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Original Research Article

Antioxidant properties, selected enzyme inhibition capacities, and a cosmetic cream formulation of Thai mango seed kernel extracts

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Abstract

Purpose: *To investigate the antioxidant properties, the inhibition of selected enzyme activities of ultrasonication-assisted mango seed kernel extract (MSKE), and to evaluate the physical stability and skin irritation properties of a cosmetic cream formulated with MSKE.*
Methods: *Choke-Anan MSKE and a Kaew cultivar of Thai mangoes were prepared by ultrasonication-assisted extraction. Antioxidant activities (DPPH, FRAP, H_2O_2 scavenging assay, ABTS), antityrosinase, anti 5-lipoxygenase, antihyaluronidase and anti α-glucosidase were determined. Cosmetic creams containing 0, 1, 2 and 3 % of MSKE were prepared and evaluated for physical stability. The most stable formulation was subjected to the clinical skin irritation test.*
Results: *The yield, total polyphenol content, antioxidant properties and inhibition of 5-lipoxygenase, hyaluronidase and α-glucosidase were higher ($p < 0.05$) for MSKE from Choke-Anan than from Kaew cultivar. The MSKE from both cultivars showed no significant difference ($p > 0.05$) in tyrosinase inhibition activity compared to arbutin. However, a slightly lower α-glucosidase inhibition activity than acarbose was observed. The cosmetic cream containing 1 % Choke-Anan MSKE had good physical stability with no skin irritation.*
Conclusion: *MSKE exhibits good antioxidant and enzyme inhibitory activity. Thus, it is a potentially natural functional ingredient for use in food and cosmetic industries.*

Keywords: *Mango, Antioxidant, Enzyme inhibitory activities, Cosmetic product stability, Skin irritation*

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INTRODUCTION

Polyphenol phytochemicals have been extensively studied and are the most well-known bioactive compounds found in plants. Polyphenols are secondary metabolites found in higher plants that contain one or more phenol units [1]. They have strong antioxidant activity, and can scavenge a variety of free radicals including reactive oxygen species (ROS) and reactive nitrogen species (RNS) [2]. Previous studies have shown the protective action of polyphenols on human health and indicate their potential use as key components of a healthy and balanced diet [3]. Currently, the use of natural antioxidants in cosmetics is of increasing interest. Previous studies show that oxidative stress, is the major cause of skin ageing and is an over production of ROS and a reduction of antioxidant activity with age [4]. Moreover, plant polyphenols have been reported to be used as sunscreens, whitening and anti-ageing agents in cosmetic products [5].

The mango (*Mangifera indica* L) fruit belongs to the *Anacardiaceae* family and is a good source of various polyphenols, which are found in the pulp, peel and seed [6]. The mango fruit and its processed products are in increasing demand in the world market. Consequently, mango seed and peel, which account for 35 - 60 % of the fruit depending on the variety, are the main by-products [7]. There are several mango varieties grown in Thailand. The most well-known cultivars are *Choke-Anan, Ok-Long, Kaew, Nam-Dorkmai, Rad and Keow-Savoey*. The *Choke-Anan* and *Kaew* cultivars are commonly used for processing in factories, and represent for 29.5 % and 27.9 %, respectively, for all mango varieties. It has been reported that industrial mango seed waste generation is as high as 1 ton annually [8].

The bioactive compounds in the mango seed kernel are tannin, gallic acid, coumarin, cafeic acid, vanillin, mangiferin, ferulicacid and cinamic acid [9]. Mango seed kernel extracts have been reported to have anti-tyrosinase, anti-inflammatory and hepatoprotective activities [10]. Therefore, mango seed kernels could be a potential source of ingredients for functional foods and cosmetics [11].

The present study aimed to determine a suitable ultrasonication time for the extraction of two cultivars of Thai mango seed kernel. The bioactivity, antioxidant activity and the effect on tyrosinase, 5-lipoxyganase, hyaluronidase and α-glucosidase activities were also studied. The application of the mango seed kernel extract in a cosmetic cream was evaluated.

EXPERIMENTAL

Plant materials

Two mango cultivars (*Mangifera indica* L.) were studied. The cultivars, *Kaew* and *Choke-Anan* were obtained from a local orchard in Nakornratchasima Province, Thailand between March and May, 2015. Mature green mangoes were selected by weight (200 - 250 g / kg). The peel and pulp were removed from the fruits using a fruit peeler and a knife, and the seeds were kept at -18 °C (Ultra Cold Freezer -80 °C, CTL 821, Thailand) for no longer than 1 month. Before use, the frozen kernels were separated from their shell with scissors.

Preparation of mango seed kernel extract (MSKE)

Crude MSKE were prepared by ultrasonic-assisted extraction as previously described [12]. All of the samples were ground and blended with 95 % ethanol (100 ml) in a blender for 5 min. The samples were incubated in a sonication water bath, at a frequency of 20 KHz and a temperature of 25 °C for 15 - 60 min. The samples were further incubated in a water bath at 80 °C and stirred every 10 min for 1 h. The mixtures were cooled at room temperature and the supernatant from each mixture was passed through Whatman filter paper no. 4. All filtrates were evaporated in a rotary evaporator at 50 °C under a vacuum until dry, and the extracts were weighed to determine the extraction yield of the soluble components.

Determination of total polyphenol content (TPC)

TPC was analysed as previously described [13]. The TPCs of the samples were expressed as mg of gallic acid equivalents per gram of MSKE.

Determination of antioxidant activities

The antioxidant activity of MSKE was evaluated using four different methods; the 2, 2-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging assay, the ferric reducing antioxidative power assay (FRAP), the hydrogen peroxide scavenging assay and the 2, 2'-azino-bis (3-ethylbenzothiazoline-6-sulphonic acid) (ABTS) radical scavenging assay. The assays were performed according to previous reports [14]. The results were expressed as mg of trolox equivalents per gram of MSKE.

Determination of enzyme inhibition activity

The tyrosinase inhibition activity was measured using a modified dopachrome method with mushroom tyrosinase and L-3, 4-dihydroxyphenylalanine as the substrate [15]. The 5-lipoxygenase inhibition activity was studied using sodium linoleate as the substrate according to a previous study [16]. The hyaluronidase inhibition activity was determined using sodium hyaluronate as substrate following a previously described method [17]. The α-glucosidase inhibition activity was measured using p-nitrophenyl-α-D-glucopyranoside as substrate [18]. All inhibitory effects of the samples were expressed as the inhibitor concentration causing a 50 % loss of enzyme activity (IC_{50}).

Preparation of cosmetic cream

The oil-in-water emulsion creams used in this study were prepared, respectively by melting the lipophilic phase including Emulium Delta (5.0 %), stearic acid (1.5 %), stearyl alcohol (2.0 %), Captex 300 (3 %) and cetyl alcohol (1.5 %) in a water bath at 80 °C and separately mixing the hydropholic phase; propylene glycol (3 %), xanthan gum (0.1 %), EDTA (0.1 %) and water in a water bath at 70 °C.

The 2 phases were mixed by homogenizer at 20,000 rpm for 3 min and cooled down at room temperature. MSKE (0, 1, 2, and 3 % w/w) and 0.1 % phenoxyethanol as preservative were added and mixed again at 10,000 rpm for 3 min.

Test for resistance to centrifugation

The resistance to centrifugation study was based on a previously described method [19]. The samples were stored at ambient temperature and humidity for 48 h. A 10 ml sample was centrifuged at 3000 rpm for 30 min. The Samples were evaluated for phase separation by measuring the supernatant after centrifugation.

Assessment of physical stability

The samples were stored at -4 °C for 24 h and then 25 °C for another 24 h and this was repeated for 6 cycles. Samples were taken every 48 h for the evaluation of pH, viscosity, phase separation, colour and TPC. The samples were centrifuged at 15000 g for 30 min at 4 °C and the supernatant was analysed for TPC using a previously described method [13].

The colour of the samples was expressed as *L* (degree of lightness), *a* (degree of redness) and *b* (degree of yellowness) values. The total colour difference (ΔE) was calculated by Eq 1.

$$\Delta E = \sqrt{(L - L')^2 + (a - a')^2 + (b - b')^2} \quad \text{........ (1)}$$

where *L, a* and *b* are the sample colours, and *L´, a´ and b´* are the colours at time zero.

Skin irritation test

MSKE cream was subjected to *in-vivo* skin irritation assessment. A total of 20 Thai men and women with normal skin, 18 years old and older, volunteered to participate in this study. Patch tests were performed on a part of the back (5x4 cm) of all volunteers. After 24 h, the patch was removed and the skin was observed for redness/ irritation after 30 min and 24 h. The method used in this study was approved by the Ethical Committee for *in vivo* Studies of Mae Fah Luang University, Thailand (reference no. REH-50005).

Statistical analysis

The results are expressed as the mean ± standard deviation (SD, n = 3) Statistical analyses were carried out by a one-way ANOVA using SPSS version 16.0. Significant differences were at $p \leq 0.05$.

RESULTS

Extraction yield and TPC

The effect of duration of ultrasonication on the extraction yield and TPC of the MSKEs from the two cultivars are shown in table 1. The results showed that a longer ultrasonication duration (up to 45 min) gave a significantly higher ($p \leq 0.05$) extraction yield and TPC of the extracts. However, the values were not significantly different ($p > 0.05$) after 45 min, indicating that the optimum duration of ultrasonication for the extraction of MSKEs under the conditions used in this experiment was 45 min. The *Choke-Anan* cultivar had a higher extraction yield and TPC than the *Kaew* cultivar. The MSKE obtained by ultrasonic-assisted extraction at 45 min gave a 55 and 63 % higher extraction yield and 92 and 55 % higher TPC for the *Kaew* and *Choke-Anan* cultivars, respectively compared to conventional ethanol extraction.

Antioxidant activity of MSKE

MSKEs prepared by the ultrasonication-assisted extraction of the two cultivars had approximately two-fold greater antioxidant activity for all the methods studied (Table 2). The higher polyphenol content in the MSKEs obtained by ultrasonication-assisted extraction (Table 1) likely contributed to the greater antioxidant activity. In addition, the *Choke-Anan* MSKE showed a higher antioxidant activity than the *Kaew* MSKE for all methods evaluated. The results corresponded to the content of TPC, which was also higher in the *Choke-Anan* MSKE (Table 1).

Enzyme inhibition capacity of MSKEs

As shown in Table 3, the *Kaew* and *Choke-Anan* MSKE were not significantly different (p > 0.05) for the tyrosinase inhibitory activity compared to arbutin and the IC_{50} values were in the range of 19.86 $\pm$ 1.2 to 20.64 $\pm$ 0.3 µg / mL. The *Choke-Anan* MSKE had significantly higher ($p \leq 0.05$) 5-lipoxygenase inhibitory activity than that the *Kaew* MSKE. However, the inhibitor concentration that caused a 50 % loss of the enzyme activity (IC_{50}) of the MSKEs was approximately 3.2 - 4.3 fold higher than rutin. The hyaluronidase inhibitory activity of the *Choke-Anan* MSKE was not significantly different (p > 0.05) compared to vitamin C. However the *Kaew* MSKE showed an approximately 1.3 fold lower inhibitory activity. The *Choke-Anan* MSKE had a significantly higher ($p \leq 0.05$) α-glucosidase inhibitory capacity than the *Kaew* MSKE. The *Choke-Anan* MSKE had an approximately 1.1 fold higher IC_{50} than acarbose, indicating a slightly lower α-glucosidase inhibitory activity.

Table 1: Effect of the ultrasonication duration on the extraction yield and TPC of MSKEs

Mango cultivars	Extraction time (min)	Yield (%)	TPC (mg GAE/g)
Kaew	0 (Ethanol extraction)	1.60±0.06^{g}	71.74±0.97^{f}
	15	1.71±0.03^{f}	70.93±0.63^{f}
	30	2.10±0.07^{e}	91.64±0.80^{e}
	45	2.48±0.03^{c}	137.49±1.15^{b}
	60	2.49±0.06^{c}	138.71±2.52^{b}
Choke-Anan	0 (Ethanol extraction)	2.16±0.02^{e}	110.02±1.06^{d}
	15	2.29±0.04^{d}	110.32±0.93^{d}
	30	2.73±0.03^{b}	124.36±1.69^{c}
	45	3.52±0.03^{a}	170.12±1.89^{a}
	60	3.56±0.02^{a}	170.63±0.93^{a}

Values are the mean ± standard deviation; (n=3); values in the same column followed by different superscript letters are significantly different ($p \leq 0.05$)

Table 2: Antioxidant capacity of MSKE by different methods

MSKE extract	Antioxidant capacity (mg Trolox/ g MSKE)			
	DPPH	FRAP	H_2O_2	ABTS
Kaew Ethanolic	92.61$\pm$3.72^{d}	91.24$\pm$3.34^{d}	49.15$\pm$4.96^{d}	82.66$\pm$1.17^{d}
Kaew Ethanolic + ultrasonication	197.00$\pm$5.83^{b}	206.32$\pm$2.46^{b}	108.79$\pm$3.05^{b}	92.40$\pm$1.55^{c}
Choke-Anan ethanolic	117.07$\pm$4.12^{c}	123.43$\pm$2.55^{c}	60.54$\pm$2.86^{c}	166.74$\pm$0.96^{b}
Choke-Anan ethanolic + ultrasonic-cation	254.64$\pm$1.15^{a}	289.47$\pm$3.26^{a}	110.24$\pm$2.26^{a}	198.68$\pm$ 0.44^{a}

Values are the mean ± standard deviation; (n = 3); values in the same column followed by different superscript letters are significantly different ($p \leq 0.05$)

Table 3: Enzyme inhibition capacity

Sample	IC_{50} (µg/mL)			
	Tyrosinase	***5-Lipoxygenase***	***Hyaluronidase***	***α-Glucosidase***
Kaew MSKE	20.64±0.32^{a}	39.77±2.41^{a}	47.61$\pm$2.92^{a}	163.19$\pm$2.33^{a}
Choke-Anan MSKE	19.86$\pm$1.22^{a}	30.94±0.32^{b}	37.28$\pm$1.67^{b}	113.51$\pm$5.85^{b}
Arbutin	20.46±0.33^{a}	-	-	-
Rutin	-	9.31±0.55^{c}	-	-
Vitamin C	-	-	39.29$\pm$0.25^{b}	-
Acarbose	-	-	-	104.42$\pm$5.54^{c}

Values are the mean ± SD (n=3); values in the same column followed by different superscript letters are significantly different ($p \leq 0.05$). IC_{50} = inhibitor concentration causing 50 % loss of enzyme activity

Physical stability of MSKE cream

After centrifugation, phase separation was not observed in any sample of MSKE cream or the control base (data not shown). A physical stability evaluation of the MSKE creams is shown in Table 4. A freeze-thaw cycling test showed that the pH and viscosity of the samples from each cycle did not exhibit significant changes ($p > 0.05$) and no phase separation was observed in any sample. The results indicate that the pH, viscosity and appearance of the MSKE creams were stable and that the MSKE did not affect the physical properties tested. In particular, the total colour (ΔE) of the 1% MSKE and the base cream was not significantly different ($p > 0.05$) for any cycle (data not shown), while the (ΔE) of the 2 and 3 % MSKE creams were significantly different ($p \leq 0.05$).

Clinical skin irritation

No volunteer exposed to MSKE cream showed an adverse reaction. Skin exposed to the MSKE cream did not respond differently than skin exposed to the negative control (data not shown).

DISCUSSION

This study found that the *Choke-Anan* and *Kaew* MSKEs had higher extraction yields and TPC when ultrasonication was applied during extraction. A higher TPC of MSKE had previously been observed when an ultrasonic-assisted aqueous two phase extraction of mango seed kernel was used [20]. Ultrasonication was shown to disrupt the cell membrane and the cell wall structure, increasing solvent diffusion through the membrane, thus facilitating the release of the cell contents [21].

MSKEs from the two cultivars prepared by ultrasonication-assisted extraction showed greater antioxidant activity for all methods studied and the *Choke-Anan* MSKE had higher antioxidant activity than the *Kaew* MSKE. The results agree with reports of concurrent antioxidant activities indicated by DPPH and ABTS methods for *Choke-Anan* MSKE when compared to several other varieties of Thai mangoes [22]. Moreover, the *Choke-Anan* and *Kaew* MSKEs had the highest antioxidant properties of eleven mango varieties studied [23].

The results showed that tyrosinase inhibitory activity of the *Kaew* and *Choke-Anan* MSKEs were similar to previously reported values. *Choke-Anan* MSKE was previously shown to inhibit tyrosinase activity up to 1.58 fold higher than arbutin [25]. These results indicated that MSKE can be a good source of phytochemicals with tyrosinase inhibitory activity.

5-Lipoxygenase catalyses the conversion of polyunsaturated fatty acids to biologically active metabolites, which are active mediators in a variety of inflammation processes [26]. A previous study showed that the IC_{50} values for the 5-lipoxygenase inhibitory activity of eight plant extracts ranged from 27.4 $\pm$ 0.6 to 66.7 $\pm$ 0.6 µg / mL [27]. These 5-lipoxygenase inhibition activities imply that MSKE has a high potential for use as natural anti-inflamatory drug compared to other plant extracts reported in previous studies.

It is well understood that the degradation of hyaluronic acid by hyaluronidase can diminish amount of hyaluronic acid in the skin, which consequently becomes dry and wrinkled [28]. An extract of the bark of *Terminaliaarjuna* (250 µg / mL) and dried fruit rinds of *Terminaliachebula* (500 µg / mL) have been reported to have 90.40 $\pm$ 5.30 % and 89.65 $\pm$ 3.90 % hyaluronidase inhibition, respectively [29]. In the present study, the *Kaew* and *Choke-Anan* MSKEs respectively gave up to 80.35 % and 97.61 % inhibition at concentrations of 70 µg / mL. These results indicate that the MSKEs, and especially *Choke-Anan* MSKEs, have a potential for cosmetic use as an anti-wrinkle agent.

The progression of diabetes mellitus can be controlled by inhibiting the absorption of dietary carbohydrates in the small intestine [30]. The α-glucosidase inhibitory activity of the *Kaew* and *Choke-Anan* MSKEs compared to acarbose showed IC_{50} values of 163.19 $\pm$ 2.3, 113.51 $\pm$ 5.8, and 104.42 $\pm$ 5.5 µg / mL, respectively. A methanol extract of mango seed from Nigeria has been reported to inhibit α-glucosidase with an IC_{50} of 340 µg / mL [31]. The results in this study revealed that MSKEs potently inhibit α-glucosidase activity.

Due to the higher bioactivity of the *Choke-Anan* MSKE, it was further evaluated for its potential use as a cosmetic ingredient. The results revealed that addition of MSKE at 1 % in a cosmetic cream caused no significant difference ($p > 0.05$) of the physicochemical

Table 4: pH, viscosity, phase separation and TPC of the MSKE creams and the base control from the freeze-thaw physical stability evaluation

Sample	Parameter	Freeze-thaw cycle						
		0	**1**	**2**	**3**	**4**	**5**	**6**
Control base	pH[NS]	5.74±0.02	5.67±0.06	5.63±0.06	5.43±0.38	5.70±0.10	5.63±0.06	5.70±0.17
	Viscosity (cPs)[NS]	15558.45±18.53	15545.04±14.73	15546.33±3.21	15536.22±4.04	15550.34±8.50	15547.14±10.11	15549.33±11.01
	Phase separation	N	N	N	N	N	N	N
	TPC (mg of GAE/ ml)	ND	ND	ND	ND	ND	ND	ND
1% MSKE	pH[NS]	5.72±0.05	5.63±0.06	5.70±0.10	5.67±0.12	5.70±0.10	5.67±0.06	5.63±0.06
	Viscosity (cPs)[NS]	15540.43±7.61	15546.33±5.85	15540.66±6.11	15549.21±10.44	15551.06±10.14	15538.66±4.04	15547.66±6.35
	Phase separation	N	N	N	N	N	N	N
	TPC (mg of GAE/ ml)	1.64±0.32[a]	1.65±0.40[a]	1.66±0.33[a]	1.62±0.33[a]	1.48±0.15[b]	1.47±0.09[b]	1.47±0.12[b]
2% MSKE	pH[NS]	5.69±0.03	5.67±0.06	5.67±0.12	5.73±0.12	5.63±0.06	5.70±0.10	5.70±0.10
	Viscosity (cPs)[NS]	15543.56±11.15	15542.66±11.05	15549.66±2.50	15539.66±6.31	15547.33±12.42	15549.66±9.60	15541±5.58
	Phase separation	N	N	N	N	N	N	N
	TPC (mg of GAE/ ml)	3.32+0.06[a]	3.34±0.14[a]	3.27±0.21[a]	3.23±0.17[a]	2.84±0.03[b]	2.79±0.13[b]	2.79±0.11[b]
3% MSKE	pH[NS]	5.70±0.06	5.67±0.06	5.70±0.10	5.73±0.12	5.67±0.12	5.67±0.06	5.63±0.06
	Viscosity (cPs)[NS]	15527.45±5.80	15529.33±5.50	15539.33±8.32	15535.66±6.69	15539.04±5.19	15538.55±6.03	15540.66±10.60
	Phase separation	N	N	N	N	N	N	N
	TPC (mg of GAE/ ml)	4.92±0.12[a]	4.90±0.21[a]	4.89±0.14[a]	4.88±0.21[a]	4.23±0.13[b]	4.24±0.31[b]	4.20±0.11[b]

Values are the mean ± SD (n = 3); values in the same row followed by different superscript letters are significantly different ($p \leq 0.05$). NS means non-significantly different, N means not observed, ND means not determined properties or the skin irritation test result of the cream. Moreover, adding MSKE to the cream contributed to the total polyphenol content of the product.

CONCLUSION

The findings of this study indicate that mango seed by-products can be used as a new ingredient source for the food, pharmaceutical and cosmetic industries. The results demonstrate that *Kaew* and *Choke-Anan* MSKEs exhibit antioxidant activities as well as inhibit tyrosinase, 5-lipoxygenase, hyaluronidase and α-glucosidase activities. A cosmetic cream containing 1 % *Choke-Anan* MSKE is physically stable and appears safe for use on human skin.

DECLARATIONS

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Conflict of Interest

No conflict of interest associated with this work.

Contribution of Authors

The authors declare that this work was done by the authors named in this article and all liabilities pertaining to claims relating to the content of this article will be borne by them.

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REFERENCES

1. *Parr AJ, Bolwell GP. Phenolic in the plant and in man. The potential for possible nutritional enhancement of the diet by modifying the phenols content or profile. J Agri Food Chem 2000; 80: 995-1012.*
2. *Hernandez I, Alegrel L, Breusegem FV, Munne-Bosch S. How relevant are flavonoids as antioxidants in plants. Trends Plant Sci 2009; 14: 125-132.*
3. *Lima GPP, Vianello F, Correa CR, Campos RAS, Borguini MG. Polyphenols in fruits and vegetablesand its effect on human health. Food Nutri Sci 2014; 5: 1065-1082.*
4. *Ma W, Wlaschek M, Tantcheva-Poor I, Schneider LA, Naderi L, Razi-Wolf Z. Chronological ageing and photoageing of the fibroblasts and the dermal connective tissue. Clin Exp Dermatol 2001; 26: 592-599.*
5. *Gonzalez S, Fernandez-Lorentey M, Gilaberte C. The latest on skin photoprotection. Clin. Exp Dermatol 2008; 26: 614-626.*
6. *Masibo M, He Q. Major mango polyphenols and their potential significance to human health. Comprehensive Rev Food Sci Food Safe 2008; 7: 309-319.*
7. *Ayala-Zavala JF, Vega-Vega V, Rosas-Dominguez C, Palafox-Carlos H. Villa-Rodriguez JA, Wasim- Siddiqui MD. Agro-industrial potential of exotic fruit by-products as a source of food additives. Food Res Int 2011; 44: 1866-1874.*
8. *Maisuthikul P, Phasuk S. Survey of mango seed waste management in the Thai food industry. University of Thai chamber commerce journal 2008; 4: 158-166.*
9. *Ahmed A, Saeid D, Eman A, Reham E. Egyptian mango by-product 1. Compositional quality of mango seed kernel. Food Chem 2007; 103: 1141-1152.*
10. *Nithitanakool S, Pithayanukul P, Bavovada R. Antioxidant and hepatoprotective activities of Thai mango seed kernel extract. Planta Med 2009; 75: 1118-1123.*
11. *Kittiphoom S. Utilization of Mango seed. Int Food Res J 2012; 19(4): 1325-1335.*
12. *Ghafoor K, Choi YH. Optimization of Ultrasound assisted extraction of phenolic compounds and antioxidants from Grape peel through response surface methodology. Journal KoreanSoc Appl Biol Chem 2009; 52: 295-300.*
13. *Singleton VL, Lamuela-Raventos RM. Analysis of total phenol and other oxidation substrates and antioxidants by means of Folin-Ciocalteu reagent. Methods Enzymol 1999; 299: 152-178.*
14. *Nishaa S, Vishnupriya M, Sasikumar JM, Hephazibah PC, Gopalakrishnan VK. Antioxidant activity of ethanolic extract of Marantaarundinacea L. Tuberous Rhizomes. Asian J of Pham Clin Res 2012; 5(4): 85-88.*
15. *Masuda T, Yamashita D, Takeda Y, Yonemori S. Screening for tyrosinase inhibitors among extracts of seashore plants and identification of potent inhibitors from Garcinia subelliptica. Biosci Biotechnol Biochem 2005; 69: 197-201.*
16. *Shinde UA, Phadke AS, Nari AM, Mungantiwar AA, Dikshit VJ, Saraf MN. Membrane stabilization activity a possible mechanism of action for the anti-inflammatory activity of Cedrus deodara wood oil. Fitoterapia 1999; 70: 25-257.*
17. *Lee KK, Cho JJ, Park EJ, Choi JD. Anti-elastase and anti-hyaluronidase activity of henolic substance from*

Areca catechu as a new anti-ageing agent. Int J CosmetSci 2001; 23(6): 341-346.

18. *Apostolidis E, Li L, Lee C, Seeram NP. In vitro evaluation of phenolic-enriched maple syrup extracts for inhibition of carbohydrate hydrolyzing enzymes relevant to type 2 diabets management. J Funct Foods 2011; 3: 100-106.*
19. *Hong YH, Jung EY, Noh DON, Suh HJ. Physiological effect of formulation containing tannase-converted green tea extract on skin care: physical stability, collagenase, elastase, and tyrosinase activities. Integr Med Res2014; 3: 25-38.*
20. *Yuntao G, Zhenfeng W, Lijun L, Jianhui D, Ding L. Optimization of ultrasound-assisted aqueous two-phase extraction of polyphenol from mango seed kernel. Transactions of Chin Soc Agricul Engine 2012; 28: 255-261.*
21. *Rostagno MA, Palma M, Barroso CG. Ultrasound-assisted extraction of soy isoflavones. J Chromatogr A 2003; 1012: 119-128.*
22. *Khammuang S, Sarnthima K. Antioxidant and antibacterial activities of selected varieties of Thai mango seed extract. J Pharm Sci 2011; 24: 37-42.*
23. *Maisuthisakul P. Antiradical scavenging activity and polyphenolic compounds extracted from Thai mango seed kernels. As J Food Ag-Ind 2008; 1(02): 87-96.*
24. *Park SH, Kim DS, Kim WG, Ryoo IJ, Lee DH, Huh CH. Terrein: a new melanogenesis inhibitor and its mechanism. Cell Mol Life Sci 2004; 61: 2878-85.*
25. *Maisuthisakul P, Gordon MH. Antioxidant and tyrosinase inhibitory activity of Mango seed kernel by product. Food chem 2009; 117: 332-341.*
26. *Alitonou GA, Avlessi F, Sohounhloue DK, Agnaniet H, Bessiere JM, Menut C. Investigation on essential oil of cymbopogongiganteus from Benin for it potential use as anti-inflammatory agent. Int J Aromather 2006; 16: 113-119.*
27. *Albano SM, Lima AS, Miguel G, Pedro LG, Barroso JG, Figueiredo AC. Antioxidant, Anti 5-lipoxygenase and anti-acetylcholinesterase Activities of Essential oils and decoction waters of some aromatic plants. Rec Nat Prod 2012; 6(1): 35-48.*
28. *Sahasrabudhe A, Deodhar M. Anti-hyaluronidase, anti-elastase activity of Garcinia indica. Int J Botany 2010; 6: 299-303.*
29. *Satardekar KV, Deodhar MA. Anti-ageing ability of Terminalia Species with special reference to hyaluronidase, elastase inhibition and collagen synthesis in vitro. Int J Pharmacog Phytochem Res 2010; 2: 30-34.*
30. *Kumar S, Narwal S, Kumar V, Prakash O. α-Glucosidase inhibitors from plants: A Natural approach to treat diabetes. Pharmacog Rev 2011; 5: 19-29.*
31. *Irondi EA, Oboh G, Akindahunsi AA, Boligon AA, Athayde ML. Phenolic composition and inhibitory activity of Mangifera indica and Mucunaurens seeds extracts against key enzymes linked to the pathology and complications of type 2 diabetes. Asian Pac Trop biomed 2014; 4(11): 903-910.*