt JD, Panchakshar, UD, Hemavathi KG, Gulati OD. (1998). Effect of Abana, an ayurvedic preparation on ethinyl stradiolinduced hypertension in rats. *Indian J Pharmacol* 30:399–403.

Bhattacharya S, Ghosh AK. (2009). Phytosomes: The emerging technology for enhancement of bioavailability of botanicals and nutraceuticals. *ISPUB* 2. doi: 10.5580/1216.

Cheng JWM. (2008). Aliskiren: Renin inhibitor for hypertension management. *Clin Ther* 30:31–47.

Dangi SY, Jolly CI, Narayanan S. (2002). Antihypertensive activity of the total alkaloids from the leaves of *Moringa oleifera*. *Pharm Biol* 40: 144–8.

Du YL, Chen SX. (2005). Combinative application of antihypertension drugs. *World Clin Drugs* 26:592–602.

Duarte CM, Verli H, Xavier J, et al. (2004). New optimized piperamide analogues with potent in *in vivo* hypotensive properties. *Eur J Pharm Sci* 23:363–9.

Gamaniel KS. (2000). Toxicity from medicinal plants and their products. *Niger J Nat Pro Med* 4:4–8.

Ghayur MN, Gilani AH. (2005). Pharmacological basis for the medicinal use of ginger in gastrointestinal disorders. *Dig Dis Sci* 50:1889–97.

Kearney PM. (2005). Global burden of hypertension: Analysis of worldwide data. *Lancet* 365:217–23.

Ke L. (2004). Review and prospect of medication of hypertension. The College of Sanitary and Management Staff of Si Chuan Province, 20, 138.

Lawal BAS, Aderibigbe AO, Essiet GA, Essien AD. (2007). Hypotensive and antihypertensive effects of *Aframomum melegueta* seeds in humans. *Int J Pharmacol* 3:311–18.

Li JX, Xue B, Chai Q, Liu ZX, Zhao AP, Chen LB. (2005). Antihypertensive effect of total flavonoid fraction of Astragalus complanatus in hypertensive rats. *Chin J Physiol* 48:101–6.

Loeb AL, Longnecker DE. (1992). Inhibition of endothelium-derived relaxing factor-dependent circulatory control in intact rats. *Am J Physiol* 262:H1494–500.

Magos GA, Vidrio H. (1991). Pharmacology of Casimiroa edulis; I. Blood pressure and heart rate effects in the anesthetized rat. *Planta Med* 57:20–4.

Manach C, Scalbert A, Morand C, et al. (2004). Polyphenols: Food sources and bioavailability. *Am J Clin Nutr* 79:727–47.

Manosroi J, Manosroi A, Rungruangsri U. (2006). Translation of Lanna medicinal plant recipes for research and development of modern pharmaceuticals and the understanding of the Lanna Thai cultures/ histories. *CMU J* 5:437–41.

Noll G, Tschudi M, Nava E, Luscher TF. (1997). Endothelium and high blood pressure. *Int J Microcirc Clin Exp* 17:273–9.

Odebiyi OO, Sofowora EA. (1978). Phytochemical screening of Nigerian medicinal plants II. *Lloydia* 41:234–46.

Patel SS, Verma NK, Ravi V, et al. (2010). Antihypertensive effect of an aqueous extract of *Passiflora nepalensis* Wall. *Int J Appl Res Nat Pro* 3:22–7.

Pechanova O, Kashiba M, Inoue M. (1999). Role of glutathione in stabilization of nitric oxide during hypertension developed by inhibition of nitric oxide synthase in the rat. *Jpn J Pharmacol* 81: 223–9.

Reagan-Shaw S, Nihal M, Ahmad N. (2008). Dose translation from animal to human studies revistied. *FASEB* 22:659–61.

Rosamond W, Flegal K, Friday G. (2007). Heart disease and stroke statistics-2007 update: A report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 115:169–71.

Sofowora A. (1982). Determination of saponin. In: *Medicinal plants and traditional medicine in Africa*. Chichester, England: John Wiley and Sons, 142–46.

Srivastava P, Raut HN, Puntambekar HM, Desai AC. (2011). Effect of storage conditions on free radical scavenging activities of crude plant material of *Piper longum*. *J Phyto* 3:23–27.

Swarup A, Umadevi K. (1998). Evaluation of eve care in the treatment of dysmenorrhoea and premenstrual syndrome. *Obs Gynae Today* 6: 369–72.

Terencio MC, Sanz MJ, Paya M. (1991). Antihypertensive action of a procyanidin glycoside from *Rhamnus lycioides*. *J Ethnopharmacol* 31: 109–14.

Vadivu R, Lakshmi KS. (2008). *In vitro* and *in vivo* anti-inflammatory activity of leaves of *Symplocos cochinchnensis* (Lour) Moore ssp *laurina*. *Bangladesh J Pharmacol* 3:121–4.

Wang Z. (2004). Progress on treatment of essential hypertension. *Job Health* 20:138.

Wang LW, Kang JJ, Chen IJ, et al. (2002). Antihypertensive and vasorelaxing activities of synthetic xanthone derivatives. *Bioorganic Med Chem* 10:567–72.

Watanabe J, Kasai K, Kanegae R, et al. (2007). Extraction of acteoside. Japanese patent JP3925828.

Whitworth JA. (2003). World Health Organization, International Society of Hypertension Writing Group. World Health Organization (WHO)/ International Society of Hypertension (ISH) statement on management of hypertension. *J Hypertens* 11:1983–92.

Williamson EM, Okpako DG, Evan FJ. (1996). *Pharmacological methods in phytotherapy research. Vol. 1 Selection, preparation and pharmacological evaluation of plant material*. Chichester, England: John wiley and Sons Ltd, 9–13.

Yodjun M, Karnchanatat A, Sangvanich P. (2012). Angiotensin I-converting enzyme inhibitory proteins and peptides from the rhizomes of Zingiberaceae plants. *Appl Biochem Biotechnol* 166:2037–50.

Zhu SJYL. (1997). Risk factors and hypertension complication. *Jpn Med Intro* 18:200–2.