UNIVERSITI PUTRA MALAYSIA

PRODUCTION OF VIABLE CELLS OF gdhA DERIVATIVE Pasteurella multocida B:2 FOR USE AS ANIMAL VACCINE

SITI NUR HAZWANI OSLAN

FBSB 2018 14

PRODUCTION OF VIABLE CELLS OF *gdhA* DERIVATIVE P*asteurella multocida* B:2 FOR USE AS ANIMAL VACCINE

By

SITI NUR HAZWANI OSLAN

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

November 2017

.

COPYRIGHT

Dedicated with love to:

my parents

Oslan Abdul Ghani
Noor Hayati Mohd. Zain

my siblings

Mohd. Lukhman
Siti Nurbaya
Muhammad Faris Firdaus
Muhammad Bazli Fahmi
Muhammad Yatimi Hakim

my family

all my friends

Who supported me all these years

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

PRODUCTION OF VIABLE CELLS OF *gdhA* DERIVATIVE *Pasteurella multocida* B:2 FOR USE AS ANIMAL VACCINE

By

SITI NUR HAZWANI OSLAN

November 2017

Chairman : Arbakariya Ariff, PhD
Faculty : Biotechnology and Biomolecular Sciences

The attenuated strain of *gdhA* derivative *Pasteurella multocida* B:2 (mutant) has demonstrated its efficacy as a live vaccine to control haemorrhagic septicaemia (HS) disease in cattle and buffaloes. However, the commercial application of this vaccine to control HS still faces some limitations such as cost effectiveness of large scale cultivation process, low cell viability and productivity, and unsuitable commercial formulation in order to sustain the cell viability of the bacterial cells in live vaccine. The main objective of this study are to develop the bioprocessing method to increase viability in terms of productivity of *gdhA* derivative *P. multocida* B:2 with minimum production cost and to develop essential formulation in powderised form with high bacterial cell survival rate for subsequent use as animal live cell vaccine.

The growth medium with the addition of histidine at a concentration of 20 mM greatly improved the cell viability of *P. multocida* B:2 mutant in cultivation using YDB as basal medium. During batch cultivation of this mutant, ammonium accumulated in the culture greatly inhibited the growth that reduced the final cell concentration and yield. The possibility of using cation-exchange resin for *in situ* removal of ammonium accumulated in the culture for the improvement of the cultivation of this mutant was investigated in this study. The ability of cation-exchange resins, which included Amberlite IRC-86, Amberlite IR120 H, and Dowex DRG8 H, to selectively adsorbed ammonium was first investigated. Amberlite IRC-86, which has capability on ammonium adsorption with Q_{max} value of 0.86 g/g as determined using sorption isotherm experiments, was chosen for *in situ* removal of ammonium in the culture of *P. multocida* B:2 mutant.

In shake flask culture, the 10 g/L of Amberlite IRC-86 improved the final viable cell concentration (7.2 x 10^{10} cfu/mL) by about 11 time higher than that obtained in cultivation without resin (6.6 x 10^{9} cfu/mL). In cultivation using 2 L stirred tank bioreactor with internal column containing Amberlite IRC-86, growth of the mutant was enhanced by 10% as compared to the cultivation without resin, agitated at 500 rpm. The final viable cell obtained in stirred tank bioreactor (1.05 x 10^{11} cfu/mL) was significantly higher than that obtained in shake flask culture. The use of trehalose as protective agent in freeze drying of *P. multocida* B:2 mutant cells greatly sustained the cell viability (93-95%). During storage at -30◦C and 4◦C, the freeze dried cells using trehalose was also able to maintain the viability (10^{6}-10^{8}cfu/mL) up to 6 and 12 month, respectively. The stored viable cells was still effective to be used as attenuated vaccine of *P. multocida* B:2.

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

PENGHASILAN BILANGAN SEL MUTAN *gdhA Pasteurella multocida* B:2 UNTUK KEGUNAAN VAKSIN HAIWAN

Oleh

SITI NUR HAZWANI OSLAN

November 2017

Pengerusi : Arbakariya Ariff, PhD
Fakulti : Bioteknologi dan Sains Biomolekul

Strain *gdhA* terbitan *Pasteurella multocida* B:2 mutan telah terbukti keberkesanannya sebagai vaksin untuk mengawal penyakit septisemia berdarah (HS) kepada lembu dan kerbau. Walau bagaimanapun, aplikasi pengkomersilan vaksin untuk mengawal HS masih menghadapi beberapa batasan seperti pemprosesan pada skala besar pada kos yang berptutan, bilangan sel dan produktiviti yang rendah, dan formula untuk pengkomersilan yang tidak sesuai untuk mengekalkan bilangan sel bakteria dalam vaksin hidup. Objektif utama kajian ini adalah untuk membangunkan satu kaedah biopemprosesan bagi meningkatkan bilangan sel yang tinggi dari segi produktiviti pada vaksin mutant bacteria dengan kos yang minimum dan untuk memformulasikan sel bakteria secara optimum dengan kadar kelangsungan hidup yang tinggi untuk pengkomersilan vaksin hidup haiwan.

Pertumbuhan bilangan sel vaksin mutan adalah bertambah baik di dalam media basal YDB dengan tambahan histidine pada kepekatan 20mm. Semasa pertumbuhan mutan ini, ammonium telah terkumpul dalam sel dan menghalang pertumbuhan dan penghasilan sel. Dalam kajian ini, penggunaan resin pertukaran kation dalam penyingkiran ammonium terkumpul di dalam sel melalui *in situ* untuk memperbaiki pertumbuhan mutan ini telah dikaji. Resin kation yang telah diuji, termasuk Amberlite IRC-86, Amberlite IR120 H, dan Dowex DRG8 H, telah dipilih untuk menyerap ammonium diuji menggunakan eksperimen penyerapan isoterma. Di dalam ekesperimen, Amberlite IRC-86 yang mempunyai keupayaan di dalam penyerapan ammonium dengan Q_{max} 0.86 g/g melalui kaedah sorption isoterma, telah dipilih dalam penyingkiran ammonium pada *P. multocida* B: 2 mutan.

Di dalam kelalang kon, penggunaan 10 g/L Amberlite IRC-86 menyebabkan kepekatan akhir sel bertambah (7.2 x 10^{10} cfu/mL) sebanyak 11 kali lebih tinggi daripada kultur tanpa resin (6.6 x 10^{9} cfu/mL). Dalam pertumbuhan kultur menggunakan 2L bioreaktor dilekatkan dengan kolum yang mengandungi Amberlite IRC-86, pertumbuhan mutan telah memingkat sebanyak 10% berbanding dengan pertumbuhan tanpa resin pada 500 rpm. Bilangan sel mutan yang diperolehi dalam bioreaktor adalah (1.05 x 10^{11} cfu/mL) adalah jauh lebih tinggi daripada yang diperolehi dalam kelalang kon. Penggunaan trehalos sebagai agen pelindung menunjukkan kadar bilangan sel yang tinggi (93-95%) semasa proses pengeringan-beku dan penyimpanan pada suhu -30°C dan 4°C, masih dapat mengekalkan bilangan sel sehingga (10^{6}- 10^{8} cfu/mL) untuk 6 ke 12 bulan penyimpanan dan masih boleh digunalkan sebagai vaksin mutant *P. multocida* B:2.

ACKNOWLEDGEMENTS

Firstly, I want to express my appreciation and gratitude to my supervisor, Prof. Dr. Arbakariya ariff for his guidance, support and supervision. The appreciation also goes to my co-supervisors, Prof. Dr. Mohd Zamri Saad and Dr. Murni Halim for their ideas and knowledge. I am particularly indebted to Dr. Tan Joo Shun who helps me to with the experiments analysis. I am grateful to my sponsors Ministry of High Education Malaysia (MyBrain15) and Universiti Putra Malaysia for the scholarships.

A special gratitude to lecturers and staffs at Biomanufacturing and Bioprocessing Research Centre Dr. Mohd Shamzi Mohamed, Dr. Fadzlie Wong Faizal Wong, Mr. Mohd. Rizal Kapri, Mrs. Liyana Ithnin, Mr. Sobri Mohd Akhir, and Mrs. Zainon Sidik. Not forgotten the technicians and post-graduate colleagues; Mrs. Roslina, Mrs. Farrah, Ms. Bainun, Mrs. Hamizah, Mrs. Amalina, Mrs. Asmaa, Ms. Subhashini, Ms. Hayatun, and Mrs. Puvaneswary, Ms. Raihan, Ms. Majdiah, and Mrs. Munirah who gave me their hands when I am in need. I would also like to extend my appreciation to Histopathology Laboratory staffs, Dr. Mazlina Mazlan, Dr. Mohd Firdaus Nawi, Dr. Shaqinah Nasruddin, Dr. Adzarina Nordi, Dr. Annas Salleh, Mrs. Jamilah Jahari, Mrs. Latifah Mohd Hanan, and Ms. Zainatulaishah Abdul Manap for their kind help.

Finally, special thanks to my beloved parents Hj. Oslan Abd Ghani and Hjh. Noor Hayati Mohd Zain, my brothers and sister; Mr. Mohd Lukhman, Dr. Hjh Siti Nurbaya, Mr. Mohd Faris Firdaus, Mr. Mohd Bazli Fahmi, and Mr. Mohd Yatimi Hakim, to my sister in law Mrs. Norazila Mohd, my nephew Mohd. Norman Danial and niece Nor Zarra Izzati for their continuous supports. Finally, special thanks to my parents for their patience and still being there when I need them. I need to thank all those who have directly and indirectly concerns and encouragements given by all during the accomplishment my study in UPM. Thank you very much from the bottom of my heart.

ALHAMDULILLAH

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

Arbakariya Ariff, PhD
Professor
Faculty of Biotechnology and Biomolecular Sciences
Universiti Putra Malaysia
(Chairman)

Mohd Zamri Saad, PhD
Professor
Faculty of Veterinary Medicine
Universiti Putra Malaysia
(Member)

Murni Halim, PhD
Senior Lecturer
Faculty of Biotechnology and Biomolecular Sciences
Universiti Putra Malaysia
(Member)

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

Date:

Declaration by graduate student

I hereby confirm that:

- this thesis is my original work;
- quotations, illustrations and citations have been duly referenced;
- this thesis has not been submitted previously or concurrently for any other degree at any other institutions;
- intellectual property from the thesis and copyright of thesis are fully-owned by Universiti Putra Malaysia, as according to the Universiti Putra Malaysia (Research) Rules 2012;
- written permission must be obtained from supervisor and the office of Deputy Vice-Chancellor (Research and Innovation) before thesis is published (in the form of written, printed or in electronic form) including books, journals, modules, proceedings, popular writings, seminar papers, manuscripts, posters, reports, lecture notes, learning modules or any other materials as stated in the Universiti Putra Malaysia (Research) Rules 2012;
- there is no plagiarism or data falsification/fabrication in the thesis, and scholarly integrity is upheld as according to the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) and the Universiti Putra Malaysia (Research) Rules 2012. The thesis has undergone plagiarism detection software.

Signature: _____Date: _____

Name and Matric No.: _____

Declaration by Members of Supervisory Committee

This is to confirm that:

- the research conducted and the writing of this thesis was under our supervision;
- supervision responsibilities as stated in the Universiti Putra Malaysia (Graduate Studies) Rules 2003 (Revision 2012-2013) are adhered to.

Signature: _____
Name of Chairman
of Supervisory
Committee _____

Signature: _____
Name of Member of
Supervisory
Committee: _____

Signature: _____
Name of Member of
Supervisory
Committee: _____

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF APPENDICES

LIST OF ABBREVIATIONS

ANOVA	Analysis of variance
BHI	Brain-heart infusion
Bp	Base pairs
ºC	Degree celcius
%	Percentage
cfu	Colony forming unit
DCW	Dry cell weight
DOE	Design of Experiments
DNA	Deoxyribonucleic acid
Dntp	Deoxyribonucleotides acid
g	Gram
gdhA	Glutamate dehydrogenase
HS	Haemorrhagic septicaemia
ISPR	*in situ* product removal
K_d	Dissociation rate
K_La	Oxygen transfer rate
L	Liter
mL	Mililiter
mM	Milimolar
PBD	Plackett-Burman Design
PBS	phosphate buffered saline
PCR	Polymerase chain reaction
Pr	Productivity
Q_{max}	Maximum adsorption capacity
RSM	Response Surface Methodology
RM	Ringgit Malaysia
SEM	Scanning electron micrograph
TB	terrific broth
Tg	Transition temperature
w/v	Weight per volume
µL	Microlitre
μ_{max}	Maximum of specific growth rate
X_{max}	Maximum of cell density
YDB	Yeast dextrose broth

CHAPTER 1

INTRODUCTION

Haemorrhagic septicaemia (HS) is an acute septicaemic contagious bacterial disease affecting primarily cattle and buffaloes (Khan et al., 2011) with high mortality rate in infected animals (Rafidah et al., 2010; Sarah, 2007). In Asia, this disease is caused by a specific serotype of *Pasteurella multocida* designated as B:2 and E:2 in Africa (Bain et al., 1982; De Alwis, 1999; Tatabaie et al., 2007). The disease is per-acute, having a short clinical course involving severe depression, pyrexia, submandibular edema and dyspnea, followed by recumbency and death (Tatabaie et al., 2007). Treatment or prevention of HS has been used to control the spread of HS. The killed whole cells vaccines are commonly used in Malaysia (Abdullah et al., 2013). Besides that, oil-adjuvant vaccines are quite unpopular among the field users because of their high viscosity, provide only short-term immunity and swelling at the site of inoculation (Tatabaie et al., 2007; Abdullah et al., 2013).

In molecular approach method, the wild type *gdhA* gene of *P. multocida* B:2 had been modified with kanamycin inserted into the *gdhA* gene to become a live attenuated vaccine, known as live attenuated *gdhA* derivative *P. multocida* B:2 (mutant) (Sarah et al., 2006). The use of mutant *P. multocida* B:2 in the field vaccination could increase herd immunity antibody for 8 to 10 months before a booster dose was required (Rafidah et al., 2011).

In the vaccination of HS using mutant *P. multocida* B:2 vaccine, the effective concentration of viable cell should be ranged from 10^5 to 10^7 (cfu/mL) (Rafidah et al. 2011). Based on the previous study using modified basal medium, the highest viable cell of this mutant at the end of cultivation was only 10^8 (cfu/mL) (Oslan, 2013). For commercial application, live cells may be formulated in powderised form to enable high stability during storage and ease of handling. Since mutant *P. multocida* B:2 is not thermophilic microorganism, freeze drying could be considered as the appropriated method to formulate the final vaccine product containing viable cells in powderised form. It is well known that significance reduction of the percentage of cell viability may occurs during freeze drying. Preservation of live attenuated mutant for use as vaccine mutant is important to retain the high viability of cells during long term storage, prior to field use (Morgan et al., 2006). Thus, improvement of the final viable cell number of mutant *P. multocida* B:2 at the end of the cultivation is required to meet the final viable cell number in the vaccine product for commercial use. Commercial formulation of vaccine product containing live cells in powderised form, that can be achieved via freeze drying techniques gives some advantages which include long term preservation with good stability, convenience in handling, storage and marketing (Carvalho et al., 2004) as well as accuracy in dosage. Generally, medium composition greatly influenced the

growth of the microorganism not only in term of cell number but also the cell viability. In order to get high cell number and viability, the optimization of medium composition shall be performed. In addition, Plackett-Burman design (PBD) may be applied in order to validate the tests, and to evaluate the influence of various different types of supplement in the medium formulation.

Ammonium has been detected as a by-product in growth of mutant *P. multocida* B:2, which subsequently influenced the culture pH and inhibited growth (Oslan, 2013). Ammonium accumulated in the culture may be removed by *in situ* addition of cation-exchange resin, which directly absorps the ammonium to their surface. The removal of ammonium may enhance growth of mutant *P. multocida* B:2, not only in term of final cell number but also the percentage of viability. Resin as an adsorbent have been used successfully in extractive fermentation to reduce end-product inhibition and improve the overall process efficiency (Sang et al., 2007; Tan et al., 2011; Tan et al., 2013). It is well known that the accumulation of cetate in the culture of recombinant *E. coli* greatly inhibited the growth nd expression of the target protein. *In situ* adsorption of acetate by anion-exchange resins in *E. coli* culture for producing periplasmic human interferon-alpha2b (PrIFN-α2b) was previously studied (Tan et al., 2011). The adsorption of target product/by-product by ion-exchange resin in extractive fermentation can be carried out either within a bioreactor or by circulating a fermentation broth through an external column that contains the adsorbent. Additionally, in the former system, the resins can either be trapped in a compartment housed inside the bioreactor or dispersed freely in the culture (Tan et al., 2013).

This study was conducted to develop high performance cultivation method of *gdhA* derivative *P. multocida* B:2 with high final cell number and viability. The selection of appropriate basal medium for the cultivation of *gdhA* derivative *P. multocida* B:2 was initially performed. The effect of the supplementation of various nutrients such as vitamins and amino acids on growth and viability of the bacterium was aslo evaluated and then optimized to obtain the maximum performance. The use of cation exchange resin for the removal of ammonium accumulated in the culture to reduce the inhibition effect on growth was first evaluated in shake flask culture and then transferred into 2 L stirred tank bioreactor with internal column for continuous removal of ammonium during the cultivation. The parameters and protective agents for the freeze drying of *gdhA* derivative *P. multocida* B:2, which gave the highest cell viability, were also searched.

The objectives of the present study were:

1. To determine the effect of basal medium, amino acids and vitamins on growth performance of *gdhA* derivative *P. multocida* B:2.
2. To improve the viability of *gdhA* derivative *P. multocida* B:2 during the cultivation by introducing *in-situ* removal of ammonium ions using selected ion exchange resins.

3. To develop an integrated system comprising 2 L stirred tank bioreactor and cation exchange column for continuous removal of ammonium during *gdhA* derivative *P. multocida* B:2 cultivation.
4. To investigate and propose freeze drying parameters suitable to maintain high cell viability of *gdhA* derivative of *P. multocida* B:2 after freeze drying.

Based on the objectives of the study, the hypotheses are:

1. Cultivation performance of gdhA derivative *P. multocida* B:2 with high cell viability could be achieved in optimum amino acid concentration in basal medium.
2. *In situ* addition of the selected ionic exchange resins may be used for the removal of the accumulated ammonium in the culture, which in turn, may improve growth and viability of mutant *P. multocida* B:2 cell.
3. Freeze drying technique with suitable type and concentration of protective and bulking agent could be used to prepare mutant *P. multocida* B:2 formulation in powdered form with maintain viable cells for application as commercial vaccine.

REFERENCES

Abadias, M., Benabarre, A., Teixido, N., Usall, J. and Vinas, I. (2001). Effect of freeze drying and protectants on viability of the biocontrol yeast *Candida sake*. *International Journal of Food Microbiology* 65:173–182.

Abbas, C.A. and Sibirny, A.A. (2011). Genetic control of biosynthesis and transport of riboflavin and flavin nucleotides and construction of robust biotechnological producers. *Microbiology and Molecular Biology Reviews* 75(2):321-360.

Abdelwahed, W., Degobert, G., Stainmesse, S. and Fessi, H. (2006). Freeze-drying of nanoparticles: Formulation, process and storage considerations *Advanced Drug Delivery Reviews* 58:1688–1713.

Abdullah, F.F.J., Abdinasir, Y. O., Lawan, A., Zunita, Z., Rasedee, A., Zamri-Saad, M. and Saharee, A.A. (2013). Haematological and biochemical aterations in calves following infection with *Pasteurella multocida* Type B: 2, Bacterial lipopolysaccharide and outer membrane protein immunogens (OMP). *Asian Journal of Animal and Veterinary Advances* 8:806-813.

Abubakar, M.S and Zamri-Saad, M. (2011). Clinico-pathological changes in buffalo calves following oral exposure to *Pasteurella multocida* B:2. *Basic and Applied Pathology* 4:130-135.

Adachi, K., Kawana, K., Yokoyama, T., Fujii, T., Tomio, A., Miura, S., Tomio, K., Kojima, S., Oda, K. and Sewaki, T. (2010). Oral immunization with a *Lactobacillus casei* vaccine expressing human papillomavirus (HPV) type 16 E7 is an effective strategy to induce mucosal cytotoxic lymphocytes against HPV16 E7. *Vaccine* 28:2810-2817.

Aebischer, T., Bumann, D., Epple, H.J., Metzger, W., Schneider, T., Cherepnev, G., Walduck, A.K., Kunkel, D., Moos, V. and Loddenkemper, C. (2008). Correlation of T cell response and bacterial clearance in human volunteers challenged with *Helicobacter pylori* revealed by randomised controlled vaccination with Ty21a-based *Salmonella* vaccines. *Gut* 57:1065-1072.

Agnieszka, C., Andrzej, L. (2011). Freeze-Drying – Application in food processing and biotechnology – A review. *Polish Journal Of Food And Nutrition Sciences* 61(3):165-171.

Aguilera, J.M. and Karel, M. (1997). Preservation of biological materials under desiccation. *Critical Reviews in Food Science and Nutrition* 37(3):287-309.

Ainaa, A.K., Shaiful, A. S.,Beh, B.K., Norhazniza, A. and Kamariah, L. (2016). The effect of different freeze dried formulations on the viability of lactic acid bacteria In lactose-free yogurt production. *Australian Journal of Basic and Applied Sciences* 10(17):164-171.

Alexandratos, S.D. (2009). Ion exchange resins. A retrospective from Industrial and engineering chemistry research. *Industrial and Engineering Chemistry Research* 48:388-398.

Alshameri, A., Ibrahim, A., Assabri, A.M., Lei, X., Wang, H. and Yan, C. (2014). The investigation into the ammonium removal performance of Yemeni natural zeolite: Modification, ion exchange mechanism, and thermodynamics, *Powder Technology* 258: 20-31.

Annas, S., Zamri-Saad M, Jesse, F.F.A and Zunita, Z. (2014). New sites of localisation of *Pasteurella multocida* B:2 in buffalo surviving experimental haemorrhagic septicaemia. *BMC Veterinary Research* 2014:10:88**.**

Bae, J., Yoo, R., Lee, E. and McCarty, P. L. (2013). Two-stage anaerobic fluidized-bed membrane bioreactor treatment of settled domestic wastewater. *Water Science and Technology* 68(2):394-399.

Baez, A. and Shiloach, J. (2014). Effect of elevated oxygen concentration on bacteria, yeasts, and cells propagated for production of biological compounds. *Microbial Cell Factories* 13:181.

Bain, R.V.S., De Alwis, M.C.L., Carter, G.R. and Gupta, B.K. (1982). Haemorhagic septicemia. FAO Animal Production and Health Paper No. 33. Food and Agriculture Organisation of the United Nations, Rome.

Bandyopadhyay, B., Humphrey, A. E., Taguchi, H. and Rao, G. (2009). Dynamic measurement of the volumetric oxygen transfer coefficient in fermentation systems. *Biotechnology and Bioengineering* 104:841-853.

Barry, E.M., Wang, J., Wu, T., Davis, T. and Levine, M.M. (2006). Immunogenicity of multivalent *Shigella*-ETEC candidate vaccine strains in a guinea pig model. *Vaccine* 24:3727-3734.

Baumann, K., Carnicer, M., Dragosits, M., Graf, A.B., Stadlmann, J., Jouhten, P., Maaheimo, H., Gasser, B., Albiol, J. and Mattanovich, D. (2010). A multi-level study of recombinant *Pichia pastoris* in different oxygen conditions. *BMC Systems Biology* 4(1):141.

Bazrafshan E., Amirian, P., Mahvi, A.H. and Ansari,-M.A. (2016). application of adsorption process for phenolic compounds removal from aqueous environments: a systematic review. *Global Nest Journal* 18(1):146-163.

Behboudi-Jobbehdar, S., Soukoulis, C., Yonekura, L. and Fisk, I. (2013). Optimization of spray-drying process conditions for the production of maximally viable microencapsulated *L. acidophilus* NCIMB 701748. *Drying Technology: An International Journal* 31:1274- 1283.

Bender, R.A. (2012). Regulation of the histidine utilization (hut) system in bacteria. *Microbiology and Molecular Biology Reviews* 76(3):565-584.

Benkirane, A. and De Alwis, M.C.L. (2002). Haemorrhagic septicaemia, its significance, prevention and control in Asia. *Veterinární medicína Journal* 47: (8):234–240.

Berny, J.F. and Hennebert, G.L. (1991). Viability and stability of yeast cells and filamentous fungus spores during freeze-drying: Effects of protectants and cooling rates. *Mycologia* 83:805–815.

Bisht, K.S., Salim, N., Hassan, L., Zunita, Z., Kamarudin, M.I. and Saharee, A.A. (2006). Temporal Patterns of haemorrhagic septicemia mortalities ion cattle and buffaloes in Peninsular Malaysia, 1993-2003. *Journal of Animal and Veterinary Advances* 5(8):651-658.

Boyce, J. D., and Adler, B. (2001). A capsular *Pasteurella multocida* B: 2 can stimulate protective immunity against pasteurellosis. *Infection and Immunity* 69(3):1943-1946.

Bozoglu, T.F., Ozilgen, M. and Bakir, U. (1987). Survival kinetics of lactic acid starter cultures during and after freeze-drying. *Enzyme and Microbial Technology* 9:531–537.

Brummelhuis, H.G.J. (1980). Methods of Plasma Protein Fractionation. Curling, J.M., Ed.; Academic Press: London, pp. 117-128.

Bumann, D., Behre, C., Behre, K., Herz, S., Gewecke, B., Gessner, J.E., von Specht, B.U. and Baumann, U. (2010). Systemic, nasal and oral live vaccines against *Pseudomonas aeruginosa*: a clinical trial of immunogenicity in lower airways of human volunteers. *Vaccine* 28:707-713.

Carter, G.R. (1984). Serotyping of *Pasteurella multocida*. In Methods in Microbiology. T. Bergman (ed.), Academic Press, London, p. 16.

Carvalho, A.S., Silva, J., Ho, P., Teixeira, P., Malcata, F.X. and Gibbs, P. (2002) Survival of freeze-dried Lactobacillus plantarum and Lactobacillus rhamnosus during storage in the presence of protectants. *Biotechnology Letters* 24:1587–1591.

Carvalho, A.S., Silva, J., Ho, P., Teixeira, P., Malcata, F.X. and Gibbs, P. (2004). Relevant factors for the preparation of freeze-dried lactic acid bacteria. *International Dairy Journal* 14:835–847.

Carvalho, A. S., Silva, J., Ho, P., Teixeira, P., Malcata, F. X. and Gibbs, P. (2004). Effects of various sugars added to growth and drying media upon thermotolerance and survival throughout storage of freeze-dried *Lactobacillus delbrueckii* ssp. *bulgaricus. Biotechnology Progress* 20:248–254.

Castro, H. P., Teixeira, P. M. and Kirby, R. (1996). Changes in the membrane of *Lactobacillus bulgaricus* during storage following freeze-drying. *Biotechnology Letters* 18:99–104.

Chandrasekaran, S., Yeap, P.C. and Saad, R. (1987). The effect of storage conditions on the stability and potency of haemorrhagic septicaemia oil adjuvant vaccine. *Kajian Veterinar* 19:71-75.

Charoenrein, S. and Owcharoen, K. (2016). Effect of freezing rates and freeze-thaw cycles on the texture, microstructure and pectic substances of mango. *International Food Research Journal* 23(2):613-620.

Chassagne-Berces, S., Fonseca, F., Citeau, M. and Marin, M. (2010). Freezing protocol effect on quality properties of fruit tissue according to the fruit, the variety and the stage of maturity. *Food Science and Technology* 43(9):1441-1449.

Chen, H., Lin, C. and Chen, M. (2006). The effects of freeze drying and rehydration on survival of microorganisms in kefir. *Asian Australasian Journal of Animal Sciences* 19(1):126-130).

Chen, J.P., Chua, M.L. and Zhang, B.P. (2002). Effects of competitive ions, humic acid, and pH on removal of ammonium and phosphorous from the synthetic industrial effluent by ion exchange resins. *Waste Management* 22:711-719.

Chen, X., Cen, P. and Chen, J. (2005). Enhanced production of human epidermal growth factor by a recombinant *Escherichia coli* integrated with *in situ* exchange of acetic acid by macroporous ion-exchange resin. *Journal of Bioscience and Bioengineering* 100(5):579-581.

Chen, Y.N., Liu, C.H., Nie, J.X., Luo, X.P. and Wang, D.S. (2013). Chemical precipitation and biosorption treating land lleachate to remove ammonium–nitrogen, *Clean Technology Environment Policy* 15:395–399.

Ciurzyńska, A. and Lenart, A. (2010). Rehydration and sorption properties of osmotically prepared freeze-dried strawberries. *Journal of Food Engineering* 97:267–274.

Commichau, F.M., Forchhammer, K. and Stu¨lke. J. (2006). Regulatory links between carbon and nitrogen metabolism. *Current Opinion in Microbiology* 9:167–172.

Commichau, F.M., Gunka,K., Landmann, J.J. and Stu¨lke, J. (2008). Glutamate metabolism in *Bacillus subtilis*: Gene expression and enzyme activities evolved to avoid futile cycles and to allow rapid responses to perturbations of the System. *Journal of Bacteriology* 190(10):3557–3564.

Confer, A.W. (1993). Immunogens of *Pasteurella. Veterinary Microbiology* 37(3–4):353-368.

Cooney, E.L., Booker, N.A., Shallcross, D.C. and Stevens, G.W. (1999). Ammonia removal from wastewaters using natural Australian zeolite. II. Pilot-scale study using continuous packed column process. *Separation Science and Technology* 34(14): 2741-2760.

Corbanie, E.A. Remon, J.P., Van Reeth, K., Landman, W.J.M. Van Eck, J.H.H. and Vervaet, C. (2007). Spray drying of an attenuated live Newcastle disease vaccine virus intended for respiratory mass vaccination of poultry. *Vaccine* 25:8306–8317.

Corbel, M.J. (1996). Reasons for instability of bacterial vaccines. Developments in Biological Standardization 87:113-24.

Corcoran, B.M., Ross, R.P., Fitzgerald, G.F. and Stanton, C. (2004). Comparative survival of probiotic *Lactobacilli* spray-dried in the presence of prebiotic substances. *Journal of Applied Microbiology* 96:1024–1039.

Costa, E., Usall, J., Teixido, N., Garcia, N. and Vinas, I. (2000). Effect of protective agents, rehydration media and initial cell concentration on viability of *Pantoea agglomerans* strain CPA-2 subjected to freeze-drying. *Journal of Applied Microbiology* 89:793–800.

Crowe, J.H., Crowe, L.M., Oliver, A.E., Tsvekova, N., Wolkers, W. and Tablin, F. (2001). The trehalose myth revisited: introduction to a symposium on stabilization of cells in the dry state. *Cryobiology* 43:89-105.

Czlircin, E., Mtszhros-Kis, A., Domokos, E. and Papp, J. (1988). Separation of ammonia from wastewater using clinoptilolite as ion exchanger. *Nuclear and Chemical Waste Management* 8:107–113.

Dashty, M. (2013). A quick look at biochemistry: carbohydrate metabolism. *Clinical Biochemistry* 46(15):1339-1352.

Davies, R.L., MacCorquodale, R. and Reilly, S. (2004). Characterisation of bovine strains of *Pasteurella multocida* and comparison with isolates of avian,ovine and pocine origin. *Veterinary Microbiology* 99:145-158.

David, M., Dexiang, C., and Debra, K. (2012). Spray drying and vaccine stabilization. *Expert Review of Vaccines* 11(10):1211-1219.

De Alwis, M.C.L. (1992). Haemorrhagic septicaemia - A general review. *British Veterinary Journal* 148:99–112.

De Alwis, M.C.L. (1993). Sri Lanka. In: Patten, B.E., Spencer, T.L., Johnson, R.B., Hoffmann, D. and Lehane, L., (Eds.), Pasteurellosis in Production Animals. Australian Centre for International Agriculture Research. Proceedings, 43:243-245.

De Alwis M.C.L: (1999). Haemorrhagic septicaemia, Australian Centre for International Agricultural Research (ACIAR) Monograph 57. Canberra, Australia.

Demir, A., Günay, A. and Debik, E. (2002). Ammonium removal from aqueous solution by ion-exchange using packed bed natural zeolite. *Water SA* 28(3):329-336.

Detmer, A. and Glenting, J. (2006). Live bacterial vaccines – a review and identification of potential hazards. *Microbial Cell Factories* 5:23.

Dhawan. S. and Kuhad, R.C. (2002). Effect of amino acids and vitamins on laccase production by the bird's nest fungus *Cyathus bulleri*. *Bioresource Technology* 84(1):35-38.

Diban, N., Aguayo, A. T., Bilbao, J., Urtiaga, A., and Ortiz, I. (2013). Membrane Reactors for *in Situ* Water Removal: A Review of Applications. *Industrial and Engineering Chemistry* 52(31):10342–10354.

Dietrich, S., Ana-Paula, M.D.S, and Isabella, L. B. (2016). Optimization of a freeze-drying process for the biocontrol agent *Pseudomonas* spp. and its influence on viability, storability and efficacy. *Biological Control* 94:74–81.

Ding, Y. and Sartaj, M. (2016). Optimization of ammonia removal by ion-exchange resin using response surface methodology. *International Journal of Environmental Science* and *Technology* 13:985–994.

Dionysios, A., Antonopoulos, R.I., Aminov, P.A., Duncan, B.A., White,R.I. and Mackie (2003). Characterization of the gene encoding glutamate dehydrogenase (gdhA) from the ruminal bacterium *Ruminococcus flavefaciens* FD-1. *Archives of Microbiology* 179:184–190.

Doran, P.M. Bioprocess Engineering Principles. Elsevier, 1995.

Dougan, G., Maskell, D., Pickard, D. and Hormaechce, C. (1987). Isolation of stable *aroA* mutants of *Salmonella typhi* Ty2: properties and preliminary characterisation in mice. *Molecular and General Genetics* 207:402-405.

Dougan, G., Maskell, D., O'Callaghan, D. , Chatfield, S., Charles, I. and Hormaeche, C. (1988). Oral vaccination. *Antonie van Leeuwenhoek* 54:447-451.

Du Preez, J.C., Van Rensburg, E. and Stephanus, G.K. (2008). Kinetics of growth and leukotoxin production by *Mannheimia haemolytica* in continuous culture. *Journal of Industrial Microbiology and Biotechnology* 35(6):611–618.

El Ouardi, M., Qourzal, S., Alahiane, S., Assabbane, A. and Douch, J. (2015). Effective removal of nitrates ions from aqueous solution using new clay as potential low-cost adsorbent. *Journal of Encapsulation and Adsorption Sciences* 5:178-190.

Elsayed, A.E. Hoda, G.O. and Hesham, A.E. (2015). Development of fed-batch cultivation strategy for efficient oxytetracycline production by *Streptomyces rimosus* at semi-industrial scale. *Brazilian Archives of Biology and Technology* 58(5):676-685.

El-Sheekh, M.M., Khairy, H.M., Gheda, S.F. and El-Shenody, R.A. (2016). Application of Plackett–Burman design for the high production of some valuable metabolites in marine alga *Nannochloropsis oculata. Egyptian Journal of Aquatic Research* 42:57–64.

Fabian, M.C., Katrin, G., Jens, J.L., and Jorg, S. (2008). Glutamate Metabolism in *Bacillus subtilis*: Gene expression and enzyme activities evolved to avoid futile cycles and to allow rapid responses to perturbations of the system. *Bacteriology* 3557–3564.

Faccin, D.J.L., Rech, R., Secchi, A. R., Cardozo, N. S. M. and Ayub, M. A. Z. (2013). Influence of oxygen transfer rate on the accumulation of poly (3-hydroxybutyrate) by *Bacillus megateriu*. *Process Biochemistry* 48:420–425.

Farrell, P., Sun, J. Gao, M., Sun, H., Pattara, B., Zeiser, A. and D'Amore, T. (2012). Development of a scaled-down aerobic fermentation model for scale-up in recombinant protein vaccine manufacturing. *Vaccine.* 30(38):5695-5698.

Feng, Y., Wang, S., Luo, F., Ruan, Y., Kang, L., Xiang, X., Chao, T., Peng, G., Zhu, C. and Mu, Y. (2008). A novel recombinant bacterial vaccine strain expressing dual viral antigens induces multiple immune responses to the Gag and gp120 proteins of HIV-1 in immunized mice. *Antiviral Research* 80:272-279.

Ferber, D.M., Khambaty, F., Ely, B. (1988). Utilization of histidine by *Caulobacter crescentus. Microbiology* 134 (8):2149-2154.

Fonseca, F., Passot, S., Cunin, O. and Marin, M. (2004) Collapse temperature of freeze dried *Lactobacillus bulgaricus* suspensions and protective media. *Biotechnology Progress* 20:229-238.

Food and Agricultural Organisation (FAO), (2004). Agriculture data FAOSTAT.

Fernández, A., Saguir, F. and Manca de Nadra, M. (2003). Effect of amino acids and peptides on growth of *Pediococcus pentosaceus* from wine. *Latin American applied research* 33(3):225-229.

Feunou, P.F., Kammoun, H., Debrie, A.S., Mielcarek, N. and Locht, C. (2010). Long-term immunity against pertussis induced by a single nasal administration of live attenuated *B. pertussis* BPZE1. *Vaccine* 28(43):7047-7053.

Fonseca, F., Passot, S., Cunin, O. and Marin, M. (2004). Collapse temperature of freeze-dried *Lactobacillus bulgaricus* suspensions and protective media. *Biotechnology Progress* 20:229-238.

Gailliot, F.P., Gleason, C., Wilson, J.J. and Zwarick, J. (1990). Fluidized bed adsorption for whole broth extraction. *Biotechnology Progress* 6:370.

Gao, Q., Liu, F.,Zhang, T., Zhang, J., Jia, S., Yu, C., Jiang, K. and Gao, N. (2010). The role of lactic acid adsorption by ion exchange chromatography. *Plos One* 5(11):e13948.

Garcia-Ochoa, F. and Gomez, E. (2009). Bioreactor scale-up and oxygen transfer rate in microbial processes: An overview. *Biotechnology Advances* 27:153–176.

Gaspard, M., Neveu, A. and Martin, G. (1983). Clinoptilolite indrinking water treatment for NH_4^+ removal. *Water Research* 17(3):279-288.

Gauthier, T., Thibault, J. and LeDuy, A. (1991). Measuring k_La with randomly pulsed dynamic method. *Biotechnology and Bioengineering* 37:889-893.

Gomez, Z.A, Tymczyszyn, E.E., De Antoni, G. and Disalvo, E.A. (2003). Action of trehalose on the preservation of *Lactobacillus delbrueckii* ssp. *bulgaricus* by heat and osmotic dehydration. *Journal of Applied Microbiology* 95:1315–1320.

Gomis, A.I.U., De Alwis, M.C.L., Radhakrishnan, S. and Thalagoda, S.A. (1989). Further studies on stability and potency of the haemorrhagic septicaemia oil adjuvant vaccine. *Sri Lanka Veterinary Journal* 36:9-20.

Grijspeerdt, K. and Vanrolleghem, P. (1999). Estimating the parameters of the Baranyi model for bacterial growth. *Food Microbiology* 16(6):593-605.

Gulsah, O., Bruno, F.U., Bernabé, L.R., Nalan, K. and Marek, B. (2016). Arsenic sorption using mixtures of ion exchange resins containing n-methyl-d-glucamine and quaternary ammonium groups. *Journal of the Chilean Chemical Society* 61(1):2752-2756.

Gunatilake S.K. (2015). Methods of Removing Heavy Metals from Industrial Wastewater. *Journal of Multidisciplinary Engineering Science Studies* 1(1):12-18.

Guowei, S., Bowen, Z., Yixin, H., He, C. and Hongchang, Wan. (2017). Optimization of cryoprotectants for Streptococcus thermophilus during freeze-drying using Box-Behnken experimental design of response surface methodology. *Emirates Journal of Food and Agriculture* 29(4):256-263.

Gupta, V. K., Sadegh, H., Yari, M., Ghoshekandi, R. S., Maazinejad, B. and Chahardori, M. (2015). Removal of ammonium ions from wastewater A short review in development of efficient methods. *Global Journal of Environmental Science and Management* 1(2):149-158.

Hamoudi, L., Goulet, J. and Ratti, C. (2007). Effect of protective agents on the viability of *Geotrichum candidum* during freeze-drying and storage. *Journal of Food Science* 72(2):45-49.

Haralambous, A., Maliou, E. and Malamis, M. (1992). The use of zeolite for ammonium uptake. Water Science Technology 25 (1):139-145.

Hariyadi, P. (2013). Freeze-drying technology: for better quality and flavor of dried products. *Foodreview Indonesia* 5(2):52-57.

Hashim, S., Kwon, D.H., Abdelal, A. and Lu, C.D. (2004). The arginine regulatory protein mediates repression by arginine of the operons encoding glutamate synthase and anabolic glutamate dehydrogenase in *Pseudomonas aeruginosa*. *Journal of Bacteriology* 186:3848-54.

Helling, R.B. (1998). Pathway choice in glutamate synthesis in *Escherichia coli. Journal of Bacteriology* 180(17):4571–4575.

Hellio C, Veron B, Ga, Y.L. (2004) Amino acid utilization by *Chlamydomonas reinhardtii*: specific study of histidine. *Plant Physiology and Biochemistry* 42(3):257-264.

Highlander, S. K. (1997). Growth of *Pasteurella haemolytica* and production of its leukotoxin in semi-defined media. *American Journal of Veterinary Research* 58:749-754.

Hills,G.M.and Spurr,E.D. (1952). The effect of temperature on the nutritional requirements of Pasteurella pestis. *Journal of General Microbiology* 6:64-73.

Ho, S.Y., Chua, S.Q., Foo, D.G., Locht, C., Chow, V.T., Poh, C.L. and Alonso, S. (2008). Highly attenuated *Bordetella pertussis* strain BPZE1 as a potential live vehicle for delivery of heterologous vaccine candidates. *Infection and Immunity* 76:111-119.

Hoft, D.F., Blazevic, A., Abate, G., Hanekom, W.A., Kaplan, G., Soler, J.H., Weichold, F., Geiter, L., Sadoff, J.C. and Horwitz, M.A. (2008). A new recombinant *Bacille Calmette-Guérin* vaccine safely induces significantly enhanced tuberculosis-specific immunity in human volunteers. *The Journal of Infectious Diseases* 198:1491-1501.

Horadagoda, N.U., Hodgson, J.C., Moon, G.M., Wijewardana, T.G. and. Eckersall, P.D. (2001). Role of endotoxin in the pathogenesis of haemorrhagic septicaemia in the buffalo. *Microbial Pathogenesis* 30:171-178.

Hu, S.P., Felice, L.J. Sivanandan, V. and Maheswaranl, S.K. (1986). Siderophore production by *Pasteurella multocida*. *Infection and Immunity* 54(3):804-810.

Hu, P., Leighton, T. Ishkhanova, G. and Kustu. S. (1999). Sensing of nitrogen limitation by *Bacillus subtilis*: Comparison to enteric bacteria. *Journal of Bacteriology* 181:5042–5050.

Huang, L., Lu, Z., Yuan, Y., Lu, F. and Bie, X. (2006). Optimization of a protective medium for enhancing the viability of freeze-dried *Lactobacillus delbrueckii* subsp. *Bulgaricus* based on response surface methodology. *Journal of Industrial Microbiology and Biotechnology* 33:55–61

Hubalek, Z. (2003). Protectants used in the cryopreservation of microorganisms. *Cryobiology* 46:205-229.

Ibrahim, H.H., Jesse, F.F.A., Chunga, E.L.T., Marza, A.D., Zamri-Saad,M., Haron, A.W. and Mohd Lila, M.A. (2016). Infection of Reproductive System of Buffaloes and Cattle with *Pasteurella Multocida*: A Review of Pathophysiological Alterations. *Pertanika Journal of Scholarly Research Reviews* 2(3):47-54.

Interior, M.M. (1993). Myanmar. In: Patten, B.E., Spencer, T.L., Johnson, R.B., Hoffmann, D. and Lehane, L., (Eds.), Pasteurellosis in Production Animals. Australian Centre for International Agriculture Research. Proceedings, 43: 254-256.

Islam, M. and Patel, R. (2011). Physicochemical characterization and adsorption behavior of Ca/Al chloride hydrotalcite-like compound towards removal of nitrate. *Journal of Hazardous Materials* 190:659-668.

Jahangiri-rad, M., Jamshidi, A., Mohammad, R. and Nabizadeh, R. (2014). Adsorption performance of packed bed column for nitrate removal using PAN-oxime-nano Fe_2O_3. *Environmental Health Science and Engineering* 12:90.

Jamaludin, R. (1993). Malaysia. In: Patten, B.E., Spencer, T.L., Johnson, R.B., Hoffmann, D. and Lehane, L., (Eds.), Pasteurellosis in Production Animals. Australian Centre for International Agriculture Research. Proceedings, 43:238-239.

Jindrich, P., Ann, H. and Paul, D.V. (2016). Impact of the freeze-drying process on product appearance, residual moisture content, viability, and batch uniformity of freeze-dried bacterial cultures safeguarded at culture collections. *Applied of Microbiology and Biotechnology* 100:6239–6249.

Jorgensen, T.C. and Weatherley, L.R. (2003). Ammonia removal from wastewater by ion exchange in the presence of organic contaminants. *Water Research* 37:1723–1728.

Ju, L.K. and Chase, G.G. (1992). Improved scale-up strategies of bioreactors. *Bioprocess Engineering* 8:49–53.

Javier, A.M. and Sergi, M. (2014). Plant amino acid-derived vitamins: Biosynthesis and function. *Amino Acids* 46:809-824.

Jeong, H., Park, J. and Kim, H. (2013). Determination of NH_4^+ in environmental water with interfering substances using the modified Nessler Method. *Journal of Chemistry* 2013:9.

Jiang, S., Rasmussen, R.A., Nolan, K.M., Frankel, F.R., Lieberman, J., McClure, H.M., Williams, K.M., Babu, U.S., Raybourne, R.B. and Strobert, E. (2007). Live attenuated *Listeria monocytogenes* expressing HIV Gag: Immunogenicity in rhesus monkeys. *Vaccine* 25:7470-7479.

Jin, T.H., Nguyen, L., Qu, T. and Tsao, E. (2011). Improved formulation and lyophilization cycle for rBCG vaccine. *Vaccine* 29:4848–4852.

Jindrich, P., Ann, H. and Paul, D.V. (2016). Impact of the freeze-drying process on product appearance, residual moisture content, viability, and batch uniformity of freeze-dried bacterial cultures safeguarded at culture collections. *Applied of Microbiology and Biotechnology* 100:6239–6249.

Josefsberg, J.O. and Buckland, B. (2012). Vaccine Process Technology. *Biotechnology and Bioengineering* 109(6):1443-1460.

Kadam, P.C. and Boone, D.R. (1996). Influence of pH on ammonia accumulation and toxicity in halophilic, methylotrophic methanogens. *Applied and Environmental Microbiology* 62(12):4486–4492.

Kaleta, C., Schäuble, S., Rinas, U. and Schuster, S. (2013). Metabolic costs of amino acid and protein production in *Escherichia coli*. *Biotechnology Journal* 8(9):1105-1114.

Kamarudin, M.I. (2005). Haemorrhagic septicaemia: Eradication is a possibility. Proceedings of the regional symposium on haemorrhagic septicaemia, December 1–2, 2005. Serdang, Malaysia: Putrajaya, UPM Press:12-15.

Kamble, M.P. and Yadav, G. D. (2017). Kinetic Resolution of (*R*,*S*)-α-Tetralol by Immobilized *Candida antarctica* Lipase B: Comparison of Packed-Bed over Stirred-Tank Batch Bioreactor. *Industrial and Engineering Chemistry Research* 56(7):1750–1757.

Kandil, S. and El Soda, M. (2015). Influence of freezing and freeze drying on intracellular enzymatic activity and autolytic properties of some lactic acid bacterial strains. *Advances in Microbiology* 5:371-382.

Kang, S.Y., Lee, J.U., Moon, S.H. and Kim, K.W. (2004). Competitive adsorption characteristics of Co2+, Ni2+, and Cr3+ by IRN-77 cation exchange resin in synthesized wastewater. *Chemosphere* 56(2):141-147.

Kang, M., Kim, Y., Lee, H., Lim, H. and Oh, J. (2012). Comparison of temperature and additives affecting the stability of the probiotic *Weissella cibaria*. *Original Article-Infection and immunology* 48(3):159–163.

Kanojia, G., Have, R.T., Soema, P.C., Frijlink, H., Amorij, J.P. and Kersten, G. (2017). Developments in the formulation and delivery of spray dried vaccines. *Human Vaccines and Immunotherapeutics* 13(10):2364-2378.

Kanojia, G., Willems, G.J., Frijlink, H.W., Kersten, G.F., Soema, P.C., Amorij, J.P. (2016). A Design of Experiment approach to predict product and process parameters for a spray dried influenza vaccine. *International Journal of* Pharmaceutics 511(2):1098–111.

Karthika, C. and Sekar, M. (2013). Comparison studies of adsorption properties on Ni(II) removal by strong and weak acid cation-exchange resins. *Chemistry Research Journal* 3(3):65–69.

Kayani, R.F.I., Naqvi, Z.H. Chaudhry, T.M. and Shauket, M. (2000). Studies on *Pasteurella multocida:* Indirect haemagglutination test for the identification of serological types. *Pakistan Journal of Biological Sciences* 3(3):503-504.

Kazzaz, J.A, Xu, J., Palaia, T.A., Mantell, L., Fein, A.M. and Horowitz, S. (1996). Cellular oxygen toxicity: Oxidant injury without apoptosis. *Journal of Biological Chemistry* 271:15182–15186.

Keller, R., Hilton, T.D., Rios, H., Boedeker, E.C. and Kaper, J.B. (2010). Development of a live oral attaching and effacing *Escherichia coli* vaccine candidate using *Vibrio cholerae* CVD 103-HgR as antigen vector. *Microbial Pathogenesis* 48:1-8.

Khaled, A.R, Shaker, L.S., Bakkar, A. and Abulmagd, S.M. (2016). Comparison of different fermentation parameters of *Pasteurella multocida* on the dry cell mass for the preparation of fowl cholera vaccine. *International Journal of Recent Scientific Research Research* 7(12):14558-14561.

Khan, A., Saleemi, M.K., Khan, M.Z., Gul, S.T., Irfan, M. and Qamar, M.S. (2011). Hemorrhagic Septicemia in Buffalo (*Bubalus bubalis*) calves under sub-tropical conditions in Pakistan. *Pakistan Journal Zoology* 43(2):295-302.

Khan, A., Munir, S., Jamal, Q., Anees, M., Shah, S.A., Sherwani, S.K., Basit, A. Ali, G. Asadullah, and Hussain, M. (2013). Biomass production of *Pasteurella multocida* using biofermenter. *International Journal of Advanced Research* 1(5):142-151.

Khan, M Z.I., Sultan, I.I.A.A., Arshad, M.M.B., Erkihun, A. and Sani, N.I. (2014). Serotyping of *Pasteurella multocida* based on capsules in ducks in Kelantan, Malaysia. *Asian Journal of Science and Technology* 5(11):713-715.

Khan, S., Chatfield, S., Stratford, R., Bedwell, J., Bentley, M., Sulsh, S., Giemza, R., Smith, S., Bongard, E. and Cosgrove, C.A. (2007). Ability of SPI2 mutant of *Salmonella typhi* to effectively induce antibody responses to the mucosal antigen enterotoxigenic *E. coli* heat labile toxin B subunit after oral delivery to humans. *Vaccine* 25:4175-4182.

Khar, U.R.V. and Myint, A. (1993). Myanmar. In: Patten, B.E., Spencer, T.L., Johnson, R.B., Hoffmann, D. and Lehane, L., (Eds.), Pasteurellosis in Production Animals. Australian Centre for International Agriculture Research. Proceedings, 43: 249-241.

Khin, M.N. and Zamri-Saad, M. (2010). The Effect of Dexamethasone on Immune Responses of Calves to Intranasal Exposures to Live Attenuated *gdhA* Derivative of *Pasteurella multocida* B:2. Pertanika Jounal Tropical Agricaltur Science 33 (2):205 – 211.

Kim, J., Kim, K. Ye, H., Lee, E., Shin, C., Mc Carty, P.L. and Bae, J. (2011). Anaerobic fluidized bed membrane bioreactor for wastewater treatment. *Environmental Science* and *Technology* 45(2):576-581.

Kim, T. and Kubica, G. (1973). Preservation of Mycobacteria: 100% viability of suspensions stored at -70C. *Applied microbiology* 25(6):956-960.

Klesius, P. and Pridgeon, J. (Eds.) (2011). Better science, better fish, better life proceedings of the ninth international symposium on tilapia in aquaculture: Proceedings: *Live Attenuated Bacterial Vaccines in Aquaculture*. Shanghai Ocean University, Shanghai: China.

Koon, J.H. and Kaufman, W.J. (1975). Ammonia removal from municipal wastewaters by ion exchange, *Journal of the Water Pollution Control Federation* 47:448.

Konz, J.O., King, J. and Cooney, C.L. (1998). Effects of oxygen on recombinant protein expression. *Biotechnology Progress* 14:393–409.

Korshunov, S., and Imlay, J.A. (2006). Detection and quantification of superoxide formed within the periplasm of *Escherichia coli*. *Journal of Bacteriology* 188:6326–6334.

Koser, S. (1968). Vitamin requirements of bacteria and yeasts. Thomas, C.C. Springfield. p. 340–345.

Kral, K., Maclean, M. and San, S. (1993). Cambodia. In: Patten, B.E., Spencer, T.L., Johnson, R.B., Hoffmann, D. and Lehane, L., (Eds.), Pasteurellosis in Production Animals. Australian Centre for International Agriculture Research. Proceedings, 43: 246-248.

Kumar, P., Singh, V.P., Agrawal, R.K. and Singh, S. (2009). Identification of *Pasteurella multocida* isolates of ruminant origin using polymerase chain reaction and their antibiogram study. *Tropical Animal Health and Production* 41:573–578.

Kunda, N.K., Wafula, D., Tram, M., Wuc, T.H. and Muttil, P. (2016). A stable live bacterial vaccine. *European Journal of Pharmaceutics and Biopharmaceutics* 103:109–117.

Kundu, P.B. (1993). India. In: Patten, B.E., Spencer, T.L., Johnson, R.B., Hoffmann, D. and Lehane, L., (Eds.), Pasteurellosis in Production Animals. Australian Centre for International Agriculture Research. Proceedings, 43: 232-233.

Kuramaa, H., Poetzschkeb, J. and Haseneder, R. (2002). The application of membrane filtration for the removal of ammonium ions from potable water. *Water Research* 36:2905–2909.

Lal, M., Priddya, S., Bourgeois, L., Walker, R., Pebley, W., Brown, J., Desai, J., Darsley, M.J., Kristensen, D. and Chen, D. (2013). Development of a fast-dissolving tablet formulation of a liveattenuated enterotoxigenic *E. coli* vaccine candidate. *Vaccine* 31:4759– 4764.

Leclair, D.A., Cranston, E.D., Xing, Z., Thompson, M.R. (2016). Optimization of spray drying conditions for yield, particle size and biological activity of thermally stable viral vectors. *Pharmaceutical Research* 33(11):2763–76.

Lee, S.F., Halperin, S.A., Wang, H. and MacArthur, A. (2002). Oral colonization and immune responses to *Streptococcus gordonii* expressing a pertussis toxin S1 fragment in mice. *FEMS Microbiology Letters* 208:175-178.

Lei, L., Li, X., and Zhang, X. (2008). Ammonium removal from aqueous solutions using microwave-treated natural Chinese zeolite. *Separation and* Purification *Technology* 58:359–366.

Leibiger, R., Niedung, K., Geginat, G., Heesemann, J. and Trülzsch, K. (2008). *Yersinia enterocolitica* Yop mutants as oral live carrier vaccines. *Vaccine* 26:6664-6670.

Leonardo, M.R., Dailly, Y. and Clark, D.P. (1996). Role of NAD in regulating the adhE gene of *Escherichia coli*. *Journal of Bacteriology* 178(20):6013-6018.

Leslie, S.B., Israeli, E. Llighthart, B. Crowe, J.H. and Crowe. L.M. (1995). Trehalose and sucrose protect both membranes and proteins in intact bacteria during drying. *Applied and Environmental Microbiology* 61:3592-3597.

Li, S., Locke, E., Bruder, J., Clarke, D., Doolan, D.L., Havenga, M.J.E., Hill, A.V.S., Liljestrom, P., Monath, T.P., Naim, H.Y., Ockenhouse, C., Tang, D.C.C., VanKampen, K.R., Viret, J.F., Zavala, F. and Dubovsky, F. (2007). Viral vectors formalaria vaccine development. *Vaccine* 25(14):2567–2574.

Li, X., Lin, C., Wang, Y., Zhao, M. and Hou, Y. (2010). Clinoptilolite adsorption capability of ammonia in pig farm. *Procedia Environmental Sciences* 2:1598–1612.

Li, X., Shi, H., Wang, Y., Zhang, S., Chu, J., Zhang, M., Huang, M. and Zhuang, Y. (2011). Effects of vitamins (nicotinic acid, vitamin B 1 and biotin) on phototrophic hydrogen production by *Rhodobacter sphaeroides* ZX-5. *International Journal of Hydrogen Energy* 36(16):9620-9625.

Liang, P., Yu, H., Huang, J., Zhang, Y. and Cao, H. (2016). The Review on adsorption and removing ammonia nitrogen with biochar on its mechanism. *Matec Web of Conferences* 67:07006.

Lin, L., Lei, Z., Wang, L., Liu, X., Zhang, Y., Wan, C., Lee, D.J. and Tay, J.H. (2013). Adsorption mechanisms of high-levels of ammonium onto

natural and NaCl-modified zeolites. *Separation and Purification Technology* 103:15–20.

Lin, S.H., and Wu, C.L. (1996). Ammonia removal from aqueous solution by ion exchange. *Industrial* and *Engineering Chemistry* Research 35:553–558

Lin, S.H. and Wu, C.L. (1996). Removal of nitrogenous compounds from aqueous solution by ozonation and ion exchange. *Water Research* 30(8):1851–1857.

Liu, J., Su, Y., Li, Q., Yue, Q. and Gao, B. (2013). Preparation of wheat straw based superabsorbent resins and their applications as adsorbents for ammonium and phosphate removal. *Bioresource Technology* 143:32-39.

Losen, M., Frollich, B., Pohl, M. and Buchs, J. (2004). Effect of Oxygen limitation and medium composition on *Escherichia coli* fermentation in shake-Flask Cultures. *Biotechnology Progress* 20:1062−1068.

Lye, G.J. and Woodley, J.M. (199). Application of in situ product-removal techniques to biocatalytic processes. *Trends in Biotechnology - Cell Press* 17(10):395–402.

Maciag, P.C., Radulovic, S. and Rothman, J. (2009). The first clinical use of a live-attenuated *Listeria monocytogenes* vaccine: a Phase I safety study of Lm-LLO-E7 in patients with advanced carcinoma of the cervix. *Vaccine* 27:3975-3983.

Madhu, A.N. Awasthi, S.P., Reddy, K.B.P.R. and Prapulla, S.G. (2011). Impact of freeze and spray drying on the retention of probiotic properties of *Lactobacillus fermentum*: An in vitro Evaluation Model. *International Journal of Microbiological Research* 2(3):243-251

Magasanik, B. and Bowser, H.R. (1955). The degradation of histidine by *Aerobacter aerogenes*. *Journal of Biological Chemistry* 213(2):571-580.

Magasanik, B., Lund, P., Neidhardt, F.C., Schwartz, D.T. (1965). Induction and repression of the histidine-degrading enzymes in *Aerobacter aerogenes*. *Journal of Biological Chemistry* 240(11):4320-4324.

Magasanik, B. (1992). Regulation of Nitrogen Utilization. *Cold Spring Harbor Monograph Archive* 21:283-317.

Malekian, R., Abedi-Koupai, J., Eslamian, S.S., Mousavi, S.F., Abbaspour, K.C., and Afyuni, M. (2011). Ion-exchange process for ammonium removal and release using natural Iranian zeolite. *Applied Clay Science* 51(3):323-329.

Malovanyy, A., Sakalova, H., Yatchyshyn, Y., Plaza, E., and Malovanyy, M. (2013). Concentration of ammonium from municipal wastewater using ion exchange process. *Desalination* (329):93-102.Manadar, P. (1991). Country Report. Proceedings IV: *International Workshop on Haemorrhagic Septicaemia,* Kandy, Sri Lanka.

Mazur, P. (1984).Freezing of living cells: Mechanisms and implications. *American Journal of Physiology* 247(3):125-142.

Md Yasin, I.S. (2009). Identification, cloning, sequencing, expression and protective capacity of the gene encoding a fimbrial protien of *Pasteurella multocida* B:2, PhD Thesis, Universiti Malaysia Terengganu, Malaysia.

Mingguan Malaysia (2008, Mei 10). 30 kerbau, lembu mati mengejut. *Utusan Malaysia* ARKIB: 11/05/2008.

Mohamed, M.S., Tan, J.S., Kadkhodaei, S., Mohamad, R., Mokhtar, M.N. and Ariff, A.B. (2014). Kinetics and modeling of microalga *Tetraselmis* sp. FTC 209 growth with respect to its adaptation toward different trophic conditions. *Biochemical Engineering Journal* 88:30-41.

Mohamed, R.A. and Abdelsalam, E.B. (2008). A review on pneumonic pasteurellosis (respiratory mannheimiosis) with emphasis on pathogenesis, virulence mechanisms and predisposing factors. *Bulgarian Journal of Veterinary Medicine* 11(3):139−160.

Mohan, S.K., Viruthagiri, T. and Arunkumar, C. (2013). Application of Plackett-Burman Design for screening the media components for tannase production from redgram husk using submerged fermentation. *International Journal of Pharma Research and Review* 2(9):24-29.

Morgan, C.A., Herman, N., White, P.A. and Vesey, G. (2006). Preservation of microorganisms by drying; A review. *Journal of Microbiological Methods* 66(2):183–193.

Murugappan, S., Patil, H.P., Kanojia, G., ter Veer, W., Meijerhof, T., Frijlink, H.W., Huckriede, A. and Hinrichs, W.L.J. (2013). Physical and immunogenic stability of spray freeze-dried influenza vaccine powder for pulmonary delivery: Comparison of inulin, dextran, or a mixture of dextran and trehalose as protectants. *European Journal of Pharmaceutics and Biopharmaceutics* 85:716–725.

Nadejda, T. (2012). Removal of ammonium and phosphates from aqueous solutions by activated and modified Bulgarian clinoptilolite. *Journal of Chemical Engineering and Materials Science* 3(5):79-85.

Nattawat, I., Yingyote, L., Jih-Ming, C., Surapol, P. and Chih-Hsiang, L. (2016). Using cation exchange resin for ammonium removal as part of

sequential process for nitrate reduction by nano iron. *Sustainable Environment Research* 26:156-160.

Naz, S., Hanif, A., Maqbool, A. Ahmed, S. and Muhammand, K. (2011). Isolation, characterization and monitoring of antibiotic resistance in *Pasteurella multocida* isolates from buffalo (*Bubalus bubalis*) herds around Lahore. *The Journal of Animal and Plant Sciences* 22(3):242-245.

Nelson, P.G., Bernárdez, P.F. and Castro, L.P. (2007). Fed-batch pediocin production on whey using different feeding media. *Enzyme and Microbial Technology* 41(3):397-406.

Neramitmansook, P. (1993). Thailand. In: Patten, B.E., Spencer, T.L., Johnson, R.B., Hoffmann, D. and Lehane, L., (Eds.), Pasteurellosis in Production Animals. Australian Centre for International Agriculture Research. Proceedings, 43: 234-237.

Nireesha, G.R., Divya, L., Sowmya, C., Venkateshan, N., Babu, M.N. and Lavakumar, V. (2013). Lyophilization/Freeze Drying-a review. *International Journal of Novel Trends in Pharmaceutical Sciences* 3(4):87-98.

Norqvist, A., Hagstrom, A. and Wolf-Watz. H. (1989). Protection of rainbow trout against vibriosis and furunculosis by use of attenuated strains of *Vibrio anguillarum*. *Applied and Environmental Microbiology* 55:1400-1405.

Nwabanne, J. T. and Igbokwe, P. K. (2012). Adsorption performance of packed bed column for the removal of Lead (ii) using oil palm fibre. *International Journal of Applied Science and Technology* 2(5):106-115.

Ohtake, S., Martin, R., Saxena, A., Pham, B., Chiueh, G., Osorio, M., Kopecko, D., Xu, D., Lechuga-Ballesteros, D. and Truong-Le, V. (2011). Room temperature Stabilization of oral, live attenuated *Salmonella enterica* serovar Typhi-vectored vaccines. *Vaccine* 29(15):2761–2771.

Oppermann, T., Busse, N. and Czermak, P. (2017). Mannheimia haemolytica growth and leukotoxin production for vaccine manufacturing — A bioprocess review. *Electronic Journal of Biotechnology* 28:95–100.

Oslan, S.N.H., Zamri-Saad, M., Rosfarizan, M. and Khairani-Bejo, S. (2014). *In vitro* and *in vivo* survivality of *gdhA* derivative *Pasteurella multocida* B:2. *Malaysian Journal of Microbiology* 10(1):63-66.

Oslan, S.N.H. (2013). *In vivo* survivality and optimization of parameters for biomass production of *gdhA* derivative of *Pasteurella multocida* B:2, Master of Science Thesis, Universiti Putra Malaysia.

Otero, M.C., Espeche, M.C. and Nader-Macıas, M.E. (2007). Optimization of the freeze-drying media and survival throughout storage of freeze-dried *Lactobacillus gasseri* and *Lactobacillus delbrueckii* subsp. *delbrueckii* for veterinarian probiotic applications. *Process Biochemistry* 42:1406–1411.

Outram, V., Lalander, C., Lee, J.G.M., Davies, E.T. and Harvey, A.P. (2017). Applied i*n situ* product recovery in ABE fermentation*. Biotechnlogy Progress* 33(3):563–579.

Özcan, A.S., Erdem, B. and Özcan, A. (2004). Adsorption of acid blue 193 from aqueous solutions onto Na-bentonite and DTMA-bentonite. *Journal of Colloid and Interface Science* 280(1): 44-54.

Ozturk, I., Altinbas, M., Koyuncu, I., Arikan, O. and Gomec-Yangin, C. (2003). Advanced physico-chemical treatment experiences on young municipal landfill leachates. *Waste Management* 23:441–446.

Paccez, J.D., Nguyen, H.D., Luiz, W.B., Ferreira, R.C., Sbrogio-Almeida, M.E., Schuman, W. and Ferreira, L.C. (2007). Evaluation of different promoter sequences and antigen sorting signals on the immunogenicity of *Bacillus subtilis* vaccine vehicles. *Vaccine* 25:4671-4680.

Pacheco, L.G., Mati, V.L., Castro, T.L., Dorella, F.A., Oliveira, S.C., Miyoshi, A., de Melo, A.L. and Azevedo, V. (2008). Oral immunization with *Salmonella harboring* a Sm14-based DNA vaccine does not protect mice against *Schistosoma mansoni* infection. *Parasitology International* 57:506-508.

Palmfeldt, J., Radstrom, P. and Hahn-Ha¨G.B. (2003). Optimisation of initial cell concentration enhances freeze-drying tolerance of *Pseudomonas chlororaphis. Cryobiology* 47:21–29.

Patnaik, K.S.K.R. and Sriharsha, K. (2010). Fluidization principles for three-phase fluidized bed bio-reactor. *Journal of Chemical Engineering and Applications* 1(3):251-255.

Paustian, M.L., May, B.J. and Kapur, V. (2002). Transcriptional response of *Pasteurella multocida* to nutrient limitation. *Journal of Bacteriology* 184(13):3734-3739.

Phoung, P.T. (1993). Vietnam. In: Patten, B.E., Spencer, T.L., Johnson, R.B., Hoffmann, D. and Lehane, L., (Eds.), Pasteurellosis in Production Animals. Australian Centre for International Agriculture Research. Proceedings, 43: 240-242.

Plackett, R. L. and Burman, J. P. (1946). The design of optimum multifactorial experiments. *Biometrika* 33:305-325.

Prajapati, J.C., Syed, H.S. and Chauhan, J. (2014). Removal of Ammonia from wastewater by ion exchange technology. *International Journal Of Innovative Research In Technology* 1(9):6-11.

Prakash, O., Nimonkar, M. and Shouche, Y.S. (2013). Practice and prospects of microbial preservation. *FEMS Microbiology Letters* 339:1–9.

Putra, A.A.G. (1993). Indonesia. In: Patten, B.E., Spencer, T.L., Johnson, R.B., Hoffmann, D. and Lehane, L., (Eds.), Pasteurellosis in Production Animals. Australian Centre for International Agriculture Research. Proceedings, 43:229-231.

Quanzhou, C., Kanggen, Z.,Yan, C., Aihe, W. and Fang, L. (2017). Removal of ammonia from aqueous solutions by ligand exchange onto a Cu(II)-loaded chelating resin: Kinetics, equilibrium and thermodynamics. *The Royal Society of Chemistry Advances* 7:12812–12823.

Rafidah, O., Zamri-Saad, M., Nasip, E., Shahiruddin, S. and Saharee, A. A. (2010). Analysis of hemorrhagic septicemia outbreaks in cattle and buffalo in Malaysia. *Online Journal of Veterinary Research* 14:325-333.

Rafidah, O., Zamri-Saad, M., Nasip, E., and Saharee, A. A. (2011). Herd immunity in buffaloes after intranasal live *gdhA* derivative *Pasteurella multocida* B:2. *Online Journal of Veterinary Research* 283-290.

Rafidah, O., Zamri-Saad, M., Shahirudin, S. and Nasip, E. (2012). Efficacy of intranasal vaccination of field buffaloes against haemorrhagic septicaemia with a live *gdhA* derivative *Pasteurella multocida* B:2. *Veterinary Record* 171(7):175.

Rahman, M.M., Salleh, M.A.M., Rashid, U., Ahsan, A., Hossain, M.M. and Chang, S.R. (2014). Production of slow release crystal fertilizer from wastewaters through struvite crystallization – A review. *Arabian Journal of Chemistry* 7(1):139–155.

Rahmani, A.R., Mahvi, A.H., Mesdaghinia, A.R., and Nasseri, S. (2004). Investigation of ammonia removal from polluted waters by Clinoptilolite zeolite. *International Journal of Environmental Science* and *Technology* 1(2):125-133.

Raina, M. M. (2008). Bacterial Growth. In: Environmental Microbiology Second Edition. Raina M. M., Ian, L. P. and Charles P. G. (Eds.), Academic Press, London, pp. 37-54.

Rajendran, A., Palanisamy, A. and Thangavelu, V. (2008). Evaluation of medium components by Plackett-Burman statistical design for lipase production by *Candida rugose* and kinetic modeling. *Chinese Journal of Biotechnology* 24(3):436-444.

Ramasamy, R., Yasawardena, S., Zomer, A., Venema, G., Kok, J. and Leenhouts, K. (2006). Immunogenicity of a malaria parasite antigen displayed by *Lactococcus lactis* in oral immunisations. *Vaccine* 24:3900-3908.

Rambhatla, S. and Pikal, M.J. (2003). Heat and mass transfer scale-up issues during freeze drying, I: Atypical radiation and the edge vial effect. *AAPS PharmSciTech Journal* 4(2):111–120.

Rey, L. and May, J. (2001). Freeze-drying/lyophilization of pharmaceutical and biological products. Book reviews. *European Journal of Pharmaceutics and Biopharmaceutics* 2001(51):163–164.

Roland, K.L., Cloninger, C., Kochi, S.K., Thomas, L.J., Tinge, S.A., Rouskey, C. and Killeen, K.P. (2007). Construction and preclinical evaluation of recombinant Peru-15 expressing high levels of the cholera toxin B subunit as a vaccine against enterotoxigenic *Escherichia coli*. *Vaccine* 25:8574-8584.

Saarela, M., Virkajärvi, I., Alakomi, H-L., Mattila-Sandholm, T., Vaari, A., Suomalainen, T. and Mättö, J. (2005). Influence of fermentation time, cryoprotectant and neutralization of cell concentrate on freeze-drying survival, storage stability, and acid and bile exposure of *Bifidobacterium animalis* ssp. *lactis* cells produced without milk-based ingredients. *Journal of Applied Microbiology* 99 (6):1330-1339.

Saharee, A.A., Salim, N., Rasedee, A. and Jainudeen, M.R (1993). Hemorrhagic septicemia carriers among cattle and buffalo in Malaysia. In: Pasteurellosis in Production Animals. Australian Centre for International Agricultural Research Proceeding No.43:89-91.

Sainz, J. Pizarro, F., Pe´ rez-Correa, J. R., and Agosin E. (2003). Modelingof yeast metabolism and process dynamics in batch fermentation. *Biotechnology and Bioengineering* 81(7): 818-828.

Saluja, V.M Amorij, J.P., Kapteyn, J.C., de Boer, A.H., Frijlink, H.W. and Hinrichs, W.L.J. (2010). A comparison between spray drying and spray freeze drying to produce an influenza subunit vaccine powder for inhalation. *Journal of Controlled Release* 144:127–133.

Sanjith, N.L. and Gatin, L.A. (1993). Freeze drying: Annealing principles and practice. *NP publication* 2:163-233.

Sarwar, N., Muhammad, K., Rabbani, M. Younus, M., Sarwar, M., Ali, M.A., Hanif, K. and Kamran, M. (2013). Optimization of physico-chemical factors augmenting *in vitro* biomass production of *Pasteurella multocida. Journal of Animal & Plant Sciences* 23(4):1085-1088.

Sollohub, K. and Cal, K. (2010). Spray drying technique: II. Current applications in pharmaceutical technology. *Journal of Pharmaceutical Sciences* 99:587–597.

Priadi, A. and Natalla. L. (2001). Protection of a live *Pasteurella multocida* B: 3.4 vaccine against haemorrhagic septicaemia. *Jurnal Ilmu Ternak dan Veteriner* 7:55-61.

Salmbandamurthy, V.K. and Jocobs, J.W.R. (2005). Live attenuated mutants of *Mycobacterium tuberculosis* as candidate vaccines against tuberculosis. *Microbes and Infection* 7(5-6):955-961.

Saltali, K., Sarý, A. and Aydýn, M. (2007). Removal of ammonium ion from aqueous solution by natural Turkish (Yýldýzeli) zeolite for environmental quality. *Journal of* Hazardous *Materials* 141(1):258-263

Sang, W.P., Se, J.H., Dong-Shik, K., Sang, J.S. (2007). Improvement of epothilone B production by *in situ* removalof ammonium using cation exchange resin in *Sorangium cellulosum* culture. *Biochemical Engineering Journal* 37:328–331.

Sarah, S.O., Zamri-Saad, M., Zunita, Z., and Raha, A.R. (2006). Molecular cloning and sequence analysis of *gdhA* gene *Pasturella multocida* B:2. *Journal of Animal and Veterinary Advances* 5:1146-1149.

Sarah, S.O. (2007). Construction of an attenuated *Pasteurella multocida* B:2 by mutation in The *gdhA* gene, Master of Science Thesis, Universiti Putra Malaysia.

Savini, M., Cecchini, C., Verdenelli, M.C., Silvi, S., Orpianesi, C. and Cresci, A. (2010). Pilot-scale production and viability analysis of freeze-dried probiotic bacteria using different protective agents. *Nutrients* 2:330-339.

Schoug, A., Olsson, J., Carlfors, J., Schnürer, J, and Håkansson, S. (2006). Freeze-drying of *Lactobacillus coryniformis* Si3—effects of sucrose concentration, cell density, and freezing rate on cell survival and thermophysical properties. *Cryobiology* 53 (1):119-127.

Scott, P.V., Markham, J.F. and Whithear, K.G. (1999). Safety and efficacy of two live *Pasteurella multocida aroA* mutant vaccines in chickens. *Avian Diseases* 43:83-88.

Selmer-Olsen, E., Birkeland, S.E. and Srhaug, T. (1999). Effect of protective solutes on leakage from and survival of immobilized *Lactobacillus* subjected to drying, storage and rehydration. *Journal of Applied Microbiology* 87:429–437.

Seo, S.U., Kim, J.J., Yang, H., Kwon, H.J., Yang, J.Y., Curtiss III, R. and Kweon, M.N. (2012). Effective protection against secondary

pneumococcal pneumonia by oral vaccination with attenuated *Salmonella* delivering PspA antigen in mice. *Vaccine* 30:6816-6823.

Shah, A., Kamboh, A., Rajput, N. and Korejo, N. (2008). Optimization of physico-chemical conditions for the growth of *Pasteurella multocida in vitro*. *Journal of agriculture and social sciences* 04:176–79.

Shin, W.S., Lee, D., Kim, Y S.. Jeong, S. and Chun G.T. (2013). Application of scale-up criterion of constant oxygen mass transfer coefficient (k_La) for production of itaconic acid in a 50L pilot-scale fermentor by fungal cells of *Aspergillus terreus*. *Journal of Microbiology and Biotechnology* 23(10):1445–1453.

Shivachandra, S.B., Viswas, K.N. and Kumar, A.A. (2011). A review of hemorrhagic septicemia in cattle and buffalo. *Animal Health Research Reviews* 12(1): 67–82.

Shukla, S. (2011). Freeze drying process: A review. *International Journal of Pharmaceutical Sciences and Research* 2(12):3061-3068.

Soltys, M.A. (1963). Bacteria and fungi pathogenic to man and animals, Chapter 15, London: Balliere Tindall and Cox. pp. 240-245.

Sonenshein, A.L. (2007). Control of key metabolic intersections in *Bacillus subtilis. Nature Reviews Microbiology* 5(12):917-927.

Soussi, N., Saklani-Jusforgues, H., Colle, J.H., Milon, G., Glaichenhaus, N. and Goossens, P.L. (2002.). Effect of intragastric and intraperitoneal immunisation with attenuated and wild-type LACK-expressing *Listeria* monocytogenes on control of murine *Leishmania* majorinfection. *Vaccine* 20:2702-2712.

Sprynskyy, M., Lebedynets, M., Zbytniewski, R., Namieœnik, J. and Buszewski, B. (2005). Ammonium removal from aqueous solution by natural zeolite, Transcarpathianmordenite, kinetics, equilibrium and column tests. *Separation and Purification Technology* 46(3):155-160.

Stanbury, P.F. and Whitaker, A. Principles of fermentation technology. Pergamon Press, 1984.

Streeter, J. (2003). Effect of trehalose on survival of *Bradyrhizobium japonicum* during desiccation. *Journal of Applied Microbiology* 95:484–491.

Stummer, S., Toegel, S., Rabenreither, M.-C., Unger, F.M., Wirth, M., Viernstein, H. and Salar-Behzadi, S.(2012). Fluidized-bed drying as a feasible method for dehydration of *Enterococcus faecium* M74. *Journal of Food Engineering* 111:156-165.

Sun, Y., Li, Y., Bai, S. and Hu, Z. (1999). Modeling and simulation of an *in situ* product removal process for lactic acid production in an airlift

bioreactor. *Industrial and Engineering Chemistry Research* 38(9):3290–3295.

Swarup, B. and Umesh, M. (2015). Continuous fixed-bed column study and adsorption modeling: Removal of Lead ion from aqueous solution by charcoal originated from chemical carbonization of rubber wood sawdust. *Journal of Chemistry* 2015:1-9.

Tabatabaei, M., MoazzeniJula, G. R., Jabbari, A. R. and Esmailzadeh, M. (2007). Vaccine efficacy in cattle against hemorrhagic septicemia with live attenuated *aroA* mutant of *Pasteurella multocida* B:2 strain. *Journal of Cell and Animal Biology* 1:62-65.

Tan, J.S., Ramanan, R.N., Ling, T.C., Shuhaim,i M., Ariff, A.B. (2011). Enhanced production of periplasmic interferon alpha-2b by *Escherichia coli* using ion-exchange resin for *in situ* removal of acetate in the culture. *Biochemical Engineering Journal* 58–59:124–32.

Tan, J.S., Ling, T.C., Mustafa, S., Tam, Y.J., Ramanan, R.N. and Ariff, A. (2013). An integrated bioreactor-expanded bed adsorption system for the removal of acetate to enhance the production of alpha-interferon-2b by *Escherichia coli*. *Process Biochemistry* 48(4):551-558.

Tang, S., Boehme, L., Lam, H. and Zhang, Z. (2009). *Pichia pastoris* fermentation for phytase production using crude glycerol from biodiesel production as the sole carbon source. *Biochemical Engineering Journal* 43(2):157-162.

Thiry, M. and Cingolani, D. (2002). Optimizing scale-up fermentation processes. *Trends Biotechnology* 20(3):103-105.

Tolner, B., Smith, L., Begent, R.H.J. and Chester, K.A. (2006). Expanded-bed adsorption immobilized-metal affinity chromatography. *Nature Protocols* 1:1213–22.

Vadgama, R. N., Odaneth, A. A. and Lali, A. M. (2015). Green synthesis of isopropyl myristate in novel single phase medium Part II: Packed bed reactor (PBR) studies. *Biotechnology Reports* 8:105-109.

Van Rensburg, E., du Preez, J.C. and Kilian, S.G. (2004) Influ-ence of the growth phase and culture medium on the survival of *Mannheimia haemolytica* during storage at different temperatures Journal of Applied Microbiology 96:154–161.

Van Rensburg, E. and Du Preez, J. C. (2006). Effect of pH, temperature and nutrient limitations on growth and leukotoxin production by *Mannheimia haemolytica* in batch and continuous culture. *Journal of Applied Microbiology* 102:1273–1282.

Du Preez, J.C., Van Rensburg, E. and Kilian, S.G. (2008). Kinetics of growth and leukotoxin production by Mannheimia haemolytica in continuous culture. *Journal of Industrial Microbiology and Biotechnology* 35 (6): 611–618.

Verma, R. and Jaiswal, T.N. (1998). Haemorrhagic septicaemia vaccines. *Vaccines* 16:1184–1190.

Vipulasiri, A.A., Wijewardana, T.G., and De Alwis, M.C.L. (1982). A note on the effect of storage temperature and time on the potency of haemorrhagic septicaemia oil adjuvant vaccine. *Sri Lanka Veterinary Journal* 30:19-21.

Vogl, C., Grill, S., Schilling, O., Stülke, J., Mack, M. and Stolz, J. (2007). Characterization of riboflavin (vitamin B2) transport proteins from *Bacillus subtilis* and *Corynebacterium glutamicum*. *Journal of Bacteriology* 189(20):7367-7375.

Wang, L.K., Vaccari, D.A., Li, Y. and Shammas, N. K. Chemical precipitation. Wang, L.K., Hung, Y.T. and Shammas, N.K. (Eds.), Physicochemical Treatment Processes, vol. 3, Humana Press, New Jersey (2004), pp. 141-198.

Wang, P., Wang, Y., Liu, Y., Shi, H. and Su, Z. (2012). Novel *in situ* product removal technique for simultaneous production of propionic acid and vitamin B12 by expanded bed adsorption bioreactor. *Bioresource Technology* 104:652–659.

Wang, Y., Li, Y. and Zhao, F.J. (2014). Bisorption of chromium(VI) from aqueous solutions by *Sargassum thunbergii* Kuntze. *Biotechnology and Biotechnological Equipment* 28(2):259-265.

Webb, S.D., Golledge, S.L., Cleland, J.L., Carpenter, J.F. and Randolph, T.W. (2002). Surface adsorption of recombinant human interferon-gamma in lyophilized and spray-lyophilized formulations. *Journal of Pharmaceutical Sciences* 91(6):1474–1487.

Wessman, G.E. (1966). Cultivation of *Pasteurella haemolytica* in a chemically defined medium. *Applied Microbiology* 14(4):597-602.

Wessman, P., Mahlin, D., Akhtar, S., Rubino, S., Leifer, K., Kessler, V. and Håkansson, S. (2011). Impact of matrix properties on the survival of freeze-dried bacteria. *Journal of Science Food Agriculture* 91(14):2518-28.

Willis, R. (2000). Expanded-bed adsorption. *Today's Chemist at Work* 9:23–8.

Wong, P.L., Royce, A.J. and Lee-Parsons, C.W.T. (2004). Improved ajmalicine production and recovery from *Catharanthus roseus* suspensions with

increased product removal rates. *Biochemical Engineering Journal* 21:253–258.

Xia, H., Lin, D. and Yao, S. (2007). Evaluation of new high-density ion exchange adsorbents for expanded bed adsorption chromatography. *Journal of Chromatography* 1145:58-66.

Xiao, X.M., Dai, D.F., Chen, H.Z., Zi, F.D. and Yu M. (2014). New correlation of volumetric oxygen mass transfer coefficient for scale-up in aerobic fermentation of recombination *E. coli. Journal of Chemical and Pharmaceutical Research* 6(7):1810-1817.

Xu, D.Q., Cisar, J.O., Osorio, M., Wai, T.T. and Kopecko, D.J. (2007). Corelinked LPS expression of *Shigella dysenteriae* serotype 1 O-antigen in live *Salmonella typhi* vaccine vector Ty21a: preclinical evidence of immunogenicity and protection. *Vaccine* 25:6167-6175.

Yanagi, K., Miyoshi, H., Fukuda, H. and Ohshima, N. (1992). A packed-bed reactor utilizing porous resin enables high density culture of hepatocytes. *Applied Microbiology Biotechnology* 37:316-320.

Yang, G.C.C. and Lee, H.L. (2005). Chemical reduction of nitrate by nano sized iron: Kinetics and pathways. *Water Research* 39:884-894.

Yang, L., Ma, Y. and Zhang, Y. (2007). Freeze-drying of live attenuated *Vibrio anguillarum* mutant for vaccinepreparation. *Biologicals* 35:265-269.

Yang, H., Cao, S., Huang, X., Liu, J., Tang, Y. and Wen, X. (2009). Intragastric administration of attenuated *Salmonella typhimurium* harbouring transmissible gastroenteritis virus (TGEV) DNA vaccine induced specific antibody production. *Vaccine* 27:5035-5040.

Yeo, B.K. and Mokhtar, I. (1993). Malaysia. In: Patten, B.E., Spencer, T.L., Johnson, R.B., Hoffmann, D. and Lehane, L., (Eds.), Pasteurellosis in Production Animals. Australian Centre for International Agriculture Research. Proceedings, 43: 112-115.

Yoshioka, S., Aso, Y. and Kojima, S. (1999). The effect of excipients on the molecular mobility of lyophilized formulations, as measured by glass transition temperature and NMR relaxation-based critical mobility temperature. *Pharmaceutical Research* 16(1):135-140.

Yu, P., Dunn, N.W. and Kim, W.S. (2002). Lactate removal by anionic-exchange resin improves nisin production by *Lactococcus lactis*. *Biotechnology Letters* 24:59–64.

Yu, R., Geng, J., Ren, H., Wang, Y. and Xu, K. (2013). Struvite pyrolysate recycling combined with dry pyrolysis for ammonium removal from wastewater. *Bioresource Technology* 132:154–159.

Yuwei, D., Yanqiu, Z. and Baojun, T. (2017). Immobilization of ammonia-oxidizing bacteria by polyvinyl alcohol and sodium alginate. *Brazilian Journal of Microbiology* 48:515–521.

Zamri-Saad, M., Ernie, Z.A. and Sabri, M.Y. (2006). Protective effect following intranasal exposure of goats to live *Pasteurella multocida* B:2. *Tropical Animal Health Production* 38:541–546.

Zamri-Saad, M. and Annas, S. (2016). Vaccination against hemorrhagic septicemia of bovines: A review. *Pakistan Veterinary Journal* 36(1):1-5.

Zayed, G. and Roos, Y.H. (2004). Influence of trehalose and moisture content on survival of *Lactobacillus salivarius* subjected to freeze-drying and storage. *Process Biochemistry* 39:1081-1086.

Zeng, Y., Fan, H., Chiueh, G., Pham, B., Martin, R., Lecguha-Ballesteros, D., Truong, V.L., Joshi, S., and Middaugh, C.R. (2009). Towards development of stable formulations of a live attenuated bacterial vaccine. *Human Vaccines* 5(5): 322-331.

Zhang, G. (2013). The essential amino acids requirements for *Oenococcus Oeni* growth and organic acids metabolism. *African Journal of Microbiology Research* 7(16):1591-1597.

Zhang, Y., Shi, Z., Chen, M., Dong, X. and Zhou, J. (2015). Evaluation of simultaneous nitrification and denitrification under controlled conditions by an aerobic denitrifier culture. *Bioresource Technology* 175:602–605.

Zhao, G., and Zhang, G. (2005). Effect of protective agents, freezing temperature, rehydration media on viability of malolactic bacteria subjected to freeze-drying. *Journal of Applied Microbiology* 99(2): 333–338.