THERMAL AND HYDROTHERMAL TREATMENT EFFECTS ON ANTINUTRITIONAL AND FUNCTIONAL PROPERTIES OF DEFATTED WINGED BEAN (Psophocarpus tetragonolobus L.DC) SEED PROTEIN POWDERS

SAMI SAADI

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DOCTOR OF PHILOSOPHY
UNIVERSITI PUTRA MALAYSIA

2014

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By

SAMI SAADI

Thesis Submitted to School of Graduate Studies, Universiti Putra Malaysia in Fulfillment of the Requirement for the Doctor of Philosophy

December 2014

DEDICATION

This thesis is dedicated to my beloved parents, brothers, and sisters; to all members of my big family SAADI and my lovely wife Nor Elhouda Nacer and her family as well. It also goes to teachers, scientists, researchers, and all seekers for knowledge.

Abstract of thesis presented to the Senate of Universiti Putra Malaysia in fulfillment of the requirements for the degree of Doctor of Philosophy

THERMAL AND HYDROTHERMAL TREATMENT EFFECTS ON ANTINUTRITIONAL AND FUNCTIONAL PROPERTIES OF DEFATTED WINGED BEAN (*PSOPHOCARPUS TETRAGONOLOBUS* L. DC) SEED PROTEINS POWDERS

By

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December 2014

Chairman: Prof. Nazamid Saari, PhD

Faculty: Food Science and Technology

The changes in the structural motif of protein by mitigating protease inhibitors like Bowman Birk Inhibitor (BBI), Kunitz type inhibitor (KTI), and lectin and other secondary metabolites such as phytic acid (PA), tannic acid (TA) and their derivative compounds of myo-inositol (MI) and gallic acid (GA) is one of the main targets of biochemists for inducing protein denaturation/unfolding and therefore, enzyme accessibility to different distinct regions of defatted protein polymeric chain (DPPC). For this reason tow method treatments named as thermal treatment (TT) and hydrothermal treatment (HT) were developed, optimized by using RSM-CCD and mathematically modeled via second order polynomial regression models to mitigate PA, MI, TA, GA, BBI, KTI and lectin after the defatting process. Under optimum conditions of TT and HT, tow model types of proteins named defatted hydrothermal treated sample (DHTS) and defatted thermal treated sample (DTTS) in addition to defatted native sample (DNS) were obtained. The subsequent digestion of the three model types (DHTS, DTTS, and DNS) with digestive enzymes of trypsin and combined trypsin-α-chymotrypsin simulated under gastrointestinal tract conditions for up six hours of hydrolysis was examined. Results showed that HT and TT conditions were successfully fitted revealing a significant correlation between dependent and independent variables, justifying the competence and accuracy of RSM-model-equations toward the formation of polymers via enzymatic hydrolysis after mitigating those polymorphic-antinutrients from defatted winged bean seeds protein (DWBSPs) matrix. The deactivation levels of KTI in the following trypsin-digests (TDJ) taking DNS as control were ordered as follow: DHTS-TDJ (47.39%) > DTTS-TDJ (46.21%). In contrast, their deactivation levels for BBI in the following trypsin-α-chymotrypsin digests (TDJ-α-CHDJ) were ordered as follow: DHTS-(TDJ-α-CHDJ) 57.87% > DTTS-(TDJ-α-CHDJ) 30.23%. Moreover, many of the encountered issues can be occurred when a solid/soft materials are subjected to certain physical, and chemical stresses such as the disorder state of atoms, re-configuration of molecules, chemical bonding dissociation and re-association. Therefore, the above mechanization effects were investigated and mechanistically interpreted by determining the denaturation/unfolding state resulting from TT and HT using differential scanning calorimetry (DSC). RSM-CCD was used to determine the denaturation/unfolding efficiency (DE/UE) by exploring their energetic model parameters of enthalpy (ΔH), entropy (ΔS) and heat capacity (ΔCp). Results showed that the DE/UE (%) based ΔH, ΔS and ΔCp were found to be more precise among sample group revealing an

excellent fitting between variables and highly significant R^2 ranging from 99.8% (ΔCp), 91.9% (ΔS), and 84.3% (ΔH). Furthermore, the comparisons in between experimental and predicted values indicated that the corresponding RSM-CCD polynomial regression models are suitable and applicable. Meanwhile, the low level of ΔG reflected a low average level of dissociated chemical bonds and vice-versa for the high level of free energy of transition. The results of DE/UE efficiency (%) were then used with other structural parameters to investigate the enzymatic catalytic rate (ECR), enzymatic catalytic efficiency (ECEF), and other associated energetic parameters such as enzymatic activation energy (EAE) and enzymatic catalytic energy (ECE) of different enzymes with distinct region of specificities in DPPC. DNS, DHTS, and DTTS protein model types were used to assess the biochemical transition states of this catalytic elements and their involvement in many of the internal mechanisms associated to substrate aggregation, adhesion, mode of inhibitions, reversible transition, and reformation of the chemical bonding during polymer formations. Different mathematical models were successfully established in order to discriminate the mobility and displacement of specific enzymes (trypsin, α-chymotrypsin, and their interaction) with other non-specific enzyme conterparts (alcalase and papain). The results showed that the specificity of the enzymes played a key role in accelerating and retarding the ECR. They revealed that the EAE and ECE of these complex system had different signatures and profiles during their biochemical transitions, thus exhibiting competitive, non-competitive, competitive-non-competitive and feed-back inhibition modes. They showed that these enzymes are capable in accessing different distinct of peptides or proteins, so, inducing significant dilatation (relaxation) and attraction through a chemical bombing at atomic levels. These behaviors helped us to understand the impact of enzymatic antagonism under electrostatic, ionic, cationic, hydrophobic, and hydrogen forces in renewing enzyme energy from the surrounded envirmental conditions of the hydrolysis process with profitable of released captivated biomaterials. The biological activities of the resulting biomaterials were validated by the degradation of the network structure constructed by the secondary metabolites of PA, TA and their derivative compounds MI) and GA using clustering statistical method. Results showed that, the chemical structure of the secondary metabolites played a pivotal role in maintaining their resistance against the exerted external forces, therefore, the combined effect of temperature (40°C), time (1.5hr) and pH (2.5) was the best options for degrading those antinutrients by avoiding their polymorphism (association) with DPPC that will undergo the enzymatic hydrolysis using specific enzymes (trypsin, α-chymotrypsin, and combined trypsin-α-chymotrypsin) and non-specific enzymes (papain and alcalase). The obtained enzymatic polymer digests were investigated from their antioxidative and antihypertensive biological effects in vitro using DPPH free radical scavenging assay, ferric chelating ability assay, and ABTS capacity assay, while the angiotensin-converting enzyme (ACE) inhibitory activity (IA) was assessed by HPLC, taking hippuric acid as bio-chemical marker for the identification. The majority of the enzymatic polymer digests yielded a variable range of antioxidant potency varying from low, middle, strong and very strong effects. While the ACE-IA assay revealed that these enzymatic polymer digests had the highest impact on the bioconversion of angiotensin I to angiotensin II, resulting in an overall inhibition values ranging from 89.76% to 97.99% for the four selected model types. Consequently, the DHTS of winged bean seed protein powders and their resulting enzymatic polymer digests are promising biomaterials in triggering certain biological effects similar to that of peptide like-hormone such as the reduction of the incidences of the oxidation stress and hypertension.

Abstrak tesis yang dikemukakan kepada Senat Universiti Putra Malaysia sebagai memenuhi keperluan untuk Ijazah Doktor Falsafah

KESAN RAWATAN HABA DAN HIDROTERMA PADA SIFAT-SIFAT ANTINUTRISI DAN PERFUNGSIAN BENIH SERBUK PROTEIN KACANG BOTOR YANG DINYAHLEMAK (*PSOPHOCARPUS TETRAGONOLOBUS* L. DC)

Oleh

SAMI SAADI

Disember 2014

Pengerusi: Prof. Nazamid Saari, PhD

Fakulti: Sains dan Teknologi Makanan

Perubahan dalam motif struktur protein dengan menggunakan kaedah mitigasi penindas protease seperti penindas Bowman Birk (BBI), penindas jenis Kunitz (KTI), dan lectin dan lain-lain metabolit sekunder seperti asid fitik (PA), asid tannik (TA) dan hasil terbitan sebatian dari myo-inositol (bt) dan asid gallik (GA) merupakan salah satu sasaran utama ahli kimia untuk menggalakkan proses denaturasi protein dan selanjutnya pengaksesan enzim ke kawasan-kawasan tertentu dalam rantaian polimeric protein yang dinyahlemak (DPPC). Oleh demikian dua kaedah rawatan yang dinamakan rawatan haba (TT) dan rawatan hidroterma (HT) yang telah dibangunkan secara optima dengan menggunakan RSM-CCD dan model matematik melalui model regresi order yang kedua telah digunakan untuk proses mitigasi PA, MI, TA, GA, BBI, KTI dan lectin selepas proses defatting. Di bawah kondisi optima TT dan HT, dua model jenis protein yang dinamakan sampel nyahlemak rawatan hidroterma (DHTS) dan sampel nyahelima rawatan haba (DTTS) selain daripada defatted sampel natif (DNS) telah diperolehi. Penghadaman yang berterusan oleh ketiga-tiga jenis model (DHTS, DTTS, dan DNS) dengan penghadaman enzim tripsin dan gabungan trypsin-α-chymotripsin di bawah kondisi simulasi saluran gastrousus sehingga enam jam menggunakan proses hydrolisis telah diperiksa. Hasil kajian menunjukkan bahawa kondisi HT dan TT adalah bersesuaian dan ia mendedahkan korelasi yang signifikan antara pembolehubah bebas dan bergantung, menjustifikasikan kecekapan dan ketepatan RSM-model-equations ke arah pembentukan polimer melalui enzim hydrolisis selepas mitigasi polimorfik-antinutrisi dari matrik benih protein kacang botor yang dinyahelimak (DWBSPs). Tahap penyahaktifan KTI dalam trypsin-digests (TDJ) menggunakan DNS sebagai kawalan diaturkan seperti berikut: DHTS-TDJ (47.39%) > DTTS-TDJ (46.21%). Manakala tahap penyahaktifannya untuk BBI di dalam tripsin-α-chymotripsin digests (TDJ-α-CHDJ) telah diaturkan seperti berikut: DHTS-(TDJ-α-CHDJ) 57.87% > DTTS-(TDJ-α-CHDJ) 30.23%. Selain itu, kebanyakkan isu-isu yang ditemui berlaku apabila bahan pepejal/lembut tertakluk kepada bentuk fizikal tertentu, dan tekanan kimia seperti keadaan gangguan atom, konfigurasi semula molekul, penceraian ikatan kimia dan persatuannya semula. Oleh itu, kesan-kesan mekanisma di atas telah disiasat dan ditafsirkan secara mekanikal dengan menentukan keadaan denaturasi akibat TT dan HT menggunakan calorimetri pengimbas pembezaan (DSC). RSM-CCD ini digunakan untuk menentukan kecekapan denaturasi (DE/UE) dengan mengkaji parameter model tenaga enthalpi (ΔH), entropy (ΔS) dan muatan haba (ΔCp). Hasil kajian menunjukkan bahawa DE/UE (%) yang berdasarkan ΔH, ΔS dan ΔCp

didapati lebih tepat antara kumpulan sampel yang menunjukkan kesesuaian terbaik antara pembolehubah dan yang mempunyai nilai signifikasi R^2 yang tinggi bermula daripada 99.8% (p)$C\Delta$), 91.9% (ΔS) dan 84.3% (ΔH). Selain itu, perbandingan di antara nilai-nilai yang diperolehi di dalam eksperimen dan ramalan yang dinyatakan RSM-CCD khususnya regresi adalah sesuai dan boleh digunakan. Sementara itu, tahap rendah ΔG mencerminkan tahap purata rendah bon dissosiasi kimia dan sebaliknya menunjukkan tahap tinggi bagi peralihan tenaga bebas. Keputusan kecekapan DE/UE (%) kemudian digunakan dengan parameter yang berlainan struktur untuk menyiasat kadar pemangkin enzim (radar ECR), kecekapan pemangkin enzim (ECEF) dan lain-lain parameter tenaga yang berkaitan seperti tenaga pengaktifan enzim (EAE) dan enzim pemangkin tenaga (ECE) untuk enzim yang berbeza dan mempunyai rantau yang spesifik di DPPC. Jenis model protein DNS, DHTS dan DTTS telah digunakan untuk menilai peralihan biokimia bagi unsur-unsur pemangkin ini dan penglibatannya dalam kebanyakkan mekanisma dalaman yang berkaitan untuk pengagregatan substrat, lekat, mod inhibisi, peralihan yang berbalik dan reformasi bond kimia semasa formasi polimer. Model matematik yang berbeza telah berjaya ditubuhkan untuk mendiskriminasi pergerakan dan anjakan enzim tertentu (trypsin, α-chymotrypsin dan interaksi mereka) dengan lain-lain conterparts-khusus enzim (alcalase dan papain). Hasil kajian menunjukkan bahawa kepentingan enzim memainkan peranan penting dalam mempercepatkan dan memperlambatkan radar ECR tersebut. Mereka mendedahkan bahawa sistem komplek EAE dan ECE ini mempunyai pengenalan yang berbeza dan boleh diprofailkan semasa ia melalui peralihan biokimia, oleh demikian ia mempamerkan mod perencatan berdaya saing,tidak-berdaya saing, berdaya saing-tidak-berdaya saing dan mod inhibisi maklum-balas. Mereka menunjukkan bahawa enzim ini mampu mengakses peptida dan protein yang berbeza, oleh itu, menggalakkan dilasasi yang signifikan (relaksasi) dan tarikan melalui pengeboman kimia di peringkat atom. Perilaku ini membantu kita untuk memahami impak enzim antagonisma di bawah elektrostatik ionik, kationik, hydrofobik, dan kuasa-kuasa hidrogen dalam memperbaharui tenaga enzim daripada keadaaan sekeliling proses hydrolisis dengan memberi untungan daripada pelepasan bahan bio yang tersimpan. Aktiviti-aktiviti biologi bahan-bio yang terhasil telah disahkan oleh kemusnahan struktur rangkaian yang dibina oleh metabolites sekunder daripada PA, TA dan sebatian terbitan mereka (MI dan GA) yang menggunakan kaedah kelompok statistik. Hasil kajian menunjukkan bahawa struktur kimia metabolites sekunder memainkan peranan penting mengekalkan penentangan mereka terhadap tekanan luaran, oleh yang demikian, kesan gabungan suhu (40° C), masa (1.5 jam) dan pH (2.5) adalah pilihan yang terbaik untuk degradasi antinutrisi tersebut dengan mengelakkan berlakunya polymorphism dengan DPPC yang akan menjalani hydrolisis enzim menggunakan enzim tertentu (trypsin-α-chymotrypsin, dan gabungan trypsin-α-chymotrypsin) dan enzim khusus (papain dan alcalase). Polimer enzim penghadaman yang diperolehi disiasat dari kesan biologi antioksidatif dan antihipertensif dalam vitro menggunakan esei DPPH assay scavenging radikal bebas, esei keupayaan pengkelat ferik dan esei kapasiti ABTS, manakala enzim penukaran angiotensin (ACE) pembantut aktiviti (IA) telah dinilai oleh HPLC, di mana asid hipurik diambil sebagai penanda bio-kimia untuk pengenalpastian. Majoriti polimer enzim penghadaman menghasilkan pelbagai pembolehubah antioksidan dengan potensi yang berbeza bermula dari kesan rendah, sederhana, kuat sehingga sangat kuat. Manakala assay ACE-IA mendedahkan bahawa polimer enzim penghadaman ini mempunyai impak tertinggi pada penukaran-bio angiotensin I angiotensin II, mengakibatkan keseluruhan nilai-nilai inhibisi yang diperolehi adalah di antara 89.76% hingga 97.99% bagi keempat-empat jenis model yang dipilih. Oleh yang demikian, DHTS benih serbuk protein kacang botor dan polimer enzim penghadaman yang terhasil menjanjikan masa depan yang cerah bagi bahan bio yang boleh mencetuskan beberapa kesan biologi yang sama dengan peptida berbentuk hormon bagi pengurangan insiden tekanan pengoksidaan dan hipertensi.

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I certify that a Thesis Examination Committee has met on December 22, 2014 to conduct the final examination of Sami Saadi thesis entitled "Thermal and Hydrothermal Treatment Effects on Antinutritional and Functional Properties of Defatted Winged Bean (*Psophocarpus tetragonolobus* L. DC) Seed Protein Powders" in accordance with the Universities and University Colleges Act 1971 and the Constitution of the Universiti Putra Malaysia [P.U.(A) 106] 15 March 1998. The Committee recommends that the student be awarded the Doctor of Philosophy.

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This thesis was submitted to the Senate of Universiti Putra Malaysia and has been accepted as fulfilment of the requirement for the degree of Doctor of Philosophy. The members of the Supervisory Committee were as follows:

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LIST OF ABBREVIATIONS

PA	Phytic acid
MI	Myo-inositol
TA	Tannic acid
GA	Gallic acid
ECR	Enzymatic catalytic rate
EAE	Enzymatic activation energy
ECE	Enzymatic catalytic energy
ECEF	Enzymatic catalytic efficiency
KTI	Kunitz-trypsin inhibitor
BBI	Bowman Birk inhibitor
FCA	Ferric chelating ability
RSA	Radical scavenging activity
ACE	Angiotensin-converting enzyme
ABTS	2.2'-azino-bis(3-ethylbenzothiazoline-6-sulphonic acid)
DPPH	1,1-diphenyl-2-picrylhydrazyl
DJ	Djest
PC	Peptide concentrations
HT	Hydrothermal treatment
TT	Thermal treatment
HD	Hydrolysis degree
HT	Hydrolysis time
PCL	Peptide chain length
PP	Polypeptides
WBS	Winged bean seeds
HPLC	High performance liquid chromatography
DWBSPs	Defatted winged bean seed proteins
HA	Hippuric acid
HHL	Hippuryl-histidyl-leucine
OPA	*O*-phthaldiadehyde
BSA	Bovine serum albumin
E	Enzyme
S	Substrate
K	Enzymatic reaction constant
PDAD	Photo- diode array detection
ANOVA	Analysis of variance
NS	Native sample
DS	Defatted sample
R^2	Coefficient of determination
RSM	Response surface methodology
CCD	Central composite design
AOAC	Association of official analytical chemists
CP	Crude protein
CL	Crude lipid
CF	Crude fiber
CH	Carbohydrates

BS	Buffer system
DSC	Differential scanning calorimetry
ΔH	Enthalpy
ΔS	Entropy
Δcp	Heat capacity
Tg	Glass transition
Tm	Maximum denaturation temperature (1/2 of protein unfolding)
pI	Net charge of peptide
2D/3D	Two dimensional/three dimensional
R^2 (*Adj*)	Adjusted coefficient of determination
ΔG	Gibbs free energy
AAs	Amino acids
LMW	Low molecular weight
TT	Thrombin time
APTT	Activated partial thromboplastin time
LAB	Lactic acid bacteria
FAA	Free amino acids
ELIZA	Enzyme-linked immunosorbent assay
BW	Body weight
SHR	Spontaneously hypertensive rat
ODS HPLC	Octadecyl-silica column-high performance liquid chromatography
GFC	Gel filtration chromatography
OR	Orientase
PR	Protease
RP-HPLC	Reverse-phase high performance liquid chromatography
ACE-IA	Angiotensin-converting enzyme inhibitory activity
NO	Nitric oxide
ESI-TOF MS/MS	Ionisation-time-flight-mass-spectrometry
ESR	Electron spin resonance
DNA	Deoxyribonucleic acid
SOSA	Superoxide anion scavenging activity
MW	Molecular weight
MTT	Methyl thiazol tetrazolium
FPLC	Fast liquid protein chromatography
LOX	Lipoxygenase
Con A	Concanavalin A
IL-2	Interleukin-two
TFN-γ	Interferon-**γ**
TBA	Thiobarbituric acid
BHA	Butylated hydroxyanisol
PUFAs	Polyunsaturated fatty acids
HPLC-MS/MS	High performance liquid chromatography-mass/mass spectrometry
LC-ESI-Q-TOF-MS/MS	Liquid chromatography-ionization-time-flight-mass-spectrometry
ROS	Reactive oxygen species
FAR-UVCD	Far-ultra-violet circular dichroism spectrometry
SEC	Size exclusion chromatography
TFA	Trifluoroacetic acid
CE	Capillary electrophoresis
CIEF	Capillary isoelectric focussing

IEC	Ion-exchange chromatography
cDNA	Cyclic deoxyribonucleic acid
GMP	Guanosine monophosphate
UF	Ultra-filtration
CAU-PAGE	Continuous acid urea polyacrylamide gel electrophoresis
SBP	Systolic blood pressure
CMP	Caseinmacropeptide
MALDI-MS	Matrix-assisted laser desorption ionization mass spectroscopy
K_{cat}	Constant indicates the catalytic efficiency of enzyme
Km	Constant parameter that gives an indication on the adhesion force between enzyme and its targeted material.
Ki	Constant parameter in the presence of an inhibitor.
V_{max}	Maximum velocity of the enzyme during enzymatic reaction.
I	Inhibitor
PepT1	Specific carrier of peptide
UGI	Upper gastrointestinal
SOD	Superoxide dismutase
CAT	Catalase
GSH-PX	Glutathione peroxidase
PEP	Prolyl endopeptidase
PEF	Pulsed electric filed
LPS	Lipopolysaccharides
PFP	Partially purified peptides
MIC	Minimum inhibition concentration
PEG	Polyethylglycol
Gly	Glycine
Ala	Alanine
Val	Valine
Leu	Leucine
Ile	Isoleucine
Met	Methionine
Phe	Phenylalanine
Trp	Tryptophan
Pro	Proline
Ser	Serine
Thr	Threonine
Cys	Cysteine
Tyr	Tyrosine
Asn	Asparagine
Gln	Glutamine
Asp	Aspartic acid
Glu	Glutamic acid
Lys	Lysine
Arg	Arginine
His	Histidine

CHAPTER 1

GENERAL INTRODUCTION

The winged bean (*Psophocarpus tetragonolobus* L. DC.) seeds are an underutilized food materials, which have a nutritive values comparable to those of soybean seeds (Garcia, & Palmer, 1980; Prakash et al., 1987, Yea et al., 2014). However, the types of proteins and their amino acid composition (Ekpenyong and Borchers, 1982), and high value-added compounds of these seeds such as carbohydrates and dietary fibers (Misra et al., 1987) have prompted scientists over the world to initiate their exploitation in the food industry. Unfortunately, the direct consumption of these seeds without pretreatment has been shown to cause an incomplete digestion of proteins in the human intestines (Henley & Kuster, 1994; Deshpande & Damodaran, 1989). This problem, in fact, is associated to the presence of antinutritional factors such as tannic acid, phytic acid, protease inhibitors and lectin (Urooj & Puttaraj, 1994; Liener, 1994; Tovar, 1991). The digestion of legume seed proteins is limited by the presence of phytic and tannic acids (Tovar, 1991). The absorption of high amounts of tannic acids by the human body after consumption might impact negatively the living organisms through the organs damage and other of membrane intestinal irritants (Garg, 1992; Terrill, 1994). Phytic acid displays a great capacity in reducing protein solubility, enzymatic activity, proteolytic digestibility, and biopeptide availability (Liu, 1998; Welch, 2002; Raboy, 2009; Kumar, 2010). Therefore, the problem of phytic acid cannot be ignored when the seeds are turned into flour, infant formula foods and as well as in paste-based fruits or vegetables products (Park, 2006). Thus, they have to be subjected to treatments that will either reduce or eliminate their contents, among which the degradation of these antinutrients can be accelerated by the addition of base or acid (Kruger, 2012). Most of these natural contaminants (e.g. phytic acid, tannic acid, protease inhibitors, and lectin) are distributed in different distinct regions of grain legumes and form and heterogeneous complex system (Liener, 1989; D'Mello, 1995). These types of anti-nutritional compounds are distinguished from other storage proteins based on their functionality, where their presence within the seeds might serve as well as particular protective effects toward the living system. The main families of protease inhibitors present in legume seeds are the Bowman Birk type inhibitors and Kunitz type inhibitors (Laskowsky and Kato, 1980; Mosolov and Valueva, 2005; Qi et al., 2005). Bowman Birk inhibitor can act as cancer preventive and suppressing agents and has shown great importance in cancer research using different *in vitro* and *in vivo* model systems (Clawson, 1996). The proper arrangement of 70 residues with seven disulphide bridges permitted a better stabilization to BBI molecules, particularly for the double-headed structural motif that may lead to better recognition for the enzymes (Odani and Ikenaka, 1973). The main characteristic of its particular reactive sites are associated to the chemical structure of amino acid residues positioned in the active site P1 (Scarafoni et al., 2007). Owing to its structural characteristics, BBI exerts a double mechanism of actions by inhibiting both of proteolytic enzymes of trypsin and chymotrypsin and termed as double-headed inhibitors (Domoney et al., 1993). On the other hand, Kunitz inhibitor polypeptide consists of one active site and it comprise of 181 residues arranged with only two disulfide bridges that maintain its stability. The low level of disulfide bridges in Kunitz inhibitor makes it more sensitive to heat compared to BBI. The high rigidity level and its compaction due to many internal disulfide bridges may the result of BBI thermal stability (Rouhana et al., 1996). It is well characterized in legume seeds with similar structure configuration (*e.g.* similar N-terminal sequence) to that of soybean trypsin. Kunitz-trypsin inhibitor possesses a molecular weight of 20 kDa and comprises with four types of cysteine residues forming a single active site, which is usually located on the protein loops (Birk, 1996; Wang and Ng, 2006). This type of inhibitor as exception case is successfully isolated from the *Mimosoidae* subfamily and constitutes of two sequence chains of polypeptides linked together with one disulfide bridge (Lin et al., 1991; Oliva et al., 2000). Lectin is a sugar binded protein complex that occurs naturally within the legume seeds, meaning that a specific type of protein possesses at least one of the non-catalytic domain that is attached reversibly to mono or oligosaccharides (Ryan, 1999). Moreover, plant is considered as one of the main sources for isolating lectin molecules, which is usually found in the fruits and vegetables that did not undergo processing (Nachbar and Oppenheim, 1980). In contrast, the abundance presences of lectin in pulse crops requires mitigation and thermal denaturation or reduction prior to human consumption. Lectin that is derived from various food sources showed to exert great impacts in modulating the immune disorders by stimulating the proliferation of lymphocytes, cytokine regulation, anti-body synthesis, and natural killer cell activity (Hartmann and Meisel, 2007). It is used to control obesity, to treat cancer diseases, and to activate some of the innate defense mechanisms (Sames et al., 2001; Wang et al., 2000).

The application of heat treatment under controlled processing conditions to legume seeds is paramount important to human health. However, the variability in the structural properties of different antinutritional factors and protease inhibitors and their degree of susceptibility during various processing treatments prompts the scientist to investigate the best conditions leading to the desired quality of legume seed proteins. Although the presence of these antinutritional compounds may impact adversely the mechanism of hydrolysis and the absorption trajectory of macro-and micro-nutrients from the entrocyte domain (e.g. big and small intestines) to portal circulation (blood). These, protease inhibitors that have been denatured have been reported to provide beneficial effects, especially on their potential effects for lowering the incidences of cancers and obesity and other physiological perturbations and immune discords within the living system (Clawson, 1996; Kennedy, 1998).

Therefore, the main objectives of this study were:

(1): To mitigate phytic acid, tannic acid, Bowman Birk Inhibitor (BBI), Kunitz-Trypsin Inhibitor (KTI) and lectin from defatted winged bean seed protein powder using thermal and hydrothermal treatments.
(2): To determine the denaturation/unfolding state and efficiency caused by thermal and hydrothermal treatments by optimization using response surface methodology (RSM-CCD).
(3): To establish different models between the structural characteristics of the hydrolysates and their energetic parameters for better understanding of the structure-function relationships.
(4): To characterize the antioxidative and antihypertensive activities of protein hydrolysates from defatted hydrothermal treated samples (DHTS) using non-specific enzymes (e.g. alcalase and papain) and specific enzymes (e.g. trypsin, α-chymotrypsin and their combinations).

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