SCALING UP OF THE PROCESSES FOR THE PRODUCTION OF OPTIMIZED EURYCOMA LONGIFOLIA EXTRACTS USING DIMENSIONAL ANALYSIS

NOOR HAFIZA BINTI MOHMAD @ HARUN

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School of Chemical and Energy Engineering Faculty of Engineering Universiti Teknologi Malaysia

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Special dedication to my beloved;

Husband & Kids: Amirul Faizi bin Abdul Muthalib Amir Hafiy bin Amirul Faizi Amni Hayfa binti Amirul Faizi Auni Husna binti Amirul Faizi Aini Hasna binti Amirul Faizi

Mother & Siblings:

Siti Khalijah binti Ahmad Hasbul Khairi bin Mohmad @ Harun Khairul Helmi bin Mohmad @ Harun Mohd Akmal bin Mohmad @ Harun

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ABSTRACT

Eurycoma longifolia (EL) extract has attracted a lot of consumer interests. However, the production of *EL* extract has long been affected by issues of low yield and weak quality assurance. Two main processing units in EL extraction that are solidliquid extraction and spray drying, became the main focus of this research work. A study on the optimization of both processes followed by scaling up using dimensional analysis and similarity study were conducted to increase the extract yield and improve the quality of *EL* extract. Crude *EL* extract yield of $8.8 \pm 0.6\%$ (w/w) was obtained under the following optimal conditions at laboratory scale: 53 minutes of extraction, solvent to raw material ratio of 12.5:1 and raw material particle size of 0.5 to 1.0 mm. Process efficiency of 39.6% was achieved following the optimization of the spray drying process (without carrier agent) which was conducted under the following optimal conditions: air inlet temperature of 137 °C, air pressure of 8 psi and feed flow rate of 2.3 ml/min. The quality of EL extracts before and after spray drying was analysed. Spray drying resulted in loss of all marker compounds with protein being the highest at 87.7%. To improve the retention of marker compounds, microencapsulation of the extracts using a carrier agent was considered. Microencapsulation with scleroglucan (sclg) at laboratory scale resulted in the best retention of compounds with the highest process efficiency of 72.3%, which was achieved under the following optimum conditions: air inlet temperature of 185 °C, feed flow rate of 4.5 ml/min, air pressure of 8 psi and sclg concentration of 3.8% (w/w). Spray drying at the optimized air inlet temperature resulted in final product yield of 4.54% (w/w) when drying without using carrier agent and 45.0% (w/w) with sclg. respectively. To scale up the extraction process, a dimensionless number denoted as $ShSc^{-1}$ number was proposed based on best fitted data. Using data at laboratory scale, $ShSc^{-1}$ number of 0.0312 was obtained at optimized EL extraction conditions. Taking into account the scale up rule of P/V being constant and the scale-up factor of 7.6, pilot scale works at $ShSc^{-1}$ number of 0.0376 (the closest to lab-scale value) satisfactorily produced EL extract yield of 8.65% (w/w) with an error of 0.06%. Due to the dissimilarity in the physical conditions of both spray dryers, scale up of the spray drying process was performed based on air inlet temperature only. Spray drying at the optimized air inlet temperature at lab-scale resulted in final pilot-scale product yield of 2.5% (w/w) and 29.2% (w/w) when drying without using carrier agent and with sclg, respectively. Microencapsulation process efficiency at pilot scale was 71.7%, and the quality of extracts after spray drying (with the exception of polysaccharides) were quite consistent with the quality obtained at laboratory scale. The outcome of this research work demonstrated that useful scale-up knowledge of the production of EL extract from laboratory scale to pilot scale had been successfully obtained.

ABSTRAK

Ekstrak Eurycoma longifolia (EL) menarik perhatian ramai pengguna. Walaupun begitu, penghasilan ekstrak EL telah lama dibelenggu dengan isu-isu seperti hasil yang rendah dan jaminan kualiti yang lemah. Dua unit pemprosesan utama dalam pengekstrakan EL iaitu pengekstrakan pepejal-cecair dan penyemburan kering menjadi fokus utama kajian ini. Penyelidikan tentang pengoptimuman bagi kedua-dua proses diikuti dengan penskalaan menggunakan analisis dimensi dan kajian kesamaan telah dijalankan untuk meningkatkan hasil dan kualiti ekstrak EL. Hasil ekstrak EL sebanyak $8.8 \pm 0.6\%$ (w/w) telah diperoleh pada keadaan optima skala makmal: masa ekstrak 53 minit, nisbah pelarut kepada bahan mentah 12.5:1 dan saiz partikel bahan mentah 0.5-1.0 mm. Kecekapan proses 39.6% telah berjaya dicapai pada keadaan optimum penyemburan kering (tanpa menggunakan agen bahan pembawa) iaitu pada: suhu udara masuk 137 °C, tekanan udara 8 psi dan kadaralir suapan 2.3 ml/min. Kualiti ekstrak EL sebelum dan selepas proses penyemburan kering telah dianalisa. Kesemua sebatian utama telah hilang semasa penyemburan kering dimana protein mempunyai jumlah kehilangan yang tertinggi iaitu 87.7%. Bagi meningkatkan ketahanan sebatiansebatian utama, mikrokapsulan ekstrak dengan penggunaan agen bahan pembawa telah diambil kira. Mikrokapsulan dengan menggunakan scleroglucan (sclg) pada skala makmal adalah yang terbaik bagi ketahanan sebatian dengan kecekapan proses tertinggi pada 72.3%, dimana dicapai pada keadaan optimum berikut: suhu udara masuk 185 °C, kadaralir suapan 4.5 ml/min, tekanan udara 8 psi dan kepekatan sclg 3.8% (w/w). Penyemburan kering pada suhu udara masuk yang optimum menghasilkan hasil produk akhir masing-masing 4.54% (w/w) bagi pengeringan tanpa agen bahan pembawa dan 45.0% (w/w) bagi menggunakan sclg. Untuk penskalaan proses pengekstrakan, satu nombor tidak berdimensi yang dinamakan sebagai nombor *ShSc⁻¹* telah dicadangkan berdasarkan data yang terbaik. Nombor *ShSc⁻¹* 0.0312 telah diperoleh pada keadaan optimum pengekstrakan EL pada skala makmal. Dengan mengambil kira hukum penskalaan P/V yang malar dan faktor penskalaan 7.6, kerjakerja penskalaan pada skala pandu menggunakan nombor ShSc⁻¹ 0.0376 (nilai paling hampir pada skala makmal) telah menghasilkan hasil ekstrak 8.65 % (w/w) dengan ralat 0.06 %. Oleh kerana ketidaksamaan keadaan fizikal bagi kedua-dua semburan kering, penskalaan penyemburan kering telah dijalankan hanya berdasarkan pada suhu udara masuk. Penyemburan kering pada suhu udara masuk optimum pada skala makmal menghasilkan hasil produk akhir pada skala pandu masing-masing 2.5% (w/w) dan 29.2% (w/w) bagi pengeringan tanpa agen bahan pembawa dan bagi pengeringan menggunakan sclg. Kecekapan proses mikrokapsulan pada skala pandu ialah 71.7% dan kualiti ekstrak selepas penyemburan kering (kecuali bagi polisakarida) didapati hampir konsisten dengan kualiti yang diperoleh dari skala makmal. Hasil keputusan kajian ini menunjukkan bahawa ilmu penskalaan dalam penghasilan ekstrak EL dari skala makmal ke skala pandu telah diperoleh dengan jayanya.

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LIST OF ABBREVIATIONS

ANOVA	-	analysis of variance
AOAC	-	low molecular weight
ASE	-	accelerated solvent extraction
BSA	-	bovine serum albumin
CCD	-	central composite design
CFD	-	computational fluid dynamics
DD	-	degree of deacetylation
DE	-	dextrose equivalent
DSC	-	Differential Scanning Calorimetry
EPP1	-	entry point project 1
ETP	-	economic transformation program
EVR	-	evaporation rate
FAO	-	Food and Agricultural Organization
FRIM	-	Forest Research Institute Malaysia
FTIR	-	Fourier Transform Infrared Spectroscopy
GAP	-	good agricultural practice
GCMS	-	Gas Chromatography Mass Spectrometry
GLP	-	good laboratory practice
GMP	-	good manufacturing practice
HPLC	-	High Performance Liquid Chromatography
HPTLC	-	High Performance Thin Layer Chromatography
HTF	-	heat transfer fluid
IBD	-	Institute of Bioproduct Development
IUPAC	-	International Union of Pure and Applied Chemistry
LCMS	-	Liquid Chromatography Mass Spectrometry
LD50	-	lethal dose, 50%
LMW	-	medium molecular weight

MARDI	-	Malaysian Agricultural Research and Development Institute
MCE	-	microwave assisted extraction
MIT	-	Massachusetts Institute of Technology
MMW	-	medium molecular weight
MS	-	Malaysian Standard
MW	-	molecular weight
NKEA	-	national key economic areas
NMR	-	Nuclear Magnetic Resonance Spectroscopy
NPRA	-	National Pharmaceutical Regulatory Agency
OFAT	-	one-factor-at-a-time
pH	-	logarithmic scale (of ion H^+)
PHWE	-	pressurized hot water extraction
PLE	-	pressurized liquid extraction
R&D	-	research and development
RM	-	Ringgit Malaysia
RSM	-	response surface methodology
SDS	-	sodium dodecyl sulfate
SFE	-	supercritical fluid extraction
SIRIM	-	Standard and Industrial Research Institute of Malaysia
SME	-	Small and Medium Enterprise
TCA	-	trichloroacetic acid
TCM	-	traditional and complementary medicine
TLC	-	Thin Layer Chromatography
TPP	-	tri-polyphosphate
US	-	United States
UV	-	Ultraviolet
WHO	-	World Health Organization

LIST OF SYMBOLS

$ ho_0$ and $ ho_1$		densities of the droplet at the initial and end of the constant rate period
%	-	percentage
$X^{w}{}_{i}$	~	mass fraction of component <i>i</i>
\dot{m}_{air}	-	air mass flow rate
<i>m</i> _{water}	-	mass flow rate of water contained in the concentrate
ΔT_{AMTD}	-	arithmetric mean temperature difference between droplet and air
C_D		drag coefficient
C_{pi}	-	specific heat of component <i>i</i>
C_s	÷	mass fraction of solid content
C _w	-	mass concentration of water
v_{tip}	÷	impeller tip speed or πND
$ ho_p$		particle density
v_t	n÷1	terminal velocity
ω_s		sinking velocity of a single particle
ΔT	÷.	temperature drop
ΔT	÷	temperature drop
Δho		density differences
A	-	cross-sectional area
а	-	exponent
A_{lm}	-	log mean area for wall
ALR _{dryer}	-	air-to-liquid ratio of both spray dryers
ALR _{nozzle}	-	air-to liquid ratio of the nozzle
A_p	-	total area of particles
Ar	+	Archimedes number
С	-	concentration of solute
Cœ	-	concentration of defined solute in the solvent
C'œ	-	concentration of solute in the dry solid (extract free)

cm	-	centimeter
cm ⁻¹	÷	reciprocal of centimeters
Ср	-	specific heat capacity
CV	040	coefficient of variation
D	- r- i -r-	impeller diameter
D or D_s or D_d	-	diffusion coefficient
<i>d</i> /2	÷	half of thickness of slab geometry of Tongkat Ali roots
D/D_{v}	÷.	impeller to vessel diameter ratio
d_0	÷	initial of constant rate period
d_1	÷	end of constant rate period
<i>D</i> ₃₂	t i t	Sauter mean diameter
d_a	· 4-	diameter of a sphere with the same volume as the particle
d_{av}	-	average diameter of the droplet
d_p	÷	particle diameter
D_{v}	4	vessel diameter
<i>E</i> *)÷	energy dissipate
e.g.	-	for example
Fa	÷	force due to acceleration (or agitation)
F_b	$(\frac{1}{2})$	buoyant force acting upward
F_D	÷	resistance or drag force acting in opposite direction to the particle motion
F_{g}	÷	gravity acting downward
Fr	4	Froude number
g	÷	gram
g	1÷1	gravitational acceleration
$g \Delta ho$	÷	weight differences
Gin	0 . 0	drying air flow rate (including water vapour)
G _{tfn}	-	nozzle atomization air flow rate (including water vapour)
Н	÷	height of liquid in the vessel
$h or h_i or h_o$	-	convective heat transfer coefficient

H/D	-	height to impeller diameter ratio
H/D_{v}	-	liquid height to vessel diameter ratio
h_m	-	convective mass transfer coefficient
J	-	Joule
Κ	-	volumetric shape factor
Κ	-	partition coefficient
Κ	-	Kelvin degree
k	-	thermal conductivity
k_b	-	thermal conductivity of air or gas
k_d	-	thermal conductivity of the droplet
kDA	-	kilo Daltons or unified atomic mass unit
kg	-	kilogram
k_m	-	mass transfer coefficient
k obs	-	order rate constant
1	-	characteristic length
m	-	meter
т	-	mass of particle
m	-	variables
mg	-	milligram
Ν	-	impeller speed
n	-	basic dimensions
n	-	exponent value
N_{js}	-	Zwietering constant or critical minimum speed
N_M	-	impeller speed of lab-scale
N_T	-	impeller speed of pilot-scale
Nu	-	Nusselt number
N_{v}	-	Dimensionless local velocities
°C	-	degree Celsius
Р	-	impeller power
P/V	-	volume-related mixing power or specific power consumption
P_o	-	Power number

ppm	-	parts per million
Pr	-	Prandtl number
Prob > F	-	probability <i>p</i> -value
R	-	scale up factor
R	-	correlation coefficient
R^2	-	determination coefficient
Re	-	Reynold number
Re_p	-	particle Reynold number
r ₀ - r _{iii}	-	inner and outer radius of the vessels
rpm	-	revolutions per minute
\$	-	second
S1	-	Tongkat Ali particle size of below 0.5 mm
S2	-	Tongkat Ali particle size between 0.5 to 1.0 mm
S3	-	Tongkat Ali particle size above 1.0 mm
Sc	-	Schmidt number
Sh	-	Sherwood number
St	-	Stanton number
t	-	time
Т	-	total amount of extract
t _c	-	residence time during the constant rate
<i>t</i> f	-	residence time during the falling rate
T_g	-	glass transition temperature
T_{wb}	-	wet-bulb temperature
V	-	volume of liquid solvent
v	-	kinematic viscosity
Λ	-	macro-scale of turbulence
V'	-	volume of solid particles
V_p	-	total volume of particles
w/w	-	mass fraction percentage
X_{I}	-	extraction duration
X_2	-	solvent to raw material ratio
X_3	-	particle size

X_b	-	equilibrium moisture content at the end of drying
Xc	-	critical moisture content at the end of constant rate period
Y	-	extract yield
Y _{in}	-	inlet drying air vapour concentration (kg vapour/kg dry air)
Yout	-	outlet drying air vapour concentration (kg vapour/kg dry air)
Y _{tfn}	-	nozzle atomization air vapour concentration (kg vapour/kg dry air)
Ζ	-	height of impeller blade from bottom of the vessel
Ζ	-	height of impeller off-bottom clearance
ΔT_{LMTD}	-	log mean temperature difference between air and droplet temperature
З	-	power per unit mass
θ	-	mixing time
θN	-	dimensionless mixing time
λ	-	local isotropic turbulence or Kolmogorov's micro- scale
μ	-	dynamic viscosity
μm	-	micrometer
π	-	Pi
ho	-	liquid density
τ	-	Torque
φ_v	-	volume fraction of solid or porosity
ω_{ss}	-	sinking velocity of swarm particle
υ	-	speed of fluid

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CHAPTER 1

INTRODUCTION

1.1 Research Background

Eurycoma longifolia or Tongkat Ali is well recognized as a traditional herbal remedy in Southeast Asia which are currently going global for its vitality and aphrodisiac properties. Today, *Eurycoma longifolia* is amongst the top selling herbal products in Malaysia. The roots of *Eurycoma longifolia* are believed to be highly potent and its decoction is consumed traditionally as a health tonic and to treat a variety of ailments such as fever, ulcer, cough, diarrhoea, postpartum treatment etc. (Bhat and Karim, 2010). Over the past few decades, numerous convincing evidences were obtained on the ability of *Eurycoma longifolia* in improving male sexual health (Thu *et al.*, 2017a). Published data and current investigations reveal *Eurycoma longifolia* as possessing cytotoxic, anti-ulcer, anti-tumor, anti-estrogenic, anti-pyretic, anti-schistosomal, anti-inflammatory, anti-bacterial, anti-fungal, anti-cancer, anti-malarial, anti-parasitic, anti-anxiolytic, and anti-diabetic activities (Mohamed *et al.*, 2015). In the most recent research, *Eurycoma longifolia* was proven to exhibit various effects such as osteoporosis preventive, hormonal, ergogenic, insecticidal and muscular (Rehman *et al.*, 2016).

Based on its intrinsic factors (i.e. cultivation, age, genetic and geographical) as well as the efficiency of processing, extracts of *Eurycoma longifolia* are comprised of

various active constituents from primary and secondary metabolites that are responsible for the pharmacological activities and therapeutic effects. One study found that quassinoids are present in higher portions than alkaloids in *Eurycoma longifolia* extract with eurycomanone compound and its derivatives being the major compounds (Chua et al., 2011). Apart from that, a eurypeptide with molecular weight of 4.3 kDa was identified as the aphrodisiac marker in Eurycoma longifolia extract (Asiah et al., 2007; Ismail et al., 2012). The standardized water soluble extract has been patented in 2004 by US patent (i.e. US 7132117 B2) after extensive examination on the sexual effects of Eurycoma longifolia on animals (Sambandan et al., 2006). The Malaysian Government has published a Malaysian Standard (MS 2409:2011) on the quality requirements of Eurycoma longifolia freeze-dried water extract based on four markers, which are eurycomanone, total protein, total glycosaponin and total polysaccharides (MS, 2011). Due to the great demand for *Eurycoma longifolia* products, Malaysia has placed this herb along with four other types of herbs (initially) as part of the herbs that are to be given emphasis by the government through National Key Economic Areas (NKEA) Agriculture Entry Point Project (EPP1) under the 10th Malaysian Plan to enhance R&D for the herbs with the target to produce safe, high quality and efficacious herbal products that are to be marketed globally (Ahmad et al., 2015).

Unfortunately, today most of the *Eurycoma longifolia* extracts used for commercial preparations still do not meet the mandatory regulatory parameter for the concentration of the marker compounds. This situation was revealed by a study based on eurycomanone level (should be between 0.8 to 1.5%), where 17 out of 41 products of *Eurycoma longifolia* obtained in Malaysia and internationally were found to not even contain this compound (Norhidayah *et al.*, 2015). *Eurycoma longifolia* products in the market is often unauthenticated. According to a previous study, the recommended consumption of *Eurycoma longifolia* extract is at the dose of 200 to 400 mg daily for adults (Mohd Effendy *et al.*, 2012). The processing technology practice must also be emphasized in order for *Eurycoma longifolia* products to be manufactured

correctly. The recent dramatic growth of manufacturers with sales of more than 200 *Eurycoma longifolia* products urges the Malaysian Government to enforce the Good Manufacturing Practice (GMP) as a guideline to control the quality, safety and efficacy of the products.

1.2 Problem Statement

Researchers studying herbal production focus on innovations in processing that include development of environmental friendly processes, application of novel processing methods and the improvement of existing process technology (Aziz, 2003). The current practice of *Eurycoma longifolia* extract production at industrial scale comprises of two main processing, namely solid-liquid extraction and spray drying (Athimulam *et al.*, 2006). However, the product yield of spray-dried *Eurycoma longifolia* extract is reported to be quite low and its quality is inconsistent. The extract yield produced at manufacturing scale was reported to be at only about 3% w/w (Athimulam *et al.*, 2006).

Most studies on the solid-liquid extraction of *Eurycoma longifolia* focused on the effect of processing parameters and their modelling in order to obtain high extract yield (Sim, 2004; Mohtar *et al.*, 2007; Kumaresan, 2008; Mohamad *et al.*, 2013; Zamri, 2014). Laboratory experimentations in a stirred vessel have shown that the crude extract yield obtained was in the region of 4.84 to 11.29% depending on the types of parameter investigated (Zamri, 2014). The maximum extractable yield of *Eurycoma longifolia* in this study was theoretically determined to be 53.96% (w/w). Currently, there is no experimental work reported for scale up of batch solid-liquid extraction of *Eurycoma longifolia* after optimization at lab scale.

For downstream processing, spray drying is mostly applied in herbal manufacturing to remove solvent for easy handling and to prolong the shelf-life of the products. *Eurycoma longifolia* extract, which has complex chemical composition, has low glass transition temperature (T_g) , which may lead to high temperature drop (ΔT) during the spray drying process and this might result in high losses. Furthermore, the technical difficulties in scaling up of spray drying are faced by most researchers due to the complexity of the spray drying process that consists of atomization (droplets formation from liquid solution) and evaporation stages (removal of moisture from the droplets).

To address the issue of low product yield and inconsistent quality, the manufacturing process (i.e. extraction and spray drying) has to be optimized, however, performing optimization at manufacturing scale is uneconomical. The way to tackle this problem is by doing optimization at lab-scale, and using dimensional analysis and similitude to scale up the process to industrial scale. Dimensional analysis can be used as a tool to quickly elaborate reliable relations among physical quantities using their dimensions, which must be accompanied by similitude principles to simulate the real conditions of the problem for a more accurate scaling-up exercise. The purpose of this work was to determine the processing parameters that permit accurate transfer of data between facilities of different scales within the ranges covered by the dimensionless numbers with the aim to increase the extract yield and amounts of marker compounds in *Eurycoma longifolia* extracts.

1.3 Objective of Study

The objectives of this study were as follows:

- (i) To optimize the processing conditions for the production of *Eurycoma longifolia* extract to obtain high yield and better product quality.
- (ii) To scale-up the production of *Eurycoma longifolia* using dimensional analysis and similitude.

1.4 Scopes of the Study

In order to accomplish this objective, the following scopes of study were implemented:

- (i) Optimizing the processing conditions of lab-scale single-step solid-liquid extraction and mini-scale spray drying of *Eurycoma longifolia* roots using response surface methodology.
- (ii) Investigating the effect of number of extraction steps in solid-liquid extraction by one-factor-at-a-time (OFAT) technique and the effect of addition of different carrier agents in spray drying process through a comparison study.
- (iii) Establishing the scale-up relationships by dimensional analysis method for solid-liquid extraction, and formulate reliable scale-up predictions for spray drying process in the production of *Eurycoma longifolia* extract.
- (iv) Validating optimum extract yield and quality of extracts at pilot-scale.
- (v) Cost analysis of production of spray-dried *Eurycoma longifolia* extract.

1.5 Significances and Original Contributions of the Study

This study offers several contributions in the optimization and scaling up of the production of *Eurycoma longifolia* extract.

- (i) To the best of current knowledge, this study is one of the first reports on the establishment of the scale-up relationships using the dimensional analysis method by taking into accounts the fundamental engineering of transport phenomena inside the solid-liquid extraction of *Eurycoma longifolia* roots. A considerable number of works were conducted on the modelling of *Eurycoma longifolia* extraction but none focused on the scaling-up technique of identical geometry based on existing pilot-scale equipment. Basically, scale-up of solid suspension in a variety of stirred vessel design have been broadly conducted using an empirical equation of ND^a = constant, however the scale-up rule is still a contradiction up to now depending on the suspension properties, flow behavior and vessel configurations. Thus, there are compelling reasons to establish best-fitted scale-up model from the developed dimensionless numbers in order to obtain similar output between laboratory and pilot-scale for *Eurycoma longifolia* extraction.
- (ii) Spray drying is well recognized as a complex process involving the occurrence of simultaneous heat and mass transfers during the droplet drying. New emerging microencapsulation data suggests that improving the process efficiency and preserving the heat-sensitive compounds can be easily controlled by the addition of appropriate wall material type and concentration. To date, specific studies on microencapsulation by spray drying (e.g. addition of maltodextrin up to 8 %) at commercial-scale have not been verified, hindering the current performance of spray drying of *Eurycoma longifolia* extract. Moreover, the use of high carrier agent concentration in common

practice (up to 10 %) is not encouraged as it affects the quality of the final product.

(iii) As each stage of main processing in the production of *Eurycoma longifolia* extract is strongly dependent on operating variables, the importance of optimization cannot be underestimated. In finding the highest yield with considerable amount of active compounds present in the final product, process optimization can provide the required link between laboratory test results and pilot-scale setting arrangement. Existing optimization works on *Eurycoma longifolia* extraction are currently performed in a different geometry and vessel design, which will result in different outcomes. Meanwhile, reports on optimization of spray drying of *Eurycoma longifolia* extract are currently scarce. Optimization of both main processing units will provide insights on the understanding of the dependence variables on the selected multi-responses.

1.6 Thesis Structure and Organization

This thesis is divided into five chapters. Chapter 1 covers a brief overview of the research backgrounds, problems statement, central objective, scopes of study, significances and originality of the study.

Chapter 2 offers an overview of Tongkat Ali products marketability, pharmacological properties, phytochemistry, issues related on its safety, efficacy, quality and standardization as well as the analytical methods used. The literatures also highlight the processing of spray-dried Tongkat Ali extract with regards to basic concepts and kinetics involved in the system.

Chapter 3 covers the overall methodologies used for the optimization and scaling up of the solid-liquid extraction and spray drying process. The equipment design characteristics and its limitation are explained for up-scaling purposes in the production of Tongkat Ali extract.

Chapter 4 presents the comprehensive results and discussions on the operating parameters effect on the multi-responses optimization, scaling-up formulations, and pilot-scale verifications of solid-liquid extraction and spray drying processes. The preliminary works on Tongkat Ali authentication, extraction modelling and spray drying thermal effect are also described in this chapter.

Chapter 5 provides the overall summary of the research findings and future recommendations for upcoming works.

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