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OPTIMISATION OF MEDIUM FORMULATION AND SCALING UP OF THREONINE AND TRYPTOPHAN PRODUCTION BY LACTIC ACID BACTERIA USING RESPONSE SURFACE METHODOLOGY

LIM YE HENG

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By

LIM YE HENG

Thesis Submitted to the School of Graduate Studies, Universiti Putra Malaysia, in Fulfilment of the Requirements for the Degree of Doctor of Philosophy

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Chair : Professor Foo Hooi Ling, PhD
Faculty : Institute of Bioscience

Increasing knowledge on the functions of amino acid (AA) in animal production has led to escalating demand of various amino acid. Threonine and tryptophan are among the most commonly employed feed AA due to their indispensable roles in enhancing the growth performance of livestocks. Currently, AA production relies heavily on non-food-grade-microorganisms such as genetically modified *Corynebacterium glutamicum* and *Escherichia coli* which was a concern as the use of genetically modified *C. glutamicum* for production of amino acid was linked to over thousand cases of a deadly syndrome, eosinophila myalgia syndrome (EMS). This has urged for search of safer alternatives by utilising food-grade-microorganisms. Recent studies reported that lactic acid bacteria (LAB) were capable to produce various AA owing to their well-established proteolytic system and presence of AA biosynthesis gene. Furthermore, they are reputed with the Generally Recognised as Safe (GRAS) status, making them an excellent candidate as food grade producer. However, there were limited studies regarding production of AA by using LAB. Hence, the objective of this study was to identify the threonine and tryptophan producing LAB and optimise the medium formulation via response surface methodology (RSM) approach, followed by scaling up their production by using constant impeller tip speed approach. It was hypothesised that threonine and tryptophan producing LAB could be identified and their production could be improved by optimisation of the medium formulation using RSM. Additionally, the production of threonine and tryptophan by the selected LAB could be scaled up constant impeller tip speed approach. In this study, 17 LAB isolates from Malaysian foods were identified phenotypically and genotypically. The isolates comprised of 3 species: *Pediococcus pentosaceus* (6 isolates), *Pediococcus acidilactici* (2 isolates), and *Lactobacillus plantarum* (9 isolates). Thereafter, the growth profile of the isolates were characterised and their proteolytic activity was determined qualitatively and quantitatively under 3 pH conditions by using skim milk agar hydrolysis assay, skim milk agar well diffusion assay and azocasein assay due

to the important role of proteolytic activity on amino acid production. All the LAB isolates exhibited versatile extracellular proteolytic system where proteolytic activity was detected over wide pH range. The highest extracellular proteolytic activity at pH 5 (15.76 U/mg) and pH 8 (19.42 U/mg) was detected in *L. plantarum* RG14. Meanwhile, *L. plantarum* RS5 and RI11 demonstrated the highest extracellular proteolytic activity of approximately 17 U/mg at pH 6.5.

The ability of the LAB isolates to produce AA was subsequently determined by cultivating in de Man Rogosa and Sharpe (MRS) medium. The production of amino acid was quantified by using high performance liquid chromatography (HPLC) analysis. The LAB isolates demonstrated the ability to produce numerous industrially important AA but the production was strain dependent. *P. pentosaceus* TL-3 demonstrated highest threonine productivity (12.88 mg/L/h) and identified as superior threonine producer in this study. Meanwhile, *P. acidilactici* TP-6 was selected as tryptophan producer with a productivity of 5.05 mg/L/h. The production of threonine and tryptophan by the selected LAB isolate was subsequently optimised by using RSM. The nutritional requirement for threonine and tryptophan production was first evaluated by using Plackett Burman Design (PBD) and subsequently optimised by using Central Composite Design (CCD). Molasses, meat extract, $(NH_4)_2SO_4$ and $MnSO_4$ were the most important components for threonine production by *P. pentosaceus* TL-3 with an optimum concentration of 30.79 g/L, 25.30 g/L, 8.59 g/L, and 0.098 g/L respectively. The net threonine produced recorded by *P. pentosaceus* TL-3 under optimised condition (125.98 mg/L) was improved by 2 fold whereas the cost of the optimised medium was reduced by 8.5% compared to MRS medium.

In comparison, the best combination of medium components for tryptophan production by *P. acidilactici* TP-6 were molasses, meat extract, urea and $FeSO_4$. The optimum concentration suggested by RSM were: molasses, 14.06 g/L; meat extract 23.68 g/L; urea, 5.56 g/L and $FeSO_4$, 0.024 g/L. Up to 68.05 mg/L of tryptophan was produced by *P. acidilactici* TP-6 under optimised condition, which was equivalent to 150% enhancement compared to the control. In contrast, the cost of the optimised medium was reduced by 11%. Furthermore, the production of threonine and tryptophan by the selected LAB isolate was successfully scaled up in 30 L stirred tank bioreactor based on constant impeller tip speed approach. Additionally, the net threonine and tryptophan produced in bioreactor cultivation was comparable to the predicted amount suggested by CCD. In conclusion, *P. pentosaceus* TL-3 and *P. acidilactici* TP-6 were identified as threonine and tryptophan producer respectively and the production of threonine and tryptophan by the selected producer strain was enhanced by 2 folds and 150% respectively through optimisation of their medium formulation using RSM approach. Additionally, the production of threonine and tryptophan was successfully scaled by based on constant impeller tip speed approach where the production in both small and large scale cultivation was comparable.

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

PENGOPTIMUMAN FORMULASI MEDIA DAN MEMPERTINGKATKAN SKALA PENGHASILAN TREONIN DAN TRIPTOFAN OLEH BAKTERIA ASID LAKTIK DENGAN MENGGUNAKAN KAEDAH RANGSANGAN PERMUKAAN

Oleh

LIM YE HENG

Disember 2017

Pengerusi : Profesor Foo Hooi Ling, PhD
Fakulti : Institut Biosains

Peningkatan pengetahuan terhadap fungsi asid amino dalam pengeluaran haiwan membawa kepada peningkatan permintaan pelbagai asid amino. Treonin dan triptofan merupakan asid amino yang paling biasa digunakan disebabkan peranan penting mereka dalam menambah baik prestasi pertumbuhan haiwan ternakan. Pada masa kini, penghasilan asid amino bergantung kepada mikroorganisma bukan gred makanan seperti *Corynebacterium glutamicum* serta *Escherichia coli* yang diubahsuai secara genetik dan ini merupakan satu kebimbangan oleh kerana penggunaan *C. glutamicum* yang diubahsuai secara genetik untuk penghasilan asid amino telah dikaitkan dengan lebih daripada ribuan kes sindrom maut iaitu sindrom eosinophila myalgia (EMS). Justeru, alternatif yang lebih selamat perlu dikaji. Baru-baru ini, terdapat laporan bahawa bakteria asid laktik (LAB) mampu menghasilkan pelbagai asid amino berikutan sistem proteolitik yang mantap serta kehadiran gen biosintesis asid amino. Tambahan pula, LAB dikenali dengan status umumnya yang diiktiraf sebagai selamat (GRAS), menjadikan mereka calon yang unggul sebagai penghasil asid amino gred makanan. Namun demikian, kajian berkaitan penghasilan asid amino dengan menggunakan LAB masih terhad. Oleh itu, objektif kajian ini adalah untuk mengenal pasti LAB yang boleh menghasilkan treonin dan triptofan serta mengoptimumkan rumusan media melalui kaedah rangsangan permukaan (RSM), disusuli dengan meningkatkan skala penghasilan dengan menggunakan kaedah kelajuan tip pendesak tetap. Hipotesis kajian ini adalah LAB yang mampu menghasilkan treonin dan triptofan dapat dikenal pasti dan penghasilannya dapat dipertingkatkan dengan pengoptimuman formulasi media dengan menggunakan RSM. Selain itu, penghasialn treonin dan triptofan oleh LAB terpilih boleh dipertingkatkan skala berdasarkan kaedah kelajuan tip pendesak tetap. Dalam kajian ini, 17 LAB yang pencilan daripada makanan Malaysia telah dikenal pasti secara fenotipik dan genotipik. LAB yang diisolasikan terdiri daripada 3 spesies: *Pediococcus pentosaceus* (6 strain), *Pediococcus acidilactici* (2 strain), dan

Lactobacillus plantarum (9 strain). Selepas itu, ciri profil pertumbuhan LAB dan aktiviti proteolitik mereka telah ditentukan secara kualitatif dan kuantitatif bawah 3 keadaan pH dengan menggunakan asai hidrolisis agar susu skim, kaedah penyebaran perigi agar susu skim serta kaedah azokasein. Semua LAB menunjukkan sistem proteolitik ekstrasel yang serba boleh di mana aktiviti proteolitik telah dikesan pada julat pH yang luas. Aktiviti proteolitik tertinggi ekstrasel pada pH 5 (15.76 U/mg) dan pH 8 (19.42 U/mg) dicatatkan oleh *L. plantarum* RG14. Sementara itu, *L. plantarum* RS5 dan RI11 menunjukkan aktiviti proteolitik ekstrasel tertinggi sekitar 17 U/mg pada pH 6.5.

Keupayaan LAB yang dipencilkan untuk menghasilkan asid amino kemudiannya ditentukan dengan pengkulturan dalam media de Man Rogosa dan Sharpe (MRS). Penghasilan asid amino diukur dengan menggunakan analisis kromatografi cecair berprestasi tinggi (HPLC). LAB yang dipencilkan menunjukkan keupayaan untuk menghasilkan pelbagai asid amino perindustrian penting namun penghasilan adalah bergantung pada strain. *P. pentosaceus* TL-3 menunjukkan produktiviti tertinggi treonin (12.88 mg/L/h) dan terpilih sebagai penghasil treonin unggul. Sementara itu, *P. acidilactici* TP-6 telah dipilih sebagai penghasil triptofan dengan produktiviti sebanyak 5.05 mg/L/h. Penghasilan treonin dan triptofan oleh LAB yang terpilih dioptimumkan seterusnya dengan menggunakan RSM. Pada mulanya, keperluan nutrien untuk penghasilan treonin dan triptofan dinilai dengan menggunakan reka bentuk *Plackett Burman* (PBD) dan kemudiannya dioptimumkan dengan menggunakan reka bentuk central composite (CCD). *Molasses*, ekstrak daging, $(NH_4)_2SO_4$ dan $MnSO_4$ adalah komponen yang paling penting untuk penghasilan treonin oleh *P. pentosaceus* TL-3 dengan kepekatan optimum sebanyak 30.79 g/L, 25.30 g/L, 8.59 g/L, dan 0.098 g/L masing-masing. Hasil treonin yang dicatatkan oleh *P. pentosaceus* TL-3 di bawah keadaan optimum (125.98 mg/L) telah meningkat sebanyak 2 kali ganda manakala kos media optimum telah dikurangkan sebanyak 8.5% berbanding dengan media MRS.

Di samping itu, kombinasi komponen media yang terbaik untuk penghasilan triptofan oleh *P. acidilactici* TP-6 adalah *molasses*, ekstrak daging, urea dan $FeSO_4$. Kepekatan optimum yang disyorkan oleh RSM adalah: ceng, 14.06 g/L; ekstrak daging, 23.68 g/L; urea, 5.56 g/L dan $FeSO_4$, 0.024 g/L. Sebanyak 68.05 mg/L triptofan telah dihasilkan oleh *P. acidilactici* TP-6 di bawah keadaan optimum, bersamaan dengan 150% peningkatan berbanding dengan kawalan. Sebaliknya, kos media optimum telah dikurangkan sebanyak 11%. Selain itu, penghasilan treonin dan triptofan oleh LAB terpilih telah berjaya dipertingkatkan skala dalam bioreaktor 30 L berdasarkan kaedah kelajuan tip pendesak tetap. Tambahan pula, hasil treonin dan triptofan yang dicatatkan di dalam pengkulturan bioreaktor adalah setanding dengan hasil yang diramalkan oleh RSM. Sebagai kesimpulan, *P. pentosaceus* TL-3 dan *P. acidilactici* TP-6 telah dikenal pasti sebagai penghasil treonin dan triptofan serta penghasilan treonin dan triptofan oleh penghasil terpilih telah dipertingkatkan sebanyak 2 kali ganda dan 150% masing-masing melalui pengoptimuman rumusan media mereka dengan menggunakan kaedah RSM. Tambahan pula, penghasilan treonin dan triptofan telah berjaya dipertingkatkan skala berdasarkan kaedah kelajuan

pendesak tetap di mana penghasilan di dalam skala kecil dan besar adalah setara.

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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:

Foo Hooi Ling, PhD
Professor
Faculty of Biotechnology and Biomolecular Sciences
Universiti Putra Malaysia
(Chairman)

Rosfarizan Mohamad, PhD
Professor
Faculty of Biotechnology and Biomolecular Sciences
Universiti Putra Malaysia
(Member)

Norhani Abdullah, PhD
Research Fellow
Institute of Tropical Agriculture and Food Security
Universiti Putra Malaysia
(Member)

_____
ROBIAH BINTI YUNUS, PhD
Professor and Dean
School of Graduate Studies
Universiti Putra Malaysia

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Name of Chairman of Supervisory Committee: Foo Hooi Ling

Signature: _____
Name of Member of Supervisory Committee: Rosfarizan Mohamad

Signature: _____
Name of Member of Supervisory Committee: Norhani Abdullah

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

LIST OF ABBREVIATIONS

% (v/v)	Percent volume per volume
% (w/v)	Percent weight per volume
$(NH_4)_2HC_6H_5O_7$	Ammonium citrate
$(NH_4)_2SO_4$	Ammonium sulphate
× *g*	Times gravity
° C	Degree in Celcius
µL	Microliter
2-(OH)-5-$(NO_2)C_6H_3COOH$	2-hydroxy-5-nitrobenzoic acid
A230	Absorbance at wavelength 230 nm
A260	Absorbance at wavelength 260 nm
A280	Absorbance at wavelength 280 nm
AA	Amino acid
AAA	Auxiliary amino acid
Abs $_{540nm}$	Absorbance at wavelength 540 nm
Ala	Alanine
ANOVA	Analysis of variance
Arg	Arginine
Asn	Asparagine
Asp	Aspartate
BLAST	Basic local alignment search tool
bp	Base pair
BSA	Bovine serum albumin
C.	*Corynebacterium*
$C_4H_4KNaO_6·4H_2O$	Sodium tartrate tetrahydrate
C_6H_5OH	Phenol
CCD	Central composite design
CEP	Cell-envelope proteinase
CFS	Cell free supernatant
CFU/mL	Colony forming unit per millilitre
$CuSO_4$	Copper (II) sulphate
Cy2	Cystine
DAD	Diode array detector
df	Degree of freedom
DNA	Deoxyribonucleic acid
DNS	Dinitrosalicylic acid
dNTPs	Deoxynucleotide triphosphates
Dpp	ATP-driven peptide transporter
DtpT	Di-/tripeptide transporter
E.	*Escherichia*
EBT	1,1'-ethylidene-bis-tryptophan
Em	Emission
EMP	Embden-Meyerhoff-Parnas
EMS	Eosinophils myalgia syndrome
Eq.	Equation
Ex	Excitation
$FeSO_4$	Iron (II) sulphate

FLD	Fluorescence detector
FMOC	9-fluorenylmethyl chloroformate
g	Gram
GABA	Gamma-aminobutyric acid
Gln	Glutamine
Glu	Glutamate
Gly	Glycine
GRAS	Generally recognised as safe
h	Hour
HCl	Hydrochloric acid
His	Histidine
HIV	Human immunodeficiency virus
HPLC	High performance liquid chromatograph
Ile	Isoleucine
ISTD	Internal standard
K_2HPO_4	Dipotassium hydrogen phosphate
kb	Kilo base
KH_2PO_4	Potassium dihydrogen phosphate
k_La	Volumetric mass transfer coefficient
L	Litre
L.	*Lactobacillus*
LAB	Lactic acid bacteria
LC	Liquid chromatography
Leu	Leucine
LNAA	Large neutral amino acid
Lys	Lysine
M	Molar
Met	Methionine
$MgCl_2$	Magnesium chloride
$MgSO_4$	Magnesium sulphate
min	Minute
mL	Millilitre
mM	Millimolar
$MnSO_4$	Manganese sulphate
MRS	de Man Rogasa and Sharpe
MSG	Monosodium glutamate
Na_2SO_3	Sodium sulfite
NaCl	Sodium chloride
$NADP^+$	Nicotinamide adenine dinucleotide phosphate
NaH_2PO_4	Sodium dihydrogen phosphate
NaOAc	Sodium acetate
NaOH	Sodium hydroxide
NH_4NO_3	Ammonium nitrate
nm	Nanometre
NMF	Natural moisturising factors
OD_{600nm}	Optical density at wavelength 600 nm
OPA	O-phthalaldehyde
Opp	Oligopeptides transporters
P.	*Pediococcus*
PBD	Plackett burman design
PCR	Polymerase chain reaction

Phe	Phenylalanine
PKP	Phosphoketolase pathway
PKU	Phenylketonuria
PMF	Protein motive force
pmol/µL	Picomole per microliter
P_r	Productivity
Pro	Proline
QPS	Qualified presumption of safety
R^2	Coefficient of determination
RC	Regenerated cellulose
rDNA	Ribosomal deoxyribonucleic acid
RNA	Ribonucleic acid
rpm	Rotation per minutes
RSM	Response surface methodology
SEM	Standard error mean
Ser	Serine
S_f	Final substrate concentration
S_i	Initial substrate concentration
S_i-S_f	Substrate consumed
SmF	Submerged fermentation
sp.	Species
SSF	Solid state fermentation
Std	Amino acid standard
Thr	Threonine
Trp	Tryptophan
Tyr	Tyrosine
UV	Ultraviolet
V	Volt
Val	Valine
X_{max}	Maximum cell concentration
$Y_{p/s}$	Product yield coefficient
$Y_{x/s}$	Growth yield coefficient
$ZnSO_4$	Zinc sulphate

CHAPTER 1

INTRODUCTION

Amino acid is one of the most crucial nutrients to ensure survival of living organisms (Sundrum *et al*., 2005). Increasing knowledge on the functions and properties of amino acid has led to diverse commercial applications and escalating global demand. Livestock industry is the largest consumer of amino acid and constitutes up to 56% of the total amino acid market, followed by food industry (32%) and other industries (12%) (Leuchtenberger et al., 2005). Intensive development has favoured over feed amino acid due to their indispensable roles in enhancing the growth performance and well-being of livestocks. Methionine and lysine were the first amino acid introduced to animal feed (Toride, 2004). However, threonine and tryptophan has gained increasing interest and applied widely in animal feed recently as they have positive impact on the growth performance of the animals (Xie *et al*., 2014; Iwuji *et al*., 2014; Duarte *et al*., 2013; Święch *et al*., 2011).

Over the past decades, production of amino acid relied heavily on modified strains of *Corynebacterium glutamicum* and *Escherichia coli*. However, the use of genetically engineered microorganisms for production of tryptophan has caused over thousand cases of eosinophila myalgia syndrome (EMS) due to production of a dimerisation product of tryptophan which is toxic. The tragedy eventually led to death of 27 victims while some of the victims experienced permanent disability. Hence, industries may still come to reluctant when using these microorganisms for production of amino acid, particularly in food industry. Moreover, use of pathogenic producer microorganisms such as *E. coli* are also rasing concern (Venkitanarayanan *et al*., 2016). This has motivated researchers to seek for safer alternatives by utilising food grade microorganisms such as lactic acid bacteria (LAB) for production of amino acid (Norfarina *et al*., 2014; Zareian *et al*., 2012).

LAB are one of the most important group of industrial microorganism. They are applied extensively for production of various cultured foods due to their Generally Recognised as Safe (GRAS) reputation (Blair & Regenstein, 2015; Mayo *et al*., 2010) and ability to produce an array of metabolites that contribute greatly to improve the preservation properties and develop unique flavours and texture of the cultured foods (Margaret & Milind, 2006). Several studies revealed that LAB possessed a well-established proteolytic system which may contribute to production of amino acid (Savijoki *et al*., 2006; Simova *et al*., 2006; Hasan, 2003). Additionally, presence of active amino acid biosynthesis pathway and the relevant genes had been reported in LAB (Zareian *et al*., 2012; Garault *et al*., 2000).

Optimisation of fermentation parameters is a crucial step in bioprocess due to its impact on the product yield (Panda *et al*., 2007) as well as influence on the economic feasibility of the fermentation process (Schmidt, 2005). Statistical

optimisation approaches are preferred over conventional optimisation approach due to its usefulness in optimising the process with minimal number of experiments. Response surface methodology (RSM) is one of the most commonly used statistical optimisation technique due to its high efficiency in determining the optimal conditions of a multivariate system and ability to explain the interactive effects of all the factors in a process with minimal experimental runs (Mander *et al*., 2013; Elibol, 2004; Liu & Tzeng, 1998). RSM has been applied extensively for optimisation of various fermentation processes involving LAB (Deepak *et al*., 2015; Tajabadi *et al*., 2015; Anvari *et al*., 2014; Hwang *et al*., 2012; Kumar *et al*., 2012; de Lima *et al*., 2010; Li *et al*., 2010; Norfarina, 2010). Another important aspect in bioprocess is the scalability of the process. The bioprocess must be able to be scaled up for industrial application. Constant impeller tip speed approach is one of the most commonly employed stategy for scaling up of bioprocesses involving microorganisms and enzymes (Keng *et al*., 2008; Stephenie *et al*., 2007; Hamdi *et al*., 2000).

However, the major challenges to utilise LAB as a safer alternative for production of amino acid were lack of documentations regarding the ability of LAB to produce amino acid as well as the optimisation and scaling up of their production. Hence, the general objective of this study was to optimise the medium formulation for threonine and tryptophan production by using LAB isolated from Malaysian foods, followed by scaling up in pilot scale bioreactor. Meanwhile, the specific objectives of this study were as follows:

1) To identify and characterise the growth and proteolytic activity of LAB isolated from various Malaysian traditional foods and select the LAB isolate for threonine and tryptophan production.
2) To optimise the medium formulation for production of threonine and tryptophan by *Pediococcus pentosaceus* TL-3 and *Pediococcus acidilactici* TP-6 respectively via RSM approach.
3) To scale up the production of threonine and tryptophan by the *Pediococcus pentosaceus* TL-3 and *Pediococcus acidilactici* TP-6 by using constant impeller tip speed approach.

REFERENCES

Adnan, A.F.M., and Tan, I.K. (2007). Isolation of lactic acid bacteria from Malaysian foods and assessment of the isolates for industrial potential. *Bioresource Technology*. 98(7): 1380-1385.

Aiba, S., Tsunekawa, H., and Imanaka, T. (1982). New approach to tryptophan production by *Escherichia coli*: genetic manipulation of composite plasmids in vitro. *Applied and Environmental Microbiology*. 43(2): 289-297.

Alexander, J.C., Beckneh, C., and Elvehjem, C.A. (1953). The alanine, cystine, glycine and serine content of meat. *Journal of Nutrition*. 51(3): 319-328.

Altekar, M., Homon, C.A., Kashem, M.A., Mason, S.W., Nelson, R.M., Patnaude, L.A., Yingling, J., and Taylor, P.B. (2006). Assay optimization: a statistical design of experiments approach. *Journal of the Association for Laboratory Automation.* 11(1): 33-41.

Anvari, M., Khayati, G., and Rostami, S. (2014). Optimisation of medium composition for probiotic biomass production using response surface methodology. *Journal of Dairy Research*. 81(01): 59-64.

Applegate, T.J., and Angel, R. (2008). *Protein and amino acids requirements for poultry* [Fact sheet]. Retrieved from https://puyallup.wsu.edu/lnm/wp-content/uploads/sites/346/2014/11/Protein-and-amino-acid-for-poultry-final.pdf.

Aro, S.O., and Aletor, V.A. (2012). Proximate composition and amino acid profile of differently fermented cassava tuber wastes collected from a cassava starch producing factory in Nigeria. *Livestock Research for Rural Development*. 24(3): 1-5.

Axelsson, L. (1998). Lactic Acid Bacteria: Classification and Physiology. In S. Salminen, A.V. Wright (Eds.). *Lactic Acid Bacteria: Microbiology and Functional Aspects* (2nd ed.) (pp. 1-58). New York: Marcel Dekker.

Azin, A., Rosfarizan, M., Raha, A.R., Rosli, M.I., Farideh, N., Tan, J.S., and Sahar, A. (2015). Cyclodextrin glycosyltransferase biosynthesis improvement by recombinant *Lactococcus lactis* NZ: NSP: CGT: medium formulation and culture condition optimization. *Biotechnology & Biotechnological Equipment*. 29(3): 555-563.

Bardowski, J., Ehrlich, S.D., and Chopin, A. (1992). Tryptophan biosynthesis genes in *Lactococcus lactis* subsp. *lactis*. *Journal of Bacteriology*. 174(20): 6563-6570.

Batra, J., Beri, D., and Mishra, S. (2014). Response surface methodology based optimization of β-glucosidase production from *Pichia pastoris*. *Applied Biochemistry and Biotechnology*. 172(1): 380-393.

Becker, J., Zelder, O., Häfner, S., Schröder, H., and Wittmann, C. (2011). From zero to hero - Design-based systems metabolic engineering of *Corynebacterium glutamicum* for L-lysine production. *Metabolic Engineering*. 13(2): 159-168.

Beganović, J., Kos, B., Pavunc, A.L., Uroić, K., Džidara, P., and Šušković, J. (2013). Proteolytic activity of probiotic strain *Lactobacillus helveticus* M92. *Anaerobe*. 20: 58-64.

Berg, J.M., Tymoczko, J.L., and Stryer, L. (2002). *Biochemistry* (5th ed.). San Francisco: W.H. Freeman Publishers.

Binod, P., Sindhu, R., and Pandey, A. (2013). Upstream Operations of Fermentation Processes. In C.R. Soccol, A. Pandey, C. Larroche (Eds.) *Fermentation Processes Engineering in the Food Industry* (pp. 75-88). Boca Raton: CRC Press.

Blair, R., and Regenstein, J.M. (2015). *Genetic Modification and Food Quality: A Down to Earth Analysis*. Chichester: John Wiley and Sons.

Blanc, B., Laloi, P., Atlan, D., Gilbert, C., and Portalier, R. (1993). Two cell-wall-associated aminopeptidases from *Lactobacillus helveticus* and the purification and characterization of APII from strain ITGL1. *Journal of General Microbiology*. 139(7): 1441-1448.

Block, R.J., Weiss, K.W., Almquist, H.J., Carroll, D.B., Gordon, W.G., and Saperstein, S. (1956). *Amino acid Handbook. Methods and Results of Protein Analysis.* Springfield: Blackwell Scientific Publications.

Bolotin, A., Wincker, P., Mauger, S., Jailon, O., Malarme, K., Weissenbach, J., Ehrlich, S.D., and Sorokin, A. (2001). The complete genome sequence of the lactic acid bacterium *Lactococcus lactis* ssp. *lactis* IL1403. *Genome Researh.* 11(5): 731-753.

Bouchard, D., Even, S., and Le Loir, Y. (2015). Lactic acid bacteria in animal production and health. In F. Mozzi, R.R Raya, G.M. Vignolo (Eds.). *Biotechnology of Lactic Acid Bacteria: Novel Applications* (pp. 144-158). New Jersey: Wiley-Blackwell.

Bouton, Y., Guyot, P., and Grappin, R. (1998). Preliminary characterization of microflora of Comté cheese. *Journal of Applied Microbiology*. 85(1): 123-131.

Bradford, M.M. (1976). A rapid and sensitive method for the quantitation of microgram quantities of protein utilizing the principle of protein-dye binding. *Analytical Biochemistry*. 72: 248-254.

Brown, R.J., De Banate, M.A., and Rother, K.I. (2010a). Artificial sweeteners: a systematic review of metabolic effects in youth. *International Journal of Pediatric Obesity*. 5(4): 305-312.

Brown, W.H., Foote, C., Iverson, B., and Anslyn, E. (2010b). *Organic Chemistry* (5th ed.). Boston: Wadsworth Cengage Learning.

Bunchasak, C. (2009). Role of dietary methionine in poultry production. *The Journal of Poultry Science*. 46(3): 169-179.

Burr, B., Walker, J., Truffa-Bachi, P., and Cohen, G.N. (1976). Homoserine kinase from *Escherichia coli* K12. *European Journal of Biochemistry*. 62(3): 519-526.

Cahyanto, M.N., Kawasaki, H., Nagashio, M., Fujiyama, K., and Seki, T. (2006). Regulation of aspartokinase, aspartate semialdehyde dehydrogenase, dihydrodipicolinate synthase and dihydrodipicolinate reductase in *Lactobacillus plantarum*. *Microbiology*: 152(1): 105-112.

Callon, C., Millet, L., and Montel, M.C. (2004). Diversity of lactic acid bacteria isolated from AOC Salers cheese. *Journal of Dairy Research*. 71(02): 231-244.

Carafa, I., Nardin, T., Larcher, R., Viola, R., Tuohy, K., and Franciosi, E. (2015). Identification and characterization of wild *Lactobacilli* and *Pediococci* from spontaneously fermented Mountain Cheese. *Food microbiology*. 48: 123-132.

Chaillou, S., Champomier-Vergès, M.C., Cornet, M., Crutz-Le Coq, A.M., Dudez, A.M., Martin, V., Beaufils, S., Darbon-Rongere, E., Bossy, R., Loux, V., and Zagorec, M. (2005). The complete genome sequence of the meat-borne lactic acid bacterium *Lactobacillus sakei* 23K. *Nature Biotechnology*. 23(12): 1527-1533.

Chauhan, K., Trivedi, U., and Patel, K.C. (2007). Statistical screening of medium components by Plackett–Burman design for lactic acid production by *Lactobacillus* sp. KCP01 using date juice. *Bioresource Technology*. 98(1): 98-103.

Chen, H., Xu, X. Q., and Zhu, Y. (2010). Optimization of hydroxyl radical scavenging activity of exo-polysaccharides from *Inonotus obliquus* in submerged fermentation using response surface methodology. *Journal of Microbiology and Biotechnology*. 20(4): 835-843.

Chen, N., Huang, J., Feng, Z.B., Yu, L., Xu, Q.Y., and Wen, T.Y. (2009). Optimization of fermentation conditions for the biosynthesis of L-threonine by *Escherichia coli*. *Applied Biochemistry and Biotechnology*. 158(3): 595-604.

Chen, Y.S., and Steele, J.L. (1998). Genetic characterization and physiological role of endopeptidase O from *Lactobacillus helveticus* CNRZ32. *Applied and Environmental Microbiology*. 64(9): 3411-3415.

Cheng, L.K., Wang, J., Xu, Q.Y., Xie, X.X., Zhang, Y.J., Zhao, C.G., and Chen, N. (2012). Effect of feeding strategy on L-tryptophan production by recombinant *Escherichia coli*. *Annals of Microbiology*. 62(4): 1625-1634.

Chopin, A. (1993). Organization and regulation of genes for amino acid biosynthesis in lactic acid bacteria. *FEMS Microbiology Reviews*. 12: 21-38.

Cleveland, J., Montville, T.J., Nes, I.F., and Chikindas, M.L. (2001). Bacteriocin safe, natural antimicrobials for food preservation. *International Journal of Food Microbiology.* 71: 1- 20.

Coppola, R., Nanni, M., Iorizzo, M., Sorrentino, A., Sorrentino, E., and Grazia, L. (1997). Survey of lactic acid bacteria isolated during the advanced stages of the ripening of Parmigiano Reggiano cheese. *Journal of Dairy Research*. 64(02): 305-310.

Coruzzi, G., Last, R., Dudareva, N., and Amrhein, N. (2015). Amino Acids. In B.B. Buchanan, W. Gruissem, R.L. Jones (Eds.) *Biochemistry and Molecular Biology of Plants* (pp. 289-336). Hoboken: John Wiley and Sons, Inc.

Corzo, A., Kidd, M.T., Dozier III, W.A., Pharr, G.T., and Koutsos, E.A. (2007). Dietary threonine needs for growth and immunity of broilers raised under different litter conditions. *Journal of Applied Poultry Research*. 16: 574-582.

Dalmış, Ü., and Soyer, A. (2008). Effect of processing methods and starter culture (*Staphylococcus xylosus* and *Pediococcus pentosaceus*) on proteolytic changes in Turkish sausages (sucuk) during ripening and storage. *Meat Science*. 80(2): 345-354.

Davati, N., Hamidi Esfahani, Z., and Shojaosadati, S.A. (2010). Optimization of medium composition for microbial production of glutamic acid from Date fruit wastes using fractional factorial method. *Iranian Journal of Food Science and Technology*. 7(2): 61-67.

De Bruyne, K., Franz, C.M., Vancanneyt, M., Schillinger, U., Mozzi, F., de Valdez, G.F., De Vuyst, L., and Vandamme, P. (2008). *Pediococcus argentinicus* sp. nov. from Argentinean fermented wheat flour and identification of *Pediococcus* species by *pheS*, *rpoA* and *atpA* sequence analysis. *International Journal of Systematic and Evolutionary Microbiology*. 58(12): 2909-2916.

de Carvalho, A.A.T., Mantovani, H.C., Paiva, A.D., and De Melo, M.R. (2009). The effect of carbon and nitrogen sources on bovicin HC5 production by *Streptococcus bovis* HC5. *Journal of Applied Microbiology*. 107(1): 339-347.

de Carvalho, I.P.C., Detmann, E., Mantovani, H.C., Paulino, M.F., Valadares Filho, S.D.C., Costa, V.A.C., and Gomes, D.I. (2011). Growth and antimicrobial activity of lactic acid bacteria from rumen fluid according to energy or nitrogen source. *Revista Brasileira de Zootecnia*. 40(6): 1260-1265.

de Giori, G.S., de Valdez, G.F., de Ruiz Holgado, A.P., and Oliver, G. (1985). Effect of pH and temperature on the proteolytic activity of lactic acid bacteria. *Journal of Dairy Science*. 68(9): 2160-2164.

de Lima, C.J.B., Coelho, L.F., and Contiero, J. (2010). The use of response surface methodology in optimization of lactic acid production: focus on medium supplementation, temperature and pH control. *Food Technology and Biotechnology*. 48(2): 175-181.

Deepak, V., Pandian, S.R K., Sivasubramaniam, S.D., Nellaiah, H., and Sundar, K. (2015). Optimization of anticancer exopolysaccharide production from probiotic *Lactobacillus acidophilus* by response surface methodology. *Preparative Biochemistry and Biotechnology*. 46(3), 288-297.

Deguchi, Y., and Morishita, T. (1992). Nutritional requirements in multiple auxotrophic lactic acid bacteria; genetic lesions affecting amino acid biosynthetic pathways in *Lactococcus lactis*, *Enteriococcus faecalis* and *Pediococcus acidilactici*. *Bioscience, Biotechnology, and Biochemistry*. 56: 913–918.

Delorme, C., Godon, J.J., Ehrlich, S.D., and Renault, P. (1993). Gene inactivation in *Lactococcus lactis*: histidine biosynthesis. *Journal of Bacteriology*. 175(14): 4391-4399.

Dey, G., Mitra, A., Banerjee, R., and Maiti, B.R. (2001). Enhanced production of amylase by optimization of nutritional constituents using response surface methodology. *Biochemical Engineering Journal*. 7(3): 227-231.

Diesveld, R., Tietze, N., Fürst, O., Reth, A., Bathe, B., Sahm, H., and Eggeling, L. (2009). Activity of exporters of *Escherichia coli* in *Corynebacterium glutamicum*, and their use to increase L-threonine production. *Journal of Molecular Microbiology and Biotechnology*. 16: 198-207.

Djekrif-Dakhmouche, S., Gheribi-Aoulmi, Z., Meraihi, Z., and Bennamoun, L. (2006). Application of a statistical design to the optimization of culture medium for α-amylase production by *Aspergillus niger* ATCC 16404 grown on orange waste powder. *Journal of Food Engineering*. 73(2): 190-197.

Dobson, C.M., Deneer, H., Lee, S., Hemmingsen, S., Glaze, S., and Ziola, B. (2002). Phylogenetic analysis of the genus *Pediococcus*, including *Pediococcus claussenii* sp. nov., a novel lactic acid bacterium isolated from beer. *International Journal of Systematic and Evolutionary Microbiology*. 52(6): 2003-2010.

Doi, K., Nishizaki, Y., Fujino, Y., Ohshima, T., Ohmomo, S., and Ogata, S. (2009). *Pediococcus lolii* sp. nov., isolated from ryegrass silage. *International Journal of Systematic and Evolutionary Microbiology*. 59(5): 1007-1010.

Dong, X., Quinn, P.J., and Wang, X. (2011). Metabolic engineering of *Escherichia coli* and *Corynebacterium glutamicum* for the production of L-threonine. *Biotechnology Advances*. 29(1): 11-23.

Dong, Z., Gu, L., Zhang, J., Wang, M., Du, G., Chen, J., and Li, H. (2014). Optimisation for high cell density cultivation of *Lactobacillus salivarius* BBE 09-18 with response surface methodology. *International Dairy Journal*. 34(2): 230-236.

Donkor, O.N., Henriksson, A., Vasiljevic, T., and Shah, N.P. (2007). Proteolytic activity of dairy lactic acid bacteria and probiotics as determinant of growth and in vitro angiotensin-converting enzyme inhibitory activity in fermented milk. *Le Lait*. 87(1): 21-38.

Du, Y.C., Long, X.H., Liu, Z.P., and Shao, H.B. (2014). Optimizing medium for producing ethanol from industrial crop Jerusalem artichoke by one-step fermentation and recombinant *Saccharomyces cerevisiae*. *Plant Biosystems*. 148(1): 118-126.

Duarte, K.F., Junqueira, O.M., Filardi, R.D.S., Siqueira, J.C.D., Puzotti, M.M., Garcia, E.A., Molino, A.D.B., and Laurentiz, A.C.D. (2013). Digestible tryptophan requirements for broilers from 22 to 42 days old. *Revista Brasileira de Zootecnia*. 42(10): 728-733.

Eggimann, B., and Bachmann, M. (1980). Purification and partial characterization of an aminopeptidase from *Lactobacillus lactis*. *Applied and Environmental Microbiology*. 40(5): 876-882.

Eikmanns, B.J., Metzger, M., Reinscheid, D., Kircher, M., and Sahm, H. (1991). Amplification of three threonine biosynthesis genes in *Corynebacterium glutamicum* and its influence on carbon flux in different strains. *Applied Microbiology and Biotechnology*. 34(5): 617-622.

El-Ghaish, S., Dalgalarrondo, M., Choiset, Y., Sitohy, M., Ivanova, I., Haertlé, T., and Chobert, J.M. (2010). Characterization of a new isolate of *Lactobacillus fermentum* IFO 3956 from Egyptian Ras cheese with proteolytic activity. *European Food Research and Technology*. 230(4): 635-643.

Elibol, M. (2004). Optimization of medium composition for actinorhodin production by *Streptomyces coelicolor* A3(2) with response surface methodology. *Process Biochemistry*. 39(9): 1057-1062.

Emanuel, V., Adrian, V., Ovidiu, P., and Gheorghe, C. (2005). Isolation of a *Lactobacillus plantarum* strain used for obtaining a product for the preservation of fodders. *African Journal of Biotechnology*. 4(5): 403-408.

Essid, I., Medini, M., and Hassouna, M. (2009). Technological and safety properties of *Lactobacillus plantarum* strains isolated from a Tunisian traditional salted meat. *Meat Science*. 81(1): 203-208.

Everson, C.W., Danner, W.E., and Hammes, P.A. (1970). Improved starter culture for semi-dry sausage. *Food Technology*. 24: 42-44.

Exterkate, F.A., and de Veer, G.J. (1987). Purification and some properties of a membrane-bound aminopeptidase A from *Streptococcus cremoris*. *Applied and Environmental Microbiology*. 53(3): 577-583.

Faehnle, C.R., Le Coq, J., Liu, X., and Viola, R.E. (2006). Examination of key intermediates in the catalytic cycle of aspartate-β-semialdehyde dehydrogenase from a Gram-positive infectious bacteria. *Journal of Biological Chemistry.* 281(41): 31031-31040.

Faghfuri, E., Fooladi, J., and Moosavi-Nejad, S.Z. (2013). L-tryptophan production by whole cells of *Escherichia coli* based on Iranian sugar beet molasses. *Jundishapur Journal of Microbiology*. 6(4): 1-5.

Felis, G., and Dellaglio, F. (2007). Taxonomy of *Lactobacilli* and *Bifidobacteria*. *Current Issues in Intestinal Microbiology*. 8(2): 44- 61.

Fernandez-Espla, M.D., Garault, P., Monnet, V., and Rul, F. (2000). *Streptococcus thermophilus* cell wall-anchored proteinase: release, purification, and biochemical and genetic characterization. *Applied and Environmental Microbiology*. 66: 4772–4778.

Foo, H.L., Loh, T.C., Lai, P.W., Lim, Y.S., Kufli, C.N., and Gulam, R. (2003). Effects of adding *Lactobacillus plantarum* I-UL4 metabolites in drinking water of rats. *Pakistan Journal of Nutrition*. 2(5): 283-288.

Forsythe, S.J. (2000). *The Microbiology of Safe Food.* Oxford: Blackwell Science.

Foucaud, C., Francois, A., and Richard, J. (1997). Development of a chemically defined medium for the growth of *Leuconostoc mesenteroides*. *Applied and Environmental Microbiology*. 63(1): 301-304.

Franz, C.M., Endo, A., Abriouel, H., Reenen, C.A.V., Gálvez, A., and Dicks, L.M. (2014). The genus *Pediococcus*. In W.H. Holzapfel, B.J.B. Wood (Eds.). *Lactic Acid Bacteria: Biodiversity and Taxonomy* (pp. 359-376). Chichester: John Wiley and Sons.

Frape, D. (2008). *Equine nutrition and feeding*. Hoboken: Blackwell Publishing.

Galia, W., Perrin, C., Genay, M., and Dary, A. (2009). Variability and molecular typing of *Streptococcus thermophilus* strains displaying different proteolytic and acidifying properties. *International Dairy Journal*. 19(2): 89-95.

Gao, X., Qiao, S.Y., and Lu, W.Q. (2009). Determination of an economical medium for growth of *Lactobacillus fermentum* using response surface methodology. *Letters in Applied Microbiology*. 49(5): 556-561.

Garault, P., Letort, C., Juillard, V., and Monnet, V. (2000). Branched-chain amino acid biosynthesis is essential for optimal growth of *Streptococcus thermophilus* in milk. *Applied and Environmental Microbiology*. 66(12): 5128-5133.

Geis, A., Bockelmann, W., and Teuber, M. (1985). Simultaneous extraction and purification of a cell wall-associated peptidase and β-casein specific protease from *Streptococcus cremoris* AC1. *Applied Microbiology and Biotechnology*. 23(1): 79-84.

Gilbert, C., Atlan, D., Blanc, B., Portalier, R., Germond, G.J., Lapierre, L., and Mollet, B. (1996). A new cell surface proteinase: sequencing and analysis of the prtB gene from *Lactobacillus delbrueckii* subsp. *bulgaricus*. *Journal of Bacteriology*. 178: 3059–3065.

Global Industry Analysts. (2015). *The Global Amino Acids Market: Trends, Drivers and Projections*. San Jose: Global Industry Analysts (GIA), Inc. Retrived from: https://www.grandviewresearch.com/press-release/global-amino-acids-market, on August 2017.

Godon, J.J., Delorme, C., Bardowski, J., Chopin, M.C., Ehrlich, S.D., and Renault, P. (1993). Gene inactivation in *Lactococcus lactis*: branched-chain amino acid biosynthesis. *Journal of Bacteriology*. 175(14): 4383-4390.

Grand View Research. (2015). *Global Amino Acids Market By Product (L-Glutamate, Lysine, Methionine, Threonine, Tryptophan, Leucine, Iso-Leucine, Valine, Glutamine, Arginine), By Source, By Application Expected to Reach USD 35.40 Billion By 2022*. San Francisco: Grand View Research, Inc.

Grobben, G.J., Boels, I.C., Sikkema, J., Smith, M.R., and De Bont, J.A. (2000). Influence of ions on growth and production of exopolysaccharides by *Lactobacillus delbrueckii* subsp. *bulgaricus* NCFB 2772. *Journal of Dairy Research*. 67(1): 131-135.

Gropper, S., and Smith, J. (2012). *Advanced Nutrition and Human Metabolism* (6th ed.). Boston: Wadsworth Cengage Learning.

Gunther, I.L., and White, H.R. (1961). The cultural and physiological characters of the *Pediococci*. *Journal of General Microbiology*. 26(2): 185-197.

György, P. (1964). The History of Vitamin B6. Introductory Remarks. In R.S. Harris, I.G. Wool, J.A. Loraine, G.F. Marrian, K.V. Thimann (Eds.) *Vitamins and Hormones*, Vol. 22 (pp. 361-365). New York: Academic Press Inc.

Hagino, H., and Nakayama, K. (1975). L-tryptophan production by analog-resistant mutants derived from a phenylalanine and tyrosine double auxotroph of *Corynebacterium glutamicum*. *Agricultural and Biological Chemistry*. 39(2): 343-349.

Hagting, A., Kunji, E.R., Leenhouts, K.J., Poolman, B., and Konings, W.N. (1994). The di-and tripeptide transport protein of *Lactococcus lactis*. A new type of bacterial peptide transporter. *Journal of Biological Chemistry*. 269(15): 11391-11399.

Hamdi, M., Hamza, S., Mtimet, N., Hmida, N., Cornelius, C., Zgouli, S., Mahjoub, A., and Thonart, P. (2000). Effect of corn steep liquor supplementation and scale up on *Lactococcus* starter production. *Bioprocess Engineering*. 22(1): 23-27.

Hamel, J.F.P., and Hunter, J.B. (1990). Modeling and Applications of Downstream Processing- A survey of innovative strategies. In J.F.P. Hamel, J.B. Hunter, S.K. Sikdar (Eds.). *Downstream Processing and Bioseparation*, Vol. 419 (pp. 1-35). Washington: ACS Publications.

Hammes, W.P., and Hertel, C. (2006). The genera *Lactobacillus* and *Carnobacterium*. In M. Dworkin, S. Falkow, E. Rosenberg, K.H. Schleifer, E. Stackebrandt (Eds.). *The Prokaryotes- A Handbook on the Biology of Bacteria, 3rd ed. Vol. 4: Archaea. Bacteria: Firmicutes, Actinomycetes* (pp. 320-403). New York: Springer Science and Business Media.

Hanan, S.A. (2012). Isolation and screening of extracellular proteases produced by new isolated *Bacillus* sp. *Journal of Applied Pharmaceutical Science*. 2(9): 71-74.

Hartzema, A.G., Porta, M.S., Tilson, H.H., Milburn, D.S., and Myers, C.W. (1991). Tryptophan toxicity: A pharmacoepidemiologic review of eosinophilia-myalgia syndrome. *Annals of Pharmacotherapy*. 25(11): 1259-1262.

Hasan, B. (2003). Fermentation of fish silage using *Lactobacillus pentosus*. *Jurnal Natur Indonesia*. 6(1): 11-15.

Henderson, J.W., Ricker, R.D., and Cliff, W.I. (2000). Rapid, accurate, sensitive and reproducible HPLC analysis of amino acids. Agilent Technologies, Appl. note: 5980-1193.

Hermann, T. (2003). Industrial production of amino acids by Coryneform bacteria. *Journal of Biotechnology*. 104(1): 155-172.

Hermann, T., and Rieping, M. (2003). *U.S. Patent No. US6562601 B2*. Washington, DC: U.S. Patent and Trademark Office.

Hertel, S.C., Hieke, M., and Gröger, D. (1991). Anthranilate synthase from *Ruta graveolens*: partial purification and properties. *Biochemie und Physiologie der Pflanzen*. 187(2): 121-129.

Higgins, C.F. (1992). ABC transporters: from microorganisms to man. *Annual Review of Cell Biology*. 8(1): 67-113.

Holzapfel, W.H., Franz, C.M., Ludwig, W., Back, W., and Dicks, L.M. (2006). The genera *Pediococcus* and *Tetragenococcus*. In M. Dworkin, S. Falkow, E. Rosenberg, K.H. Schleifer, E. Stackebrandt (Eds.). *The Prokaryotes-A Handbook on the Biology of Bacteria, 3rd ed. Vol. 4: Archaea. Bacteria: Firmicutes, Actinomycetes* (pp. 320-403). New York: Springer Science and Business Media.

Holzapfel, W.H.N., and Wood, B.J.B. (2012). *The Genera of Lactic Acid Bacteria* (Vol. II). New York: Springer Science and Business Media.

Hopkins, F.G., and Cole, S.W. (1901). A contribution to the chemistry of proteids. Part I. A preliminary study of a hitherto undescribed product of tryptic digestion. *The Journal of Physiology*. 27(4-5): 418-428.

Hugenholtz, J., and Kleerebezem, M. (1999). Metabolic engineering of lactic acid bacteria: Overview of the approaches and results of pathway rerouting involved in food fermentations. *Current Opinion in Biotechnology*. 10(5): 492-497.

Hutkins, R.W. (2008). *Microbiology and technology of fermented foods*, Vol. 22. Iowa: Blackwell Publishing.

Hwang, C.F., Chang, J.H., Houng, J.Y., Tsai, C.C., Lin, C.K., and Tsen, H.Y. (2012). Optimization of medium composition for improving biomass production of *Lactobacillus plantarum* Pi06 using the Taguchi array design and the Box-Behnken method. *Biotechnology and Bioprocess Engineering*. 17(4): 827-834.

Igarashi, Y., Kodama, T., and Minoda, Y. (1982). Excretion of L-tryptophan by analogue-resistant mutants of *Pseudomonas hydrogenothermophila* TH-1 in autotrophic cultures. *Agricultural and Biological Chemistry*. 46(6): 1525-1530.

Ikeda, K. (2002). New seasonings. *Chemical Senses*. 27(9): 847-849.

Ikeda, M. (2003). Amino acid production processes. In R. Faurie, J. Thommel (Eds.) *Microbial production of L-amino acids* (pp. 1-35). Berlin: Springer Berlin Heidelberg.

Ikeda, M., and Katsumata, R. (1992). Metabolic engineering to produce tyrosine or phenylalanine in a tryptophan-producing *Corynebacterium glutamicum* strain. *Applied and Environmental Microbiology*. 58(3): 781-785.

Ikeda, M., and Katsumata, R. (1995). Tryptophan production by transport mutants of *Corynebacterium glutamicum*. *Bioscience, biotechnology, and biochemistry*. 59(8): 1600-1602.

Ikeda, M., and Katsumata, R. (1999). Hyperproduction of tryptophan by *Corynebacterium glutamicum* with the modified pentose phosphate pathway. *Applied and Environmental Microbiology*. 65(6): 2497-2502.

Ikeda, M., and Takeno, S. (2013). Amino Acid Production by *Corynebacterium glutamicum*. In H. Yukawa, M. Inui (Eds.). *Microbiology Monographs 23, Corynebacterium glutamicum* (pp. 107-147). Berlin: Springer.

Ikeda, M., Nakanishi, K., Kino, K., and Katsumata, R. (1994). Fermentative production of tryptophan by a stable recombinant strain of *Corynebacterium glutamicum* with a modified serine-biosynthetic pathway. *Bioscience, Biotechnology, and Biochemistry*. 58(4): 674-678.

Inamdar, S.T.A. (2012). *Biochemical Engineering: Principles and Concepts* (3rd ed.). New Delhi: PHI Learning Pvt. Ltd.

Iwuji, T.C., Akinmutimi, A.H., Ogbuewu, I.P., Etuk, I.F., and Odoemelam, V.U. (2014). Roles of tryptophan in monogastric nutrition: a review. *Advances in Agriculture, Sciences and Engineering Research*. 4(3): 1544-1556.

Izumi, Y., Chibata, I., and Itoh, T. (1978). Production and utilization of amino acids. *Angewandte Chemie International Edition in English*. 17(3): 176-183.

Jenkins, J.K., and Courtney, P.D. (2003). *Lactobacillus* growth and membrane composition in the presence of linoleic or conjugated linoleic acid. *Canadian Journal of Microbiology*. 49(1): 51-57.

Jones, B.V., Sun, F., and Marchesi, J.R. (2007). Using skimmed milk agar to functionally screen a gut metagenomic library for proteases may lead to false positives. *Letters in Applied Microbiology*. 45(4): 418-420.

Jung, S.H., Park, J.W., Cho, I.J., Lee, N.K., Yeo, I.C., Kim, B.Y, Kim, H.K., and Hahm, Y.T. (2012). Characterization of lactic acid bacteria isolated from sauce-type kimchi. *Preventive Nutrition and Food Science*. 17(3): 217-222.

Junker, B.H. (2004). Scale-up methodologies for *Escherichia coli* and yeast fermentation processes. *Journal of Bioscience and Bioengineering*. 97(6): 347-364.

Kadam, S.R., Patil, S.S., Bastawde, K.B., Khire, J.M., and Gokhale, D.V. (2006). Strain improvement of *Lactobacillus delbrueckii* NCIM 2365 for lactic acid production. *Process Biochemistry*. 41(1): 120-126.

Kammoun, R., Naili, B., and Bejar, S. (2008). Application of a statistical design to the optimization of parameters and culture medium for α-amylase production by *Aspergillus oryzae* CBS 819.72 grown on gruel (wheat grinding by-product). *Bioresource Technology*. 99(13): 5602-5609.

Kandler, O., and Weiss, N. (1986). Regular Non-sporing Gram Positive Rods. In P.H. Sneath, N. Mair, M.E. Sharpe, J.G. Holt (Eds.). *Bergey's Manual of Systematic Bacteriology* (pp. 1208–1234). Baltimore: William and Wilkins.

Kaufman, S. (1977). Phenylketonuria: biochemical mechanisms. In B.W. Agranoff, M.H. Aprison (Eds.) *Advances in Neurochemistry* (pp. 1-132). New York: Springer Science and Business Media.

Keng, P.S., Basri, M., Ariff, A.B., Abdul Rahman, M.B., Abdul Rahman, R.N.Z., and Salleh, A.B. (2008). Scale-up synthesis of lipase-catalyzed palm esters in stirred-tank reactor. *Bioresource Technology*. 99(14): 6097-6104.

Khayati, G. (2013). Optimization of propionic acid extraction by aqueous two-phase system using response surface methodology. *Chemical Engineering Communications*. 200(5): 667-677.

Khayati, G., and Kiyani, F. (2012). A statistical approach for optimization of lipase production by using rice straw: analysis of different inducers and nitrogen sources effect. *Minerva Biotecnologica*. 24(3): 83-89.

Khuri, A.I., and Mukhopadhyay, S. (2010). Response surface methodology. *Wiley Interdisciplinary Reviews: Computational Statistics*. 2(2): 128-149.

Kiefer, P., Heinzle, E., and Wittmann, C. (2002). Influence of glucose, fructose and sucrose as carbon sources on kinetics and stoichiometry of lysine production by *Corynebacterium glutamicum*. *Journal of Industrial Microbiology and Biotechnology*. 28(6): 338-343.

Kiefer-Partsch, B., Bockelmann, W., Geis, A., and Teuber, M. (1989). Purification of an X-prolyl-dipeptidyl aminopeptidase from the cell wall proteolytic system of *Lactococcus lactis* subsp. *cremoris*. *Applied Microbiology and Biotechnology*. 31(1): 75-78.

Kim, D.J., Chung, S.G., Lee, S.H., and Choi, J.W. (2012). Relation of microbial biomass to counting units for *Pseudomonas aeruginosa*. *African Journal of Microbiology Research*. 6(21): 4620-4622.

Kim, J.H., Patterson, P.H., and Kim, W.K. (2014). Impact of dietary crude protein, synthetic amino acid and keto acid formulation on nitrogen excretion. *International Journal of Poultry Science*. 13(8): 429-436.

Kinoshita, S., Udaka, S., and Shimono, M. (1957). Studies on the amino acid fermentation. *The Journal of General and Applied Microbiology*. 3(3): 193-205.

Kircher, M., and Pfefferle, W. (2001). The fermentative production of L-lysine as an animal feed additive. *Chemosphere*. 43: 27-31.

Klaenhammer, T.R., Barrangou, R., Buck, B.L., Azcarate-Peril, M.A., and Altermann, E. (2005). Genomic features of lactic acid bacteria effecting bioprocessing and health. *FEMS Microbiology Reviews*. 29(3): 393-409.

Kleerebezem, M., Boekhorst, J., van Kranenburg, R., Molenaar, D., Kuipers, O.P., Leer, R., Tarchini, R., Peters, S.A., Sandbrink, H.M., Fiers, M.W.E.J., Stiekema, W., Lankhorst, R.M.K., Bron, P.A., Hoffer, S.M., Groot, M.N.N., Kerkhoven, R., de Vries, M., Ursing, B., de Vos, W.M., and Siezen, R.J. (2003). Complete genome sequence of *Lactobacillus plantarum* WCFS1. *Proceedings of the National Academy of Sciences*. 100(4): 1990-1995.

Klein, G., Pack, A., Bonaparte, C., and Reuter, G. (1998). Taxonomy and physiology of probiotic lactic acid bacteria. *International Journal of Food Microbiology*. 41(2): 103-125.

Kocabaş, P., Çalık, P., and Özdamar, T.H. (2006). Fermentation characteristics of L-tryptophan production by thermoacidophilic *Bacillus acidocaldarius* in a defined medium. *Enzyme and Microbial Technology*. 39(5): 1077-1088.

Kostrzewa, R.M., Nowak, P., Kostrzewa, J.P., Kostrzewa, R.A., and Brus, R. (2005). Peculiarities of L-DOPA treatment of Parkinson's disease. *Amino Acids*. 28(2): 157-164.

Kroner, Z. (2011). *Vitamins and minerals*. Santa Barbara: ABC-CLIO Greenwood.

Kruse, D., Krämer, R., Eggeling, L., Rieping, M., Pfefferle, W., Tchieu, J.H., Chung, Y.J., Saier Jr, M.H., and Burkovski, A. (2002). Influence of threonine exporters on threonine production in *Escherichia coli*. *Applied Microbiology and Biotechnology*. 59: 205-210.

Kumar, M., Jain, A.K., Ghosh, M., and Ganguli, A. (2012). Statistical optimization of physical parameters for enhanced bacteriocin production by *L. casei. Biotechnology and Bioprocess Engineering.* 17: 606-616.

Kunji, E.R., Mierau, I., Hagting, A., Poolman, B., and Konings, W.N. (1996). The proteotytic systems of lactic acid bacteria. *Antonie van Leeuwenhoek*. 70(2-4): 187-221.

Lee, A.C., and Fujio, Y. (1999). Microflora of banh men, a fermentation starter from Vietnam. *World Journal of Microbiology and Biotechnology*. 15(1): 51-55.

Lee, K., Lee, J., Kim, Y.H., Moon, S.H., and Park, Y.H. (2001). Unique properties of four *Lactobacilli* in amino acid production and symbiotic mixed culture for lactic acid biosynthesis. *Current Microbiology*. 43(6): 383-390.

Lee, M.H., Lee, H.W., Park, J.H., Ahn, J.O., Jung, J.K., and Hwang, Y.I. (2006). Improved L-threonine production of *Escherichia coli* mutant by optimization of culture conditions. *Journal of Bioscience and Bioengineering*. 101(2): 127-130.

Lee, Y.A. (2002). *Purification and Characterisation of Bacteriocin Produced by Lactococcus lactis Subsp. lactis RW18 Isolated from Steamed Fish* (*Rastrelliger* sp.). Unpublished master dissertation, Universiti Putra Malaysia, Malaysia.

Lei, V., and Jakobsen, M. (2004). Microbiological characterization and probiotic potential of koko and koko sour water, African spontaneously fermented millet porridge and drink. *Journal of Applied Microbiology*. 96(2): 384-397.

Leroy, F., and De Vuyst, L. (2004). Lactic acid bacteria as functional starter cultures for the food fermentation industry. *Trends in Food Science and Technology*. 15(2): 67-78.

Lessire, M., Hallouis, J.M., Bordeau, T., Primot, Y., Corrent, E., Fraysse, P., Tesseraud, S., and Berri, C. Study of the lysine requirement of broiler finishers: effects on growth performance. Proceedings of the 10th Research Meeting of Poultry and Waterfowl Foie Gras, La Rochelle, France, Mar. 26-28, 2013. Institut Technique de l'Aviculture: Paris, 2013.

Leuchtenberger, W., Huthmacher, K., and Drauz, K. (2005). Biotechnological production of amino acids and derivatives: current status and prospects. *Applied Microbiology and Biotechnology*. 69(1): 1-8.

Li, H., Qiu, T., Gao, D., and Cao, Y. (2010). Medium optimization for production of gamma-aminobutyric acid by *Lactobacillus brevis* NCL912. *Amino acids*. 38(5): 1439-1445.

Li, J., Ma, C., Ma, Y., Li, Y., Zhou, W., and Xu, P. (2007a). Medium optimization by combination of response surface methodology and desirability function: an application in glutamine production. *Applied Microbiology and Biotechnology*. 74(3): 563-571.

Li, J.Y., Zhang, L.W., Du, M., Han, X., Yi, H.X., Guo, C.F., Zhang, Y.C., Luo, X., Zhang, Y.H., Shan, Y.J., and Hou, A.J. (2011). Effect of tween series on growth and cis-9, trans-11 conjugated linoleic acid production of *Lactobacillus acidophilus* F0221 in the presence of bile salts. *International Journal of Molecular Sciences*. 12(12): 9138-9154.

Li, Y., Liu, Z., Zhao, H., Xu, Y., and Cui, F. (2007b). Statistical optimization of xylanase production from new isolated *Penicillium oxalicum* ZH-30 in submerged fermentation. *Biochemical Engineering Journal*. 34(1): 82-86.

Lien, E.L. (2003). Infant formulas with increased concentrations of α-lactalbumin. *The American Journal of Clinical Nutrition*. 77(6): 1555S-1558S.

Liew, S.L. (2004). *Pilot-scale Production of Lactobacillus rhamnosus ATCC 7469*. Unpublished doctoral dissertation, Universiti Putra Malaysia, Malaysia.

Lim, Y.S. (2003). *Isolation of Bacteriocinogenic Lactic Acid Bacteria and Purification of Selected Bacteriocins from Traditional Fermented Foods*. Unpublished master dissertation, Universiti Putra Malaysia, Malaysia.

Lin, M.Y., and Young, C.M. (2000). Folate levels in cultures of lactic acid bacteria. *International Dairy Journal*. 10(5): 409-413.

Lin, X., Xu, S., Yang, Y., Wu, J., Wang, H., Shen, H., and Wang, H. (2009). Purification and characterization of anthranilate synthase component I (TrpE) from *Mycobacterium tuberculosis* H37Rv. *Protein Expression and Purification*. 64(1): 8-15.

Liu, B.L., and Tzeng, Y.M. (1998). Optimization of growth medium for the production of spores from *Bacillus thuringiensis* using response surface methodology. *Bioprocess Engineering*. 18(6): 413-418.

Liu, L., Duan, X., & Wu, J. (2016). L-tryptophan production in *Escherichia coli* improved by weakening the Pta-AckA pathway. *PLoS ONE*. 11(6): e0158200.

Liu, L., Zhang, B., Tong, H., and Dong, X. (2006). *Pediococcus ethanolidurans* sp. nov., isolated from the walls of a distilled-spirit-fermenting cellar. *International Journal of Systematic and Evolutionary Microbiology*. 56(10): 2405-2408.

Liu, M., Bayjanov, J.R., Renckens, B., Nauta, A., and Siezen, R.J. (2010). The proteolytic system of lactic acid bacteria revisited: a genomic comparison. *BMC genomics*. 11(36): 1-15.

Liu, Q., Cheng, Y., Xie, X., Xu, Q., and Chen, N. (2012). Modification of tryptophan transport system and its impact on production of L-tryptophan in *Escherichia coli*. *Bioresource technology*. 114: 549-554.

Liu, S. (2013). *Bioprocess Engineering: Kinetics, Biosystems, Sustainability, and Reactor Design*. Amsterdam: Elsevier.

Liu, S.Q., Holland, R., McJarrow, P., and Crow, V.L. (2003). Serine metabolism in *Lactobacillus plantarum*. *International Journal of Food Microbiology*. 89(2): 265-273.

Livshits, V.A., Zakataeva, N.P., Aleshin, V.V., and Vitushkina, M.V. (2003). Identification and characterization of the new gene *rht*A involved in threonine and homoserine efflux in *Escherichia coli*. *Research in Microbiology*. 154(2): 123-135.

Llorente-Bousquets, A., Pérez-Munguía, S., and Farrés, A. (2008). Novel extracellular proteolytic activity in *Pediococcus acidilactici* ATCC 8042. *Canadian Journal of Microbiology*. 54(8): 694-699.

Mahrous, H., Mohamed, A., El-Mongy, M.A., El-Batal, A., and Hamza, H. (2013). Study bacteriocin production and optimization using new isolates of *Lactobacillus* spp. isolated from some dairy products under different culture conditions. *Food and Nutrition Sciences*. 4: 342-356.

Mahyidin, M.N. (2016). *Bioconversion of Palm Kernel Cake Mediated by Selected Lactic Acid Bacteria via Solid State Fermentation*. Unpublished master dissertation, Universiti Putra Malaysia, Malaysia.

Malumbres, M., Mateos, L.M., Lumbreras, M.A., Guerrero, C., and Martin, J.F. (1994). Analysis and expression of the thrC gene of *Brevibacterium lactofermentum* and characterization of the encoded threonine synthase. *Applied and Environmental Microbiology*. 60(7): 2209-2219.

Manca de Nadra, M.C., Arena, M.E., and Saguir, F.M. (2003). Nutritional requirements and amino acids utilization by lactic acid bacteria from wine - A short review. *Journal of Food Agriculture and Environment*. 1(3&4): 76-79.

Manca de Nadra, M.C. (2007). Nitrogen Metabolism in Lactic Acid Bacteria from Fruits: A Review. In A. Méndez-Vilas (Ed.). *Communicating Current Research and Educational Topics and Trends in Applied Microbiology* (pp. 500-510). Barcelona: Formatex.

Mander, P., Choi, Y.H., Seong, J.H., Na, B.H., Cho, S.S., Lee, H.J., and Yoo, J.C. (2013). Statistical optimization of a multivariate fermentation process for enhancing antibiotic activity of *Streptomyces* sp. CS392. *Archives of Pharmacal Research*. 36(8): 973-980.

Margaret, A.R., and Milind, A.C. (2006). *Bacteriocins: Ecology and Evolution*. New York: Springer Science and Business Media.

Marroki, A., and Bousmaha-Marroki, L. (2014). *Lactobacilli* isolated from Algerian goat's milk as adjunct culture in dairy products. *Brazilian Archives of Biology and Technology*. 57(3): 410-420.

Masuda, M., Takamatsu, S., Nishimura, N., Komatsubara, S., and Tosa, T. (1992). Improvement of nitrogen supply for L-threonine production by a recombinant strain of *Serratia marcescens*. *Applied Biochemistry and Biotechnology*. 37(3): 255-265.

Matalon, R., Surendran, S., Matalon, K.M., Tyring, S., Quast, M., Jinga, W., Ezell, E., and Szucs, S. (2003). Future role of large neutral amino acids in transport of phenylalanine into the brain. *Pediatrics*. 112(6): 1570-1574.

Mateus, D.M.R., Alves, S.S., and Da Fonseca, M.M.R. (2004). Kinetics of L-tryptophan production from indole and L-serine catalyzed by whole cells with tryptophanase activity. *Journal of Bioscience and Bioengineering*. 97(5): 289-293.

Matthews, B.F., and Widholm, J.M. (1978). Regulation of lysine and threonine synthesis in carrot cell suspension cultures and whole carrot roots. *Planta*. 141(3): 315-321.

Mayo, B., Aleksandrzak-Piekarczyk, T., Fernandez, M., Kowalczyk, M., Alvarez-Martin, P., and Bardowski, J. (2010). Updates in the metabolism of lactic acid bacteria. In F. Mozzi, R.R. Raya, G.M. Vignola (Eds.) *Biotechnology of Lactic Acid Bacteria-novel Applications* (pp. 3-33). New Jersey: Wiley-Blackwell.

McDowell, L.R. (2000). *Vitamins in Animal and Human Nutrition* (2nd ed.). Ames: Iowa State University Press.

McSweeney, P.L., and Sousa, M.J. (2000). Biochemical pathways for the production of flavour compounds in cheeses during ripening: A review. *Le Lait*. 80(3): 293-324.

Menconi, A., Kallapura, G., Latorre, J.D., Morgan, M.J., Pumford, N.R., Hargis, B.M., and Tellez, G. (2014). Identification and characterization of lactic acid bacteria in a commercial probiotic culture. *Bioscience of Microbiota, Food and Health*. 33(1): 25-30.

Miller, G.L. (1959). Use of Dinitrosalicylic acid reagent for determination of reducing sugar. *Analytical Chemistry*. 31(3): 426-428.

Miller, J.N. (2013). Experimental design and optimisation (4): Plackett–Burman designs. *Analytical Methods*. 5(8): 1901-1903.

Miwa, K., Tsuchida, T., Kurahashi, O., Nakamori, S., Sano, K., and Momose, H. (1983). Construction of L-threonine overproducing strains *of Escherichia coli* K-12 using recombinant DNA techniques. *Agricultural and Biological Chemistry*. 47(10): 2329-2334.

Miyajima, R., and Shiio, I. (1972). Regulation of aspartate family amino acid biosynthesis in *Brevibacterium flavum* V. Properties of Homoserine Kinase. *Journal of Biochemistry*. 71(2): 219-226.

Mohamad, R. (2000). *Kinetics, modelling and scaling-up of kojic acid fermentation by Aspergillus flavus 44-1 using different carbon sources*. Unpublished doctoral dissertation, Universiti Putra Malaysia, Malaysia.

Momose, H., and Takagi, T. (1978). Glutamic acid production in biotin-rich media by temperature-sensitive mutants of *Brevibacterium lactofermentum*, a novel fermentation process. *Agricultural and Biological Chemistry*. 42(10): 1911-1917.

Montserrat, S., Iñaki, R., François, O., Francesc, G., and Carles, C. (1993). Application of factorial design to the optimization of medium composition in batch cultures of *Streptomyces lividans* TK21 producing a hybrid antibiotic. *Biotechnology Letters*. 15(6): 559-564.

Moshirfar, A., Kamara, K., and Castonguay, T.W. (1996). Intragastrically administered tryptophan blocks gluconeogenesis in 48-hr starved rats. *The Journal of Nutritional Biochemistry*. 7(10): 567-570.

Mozzi, F., Raya, R.R., and Vignola, M.G. (2010). *Biotechnology of Lactic Acid Bacteria.* New Jersey: Wiley-Blackwell.

Mtshali, P.S., Divol, B., and du Toit, M. (2013). Evaluating *Lactobacillus* and *Pediococcus* strains for enzyme-encoding genes related to peptide and amino acid utilization in wine. *Annals of Microbiology*. 63(1): 233-239.

Mugula, J.K., Nnko, S.A.M., Narvhus, J.A., and Sørhaug, T. (2003). Microbiological and fermentation characteristics of togwa, a Tanzanian fermented food. *International Journal of Food Microbiology*. 80(3): 187-199.

Myers, R.H., Montgomery, D.C., and Anderson-Cook, C.M. (2016). *Response Surface Methodology: Process And Product Optimization Using Designed Experiments*. New Jersey: John Wiley and Sons.

Nadeem, S., Niaz, B., Muzammil, H.M., Rana, S.M., Rajoka, M.I., and Shakoori, A.R. (2011). Optimising carbon and nitrogen sources for L-glutamic acid production by *Brevibacterium* strain NIAB SS-67. *Pakistan Journal of Zoology*. 43(2): 285-290.

Nakayama, K., Kitada, S., and Kinoshita, S. (1961). Studies on lysine fermentation I. The control mechanism on lysine accumulation by homoserine and threonine. *Journal of General and Applied Microbiology*. 7(3): 145-154.

Nampoothiri, K.M., and Pandey, A. (1995). Effect of different carbon sources on growth and glutamic acid fermentation by *Brevibacterium* sp. *Journal of Basic Microbiology*. 35(4): 249-254.

Nampoothiri, K.M., and Pandey, A. (1996). Solid state fermentation for L-glutamic acid production using *Brevibacterium* sp. *Biotechnology Letters*. 18(2): 199-204.

Naveena, B.J., Altaf, M., Bhadriah, K., and Reddy, G. (2005). Selection of medium components by Plackett–Burman design for production of L (+) lactic acid by *Lactobacillus amylophilus* GV6 in SSF using wheat bran. *Bioresource Technology*. 96(4): 485-490.

Nester, E.W., Anderson, D.G., Roberts, J.C., and Nester, M.T. (2009). *Microbiology: A Human Perspective* (6th ed). New York: McGraw-Hill.

Neysens, P., Messens, W., and De Vuyst, L. (2003). Effect of sodium chloride on growth and bacteriocin production by *Lactobacillus amylovorus* DCE 471. *International Journal of Food Microbiology*. 88(1): 29-39.

Norfarina, M.N. (2011). *Optimization of Medium Formulation for Folate Biosynthesis by Lactobacillus plantarum I-UL4 Using Response Surface Methodology*. Unpublished master dissertation, Universiti Putra Malaysia, Malaysia.

Norfarina, M.N., Loh, T.C., Raha, A.R., Foo, H.L., Zuhainis, W.S., and Rosfarizan, M. Evaluation of Lactic Acid Bacteria as Amino Acid Producer for Poultry Feed Additive Formulation. Proceedings of the 1st Asean Regional Conference on Animal Production 2014 and 35th Annual Conference of Malaysian Society of Animal Production (MSAP), Kuching, Malaysia, Jun. 4-6, 2014. Panandam J.M., Alimon A.R., Yaakub H., Wahid H., Omar M.A., Wan Khadijah W.E. (Eds.); Malaysian Society of Animal Production: Serdang, 2014.

Norfarina, M.N., Rosfarizan, M., Foo, H.L., and Raha, A.R. (2010). Improvement of folate biosynthesis by lactic acid bacteria using response surface methodology. *Food Technology and Biotechnology*. 48(2): 243-250.

Odunfa, S.A., Adeniran, S.A., Teniola, O.D., and Nordstrom, J. (2001). Evaluation of lysine and methionine production in some *Lactobacilli* and yeasts from Ogi. *International Journal of Food Microbiology*. 63(1): 159-163.

Oh, H., Wee, Y.J., Yun, J.S., Han, S.H., Jung, S., and Ryu, H.W. (2005). Lactic acid production from agricultural resources as cheap raw materials. *Bioresource Technology*. 96(13): 1492-1498.

Oh, S., Rheem, S., Sim, J., Kim, S., and Baek, Y. (1995). Optimizing conditions for the growth of *Lactobacillus casei* YIT 9018 in tryptone-yeast extract-glucose medium by using response surface methodology. *Applied and Environmental Microbiology*. 61(11): 3809-3814.

Okamoto, K., and Ikeda, M. (2000). Development of an industrially stable process for L-threonine fermentation by an L-methionine-auxotrophic mutant of *Escherichia coli*. *Journal of Bioscience and Bioengineering*. 89(1): 87-89.

Okamoto, K., Kino, K., and Ikeda, M. (1997). Hyperproduction of L-threonine by an *Escherichia coli* mutant with impaired L-threonine uptake. *Bioscience, Biotechnology, and Biochemistry*. 61(11): 1877-1882.

Oogai, Y., Yamaguchi, M., Kawada-Matsuo, M., Sumitomo, T., Kawabata, S., and Komatsuzawa, H. (2016). Lysine and threonine biosynthesis from aspartate contributes to *Staphylococcus aureus* growth in calf serum. *Applied and Environmental Microbiology*. 82(20): 6150-6157.

Ooi, M.F., Nurzafirah, M., Foo, H.L., Loh, T.C., Rosfarizan, M., Raha, A.R., and Arbakariya, A. (2015). Effects of carbon and nitrogen sources on bacteriocin-inhibitory activity of postbiotic metabolites produced by *Lactobacillus plantarum* I-UL4. *Malaysian Journal of Microbiology*. 11(2): 176-184.

Oren, A. (2010). Acidophiles. In *Encyclopedia of Life Sciences* (ELS). Chichester: John Wiley and Sons Ltd.

Osborne, A., Thorneley, R.N., Abell, C., and Bornemann, S. (2000). Studies with substrate and cofactor analogues provide evidence for a radical mechanism in the chorismate synthase reaction. *Journal of Biological Chemistry*. 275(46): 35825-35830.

Pailin, T., Kang, D.H., Schmidt, K., and Fung, D.Y.C. (2001). Detection of extracellular bound proteinase in EPS-producing lactic acid bacteria cultures on skim milk agar. *Letters in Applied Microbiology*. 33(1): 45-49.

Panda, B.P., Ali, M., and Javed, S. (2007). Fermentation process optimization. *Research Journal of Microbiology*. 2(3): 201-208.

Paranthaman, R., Vidyalakshmi, R., Murugesh, S., and Singaravadivel, K. (2008). Optimisation of fermentation conditions for production of tannase enzyme by *Aspergillus oryzae* using sugarcane baggase and rice straw. *Global Journal of Biotechnology & Biochemistry*. 3(2): 105-110.

Pastar, I., Tonic, I., Golic, N., Kojic, M., Van Kranenburg, R., Kleerebezem, M., Topisirovic, L., and Jovanovic, G. (2003). Identification and genetic characterization of a novel proteinase, PrtR, from the human isolate *Lactobacillus rhamnosus* BGT10. *Applied and Environmental Microbiology*. 69(10): 5802-5811.

Patel, B., Gohel, V., and Raol, B. (2007). Statistical optimisation of medium components for chitinase production by *Paenibacillus sabina* strain JD2. *Annals of Microbiology*. 57(4): 589-597.

Pederson, J.A., Mileski, G.J., Weimer, B.C., and Steele, J.L. (1999). Genetic characterization of a cell envelope-associated proteinase from

Lactobacillus helveticus CNRZ32. *Journal of Bacteriology*. 181(15): 4592-4597.

Pinto, A., Conti, P., Tamborini, L., and De Micheli, C. (2009). A novel simplified synthesis of acivicin. *Tetrahedron: Asymmetry*. 20(4): 508-511.

Pinto, G., Caira, S., Cuollo, M., Lilla, S., Chianese, L., and Addeo, F. (2012). Bioactive Casein Phosphopeptides in Dairy Products as Nutraceuticals for Functional Foods. In W.L. Hurley (Ed.). *Milk Protein* (pp. 3-44). Rijeka: InTech.

Pirie, P., Naeimpoor, F., and Hejazi, P. (2011). A microcosm study on P-Nitrophenol biodegradation in soil slurry by *Alcaligenes faecalis*: Plackett-Burman Design. *Iranian Journal of Chemical Engineering*. 8(2): 57-68.

Pot, B., Felis, G.E., Bruyne, K.D., Tsakalidou, E., Papadimitriou, K., Leisner, J., and Vandamme, P. (2014). The genus *Lactobacillus*. In W.H. Holzapfel, B.J. Wood (Eds.). *Lactic Acid Bacteria: Biodiversity and Taxonomy* (pp. 249-353). Chichester: John Wiley and Sons.

Powers, H.J. (2003). Riboflavin (vitamin B-2) and health. *The American Journal of Clinical Nutrition*. 77(6): 1352-1360.

Putnam, D., and Kopeček, J. (1995). Polymer conjugates with anticancer activity. In N.P. Peppas, R.S. Langer (Eds.) *Biopolymers II* (pp. 55-123). Berlin: Springer-Verlag Berlin Heidelberg.

Rao, R.S., Prakasham, R.S., Prasad, K.K., Rajesham, S., Sarma, P.N., and Rao, L.V. (2004). Xylitol production by *Candida* sp.: parameter optimization using Taguchi approach. *Process Biochemistry*. 39(8): 951-956.

Rawlings, A.V., and Harding, C.R. (2004). Moisturization and skin barrier function. *Dermatologic Therapy*. 17(s1): 43-48.

Reinscheid, D.J., Kronemeyer, W., Eggeling, L., Eikmanns, B.J., and Sahm, H. (1994). Stable expression of hom-1-thrB in *Corynebacterium glutamicum* and its effect on the carbon flux to threonine and related amino acids. *Applied and Environmental Microbiology*. 60(1): 126-132.

Rieping, M., and Hermann, T. (2006). L-Threonine. In V.F. Wendisch (Ed.) *Amino Acid Biosynthesis- Pathways, Regulation and Metabolic Engineering* (pp. 71-92). Berlin: Springer-Verlag Berlin Heidelberg.

Rodarte, M.P., Dias, D.R., Vilela, D.M., and Schwan, R.F. (2011). Proteolytic activities of bacteria, yeasts and filamentous fungi isolated from coffee fruit (*Coffea arabica L*.). *Acta Scientiarum. Agronomy*. 33(3): 457-464.

Rodrigues, L., Teixeira, J., Oliveira, R., and Van Der Mei, H.C. (2006). Response surface optimization of the medium components for the production of biosurfactants by probiotic bacteria. *Process Biochemistry*. 41(1): 1-10.

Rodwell, V., Bender, D., Botham, K.M., Kennelly, P.J., and Weil, P.A. (2015). *Harper's Illustrated Biochemistry* (30th ed.). New York: McGraw-Hill Education.

Rollán, G.C., Farias, M.E., and de Nadra, M.M. (1993). Protease production by *Leuconostoc oenos* strains isolated from wine. *World Journal of Microbiology and Biotechnology*. 9(5): 587-589.

Rollán, G.C., Farías, M.E., and de Nadra, M.M. (1995). Characterization of two extracellular proteases from *Leuconostoc oenos*. *World Journal of Microbiology and Biotechnology*. 11(2): 153-155.

Rosebrough, R.W. (1996). Crude protein and supplemental dietary tryptophan effects on growth and tissue neurotransmitter levels in the broiler chicken. *British Journal of Nutrition*. 76(1): 87-96.

Rosen, K. (2012). Production of Baker's Yeast, In D.R. Berry, I. Russell, G.C. Steward (Eds.) *Yeast Biotechnology* (pp. 471-500). London: Unwin Hyman Ltd.

Roy, A., and Mukhopadhyay, S.K. (2011). L-Tryptophan production by auxotrophic and analogue resistant mutants of *Aureobacterium flavescens*. *International Journal of Tryptophan Research*. 4: 39-46.

Roy, D.K., and Chatterjee, S.P. (1989). Production of glutamic acid by *Arthrobacter globiformis*: Influence of cultural conditions. *Folia Microbiologica*. 34(1): 11-24.

Saeed A.H., and Salam A.I. (2013). Current limitations and challenges with lactic acid bacteria: A review. *Food and Nutrition Sciences*. 2013(4): 73-87.

Safari, R., Motamedzadegan, A., Ovissipour, M., Regenstein, J.M., Gildberg, A., and Rasco, B. (2012). Use of hydrolysates from yellowfin tuna (*Thunnus albacares*) heads as a complex nitrogen source for lactic acid bacteria. *Food and Bioprocess Technology*. 5(1): 73-79.

Saraniya, A., and Jeevaratnam, K. (2014). Optimization of nutritional and non-nutritional factors involved for production of antimicrobial compounds from *Lactobacillus pentosus* SJ65 using response surface methodology. *Brazilian Journal of Microbiology*. 45(1): 81-88.

Saravanamuthu, R. (2004). Microbial Growth and Population Dynamics. In D.P. Singh, S.K. Dwivedi (Eds.). *Environmental Microbiology and Biotechnology* (pp. 10-58). New Delhi: New Age International.

Saris, P.E. (2014). Biopreservation by Lactic Acid Bacteria. In B. Ozer, G. Akdemir-Evrendilek (Eds.). *Dairy Microbiology and Biochemistry: Recent Developments* (pp. 86-94). New York: CRC Press.

Satyanarayana, U., and Chakrapani, U. (2014). *Biochemistry* (4th ed.). Amsterdam: Elsevier Health Sciences.

Savijoki K., Ingmer H., and Varmanen P. (2006). Proteolytic systems of lactic acid bacteria. *Applied Microbiology and Biotechnology*. 71: 394-406.

Schmidt, F.R. (2005). Optimization and scale up of industrial fermentation processes. *Applied Microbiology and Biotechnology*. 68(4): 425-435.

Sharma, R. (2012). Enzyme Inhibition: Mechanisms and Scope. In R. Sharma (Ed.) *Enzyme Inhibition and Bioapplications*. Rijeka: InTech.

Sharp, C.P., and Pearson, D.R. (2010). Amino acid supplements and recovery from high-intensity resistance training. *The Journal of Strength and Conditioning Research*. 24(4): 1125-1130.

Shen, T., Liu, Q., Xie, X., Xu, Q., and Chen, N. (2012). Improved production of tryptophan in genetically engineered *Escherichia coli* with *TktA* and *PpsA* overexpression. *Journal of Biomedicine and Biotechnology*. 2012: 1-8.

Sidransky, H. (2001). *Tryptophan: Biochemical and Health Implications*. Florida: CRC Press.

Siezen, R.J. (1999). Multi-domain, Cell-envelope Proteinases of Lactic Acid Bacteria. In W.N. Konings, O.P. Kuipers, J.H.J. Huis In't Veld (Eds.) *Lactic Acid Bacteria: Genetics, Metabolism and Applications* (pp. 139-155). Springer Netherlands.

Simic, P., Willuhn, J., Sahm, H., and Eggeling, L. (2002). Identification of glyA (encoding serine hydroxymethyltransferase) and its use together with the exporter ThrE to increase L-threonine accumulation by *Corynebacterium glutamicum*. *Applied and Environmental Microbiology*. 68(7): 3321-3327.

Simova E., Simov Z., Beshkova D., Frengova G., Dimitrov Z., and Spasov Z. (2006). Amino acid profiles of lactic acid bacteria, isolated from kefir grains and kefir starter made from them. *International Journal of Food Microbiology*. 107(2): 112-123.

Simpson, W.J. and Taguchi, H. (1995). The genus *Pediococcus*, with notes on the genera *Tetragenococcus* and *Aerococcus*. In B.J.B. Wood, W.H. Holzapfel (Eds.). *The Genera of Lactic Acid Bacteria* (pp. 125–172). Glasgow: Blackie Academic and Professional.

Smit, G., Smit, B.A., and Engels, W.J. (2005). Flavour formation by lactic acid bacteria and biochemical flavour profiling of cheese products. *FEMS Microbiology Reviews*. 29(3): 591-610.

Smith, J.E. (2012). Concepts of Industrial Antibiotic Production. In D.I. Alani, M. Moo-Young (Eds.) *Perspectives in Biotechnology and Applied Microbiology* (pp. 105-142). New York: Springer Science and Business Media.

Sprenger, G.A. (2006). Aromatic Amino Acids. In V.F. Wendisch (Ed.). *Amino Acid Biosynthesis- Pathways, Regulation and Metabolic Engineering* (pp. 93-127). Berlin: Springer-Verlag Berlin Heidelberg.

Stamer, J.R. (1983). Lactic Acid Fermentation of Cabbage and Cucumbers. In H.J. Rehm, G. Reed (Eds.). *Biotechnology*, Vol. 5 (pp. 365-378). Weinheim: Verlag Chemie.

Stenesh, J. (1998). *Biochemistry: 1V. Transfer of Genetic Information*. New York: Plenum Press.

Stephenie, W., Kabeir, B.M., Shuhaimi, M., Rosfarizan, M., & Yazid, A.M. (2007). Influence of pH and impeller tip speed on the cultivation of *Bifidobacterium pseudocatenulatum* G4 in a milk-based medium. *Biotechnology and Bioprocess Engineering*. 12(5): 475-483.

Stiles, M.E., and Holzapfel, W.H. (1997). Lactic acid bacteria of foods and their current taxonomy. *International Journal of Food Microbiology*. 36(1): 1-29.

Stranix, B.R., Lavallée, J.F., Sévigny, G., Yelle, J., Perron, V., LeBerre, N., Herbart, D., and Wu, J.J. (2006). Lysine sulfonamides as novel HIV-protease inhibitors: *N*ε-acyl aromatic α-amino acids. *Bioorganic and Medicinal Chemistry Letters*. 16(13): 3459-3462.

Sundrum, A., Schneider, K., and Richter, U. (2005). *Possibilities and limitations of protein supply in organic poultry and pig production.* Witzenhausen: Organic Revision.

Święch, E., Boryczka, M., Taciak, M., and Buraczewska, L. (2011). The effect of graded levels of dietary threonine on nitrogen retention and structure of the small intestine in young pigs. *Journal of Animal and Feed Sciences*. 20: 350-360.

Tajabadi, N., Ebrahimpour, A., Baradaran, A., Raha, A.R., Mahyudin, N.A., Manap, M.Y.A., Fatimah, A.B., and Saari, N. (2015). Optimization of γ-

aminobutyric acid production by *Lactobacillus plantarum* Taj-Apis362 from Honeybees. *Molecules*. 20(4): 6654-6669.

Tang, Y.W., Ellis, N.M., Hopkins, M.K., Smith, D.H., Dodge, D.E., and Persing, D.H. (1998). Comparison of phenotypic and genotypic techniques for identification of unusual aerobic pathogenic Gram-negative *Bacilli*. *Journal of Clinical Microbiology*. 36(12): 3674-3679.

Tarek, M., and Hesham, H.M. (2010). Screening of potential infants' *Lactobacilli* isolates for amino acids production. *African Journal of Microbiology Research*. 4: 226-232.

Tavakkoli, M., Hamidi-Esfahani, Z., and Azizi, M.H. (2012). Optimization of *Corynebacterium glutamicum* glutamic acid production by response surface methodology. *Food and Bioprocess Technology*. 5(1): 92-99.

Theze, J., Kleidman, L., and Saint Girons, I. (1974). Homoserine kinase from *Escherichia coli* K-12: properties, inhibition by L-threonine, and regulation of biosynthesis. *Journal of Bacteriology*. 118(2): 577-581.

Thung, T.Y. (2012). *Isolation and Purification of Proteolytic Enzyme Produced by Lactic Acid Bacteria from Budu and Bambangan*. Unpublished master dissertation, Universiti Putra Malaysia, Malaysia.

Todorov, S.D., and Dicks, L.M. (2005). Pediocin ST18, an anti-listerial bacteriocin produced by *Pediococcus pentosaceus* ST18 isolated from boza, a traditional cereal beverage from Bulgaria. *Process Biochemistry*. 40(1): 365-370.

Todorov, S.D., and Dicks, L.M. (2007). Bacteriocin production by *Lactobacillus pentosus* ST712BZ isolated from boza. *Brazilian Journal of Microbiology*. 38(1): 166-172.

Tomas, J.M.S., Bru, E., and Nader-Macia, M.E. (2010). Different combinations of salts affect the growth and bacteriocin production by *Lactobacillus salivarius* CRL 1328. *Journal of Chemical Technology and Biotechnology.* 85(1): 91-99.

Toride, Y. Lysine and other amino acids for feed: production and contribution to protein utilization in animal feeding. Proceedings of FAO Expert Consultation and Workshop on Protein Sources for the Animal Feed Industry, Bangkok, Thailand, Apr. 29-May 3, 2002. FAO: Rome, 2004.

Tripuraneni, S. (2011). *Effect of Nutrient Supplements on Cucumber Fermentation by Lactic Acid Bacteria*. Unpublished master dissertation, University of Arkansas, USA.

Turner, E.H., Loftis, J.M., and Blackwell, A.D. (2006). Serotonin a la carte: supplementation with the serotonin precursor 5-hydroxytryptophan. *Pharmacology and Therapeutics*. 109(3): 325-338.

Työppönen, S., Petäjä, E., and Mattila-Sandholm, T. (2003). Bioprotectives and probiotics for dry sausages. *International Journal of Food Microbiology.* 83(3): 233-244.

Vafopoulou-Mastrojiannaki, A., Litopoulou-Tzanetaki, E., and Tzanetakis, N. (1994). Proteinase, peptidase and esterase activity of crude cell-free extracts of *Pediococcus pentosaceus* isolated from cheese. *LWT-Food Science and Technology.* 27(4): 342-346.

Valasaki, K., Staikou, A., Theodorou, L.G., Charamopoulou, V., Zacharaki, P., and Papamichael, E.M. (2008). Purification and kinetics of two novel thermophilic extracellular proteases from *Lactobacillus helveticus*, from

kefir with possible biotechnological interest. *Bioresource Technology*. 99(13): 5804-5813.

Vallino, J.J., and Stephanopoulos, G. (2000). Metabolic flux distributions in *Corynebacterium glutamicum* during growth and lysine overproduction. *Biotechnology and Bioengineering*. 67(6): 872-885.

van Balken, J.A.M. (Ed.). (1997). *Biotechnological innovations in chemical synthesis*. Oxford: Butterworth-Heinemann.

Van der Zant, W.C., and Nelson, F.E. (1953). Characteristics of an endocellular proteolytic enzyme system of *Streptococcus lactis*. *Journal of Dairy Science*. 36(11): 1212-1222.

van Kranenburg, R., Kleerebezem, M., van Hylckama Vlieg, J.E.T., Ursing, B.M., Boekhorst, J., Smit, B.A., Ayad, E.H.E., Smit, G., and Siezen, R.J. (2002). Flavour formation from amino acids by lactic acid bacteria: predictions from genome sequence analysis. *International Dairy Journal*. 12: 111–121.

van Niel E.W.J., and Hahn-hagerdal B. (1999). Nutrient requirements of *Lactococci* in defined growth media. *Applied Microbiology and Biotechnology*. 52: 617-627.

Velly, H., Renault, P., Abraham, A.L., Loux, V., Delacroix-Buchet, A., Fonseca, F., and Bouix, M. (2014). Genome sequence of the lactic acid bacterium *Lactococcus lactis* subsp. *lactis* TOMSC161, isolated from a nonscalded curd pressed cheese. *Genome Announcements*. 2(6): e01121-14.

Venkitanarayanan, K., Kollanoor-Johny, A., and Doyle, M.P. (2016). Microbiological Safety of Foods. In C.D. Berdanier, J.T. Dwyer, D. Heber (Eds.) *Handbook of Nutrition and Food* (3rd ed.) (pp. 43-80). Boca Raton: CRC Press.

Verellen, T.L., Bruggeman, G., Van Reenen, C.A., Dicks, L.M., and Vandamme, E.J. (1998). Fermentation optimisation of plantaricin 423, a bacteriocin produced by *Lactobacillus plantarum* 423. *Journal of Fermentation and Bioengineering*. 86(2): 174-179.

Vidotti, R.M., Viegas, E.M.M., and Carneiro, D.J. (2003). Amino acid composition of processed fish silage using different raw materials. *Animal Feed Science and Technology*. 105(1): 199-204.

Viswanathan, P., and Surlikar, N.R. (2001). Production of α-amylase with *Aspergillus flavus* on *Amaranthus* grains by solid-state fermentation. *Journal of Basic Microbiology*. 41(1): 57-64.

Voet, D., and Voet, J.G. (2004). *Biochemistry* (3rd ed.). Hoboken: John Wiley and Sons, Inc.

Vohra, A., and Satyanarayana, T. (2002). Statistical optimization of the medium components by response surface methodology to enhance phytase production by *Pichia anomala*. *Process Biochemistry*. 37(9): 999-1004.

Wagner, I., and Musso, H. (2003). New naturally occurring amino acids. *Angewandte Chemie International Edition in English*. 22: 816-828.

Wang, J., Cheng, L.K., and Chen, N. (2014). High-level production of L-threonine by recombinant *Escherichia coli* with combined feeding strategies. *Biotechnology and Biotechnological Equipment*. 28(3): 495-501.

Wang, J., Cheng, L.K., Wang, J., Liu, Q., Shen, T., and Chen, N. (2013). Genetic engineering of *Escherichia coli* to enhance production of L-tryptophan. *Applied Microbiology and Biotechnology*. 97(17): 7587-7596.

Weiss, N. (1992). The genera *Pediococcus* and *Aerococcus*. In A. Balows, H.G. Truper, M. Dworkin, W. Harder, K.H. Schleifer (Eds.). *The Prokaryotes-A Handbook on the Biology of Bacteria*, *3nd ed. Vol. 2: Ecophysiology and Biochemistry* (pp. 1502-1507). New York: Springer-Verlag.

Weuster-Botz, D. (2000). Experimental design for fermentation media development: statistical design or global random search?. *Journal of Bioscience and Bioengineering*. 90(5): 473-483.

Widholm, J. (1972). Anthranilate synthetase from 5-methyltryptophan-susceptible and-resistant cultured Daucus carota cells. *Biochimica et Biophysica Acta*. 279(1): 48-57.

Wright, J.K., Feldman, J., and Takahashi, M. (1976). Cobalt (III) affinity-labeled aspartokinase. Formation of substrate and inhibitor adducts. *Biochemistry*. 15(17): 3704-3710.

Xie, M., Zhang, L., Wen, Z.G., Tang, J., Huang, W., and Hou, S.S. (2014). Threonine requirement of white Pekin ducks from hatch to 21 d of age. *British Poultry Science*. 55(4): 553-557.

Yuan, L.L., Li, Y.Q., Wang, Y., Zhang, X.H., and Xu, Y.Q. (2008). Optimization of critical medium components using response surface methodology for phenazine-1-carboxylic acid production by *Pseudomonas* sp. M-18Q. *Journal of Bioscience and Bioengineering*. 105(3): 232-237.

Zalán, Z., Hudáček, J., Štětina, J., Chumchalová, J., and Halász, A. (2010). Production of organic acids by *Lactobacillus* strains in three different media. *European Food Research and Technology*. 230(3): 395-404.

Zalkin, H., and Kling, D. (1968). Anthranilate synthetase. Purification and properties of component I from Salmonella typhimurium. *Biochemistry*. 7(10): 3566-3573.

Zarandi, M. (2007). Amino acids. In J.S. Davies (Eds.) *Amino acids, peptides and proteins*, Vol. 36 (pp. 19-81). Cambridge: Royal Society of Chemistry.

Zareian, M., Ebrahimpour, A., Bakar, F.A., Mohamed, A.K.S., Forghani, B., Ab-Kadir, M.S.B., and Saari, N. (2012). A glutamic acid-producing lactic acid bacteria isolated from Malaysian fermented foods. *International Journal of Molecular Sciences*. 13(5): 5482-5497.

Zhang, B., Tong, H., and Dong, X. (2005). *Pediococcus cellicola* sp. nov., a novel lactic acid coccus isolated from a distilled-spirit-fermenting cellar. *International Journal of Systematic and Evolutionary Microbiology*. 55(5): 2167-2170.

Zhang, H., Huang, Y., Huang, Z., and Xu, Y. (2014). Optimization of the fermentation conditions of sweet oats by response surface methodology. *Agricultural Science and Technology*. 15(3): 483.

Zhang, J.G., Cai, Y., Kobayashi, R., and Kumai, S. (2000). Characteristics of lactic acid bacteria isolated from forage crops and their effects on silage fermentation. *Journal of the Science of Food and Agriculture*. 80(10): 1455-1460.

Zhang, X., Yan, J., Yu, L., Zhang, G., Zhang, Y., Chen, N., and Wen, T. (2009). Construction of recombinant plasmids containing threonine operon and their effects on L-threonine accumulation. *Acta Microbiologica Sinica*. 49(5): 591-596.

Zhao, Z., Chen, S., Wu, D., Wu, J., and Chen, J. (2012). Effect of gene knockouts of L-tryptophan uptake system on the production of L-tryptophan in *Escherichia coli*. *Process Biochemistry*. 47(2): 340-344.

Zhu, L.W., Wang, C.C., Liu, R.S., Li, H.M., Wan, D.J., and Tang, Y.J. (2012). *Actinobacillus succinogenes* ATCC 55618 fermentation medium optimization for the production of succinic acid by response surface methodology. *Journal of Biomedicine and Biotechnology*. 2012: 1-9.

Zourari, A., Accolas, J.P., and Desmazeaud, M.J. (1992). Metabolism and biochemical characteristics of yogurt bacteria. A review. *Dairy Science and Technology*. 72(1): 1-34.