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ENHANCEMENT OF BACTERIOCIN PRODUCTION BY Lactobacillus plantarum STRAIN I-UL4 AND RS5 THROUGH OPTIMISATION OF CULTURAL CONDITIONS IN DIFFERENT SIZES OF STIRRED TANK BIOREACTORS

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By

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Postbiotic is defined as the bioactive metabolites produced by probiotic lactic acid bacterium (LAB) which mediates beneficial probiotic effects. The postbiotics produced by *Lactobacillus plantarum* strains I-UL4 and RS5 are found important for various industrial applications. The postbiotic produced by *Lactobacillus plantarum* I-UL4 (postbiotic I-UL4) was found to have high potential as human health supplement and as in-feed additive to replace antibiotic growth promoter for Tilapia fish in aquaculture industry. Meanwhile, the postbiotic produced by *Lactobacillus plantarum* RS5 (postbiotic RS5) emerged as promising feed supplement for broilers and laying hens in livestock industry. One of the prominent attributes of postbiotic as alternative in-feed growth promoter is its antimicrobial activity. Bacteriocin is one of the postbiotic compounds contributes to the antimicrobial activity of postbiotic. However, the production of bacteriocin is not naturally optimised for maximum production rates and it was affected by cultural conditions encompass medium composition and physical parameters. Besides, the optimum condition for bacteriocin production by LAB was also found strain-dependent. There is no optimisation study has been conducted to enhance the bacteriocin-inhibitory activity of postbiotic I-UL4 and postbiotic RS5. In view of the importance to meet the need for different industrial applications, it is crucial to optimise the cultural conditions for enhancement of bacteriocin-inhibitory activity of postbiotic I-UL4 and postbiotic RS5 respectively.

The optimisation study for cultural conditions which involves a huge number of experiments is more practical to be conducted in small scale cultivation using universal bottle. However, to determine the feasibility of production for industrial application, it is paramount to check the reproducibility of optimised cultural conditions in bioreactor level. Therefore, the general objective of this study was

to enhance the bacteriocin-inhibitory activity of postbiotic I-UL4 and postbiotic RS5. The first and second specific objectives were to optimise the cultural conditions for the production of bacteriocin-inhibitory activity of postbiotic I-UL4 and postbiotic RS5 in universal bottle by using combination approaches of "one factor at a time" and response surface methodology. The optimised culture condition has enhanced bacteriocin-inhibitory activity of postbiotic I-UL4 to 100% in comparison to the activity achieved in de Man Rogosa Sharpe (MRS) medium. The bacteriocin-inhibitory activity of postbiotic I-UL4 achieved 1440 MAU/mL when *L. plantarum* I-UL4 was cultivated in optimised medium at 27 ^{o}C, initial pH at 6.72 and inoculum of 6.60 % (v/v). The optimised medium comprised of 20 g/L glucose, 36.20 g/L of yeast extract, 3.75 g/L of sodium acetate, 0.76 g/L of tween 80 and 0.03 g/L of manganese sulphate terahdyrate. For *L. plantarum* RS5, the optimised culture condition has enhanced bacteriocin-inhibitory activity to 112.5 % as compared to MRS medium. The bacteriocin-inhibitory activity of postbiotic RS5 was increased to 1360 MAU/mL when cultivated in optimised medium at 30 ^{o}C, initial pH at 6.40 and inoculum of 5.22 % (v/v). The optimised medium for *L. plantarum* RS5 consists of 20 g/L of glucose, 27.84 g/L of yeast extract, 5.75 g/L of sodium acetate, 1.12 g/L of tween 80 and 0.05 g/L of manganese sulphate terahydrate.

The third specific objective was to determine the optimum agitation speed for 2 L batch cultivation of *L. plantarum* I-UL4 and *L. plantarum* RS5 using optimised medium and physical parameters in stirred tank bioreactor. The maximum level of bacteriocin-inhibitory activity (1440 MAU/mL), product yield coefficient of bacteriocin-inhibitory activity (100.28 x10^3 MAU/g) and biomass (5.54 g/L) were achieved when *L. plantarum* I-UL4 was cultivated at optimum agitation speed of 100 rpm under anaerobic condition. Meanwhile, the maximum level of bacteriocin-inhibitory activity (1600 MAU/mL), product yield coefficient of bacteriocin-inhibitory activity (87.15 x 10^3 MAU/g) and biomass (3.59 g/L) were achieved when *L. plantarum* RS5 was cultivated at optimum agitation speed of 150 rpm under anaerobic condition. The corresponding impeller tip speed for *L. plantarum* I-UL4 and *L. plantarum* RS5 was 0.34 m/s and 0.50 m/s respectively based on respective optimum agitation speed.

The last specific objective was to scale-up the production of bacteriocin-inhibitory activity of postbiotic I-UL4 and postbiotic RS5 using optimised cultural conditions in 20 L batch cultivation based on constant impeller tip speed. For both *L. plantarum* strains, same level of maximum bacteriocin-inhibitory activities and comparable kinetic parameter values were achieved in 2 L and 20 L batch cultivations respectively, indicating the production of postbiotic I-UL4 and postbiotic RS5 were successfully scale-up based on constant impeller tip speed.

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

PENINGKATAN PENGHASILAN BAKTERIOSIN OLEH STRAIN *Lactobacillus plantarum* I-UL4 DAN RS5 MELALUI OPTIMISASI KEADAAN KULTUR DALAM BIOREAKTOR BERPENGADUK YANG BERBEZA SKALA

Oleh

OOI MAY FOONG

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Posbiotik ialah metabolit bioaktif hasilan Bakteria Asid Laktik yang memberikan kesan probiotik yang berfaedah. Posbiotik yang dihasilkan oleh *L. plantarum* I-UL4 dan *L. plantarum* RS5 didapati penting untuk gunaan dalam pelbagai aplikasi industri. Posbiotik yang dihasilkan oleh *Lactobacillus plantarum* I-UL4 (posbiotik I-UL4) didapati mempunyai potensi tinggi sebagai makanan sihat manusia dan sebagai agen perangsang pertumbuhan ikan Tilapia di industri akuakultur. Manakala, posbiotik yang dihasilkan oleh *Lactobacillus plantarum* RS5 (posbiotik RS5) mempunyai potensi tinggi sebagai pengganti kepada antibiotik yang digunakan sebagai agen perangsang pertumbuhan ayam di industri penternakan. Kesesuaian posbiotik sebagai agen perangsang pertumbuhan haiwan di industri penternakan adalah disebabkan posbiotik mengandungi kesan antimikrob. Bakteriosin ialah salah satu sebatian dalam posbiotik yang menyumbangkan kesan antimikrob tersebut. Oleh itu, objektif utama kajian ini adalah untuk meningkatkan aktiviti bakteriosin dalam posbiotik I-UL4 dan posbiotik RS5. Objektif spesifik pertama dan kedua kajian ini adalah untuk mengoptimakan keadaan kultur untuk penghasilan aktiviti bakteriosin posbiotik I-UL4 dan posbiotik RS5 di botol universal melalui kombinasi kaedah optimasi “Satu Faktor Pada Satu Masa” dan “Metode Permukaan Respon”. Keadaan kultur yang optima meningkatkan aktiviti bakteriosin posbiotik I-UL4 sebanyak 100 % dan kos medium yang optima menurun sebanyak 90 % berbanding dengan medium de Man Rogosa and Sharpe (MRS).

Aktiviti bakteriosin posbiotik I-UL4 mencapai 1440 MAU/mL apabila dikulturkan di dalam medium yang optima pada suhu 27 ^{o}C, pH awal medium pada 6.72 dan saiz inoculum pada 6.60 % (v/v). Kandungan medium yang optima untuk *L. plantarum* I-UL4 terdiri daripada glukosa (20 g/L), ekstrak yis (36.20 g/L),

natrium asetat (3.75 g/L), tween 80 (0.76 g/L) dan mangan sulfat terahidrat (0.03 g/L). Bagi *L. plantarum* RS5, keadaan kultur yang optima meningkatkan aktiviti bakteriosin posbiotik RS5 sebanyak 112.5 % dan kos medium yang optima menurun sebanyak 91 % berbanding dengan medium de Man Rogosa and Sharpe (MRS). Aktiviti bakteriosin posbiotik RS5 mencapai 1360 MAU/mL apabila dikulturkan di medium yang optima pada suhu 30 ^{o}C, pH awal medium pada 6.40 dan saiz inoculum pada 5.22 % (v/v). Kandungan medium yang optima untuk *L. plantarum* RS5 terdiri daripada glukosa (20 g/L), ekstrak yis (27.84 g/L), natrium asetat (5.75 g/L), tween 80 (1.12 g/L) dan mangan sulfat terahidrat (0.05 g/L). Objektif spesifik ketiga kajian ini adalah untuk menentukan kelajuan putaran yang optima untuk fermentasi *L. plantarum* I-UL4 dan *L. plantarum* RS5 yang berisipadu 2 L di bioreaktor berpengaduk. Aktiviti bakteriosin yang maksimum (1440 MAU/mL), pemalar aktiviti bakteriosin berasaskan substrat (100.28 x10^3 MAU/g) dan pertumbuhan sel (5.54 g/L) yang tinggi dicapai apabila *L. plantarum* I-UL4 dikulturkan di bawah kelajuan putaran pada 100 rpm dalam keadaan anaerobik. Manakala, aktiviti bakteriosin yang maksimum (1600 MAU/mL), pemalar aktiviti bakteriosin berasaskan substrat (87.15 x10^3 MAU/g) dan pertumbuhan sel (3.59 g/L) yang tinggi dicapai apabila *L. plantarum* RS5 dikulturkan di bawah kelajuan putaran pada 150 rpm dalam keadaan anaerobik. Halaju hujung pengaduk untuk *L. plantarum* I-UL4 dan *L. plantarum* RS5 adalah bernilai 0.34 m/s dan 0.50 m/s berasaskan kelajuan putaran yang optima masing-masing. Objektif spesifik terakhir kajian ini adalah untuk menjalankan peningkatan skala penghasilan aktiviti bakteriosin posbiotik I-UL4 dan posbiotik RS5 berisipadu 20 L berasaskan halaju hujung pengaduk yang tetap. Untuk kedua-dua *L. plantarum* strain, aktiviti bakteriosin yang sama dan nilai-nilai parameter kinetik yang setanding dicapai di fermentasi berisipadu 2 L dan 20 L masing-masing. Ini juga menunjukkan bahawa peningkatan skala penghasilan posbiotik I-UL4 dan posbiotik RS5 telah berjaya dijalankan berasaskan halaju hujung pengaduk yang tetap.

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This thesis was submitted to the Senate of the 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

AGP	Antibiotic growth promoter
ANOVA	Analysis of variance
ATP	Adenosine triphosphate
AU/mL	Arbitrary unit/mL
BHI	Brain heat infusion
C/N	Carbon to nitrogen ratio
Ca^{2+}	Calcium ion
CCD	Central composite design
Cl^{-}	Chloride ion
Di	Diameter of impeller
Dt	Diameter of tank
DCW	Dry cell weight
DOT	Dissolved oxygen tension
Fe^{2+}	Ferric ion
FFD	Fractional factorial design
g	Gravitational force
H:D-ratio	Ratio of height to diameter of tank
Hi	Height of impeller
HNSCC	Three head and neck squamouse cell carcinoma
K^{+}	Potassium ion
KH_2PO_4	Potassium dihydrogen phosphate
K_2HPO_4	Dipotassium hydrogen phosphate
KLa	Volumetric coefficient of oxygen transfer

L	Length of impeller blades
LAB	Lactic acid bacteria
LAPTg	Yeast autolysate-peptone-tryptone-tween 80-glucose
MAU/mL	Modified bacteriocin activity
Mg^{2+}	Magnesium ion
Mn^{2+}	Manganese ion
$MgSO_4$	Magnesium sulphate
$MnSO_4$	Manganese sulphate
MRS	de-Man Rogosa Sharpe
MRSA	Methicillin-resistance *S. aureus*
N	Nitrogen
N/A	Not available
Na^+	Sodium ion
nm	nanometer
OD	Optical density
OFAT	One factor at a time
pln	plantaricin
Pmax	Maximum product
PBD	Placket-Burman design
Postbiotic I-UL4	Postbiotic produced by *L. plantarum* I-UL4
Postbiotic RS5	Postbiotic produced by *L. plantarum* RS5
Pr	Productivity of product
PTS	Phosphoenolpyruvate-dependent phosphotransferase system
R^C	Coefficient of determination

RPM	Rotation per minute
RSM	Response surface methodology
SAS	Statistical analysis system
SEM	Standard error of the mean
TGYE	Trypticase Glucose Yeast Extrac
t_x	Cultivation time
μ	Specific growth rate
VRE	Vancomycin-resistance *E. faecalis*
W	Width of impeller blades
WHO	World Health Organisation
Xmax	Maximum biomass
$Y_{x/s}$	Growth yield coefficient
$Y_{P/S}$	Product yield coefficient
$Y_{p/x}$	Coefficient of cell efficient to produce bacteriocin-inhibitory activity

CHAPTER 1

INTRODUCTION

Lactic acid bacteria (LAB) are generally described as gram positive bacteria which predominantly produce lactic acid as end product in carbohydrate fermentation. They are non-sporulating, non-motile and anaerobic or facultative anaerobic in nature (Khalid, 2011). LAB are ubiquitous microorganisms in nature which are usually found in carbohydrate-rich environment such as plant, fermented food products and the mucosal surfaces of human, terrestrial and marine animals (Florou-Paneri et al., 2013).

Many genera of LAB are important groups of microorganism renowned for their essential role in food, agricultural and clinical applications (Florou-Paneri et al., 2013; Saeed & Salam, 2013). *Lactobacillus* is one of the core genera of LAB consist of high number of Generally Regarded as Safe species (Khalid, 2011) and play important roles as biopreservative agent in food industry, as starter culture in food and feed fermentation and as probiotic or as vaccine carrier (Goh & Klaenhammer, 2009; Salvetti et al., 2012). The broad applications of LAB were attributed to their fast growing characteristics and the production of various beneficial metabolites (Saeed & Salam, 2013).

Recently, the term “postbiotic” was used to describe the bioactive metabolites produced by probiotic LAB which mediates beneficial probiotic effects (Cicenia et al., 2014; Tsilingiri et al., 2012). The postbiotic produced by LAB commonly comprised of bacteriocin, organic acid, ethanol, diacetyl, acetaldehydes and hydrogen peroxide (Suskovic et al., 2010). Several previous reports showed that postbiotics produced by *Lactobacillus plantarum* isolated from Malaysian fermented food exhibited broad inhibitory activity towards closely related and pathogenic bacteria (Foo et al., 2003; Thanh et al., 2010) and emerged as a promising replacer to antibiotic growth promoter (AGP) for livestock industries (Loh et al., 2010; Thu et al., 2011; Loh et al., 2013). The high potential use of postbiotics as in-feed growth promoter fulfilled the critical need as the alternative AGP for the indiscriminate use of antibiotic growth promoter leading to antibiotic resistance effect which imparts hazardous effects on human and environment [World Health Organisation (WHO), 2014].

One of the prominent attributes of postbiotic as in-feed growth promoter is antimicrobial activity. Bacteriocin is one of the postbiotic compounds contributing to the antimicrobial activity (Rattanachaikunsopon & Phumkhachorn, 2010). Bacteriocin comprised a huge family of ribosomally synthesised peptides which are biologically active with antimicrobial actions against other bacteria, predominantly closed related species (Parada et al., 2007; Perez et al., 2014). Bacteriocins produced by LAB are able to tolerate high thermal stress and

remain active in a wide pH range (Perez et al., 2014). Bacteriocins are proteinaceous compounds which are susceptible to degradation by proteolytic enzymes. Therefore, bacteriocins do not reside long in the human body and this minimise the risk of development of resistance effect. So far, no report about the development of resistance was found even though bacteriocins are applied long in industry (Perez et al., 2014). Recent reports also showed that bacteriocin produced by probiotic LAB might contribute to the probiotic functionality in the host (Dobson et al., 2012). Bacteriocin may act as killing peptides which directly eliminates pathogens. They may also function as colonising peptides for probiotics to compete with the resident microbiota in gut. Bacteriocins may also act as signalling peptides in quorum sensing (Kleerebezem et al., 1997; Meijerink et al., 2010; van Hemert et al., 2010). All these positive attributes make bacteriocin especially attractive for various applications (Chen & Hoover, 2003; Cleveland et al., 2001; van Heel et al., 2011).

Among the postbiotic produced by *L. plantarum* isolated from Malaysia fermented food, the postbiotic produced by *L. plantarum* I-UL4 (postbiotic I-UL4) was found to have high potential as human health supplement (Tan et al., 2015) and as in-feed additive to replace antibiotic growth promoter for Tilapia fish in aquaculture industry (Anuradha et al., 2013). Meanwhile, the postbiotic produced by *L. plantarum* RS5 (postbiotic RS5) emerged as promising in-feed growth promoter for broilers and laying hens in livestock industry (Thu et al., 2011; Loh et al., 2014). These two postbiotics with antimicrobial activity are important for aquaculture and livestock industries. However, no optimisation study has been conducted to enhance the bacteriocin-inhibitory activity of postbiotic I-UL4 and postbiotic RS5. Just as other metabolic activities, the bacteriocin production by LAB is not naturally optimised for maximum production rates (Sanchez & Demain, 2008). The production of bacteriocin is usually strain-dependent (Carolissen-Mackay et al., 1997) and is affected by both cultural conditions encompassing biochemical environment and physical parameters (Saeed & Salam, 2013). Biochemical environment includes nutritional requirement which is made available through the culture medium (Saeed & Salam, 2013). Meanwhile, physical parameters include cultivation conditions, for instance incubation temperature, initial pH of medium and others (Kumar et al., 2012; Patel et al., 2009; Vijayalakshmi & Rajakumar, 2010). Previous reports also showed that the bacteriocin production by LAB had been successfully enhanced after the optimisation of cultural conditions (Lee et al., 2012; Li et al., 2002; Malheiros et al., 2015). Therefore, it is essential to optimise the cultural conditions encompass medium composition and physical parameters to enhance the bacteriocin-inhibitory activity of postbiotic I-UL4 and postbiotic RS5.

Keeping in view to the complexity of cultural conditions contributing to bacteriocin production, the identification of factors influencing the production is crucial for subsequent optimisation (Delgado et al., 2007). Therefore, preliminary identification of factors influencing production of desired compound was usually performed preceeding the statistical optimisation of concentration of desired compound. The approach of “One factor at a time” was generally employed in

preliminary identification while Response Surface Methodology (RSM) was applied in statistical optimisation (Preetha et al., 2007; Suganthi & Mohanasrinivasan, 2014). RSM is a gathering of statistical techniques for designing experiments, evaluating the effects of factors and determining optimum conditions of factors to achieve a desirable outcome (Lee et al., 2012). This method had been successfully applied for the optimisation of microorganims' metabolite production (He et al., 2004; Venil & Lakshmanaperumalsamy, 2009), conditions of enzymatic hydrolysis (Eslahi et al., 2013), parameters of food preservation (Gupta et al., 2013) and fermentation processes (Peng et al., 2015). Besides, RSM has also been shown as a powerful tool for the optimisation of bacteriocin production by various LAB such as *Lactobacillus sakei* (Malheiros et al., 2015), *Pediococcus acidilactici* (Suganthi & Mohanasrinivasan, 2014), *Lactobacillus brevis* (Lee et al., 2012) and *Streptococcus phocae* (Kanmani et al, 2011). Optimisation study which involved a few factors at a same time will involve a huge number of experiments. Therefore, it is more practical to conduct in small scale cultivation using universal bottle or shake flask, before performing the cultivation with optimised conditions at large scale in bioreactor (Kennedy & Krouse, 1999). In cultivation using stirred tank bioreactor, an optimum agitation speed is important to ensure the uniform suspension of microorganisms in the medium without introducing excessive shear stress to the microorganisms. Moreover, the understanding of agitation speed effect on the cultivation of microorganisms would affect the selection of strategy to scale-up to larger volume of bioreactor. The selection of scale-up strategy is subjected to the process conditions (Stephenie et al., 2007). There are various scale-up strategies including the scale-up based on volumetric coefficient of oxygen transfer (kLa) that is usually applied in aerobic cultivation and scale-up based on constant impeller tip speed which takes mixing and shear stress into consideration (Junker, 2004).

In view of various factors affecting the production of bacteriocin-inhibitory activity of postbiotic in different scales of cultivation, the general objective of this study was to enhance the bacteriocin-inhibitory activity of postbiotics produced by *Lactobacillus plantarum* I-UL4 (postbiotic I-UL4) and *Lactobacillus plantarum* RS5 (postbiotic RS5). The specific objectives of this study were as follow:

(i) To develop an optimised medium formulation for the enhancement of bacteriocin-inhibitory activity of postbiotic I-UL4 and postbiotic RS5 in universal bottle by using combination approaches of "One Factor at a Time" and RSM.
(ii) To optimise the physical parameters for the enhancement of bacteriocin-inhibitory activity of postbiotic I-UL4 and postbiotic RS5 in universal bottle by using RSM.
(iii) To determine the optimum agitation speed for the enhancement of bacteriocin-inhibitory activity of postbiotic I-UL4 and postbiotic RS5 in 6.5 L stirred tank bioreactor.

(iv) To scale-up the production of bacteriocin-inhibitory activity of postbiotic I-UL4 and postbiotic RS5 based on constant impeller tip speed in 30 L stirred tank bioreactor.

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APPENDICES

APPENDIX A

Determination of carbon content in glucose

To determine the carbon content (mM C) of glucose in modified MRS medium, the percentage of carbon (f_1) and conversion of carbon concentration (g/L) into milimolar (mM) concentration of carbon (f_2) were first determined.

(i) Percentage of carbon (C) within glucose molecule ($C_6H_{12}0_6$) (f_1)
= [(Ar C) × (no of C atom)] /MW glucose
= [12 × 6] /180
= 0.40

where Ar C is relative atomic mass of carbon, MW glucose is molecular weight of glucose

(ii) Conversion of carbon concentration (g/L) into milimolar (mM) (f_2)
= [(1/12) ×1000]
= 83.33

Determination of carbon content of glucose in modified MRS medium

Total carbon content of *y* g/L of glucose = [(*y*) × f_1 × f_2] mM C

(Equation 1A)

Table 1A : Total carbon content of different concentrations of glucose in modified MRS medium

Concentration (g/L)	mM C*
0	0
5	166.67
10	333.32
15	499.98
20	666.64
40	1333.28

* The total carbon content is calculated based on Equation 1A

For instance:
Total carbon content of 20 g/L of glucose = 20 × 0.40 × 83.33 = 666.64 mM C

Determination of nitrogen content in KAT yeast extract

(i) Determination of percentage of nitrogen of KAT yeast extract using Kjeldahl method

The percentage of nitrogen of KAT yeast extract was determined by using Kjeltec™ 2400 (FOSS, UK). A mixture of 1.5 g of KAT yeast extract with 0.8 g of catalyst was reacted with concentrated sulphuric acid prior to heating in digestion block. A volume of 10 mL distilled water was added into the reaction mixture when the colour of reaction mixture changed into clear solution. A volume of 10 mL 45 % (w/v) sodium hydroxide was added subsequently into the reaction mixture. The reaction mixture was then distilled in distillation unit with 10 mL 0.5 N boric acid and 2 drops of indicator. The unreacted boric acid was then titrated with 0.05 N H_2S0_4 until neutrality is reached. Same procedure was conducted for blank without inclusion of KAT yeast extract as sample.

The percentage of nitrogen content was calculated based on Equation 2.1A.

$$\% \text{ of N} = \frac{(I_S - I_b) \times N \times 14}{W}$$

Equation 2.1A

where *Is* is volume of H_2S0_4 to titrate boric acid for sample; *Ib* is the volume of H_2S0_4 to titrate boric acid for blank; *N* is normality of H_2SO_4; W is weight of sample.

The percentage of nitrogen of KAT yeast extract (f_1)

$$\% \text{ of N} = \frac{(31.70 - 10.10) \times 0.05 \times 14}{1.50}$$

$$= 10.08 \%$$

$$= 0.1008 (f_1)$$

The percentage of nitrogen was assigned as f_1 for calculation of equation 2.2A

(ii) Conversion of nitrogen concentration (g/L) into milimolar (mM) (f_2)
= [(1/14) ×1000]
= 71.33

Determination of nitrogen content of KAT yeast extract in modified MRS medium

Total nitrogen content of *z* g/L of yeast extract = [(*z*) × f_1 × f_2] mM N

(Equation 2.2A)

Table 2A : Total nitrogen content of different concentrations of KAT yeast extract in modified MRS medium

Concentration (g/L)	mM N*
11.89	85.49
27.84	200.18
36.20	260.28
44.55	320.32

* The total nitrogen content is calculated based on Equation 2.2A

For instance:
Total nitrogen content of 36.20 g/L of KAT yeast extract
= 36.20 × 0.1008 × 71.33
= 260.28 mM N

The carbon to nitrogen ratio is calculated based on Equation 2.3A

$$C/N = \frac{\text{Carbon content (mM C)}}{\text{Nitrogen content (mM N)}}$$

(Equation 2.3A)

BIODATA OF STUDENT

Ooi May Foong was born in Penang, Malaysia in 1985. She completed her primary education by 1997 in SRJK (C) Chung Hwa Confucian (B), secondary education by 2002 and pre-university education by 2004 in Penang Chinese Girls' High School. She finished her bachelor's degree in Biotechnology by 2008 in Faculty of Biotechnology and Biomolecular Sciences, Universiti Putra Malaysia. Later, she pursues her full time of degree of Doctor of Philosophy in Industry Biotechnology under Graduate Research Fellowship (GRF) scheme.

LIST OF PUBLICATIONS

Ooi, M.F., Mazlan, N., *****Foo, H.L., Loh, T.C., Mohamad, R., Abdul Rahim, R., Ariff, 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.

Kareem, K.Y., Loh, T.C., Foo, H.L., Samsudin, A.A., Henny, A., Nazim, R.A., **Ooi, M.F.** (2015). Carcass, meat and bone quality of broiler chickens fed with postbiotic and prebiotic combinations. *International Journal of Probiotics and Prebiotics*, 10 (1): 23-30.

Kareem, K.Y., Foo, H.L., Loh, T.C., **Ooi, M.F.**, Samsudin, A.A. (2014). Inhibitory activity of postbiotic produced by strains of *Lactobacillus plantarum* using reconstituted media supplemented with inulin. *Gut Pathogens*, 6 (23): 1-7.

LIST OF PROCEEDINGS PRESENTED IN CONFERENCES

Ooi, M.F., Foo, H. L., Loh, T. C., Rosfarizan, M., Raha, A. R., and Arbakariya, A. (2015). Comparative study on medium optimisation for enhancement of bacteriocin-inhibitory activity of postbiotic produced by *Lactobacillus plantarum* strains I-UL4 and RS5. Asian Congress on Biotechnology 2015: Biotechnology and bioeconomy for sustainable future. Istana Hotel, Kuala Lumpur, Malaysia, 15-19 November. pp. 308. (Poster Presenter)

Ooi, M.F., Foo, H.L., Loh, T.C., Rosfarizan, M., Raha, A.R. and Arbakariya, A. (2015). Enhancement of bacteriocin-inhibitory activity of postbiotic produced by *Lactobacillus plantarum* RS5 through optimisation of cultural conditions. The 8thAsian Conference on Lactic Acid Bacteria 2015, The Emerald Hotel, Bangkok, Thailand, 8-10 July. pp. 41.(Oral presenter)

Ooi, M. F., Arbakariya, A., Raha, A. R., Rosfarizan, M., Loh, T. C. and Foo, H. L.(2013).Improvement of postbiotic metabolite production by *Lactobacillus plantarum* I-UL4 under optimized cultural condition. International Congress of the Malaysian Society for Microbiology 2013. Langkawi, Malaysia, 12-15 December. pp.20. (Oral presenter)

Ooi, M. F., Foo, H. L., Rosfarizan, M., Loh, T. C., Raha, A. R. and Arbakariya, A. (2014). Comparative evaluation of postbiotic production by *Lactobacillus plantarum* I-UL4 and *Lactobacillus plantarum* RS5 under optimised cultural condition. 1st Asean Regional Conference on Animal Production 2014 and 35th Annual Conference of Malaysian Society of Animal Production (MSAP). Kuching, Sarawak, Malaysia, 4-6 June. pp. 157-158.(Poster presenter)

Ooi, M. F., Arbakariya, A., Rosfarizan, M., Raha, A. R., Loh, T. C. and Foo, H.L. (2011). Medium optimization for bacteriocin production by *Lactobacillus plantarum* I-UL4 using response surface methodology. International Congress of the Malaysian Society for Microbiology 2011. Penang, Malaysia, 8 – 11 December. pp. 445-447. (Poster presenter).

Ooi, M. F., Nadia, S. O. M. O., Norkhalidah, J., Norhazira, S. Y., Arbakariya, A., Rosfarizan, M., Raha, A. R., Loh, T. C. and Foo, H.L. (2009). Effects of pH, temperature and carbon to nitrogen ratio on bacteriocin production by *Lactobacillus plantarum* I-UL4. International Congress of Malaysian Society for Microbiology. Penang, Malaysia, 1 – 4 December. pp. 319. (Poster presenter)

AWARDS AND ACHIEVEMENTS

1. Recipient of "Young Scientist Scholarship" awarded by Yakult Thailand in The 8th Asian Conference on Lactic Acid Bacteria 2015.

2. Best Poster Presenter for 1st Asean Regional Conference on Animal Production 2014 and 35th Annual Conference of Malaysian Society of Animal Production (MSAP).

3. Best Oral Presenter for International Congress of Malaysian Society for Microbiology (ICMSM), 2013

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