UNIVERSITI PUTRA MALAYSIA

POSTBIOTICS AS ANTIOXIDANT AND ANTIMICROBIAL AGENTS ON THE ENHANCEMENT OF GROWTH PERFORMANCE, IMMUNITY, BIOMARKER RESPONSES, MEAT QUALITY AND CARCASS CHARACTERISTICS IN BROILERS UNDER HEAT STRESS

HUMAM ALI MERZZA

FP 2020 20

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By

HUMAM ALI MERZZA

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

February 2020

DEDICATION

I would like to dedicate this work to:

My beloved father and mother who always prays for my success

My beloved wife (Amina) and kids (Tiba, Shams and Adam) for being my inspiration

My brothers and sisters for their constant encouragement and support

My family-in-law, without their support, I could not have accomplished this work

My relatives for their continuous moral support

My friends and colleagues

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

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February 2020

Chairman : Professor Loh Teck Chwen, PhD
Faculty : Agriculture

Three experiments were conducted to study the effects of feeding postbiotics of *L. plantarum* on the performance of broiler chickens under heat stress. *In vitro* study was initially conducted to determine the antioxidant capacity and inhibitory activity against pathogens of six postbiotics (RG14, RG11, RI11, TL1, RS5, and UL4) obtained from different strains of *Lactobacillus plantarum* and then to select the best postbiotics based on the antioxidant activity. The 2,2-Diphenyl-1-Picryl-hydrazyl (DPPH) and 2,2'-azino-bis (3-thylbenzothiazoline-6-sulfonic) acid (ABTS) assays were used to examine the antioxidant activity of all postbiotics and ascorbic acid was used as standard antioxidant. The modified inhibitory activity (MAU) of the postbiotics was tested against pathogenic microorganisms such as *Pediococcus acidilactici, Salmonella enterica, Escherichia coli*, vancomycin-resistant enterococci (VRE) and *Listeria monocytogenes*. The oxytetracycline (OTC) was used as a positive control. The results indicated that all postbiotics showed activity to scavenging free radicals in both DPPH and ABTS assays. The RI11 demonstrated the highest scavenge of free radicals, followed by UL4, then RS5 as compared to other postbiotics (RG14, RG11 and TL1). All postbiotics (RI11, RS5 and UL4) had higher MAU/mL than OTC against all indicator organisms except VRE. Among the postbiotics, there was no different in MAU/mL against *E.coli*, VRE and *L. monocytogenes*. Postbiotic RS5 had higher inhibition activity against *P. acidilactici* and *Salmonella* than UL4, whereas RS5 was not different with RI11. Postbiotics RS5 and RI11 had higher optical density and lower pH, which corresponds to increase in inhibitory activity against indicator organisms. The results of the present study showed that postbiotics (RI11, RS5 and UL4) have the highest ability to scavenge free radicals and prevent the proliferation of pathogenic bacteria and thus chosen for evaluation in the following *in vivo* study.

A feeding trial was then conducted to examine the effect of postbiotics on growth performance, nutrient digestibility, gut microbial population and histology, immune status, acute phase proteins and HSP70, antioxidant activity, meat quality and gene expression related to growth in broilers under heat stress. A total of 252 one-day-old male broiler chicks (Cobb 500) were randomly assigned in cages in identical environmentally controlled chambers. During the starter period from 1 to 21 days, all the birds were fed the same basal diet. On day 22, the birds were weighed and randomly divided into six treatment groups and exposed to cyclic high temperature at 36 ± 1 °C for 3 h per day from 11:00 to 14:00 until the end of the experiment. From day 22 to 42 (finisher period), an equal number of birds were subjected to one of the following diets: NC (negative control) basal diet; OTC (positive control) basal diet + 0.02% oxytetracycline; or AA (ascorbic acid) basal diet + 0.02% ascorbic acid. The other three groups (RI11, RS5 and UL4) were basal diet + 0.3% different postbiotics. The results demonstrated that birds fed RI11 diets had higher final body weight, total weight gain and average daily gain than the birds that received the NC, OTC and AA treatments. The feed conversion ratio was higher in the RI11 group compared with other groups. Dry matter (DM), organic matter (OM) and crude protein (CP) digestibility increased in broilers fed postbiotics RI11 and UL4 compared to NC and OTC groups. Carcass parameters were not affected by the postbiotic-supplemented diet. Postbiotic supplementation improved villi height in the duodenum, jejunum and ileum compared to the NC, OTC and AA treatments. The crypt depth of the duodenum and ileum was higher in NC group compared to other treatment groups except RI11 in duodenum, and UL4 in ileum was not different with NC groups. The villus height to crypt depth ratio of duodenum and ileum was higher for the postbiotic treatment groups and AA than the OTC and NC treatment groups. The postbiotic RI11 group recorded higher caecum total bacteria and *Lactobacillus* counts and lower *Salmonella* count compared to the NC and OTC treatment groups. The *Bifidobacterium* population in the NC group was lower compared to the other treatment groups. The postbiotic (RI11, RS5 and UL4) and AA treatment groups showed lower Enterobacteriaceae and *E. coli* counts and caecal pH than the NC and OTC treatment groups. The plasma immunoglobulin M (IgM) level was higher in the birds receiving postbiotic RI11 than those receiving other treatments. The plasma immunoglobulin G (IgG) level was higher in the RI11 treatment group than in the NC, AA and RS5 groups. The plasma immunoglobulin A (IgA) level was not affected by postbiotic supplements. Addition of postbiotics especially RI11 in broiler diets reduced plasma concentration of the α1-AGP (alpha1-acid glycoprotein) and CPN (ceruloplasmin) compared to other groups. The plasma T-AOC, CAT and GSH concentration was higher in RI11 and UL4 groups compared to other groups. The meat MDA (malondialdehyde) level for lipid peroxidation was lower in postbiotics and AA groups than NC and OTC groups. Feeding RI11, RS5 and UL4 decreased drip loss, cooking loss and shear force of breast meat compared to other groups. The RI11 increased the meat pH and decreased L* and b* as compared to NC and OTC groups. However, there was no difference between postbiotics and AA in meat pH, shear force and L* colour. The hepatic GHR mRNA expression level was increase in birds fed postbiotics RI11, RS5 and UL4, AA and OTC compared to the NC-fed birds. Postbiotic RI11 led to higher hepatic IGF-1 mRNA expression level compared to the NC, OTC, and AA treatments. Mortality was not significantly different among all the treatments. In conclusion, among the postbiotics applied in the current study as compared with NC, OTC and AA, postbiotic produced from *L. plantarum* RI11 could

be used as a potential alternative to antibiotic growth promoter and source of antioxidant in the poultry industry.

The subsequent feeding trial was conducted to examine the effects of feeding different levels of postbiotic RI11 on growth performance, digestibility, intestinal histomorphology, gut microbiota, lipid profile, antioxidant enzyme activity, immune response, meat quality, acute phase proteins and HSP70 mRNA expression, gene expression of mucosal immunity and intestinal barrier function and growth hormones in broilers under heat stress. In this experiment, the same animals, environment and management as described in previous experiment. The birds were fed on the following diets: 0.0% (negative control) basal diet; OTC (positive control) basal diet + 0.02% oxytetracycline; AA (ascorbic acid) basal diet + 0.02% ascorbic acid. Four further groups were the basal diet + (0.2%, 0.4%, 0.6% and 0.8%) postbiotic RI11 of the respective levels. Supplementation of 0.4%, 0.6% and 0.8% RI11 increased final body weight, total weight gain, average daily gain, digestibility of DM, CP, EE (ether extract) and better FCR than the birds fed the 0.0% RI11, OTC and AA treatments. Increasing the level of postbiotic RI11 in diet increased growth performance, nutrient digestibility, FCR, EE digestibility, total bacteria and *Bifidobacterium* population and decreased ceacal pH, *E.coli* and *Clostridium* population. Supplementation of different levels of postbiotic RI11 increased beneficial bacteria population, villi height, VH: CD (Villi height: crypt depth) ratio in the duodenum, jejunum and ileum, increased plasma glutathione peroxidase (GPx), catalase (CAT) and glutathione (GSH) enzyme activity, plasma IgM and mucosal IgA concentration, and reduced pathogen load, intestinal crypt depth, decreased MDA concentration of meat, decreased plasma α1-AGP and CPN concentration as compared to negative control and OTC groups. Feeding various dosage of postbiotic RI11 decreased the drip loss, cooking loss, shear force, lightness and yellowness of breast meat, increased the pH of meat, decreased total cholesterol, triglyceride, low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) as compared to 0.0% RI11 and OTC groups. However, no difference was observed in blood HDL, meat redness, OM and ash digestibility and plasma IgG levels. Different levels of RI11 in broiler diets showed improvement in meat quality after 7 days storage period and decreased MDA level as compared to negative and OTC groups. Postbiotic RI11 groups increased the mRNA expression of hepatic IGF-1, GHR, IL-10 and decreased of IL-8, TNF, HSP70 and α1-AGP levels compared to the negative control and OTC groups. Postbiotics also improved the integrity of the intestinal barrier by the upregulation of ZO-1 and MUC2 mRNA expression. However, no difference was observed in CLDN1 expression, but down-regulation for OCLN expression in birds fed RI11 as compared with the 0.0% RI11. Supplementation of postbiotic RI11 in different levels quadratically increased the villi height, duodenum VH:CD ratio, plasma GPx, CAT and GSH activities, mucosal IgA and plasma IgM concentration, IGF-1, GHR, IL-10, MUC2 and ZO-1 mRNA expression, and reduced intestinal crypt depth, cholesterol profile, plasma CPN level, IL-8, TNF, α1-AGP and HSP70 mRNA expression. Supplementation of postbiotic RI11 at level 0.6% was sufficient to achieve the improvement in health and growth performance of broiler chickens under heat stress as compared to other levels. In conclusion, the results suggested that 0.6% (v/w) of postbiotic produced from *L. plantarum* RI11 could be a prospective alternative to the antibiotic as a growth promoter and antioxidant additives in the poultry industry.

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

POSBIOTIK SEBAGAI AGEN ANTIOKSIDAN DAN ANTIMIKROB TERHADAP PENAMBAHBAIKAN PRESTASI TUMBESARAN, IMUNITI, TINDAK BALAS BIOPENANDA, KUALITI DAGING DAN SIFAT KARKAS PADA AYAM PEDAGING BAWAH TEGASAN HABA

Oleh

HUMAM ALI MERZZA

Februari 2020

Pengerusi : Profesor Loh Teck Chwen, PhD
Fakulti : Pertanian

Tiga experiment telah dikendalikan untuk mengkaji kesan pemberian posbiotik *L. plantarum* terhadap tumbesaran ayam pedaging di bawah tegasan haba. Kajian *in vitro* dikendalikan terlebih dahulu untuk menentukan keupayaan antioksidan dan aktiviti rencatan terhadap patogen oleh enam posbiotik (RG14, RG11, RI11, TL1, RS5, dan UL4) yang diperolehi daripada strain *Lactobacillus plantarum* yang berlainan dan kemudian untuk memilih strain posbiotik terbaik berdasarkan aktiviti antioksidan. Cerakin 2,2-Diphenyl-1-Picryl-hydrazyl (DPPH) dan 2,2'-azino-bis (3-thylbenzothiazoline-6-sulfonic) acid (ABTS) digunakan untuk memeriksa aktiviti antioksidan kesemua posbiotik dan asid askorbik digunakan sebagai piawai antioksidan. Aktiviti rencatan terubah suai (MAU) posbiotik diuji terhadap mikroorganisma patogen seperti *Pediococcus acidilactici*, *Salmonella enterica*, *Escherichia coli*, vancomycin-resistant enterococci (VRE) and *Listeria monocytogenes*. Oxytetracycline (OTC) digunakan sebagai kawalan positif. Keputusan menunjukkan yang kesemua posbiotik menunjukkan aktiviti untuk carian radikal bebas pada kedua-dua cerakin DPPH dan ABTS. RI11 menunjukkan carian radikal bebas tertinggi, diikuti dengan UL4, kemudian RS5 dibandingkan dengan posbiotik yang lain (RG14, RG11 dan TL1). Kesemua posbiotik (RI11, RS5 dan UL4) mendapat MAU/mL lebih tinggi ($p < 0.05$) berbanding OTC terhadap organisma penunjuk kecuali VRE. Antara posbiotik, tiada perbezaan ($p > 0.05$) pada MAU/mL pada *E. coli*, VRE dan *L. monocytogenes*. Posbiotik RS5 mendapat aktiviti rencatan lebih tinggi ($p < 0.05$) pada *P. acidilactici* dan *Salmonella* berbanding UL4, manakala RS5 tidak berbeza ($p > 0.05$) dengan RI11. Posbiotik RS5 dan RI11 mendapat ketumpatan optik lebih tinggi dan pH lebih rendah, yang serupa dengan peningkatan dalam aktiviti rencaran terhadap organisma penunjuk. Keputusan kajian semasa menunjukkan yang posbiotik (RI11, RS5 dan UL4) mempunyai keupayaan tertinggi

untuk carian radikal bebas dan menghalang pertambahan bakteria potogen dan kemudian dipilih untuk penilaian dalam kajian *in vivo* seterusnya.

Satu percubaan pemberian makanan dikendalikan untuk memeriksa kesan posbiotik terhadap prestasi pertumbuhan, kebolehcernaan nutrisi, populasi mikrob perut dan histologi, status imun, protin fasa akut dan HSP70, aktiviti antioksidan, profil lipid, kualiti daging dan ungkapan gen berkait rapat dengan pertumbuhan ayam pedaging di bawah tegasan haba. Sejumlah 252 anak ayam pedaging berumur sehari diletakkan secara rawak di dalam sangkar persekitaran terkawal yang sama. Semasa tempoh pemula dari hari 1 ke 21, semua ayam diberi makan diet asas yang sama. Pada hari 22, ayam ditimbang dan dibahagikan secara rawak kepada enam kumpulan rawatan dan didedahkan kepada suhu tinggi berkitar pada 36 ± 1 °C untuk 3 h setiap hari dari 11:00 sehingga 14:00 sehingga akhir eksperimen. Dari hari 22 ke 42 (tempoh penamat), bilangan ayam yang sama ditentukan kepada setiap diet berikut: NC (kawalan negative) diet asas; OTC (kawalan positif) diet asas + 0.02% oxytetracycline; atau AA (asid askorbik) diet asas + 0.02% asid askorbik. Tiga kumpulan yang lain (RI11, RS5 dan UL4) adalah diet asas + 0.3% posbiotik berlainan. Keputusan menunjukkan yang ayam diberi makan diet RI11 mempunyai berat badan akhir, jumlah kenaikan berat dan purata kenaikan berat harian lebih tinggi berbanding ayam yang menerima rawatan NC, PC dan AA. Nisbah pertukaran makanan lebih tinggi dalam kumpulan RI11 berbanding kumpulan lain. Parameter karkas tidak dipengaruhi oleh diet tambahan posbiotik. Tambahan posbiotik meningkatkan tinggi vilus dalam duodenum, jejunum dan ileum dibandingkan dengan rawatan NC, PC dan AA. Kedalaman krip duodenum dan ileum lebih tinggi dalam kumpulan NC dibandingkan dengan kumpulan rawatan lain kecuali RI11 pada duodenum, dan UL4 pada ileum tidak berbeza dengan kumpulan NC. Nisbah ketinggian vilus kepada krip pada duodenum dan ileum lebih tinggi untuk kumpulan rawatan posbiotik dan AA berbanding kumpulan rawatan PC dan NC. Kumpulan posbiotik RI11 merekodkan bilangan bakteria keseluruhan dan *Lactobacillus* sekum lebih tinggi dan bilangan *Salmonella* lebih rendah dibandingkan dengan kumpulan rawatann NC dan PC. Populasi *Bifidobacterium* pada kumpulan NC lebih rendah dibandingkan dengan kumpulan rawaran yang lain. Kumpulan rawatan posbiotik (RI11, RS5 dan UL4) dan AA menunjukkan bilangan Enterobacteriaceae dan *E. coli* dan pH sekum lebih rendah berbanding kumpulan rawatan NC dan PC. Paras plasma immunoglobulin M (IgM) lebih tinggi pada ayam menerima posbiotik RI11 berbanding dengan ayam yang menerima rawatan lain. Plasma immunoglobulin G (IgG) lebih tinggi dalam kumpulan rawatan RI11 berbanding dalam kumpulan NC, AA dan RS5. Paras plasma imunoglobulin A (IgA) tidak dipengaruhi oleh penambahan posbiotik. Penambahan posbiotik terutamanya RI11 dalam diet ayam pedaging mengurangkan kepekatan plasma α1-AGP dan CPN berbanding dengan kumpulan lain. Kepekatan plasma T-AOC, CAT dan GSH lebih tinggi dalam kumpulan RI11 dan UL4 berbanding dengan kumpulan lain. Paras daging MDA lebih rendah dalam kumpulan posbiotik dan AA berbanding kumpulan NC dan OTC. Pemberian makanan RI11, RS5 dan UL4 mengurangkan kehilangan air melalui titisan, kehilangan air melalui masakan dan daya ricihan daging dada berbanding kumpulan lain. RI11 meningkatkan pH daging dan mengurangkan L* dan B* dibandingkan dengan kumpulan NC dan OTC. Namun begitu, tiada perbezaan antara posbiotik dan AA dalam pH, daya ricihan dan warna L* daging. Takat ungkapan hepatik GHR mRNA meningkat dalam ayam diberi makan

posbiotik RI11, RS5 dan UL4, AA dan PC berbanding ayam diberi makan NC. Posbiotik RI11 membawa kepada takat ungkapan hepatic IGF-1 mRNA lebih tinggi berbanding dengan rawatan NC, OTC dan AA. Tiada perbezaan kematian ketara di antara kesemua rawatan. Kesimpulannya, antara posbiotik digunakan dalam kajian semasa, posbiotik dihasilkan dari *L. plantarum* berpotensi untuk digunakan sebagai alternatif antibiotik penggalak pertumbuhan dan sumber antioksidan dalam industri poltri.

Percubaan pemberian makanan seterusnya dijalankan untuk memerikasa kesan-kesan memberi makan posbiotik RI11pada takat berbeza terhadap prestasi pertumbuhan, kebolehcernaan, histomorfologi usus, microbiota perut, profil lipid, aktiviti enzim antioksidan, tindakbalas imun, kualiti daging, protin fasa akut dan ungkapan mRNA HSP70, ungkapan gen keimunan mukosa dan fungsi halangan usus dan hormon pertumbuhan pada ayam pedaging bawah tegasan haba. Dalam kajian ini, persekitaran dan pengurusan ayam yang sama telah diterangkan pada kajian sebelumnya. Ayam diberi makan diet berikut: 0.0% (kawalan negatif) diet asas; OTC (kawalan positif) diet asas + 0.02% oxytetracycline; AA (asid askorbik) diet asas + 0.02% asid askorbik. Empat lanjutan kumpulan adalah diet asas + (0.2%, 0.4%, 0.6% dan 0.8%) tahap posbiotik RI11 masing-masing. Penambahan 0.4%, 0.6% dan 0.8% RI11 meningkatkan berat badan akhir, berat badan keseluruhan, purata penambahahan berat harian, kebolehcernaan DM, CP, EE dan FCR lebih baik berbanding ayam diberi makan rawatan 0.0% RI11, OTC dan AA. Peningkatan tahap posbiotik RI11 dalam diet meningkatkan prestasi tumbesaran, kebolehcernaan nutrisi, FCR dan kebolehcernaan EE, keseluruhan bakteria dan populasi *Bifidobacterium* dan mengurangkan pH, *E. coli* dan *Clostridium* sekum. Penambahan tahap posbiotik RI11 berbeza meningkatkan populasi bakteria baik, ketinggian vilus, nisbah ketinggian vilus kepada delaman krip (VH:CD) pada duodenum, jejunum dan ileum, meningkatkan aktiviti enzim plasma gluthathione peroxidase (GPx), catalase (CAT) dan gluthathione (GSH), kepekatan plasma IgM dan IgA mukosa, dan mengurangkan populasi patogen, kedalaman krip usus, mengurangkan kepekatan MDA daging, mengurangkan kepekatan plasma α1-AGP and CPN dibandingkan dengan kumpulan kawalan negatif dan OTC. Pemberian dos posbiotik RI11 berbeza mengurangkan kehilangan air melalui titisan, kehilangan air melalui masakan, daya ricihan, kecerahan dan kekuningan daging dada, meningkatkan pH daging, mengurangkan jumlah kolesterol, trigliserida, lipoprotin berketumpatan rendah (LDL) dan lipoprotin berketumpatan sangat rendah (VLDL) dibandingkan dengan kumpulan 0.0% RI11 dan OTC. Walau bagaimanapun, tiada perbezaan diperhatikan dalam HDL darah, kemerahan daging, kebolehcernaan OM dan abu dan takat plasma IgG. Perbezaan tahap RI11 dalam diet ayam pedaging menunjukkan peningkatan dalam kualiti daging selepas 7 hari tempoh penyimpanan dan mengurangkan takat MDA dibandingkan dengan kumpulan negative dan OTC. Kumpulan posbiotik RI11 meningkatkan takat ungkapan mRNA hepatic IGF-1, GHR, IL-10 dan mengurangkan Il-8, TNF, HSP70 dan α1-AGP dibandingkan kumpulan kawalan negatif dan OTC. Posbiotik juga memperbaiki integriti halangan usus dengan peningkatan kawalan mRNA ZO-1 dan MUC2. Walau bagaimanapun, tiada perbezaan diperhatikan dalam ungkapan CLDN1, tetapi pengurangan kawalan OCLD berbanding dengan kawalan negatif. Penambahan tahap berbeza posbiotik RI11 meningkatkan ketinggian vilus, nisbah VH:CD duodenum, aktiviti plasma GPx, CAT dan GSH, kepekatan IgA mukosa dan plasma

IgM dan ungkapan IGF-1, GHR, IL-10, MUC dan ZO-1 dan mengurangkan kedalaman krip usus, profil kolesterol, takat plasma CPN, ungkapan mRNA IL-8, TNF, α1-AGP dan HSP70. Penambahan posbiotik RI11 pada kadar 0.6% mencukupi untuk mencapai peningkatan dalam kesihatan dan prestasi pertumbuhan ayam pedaging di bawah tegasan haba jika dibandingkan dengan kadar yang lain. Kesimpulanya, keputusan mencadangkan yang 0.6% posbiotik dihasilkan dari *L. plantarum* RI11 boleh menjadi alternatif prospektif kepada antibiotik sebagai penggalak tumbesaran dan penambah antioksidan dalam industri poultri.

ACKNOWLEDGEMENTS

In the name of Allah, the Most Gracious and the Most Merciful. Alhamdulillah, all praises to Allah for the strengths and His blessing in completing this work.

The work presented in this thesis would have not been possible without the involvement of many people. First and foremost, I would like to express my sincere gratitude to my supervisor Prof. Dr. Loh Teck Chwen for his guidance, advice, patient, and continuous support throughout my PhD degree. I am also indebted to my supervisory committee member, Prof. Dr. Anjas Asmara @ Ab. Hadi Samsudin and Prof. Dr. Noordin Mohamed Mustapha for their support and assistance. My thank is also extended to Prof. Dr. Foo Hooi Ling for her great contribution and approval for the use of *L. plantarum* strains to produce postbiotics as a feed additive.

An appreciation should also go to Dr. Ooi May Foong and Dr. Lim Ye Heng for introducing me the basic microbiology practice and guidance in producing postbiotics and fellow lab mates in Prebiotics and Probiotics Laboratory, Institute of Bioscience UPM. Besides, many thanks to the office, laboratory and farm staffs of the Department of Animal Science in the Faculty of Agriculture UPM for their assistance and technical guidance during documentation work, feeding trial and laboratory work. Not to forget the staffs of Animal Research Centre, Laboratory of Animal Production in Institute of Tropical Agriculture and Food Security (ITAFoS) UPM. Special thanks to the team under Prof. Loh's supervision which are Wan Ahmad Izuddin, Nurhazirah Shazali, Dr. Mohamed Alshelmani, Goh Chong Hau, Dr. Jannatara Khatun, Ali Reza Nadim, Chang Hui Mei, Yohanna Danladi and Azizi for the support, advice and always ready to give timely help whenever required.

Being in the Department of Animal Science during my study, I was blessed with good friends. I owe them a deepest gratitude for the friendship, words of advice and help throughout my study. They are Hatem Rashid, Jamil Rashid, Dr. Tanbir, Dr. Salah Noory, Dr. Jurhamid Imlan, Siti Nadirah, Dr. Dalia, Dr. Ubedullah Kaka, Dr. Azad, Abu Bakar, Ahmed Shawqi, Amer al-Jubouri, Umar Sani, Dr. Osama, Dr. Leo, Hasfar, Pristian, Nurfadzmira, and Aliyu, Muideen, Dr. Mohammed Farooq, Dr. Wael al-Sultan, Osama from Yemen, Omar al-Jubouri. An especial appreciation to Dr. Elmutaz Atta Awad for his help and advice throughout my study.

My thankful to Prof. Dr. Abbas Shyaa Alwan, Prof. Dr. Ahmad al-Mashhadani, Prof. Dr. Hisham al-Mashhadani, Dr. Jaffer Ramadan, Prof. Dr. Naser Al-Anbari, Prof. Dr. Hazim Al-Daraji, Prof. Dr Mohamad Ishak, Prof. Dr. Khaldun, Prof. Dr. Abbas alawy, Prof. Dr. Mohammed Abdul-Abass, Dr. Sanaa, Prof. Dr. Hamza Al-Zubaidi, Prof. Dr. Dia Al-Hassani, Prof. Dr. Shakir Al-Attar, Dr. Hassanein, Dr. Hassan, for supporting me in term of getting the Iraqi's scholarship. My thanks to Ministry of Higher Education and Scientific Research of Iraq for selecting me as a scholarship candidate and funding me.

Last but not least, I would like to express my deepest appreciation to my parents, wife, kids, siblings, family-in-law and relative for the sacrifices and unconditional love. As always, it is impossible to mention everybody who had an impact to this work, I humbly extend my appreciation to all of you and pray the best for the all of you

Declaration by graduate student

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LIST OF ABBREVIATIONS

%	Per cent
µL	microlitre
µM	micromolar
FBW	Final body weight
ADG	Average daily gain
CWG	Cumulative weight gain
IF	Feed intake
FCR	Feed conversion ratio
bp	Base pair
cDNA	complementary deoxyribonucleic acid
CLDN-1	Claudin 1
NC	Negative control
CP	Crude protein
DM	Dry matter
DNA	Deoxyribonucleic acid
EDTA	Ethylenediaminetetraacetic acid
EE	Ether extract
g	Gram
GAPDH	Glyceraldehyde-3-phosphate dehydrogenase
GHR	Growth hormone receptor
h	Hour
IFN	Interferon
IgA	Immunoglobulin A
IGF-1	Insulin like growth factor 1

IL	Interleukin
kg	kilogram
L	Litre
LAB	Lactic acid bacteria
M	Molar
mg	milligram
min	minute
mL	millilitre
mM	millimolar
ng	nanogram
nm	nanometre
OCLD	Occludin
OM	Organic matter
ppm	parts per million
RNA	Ribonucleic acid
rpm	revolution per minute
SAS	Statistical analysis system
Th	T helper
TJP	Tight junction protein
TNF-α	Tumour necrosis factor alpha
v/w	volume/weight
w/w	weight/weight
VRE	Vancomycin-resistant enterococci
α	alpha
β	beta
ZO-1	Zonula occludin 1

MUC2	Mucin 2
HSP70	Heat shock protein70
APPs	Acute phase proteins
α1-AGP	Alpha1-acid glycoprotein
CPN	Ceruloplasmin
VL	Villi height
CD	Crypt depth
WHC	Water holding capacity
VLDL	Very low-density lipoprotein
TiO_2	Titanium dioxide
GLM	General linear model
AGP	Antibiotic growth promoter
AID	Apparent ileal digestibility
b*	Yellowness
a *	Redness
CFU	Colony forming units
GHR	Growth hormone receptor
GIT	Gastrointestinal tract
H_2O_2	Hydrogen peroxide
H_2SO_4	Sulphuric acid
HDL	High density lipoprotein
DPPH	2,2-Diphenyl-1-Picryl-hydrazyl
ATBS	2,2'-azino-bis (3-thylbenzothiazoline-6-sulfonic) acid

CHAPTER 1

GENERAL INTRODUCTION

Over the world, animals in commercial housing are subjected to various varieties of environmental challenges, such as diseases and adverse high temperatures, which can affect their health and lead to low productivity (Najafi, *et al.*, 2015a). Heat stress is a significant problem in commercial broiler production in the humid tropical countries, including Malaysia, because commercial broilers are often incapable to dissipate their body heat fast enough to maintain their body temperature within the comfort zone (Jahromi *et al.*, 2016). Exposure of broilers to heat stress affects nutrient digestibility, intestinal mucosa and microbiota (Quinteiro-Filho *et al.*, 2010) and results in lower feed intake and digestive capacity, thus negatively affect the productivity (Tufarelli *et al.*, 2007).

Antibiotics are widely used at sub-therapeutic levels as a growth promoter to counteract stress and infectious diseases to sustain productivity in commercial broiler farms. There are several studies reported that feeding broilers with the diet containing antibiotics (oxytetracycline or virginiamycin) under heat stress lead to improvement of the growth performance of broilers (Zulkifli *et al.*, 2000; Rahimi & Khaksefidi, 2006). However, due to the concern of the possible antibiotic residue in animal products (Metli *et al.*, 2015) and development of antibiotic-resistant bacteria attributed to excessive usage of antibiotics in animal feeds and their effects on both poultry and humans health, the use of antibiotics as growth promoter has been banned in several countries (Regulation, 2003; Awad *et al.*, 2009; Van Boeckel *et al.*, 2015).

Ascorbic acid as an antioxidant and health-promoting agent is an alternative to growth promoter antibiotics in broiler chickens (Tajkarimi & Ibrahim, 2011; Verghese *et al.*, 2017) and potentially be advantageous under heat-stress conditions. Dietary antioxidants such as ascorbic acid have been shown to be useful in compensating for inadequate biosynthesis of ascorbic acid in broiler chickens under heat stress and mitigating the negative effects of heat stress (Njoku, 1986). Ascorbic acid supplementation in heat-stressed broilers has been shown to alleviate the reduction of growth and feed intake (Kutlu & Forbes, 1993; Kadim *et al.*, 2008), improve growth, feed efficiency and carcass traits, reduce serum concentrations of corticosterone, malondialdehyde (lipid peroxidation), HSP70 and APPs (Sahin *et al.*, 2003b; Mahmoud *et al.*, 2004), and enhance meat quality (Ferreira *et al.*, 2015).

Probiotics are another alternative to antibiotics and have received extensive attention and use for many years as supplement in animals feed to improve productivity. (Shokryazdan *et al.*, 2014a, 2014b). Lactic acid bacteria (LAB) are an essential group of probiotic bacteria used in food and feed industries (Ali, 2010; Argyri *et al.*, 2013). The probiotic ability of LAB comes from their capacity to produce lactic and other organic acids, bacteriocin, hydrogen peroxide, and other compounds (Caplice & Fitzgerald, 1999; Soomro *et al.*, 2002; Leroy & De Vuyst, 2004; De Vuyst & Leroy,

2007), which can beneficially improve the gut health of the host. The general concept of using probiotics in poultry production is to improve the intestinal microbial balance which is assumed to provide better protection against various diseases (Gibson *et al.*, 1997; Fuller, 2012; Al-Khalaifah, 2018). Moreover, a recent study showed that probiotic feeding in heat-stressed chickens resulted in significant weight gain and feed efficiency, as well as enhanced antioxidant capacity in liver tissue and skeletal muscle (Jahromi *et al.*, 2016). Despite the benefits, some probiotic strains possess antibiotic resistance genes that are transmissible between organisms (Marteau & Shanahan, 2003; Egervärn *et al.*, 2009; Gueimonde *et al.*, 2013; Shazali *et al.*, 2014). Another drawback associated with probiotic products is the difficulty in maintaining the bacteria viability both at the manufacturing and storage phases (Shah & Prajapati, 2014). Therefore, these limitations may compromise the expected health benefits provided by probiotic products in poultry.

The current advancement of probiotic use to substitute antibiotics is the use of probiotic metabolites which are known as postbiotics. Postbiotics obtained from *Lactobacillus plantarum* have been demonstrated to promote growth performance and health of the broilers (Loh *et al.*, 2010; Kareem *et al.*, 2016b), layers (Loh *et al.*, 2014), piglets (Thu *et al.*, 2011; Loh *et al.*, 2013a;) and lambs (Izuddin *et al.*, 2018; Izuddin *et al.*, 2019a, 2019b). Postbiotics have the same mechanism of action and capacity as probiotics but without living cell (Thanh *et al.*, 2009). The action of postbiotics may come from the presence of antimicrobial metabolites, such as organic acids, bacteriocins and other molecules components which can reduce the gut pH and inhibit the proliferation of opportunistic pathogens in the feed and gut of animals (Aguilar-Toalá *et al.*, 2018). This inhibitory function of postbiotics has been shown on various bacteria pathogens including *Listeria monocytogenes*, *Salmonella typhimurium*, *Escherichia coli* and vancomycin-resistant enterococci *in vitro* (Thanh *et al.*, 2010; Thu *et al.*, 2011; Choe *et al.*, 2013; Kareem *et al.*, 2014). These abilities of postbiotics have led to the improvements in broiler growth performance, faecal lactic acid bacteria and villus height, up-regulation of insulin-like growth factor1 (IGF-1) and growth hormone receptor (GHR) mRNA in the liver, immunoglobulins (G and M), cytokines mRNA, meat quality, and reduced plasma cholesterol, faecal pH, and cecum Enterobacteriaceae group were observed when postbiotics were added to the feed of broilers (Thanh *et al.*, 2009; Loh *et al.*, 2010; Thu *et al.*, 2011; Thu *et al.*, 2010; Choe *et al.*, 2013; Loh *et al.*, 2013b; Kareem *et al.*, 2015; Kareem *et al.*, 2016a, 2016b)**.**

In the context of postbiotics, apart from the ability to promote healthier gut environment, the potential capacity of postbiotics obtained from *L. plantarum* as antioxidant is to be discovered particularly under heat stress condition. The *Lactobacillus*, particularly *L. plantarum* cultures have shown high antioxidative activities (He *et al.*, 2015; Ji *et al.*, 2015). In heat stressed broilers, *Lactobacillus* was shown to increase the hepatic antioxidant capacity (Jahromi *et al.*, 2016; Sugiharto *et al.*, 2017). It is believed that postbiotics from *L. plantarum* are expected to provide similar benefits of probiotic bacteria. Li *et al.* (2012) reported that *L. plantarum* strain isolated from traditional Chinese fermented foods showed high free radical scavenging activity, increased the level of antioxidant enzymes activity, and decreased

the level of malondialdehyde in the mice liver. However, the information of the postbiotic ability as antioxidant source in the broiler diets is still unknown.

Despite the data showing the benefits of postbiotics on the growth performance, gut health, and immunity in poultry, there is still a paucity of information on the role of postbiotics under heat stress. Hence, it is hypothesised that in vitro study is needed to estimate the antioxidant capacity of different postbiotics for selection and inclusion the effective type of postbiotic in different levels for in vivo study. Also, supplementation of postbiotics in broiler diets would improve growth performance, intestinal histomorphology, gut microbiota, meat quality, antioxidant enzymes activities, lipid peroxidation, acute phase proteins, heat shock protein70 and related gene expression of broiler under heat stress condition. Thus, the objectives of this current study were:

I. To determine the antioxidant activity of postbiotics produced by *Lactobacillus plantarum* RG11, RG14, RI11, UL4, TL1 and RS5 and their inhibitory activity against pathogens.
II. To investigate the effects of feeding different postbiotics on growth performance, gut morphology, nutrient digestibility, cecum bacteria, meat quality, immune status, antioxidant enzyme activity, acute phase proteins, heat shock protein70 and hepatic IGF-1 and GHR mRNA expressions in broiler chickens under heat stress condition.
III. To determine the impacts of feeding different levels of postbiotic (concluded the best postbiotic from objective 2) on growth performance, gut health, meat quality, antioxidant status and expression of acute phase proteins, heat shock protein70, cytokines, IGF-1 and GHR genes in broiler chickens under heat stress.

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