SUBCRITICAL WATER EXTRACTION OF 6-GINGEROL AND 6-SHOGAOL
FROM *Zingiber Officinale*

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To my mum, Ramlah Ibrahim, my dad Md Sarip Baba, my wife Nor Hasmi Abd Ghani and my family members.

With all love and gratitude

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# ABSTRACT

Nowadays, natural products extract as a nutritional supplement becomes a part of healthy lifestyle. However, numerous scientific evidences suggested that the processing methods that mainly use organic solvents in extraction processes may result an undesired toxic residues in the product. Thus, the so called ‘green’ solvent that is water seems to be best alternative to substitute the organic solvent in the natural herb extraction process. In this study, the effect of subcritical water extraction (SWE) was employed for the extraction of bioactive compounds from *zingiber officinale* namely 6-gingerol, 6-shogaol and 10-gingerol. Two types of SWE equipment which are ASE 200 and CLEAR SWE prototype had been utilized. The ASE 200 with the capacity of 24 ml was used to evaluate the performance of the CLEAR SWE prototype with capacity of 1000 ml. Three parameters were manipulated in the SWE optimization process that are extraction temperature (100 to 200$^{o}$C), static extraction time (10-60 minutes) and solvent to sample ratio (28/3-28/1 ml/g) at a fixed pressure of 3.5 MPa. The analysis was done using the High Performance Liquid Chromatography. Two main bioactive compounds namely 6-gingerol and 6-shogaol were extracted with the traces of 10-gingerol. The extraction and fractionation of 6-gingerol and 6-shogaol were obtained at the lower and higher temperature; respectively. The optimum conditions for the 6-gingerol was at the temperature of 130$^{o}$C, in 30 minutes and solvent to sample ratio of 28/2 ml/g with the overall mass transfer coefficient of 8.1179 x10 $^{-7}$ m/s. Meanwhile the optimum condition for the 6-shogaol was at the temperature of 170$^{o}$C, in 20 minutes and solvent to ratio of 28/2 ml/g with the overall mass transfer coefficient of 18.3764 x 10$^{-7}$ m/s. It is found that the ginger bioactive compounds will be started to degrade at a temperature above 180 $^{o}$C.

# ABSTRAK

Kini, pengambilan ekstrak produk herba sebagai makanan tambahan.adalah kebiasaan dalam amalan gaya hidup sihat. Namun, banyak bukti saintifik menunjukkan bahawa kaedah pemprosesan yang kebanyakannya menggunakan pelarut organik dalam proses pengekstrakan boleh mengakibatkan sisa toksik yang tidak diingini dalam produk tersebut. Oleh itu, pelarut teknologi hijau, iaitu air menjadi alternatif terbaik untuk menggantikan pelarut organik dalam proses pengekstrakan herba semula jadi. Dalam kajian ini, pengekstrakan sub lampau genting (SWE) telah dikaji untuk mengekstrak sebatian bioaktif, iaitu 6-gingerol, 6-shogaol dan 10-gingerol daripada *zingiber officinale*. Dua jenis peralatan SWE, iaitu ASE 200 dan prototaip CLEAR SWE digunakan. ASE 200 yang berkapasiti 24 ml digunakan untuk menilai prestasi prototaip CLEAR SWE yang berkapasiti 1000 ml. Tiga parameter telah dimanipulasi dalam proses pengoptimuman SWE iaitu suhu (100 hingga 200$^{o}$C), masa (10-60 minit) dan nisbah pelarut kepada sampel (28/3-28/1 ml / g) pada tekanan tetap iaitu 3.5 MPa. Hasil ekstrak dianalisa dengan menggunakan Kromatografi Cecair Prestasi Tinggi. Dua sebatian bioaktif utama iaitu 6-gingerol dan 6-shogaol dan hanya sedikit 10-gingerol dapat diekstrak. Dengan mengunakan proses SWE, pengekstrakan dan pemisahan 6-gingerol dan 6-shogaol dapat dicapai pada suhu yang berbeza. Keadaan optima untuk pengekstrakan 6-gingerol adalah pada suhu 130$^{o}$C, dalam masa 30 minit dan nisbah pelarut kepada sampel adalah 28/2 ml/g dengan nilai pekali pemindahan jisim keseluruhan, iaitu 8.1179 x10 $^{-7}$ m/s manakala keadaan optimum untuk 6-shogaol pula adalah pada suhu 170$^{o}$C, dalam masa 20 minit dan nisbah pelarut kepada sampel adalah 28/2 ml/g dengan nilai pekali pemindahan jisim keseluruhan iaitu 18.3764 x 10$^{-7}$ m/s. Sebatian bioaktif halia mula merosot pada suhu melebihi 180$^{o}$C.

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## LIST OF ABBREVIATIONS

| | | |
|---|---|---|
| ASE | - | Accelerated solvent extraction |
| DNA | - | Deoxyribonucleic acid |
| EPSM | - | Environmental protection society of malaysia |
| FOA | - | Food and agriculture organization of the united nations |
| HPLC | - | High performance liquid chromatography |
| H | - | Enthalpy |
| H- bonds | - | Hydrogen bond |
| IAPWS. | - | The international association for the properties of water and steam |
| MPS | - | Mean particles size |
| MOA | - | Malaysia ministry of agriculture |
| P-T diagram | - | Pressure-temperature diagram |
| P-v diagram | - | Pressure-volume diagram |
| P | | Pressure |
| RT | - | Retention time |
| SWE | - | Subcritical water extraction |
| SFE | - | Supercritical fluid extraction |
| T-v diagram | - | Temperature-volume diagram |
| $T_{cr}$ | | Critical temperature |
| T | | Temperature |
| UTM | | Universiti Teknologi Malaysia |
| UiTM | | Universiti Teknologi MARA |
| U | - | Internal energy |

# LIST OF SYMBOLS

| | | |
|---|---|---|
| $A_T$ | - | Particle surface area |
| c | - | Coefficient representing the intercept-y. |
| $C_1$ | - | Compound concentration in liquid |
| $C_s$ | - | Solid concentration. |
| $C_{1(sat)}$ | - | Initial concentration in the solid |
| $C_{1(sat)6\text{-gingerol}}$ | - | 6-gingerol initial concentration |
| $C_{1(sat)6\text{-shagaol}}$ | - | 6-shagaol initial concentration |
| $CO_2$ | - | Carbon dioxide |
| $C_p$ | - | Heat capacity |
| $D_p$ | - | Particle diameter |
| D | - | Diameter of bed |
| $H_2O$ | - | Water |
| h | - | Bed height |
| k | - | Overall mass transfer coefficient |
| $k_i$ | - | Intra-particle diffusion coefficient |
| $k_e$ | - | External mass transfer coefficient |
| $m_s$ | - | Total mass of solid |
| m | - | Coefficient representing the slope |
| O | - | Oxygen |
| $\rho$ | - | Particle density |
| $\rho_e$ | - | Density of ethanol |
| RSD % | - | Relative standard deviation |
| $r^2$ | - | Coefficient of determination |
| r | - | Correlation coefficient |

| | | |
|---|---|---|
| $S_{upper}$ | - | Upper sieve size |
| $S_{lower}$ | - | Lower sieve size |
| $s_{bl}$ | - | The standard deviation of the blank measurement |
| $\mu$ | - | Mean |
| $V_L$ | - | Volume of the solution or bed |
| W | - | Weight of mixture of ethanol and ginger particles |
| $W_f$ | - | Weight of the round bottom flask after purification process, g. |
| $W_b$ | - | Weight of the round bottom flask before purification process, g. |
| $W_s$ | - | Weight of the sample matrix, g. |
| $W_i$ | - | Initial weight of volumetric flask |
| $x_1$ | - | The lowest measurement |
| $x_{bl}$ | - | Mean of the blank measurement |
| $Y_{\%}$ | - | Overall yield percentage, % (w/w) |
| $\varepsilon$ | - | Dielectric constant |
| $\Phi_s$ | - | Particles sphericity |
| $\sigma$ | - | Standards deviation |
| $\sigma$ | - | Surface tension |

## LIST OF APPENDICES

# CHAPTER 1

# INTRODUCTION

## 1.1 Introduction

Water is known as a universal solvent and it is cheap, abundant, highly pure, non-toxic and easily handled. Normally, water was regarded as the poor solvent for the most organic compounds because of its highly polar or high dielectric constant (Smith, 2006). These make water as an ineffective solvent in an extraction process. Water utilization in the extraction process only can be effective at high temperature because the dielectric constants of water would decrease as the temperature increases and make water mimic the organic solvent dielectric constant. By that, the solubility of organic compounds in water is also increased which consequently increase the extraction efficiency.

Furthermore, other physicochemical properties of water such as viscosity and surface tension also decrease with the temperature increased and enhanced the extraction efficiency through the promoting mass transfer properties and matrix particle penetration (Wiboonsirikul & Adachi, 2008). However, the extraction above the critical point is not favourable because it can promote degradation of the extract (Eikani *et al*., 2006).

Smith (2006) stated that the interest region in the utilization of water in the separation technology is between the boiling point (100°C) and critical point (374°C) (Smith, 2006). In this region, water already vaporized and modest pressure was needed to force it in the liquid phase as referred to the water phase diagram as shown in Figure 1.1 to avoid the possible degradation of the interest organic compound. The pressure is required to ensure the water in the liquid phase depends on the operating temperature. This region is described and named differently by the researchers such as subcritical water (Amashukeli *et al*., 2007; Ayala & Castro, 2001; Budrat & Shotipruk, 2008; Ghoreishi *et al*., 2008), superheated water (Ammann *et al*., 1999; Eikani *et al*., 2007; Smith, 2006), pressurized water (Cacace & Mazza, 2006; Markom *et al*., 2010), pressurized hot water (Teo *et al*., 2010), pressurized low polarity water (Cacace & Mazza, 2006) and compressed hot water (Liu & Wyman, 2005). In this study, water in this state is referred as subcritical water.

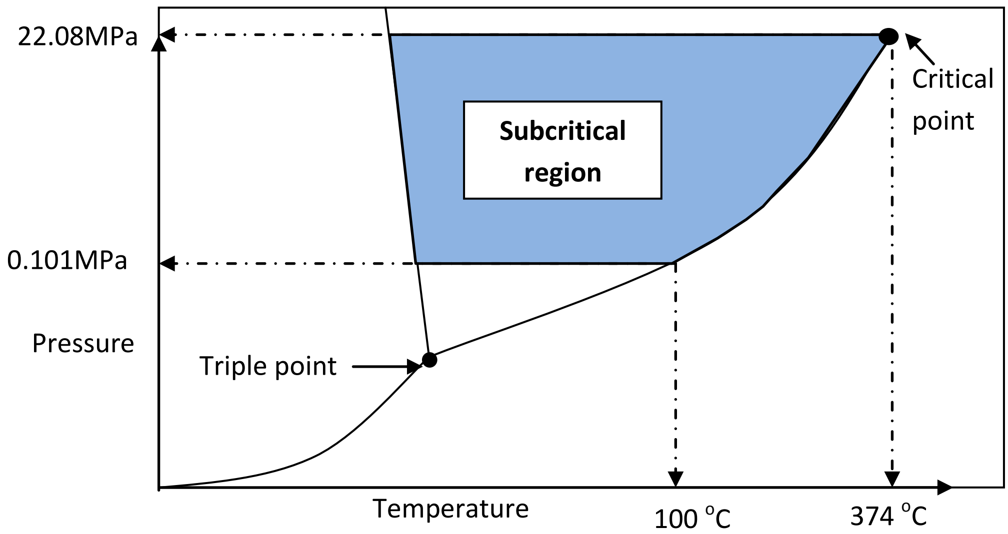


**Figure 1.1**: Water phase diagram: Temperature versus pressure

Since 1980s, the subcritical water extraction (SWE) have been applied in the numerous organic compound extraction such as Gallic acid (Markom *et al*., 2010), polyphenolic compound (Antuono, 2009; Kim *et al*., 2010; Turner *et al*., 2006), monoterpenoid phenol (Ozel *et al*., 2002), ellagic acid (Rangsriwong *et al*., 2008), asiatic acid (Kim *et al*., 2009) and magiferin (Kim, *et al*., 2010). In 1994, Hawthorne demonstrated that water can be used to extract polar, moderately polar and non-polar compound by varying the temperature from $50^oC$ to $400^oC$ (Hawthorne *et al*., 1994). Hawthorne also reported on his extended work that SWE can be utilized to extract largely polar compound at the lower temperature and less polar compound at the higher temperature (Hawthorne *et al*., 2000). This work gives the idea of the selective extraction and will be the most important features of SWE. Besides that, SWE implementation when compared with the traditional method provides a lot advantages such as low extraction time, high quality extract, inexpensive solvent and environmentally benign (Basile *et al*., 1998; Herrero *et al*., 2006; Saim & Osman, 2008). In order to evaluate the efficiency of the SWE process, a well-known natural herb, common gingers is used in this study.

Ginger is an everyday term for members of the *Zingiberaceae family(Grieve, 1992)*. Most *Zingiberaceae* family is native to tropical and subtropical locations. Ginger is classified in the division Mahnoliophyta, class Liliopsida, and order Zingiberales, family Zingiberaceae. There are 18 known genera with more than 160 species of *Zingiberaceae* in Peninsula Malaysia. Among these myriad of species, the common ginger is known as *Zingiber officinale*. Ginger originates from Southern China and widely believed to possess many medicinal benefits in the ancient Orient, and Indian Peninsula. The name “ginger” itself is derived from the Gingi district in India, where the upsets stomach is treated with ginger tea. Nowadays, ginger rhizomes are actively cultivated in the warmer parts of the globe such as India, the Middle East, and the Far East. The useful part of ginger was its tuberous rhizome that yields oleoresin or oil depends on the type of extraction. Ginger oil normally used in the fragrances and beverage industry for its unique flavour properties. Meanwhile, ginger oleoresins are used in the health food and pharmaceutical industry for its healing properties. Ginger oleoresin composed of non-volatiles pungent and non-pungent constituent including the bioactive compounds such as 6-gingerol, 6-shogaol, 8-gingerol and 10-gingerol. Other compounds such as 6-paradols, zingerone, zingiberene, gingerdiols and gingerdiones were the minor components. As the well-known herb, ginger oleoresin are scientifically proven for its anti-cancer (Abdullah *et al*., 2010; Harliansyah *et al*., 2007), anti-oxidants (Harliansyah *et al*., 2007) and anti-tumour properties (Vimala *et al*., 1999). This pharmacological study is not limited on the ginger oleoresin but selectively tested on the individual compound such as 6-gingerol, 6-shogaol and 10-gingerol. 6-gingerol is proven to medicated cardiac contractile (Antipenko *et al*., 1999) and gives the positive response on the anti-oxidant, anti-proliverative and apoptosis properties (Harliansyah *et al*., 2007). Meanwhile, 6-shogaol is proven to medicate the spinal cord injury (Kyung *et al*., 2006) and lessens the human oral cancer (Chen *et al*., 2010). 10-gingerol, another series of gingerol is proven to give the positive response on the anti-bacterial (Park *et al*., 2008) and anti-microbial activities (Nagoshi *et al*., 2006).

## 1.2 Problem Statement

There are several methods that can be used in the natural herb extraction process such as solvent extraction, hydro distillation, supercritical fluid extraction (SFE), cold pressing and vapour cracking. Among that, the most common ones are solvent extraction and hydro distillation due to their simplicity and economical characteristics. Solvent extraction refers to separation method using organic solvents such as hexane, ethanol, iso-propanol, acetone or methanol to extract oleoresin from plants. Nevertheless, due to demands on 'green' technology, this method is not preferred as the use of organic solvents may lead to the formation of toxic residue in the extract which will eventually be marketed for consumption by consumers (Basile *et al*., 1998). The purification or solvent removal process may not promise the total toxic elimination. Complete removal of the solvent residues may be possible, if the high sensitive equipment is implemented but it would increase the production cost. Furthermore, the tedious handling procedure may cause the pollution in the workplace and effect to the worker in a long term effect. The current climate of environmental awareness has given rise to various organizations such as Greenpeace, Environmental Protection Society of Malaysia (EPSM), and Environmental Protection Agencies to help educate the public to matters that can cause harm to the environment. Thus, with the availability of various knowledge sources, people are also, now more than ever, aware about the environmental impacts of non-eco-friendly processes. Other than that, the solvent extraction require a long extraction time from 5 to 10 hours which consumed a lot of energy.

Another extractions process known as supercritical fluid extraction (SFE) was a new 'green' extraction process with the unique features. The process involve the utilization of the common gases normally $CO_2$ at its supercritical phase. It was recognized as the most eco-friendly extraction method. However, the polarity or dielectric constants of supercritical $CO_2$ are too low to obtain the efficient extraction (Hawthorne *et al*., 1994; Herrero *et al*., 2009). Thus, it is only efficient for the non-polar organic compound (Hawthorne *et al*., 2000). In fact, many researchers have tried to increase the polarity by adding the organic modifier and this process cannot be considered as completely 'green' anymore. Furthermore, the need of dried sample in the SFE process to avoid the reaction between carbon dioxide and water will increased the pre-treatment cost. Besides that, the possible cuticular wax and lipid extraction in this process make it not preferable for natural herb extraction (Castro *et al*., 1999). In addition, the extremely high pressure process requirement for the SFE equipment from its critical pressure (7.38 MPa) up to 20 MPa and if carbon dioxide need to be recycle the high end compressor system is required, adds up to expensive operating costs (Castro *et al.*, 1999; Smith, 2002). Indeed, the involvement of high pressure process also needs additional safety consideration and experienced operator.

Therefore, with the general consensus of water as a "green" solvent, it seems to be the best available solution to reduce health and environmental problems in industries. The conventional water extraction or so called hydro distillation is not suitable and uneconomic due to the long extraction time. The energy cost of hydro distillation was estimated to be 20 times more compared with the SWE process (Wiboonsirikul & Adachi, 2008). For example, the extraction of marjoram leaves using SWE for 15 minutes yield five times more oil compare with the three hours of hydro distillation process (Jimenez-Carmona *et al*., 1999). This would lead to the waste of energy and contribute to further global warming. So, this SWE process is seen to be an alternative way for the herbal product extraction which offers the 'green' and economic process. Furthermore, the possibilities for the selective extraction using SWE may contribute to local herb added value not only for the ginger (Galkin & Lunin, 2005; Hawthorne, *et al*., 1994). Besides that, the different benefit and medicinal properties of ginger bioactive compounds namely 6-gingerol, 6-shogaol and 10-gingerol creating the increase on the ginger selective extraction. Thus, the aim of this study is to investigate the feasibility of the subcritical water extraction to extract ginger bioactive compounds namely 6-gingerol, 6-shagoal and 10-gingerol. Various operating conditions will be experimented to find an optimum operating condition. The study will also explore on the selective extraction on that bioactive compounds using SWE. Furthermore, two type of SWE equipment will utilized in this research that is CLEAR SWE prototype and accelerated solvent extractor, ASE 200.

## 1.3 Objective of the Study

A. To study the effect of temperature, time and ratio of solvent to ginger bioactive compounds (6-gingerol, 6-shogaol and 10-gingerol) using CLEAR SWE prototype.

B. To evaluate the competence of CLEAR SWE prototype by comparing with ASE 200 equipment.

C. To explain the SWE mechanism using overall mass transfer coefficient model for 6-gingerol and 6-shagoal at different temperature.

## 1.4 Scope of the Study

In order to achieve the objectives of the study, the following tasks will be carried out:

A. The sample pre-treatment process for the mean particles size optimization using ethanol extraction was done prior to the SWE process. There are three mean particles sizes (MPS) used in this process that are 0.75 mm, 1.5 mm and 2.68 mm. The optimum MPS will be standardized throughout SWE study.

B. The establishment of quantitative analysis method for ginger bioactive compounds (6-gingerol, 6-shogaol and 10-gingerol) using High Performance Liquid Chromatography, HPLC (Water, USA) for water based ginger extract.

C. The optimization of SWE process using CLEAR SWE prototype for the extraction of ginger bioactive compounds that is 6-gingerol, 6-shogaol and 10-gingerol. The parameter involve in this optimization process was temperature, extraction times and solvent to sample ratio.

D. The performance evaluation for CLEAR SWE prototype is done by the comparison with ASE 200 equipment data on the effect of temperature to the ginger bioactive compounds that is 6-gingerol, 6-shogaol and 10-gingerol. An ASE 200 was the commercial accelerated solvent extractor which commonly used by the researcher for SWE implementation. The temperature range is from 130$^{o}$C to 200$^{o}$C.

E. The measurement of the overall mass transfer coefficient for 6-gingerol and 6-shagoal extraction using SWE process from the temperature of 110$^{o}$C to 170 $^{o}$C.

## 1.5 Thesis Summary

This thesis is divided into five chapters. Chapter one is the introduction of the study which consists of research objective, scope of the study and the research problem. Chapter two gives the review on the raw material used, the extraction process for the natural herb product and the relationship between the physicochemical properties of water with extraction process. Chapter three describes the research methodology of the study. This chapter discuss the detail experimental procedures of pre-treatment process, the analytical method, SWE optimization and the modelling for the SWE process. The result finding is discussed in the chapter four. The study has been concluded in the chapter five together with the some recommendation on the future work.

## 1.6 Significance Contribution

The significant contribution of this study can be divided into two aspects; scientific and industry. The scientific data provide in this research would enhance the understanding of the SWE application from the view of physicochemical properties of water specifically the dielectric constants. Furthermore, the non-existence of research on the SWE application to the ginger bioactive extraction would make this research finding useful to support the product development of this commodity. Not limited to that, the modelling on the two different compounds mechanism of extraction namely 6-gingerol and 6-shogaol in the SWE process would provide the useful insight on the extraction rate of the ginger bioactive compound extraction. The data can be utilized for the prediction of other local herbs in Malaysia and for the purpose of scaling up elsewhere.

Form the industrial point of view, this newly improved method of herbal extraction will reduce the usage of organic solvents and hence support the recent awareness to create ‘greener’ environment by the use of natural solvent. This process is also believed to increase the value of herbal products through selective extraction that would benefit the manufacture. Recommendation on optimum operational condition also will help the industries to scale up the process for commercialization. This technology is also predicted to be beneficial not only to industry based on ginger, but to other herbal industries, as it is proven to be effective for the extraction of essential oils from black pepper, cumin, wheat bran, turmeric and coriander seeds.

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