ULTRASONIC ASSISTED EXTRACTION OF THYMOL FROM Plectranthus amboinicus (Lour.) Spreng LEAVES

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Chairman : Luqman Chuah Abdullah, PhD
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Plectranthus amboinicus is a medicinal herb with aromatic smells. They are commonly used in food processing and eaten as vegetables. *P.amboinicus* is also used to relief burn and control asthma. Scientific research on the leaves of this plant reveals that it possesses many beneficial bioactivities and its extract from leaves has a great potential to be used in developing commercial products. However, there is a lack of research on the processing aspects to process its bioactive extract. This research studied two main processes including drying of the leaves using tray dryer and solid-liquid extraction using ultrasonic assisted extraction (UAE). Drying kinetics and mathematical modelling on *P. amboinicus* leaves were studied. The durations for the drying process are 18, 46 and 74h for 55, 45 and 35 °C, respectively. Midilli and Kucuk model was found to be the most fitted model on the drying kinetic modelling with R2 of 0.998, 0.999 and 0.979 for temperatures of 55, 45 and 35 °C, respectively. The effective moisture diffusivity, *Deff* was calculated with values of 7.63 x 10-9 m2/s (55 °C), 2.29 x 10-9 m2/s (45 °C) and 1.14 x 10-9 m2/s (35 °C). The activation energy is at 77.78 kJ/mol. The DPPH scavenging values are 80.63, 71.70, and 60 % for each sample dried at temperatures of 35, 45 and 55 °C, respectively. Ultrasonic assisted extraction (UAE) was used as the extraction method to extract thymol concentration. The extraction kinetics and modelling were done at 3 different temperatures. The extracted thymol concentration is the lowest at 60 °C as compared to 40 and 25 °C. The Equilibrium-dependent solid-liquid extraction (EDSLE) model was chosen as the best-fitted model for the kinetic modelling. The R^2 values are 0.99, 0.95 and 0.93 for temperatures of 25, 40 and 60 °C, respectively. The optimum parameters for thymol extraction from *P.amboinicus* are at temperature of 55°C, 23 min of extraction and ratio of solute to solvent (g/mL) at 1: 35. The mechanism of UAE was explained based on observation of the structure changes using Scanning Electron Microscope (SEM). The finding of this study suggested that, increasing of drying temperature will shorten the drying time using the tray drier. UAE is a suitable method to extract thymol from *P. amboinicus* leaves.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk ijazah Master Sains

PENGEKSTRAKAN TIMOL DARIPADA DAUN *Plectranthus amboinicus* (Lour.) Spreng DENGAN BANTUAN ULTRASONIK

Oleh

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Plectranthus amboinicus adalah herba perubatan dengan bau aromatik. Mereka biasanya digunakan dalam pemprosesan makanan dan juga dimakan sebagai sayuran. *P. amboinicus* digunakan untuk melegakan melecur dan merawat athma. Penyelidikan saintifik pada daun ini mendedahkan bahawa ia mempunyai banyak bahan bioaktif yang bermanfaat dan ekstrak dari daun ini mempunyai potensi besar untuk membangunkan produk kormesial. Walaubagaimanapun, terdapat kekurangan penyelidikan mengenai aspek pemprosesan untuk memproses ekstrak bioaktifnya. Penyelidikan ini mengkaji dua proses utama termasuk pengeringan daun mengunakan pengering dulang dan pengestrakan pepejal-larutan mengunakan pengekstraktor dengan bantuan ultrasonik (UAE). Pengeringan kinetik dan permodelan pada daun *P. amboinicus* telah dikaji. Tempoh bagi proses pengeringan ialah 18, 46 dan 74 jam untuk 55, 45 dan 35 °C. Model Midilli dan Kucuk didapati paling sesuai untuk model pengeringan kinetik dengan nilai R^2, 0.998, 0.999 dan 0.979 untuk suhu 55, 45 and 35 °C. Keberkesanan kekurangan kelembapan, *Deff* telah dikira dan nilainya adalah 7.63 x 10-9 m2/s (55 °C), 2.29 x 10-9 m2/s (45 °C) and 1.14 x 10-9 m2/s (35 °C). Tenaga pengaktifan adalah sebanyak 77.78 kJ/mol. Kadar pemusnahan DPPH adalah 80.63, 71.70, and 60 % untuk daun yang dikeringkan dengan suhu 35, 45 dan 55 °C. Pengestrakan dengan ultrasonik digunakan sebagai kaedah pengekstrakan untuk mengekstrak kepekatan timol. Permodelan kinetik ekstrak dilakukan pada tiga suhu berbeza. Kepekatan timol yang diekstrak adalah paling rendah pada 60 °C berbanding 40 dan 25 °C. Model EDSLE dipilih sebagai model terbaik untuk permodelan kinetik. Nilai R^2 adalah 0.99, 0.95 and 0.93 pada suhu 25, 40 and 60 °C. Parameter yang optimum untuk mengekstrak timol dari daun *P. amboinicus* ialah pada suhu 55 °C, 23 minit masa ekstrak dan nisbah pepejal dan pelarut (g/mL) adalah 1:35. Mekanisma UAE dijelaskan berdasarkan pemerhatian perubahan struktur mengunakan Mikroskop pengimbas electron (SEM). Hasil kajian ini mencadangkan peningkatan suhu pengeringan dapat memendekkan masa pengringan dengan mengunakan pengering dulang. UAE adalah kaedah yang sesuai untuk mengekstrak timol dari daun *P. amboinicus*.

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LIST OF ABBREVIATIONS

UAE	Ultrasonic Assisted Extraction
CCD	Central Composite Design
RSM	Respond Surface Methodology
MR	Moisture Ratio
SEM	Scanning Electron Microscope
GC	Gas Chromatography
RMSE	Root Mean Square Error
DPPH	1 1,2-diphenyl-2-picrylhydrazyl
EDSLE	Equilibrium-dependent solid-liquid extraction
ANOVA	Analysis of Variance
R^2	Coefficient of Determination
χ^2	Chi square
D_{eff}	Effective moisture diffusivity
M_t	Moisture content at specific time
M_o	Initial moisture content
M_e	Equilibrium moisture content
M_{pre}	Predicted moisture content
M_{exp}	Experimental moisture content
Ea	Activation energy
R	Ideal gas constant
Ab_s	Absorbance sample
Ab_c	Absorbance control

CHAPTER 1

INTRODUCTION

1.1 Herbal Medicine

Herbal medicine is the oldest and still the most widely used system of medicine in the world today. The medicine is basically made exclusively from plant. It is used in all societies and is common to all cultures in the world. Nowadays, the plant-based medicines are most used in various field such as in public health practices and to maintain a good health. According to a report of World Health Organization (WHO), more than 80% of world's populations depend on traditional medicine for their primary health care needs (Swamy *et al*., 2011). Knowledge of the phytochemicals is desirable not only for the discovery of healthcare products, but also in disclosing new sources of economic materials like alkaloids, tanins, oils, gums etc. (Swamy *et al*., 2011). The use of herbal supplements has increased dramatically over the past 30 years. Herbal medicine is used to treat many conditions, such as allergies, asthma, eczema, premenstrual syndrome, rheumatoid arthritis, fibromyalgia, migraine, menopausal symptoms, chronic fatigue, irritable bowel syndrome, and cancer, among others. It is best to take herbal supplements under the guidance of a trained provider. For example, one study found that 90% of people with arthritic use alternative therapies, such as herbal medicine. Since herbal medicines can potentially interact with prescription medications, and may worsen certain medical conditions (Ernst, 2019).

World Health Organization (WHO) estimates that the global market is approximately USD 83 billion annually. It is difficult to calculate the data regarding the usage of herb worldwide due to the varied ways which herbs are used, e.g. food products, energy drinks, multivitamins and raw form (Robinson & Zhang, 2011). The national survey conducted in year 2007 by the National Centre for Complementary and Alternative Medicine (NCCAM) showed that 17.7 % of adults have used natural products (primarily herbs) in a one-year period (Rivera *et al.*, 2013). In Western countries, the trend of using medical herb are involved by adding the herbs to energy drinks and weight loss and nutritional products. In some countries, herbs can serve as a major way of treating certain conditions or diseases more cost effectively, especially if the herb can be grown locally or regionally (Rivera *et al.*, 2013).

In the scientific community, they highly interest with the essential oils that found in the natural product. The essential oils are complex mixture rich in terpenes with different degrees of lipophilicity and relative hydrophilicity (De Lira Mota *et al.*, 2012). Essential oils are aromatic liquid frequently obtained by steam distillation of the several plant materials. They commonly composed of volatile metabolites such as terpenoids and phenylpropanoid. Some report state that crude essential oils and their compound are used in folk medicine, indicating the pharmaceutical potential of the compound (Dos Santos *et al.,* 2015). Essential oil is the essence from a plant which is important for pharmaceuticals. Thus, the concentration of essential oil is a vital element in this study.

An appropriate solvent is needed to maximize the amount of oils extracted (Kuok Loong *et al.*, 2014).

Extraction process is the process of separation of medicinally active portion of plant or animal tissue from the inactive or inert component by using selective solvent in standard extraction procedure. The aim of the extraction process is for the crude drugs are attain the therapeutically desired and to eliminate the inert material by treatment with a selective solvent. There are some general methods for the extraction of medical herb which are, maceration, infusion, digestion, Soxhlet, ultrasound extraction (sonication), and many more (Sukhdev *et al.*, 2008). The extraction process is the key step to study of the medical plant, because extraction process is the step in the processing of the bioactive constituent from the plant material. Traditional methods such as maceration and Soxhlet extraction are commonly used at the small research setting or at Small Manufacturing Enterprise (SME) level. Some modification has been done in the processing of medicinal plants such as the modern extraction methods; microwave-assisted (MAE), ultrasound-assisted extraction (UAE) and supercritical fluid extraction (SFE), in which these advances are aimed to increase yield at lower cost. Moreover, modifications on the methods are continuously developed with such variety of methods present (Azwanida, 2015).

1.2 Herbal Processing

Herbs are mostly used in food and health industries. The presence of phytochemical ingredient gives a lot of beneficial effect to the human as in health improvement and beauty. The increase of popularity of herbal usage by the global market which also experience similar growth. Herbal medicine not only included the finished product but also need to look more such as the medicinal plant itself, herbal materials, and the herbal preparation. All these criteria are moving into the international commerce and the global trade arena, which indicate increase of economic value and importance. Hence the quality of herbal medicine of every stage production have been major concern to the health authorities, healthcare provider, the herbal industries and public itself (WHO, 2018). The flow chart in Figure 1.1 shows the general step in herbal processing.

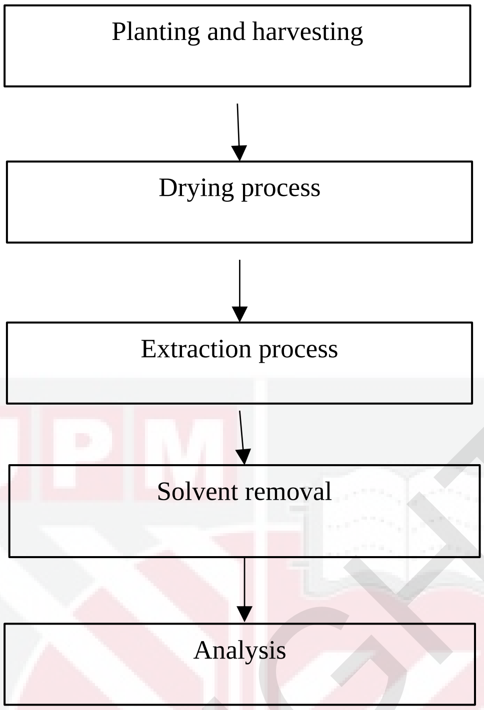

Figure 1.1: Flow chart of herbal processing.

One of the popular methods for preservation is drying process. The process involving the removal of water content or moisture from the herb to the acceptable content for aim to marketing, storage or processing purpose. Conventional method of drying process usually is the oven drying method. Nowadays, there are lots of method have been introduced to herbal drying process such as using tray dryer. Tray dryer was said that to be mostly used because of it shape and economic design. The concept of tray dryer is by transferring the hot air steam across the tray where the sample have been put. A lot of sample can be dried at the same time since tray dryer can be loaded with extra tray for carrying sample in different level (Misha *et al*., 2013).

After the drying process the next method is extraction process. Solid-liquid extraction (SLE) is the method for extraction process. Ultrasonic assisted extraction (UAE) is one of the SLE method. UAE has been stated that as a sustainable alternative compare to conventional method because it required low solvent and energy consumption. Besides, easy to handle equipment, safe, economic and can be operated at atmospheric pressure and ambient temperature are among other advantages of using this method. UAE process produces acoustic cavitation that damage the cell wall of the herbal sample which will cause the bioactive compound to be released to the solvent (Medina-Torres, N *et al*., 2017). Once the bioactive compound had been released to the solvent, the solvent will be separated using rotary evaporator. The crude extract collected after the separation process will undergo certain analysis for bioactive compound determination.

1.3 Problem Statements

Herbal industries once an unpopular industry but has now grown over the years which give billion worth of benefits and wealth. There are lots of good quality product in the local market which is not enough to meet the demand of public desired. There are lots of way to develop and introduce new herbal product.

P. amboinicus leaves is one of the herbal medical plant that found in Malaysia and it origin are found in in Africa and India. They also available in Asian country such as China, Indonesia, Thailand, Philipines, Vietnam, and Cambodia. Some are found in South Africa, Fiji, Cuba, Germany, Guyana, Puerto Rico, and USA (Arumugam *et al*., 2016). It contains many biochemical components. *P. amboinicus* leaves is not only valuable in medical aspect but also in food industry because of its pleasant smell. The active compound found in the *P. amboinicus* leaf which is thymol contributing to numerous benefits to human. Many analyses have been carried out on *P. amboinicus* leaf but there is limited research working on single active compound inside the leaves. *P. amboinicus* one of the alternative sources to provide thymol in Malaysia. Since lot of thymol are found in thyme which is not easy to find in Malaysia. The suitable conditions for extracting thymol from the leaves are yet studied.

P. amboinicus leaf is perishable and therefore always subject to quick spoilage and lead to become waste product. The resulted spoilage is from dehydration, fungal infection, dechlorophyll and others. There are many actions taken to resolve this problem such as drying process, chemical treatment, various way of storage, packaging method and materials. Extraction of essential oils will provide a way to resolve the leaves from becoming waste product. Usually drying process was done using conventional method such as oven method or sundried method, however some of other methods are more convenient, faster and hygiene compare to conventional. In this study, tray dryer was used instead of conventional method.

There is limited research on the extraction process of *P. amboinicus* leaf. Therefore, study needs to be carried out to obtain the optimum process parameters to maximize the quality of extract of the *P. amboinicus* leaf. The usage of ultrasound energy in laboratory-based technique for assisting the extraction from plant materials is widely published. The ultrasonic assisted study (UAE) has been recognized for potential in industry application for Phyto-chemical industry for wide range of herbal extraction. There is also limited research reported on the UAE for *P. amboinicus* leaf extract. The conventional methods, such as maceration and Soxhlet, are commonly used for herbal processing. However, there are certain advantages and disadvantages of these methods. By using UAE, some improvements can be achieved in the extraction process, such as to shorten the extraction duration and the solvent usage.

1.4 Objectives

1. To investigate effect of temperature (35, 45 and 55 °C) on drying of *P. amboinicus* leaves using tray dryer, its drying kinetic and effect of drying temperature on antioxidant activity.

2. To determine the extraction kinetic and applying mathematical model on thymol extraction from *P. amboinicus* leaves using UAE.

3. To determine the optimum process parameters including the temperature (40 to 60 °C), time (20 to 40 min) and solid to solvent ratio (1:30 to 1:40) for thymol extraction from *P. amboinicus* leaves using UAE.

1.5 Thesis outline

This thesis is divided into five chapter. The thesis starts with introduction in Chapter one, which include on the herbal medicine and processing, problem statements, objectives, thesis outline and the scope of study.

Chapter two present the overview of the *P. amboinicus* herbs and it benefits. This chapter also present on drying and extraction process along with their kinetics modelling.

Chapter three describe the methodology flow chart of this research. Firstly, on the drying process of the *P. amboinicus* leaves using the tray dryer. Mathematical model and fitting model were described. Antioxidant activity method was described. Secondly, the extraction kinetic part where the extraction kinetic modelling was described. Third, the optimization part where the design of experiment was done using Design expert software. Lastly the analysis of the *P. amboinicus* leave surface structure using Scanning Electron Microscope (SEM).

Chapter four present the result of drying and extraction kinetic and their mathematical modelling. Optimization result as given by Design Expert software and analysis of leaves surface structure was shown. The results presented in graphical form, table, and statistical analysis.

Chapter five present the conclusion for the research together with recommendation for future study

1.6 Scope of Study

The scope of this work covered two process involved in producing bioactive extract of *P. amboinicus* leaves namely drying of raw material and ultrasonic assisted extraction, UAE. Drying of raw material is the first post-harvest step to keep the quality of the dried leaves for the extraction process. The effect of the drying temperature on the quality of the leaves and drying kinetic were studied in order to determine the optimum drying temperature and the time of drying. Thin layer models were used to describing the drying process.

The effectiveness of UAE is done by numbers of parameters. The parameters that were considered to be use in the extraction process are the solid to solvent ratio, extraction temperature and the time of extraction. The suitable duration was determined by studying the extraction kinetic. Mathematical models were proposed for predicting the extraction process. The influence of the parameters listed were optimized using Central Composite Design (CCD) of the Respond Surface Methodology (RSM).

REFERENCES

AhmadSoraya I., Sulaiman C., Basri M., Reza H., Masoumi F., Chee, W. J., & Ashari S. E. (2017). Effects of temperature, time, and solvent ratio on the extraction of phenolic compounds and the anti-radical activity of *Clinacanthus nutans Lindau* leaves by response surface methodology. *Chemistry Central Journal*, 1–11. https://doi.org/10.1186/s13065-017-0285-1

Akpinar E. K., & Bicer Y. (2007). Modelling of thin layer drying kinetics of sour cherry in a solar dryer and under open sun. *Journal of Scientific and Industrial Research,* 66, 764-771.

Alibas I. (2014). Mathematical modeling of microwave dried celery leaves and determination of the effective moisture diffusivities and activation energy. *Food Science and Technology*, *34*(2), 394–401.

Arumugam G., Swamy M. K., & Sinniah, U. R. (2016). *Plectranthus amboinicus* (Lour.) Spreng: Botanical, phytochemical, pharmacological and nutritional significance. *Molecules*, *21*(4), 369.

Ashtiani S. H. M., Salarikia A., & Golzarian M. R. (2017). Analyzing drying characteristics and modeling of thin layers of peppermint leaves under hot-air and infrared treatments. *Information Processing in Agriculture*, *4*(2), 128-139.

Asiimwe S., Karlsson A. B., Azeem M., Mugisha K. M., Namutebi A., & Gakunga N. J. (2014). Chemical composition and toxicological evaluation of the aqueous leaf extracts of *Plectranthus amboinicus* Lour. Spreng. *International Journal of Pharmaceutical Science Invention*, *3*(2), 19–27.

Azmin S. N. H. M., Manan Z. A., Alwi S. R. W., Chua L. S., Mustaffa A. A., & Yunus N. A. (2016). Herbal processing and extraction technologies. *Separation and Puification Reviews*, *45* (4), 305-320.

Azwanida N. (2015). A review on the extraction methods use in medicinal plants, principle, strength and limitation. *Medicinal & Aromatic Plants*, *4*(3), 3–8.

Basch E., Ulbricht C., & Basch E. (2014). Thyme (*Thymus vulgaris L.*), Thymol thyme (Thymus vulgaris L .), Thymol. *J Herb Pharmacother*., *4*(1), 49-67.

Chan C. H., Yusoff R., & Ngoh G. C. (2014). Modeling and kinetics study of conventional and assisted batch solvent extraction. *Chemical engineering research and design*, *92*(6), 1169-1186.

Chemat F., Rombaut N., Sicaire A. G., Meullemiestre A., Fabiano-Tixier A. S., & Abert-Vian M. (2017). Ultrasound assisted extraction of food and natural products. Mechanisms, techniques, combinations, protocols and applications. A review. *Ultrasonics Sonochemistry*, *34*, 540–560.

Cheung Y., Siu K., & Wu J. (2013). Kinetic models for ultrasound-assisted extraction of water-soluble components and polysaccharides from medicinal fungi. *Food Bioprocess Technol., 6*, 2659–2665.

Darvishi H., Rezaie A., Asghari A., Azadbakht M., Najafi G., & Khodaei J. (2014). Study of the drying kinetics of pepper. *Journal of the Saudi Society of Agricultural Sciences*, *13*(2), 130–138.

De Lira Mota K. S., De Oliveira Pereira F., De Oliveira W. A., Lima I. O., & De Oliveira Lima E. (2012). Antifungal activity of *Thymus vulgaris L*. essential oil and its constituent phytochemicals against rhizopus oryzae: Interaction with ergosterol. *Molecules*, *17*(12), 14418–14433.

Dias A. L. B., Sergio C. S. S., Santos P., Barbero G. F., Rezende C. A., Martinez J. (2017). Ultrasound-assisted extraction of bioactive compounds from dedo de moça pepper (*Capsicum baccatum L.*): Effects on the vegetable matrix and mathematical modeling. *Journal of Food Engineering*, 198, 36-44.

Dong Z., Gu F.J., Xu F., Wang Q., (2014) Comparison of four kinds of extraction techniques and kinetics of microwave-assisted extraction of vanillin from *Vanilla planifolia* Andrews. *Food Chemistry*, 149, 54.61.

Dos Santos N. O., Mariane B., Lago J. H. G., Sartorelli P., Rosa, W., Soares, M. G., da Silva, A.M., Lorenzi, H., Vallim, M.A., & Pascon, R. C. (2015). Assessing the chemical composition and antimicrobial activity of essential oils from Brazilian plants - *Eremanthus erythropappus* (Asteraceae), *Plectrantuns barbatus,* and *P. amboinicus* (Lamiaceae). *Molecules*, *20*(5), 8440–8452.

Erbay Z., & Icier F. (2010). A review of thin layer drying of foods: Theory, modeling and experimental results. *Critical Reviews in Food Science and Nutrition*, *50*(5), 441–464.

Ernst E. (2019). Herbal medicine in the treatment of rheumatic diseases. *Rheumatic Disease Clinics of NA*, *37*(1), 95–102.

Evin D. (2011). Food and bioproducts processing thin layer drying kinetics of *Gundelia tournefortii L . Food and Bioproducts Processing*, *90*(2), 323–332.

Falcone P., Speranza B., Nobile M. A. D. E. L., & Corbo M. R. (2005). A study on the antimicrobial activity of thymol intended as a natural preservative, *68*(8), 1664–1670.

Giacometti J., Žauhar G., & Žuvi´ M. (2018). Optimization of ultrasonic-assisted extraction of major phenolic compounds from olive leaves (Olea europaea L.) using response surface methodology. *Foods*, *7*(149), 1–14.

Gujar J. G., Wagh S. J., & Gaikar V. G. (2010). Experimental and modeling studies on microwave-assisted extraction of thymol from seeds of *Trachyspermum ammi* (TA). *Separation and Purification Technology, 70*, 257–264.

Habibullah W., & Devi C. (2016, November). Ultrasonic-assisted extraction of essential oil from *Botryophora geniculate* using different extracting solvents. In *American Institute of Physics Conference Series* (Vol. 1787, No. 4).

Handa S. S. (2008). An overview of extraction techniques for medicinal and aromatic plants. *Extraction technologies for medicinal and aromatic plants, 1*.

Hossain M.B., Brunton N.P., Patras A., Tiwari B., O'Donnell C.P., Martin-Diana A.B., & Barry-Ryan C. (2012). Optimization of ultrasound assisted extraction of antioxidant compounds from Marjoram (*Origanum majorana* L.) using response surface methodology, *Ultrason Sonochem*., *19*(3), 582–590.

Inyang U. E., Oboh I. O., & Etuk B. R. (2018). Kinetic models for drying techniques — Food materials. *Advances in Chemical Engineering and Science*, *8*, 27–48.

Jang S., Lee A. Y., Lee A. R., Choi G., & Kim,H. K. (2017). Optimization of ultrasound-assisted extraction of glycyrrhizic acid from licorice using response surface methodology. *Integrative Medicine Research*, *6*(4), 388-394.

Jennan S., Farah A., & Mahjoubi F. (2015). Optimisation of ultrasound assisted extraction of *T. hyemalis* using the response surface methodology, *J. Mater. Environ. Sci*., *6*(3), 773–778.

Jian K., Tong W., Hongyuan Z., & Leilei S. (2013). The extraction and mass transfer process of soluble solids in Russian olive. *African Journal of Plant Science*, *7*(9), 407-413.

Jing C., Dong X., & Tong J. (2015). Optimization of ultrasonic-assisted extraction of flavonoid compounds and antioxidants from alfalfa using response surface method, *Molecules*, *20*(9), 15550–15571.

Kaur B. P., Sharanagat V. S., & Nema P. K. (2015). Fundamentals of drying, in "Drying technologies for foods: Fundamentals & applications" Prabhat K. Nema, Barjinder Pal Kaur, Arun, S. Mujumdar, (Eds.), Chapter 1, New India Publishing Agency, New Delhi.

Khani S., B.Khoshandam & Mirhaj M. (2013). Calculation of moisture content and drying rate during microwave drying. *Applied Mechanics and Materials*, *423-426*, 746-749.

Kitanovi'c S., Milenovi'c D., & Vlada B., V. (2008). Empirical kinetic models for the resinoid extraction from aerial parts of St. John' s wort (Hypericum perforatum L .). *Biochemical Engineering Journal*, *41* (1), 1–11.

Kowalski R., & Wawrzykowski J. (2009). Effect of ultrasound-assisted maceration on the quality of oil from the leaves of thyme *Thymus vulgaris* L. *Flavour and Fragrance Journal*, *24*(2), 69-74.

Kuok Loong N. G., Wahida P. F., & Chong C. H. (2014). Optimisation of extraction of thymol from plectranthus amboinicus leaves using response surface methodology. *Journal of Engineering Science and Technology*, *9*(Spec. Issue on Eureca 2013), 79–88.

Lai J., Xin C., Zhao Y., Feng B., He C., Dong Y., Fang Y. & Wei S. (2013). Optimization of ultrasonic assisted extraction of antioxidants from black soybean (*glycine max var*) sprouts using response surface methodology, *Molecules*, *18*(1), 1101–1110.

Lazar L., Iulia A., Volf I., & Popa V. I. (2016). Ultrasonics sonochemistry kinetic modeling of the ultrasound-assisted extraction of polyphenols from picea abies bark. *Ultrasonics Sonochemistry*, *32*, 191–197.

Lee A. Y., Kim H. S., Choi G., Kang Y. M., & Kim H. K. (2015). Optimization of ultrasonic-assisted extraction of daurisoline and dauricine from menispermi rhizoma by response surface methodology. *Journal of Liquid Chromatography & Related Technologies*, *38* (16), 1561-1570.

Medina-Torres N., Ayora-Talavera T., Espinosa-Andrews H., Sánchez-Contreras A., & Pacheco N. (2017). Ultrasound assisted extraction for the recovery of phenolic compounds from vegetable sources. *Agronomy*, *7*(3), 47.

Meisami-asl E., & Rafiee S. (2009). Mathematical modeling of kinetics of thin-layer drying of apple (var . Golab), *Agricultural Engineering International: the CIGR Ejournal. Vol. XI,* Manuscript 1185.

Misha S., Mat S., Ruslan M. H., Sopian K., & Salleh E. (2013). Review on the application of a tray dryer system for agricultural products. *World applied sciences journal*, *22*(3), 424-433.

Mirzaee E., Rafiee S., & Keyhani A. (2014). Determining of moisture diffusivity and activation energy in drying of apricots. *Res. Agr. Eng.*, *55*(3), 114–120.

Mnayer, D., Fabiano-Tixier, A. S., Petitcolas, E., Ruiz, K., Hamieh, T., & Chemat, F. (2017). Extraction of green absolute from thyme using ultrasound and sunflower oil. *Resource-Efficient Technologies*, *3*(1), 12-21.

Mohamad M., Ali M. W., Ripin A., & Ahmad, A. (2013). Effect of extraction process parameters on the yield of bioactive compounds from the roots of *Eurycoma Longifolia*. *Jurnal Teknologi*, *60* (1), 51–57.

Mundada M., Singh B., & Maske S. (2010). Convective dehydration kinetics of osmotically pretreated pomegranate arils. *Biosystems Engineering*, *107*(4), 307–316.

Naidu M. M., Vedashree M., Satapathy P., Khanum, H., Ramsamy, R., & Hebbar, H. U. (2016). Effect of drying methods on the quality characteristics of dill (*Anethum graveolens*) greens. *Food Chemistry*, *192*, 849–856.

Nguyen T., Nguyen M., Nguyen D., Bach L., & Lam T. (2019). Model for Thin Layer Drying of Lemongrass (Cymbopogon citratus) by Hot Air. *Processes*, *7*(1), 21.

Nor S., Syed F., Rahman A., Wahid R., & Ab N. (2015). Drying kinetics of *Nephelium Lappaceum* (Rambutan) in a drying oven. *Procedia - Social and Behavioral Sciences*, *195*, 2734–2741.

Novak J., & Lukas B. (2010). Temperature influences thymol and carvacrol differentially in *Origanum* temperature influences thymol and carvacrol differentially in *Origanum spp.* (Lamiaceae), *Journal of Essential Oil Research*, *22*(5), 412-415.

Nurafifah F., Chuah A. L., & Wahida M. P. F. (2018). Drying of *Plectranthus amboinicus* (lour) spreng leaves by using oven dryer. *Engineering in Agriculture, Environment and Food*, *11*(4), 239-244

Omolola A. O., Kapila P. F., & Silungwe H. M. (2019). Mathematical modeling of drying characteristics of Jew's mallow (Corchorus olitorius) leaves. *Information processing in agriculture*, *6*(1), 109-115.

Panda D., & Manickam S. (2019). Cavitation technology—The future of greener extraction method: A review on the extraction of natural products and process intensification mechanism and perspectives. *Applied Sciences*, *9*(4), 766.

Pandey, A. K. (2017). Harvesting and post-harvest processing of medicinal plants: Problems and prospects.

Peleg M., (1988). An empirical model for the description of moisture sorptioncurves. *Food Science* 53, 1216–1219.

Pillai P. G., Suresh P., Aggarwal G., Doshi G., & Bhatia V. (2011). Pharmacognostical standardization and toxicity profile of the methanolic leaf extract of P*lectranthus amboinicus* (Lour) Spreng. *Journal of Applied Pharmaceutical Science*, *1*(2), 76–81.

Pin K. Y., Chuah A. L., Rashih A. A., Rasadah M. A., Law C. L., & Choong T. S. Y. (2009). Solid-liquid extraction of betel leaves (*Piper betle* L.). *Journal of Food Process Engineering*, *34*, 549–565.

Pinelo M., Sineiro J., & Núñez M. J. (2006). Mass transfer during continuous solid–liquid extraction of antioxidants from grape byproducts. *Journal of Food Engineering*, *77*(1), 57-63.

Rivera J., Loya A., & Ceballos R. (2013). Use of herbal medicines and implications for conventional drug therapy medical sciences. *Alternative and Integrative Medicine*, *2*(6), 1–6.

Rocha R. P., & Melo E. C. (2011). Influence of drying process on the quality of medicinal plants: A review. *Journal of Medicinal Plants Research*, *5*(33), 7076-7084.

Robinson M. M., & Zhang X. (2011). Traditional medicines: Global situation, issues and challenges. *The World Medicines Situation (3rd Ed.) WHO Geneva*, 1–14.

Roldán-Gutiérrez J. M., Ruiz-Jiménez J., & De Castro M. L. (2008). Ultrasound-assisted dynamic extraction of valuable compounds from aromatic plants and flowers as compared with steam distillation and superheated liquid extraction. *Talanta*, *75*(5), 1369-1375.

Roshan P., Naveen M., Manjul P. S., Gulzar A., Anita S., & Sudarshan S. (2010). *Plectranthus amboinicus* (Lour) spreng: An overview. *The Pharma Research*, *4*, 1–15.

Sathasivam A., & Elangovan K. (2011). Evaluation of phytochemical and antibacterial activity of *Plectranthus Amboinicus*. *International Journal of Research in Ayurveda & Pharmacy*, *2*(1), 292–294.

Senthilkumar A., & Venkatesalu V. (2010). Chemical composition and larvicidal activity of the essential oil of Plectranthus amboinicus (Lour.) Spreng against Anopheles stephensi: a malarial vector mosquito. *Parasitology research*, *107*(5), 1275-1278.

Seyedabadi E. (2015). Drying kinetics modelling of basil in microwave dryer. *Agricultural Comunications*, *3*(4), 37–44.

Shakir I. K. (2017). Mass transfer coefficients of the extraction process of essential oil from *Myrtus Communis L.* plants using different solvents. In Proceeding of the Eighth Jordan International Chemical Engineering Conference (JIChEC 2017). 7-9 November, 2017, Amman, Jordan.

Shahi N. C., Singh A., & Kate A. E. (2014). Activation energy kinetics in thin layer drying of basil leaves. *International Journal of Science and Research*, *3*(7), 1836-1840.

So'bah A., Mohd Shamsul A., Farah Saleena T., Rosnah S. and Siti Roha A. (2017). Effective moisture diffusivity and activation energy of rambutan seed under different drying methods to promote storage stability. In *IOP Conference Series: Materials Science and Engineering Volume 203,* 012025.

Sovova H., (1994). Rate of the vegetable oil extraction with supercritical CO_2 -I. Modeling of extraction curves. *Chemical Engineering Science*. 49, 409-414.

Sreedharren B., Jaiganesh K. P., Kannappan N., & Sulochna N. (2010). Pharmacognostic studies on *Plectranthus amboinicus* Lour. *Research Journal of Pharmaceutical, Biological and Chemical Sciences*, *1*(4), 413–424.

Sukhdev S. H., Suman P. S. K., Gennaro L., & Dev D. R. (2008). Extraction technologies for medicinal and aromatic plants. *United Nation Industrial Development Organization and the International Center for Science and High Technology*, 116.

Swamy K. M., Pokharen N., & Dahal S. (2011). Phytochemical and antimicrobial studies of leaf extract of *Euphorbia neriifolia*. *Journal of Medicinal Plants Research*, *5*(24), 5785–5788.

Tabaraki R., & Nateghi A. (2011). Optimization of ultrasonic-assisted extraction of natural antioxidants from rice bran using response surface methodology. *Ultrasonics Sonochemistry 18*(6), 1279-1286.

Taheri-garavand A., Rafiee S., & Keyhani A. (2011). Mathematical modeling of thin layer drying kinetics of tomato influence of air dryer conditions. *International Transaction Journal of Engineering, Management & Applied Sciences & Technologies*, *2*(2), 147–160.

Tchabo W., Ma, Y., Kwaw E., Xiao L., Wu M., & Apaliya M. T. (2018). Impact of extraction parameters and their optimization on the nutraceuticals and antioxidant properties of aqueous extract mulberry leaf. *International Journal of Food Properties*, *21*(1), 717–732.

Tuˇsek A.J., Benkovi´c M., Cvitanovi´c A.B., Valinger D., Jurina T., Kljusuri´c J.G. (2016). Kinetics and thermodynamics of the solid-liquid extraction process of total polyphenols, antioxidants and extraction yield from *Asteraceae* plants. *Industrial Crops and Products,* 91, 205-214

Vankar P. S., & Srivastava J. (2010). Ultrasound-assisted extraction in different solvents for phytochemical study of *Canna indica*. *International Journal of Food Engineering*, *6*(3).

Villanueva Bermejo D., Angelov I., Vicente G., Stateva R.P., Rodriguez García-Risco, M., Reglero G., Ibañez E., & Fornari T. (2015). Extraction of thymol from different varieties of thyme plants using green solvents. *J Sci Food Agric.*, *95*(14), 2901-2907.

Wang L., & Weller C. L. (2006). Recent advances in extraction of nutra- ceuticals from plants, *Trends in Food Science & Technology*, *17*, 300–312.

WHO Guidelines on Good Herbal Processing Practices for Herbal Medicines. WHO Technical Report Series, No. 1010, 2018, Annex 1

Woo C. L., Yeoh H. S., Go S. K., & Chong, G. H. (2014). Green drying: Continuous dehumidified-air dryer. *Engineering Journal*, *18*(2), 119–126.

Yadav K. C. (2018). Optimization of process parameters in extraction of thyme oil using response surface methodology (RSM). *International Journal of Science, Engineering and Technology, 4*(1), 248-256.

Yang L., Yin P., Fan H., Xue Q., Li K., Li X., Sun L., & Liu Y. (2017). Optimization of ultrasonic-assisted extraction by response surface methodology with maximal phenolic yield and antioxidant activity from Acer truncatum leaves. *Molecules*, *22*, 232.

Yuan J., Huang J., Wu G., Tong J., Xie G.-Y., Duan J., & Qin M. (2015). Multiple responses (optimization of ultrasonic-assisted extraction by response surface methodology (RSM) for rapid analysis of bioactive compounds in the flower head of Chrysanthemum morifolium Ramat. *Industrial Crops and Products, 74,* 192-199.

Zhang H., Xie G., Tian M., Pu Q., & Qin M. (2016). Optimization of the ultrasonic-assisted extraction of bioactive flavonoids from *Ampelopsis grossedentata* and subsequent separation and purification of two flavonoid aglycones by high-speed counter-current chromatography. *Molecules 21*, 1–17.

Zhao C., Ren X., Li C., Jiang H., & Guan J. (2019). Coupling ultrasound with heat-reflux to improve the extraction of quercetin, kaempferol, ginkgetin and sciadopitysin from Mairei Yew Leaves. *Applied Science*, *9*, 1–15.