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Full Length Research Paper

Determination of total xanthones in *Garcinia mangostana* fruit rind extracts by ultraviolet (UV) spectrophotometry

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Garcinia mangostana **(Guttiferae) is an important botanical source of xanthones; these compounds have remarkable pharmacological properties such as anti-cancer, anti-inflammatory and anti-microbial effects. Xanthones-rich extracts have been widely used in nutritional supplements, herbal cosmetics and pharmaceutical preparations. In order to maintain consistency of the pharmacological and clinical outcomes, standardization of crude extracts is crucial for quality control assurance. This study reports development and validation of a ultraviolet-visible (UV-Vis) spectrophotometric method for determination of total xanthones in various *G. mangostana* fruit rind extracts. The method was validated at 4 wavelengths viz. 243.4, 254, 316.4 and 320 nm. Linearity was in the range of 0.5 to 20 µg/ml; intra-day and inter-day precision, as a relative standard deviation, was 1.1 and 1.8%, respectively; accuracy, limit of detection (LOD) and limit of quantification (LOQ) were in the range of 99 to 104%, 0.101 to 0.124 µg/ml and 0.307 to 0.375 µg/ml, respectively. The highest and lowest xanthones concentration was obtained in toluene extract (99.8%) and methanolic sub-extract (14.6%). The developed method showed high accuracy, sensitivity and selectivity towards xanthones, therefore, it may have an interesting application in routine standardization of *G. mangostana* extracts and its commercial products.**

Key words: *Garcinia mangostana*, total xanthones, ultraviolet-visible (UV-Vis) spectrophotometry.

INTRODUCTION

Garcinia mangostana L. or Mangosteen is a tropical tree from the family Guttiferae. The tree has been cultivated for centuries in the tropical rainforests of Southeast Asia, and can be found in many countries worldwide (Ji et al., 2007). Pericarps of the fruit have been used in folk medicine by Southeast Asians in treatment of several human illnesses including skin and wound infections, hemorrhoids, arthritis, tuberculosis, inflammation, genitourinary tract infections, fever, and amoebic dysentery (Moongkarndi et al., 2004; Suksamrarn et al., 2006; Harborne et al., 1999). Several commercial products of the whole fruit or fruit rinds are available worldwide including nutritional supplements, herbal cosmetics and pharmaceutical products.

Previous phytochemical studies on *G. mangostana* have reported this plant as one of the richest sources of xanthones where more than 50 compounds have been isolated including α-, β- and γ-mangostin and many other compounds (Ee et al., 2006; Peres et al., 2000; Pedraza-Chaverri et al., 2008; Zhang et al., 2010). In recent years, there has been strong interest in the *G. mangostana* xanthones due to their remarkable pharmacological effects such as analgesic (Cui et al., 2010), anti-oxidant

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(Jung et al., 2006), anti-cancer (Akao et al., 2008; Doi et al., 2009; Aisha et al., 2012b), anti-inflammatory (Chen et al., 2008; Tewtrakul et al., 2009), anti-allergy (Nakatani et al., 2002), anti-bacterial (Sakagami et al., 2005; Chomnawang et al., 2009), anti-tuberculosis (Suksamrarn et al., 2003), anti-fungal (Kaomongkolgit et al., 2009), anti-viral activity (Chen et al., 1996) and enhancement of the immune system (Tang et al., 2009). Because of the growing commercial interest in *G. mangostana*, reliable procedures are needed for quantitative determination of its bioactive principles and for quality control assurance. Few analytical methods have been reported for the standardization and quality control of *G. mangostana* herbal preparations including high performance liquid chromatography (HPLC) and liquid chromatography-mass spectrometer (LC-MS) methods (Walker, 2007; Pothitirat and Gritsanapan, 2009; Yodhnu et al., 2009; Ji et al., 2007). Though these are reliable methods, there is a need for cost effective methods for routine standardization purposes.

The ultraviolet-visible (UV-Vis) spectrophotometric method is frequently used in quantitative analysis of primary and secondary metabolites in herbal medicines such as total phenolics, flavonoids, proteins and polysaccharides (Ainsworth and Gillespie, 2007; Chen et al., 2010; Hussain et al., 2008). Xanthones of *G. mangostana* have unique UV-Vis spectra that allow accurate quantitative analysis by using UV-Vis spectrophotometry. This study was performed in order to develop and validate a new UV-Vis spectrophotometric method for determination of total xanthones in *G. mangostana* fruit rind extracts.

MATERIALS AND METHODS

Plant raw material

Ripened *G. mangostana* fruit was obtained from a local fruit farm at the Island of Penang, Malaysia, on June, 2009. Taxonomic authentication was performed by Taxonomist, University Science Malaysia (USM). A voucher specimen (No: 11155) was deposited at the Herbarium at School of Biological Sciences, USM, Malaysia. The fruit rinds were separated from the edible part and the rinds were chopped using an electric grinder before drying at 45 to 50°C for 24 h.

Chemicals and reagents

α--Mangostin reference compound (97% purity) was purchased from ChromaDex, (Irvine, California). Analytical grade solvents were acquired from Avantor Performance Materials (Petaling Jaya, Selangor, Malaysia).

Preparation of the fruit rind extracts

Three extracts were prepared including methanolic, 75% ethanolic and toluene, and 4 sub-extracts were prepared from the methanolic extract (Table 1). Extracts were prepared by the maceration method at 60°C for 48 h. Methanolic extract was dried using rotavapor, and 12.5 g was then macerated sequentially (3 × 100 ml, 10 min each) in petroleum ether, chloroform, ethyl acetate and methanol. Ethanolic and toluene extracts were concentrated by rotavapor at 50°C (ethanol) and 60°C (toluene) and kept at 2 to 8°C for 24 h. A yellow precipitate was formed, collected and further dried to obtain the ethanolic and toluene xanthones-rich extracts.

Instrumentation

Spectrophotometric measurements were performed in 1.0 cm quartz cuvettes using Lambda 25 spectrophotometer system with UV WinLab V2.85 software (Perkin-Elmer, USA).

Preparation of stock solutions

A stock solution of α-mangostin reference compound was prepared in methanol at 100 µg/ml and was further diluted to obtain 20, 16, 12, 8, 4, 2 and 0.5 µg/ml. Stock solutions of the fruit rind extracts were also prepared in methanol at 1 mg/ml and were further diluted to obtain 20 µg/ml. The stock solutions were filtered through 0.45 µm syringe filters.

UV-Vis spectroscopy

UV-Vis spectra of reference compound and extracts were collected in the wavelength range of 500 to 200 nm.

Method validation

The method was validated at 4 wavelengths according to the ICH guidelines (ICH, 1997). The following validation parameters were evaluated: selectivity, linearity, precision, accuracy and the limit of detection (LOD) and limit of quantification (LOQ).

Selectivity

Method's selectivity was confirmed by comparing the UV-Vis spectra obtained from 7 different extracts of *G. mangostana* with that of α-mangostin.

Linearity

Linearity was determined by using the reference compound at 0.5 to 20 µg/ml. The calibration curves were constructed by plotting the optical density versus concentration, and regression analysis was employed to determine the linearity of calibration curves.

Precision

Intra-day and inter-day precisions were determined by calculating the relative standard deviation (%RSD) of 5 replicates carried out within the same day and 5 replicates performed on different days, respectively.

Accuracy

Accuracy of the method was determined by performing a recovery study of α-mangostin reference compound at 5 concentrations. The experiment consisted of 3 groups; in group (A) 1 ml of α-mangostin standard solution at 20, 40, 60, 80 and 100 µg/ml was added to 9

Table 1. *G. mangostana* fruit rind extracts.

Extract	Yield (wt/wt)%
Toluene	5.0
Methanol	13.4
Petroleum ether [a]	0.4
Chloroform [b]	31.0
Ethyl acetate [c]	5.0
Methanol [d]	47.0
75% Ethanol	7.5

[a to d] refer to sub-extracts of methanolic extract.

ml methanol to obtain a final concentration of 2, 4, 6, 8 and 10 µg/ml. In group (B), 1 ml of α-mangostin standard solution at 20, 40, 60, 80 and 100 µg/ml was added to 9 ml pre-analyzed solution of toluene extract at 10 µg/ml. In the third group (C), 1 ml methanol was added to 9 ml solution of the toluene extract at 10 µg/ml. The concentration of α-mangostin and the toluene extract was kept constant in all groups, and the total volume was also kept constant at 10 ml.

The samples were re-analyzed and the percentage recovery was calculated by substituting the optical density in the following formula:

Percentage recovery = ((B – C) / A) × 100%.

Determination of LOD and LOQ

Sensitivity of the method was determined in terms of LOD and LOQ. The values were calculated through the slope and standard deviation method according to ICH guidelines (ICH, 1997) using the following formula:

LOD = (3.3 × δ) / S

LOQ = (10 × δ) / S

Where δ, Standard deviation of the Y intercept of the linear regression equations of calibration curves; S, slope of regression equations.

Measurement of total xanthones in *Garcinia mangostana* fruit rind extracts

Optical density of *G. mangostana* extracts was taken at 20 µg/ml, and the concentration of total xanthones was calculated by applying the linear regression equations of α-mangostin calibration curves. The (wt/wt)% was then determined using the formula:

Xanthones (wt/wt)% = (calculated concentration / theoretical concentration) × 100%.

Statistical analysis

Statistical calculations were carried out using the SPSS 16.0 for Windows software package. For comparison of mean values, one-way analysis of variance (ANOVA) was applied and differences were considered significant at $P < 0.05$.

RESULTS

Extraction

Extraction results are presented as (wt/wt) percentage yield relative to the dried raw material or to the crude extract (Table 1).

UV-Vis spectrophotometry

The UV-Vis spectra of α-mangostin revealed the presence of 2 peaks at 243.4 and 316.4 nm (Figure 1). Similarly, the extracts showed the same peaks with a minor shift in the wavelength. These 2 wavelengths were considered as the λ_{max} values and were used in the method validation. Another 2 commonly used wavelengths (254.0 and 320.0 nm) were also studied.

Selectivity

The method's selectivity was confirmed by comparing the UV-Vis spectra of *G. mangostana* fruit rind extracts with that of α-mangostin standard. Figure 1 shows the UV-Vis spectra of various extracts prepared in different solvents covering a wide range of polarity. The Figure 1 revealed almost identical spectra of all extracts and the reference compound.

Linearity

Good linearity was obtained at all studied wavelengths in the concentration range 0.5 to 20 µg/ml. The correlation coefficients (R^2) were more than 0.999.

Precision

The intra-day and inter-day precision was obtained from the %RSD in the concentration range 0.5 to 20 µg/ml by replicate analysis (n = 5) of the standard compound at 7 concentration points. The average %RSD in the intra-day data was 1.1% and that for inter-day data was 1.8% (Table 2). Statistical analysis showed no significant effect of the wavelength on the method's precision, $P = 0.973$ (intra-day), and 0.914 (inter-day).

Accuracy and recovery

Accuracy of the method was validated by the standard addition method and the results are presented as average percentage recovery. Recovery of the reference compound was evaluated at 5 concentrations (2, 4, 6, 8 and 10 µg/ml) in triplicates. The percentage recovery was

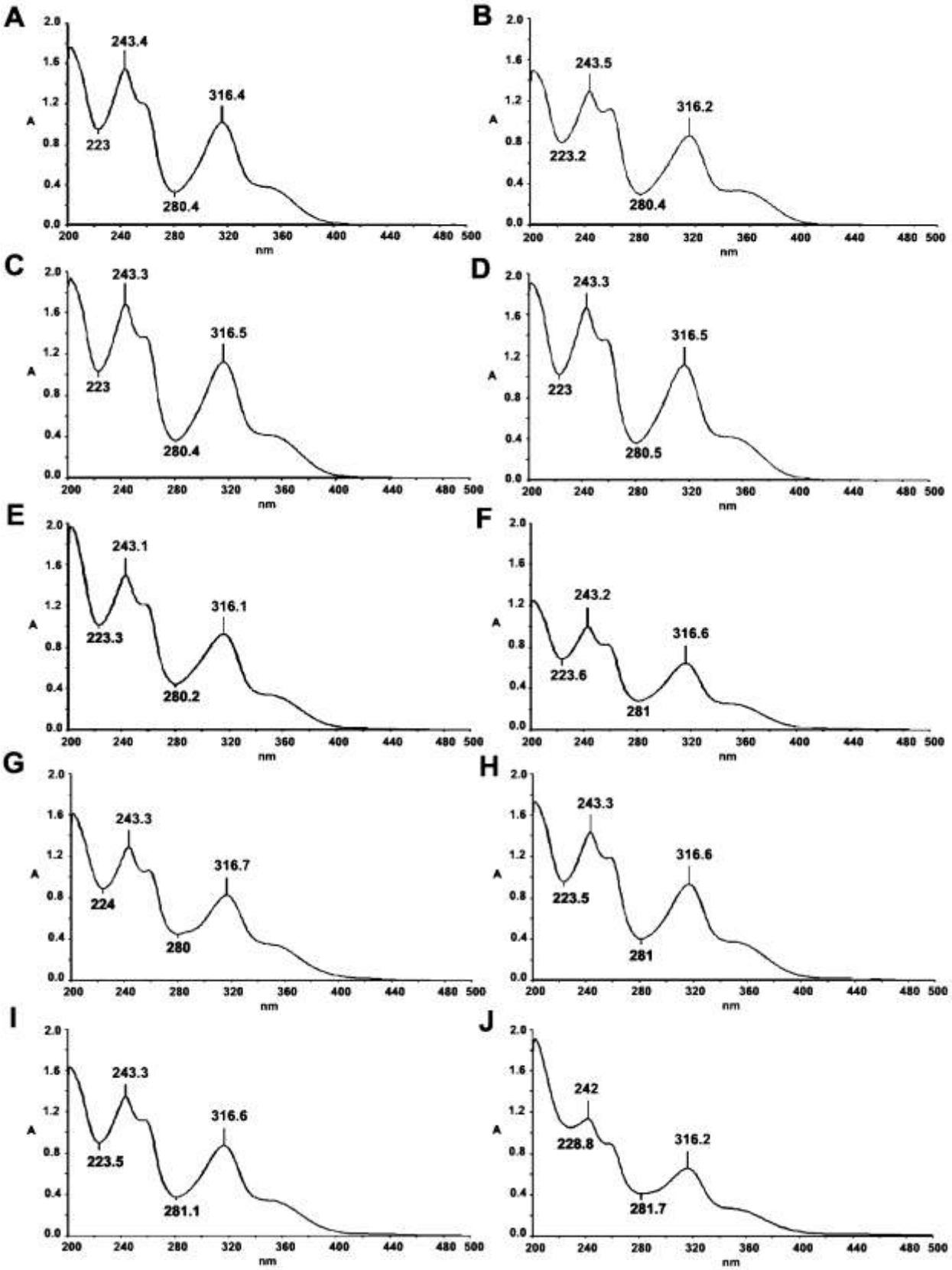

Figure 1. UV-Vis spectra of *G. mangostana* extracts. (A), α-Mangostin reference; (B), 75% ethanolic extract; (C, D and E), 3 batches of toluene extract; (F), methanolic extract; (G), petroleum ether sub-extract; (H), chloroform sub-extract; (I), ethyl acetate sub-extract; (J), methanolic sub-extract.

Table 2. Precision of the UV-Vis spectrophotometric method.

Concentration (µg/ml)	Percentage relative standard deviation			
	243.4 nm	254.0 nm	316.4 nm	320.0 nm
Intra-day data				
0.5	1.6	1.9	1.5	1.6
2	1.1	1.2	1.1	1.1
4	1.2	1.3	1.1	1.2
8	0.6	0.6	0.7	0.6
12	0.9	0.9	1.0	1.1
16	1.2	1.3	1.3	1.3
20	0.7	0.7	1.0	0.8
Inter-day data				
0.5	2.5	3.3	2.8	4.1
2	1.7	2.1	1.4	1.4
4	1.3	1.4	1.3	1.3
8	1.8	1.8	1.7	1.7
12	2.0	2.1	2.0	2.0
16	1.4	1.5	1.4	1.4
20	1.0	1.0	0.9	0.9

The results are presented as %RSD, (n = 5).

in the range of 99 to 104% (Table 3). Statistical analysis by one-way ANOVA indicates that the percentage recovery is significantly affected by changing the wavelength, $P = 0.028$.

LOD and LOQ

LOD was in the range of 0.101 to 0.124 µg/ml, and LOQ was in the range 0.307 to 0.375 µg/ml (Table 4). The wavelength was found to have a statistically significant effect on LOD and LOQ values, $P = 0.0$. The lowest LOD and LOQ values were obtained at 243.4 nm, whereas the highest values were obtained at 320.0 nm.

Total xanthones content in *G. mangostana* fruit rind extracts

Concentration of total xanthones in *G. mangostana* fruit rind extracts was calculated by applying the linear regression equations of α-mangostin calibration curves. The extracts showed a wide range of total xanthones content with the highest concentration obtained in toluene extracts and the lowest content achieved in methanolic sub-extract (Table 5).

DISCUSSION

The widespread availability of mangosteen commercial products requires the availability of reliable standardization methods for routine quality assurance. The UV-Vis spectrophotometry provides a cost effective, easy and accurate method for simultaneous determination of secondary and primary metabolites in herbal preparations. Hence, this study was conducted to develop and validate a UV spectrophotometric method for standardization of *G. mangostana* fruit rind extracts. *G. mangostana* extracts contain high concentration of α-mangostin, and hence this compound was selected as a reference compound. UV-Vis spectroscopy of *G. mangostana* extracts and α-mangostin showed almost identical spectra, the spectra were reproduced in 7 extracts prepared with solvents of different polarity. These results indicate selectivity of the proposed method, and provide the basis for determination of total xanthones in *G. mangostana* fruit rind extracts by UV spectrophotometry. The λ_{max} values were found to be 243.4 and 316.4 nm and these 2 wavelengths were employed in method's validation.

A previous study reported the λ_{max} values to be 243.0 and 320.0 nm, and reported the quantitative determination of total mangostins in *G. mangostana* fruit rind extracts at 320 nm (Pothitirat and Gritsanapan, 2008). This method has been validated at 243.4, 254.0, 316.4 and 320.0 nm in order to study the effect of wavelength on the validation parameters and to select the optimum wavelength for determination of *G. mangostana* total xanthones.

Regression analysis indicates good linearity of the developed method ($R^2 > 0.999$), and the linearity was not affected by changing the wavelength. Likewise, analysis

Table 3. Accuracy of the UV spectrophotometric method.

Concentration (µg/ml)	Percentage recovery of α-mangostin			
	243.4 nm	254.0 nm	316.4 nm	320.0 nm
10	101.6 ± 0.8	101.7 ± 0.8	102.9 ± 0.9	102.8 ± 0.8
8	100.0 ± 0.4	100.2 ± 0.5	101.5 ± 0.4	101.4 ± 0.5
6	99.4 ± 0.3	99.5 ± 0.3	101.0 ± 0.6	100.8 ± 0.6
4	101.3 ± 0.9	101.5 ± 0.9	103.7 ± 0.6	103.5 ± 0.6
2	101.0 ± 1.5	100.9 ± 1.4	104.1 ± 1.4	104.1 ± 1.5

The results are presented as average percentage recovery ± SD (n = 3).

Table 4. Calibration data of the UV spectrophotometric method.

Wavelength (nm)	*a*	*b*	LOD (µg/ml)	LOQ (µg/ml)	R^2
243.4	0.083 ± 0.001	0.028 ± 0.003	0.101 ± 0.001	0.307 ± 0.002	0.999 ± 0.001
254.0	0.066 ± 0.001	0.022 ± 0.002	0.114 ± 0.001	0.345 ± 0.002	0.999 ± 0.001
316.4	0.056 ± 0.001	0.018 ± 0.002	0.104 ± 0.001	0.315 ± 0.003	0.999 ± 0.001
320.0	0.053 ± 0.001	0.018 ± 0.001	0.124 ± 0.001	0.375 ± 0.002	0.999 ± 0.001

Results are presented as average ± SD (n = 5). The linear regression equation of the reference compound was: $y = ax + b$.

Table 5. Total xanthones content in *G. mangostana* fruit rind extracts.

Extract	Total xanthones content (wt/wt)%			
	243.4 (nm)	254.0 (nm)	316.4 (nm)	320.0 (nm)
Toluene (1st batch)	99.8 ± 0.6	102.8 ± 0.7	99.6 ± 0.7	100.1 ± 0.7
Toluene (2nd batch)	98.9 ± 0.5	101.9 ± 0.6	98.2 ± 0.6	98.7 ± 0.6
Toluene (3rd batch)	97.2 ± 1.3	100.0 ± 1.3	96.6 ± 1.3	97.1 ± 1.3
Methanol	59.9 ± 0.1	60.7 ± 0.1	55.5 ± 0.1	56.0 ± 0.1
Petroleum ether [a]	76.3 ± 0.2	78.9 ± 0.2	72.0 ± 0.2	73.0 ± 0.2
Chloroform [b]	84.3 ± 0.1	88.8 ± 0.1	76.5 ± 0.5	77.3 ± 0.2
Ethyl acetate [c]	79.1 ± 0.4	83.4 ± 0.4	76.5 ± 0.5	77.5 ± 0.5
Methanol [d]	14.6 ± 0.3	14.7 ± 0.2	12.1 ± 0.2	12.1 ± 0.2
75% Ethanol	86.5 ± 0.5	89.2 ± 0.5	81.5 ± 0.4	82.0 ± 0.3

Results are presented as average (wt/wt) percentage ± SD (n = 3). [a to d] refer to sub-extracts of methanolic extract.

of the precision data indicates no significant effect of the wavelength on the %RSD. On the contrary, the wavelength was found to have a significant effect on the method's accuracy and sensitivity. The LOD and LOQ values were in the order of 320 > 254 > 316.4 > 243.4 nm. The highest accuracy was obtained at 243.4 and 254.0 nm as indicated by the average percentage recovery of α-mangostin at these 2 wavelengths (100.6 ± 0.9 and 100.8 ± 0.9)%. The average recovery at 316.4 and 320 nm was (102.5 ± 1.4) and (102.7 ± 1.4)% which indicates lower accuracy. The wavelength was also found to have a significant effect on total xanthones content in *G. mangostana* extracts; however, it can be concluded, based on accuracy data, that measurements of total xanthones at 243.4 and 254.0 nm more closely resemble the actual concentration. Though the highest sensitivity and accuracy were obtained at 243.4 nm, the method can still be used at the other wavelengths since the highest LOD and LOQ were 0.124 and 0.375 µg/ml, and the percentage error was less than 3%.

Our method provides higher sensitivity, with LOD and LOQ values in the range 0.1 to 0.12 and 0.31 to 0.37 µgml, than the method reported previously by Pothitirat and Gritsanapan (2008) (LOD and LOQ were 0.16 and 0.49 µgml), however with similar linearity, precision and accauracy. Another advantage of our method over the exisitng one is the flexibility of the wavelength. It is noteworthy to mention that the developed method was

successfully applied in determination of entrapment efficiency and drug content in 2 drug delivery systems including solid dispersions of α-mangostin and nanoparticles of *G. mangostana* toluene extract (Aisha et al., 2012a).

In conclusion, the developed method provides a cost effective, rapid, and accurate analytical tool for standardization of *G. mangostana* extracts and may also be applied in routine quality control assurance of mangosteen commercial products.

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REFERENCES

Ainsworth EA, Gillespie KM (2007). Estimation of total phenolic content and other oxidation substrates in plant tissues using Folin–Ciocalteu reagent. Nat. Protoc. 2(4):875-877.

Aisha AF, Ismail Z, Abu-Salah KM, Majid AM (2012a). Solid dispersions of alpha-mangostin improve its aqueous solubility through self-assembly of nanomicelles. J. Pharm. Sci. 101(2):815-825.

Aisha AFA, Abu-Salah KM, Ismail Z, Majid AMSA (2012b). α-Mangostin enhances betulinic acid cytotoxicity and inhibits cisplatin cytotoxicity on HCT 116 colorectal carcinoma cells. Molecules 17(3):2939-2954.

Akao Y, Nakagawa Y, Iinuma M, Nozawa Y (2008). Anti-cancer effects of xanthones from pericarps of mangosteen. Int. J. Mol. Sci. 9(3):355-370.

Chen LG, Yang LL, Wang CC (2008). Anti-inflammatory activity of mangostins from *Garcinia mangostana*. Food Chem. Toxicol. 46(2):688-693.

Chen SX, Wan M, Loh BN (1996). Active constituents against HIV-1 protease from *Garcinia mangostana*. Planta Med. 62(4):381-382.

Chen Y, Wang J, Wan D (2010). Determination of total flavonoids in three Sedum crude drugs by UV–Vis spectrophotometry. Pharmacogn. Mag. 6(24):259.

Chomnawang MT, Surassmo S, Wongsariya K, Bunyapraphatsara N (2009). Antibacterial activity of Thai medicinal plants against methicillin-resistant Staphylococcus aureus. Pytotherapy 80(2):102-104.

Cui J, Hu W, Cai Z, Liu Y, Li S, Tao W, Xiang H (2010). New medicinal properties of mangostins: Analgesic activity and pharmacological characterization of active ingredients from the fruit hull of *Garcinia mangostana* L. Pharmacol. Biochem. Behav. 95(2):166-172.

Doi H, Shibata MA, Shibata E, Morimoto J, Akao Y, Iinuma M, Tanigawa N, Otsuki Y (2009). Panaxanthone isolated from pericarp of *Garcinia mangostana* L. suppresses tumor growth and metastasis of a mouse model of mammary cancer. Anticancer Res. 29(7):2485-2495.

Ee GC, Daud S, Taufiq-Yap YH, Ismail NH, Rahmani M (2006). Xanthones from *Garcinia mangostana* (Guttiferae). Nat. Prod. Res. 20(12):1067-1073.

Harborne JB, Baxter H, Moss GP (1999). Phytochemical dictionary: A handbook of bioactive compounds from plants, CRC.

Hussain K, Ismail Z, Sadikun A, Ibrahim P (2008). Analysis of proteins, polysaccharides, glycosaponins contents of Piper sarmentosum Roxb. and anti-TB evaluation for bio-enhancing/interaction effects of leaf extracts with Isoniazid (INH). Nat. Prod. Rad. 7(5):402-408.

ICH (1997). Guidance for Industry, Q2B: Validation of Analytical Procedures: Methodology. USA: International Conference on Harmonisation.

Ji X, Avula B, Khan IA (2007). Quantitative and qualitative determination of six xanthones in *Garcinia mangostana* L. by LC-PDA and LC-ESI-MS. J. Pharm. Biomed. Anal. 43(4):1270-1276.

Jung HA, Su BN, Keller WJ, Mehta RG, Kinghorn AD (2006). Antioxidant xanthones from the pericarp of *Garcinia mangostana* (Mangosteen). J. Agric. Food Chem. 54(6):2077-2082.

Kaomongkolgit R, Jamdee K, Chaisomboon N (2009). Antifungal activity of alpha-mangostin against *Candida albicans*. J. Oral Sci. 51(3):401-406.

Moongkarndi P, Kosem N, Kaslungka S, Luanratana O, Pongpan N, Neungton N (2004). Antiproliferation, antioxidation and induction of apoptosis by *Garcinia mangostana* (mangosteen) on SKBR3 human breast cancer cell line. J. Ethnopharmacol. 90(1):161-6.

Nakatani K, Atsumi M, Arakawa T, Oosawa K, Shimura S, Nakahata N, Ohizumi Y (2002). Inhibitions of histamine release and prostaglandin E2 synthesis by mangosteen, a Thai medicinal plant. Biol. Pharm. Bull. 25(9):1137-1141.

Pedraza-Chaverri J, Cardenas-Rodriguez N, Orozco-Ibarra M, Perez-Rojas JM (2008). Medicinal properties of mangosteen (*Garcinia mangostana*). Food Chem. Toxicol. 46(10):3227-3239.

Peres V, Nagem TJ, de Oliveira FF (2000). Tetraoxygenated naturally occurring xanthones. Phytochemistry 55(7):683-710.

Pothitirat W, Gritsanapan W (2008). Quantitative analysis of total mangostins in *Garcinia mangostana* fruit rind. J. Health Res. 22(4):161-166.

Pothitirat W, Gritsanapan W (2009). HPLC quantitative analysis method for the determination of alpha-mangostin in mangosteen fruit rind extract. Thai J. Agri. Sci. 42(1):7-12.

Sakagami Y, Iinuma M, Piyasena KG, Dharmaratne HR (2005). Antibacterial activity of alpha-mangostin against vancomycin resistant Enterococci (VRE) and synergism with antibiotics. Phytomedicine 12(3):203-8.

Suksamrarn S, Komutiban O, Ratananukul P, Chimnoi N, Lartpornmatulee N, Suksamrarn A (2006). Cytotoxic prenylated xanthones from the young fruit of *Garcinia mangostana*. Chem. Pharm. Bull. 54(3):301-305.

Suksamrarn S, Suwannapoch N, Phakhodee W, Thanuhiranlert J, Ratananukul P, Chimnoi N, Suksamrarn A (2003). Antimycobacterial activity of prenylated xanthones from the fruits of *Garcinia mangostana*. Chem. Pharm. Bull. 51(7):857-859.

Tang YP, Li PG, Kondo M, Ji HP, Kou Y, Ou B (2009). Effect of a mangosteen dietary supplement on human immune function: A randomized, double-blind, placebo-controlled trial. J. Med. Food 12(4):755-763.

Tewtrakul S, Wattanapiromsakul C, Mahabusarakam W (2009). Effects of compounds from *Garcinia mangostana* on inflammatory mediators in RAW264.7 macrophage cells. J. Ethnopharmacol. 121(3):379-382.

Walker EB (2007). HPLC analysis of selected xanthones in mangosteen fruit. J. Sep. Sci. 30(9):1229-1234.

Yodhnu S, Sirikatitham A, Wattanapiromsakul C (2009). Validation of LC for the determination of alpha-mangostin in mangosteen peel extract: a tool for quality assessment of *Garcinia mangostana* L. J. Chromatogr. Sci. 47(3):185-189.

Zhang Y, Song Z, Hao J, Qiu S, Xu Z (2010). Two new prenylated xanthones and a new prenylated tetrahydroxanthone from the pericarp of *Garcinia mangostana*. Pytotherapy 81(6):595-599.