

PERFORMANCE OF SONIC ASSISTED SOLVENT MIMICRY USING WATER
ON GINGER BIOACTIVE COMPOUNDS EXTRACTION

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Specially dedicated to my husband, Syed Ridhwan Bin Syed Hamid, my children,
Syed Ahmad Zafri, Syarifah Amna Zahra and also my other family members.

With all love and gratitude.

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ABSTRACT

The uses of water in subcritical conditions have several drawbacks, which include safety features, increase of production costs and possible degradation of bioactive compounds due to high operating conditions. To overcome these problems, sonic energy and entrainer were used as external interventions in decreasing the dielectric constant of water at milder operating conditions. The extraction efficiencies were compared and related to the solubility curve of ginger bioactive compounds in hot water, which was calculated using conductor-like screening model for real solvents (COSMO-RS). A sonic-assisted water extraction (SAWE) prototype with 1.5 liter capacity was designed and fabricated using a high frequency sonication probe (800kHz, Shinka Industry Co., Japan). The effect of low (28 kHz) and high (800 kHz) frequencies of sonication in the extraction of four major ginger bioactive compounds (6-, 8-, 10-gingerol, and 6-shogaol) were compared. Six parameters were studied, which were mean particle size (MPS, mm), time of extraction (15 to 60 minutes), applied power (40 to 80 Watt), sample to solvent ratio (w/v), temperature of extraction (25 to 45 °C), and the percentage of entrainer (5 to 15 %, v/v). The optimum conditions for the high frequency SAWE prototype were MPS 0.89-1.77mm, 45 minutes, 40W applied power, 1:30 (w/v) and 45 minutes. The concentration and recovery of 6-gingerol from the high frequency of the SAWE prototype was 2.69 times higher than the low frequency of SAWE at the optimum conditions. The performance of high frequency SAWE was improved with a pump around process with distilled water ($13.0681 \pm 0.0210 \text{mg/g}$), which was slightly higher than with 10% ethanol as the solvent in the batch system ($12.9733 \pm 0.3186 \text{mg/g}$) for 6-gingerol extract. It was found that milder operating conditions can be achieved using high frequency SAWE compared to subcritical water extraction (135- 200°C, 0.1 MPa).

ABSTRAK

Penggunaan air dalam keadaan subgenting menyebabkan beberapa isu yang melibatkan hal-hal keselamatan, kenaikan kos pengeluaran, dan degradasi sebatian bioaktif yang disebabkan oleh keadaan operasi yang tinggi. Oleh itu, tenaga sonik dan pelarut organik digunakan sebagai intervensi luar untuk menurunkan nilai pemalar dielektrik air dalam keadaan kendalian yang lebih sederhana. Kecekapan pengekstrakan telah dibandingkan dan dikaitkan dengan lengkung kelarutan sebatian bioaktif halia dengan menggunakan model saringan seperti konduktor untuk pelarut sebenar (COSMO-RS). Prototaip pengekstrakan air yang dibantu oleh tenaga sonik (SAWE) dengan kapasiti 1.5 liter telah direka dan dicipta dengan menggunakan tenaga sonik frekuensi tinggi. Kesan frekuensi rendah (28 kHz) dan frekuensi tinggi (800 kHz) tenaga sonik terhadap pengekstrakan empat sebatian bioaktif halia bioaktif yang utama (6-, 8-, 10-gingerol, dan 6-shogaol) telah dibandingkan. Enam parameter yang dikaji ialah saiz zarah purata (MPS, mm), masa pengekstrakan (15 hingga 60 minit), kuasa dikenakan (40 hingga 80 Watt), nisbah sampel kepada pelarut (w/v), suhu pengekstrakan (25 hingga 45°C), dan peratusan pelarut organik (5 hingga 15%, v/v). Keadaan optimum untuk frekuensi tinggi prototaip SAWE ialah MPS 0.89 - 1.77 mm, 45 minit, 40 Watt kuasa dikenakan, 1:30 (w/v), dan suhu 45°C. Kepekatan dan pemulihan 6-gingerol daripada frekuensi tinggi prototaip SAWE ialah 2.69 kali ganda lebih tinggi daripada frekuensi rendah SAWE pada keadaan optimum. Prestasi frekuensi tinggi SAWE dipertingkatkan dengan menggunakan proses pam kitar dengan air suling (13.0681 ± 0.0210 mg/g), iaitu lebih tinggi berbanding 10% etanol sebagai pelarut dalam sistem kelompok (12.9733 ± 0.3186 mg/g) untuk ekstrak 6-gingerol. Didapati bahawa keadaan kendalian yang lebih sederhana boleh dicapai dengan menggunakan frekuensi tinggi SAWE berbanding pengekstrakan air subgenting (135- 200°C, 0.1 MPa).

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LIST OF ABBREVIATIONS

AAD	-	absolute average deviation
ANOVA	-	Analysis of Variance
COSMO-RS	-	conductor-like screening model for real solvents
DPPH	-	1,1'-Diphenyl-2-picrylhydrazyl
GCMs	-	group contribution methods
HCW	-	Hot compressed water
HPLC	-	High performance liquid chromatography
H bond	-	Hydrogen bond
IAPWS.	-	The international association for the properties of water and steam
LLE	-	liquid-liquid equilibrium
MPS	-	Mean particles size
NRTL	-	Non-Random Two-Liquid
PDA	-	Photo-diode Array Detector
PHWE	-	pressurised hot water extraction
REDOX	-	reduction and oxidation
SAWE	-	Sonic Assisted Water Extraction
SCCO ₂	-	supercritical carbon dioxide
SCW	-	Subcritical water
SEM	-	Scanning Electron Microscopy
SFE	-	supercritical fluid extraction
UAE	-	Ultrasonic assisted extraction
US\$	-	United States dollar
T _{cr}	-	Critical temperature

LIST OF SYMBOLS

A_b	-	Bottom area of the reaction vessel
C_p	-	Heat capacity
D	-	Diffusion coefficient
D_N	-	Molecular diffusion coefficient
D_U	-	Eddy diffusion coefficient
ϵ, ϵ'	-	Dielectric constant
ϵ''	-	Loss factor
f	-	Frequency
f^{ref}	-	Fugacity at the reference state
G_{ij}	-	Excess Gibbs energy for two liquid interactions in binary mixtures
I	-	Ultrasonic intensity
m	-	Liquid mass in the vessel
σ	-	Sigma (σ -profiles)
ρ	-	Density of the medium
$P_{a,\text{max}}$	-	Maximum amplitude of the wave
P_o	-	Average power
P_a	-	Acoustic pressure
P_h	-	Hydrostatic pressure
Π	-	Power density
r^2	-	Coefficient of determination
R_0	-	Bubble average diameter
S_{upper}	-	Upper sieve size
S_{lower}	-	Lower sieve size

T	-	Temperature
t	-	Time
μ	-	Mean
W	-	Weight of mixture of ethanol and ginger particles
W_f	-	Weight of the round bottom flask after purification process
W_b	-	Weight of the round bottom flask before purification process
W_s	-	Weight of the sample matrix
W_i	-	Initial weight of volumetric flask
w/v	-	Weight per volume
v/v	-	Volume per volume
v	-	Velocity of propagation
x_1	-	The lowest measurement
x_{bl}	-	Mean of the blank measurement
x_i^I, x_i^{II}	-	Mole fraction of liquid phase I and II for species i
γ	-	Activity coefficient
$Y_{\%}$	-	Overall yield percentage, % (w/w)

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CHAPTER 1

INTRODUCTION

1.1 Introduction

Recently, with the global increase in environmental awareness and intensifying health and safety consciousness in society, scientists and engineers are looking for alternative environmentally friendly processes (Chemat *et al.*, 2015). This includes replacing traditional toxic solvents in the extraction process, such as hexane or methanol. Solvents with a high level of toxicity are not recommended in food related industries, as the residue will have a long-term effect on users. When using these kinds of solvents, disposal as well as workers safety requirements are the major issue and concern. Due to these problems, the uses of environmentally friendly methods which use green solvents such as pressurised hot water extraction and supercritical fluid extraction have acquired attention where functional bioactives related extracts are concerned. Pressurised hot water extraction uses water as the solvent while supercritical fluid extractions commonly use carbon dioxide at critical conditions (31.3 °C and 7.28MPa). The utilization of those green technology and environmental friendly solvents are intended to supplant the toxic solvents used in the conventional extraction process.

The “Green Era” of chemistry, especially solvents, started almost 19 years ago (Kislik, 2012). As a result, four types of green solvent have been developed, which are superheated water, supercritical fluids, ionic liquids and renewable organics. Those solvents have their advantages and disadvantages. For instance, renewable organics can reduce the toxicity and environmental risks but it still possesses flammability and low transparency in some wavelength ranges. As for ionic liquid, even if it used the low temperature melting salt, low vapour pressure and varied polarity as a function of cations and anions, it still caused the toxicity from some anions or cations and green synthesis is not always possible. The advantages of supercritical fluids are that it has the average properties between gas and liquids, for instance, the polarity of supercritical carbon dioxide (SCCO₂) is low and it also has easy pre-concentration. Meanwhile, the disadvantages of supercritical fluids are the equipment used is expensive and need careful control of temperature and pressure. The benefits of superheated water include the polarity are modifiable with temperature and pressure, environmental friendly and green solvent, cheaper alternative with no toxicity. However, the drawbacks of superheated water are that it uses high temperature and pressure, which causes additional expended energy, and also precipitation after cooling problem (Kislik, 2012).

Out of this four solvents, water is the most abundant, safe, cheap and environmentally friendly pure solvent. Because of this, water seems to be of crucial importance for further development of the chemistry of subcritical and supercritical fluids (Galkin and Lunin, 2005). Water based extraction at high temperature and pressure is gaining popularity for its use as a solvent. Subcritical water extraction, hot compressed water extraction, pressurised liquid extraction or accelerated solvent extraction using water are the other terms of pressurised hot water extraction (Plaza and Turner, 2015; Mukhopadhyay and Panja, 2010). Among these terms, subcritical water is most commonly used and preferred (Kislik, 2012). Subcritical water encompasses wider operating conditions compared to hot compressed water. Subcritical water is liquid water below its critical point 374 °C and 22.1 MPa at all pressure conditions and may operate below its normal boiling point of 100 °C and atmospheric pressure, 0.1MPa (Morad *et al.*, 2011). While hot compressed water usually used below its boiling point of 100 °C (Sarip *et al.*, 2014).

The ability of subcritical water extraction in the selective extraction of different ginger bioactive compounds at different temperature was proven. Among the bioactive compounds in the ginger oleoresin extracted, 6-gingerol was dominant at 135°C, while 6-shogaol and 10-gingerol appeared significantly at 165°C and 200°C, respectively (Sarip, 2012). This shows that the properties of water has high potential to be discovered, for example, the dielectric constant of water since it has a wide range of polarity at different temperatures and pressures. The equilibrium and transport properties, such as solubility and diffusion coefficient, are very useful for process design (Higashi *et al.*, 2001). In order to establish the feasibility of an extraction, the solubility of a substance is a fundamental property (Carr *et al.*, 2011).

Milder operating conditions such as ultrasonic assisted extraction (UAE) and usage of water as a solvent in the herbal extraction are the focus of this study in order to meet the green technology requirement. Ultrasound-assisted extraction or ultrasonic extraction has been extensively explored in the last two decades as an efficient extraction method in the food and pharmaceutical industries, as indicated by the exponential increase in papers published in this area (Esclapez *et al.*, 2011). The sonication of ultrasound energy creates cavitation, which can accelerate and enhance the mass transfer process in the extraction at low temperature and pressure to produce high quality food extracts economically.

1.2 Problem Statement

Nowadays, consumer interest in functional foods that include nutrients to help promote health and prevent disease has increased. Owing to this situation, it is very useful and important to have methods of processing food that can preserve the nutritional, sensorial quality and bioactivity of their constituents. Chemical and physical changes of some nutrients, which may impair the organoleptic properties and reduce the content or bioavailability, may increase during the heat processing,

particularly under severe conditions. Apart from reducing the heat or temperature of the process, there are also requirements to reduce the use of toxic solvents that will affect human safety and environment in extraction.

Although subcritical water extraction only used water as the solvent, there are some drawbacks especially the use of high pressure and temperature conditions during the extraction process. These conditions not only require higher investment cost in the pressure vessels but also additional heating cost is needed during the process (Filly *et. al.*, 2016). Moreover, temperature sensitive compounds would be degraded at high temperatures (Sarip, 2012; Soria and Villamiel, 2010). The possibility is therefore manipulating water properties, such that it can mimic other solvents. The use of external interventions, such as sonic energy effect and entrainer can be used to achieve the target properties that will influence the extraction efficiency of water, namely, the dielectric constant. The outcome of the findings makes water very attractive as a solvent or for reducing the use of toxic solvents, and, furthermore, the application can be easily extended for other uses. This technology will not only use lower temperature and normal atmospheric pressure but can also be conducted more safely.

UAE is environmentally friendly, safer and has been proven in the lab-scale as well in the industrial applications for pharmaceutical products (Farooq, 2012). It is a big challenge in developing the green technologies by using water as a solvent and ultrasonic energy as the external intervention in manipulating the properties of water to mimic the organic solvents. However, to our best knowledge, there are no detailed studies reported on the effect of sonication to the solvent properties. Therefore, the effect of sonication to the water property especially dielectric constant of water is important to study.

The main objective of this study is to manipulate the properties of water and study the efficiency of extraction using sonic energy and entrainer. The main property of water that affects the extraction process and which is considered in this

study is dielectric constant and it relates to the solubility for extraction efficiency. The outcome makes the use of water as a solvent appealing as it simultaneously reduces the use of toxic solvents, and, furthermore, the application can be easily extended for other fields of usage. The effectiveness of using sonic energy in water as a solvent was demonstrated through the extraction of ginger oleoresin. It covers the fundamental studies on sonic-assisted extraction mechanisms including the kinetics, mass transfer, thermodynamics, sonochemistry and selectivity.

1.3 Research Objectives

There are four objectives identified in this study:-

1. To design and fabricate high frequency sonic assisted water extractor (SAWE) prototype.
2. To conduct and compare sonic assisted ginger compounds extraction using water at low and high frequencies.
3. To analyse ginger bioactive compounds extracted using High Performance Liquid Chromatography (HPLC) and compare the efficiencies of both frequencies.
4. To determine the relationship of extraction efficiency between experimental methods of high frequency of Sonic Assisted Water Extractor (SAWE) prototype with the benchmark of solubility prediction using conductor-like screening model for real solvents (COSMO-RS) calculations.

1.4 Scope of the Study

Ginger was used as the reference of herbal extraction using the sonic assisted water extractor (SAWE) prototype since extensive studies have been conducted on ginger extraction regarding the extraction methods, applications and the physicochemical properties. This study was done in Iwai Lab, Department of Chemical Engineering, Kyushu University, Japan and SHIZEN i-kohza (formerly known as CLEAR i-kohza), Malaysia-Japan International Institute of Technology (MJIIT), Universiti Teknologi Malaysia (UTM) Kuala Lumpur. The study done in Iwai lab was focused on the solubility prediction of ginger bioactive compounds in hot water (binary system) and with entrainer (ternary system). The prediction was done using conductor-like screening model for real solvents (COSMO-RS) calculations during the three months attachment in Iwai Lab.

In the meantime, the lab scale of Sonic Assisted Water Extractor (SAWE) was designed and fabricated in Shizen i-kohza, UTM KL using high frequency (800 kHz) of ultrasonic probe. The performance of high frequency SAWE was compared to low frequency (28kHz) of SAWE using ultrasonic bath. The parameters that affected the sonic assisted water extraction (SAWE) for both low and high frequencies include mean particle size (MPS), time of extraction, power of ultrasonic generator, the ratio of sample to solvent (w/v), the temperature of extraction (T) and the percentage of entrainer (v/v), which were then analysed and compared.

Four main ginger bioactive compounds were detected which are 6-gingerol, 8-gingerol, 10-gingerol and 6-shogaol. The analysis of ginger bioactive compounds concentration was done using the High Performance Liquid Chromatography (HPLC). While the physical properties such as the structure of the ginger samples were analysed using Scanning Electron Microscopy (SEM).

This research covers the fundamental study to explain the effects of external interventions, which are sonic energy and entrainer on the changes of dielectric constant of water. The extraction efficiency was compared through the graph of solubility prediction and experimental data from different methods of extraction especially ethanol extraction, low frequency of SAWE and high frequency of SAWE. The discussion was done in order to find out the effect of sonic energy in the solvation and mechanism of extraction and compared the effect of low and high frequencies. This covers the use of sonic energy in escalating the process, the ability to force component or active compound out from matrix (sample) and total energy required penetrating sample into the core and passing through. It also compared the effects of both low and high frequencies of SAWE. The findings of this study would contribute to the new application of high frequency SAWE in herbal extraction as well as other separation of other thermo-labile compounds.

1.5 Research Questions

The demand for green solvent and application of sonic energy in mild conditions and environmental friendly process, which includes time, energy and cost reduction, has raised some research questions:-

1. How do process parameters give effects to the water properties?
2. What is the important property affected in establishing the feasibility of extraction process and how does the interaction and solute polarization plays their roles in the process?
3. How much is the difference of extraction efficiency by using water as a solvent with and without ultrasonic intervention?
4. How can sonication change the polarity of water as the solvent at lower temperature and ambient pressure condition?

5. How does sonic energy works in increasing the yield along with shorter time of extraction process?
6. What are the potential advantages of using high frequency of SAWE in ginger bioactive compounds extraction compared to low frequency?

1.6 Structure of Thesis

This thesis is structured into five chapters. Chapter 1 is the introduction of the thesis, which covers the problem statement, research objectives, scope of study, research questions, and the expected findings. Then, Chapter 2 is the literature review on the current extraction techniques, water as the green solvent extraction, ginger bioactive compounds, the extraction mechanism of sonic assisted water extraction (SAWE), the different range of frequencies and their application, and the comparison of low and high frequencies of SAWE. Chapter 3 presents the prediction of solubility, experimental procedures and the analysis done in this study. Next, Chapter 4 discusses the results obtained from both prediction and experimental studies and compared the effect of both low and high frequencies of SAWE. The effect of sonication to the polarity of water was also observed. Finally, Chapter 5 concludes the findings and contribution of this thesis as well as proposes the recommendations or improvements of this study.

1.7 The Significance of the Study

The important finding of this study is the manipulation of water property; especially the dielectric constants of water at lower temperature and ambient pressure which was done using sonication. Although the changes of dielectric constant of water were not really significant, it shows that there were slight changes or decrease with sonication and entrainer. This means that the interaction between water molecules was disturbed and the polarity of water as the solvents decreased to mimic the non-polar solvents. This is important since water under different conditions can mimic the properties of various solvents, which have been proven through pressurised hot water extraction or subcritical water extraction. The fundamental study on the mechanisms of sonic energy in changing the properties of water in the ginger oleoresin extraction is important in order to relate the theory to the real application. This study also discusses the solvation phenomena that occurred during the extraction process in order to enhance the extraction efficiency.

Since reference to high frequency of ultrasonic assisted extraction (UAE) is still scarce, this study has pushed the boundary of knowledge by discussing the effects of high frequency in herbal and water based extraction. The prediction of solubility for ginger bioactive compounds in hot water for the binary and ternary systems with ethanol as the entrainer was also the commencement of this herbal and green extraction field. Apart from these significances of this study to the body of knowledge, the applications of this manipulated water property was implemented in 1.5 litre lab scale Sonic Assisted Water Extractor (SAWE), which was designed and fabricated through this study. The advantages of using sonic assisted extraction have been reported as being a milder process, as well as reducing the cost and time of extraction while still using an organic solvent.

Thus, the uses of water as the solvent and sonic assisted extraction would encourage the development of green technology since it is operated at milder temperature and ambient pressure. Knowing the properties of water that can be

manipulated to mimic common solvents with sonic energy intervention will help to reduce the use of toxic solvents in the extraction at the lab scale as well as in industry, and, indirectly, reduce the cost, energy and time required, while at the same time providing an environmentally friendly process.

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APPENDIX A

List of Publication and Awards

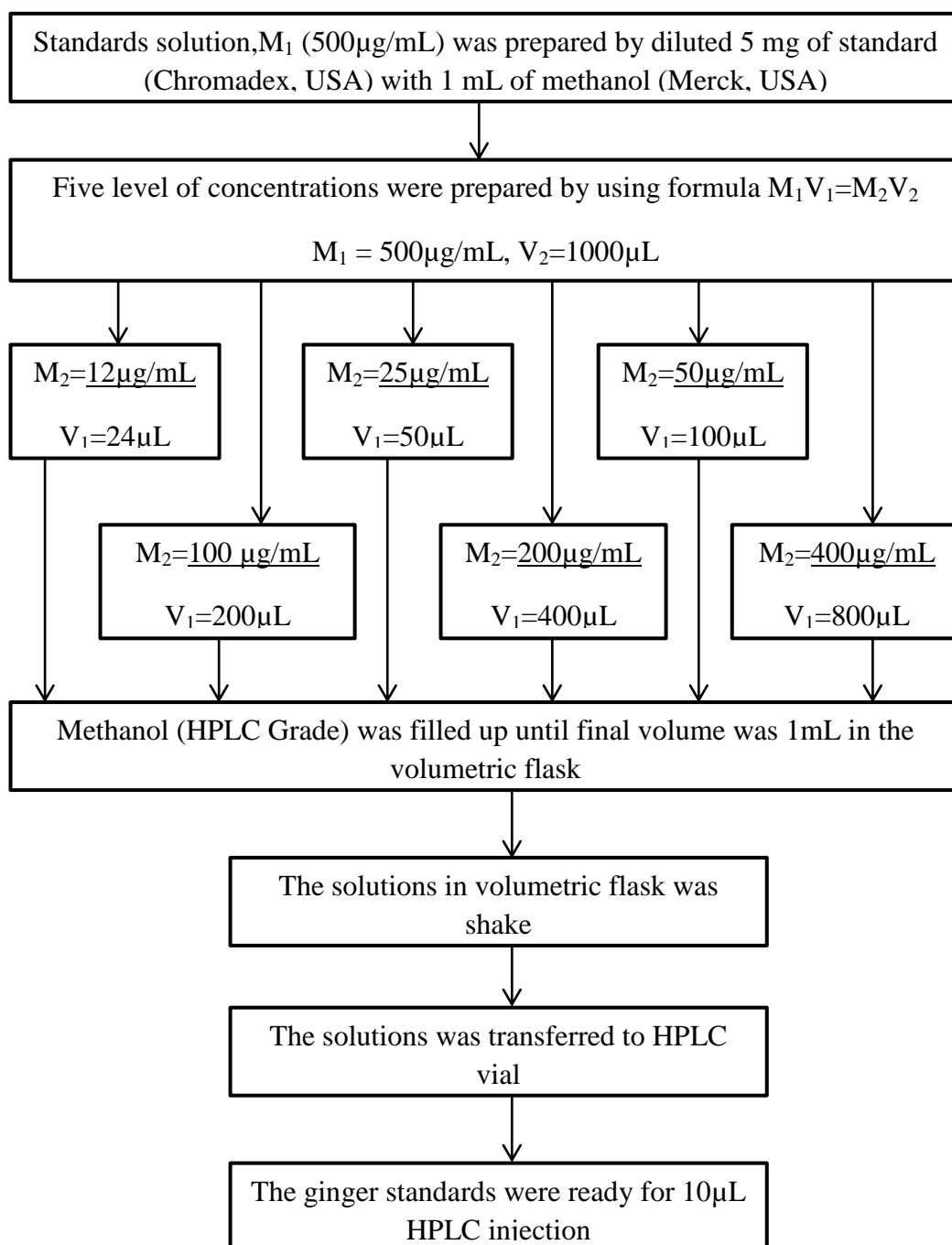
1. Syaripah Zaimah Syed Jaapar, Noor Azian Morad, Yoshio Iwai, Mohd Sharizan Md. Sarip, Mohd Azizi Che Yunus, and Yasmin Anum Mohd Yusuff (2015). Estimation of ginger bioactive compound solubilities in hot compressed water and enhancement with entrainer. *Fluid Phase Equilibria* (393) 40–47. doi.org/10.1016/j.fluid.2015.02.021. (IF:2.241)
2. Syaripah Zaimah Syed Jaapar, Noor Azian Morad, Yoshio Iwai. (2015). Solubilities Prediction of Ginger Bioactive Compounds in Liquid Phase of Water by the COSMO-RS Method. In K. S. Ford Lumban Gaol, Jamil Akhtar (Ed.), *Recent Trends in Physics of Material Science and Technology* (Vol. 204, pp. 196). Springer.
3. Syaripah Zaimah Syed Jaapar, Yoshio Iwai and Noor Azian Morad (2014) Effect of Co-solvent on the Solubility of Ginger Bioactive Compounds in Water Using COSMO-RS Calculations. *Applied Mechanics and Materials* Vol. 624: 174-178. doi:10.4028/www.scientific.net/AMM.624.174 (SCOPUS INDEXED)
4. Syaripah Zaimah Syed Jaapar, Noor Azian Morad and Yoshio Iwai (2013) Prediction of solubilities for ginger bioactive compounds in hot water by the COSMO-RS method. *Journal of Physics: Conference Series* 423(1): 012066. DOI: 10.1088/1742-6596/423/1/012066 (SCOPUS INDEXED)
5. Syaripah Zaimah Syed Jaapar, Noor Azian Morad, Yoshio Iwai. Effect of Sonication on the Dielectric Constant of Water and Water + Ethanol in Ginger Extraction. 2nd Asia-Oceania Sonochemical Society Conference (AOSS 2). The Westin, Kuala Lumpur (25-28 July 2015)
6. Syaripah Zaimah Syed Jaapar, Yoshio Iwai and Noor Azian Morad. Effect of Co-solvent on the Solubility of Ginger Bioactive Compounds in Water Using

- COSMO-RS Calculations. 2014 5th International Conference on Manufacturing Science and Technology (ICMST 2014). Curtin University, Sarawak. (7-8 June 2014)
7. Syaripah Za'imah Syed Jaapar, Yoshio Iwai, Noor Azian Morad, Mohd Sharizan MD Sarip. The Solubility of 6-gingerol and 6-shogaol in Hot Compressed Water: Experimental and COSMO-RS Prediction. 2013 Joint of Japan/Taiwan/Korea Chemical Engineering Conference. Kumamoto, Japan.(8-10 Nov 2013)
 8. Syaripah Zaimah Syed Jaapar, Noor Azian Morad and Yoshio Iwai. Prediction of solubilities for ginger bioactive compounds in hot water by the COSMO-RS method. International Conference on Science & Engineering in Mathematics, Chemistry & Physics: SCIETECH 2013. Aston Rasuna Hotel, Jakarta, Indonesia.(24-25 Jan 2013)
 9. 1ST RUNNER UP POSTER AWARD in 2nd Asia-Oceania Sonochemical Society Conference (AOSS-2) 2015, organized by The University of Nottingham, Malaysia.
 10. BEST WRITTEN PROPOSAL in JACTIM Research Proposal Writing Competition 2012, MJIIT, UTM KL.

APPENDIX B

Quantitative Analytical Method using High Performance Liquid Chromatogram (HPLC)

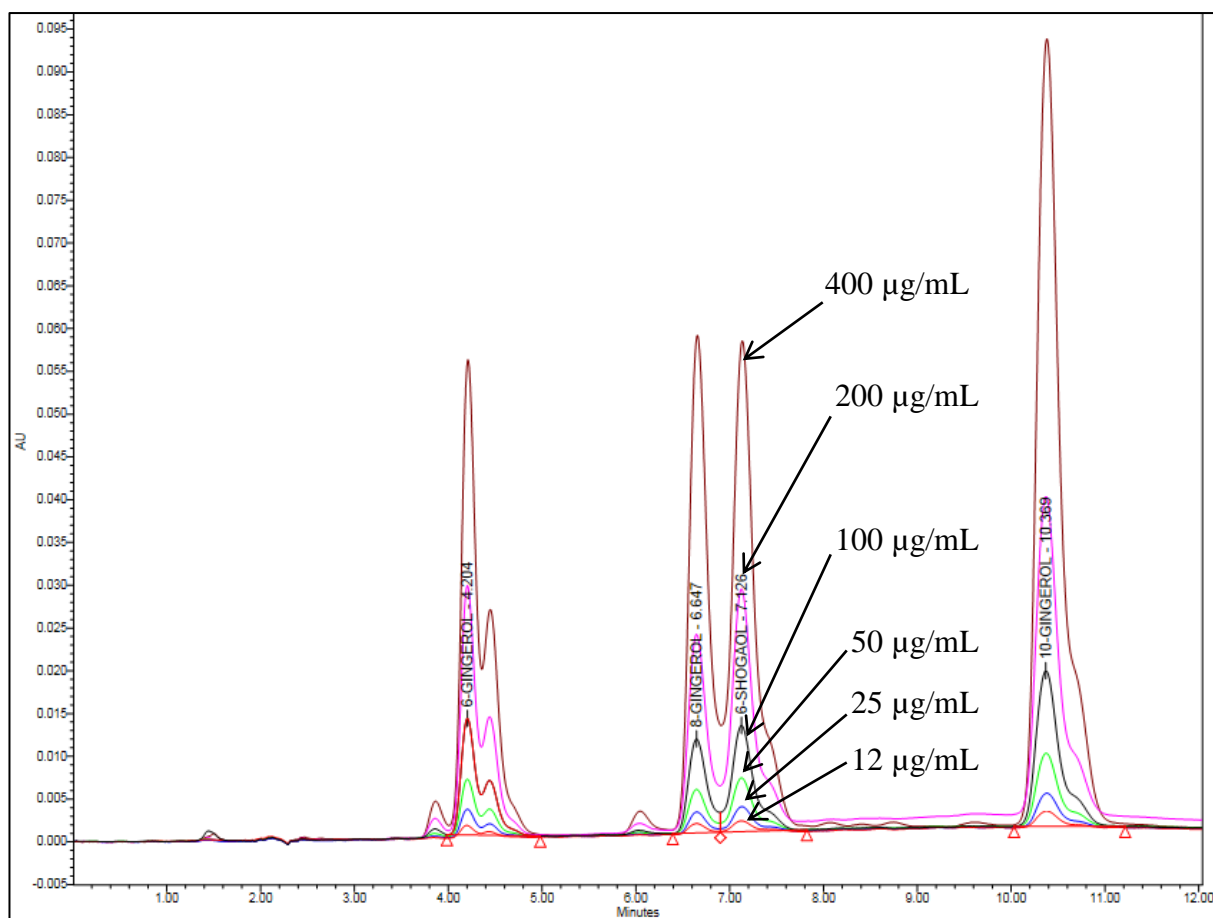
- (a) The preparation of ginger bioactive compounds standard (6-gingerol, 6-shigaol, 8-gingerol and 10-gingerol



(b) Preparation of mobile phase.

There are two mobile phases prepared for HPLC analysis which were 50% (v/v) methanol and 100% (v/v) acetonitrile, both are HPLC grade. After mixed, both mobile phases were filtered through 0.22 μ m nylon membrane filter with vacuum pump. Then, both mobile phases were degassing using low frequency of sonication for 15 minutes to make sure there were no gas entrapped in the liquid.

(c) The standard chromatogram of 6-gingerol, 6-shogaol, 8-gingerol and 10-gingerol at different concentration.

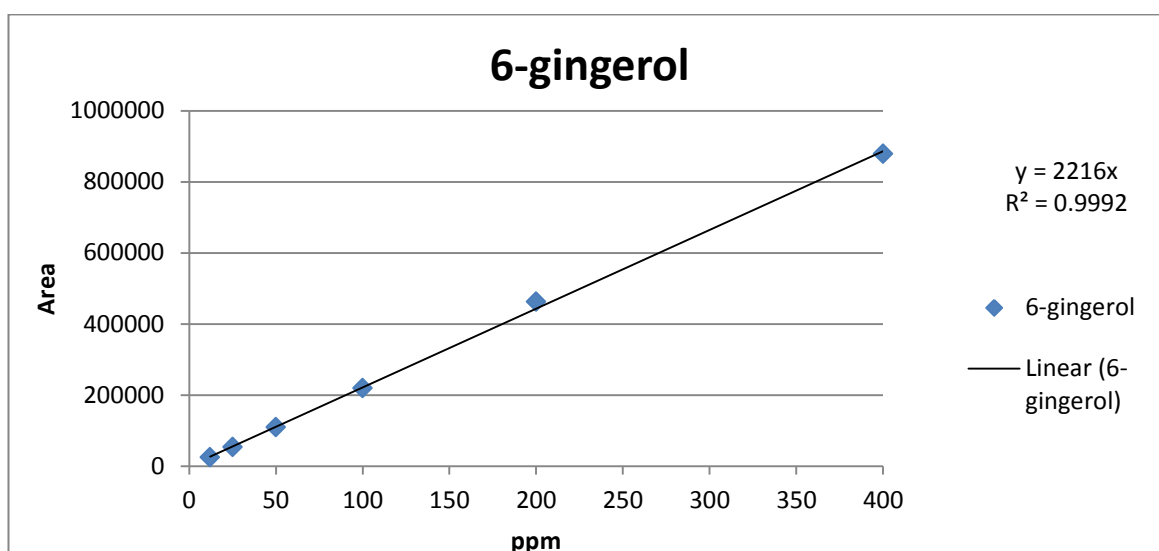


(d) HPLC results and calibration curves

(i) 6-gingerol

Peak: 6-GINGEROL

	Sample Name	Result Id	Peak Name	Level	X Value	Response	Calc. Value	% Deviation	Manual
1	12 ppm	2994	6-GINGEROL		12.000	24181.635	10.625	-11.46	No
2	25 ppm	2995	6-GINGEROL		25.000	53346.159	23.801	-4.80	No
3	50 ppm	2996	6-GINGEROL		50.000	109230.520	49.047	-1.91	No
4	100 ppm	2997	6-GINGEROL		100.000	219396.756	98.816	-1.18	No
5	200 ppm	2998	6-GINGEROL		200.000	461874.427	208.359	4.18	No
6	400 ppm	2999	6-GINGEROL		400.000	878003.977	396.352	-0.91	No



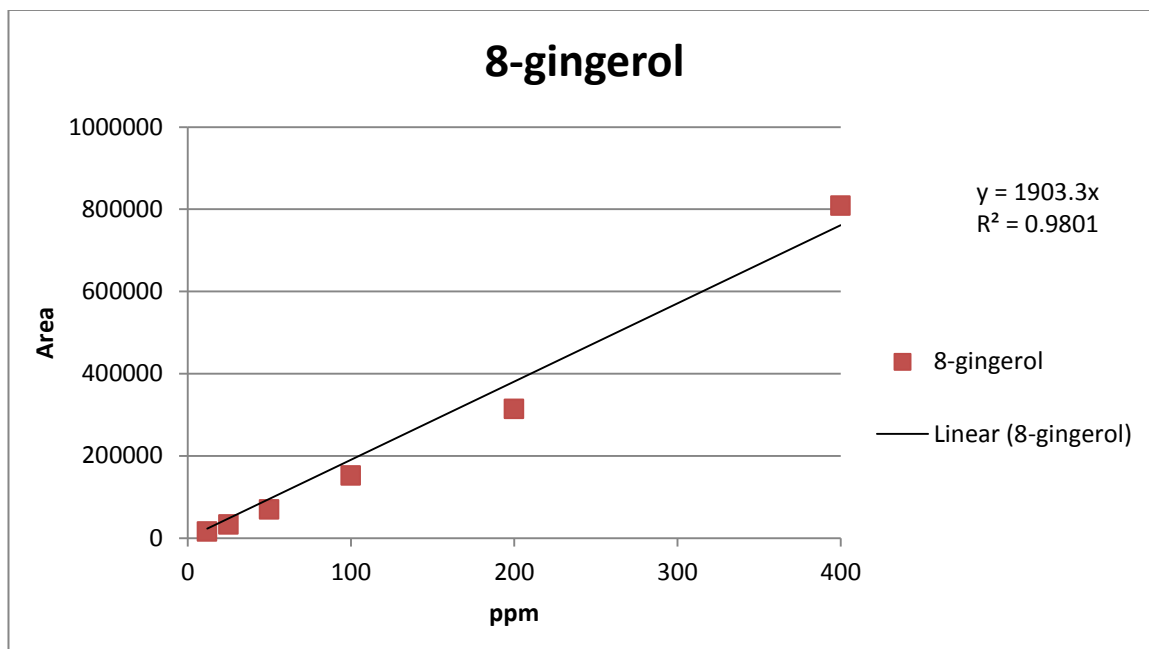
(ii) 8-gingerol

Peak: 8-GINGEROL

	Sample Name	Result Id	Peak Name	Level	X Value	Response	Calc. Value	% Deviation	Manual
1	12 ppm	2994	8-GINGEROL		12.000	15646.621	24.498	104.15	No
2	25 ppm	2995	8-GINGEROL		25.000	33004.162	33.053	32.21	No
3	50 ppm	2996	8-GINGEROL		50.000	69391.001	50.987	1.97	No
4	100 ppm	2997	8-GINGEROL		100.000	152054.466	91.729	-8.27	No
5	200 ppm	2998	8-GINGEROL		200.000	313573.505	171.336	-14.33	No

Peak: 8-GINGEROL

	Sample Name	Result Id	Peak Name	Level	X Value	Response	Calc. Value	% Deviation	Manual
6	400 ppm	2999	8-GINGEROL		400.000	808763.807	415.398	3.85	No



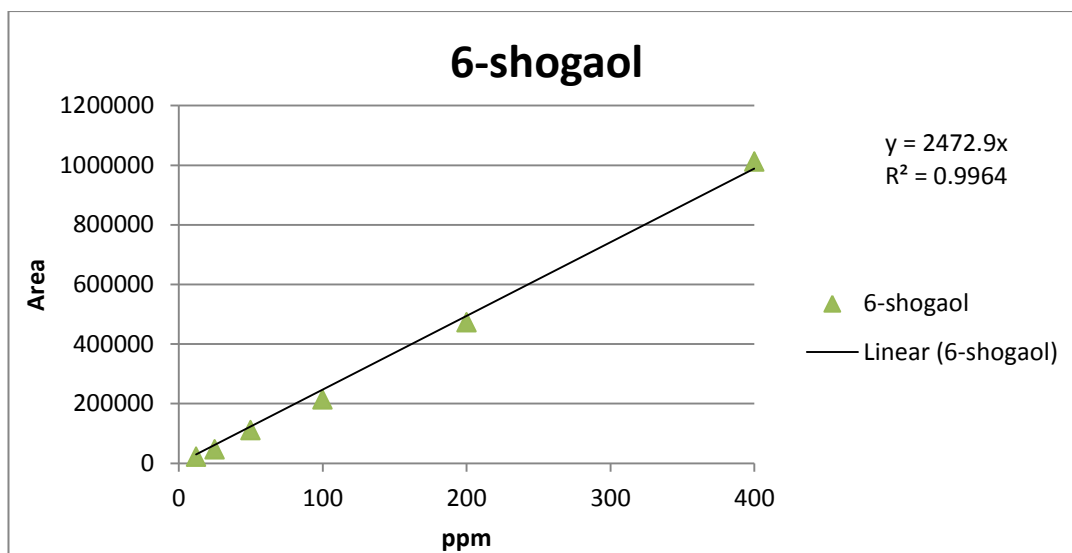
(iii) 6-shogaol

Peak: 6-SHOGAOL

	Sample Name	Result Id	Peak Name	Level	X Value	Response	Calc. Value	% Deviation	Manual
1	12 ppm	2994	6-SHOGAOL		12.000	21243.984	17.169	43.07	No

Peak: 6-SHOGAOL

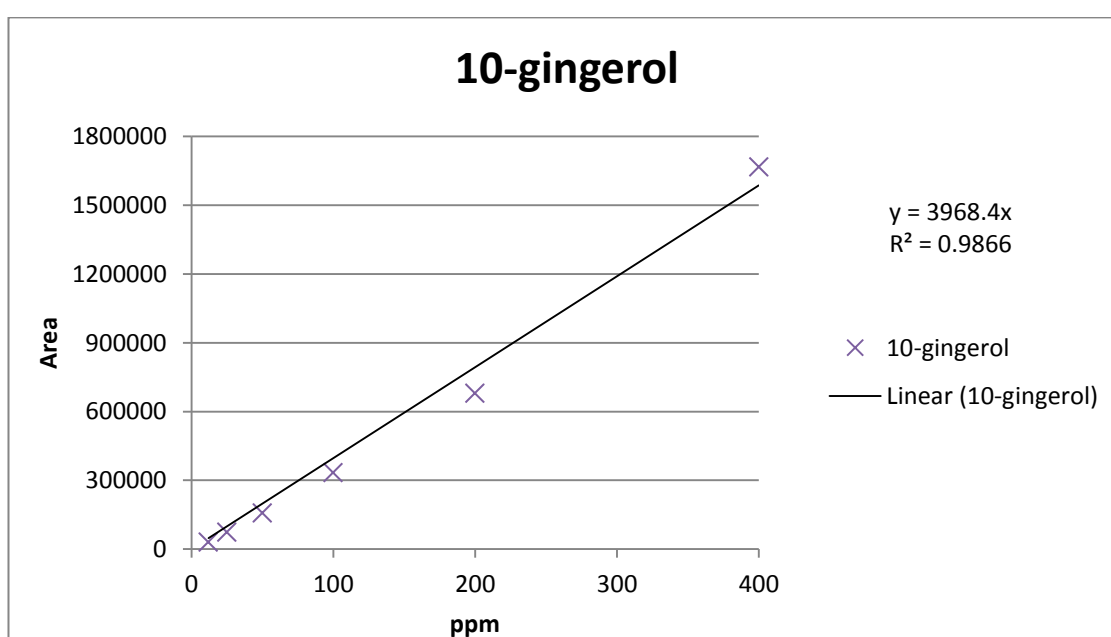
	Sample Name	Result Id	Peak Name	Level	X Value	Response	Calc. Value	% Deviation	Manual
2	25 ppm	2995	6-SHOGAOL		25.000	46862.137	27.189	8.76	No
3	50 ppm	2996	6-SHOGAOL		50.000	110411.340	52.047	4.09	No
4	100 ppm	2997	6-SHOGAOL		100.000	213387.757	92.327	-7.67	No
5	200 ppm	2998	6-SHOGAOL		200.000	472792.976	193.795	-3.10	No
6	400 ppm	2999	6-SHOGAOL		400.000	1011394.937	404.473	1.12	No



(iv) 10-gingerol

Peak: 10-GINGEROL

	Sample Name	Result Id	Peak Name	Level	X Value	Response	Calc. Value	% Deviation	Manual
1	12 ppm	2994	10-GINGEROL		12.000	29958.439	21.170	76.42	No
2	25 ppm	2995	10-GINGEROL		25.000	74349.042	31.778	27.11	No
3	50 ppm	2996	10-GINGEROL		50.000	156842.200	51.491	2.98	No
4	100 ppm	2997	10-GINGEROL		100.000	332964.941	93.578	-6.42	No
5	200 ppm	2998	10-GINGEROL		200.000	680079.609	176.525	-11.74	No
6	400 ppm	2999	10-GINGEROL		400.000	1667395.512	412.458	3.11	No



It is observed that r^2 for all four ginger bioactive compounds were more than 0.9800. Those graphs were considered a good linear correlation since $r^2 > 0.960$. Based on the equation obtained from calibration curve, the ginger bioactive compounds concentration for different ginger extracts were calculated as equations below:

$$y = mx \quad (1)$$

$y =$ peak area, $x =$ ginger bioactive concentrations

$$(i) \quad 6\text{-gingerol}, C_{6G} = \frac{\text{Peak Area}}{2216} \quad (2)$$

$$(ii) \quad 8\text{-gingerol}, C_{8G} = \frac{\text{Peak Area}}{1903.3} \quad (3)$$

$$(iii) \quad 6\text{-shogaol}, C_{6S} = \frac{\text{Peak Area}}{2472.9} \quad (4)$$

$$(iv) \quad 10\text{-gingerol}, C_{10G} = \frac{\text{Peak Area}}{3968.4} \quad (5)$$

(e) The calculation concentration of 6-gingerol, 6-shogaol, 8-gingerol and 10-gingerol

Ethanol Extraction

Based on the HPLC result below, the concentration of ginger bioactive compounds was calculated as follows:-

$$\text{Concentration} \left(\frac{\text{mg}}{\text{g}} \right) = \frac{V \times \text{DF} \times C_{6G} \left(\frac{\mu\text{g}}{\text{mL}} \right) \left(\frac{1\text{mg}}{1000 \mu\text{g}} \right)}{W}$$

where V = volume of solvent, DF = dilution factor, W= weight of sample

For example

6- gingerol:	$C_{6G} \left(\frac{\mu\text{g}}{\text{mL}} \right) = \frac{8870576}{2216} = 4002.967509 \mu\text{g}/\text{mL}$ $\text{concentration} \left(\frac{\text{mg}}{\text{g}} \right) = \frac{200\text{mL} \times 1 \times 4002.9675 \frac{\mu\text{g}}{\text{mL}} \times \left(\frac{1\text{mg}}{1000 \mu\text{g}} \right)}{20\text{g}}$ $= 40.0296751\text{mg}/\text{g}$
8- gingerol:	$C_{6G} \left(\frac{\mu\text{g}}{\text{mL}} \right) = \frac{833126}{1903.3} = 2039.707876 \mu\text{g}/\text{mL}$ $\text{concentration} \left(\frac{\text{mg}}{\text{g}} \right) = \frac{200\text{mL} \times 1 \times 2039.7079 \frac{\mu\text{g}}{\text{mL}} \times \left(\frac{1\text{mg}}{1000 \mu\text{g}} \right)}{20\text{g}}$ $= 20.3970788\text{mg}/\text{g}$
6- shogaol:	$C_{6G} \left(\frac{\mu\text{g}}{\text{mL}} \right) = \frac{3882176}{2472.9} = 807.187917 \mu\text{g}/\text{mL}$ $\text{concentration} \left(\frac{\text{mg}}{\text{g}} \right) = \frac{200\text{mL} \times 1 \times 807.1879 \frac{\mu\text{g}}{\text{mL}} \times \left(\frac{1\text{mg}}{1000 \mu\text{g}} \right)}{20\text{g}}$ $= 8.0718792 \text{ mg}/\text{g}$
10- gingerol:	$C_{6G} \left(\frac{\mu\text{g}}{\text{mL}} \right) = \frac{1996095}{3698.4} = 502.9974297 \mu\text{g}/\text{mL}$ $\text{concentration} \left(\frac{\text{mg}}{\text{g}} \right) = \frac{200\text{mL} \times 1 \times 502.9974 \frac{\mu\text{g}}{\text{mL}} \times \left(\frac{1\text{mg}}{1000 \mu\text{g}} \right)}{20\text{g}}$ $= 5.0299743\text{mg}/\text{g}$

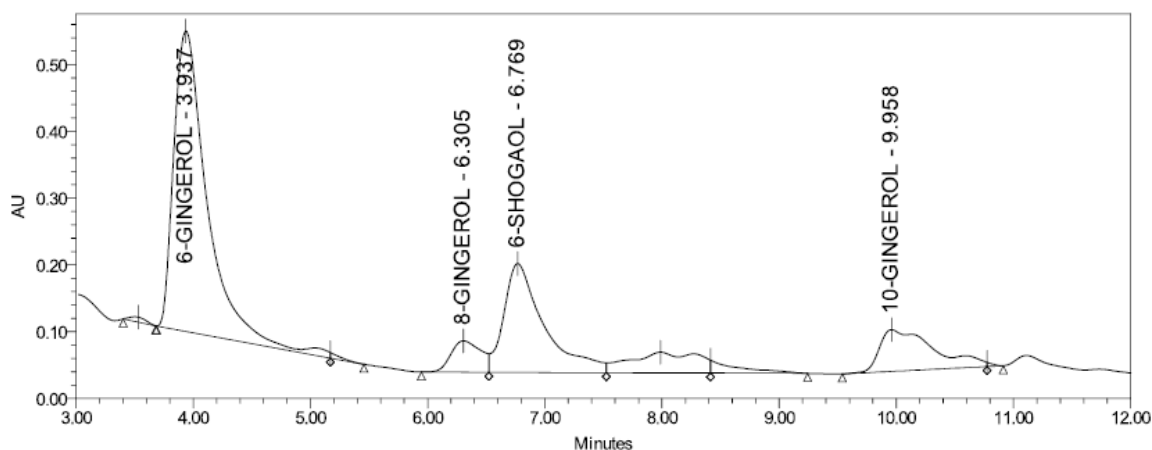
HPLC Results for ethanol extraction



Injection Summary Report

SAMPLE INFORMATION

Sample Name:	1.18mm soxh 021114 direct	Acquired By:	System
Sample Type:	Unknown	Sample Set Name:	zaimah 03nov14
Vial:	102	Acq. Method Set:	ginger
Injection #:	1	Processing Method:	GINGER STD_141014_A
Injection Volume:	20.00 ul	Channel Name:	2998 Ch1 282nm@1.2nm
Run Time:	20.0 Minutes	Proc. Chnl. Descr.:	2998 Ch1 282nm@1.2nm
Date Acquired:	11/3/2014 11:54:20 PM MYT		
Date Processed:	11/4/2014 1:26:43 PM MYT		



Channel: 2998 Ch1 282nm@1.2nm; Processed Channel: 2998 Ch1 282nm@1.2nm; Result Id: 3827; Processing Method: GINGER STD_141014_A

Processed Channel Descr.: 2998 Ch1 282nm@1.2nm

	Processed Channel Descr.	Peak Name	RT	Area	% Area	Height
1	2998 Ch1 282nm@1.2nm	6-GINGEROL	3.937	8870576	51.34	449590
2	2998 Ch1 282nm@1.2nm	8-GINGEROL	6.305	833126	4.82	47049
3	2998 Ch1 282nm@1.2nm	6-SHOGAOL	6.769	3882176	22.47	162973
4	2998 Ch1 282nm@1.2nm	10-GINGEROL	9.958	1996095	11.55	62535

Processed Channel Descr.: 2998 Ch1
282nm@1.2nm

	Amount	Units		Amount	Units		Amount	Units
1	4007.111	ppm	2	427.406	ppm	3	1527.399	ppm

Reported by User: System
 Report Method: Injection Summary Report
 Report Method ID: 3175
 Page: 1 of 2

Project Name: ginger\sept2014
 Date Printed:
 11/4/2014
 1:27:00 PM Asia/Kuala_Lumpur

APPENDIX C

Significant test was done using one way ANOVA analysis from Excel worksheet. From the data on the effect of entrainer in high frequency of SAWE, the result of ANOVA single factor was as follows:

Anova: Single Factor

SUMMARY					
Groups	Count	Sum	Average	Variance	
0	3	27573.88	9191.295	28478149	
5	3	30794.02	10264.67	32308239	
10	3	38920.11	12973.37	28104591	
15	3	58200.6	19400.2	1.23E+08	

ANOVA						
Source of Variation	SS	df	MS	F	P-value	F crit
Between Groups	1.89E+08	3	62944251	1.186067	0.374527	4.066181
Within Groups	4.25E+08	8	53069713			
Total	6.13E+08	11				

Groups were represented the range of the parameters studied, which for this case was the percentage of ethanol as the entrainer.

Count was represented how many trials were done, and for this case the experiment was done in triplicate.

Sum was the total concentration and average was the mean value of the concentration.

SS is sum of the square, where

SS between groups (B): $SS_B = \sum_j n_j (\bar{x}_j - \bar{x})^2$	SS within groups (W): $SS_W = \sum_j SS_j = \sum_j \sum_i (x_{ij} - \bar{x}_j)^2$	SS total groups (T): $SS_T = \sum_j \sum_i (x_{ij} - \bar{x})^2$
---	--	---

df is degree of freedom

$$df_T = n - 1 \quad df_B = k - 1 \quad df_W = \sum_{j=1}^k (n_j - 1) = n - k$$

MS is mean square and is defined as

$$MS = SS/df$$

while

$$MS_T = SS_T / df_T \quad MS_B = SS_B / df_B \quad MS_W = SS_W / df_W$$

MS_T is the variance for the total sample. MS_W is the sum of the group sample variances. MS_B is the variance for the “between sample”

F is the value of F-Test

P is the significant value, thus $P=0.37 > 0.05$, the effect of entrainer was not significant.

APPENDIX D

(a) The calculation of extraction yield was as follows:

$$\text{Yield (g/g)} = \frac{(W_f - W_b)}{W_s}$$

where;

W_f = weight of the round bottom flask after purification process (g) = 265.34 g

W_b = weight of the round bottom flask before purification process (g) = 267.04 g

W_s = weight of the sample matrix (g) = 20g

Thus,

$$\text{Yield (g/g)} = \frac{(267.04 - 265.34)\text{g}}{20\text{g}} = 0.085$$

(b) Yield percentage was

$$\text{Yield (\%)} = \text{Yield (g/g)} \times 100 = 8.5\%$$

(c) Recovery

$$\text{Recovery (\%)} = \frac{\text{Compound concentration } \left(\frac{\mu\text{g}}{\text{g}}\right)}{\text{Maximum or initial compound content } \left(\frac{\mu\text{g}}{\text{g}}\right) \text{ from ethanol extraction}} \times 100$$

For example, the recovery of 6-gingerol for third runs of 10% of entrainer using high frequency of SAWE was calculated as follows:

$$\text{Recovery (\%)} = \frac{18839.45832 \frac{\mu\text{g}}{\text{g}}}{41447.12 \frac{\mu\text{g}}{\text{g}}} \times 100 = 45.4542\%$$

(d) Mean Particle Size, MPS calculation

$$\text{MPS} = \frac{S_{\text{upper}} + S_{\text{lower}}}{2} = \frac{2.36 \text{ mm} + 1.18 \text{ mm}}{2} = 1.77 \text{ mm}$$

$$\text{MPS} = \frac{S_{\text{upper}} + S_{\text{lower}}}{2} = \frac{1.18 \text{ mm} + 0.60 \text{ mm}}{2} = 0.89 \text{ mm}$$

$$\text{MPS} = \frac{S_{\text{upper}} + S_{\text{lower}}}{2} = \frac{0.60 \text{ mm} + 0 \text{ mm}}{2} = 0.30 \text{ mm}$$

APPENDIX E

Mass balance calculation, total mass in = total mass out

The mass of solvent, $m = \rho V$

Total mass in:

density g/mL	Different conditions	before extract		in
		weight of ginger (g)	volume of solvent (mL)	
1.0000	1:10	70.0000	700.0000	770.0000
1.0000	1:20	35.0000	700.0000	735.0000
1.0000	1:30	23.3300	700.0000	723.3300
1.0000	1:50	14.0000	700.0000	714.0000
1.0000	45 °C	23.3300	700.0000	723.3300
1.0000	55 °C	23.3300	700.0000	723.3300
1.0000	recycle DW i	26.6700	800.0000	826.6700
1.0000	recycle DW ii	26.6700	800.0000	826.6700
0.9769	recycle 10% EtOH i	26.6700	781.4800	808.1500
0.9769	recycle 10% EtOH ii	26.6700	781.4800	808.1500
0.9850	5% EtOH	23.3300	689.5070	712.8370
0.9769	10% EtOH	23.3300	683.7950	707.1250
0.9691	15% EtOH	23.3300	678.3770	701.7070
0.9769	5% EtOH	23.3300	683.7950	707.1250
0.9850	10% EtOH	23.3300	689.5070	712.8370
0.9691	15% EtOH	23.3300	678.3770	701.7070
1.0000	800 mL	26.6700	800.0000	826.6700
1.0000	900 mL	30.0000	900.0000	930.0000
1.0000	1000 mL	33.3300	1000.0000	1033.3300
1.0000	800 mL	26.6700	800.0000	826.6700
1.0000	900 mL	30.0000	900.0000	930.0000
1.0000	1000 mL	33.3300	1000.0000	1033.3300

Total mass out:

after extract		out	loss	% of loss
weight of ginger (g)	volume of solvent (mL)			
238.2400	500	738.2400	31.7600	4.1247
135.3400	555	690.3400	44.6600	6.0762
92.4500	595	687.4500	35.8800	4.9604
60.4500	600	660.4500	53.5500	7.5000
91.3800	590	681.3800	41.9500	5.7996
99.4800	580	679.4800	43.8500	6.0622
120.8000	690	810.8000	15.8700	1.9198
121.5500	700	821.5500	5.1200	0.6194
106.7800	680	786.7800	21.3700	2.6443
101.5500	650	751.5500	56.6000	7.0037
95.8500	565	660.8500	51.9870	7.2930
92.0700	610	702.0700	5.0550	0.7149
92.2700	595	687.2700	14.4370	2.0574
98.6900	583	681.6900	25.4350	3.5970
97.6000	593	690.6000	22.2370	3.1195
87.8100	529	616.8100	84.8970	12.0986
107.7500	695	802.7500	23.9200	2.8935
122.7000	735	857.7000	72.3000	7.7742
138.2900	830	968.2900	65.0400	6.2942
117.7900	647	764.7900	61.8800	7.4855
127.9100	741	868.9100	61.0900	6.5688
137.8300	765	902.8300	130.5000	12.6291
average				5.419808

$$\text{The percentage of loss} = \frac{(\text{total mass in} - \text{total mass out})}{\text{total mass in}} \times 100$$

$$\text{Average percentage of loss} = \frac{\text{Total percentage of loss}}{22}$$

$$\text{Average percentage of loss} = 5.4198 \%$$

$$\text{AAD} = \frac{\sum \left(\frac{|x_i - x_{\text{avg}}|}{x_i} \right)}{n} = 2.5043$$

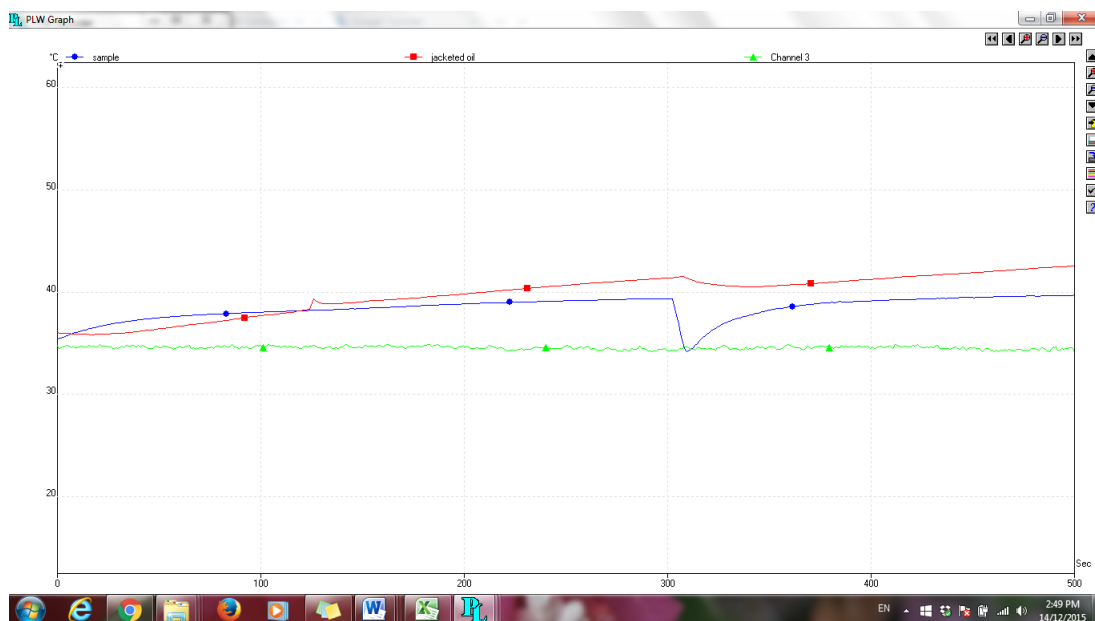
Thus, the average percentage of loss = 5.4198±2.5043%

APPENDIX F

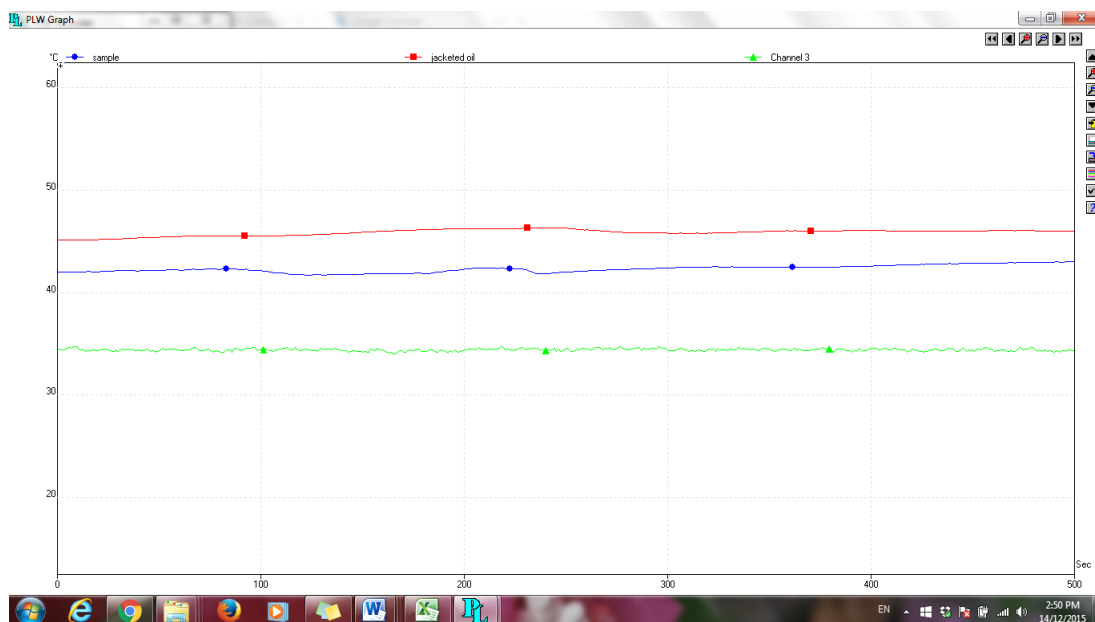
Example of Temperature Profile of High Frequency Sonic Assisted Water Extractor (SAWE) Vessel

Pump around process of ginger extraction using 100% distilled water.

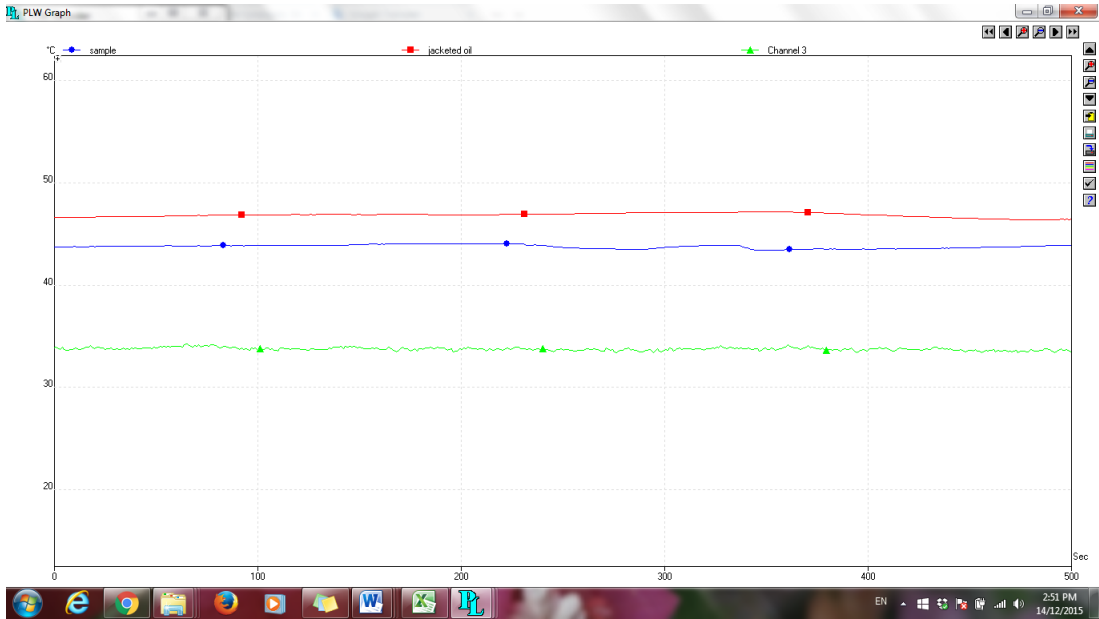
Part 1:



Part 2:



Part 3:



Part 4:

