บทความวิจัย

การศึกษาทางเคมีคำนวณของ ^{1}H-NMR และ ^{13}C-NMR สเปกโทรสโกปี ของ α-mangostin, γ-mangostin และ Garcinone D

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บทคัดย่อ

งานวิจัยนี้เป็นศึกษาทางเคมีคำนวณหา chemical shift ของ ^{1}H and ^{13}C NMR ของอนุพันธุ์ของแมงโกสติน ได้แก่ แอลฟา-แมงโกสติน แกมมา-แมงโกสติน และการ์ซิโนน ดี ด้วยระเบียบวิธี WP04, WC04 และ B3LYP โดยใช้ 6-311+G(2d,p) basis set ทั้งนี้พบว่า ค่าที่ได้จากการคำนวณมีความสอดคล้องกับค่าที่มีการรายงานจากการทดลอง การเปรียบเทียบความสามารถในการคำนวณ chemical shift ของ ^{1}H และ ^{13}C NMR ด้วยระเบียบวิธีทั้งสามข้างต้นนั้นได้รายงานในรูปแบบของกราฟแสดงค่าผิดพลาดสัมบูรณ์ต่อช่วงการทำนาย chemical shift ซึ่งพบว่าระเบียบวิธี WP04 และ B3LYP สามารถให้ข้อมูล chemical shift ของ ^{1}H NMR ที่ใกล้เคียงค่าจากการทดลองมากที่สุดในช่วงของ downfield region นอกจากนี้งานวิจัยยังได้รายงานการวิเคราะห์การถดถอยเชิงเส้น (linear regression analysis) เพื่อแสดงความสัมพันธ์ระหว่าง chemical shift ของ ^{1}H และ ^{13}C NMR ที่ได้จากการคำนวณกับข้อมูลที่ได้จากการทดลอง ซึ่งพบว่าระเบียบวิธี WP04, WC04 และ B3LYP มีประสิทธิภาพในการทำนาย chemical shift ของ ^{1}H และ ^{13}C NMR ของอนุพันธ์ของแมงโกสติน คือ แอลฟา-แมงโกสติน แกมมา-แมงโกสติน และการ์ซิโนน ดี ได้เป็นอย่างดี

คำสำคัญ: แอลฟา-แมงโกสติน แกมมา-แมงโกสติน การ์ซิโนน ดี ^{1}H NMR ^{13}C NMR

ภาควิชาเคมี คณะวิทยาศาสตร์ มหาวิทยาลัยศรีนครินทรวิโรฒ

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Computational Study of the ^{1}H-NMR and ^{13}C-NMR Spectroscopy of α-Mangostin, γ-Mangostin and Garcinone D

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ABSTRACT

This work reveals the calculation methods in characterizing ^{1}H and ^{13}C NMR chemical shifts of xanthone derivatives, α-mangostin, γ-mangostin and garcinone D. The calculated chemical shifts were computed at WP04, WC04 and B3LYP density functional levels with the 6-311+G(2d,p) basis set. The calculation values for both ^{1}H and ^{13}C chemical shifts fitted well with experimental values. The performance of the WP04, WC04 and B3LYP functional for ^{1}H and ^{13}C chemical shift prediction is compared to other methods as the plot of absolute errors in the chemical shift prediction. An analysis of errors in ^{1}H chemical shift as a function of the experimental chemical shift values indicates that there are more accurate in the downfield region for both WP04 and B3LYP. The errors show the large significant error in the upfield region for ^{1}H chemical shift. The linear regression comparisons of theoretical and experimental ^{1}H and ^{13}C chemical shift data are also reported in this work. It is found that WP04, WC04 and B3LYP have shown the regression slopes and intercepts most near unity for α-mangostin, γ-mangostin and garcinone D.

Keywords: α-mangostin, γ-mangostin, garcinone D, ^{1}H NMR, ^{13}C NMR

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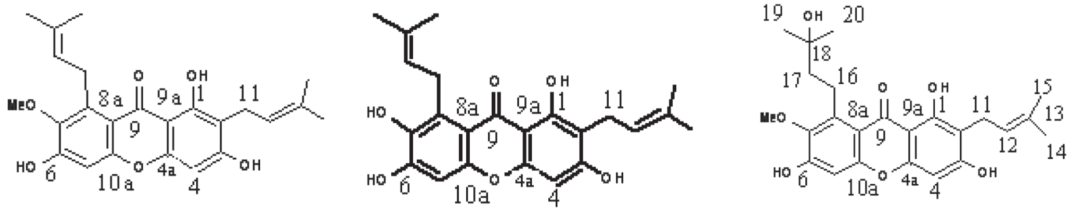
Introduction

Mangosteen, *Garcinia mangostana L.,* is a tropical fruit that is grown in hot, humid climates of Southeast Asia. Today, it has been found that mangosteen contain the compounds known as prenalated xanthone [1,2]. Previous works have suggested that xanthones have anti-cancer effects in test tube study. The molecular structures of prenylated xanthones can be identified using Nuclear Magnetic Resonance (NMR) spectroscopy. Its observation can lead to precious information about molecular geometries.

Recently many calculation models [3-6] have been developed and assisted in the interpretation of the experimental chemical shifts. It has been well known that the use of ab initio calculations is one of the methods could be used to support the interpretation and assignment of NMR spectra.

Miranda et al. [3] investigated the NMR properties based on ab initio and DFT calculations of two naturally occurring xanthones:1,5-dihydroxy-2,3-dimethoxyxanthone and 1-hydroxy-5-methoxy-2,3-methylenedioxyxanthone. NMR properties were calculated at HF and hybrid DFT/HF method, utilizing B3LYP with the 6-31G(d,p) basis set. It is found that the calculated NMR chemical shifts fitted very well to experimental values, except for the hydroxyl proton, because of the hydrogen bonding. Cramer et al. [4-6] have developed two hybrid generalized-gradient approximation density functionals, WC04 and WP04, to predicted ^{13}C and ^{1}H chemical shifts. It is reported that the WC04 and WP04 models provide results more accurate than those from equivalent B3LYP calculation. For ^{13}C chemical shifts, WC04 is more accurate than WP04.

We are interested in the structures of xanthones derivatives which are isolated from the fruit hulls of *Garcinia mangostana L.,* α-mangostin, γ-mangostin, and garcinone D (Figure 1). The structures of these compounds have been examined experimentally using ^{1}H and ^{13}C NMR techniques [1]. In this work we are interested in computing the chemical shifts of α-mangostin, γ-mangostin and garcinone D. The predicted ^{1}H and ^{13}C chemical shifts of α-mangostin, γ-mangostin and garcinone D were examined theoretically using WP04, WC04 and B3LYP methods and will be compared with the available experimental data.

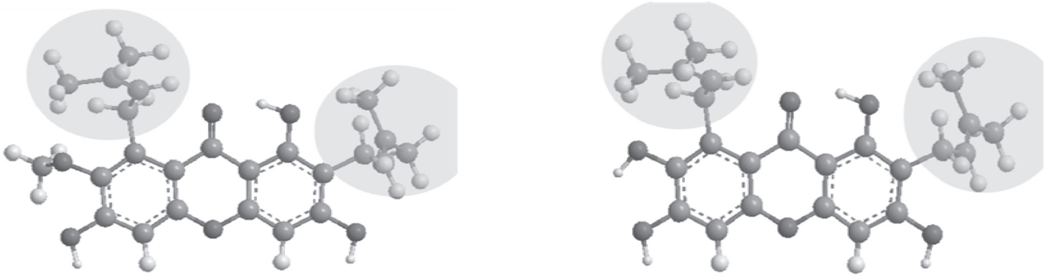


α-mangostin γ-mangostin Garcinone D

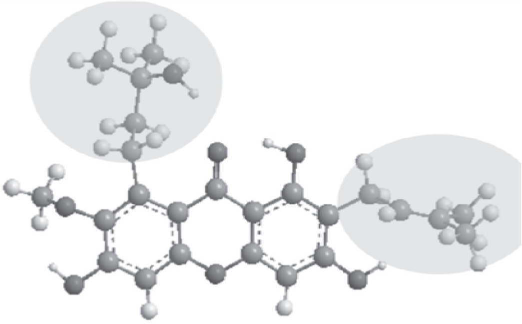
Figure 1 A set of prenylated xanthones, α-mangostin, γ-mangostin and garcinone D investigated in the study.

Materials and Methods

A set of conformers of α-mangostin, γ-mangostin and garcinone D (Figure 2) in gas phase were fully optimized at the Hartree-Fock level with a heteroatom-polarized valence-double-zeta basis set (HF/MIDI!). The ten most stable conformers for each molecule are selected for further study. We examined using three hybrid generalized-gradient approximation density functional, WP04, WC04, and B3LYP for predicting ^{1}H and ^{13}C chemical shifts. For each optimized geometries, ^{1}H and ^{13}C chemical shifts were computed relative to TMS using the gauge including atomic orbital (GIAO) formalism and the basis set 6-311+G(2d,p). Isotropic atomic chemical shifts σ in units of ppm were computed as differences between atomic isotropic shielding in solutes and corresponding reference atoms in tetramethylsilane (TMS) for each family. When more than a single conformer is considered, σ values are reported as an average value of conformers. Theoretical chemical shift data were evaluated relative to experiment based on linear correlation (R^2) in order to assess the ability of the various approaches. The calculations were carried out with Gaussian 03 [7].



a) α-mangostin b) γ-mangostin



c) garcinone D

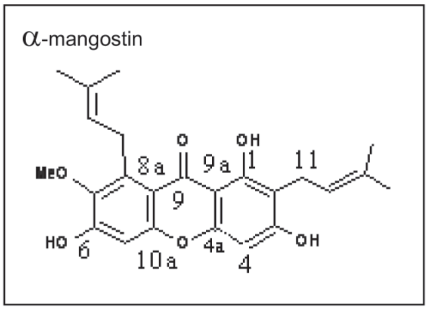
Figure 2 A model for each conformer of a) α-mangostin, b) γ-mangostin and c) garcinone D is different in geometries of groups of the atoms highlighted.

Results

α-mangostin

All calculations used HF/MIDI! geometries. The ^{1}H chemical shifts for α-mangostin were computed at WP04/6-311+G(2d,p) and B3LYP/6-311+G(2d,p). And the ^{13}C chemical shifts were computed at WC04/6-311+G(2d,p) and B3LYP/6-311+G(2d,p). The chemical shifts over a set of conformers were averaged and compared to experimental ^{1}H and ^{13}C NMR data (Table 1). The atomic labels related to the structure of α-mangostin represent the position of proton and carbon which are considered. The performance of the optimized WP04, WC04 and B3LYP functional for ^{1}H and ^{13}C chemical shift prediction is compared to other methods as shown in the plot of absolute errors in the chemical shift prediction (Figures 3 and 4). From the comparison of ^{1}H NMR chemical shifts, it is found that the calculation values obtained from WP04, and B3LYP are in good agreements with experimental values, except for hydroxyl proton. They are accurate to within 0.2 ppm for chemical shift less than 4 ppm. For ^{13}C NMR chemical shifts, the accuracies for both methods are within 12 ppm.

Table 1 Chemical shift prediction of α-mangostin calculated from (method)/6-311+G(2d,p)//HF/MIDI!.



Atomic label	^{1}H (δ)			^{13}C (δ)		
	WP04	B3LYP	experiment[1]	WC04	B3LYP	experiment[1]
1	12.86	13.07	13.71	162.16	167.02	159.8
2				103.07	116.59	109.6
3				160.47	165.13	162.3
4	5.71	5.81	6.33	80.35	92.06	92.2
4a				155.65	160.15	154.1
5	6.16	6.29	6.78	90.70	101.68	101.8
6				154.84	160.88	154.6
7				134.12	148.35	143.3
7OMe	3.60	3.76	3.68	54.11	61.28	60.1
8				142.58	147.87	136.3
8a				102.59	116.57	109.8
9				179.91	184.08	181.29
10a				154.70	160.79	156.9
11	3.29	3.37	3.2	20.14	25.28	20.9
12	5.72	6.01	5.15	119.73	127.14	122.4
13				129.69	140.46	130.3
14	1.79	1.89	1.71	17.10	19.17	17.67
15	1.55	1.64	1.6	26.47	28.24	25.54
16	4.16	4.28	3.99	23.88	30.27	25.4
17	5.45	5.70	5.15	119.38	128.37	123.6
18				131.41	141.12	130.3
19	1.54	1.63	1.75	17.85	19.69	17.97
20	1.80	1.89	1.6	26.57	28.39	25.69

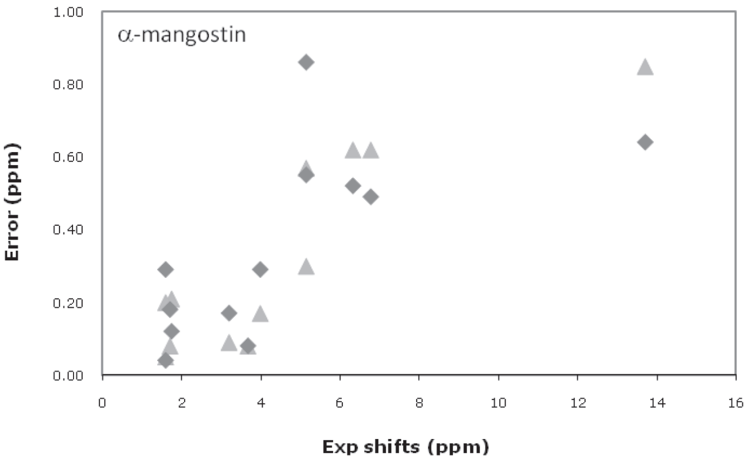


Figure 3 Absolute errors in 12 ^{1}H chemical shift predictions for WP04 (triangles) and B3LYP (diamond) as a function of chemical shift.

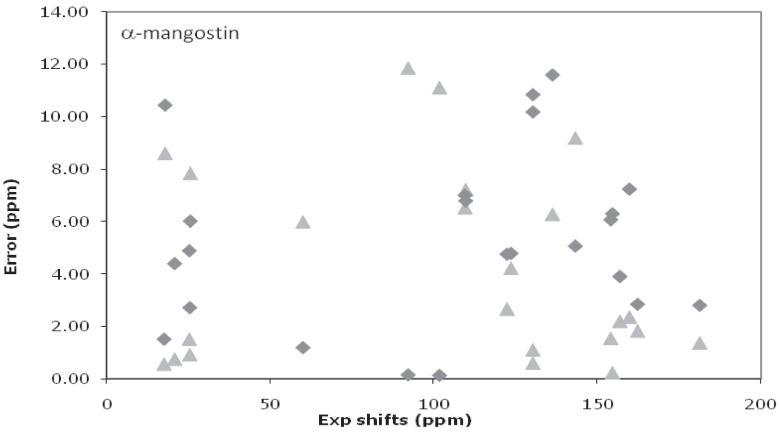
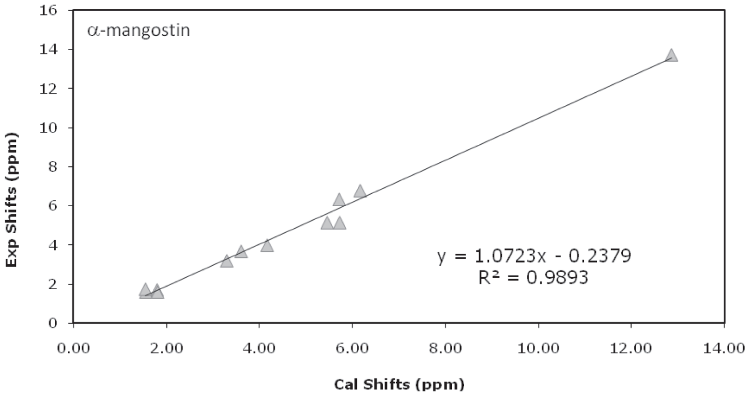


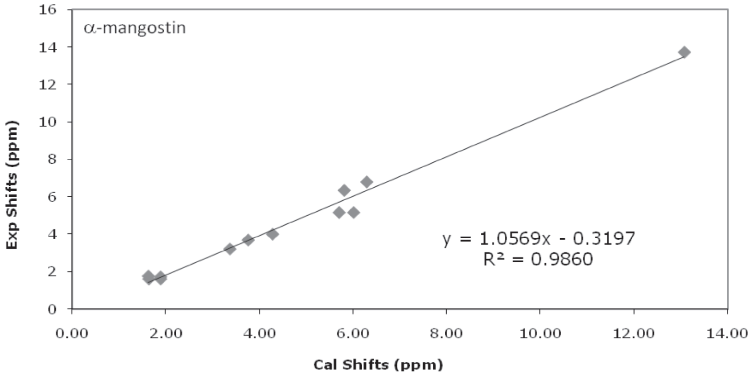
Figure 4 Absolute errors in 23 ^{13}C chemical shift predictions for WC04 (triangles) and B3LYP (diamonds) as a function of chemical shift.

An analysis of errors in ^{1}H chemical shift as a function of the experimental chemical shift values indicates that the optimized functionals are more accurate especially in the downfield region. The errors show the large significant error in the upfield region. The calculation results show the similarity of the chemical shift at WP04 and B3LYP calculation. For ^{13}C, the errors are in various ranges over an observed region. Overall the calculated absolute values are within the range of about 16% and 13% compared to the experimental results for ^{1}H and ^{13}C respectively. We also have compared the results with the calculated values taken from the global minimum energy conformer. It is interesting to note that the average chemical shift values are similar to the chemical shift values calculated from the global minima structure.

The linear regression comparisons of theoretical and experimental ^{1}H and ^{13}C chemical shift data are represented in Figures 5 and 6. It is found that WP04, B3LYP and WC04 have shown the regression slopes and intercepts close to a unity for ^{1}H and ^{13}C. From the plot between the predicted versus observed ^{1}H chemical shift, R^2 equals to 0.9893 and 0.9860 for WP04 and B3LYP, respectively. The better linear relationships are shown in the plot between the predicted versus observed ^{13}C chemical shift. The R^2 value for WC04 is 0.9915 and for B3LYP is 0.9954.

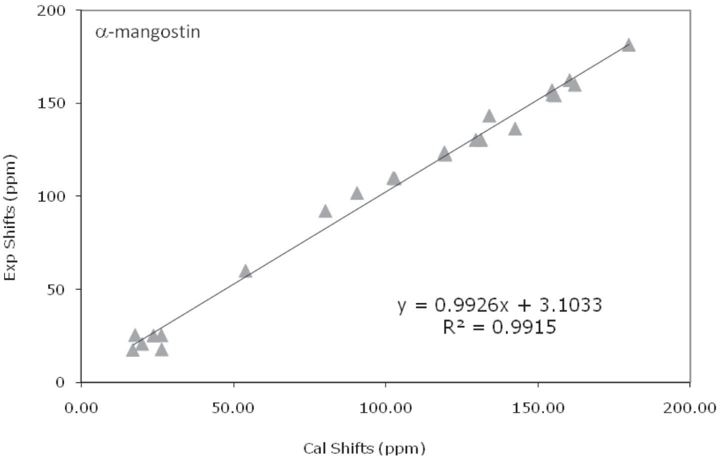


a) WP04

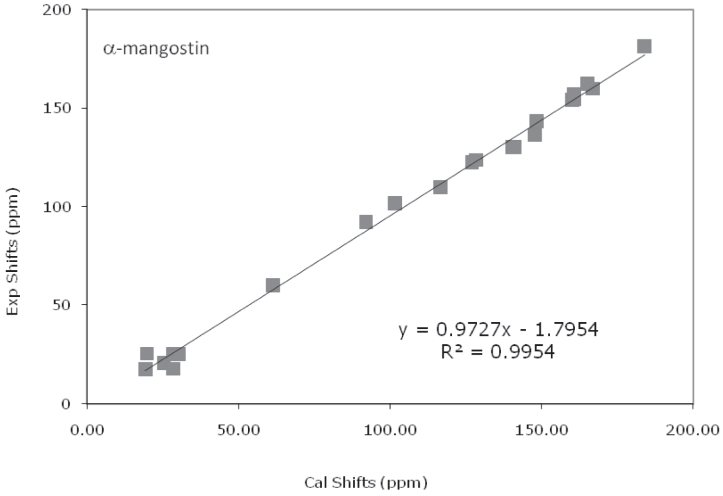


b) B3LYP

Figure 5 The predicted vs. observed ^{1}H chemical shift for a) WP04 (triangles) with $R^2 = 0.9893$ and for b) B3LYP (diamonds) with $R^2 = 0.9860$.



a) WC04



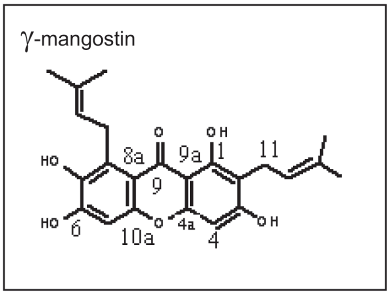
b) B3LYP

Figure 6 The predicted vs observed ^{13}C chemical shift for a) WC04 (triangles) with $R^2 = 0.9915$ and for b) B3LYP (diamonds) with $R^2 = 0.9954$.

γ-mangostin and garcinone D

To further the use of WP04, WC04, and B3LYP methods in order to predict the ^{1}H and ^{13}C chemical shifts for a family of prenylated xanthones, we examined the calculated ^{1}H and ^{13}C chemical shift for a set of conformers of another two molecules, γ-mangostin and garcinone D. The chemical shifts were computed at WP04/6-311+G(2d,p)//HF/MIDI! and B3LYP/6-311+G(2d,p)//HF/MIDI! for ^{1}H chemical shifts. The WC04/6-311+G(2d,p)//HF/MIDI! and B3LYP/6-311+G(2d,p)//HF/MIDI! are used for computing ^{13}C chemical shifts. The chemical shifts over a set of conformers for γ-mangostin and garcinone D were averaged and compared to their experimental ^{13}C and ^{1}H NMR data [1] which are shown in Tables 2 and 3, respectively. The performance of the optimized WP04, B3LYP and WC04 functional for ^{1}H and ^{13}C chemical shift prediction are represented in Figures 7 and 8 for γ-mangostin and Figures 11 and 12 for garcinone D. The linear regression comparisons of theoretical and experimental ^{1}H and ^{13}C chemical shift data for γ-mangostin (Figures 9 and 10) and garcinone D (Figures 13 and 14) are also shown here.

Table 2 Chemical shift prediction of γ-mangostin calculated from (method)/6-311+G(2d,p)//HF/MIDI!.



Atomic label	**^{1}H (δ)**			**^{13}C (δ)**		
	WP04	**B3LYP**	**experiment** [1]	**WC04**	**B3LYP**	**experiment** [1]
1	12.86	13.08	13.88	162.31	173.00	159.8
2				103.10	122.59	109.3
3				160.47	170.97	162
4	5.70	5.79	6.31	80.05	97.73	92
4a				155.69	165.92	151.9
5	6.19	6.32	6.73	89.96	105.54	100.1
6				145.76	157.60	152.5
7				132.47	150.71	140.9
8				133.40	144.57	127.6
8a				103.77	123.01	109.9
9				180.77	190.95	181.6
9a				93.86	113.87	101.9
10a				150.64	163.27	154.2
11	3.29	3.37	3.2	20.22	31.28	20.9
12	5.72	6.01	5.16	119.67	133.10	122.6
13				129.52	146.16	130.3
14	1.77	1.88	1.71	17.06	24.94	17.71
15	1.53	1.62	1.6	26.43	34.14	25.51
16	4.27	4.42	4.02	23.21	35.26	25.3
17	5.85	6.13	5.16	118.50	132.97	123.7
18				131.35	147.40	130
19	1.56	1.65	1.75	26.67	34.41	18.09
20	1.85	1.95	1.6	17.37	25.49	25.65

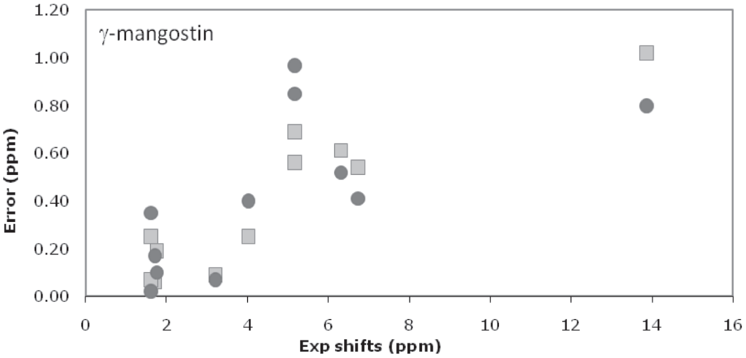


Figure 7 Absolute errors in 11 ^{1}H chemical shift predictions for WP04 (rectangulars) and B3LYP (cycles) as a function of chemical shift.

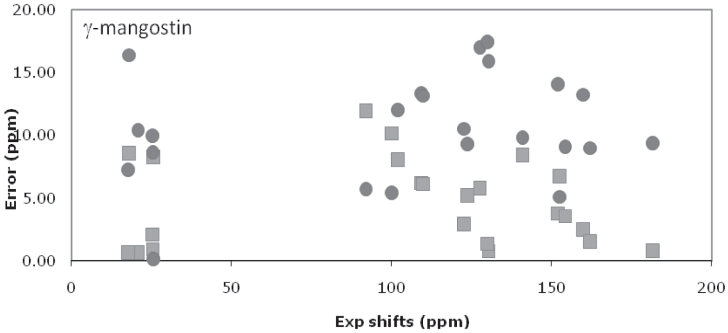
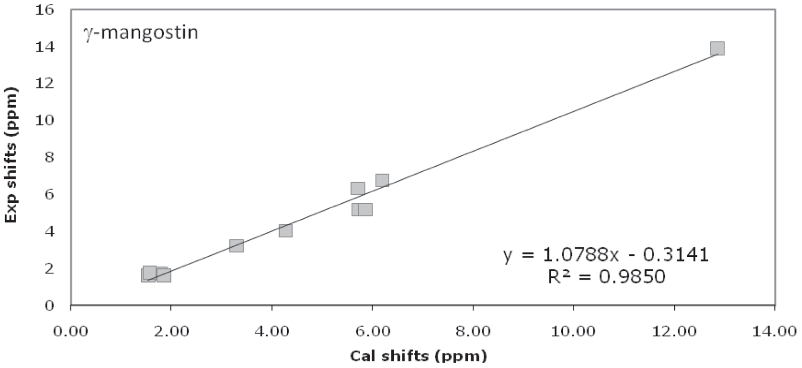
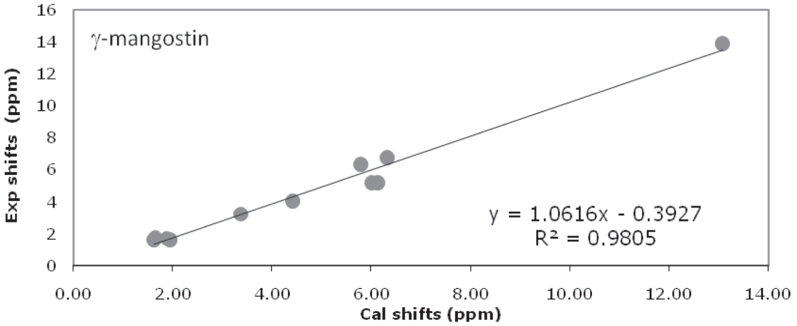


Figure 8 Absolute errors in 23 ^{13}C chemical shift predictions for WC04 (rectangulars) and B3LYP (cycles) as a function of chemical shift.

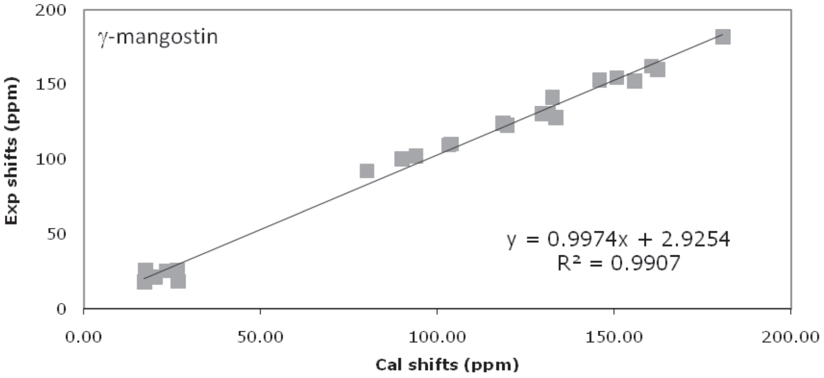


a) WP04

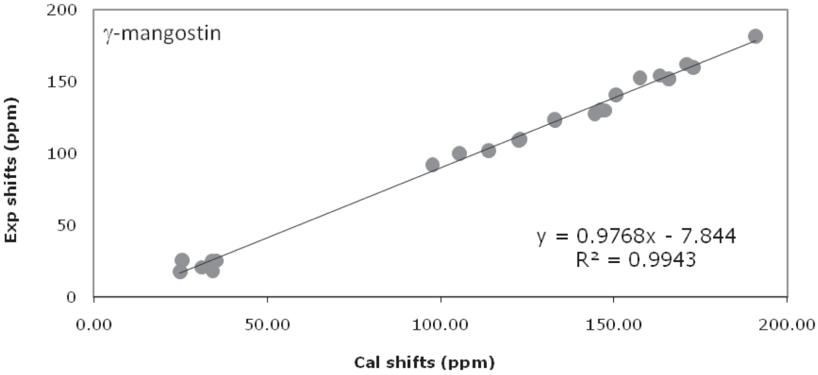


b) B3LYP

Figure 9 The predicted vs observed ^{1}H chemical shift for a) WP04 (rectangulars) with $R^2 = 0.9850$ and for b) B3LYP (cycles) with $R^2 = 0.9805$.



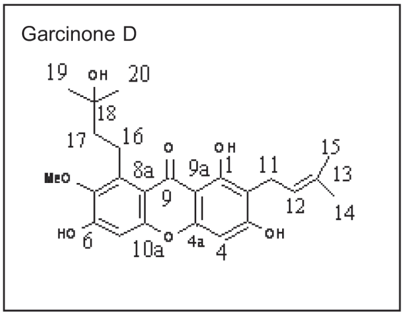
a) WC04



b) B3LYP

Figure 10 The predicted vs observed ^{13}C chemical shift for a) WC04 (rectangulars) with $R^2 = 0.9907$ and for b) B3LYP (cycles) with $R^2 = 0.9943$.

Table 3 Chemical shift prediction of garcinone D calculated from (method)/6-311+G(2d,p)//HF/MIDI!.



Atomic label	^{1}H (δ)			^{13}C (δ)		
	WP04	**B3LYP**	**experiment** [1]	**WC04**	**B3LYP**	**experiment** [1]
1	12.86	13.08	13.88	162.31	173.00	159.8
1	12.71	12.92	13.81	162.48	167.02	161.67
2				100.05	114.05	111.02
3				162.37	166.88	162.98
4	6.06	6.13	6.39	82.16	94.04	93.09
4a				156.11	160.66	155.69
5	6.60	6.7	6.80	91.45	102.16	102.48
6				155.32	160.63	157.4
7				133.35	147.36	144.41
7-Ome	3.64	3.78	3.84	55.24	62.56	61.59
8				141.84	147.34	140.06
8a				101.53	115.35	111.99
9				180.63	184.59	182.81
9a				92.04	106.84	103.59
10a				155.56	161.34	156.28
11	3.38	3.46	3.33	19.59	24.74	21.95
12	5.46	5.71	5.27	120.89	128.19	123.44
13				131.13	141.89	131.35
14	1.74	1.83	1.77	16.86	18.59	25.86
15	1.62	1.7	1.63	26.31	28.26	17.87
16	3.47	3.54	3.47	21.48	26.35	23.21
17	1.69	1.74	1.72	42.02	48.18	45.64
18				61.54	75.83	70.53
19	1.16	1.19	1.30	27.71	28.79	29.8
20	1.13	1.17	1.30	30.44	31.56	29.8

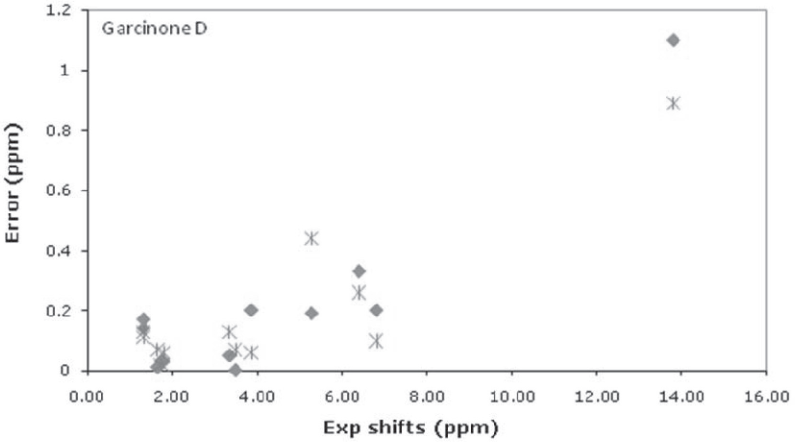


Figure 11 Absolute errors in 12 ^{1}H chemical shift predictions for WP04 (diamonds) and B3LYP (stars) as a function of chemical shift.

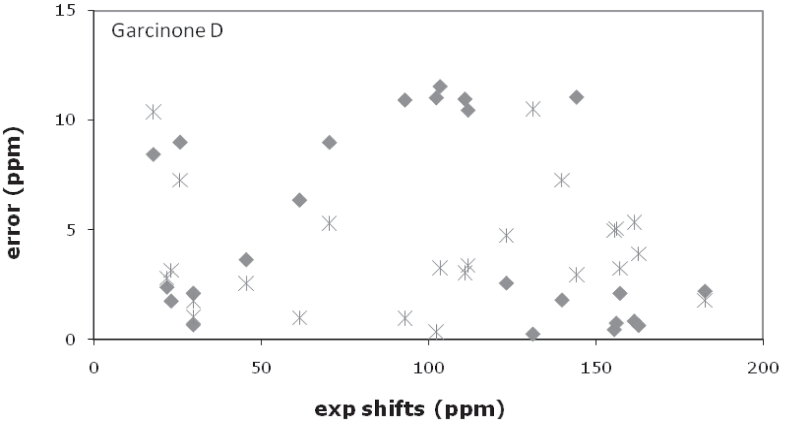
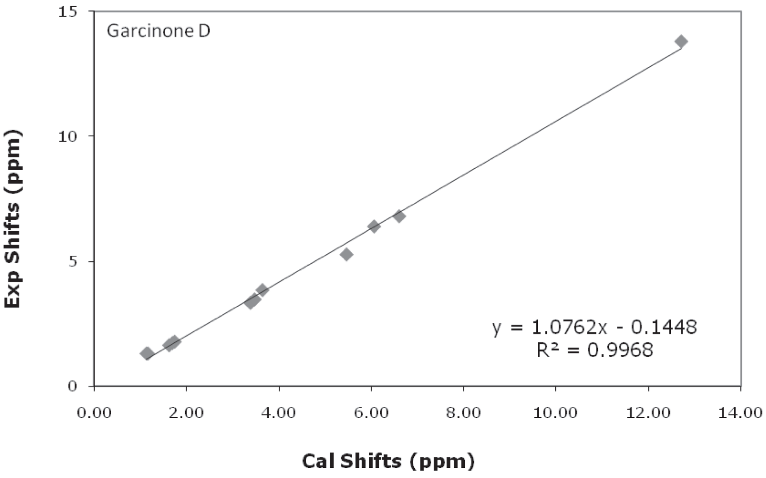
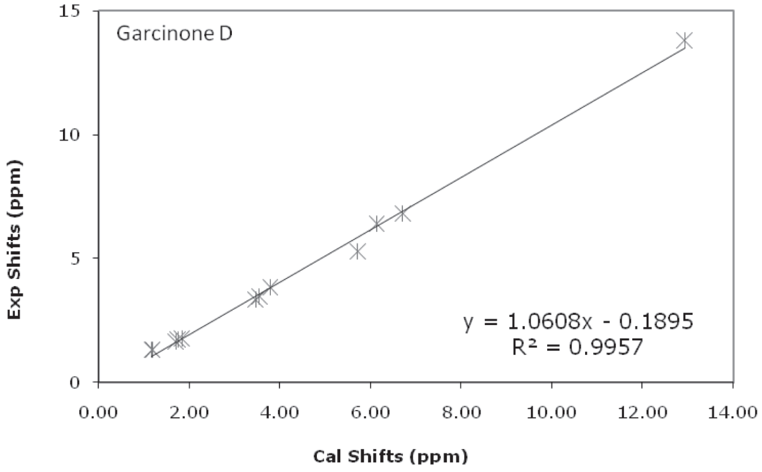


Figure 12 Absolute errors in 24 ^{13}C chemical shift predictions for WC04 (diamonds) and B3LYP (stars) as a function of chemical shift.

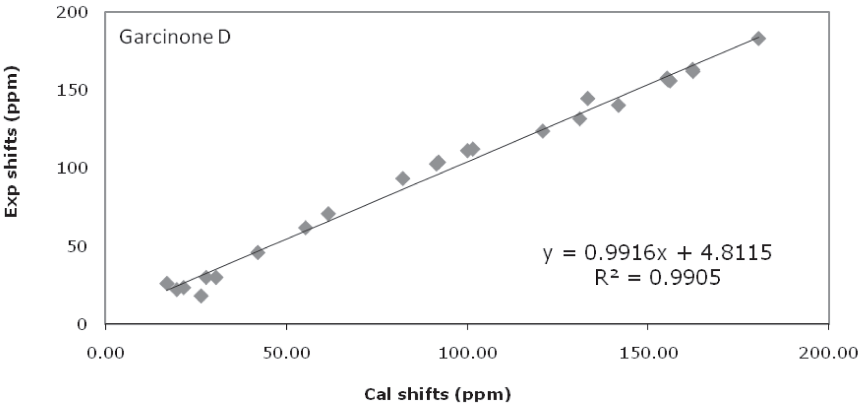


a) WP04

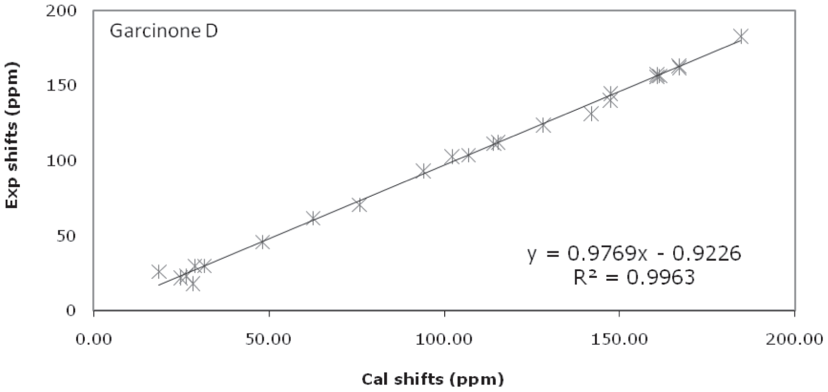


b) B3LYP

Figure 13 The predicted vs observed ^{1}H chemical shift for a) WP04 (diamonds) with $R^2 = 0.9968$ and for b) B3LYP (diamonds) with $R^2 = 0.9957$.



a) WC04



b) B3LYP

Figure 14 The predicted vs observed ^{13}C chemical shift for a) WC04 (diamonds) with $R^2 = 0.9905$ and for b) B3LYP (diamonds) with $R^2 = 0.9963$.

The calculated absolute values of ^{1}H and ^{13}C chemical shifts for both families are shown in the same ranges as for α-mangostin. By comparison the calculating ^{1}H shift for both γ-mangostin and garcinone D with the experimental data, it is found that there are small errors shown in a downfield for both WP04 and B3LYP calculation. For ^{13}C chemical shifts, the calculated values are similar for both obtained from WC04 and B3LYP methods. Table 4 shows the linear regression for each method calculated over a set of α-mangostin, γ-mangostin and garcinone D. The WP04, B3LYP and WC04 methods have shown the regression slopes and intercepts most near unity for these three molecules.

Table 4 The linear regression for each method calculated over a set of α-mangostin, γ-mangostin and garcinone D.

Method	**α-mangostin**		**γ-mangostin**		**garcinone D**	
	^{1}H	**^{13}C**	**^{1}H**	**^{13}C**	**^{1}H**	**^{13}C**
WP04	0.9893	-	0.9850	-	0.9968	-
B3LYP	0.9860	0.9954	0.9805	0.9943	0.9957	0.9963
WC04	-	0.9915	-	0.9907	-	0.9905

Conclusion and Discussion

Density functional models can successfully aid in the assignment of ^{1}H and ^{13}C chemical shifts for α-mangostin, γ-mangostin, and garcinone D. For ^{1}H chemical shift, the WP04 model shows the accuracy in the prediction of the chemical shift the same as the B3LYP model. For ^{13}C chemical shift prediction, the B3LYP model shows the better results than the other. However there are some differences in accuracy for these three models, the correlation coefficients (R^2) are in acceptable ranges. It is believed that these models can be used to predict the ^{1}H chemical shift of other prenylated xanthones.

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