EFFECT OF A LACTOBACILLI PROBIOTIC ON LONGEVITY AND MOBILITY OF MALE *DROSOPHILA MELANOGASTER* WITH ALZHEIMER'S DISEASE

LIM CHIN PENG

UNIVERSITI SAINS MALAYSIA
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PUSAT PENGAJIAN TEKNOLOGI INDUSTRI
UNIVERSITI SAINS MALAYSIA

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SATU (1) NASKAH

Nama Penyelia: **Prof. Liong Min Tze**

Bahagian: **Teknologi Bioproses**

Saya telah menyemak semua pembetulan/pindaan yang dilaksanakan oleh Encik/Puan/Cik **Lim Chin Peng**

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2. Saya ingin mengesahkan bahawa saya berpuashati dengan pembetulan/pindaan yang dilaksanakan oleh calon.

Sekian, terima kasih.

PROF. DR LIONG MIN TZE
Ph.D. (Melb) Australia
School of Industrial Technology
Universiti Sains Malaysia. (USM)
11800 Penang, Malaysia

(Tandatangan dan cop)

15/7/2020

Tarikh

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by

LIM CHIN PENG

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DECLARATION BY AUTHOR

This dissertation is composed of my original work, and contains no material previously published or written by another person except where due reference has been made in the text. The content of my dissertation is the result of work I have carried out since the commencement of my research project and does not include a substantial part of work that has been submitted to qualify for the award of any other degree or diploma in any university or other tertiary institution.

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LIM CHIN PENG

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Lim Chin Peng

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LIST OF SYMBOLS AND ABBREVIATIONS

Symbol	Caption
α	Alpha
β	Beta
$	Dollar sign
γ	Gamma
κ	Kappa
μ	Micro
%	Percent

Abbreviations	Caption
Aβ42	Amyloid beta 42 peptide
AD	Alzheimer's disease
ADI	Alzheimer's Disease International
AMPK	Adenosine monophosphate-activated kinase
ANOVA	Analysis of variance
APP	Amyloid precursor protein
BACE	Beta-secretase
BBB	Blood-brain-barrier
BDNF	Brain-derived neurotrophic factor
cAMP	Cyclic adenosine monophosphate
cfu	Colony-forming unit
cm	Centimetre
CNS	Central nervous system
CREB	cAMP response element-binding protein
dAPPl	Drosophila APP-like
DNA	Deoxyribonucleic acid
DR9	*Lactobacillus fermentum* DR9
GABA	γ-aminobutyric acid
GRAS	Generally regarded as safe
HSD	Honestly significant difference
IGF	Insulin-like growth hormone
kg	Kilogram

KGGR	Kyoto Drosophila Genome and Genetic Resource
LAB	Lactic acid bacteria
LTP	Long-term potentiation
MDA	Malondialdehyde
mGluRs	Metabotropic glutamate receptors
mm	Millimetre
MMSE	Mini-mental state examination
MRS	De Mann, Rogosa, and Sharp
NF-κB	Nuclear factor kappa-light-chain-enhancer of activated B cells
NMDAR	Anti–N-Methyl-D-Aspartate Receptor
PS	Presenilin
PUFA	Polyunsaturated fatty acids
RNA	Ribonucleic acid
ROS	Reactive oxygen species
SPSS	Statistical Package for the Social Science
UAS	Upstream activation sequence
WHO	World Health Organization

KESAN PROBIOTIK LACTOBACILLI TERHADAP TEMPOH HAYAT DAN MOBILITI *DROSOPHILA MELANOGASTER* JANTAN YANG MENGHIDAPI PENYAKIT ALZHEIMER

ABSTRAK

Kira-kira 50 juta orang di dunia didiagnosis dengan penyakit Alzheimer seperti yang dilaporkan pada tahun 2019. Kerosakan lokomotor berlaku pada peringkat awal penyakit dan penurunan prestasi pesakit selalunya berkaitan rapat dengan penuaan. Tiada rawatan yang berkesan lagi dapat dijalankan secara meluas walaupun banyak kajian saintifik telah dilakukan. Kajian ini bertujuan untuk menilai kesan *Lactobacillus fermentum* DR9 terhadap tempoh hayat *Drosophila melanogaster* yang menghidapi penyakit Alzheimer dan mengkaji kesan *Lactobacillus fermentum* DR9 terhadap mobiliti *Drosophila melanogaster* yang menghidapi penyakit Alzheimer. Kajian dari segi tempoh hayat dan kemampuan pendakian telah dijalankan dalam peniga untuk mengetahui kesan rawatan menggunakan *Lactobacillus fermentum* DR9 dalam mengurangkan kadar pemendekan jangka hayat dan penurunan mobiliti *Drosophila melanogaster* yang menghidapi penyakit Alzheimer. Berdasarkan hasil kajian, tempoh hayat Actin5C-Aβ42.DR9 menunjukkan penurunan yang lebih perlahan dan menyimpang daripada Actin5C-Aβ42.nf mulai hari ke-11. Pada hari ke-23, tempoh hayat Actin5C-Aβ42.DR9 adalah 23% lebih tinggi daripada Actin5C-Aβ42.nf. Kebanyakan aspek pendakian menunjukkan hasil kajian yang menarik bahawa Actin5C-Aβ42.DR9 mengalami peningkatan yang baik dari hari kelima sehingga hari ke-20 selepas menerima rawatan probiotik. Perkaitan antara aspek-aspek pendakian turut menyokong bahawa rawatan probiotik dapat dipertimbangkan untuk mengurangkan kemerosotan mobiliti. Penurunan kelajuan pendakian Actin5C-Aβ42.DR9 telah dikurangkan secara ketara, seterusnya menyumbang kepada waktu

yang lebih pendek untuk melintasi garis tengah dan juga ketinggian yang lebih tinggi berbanding dengan Actin5C-Aβ42.nf. Kami yakin bahawa rawatan probiotik menggunakan *L. fermentum* DR9 berpotensi untuk menyelamatkan keadaan pemendekan tempoh hayat dan kemerosotan mobiliti *Drosophila melanogaster* yang menghidapi penyakit Alzheimer.

EFFECT OF A LACTOBACILLI PROBIOTIC ON LONGEVITY AND MOBILITY OF MALE DROSOPHILA MELANOGASTER WITH ALZHEIMER'S DISEASE

ABSTRACT

Approximately 50 million people are diagnosed with Alzheimer's disease (AD) in the world as reported in 2019. Locomotor impairment were present in the early stage of the disease and the decline in the performance of AD patients is often related to aging. Effective treatment has yet to be conducted extensively even though considerable amounts of studies had been performed. This study aimed to evaluate the effect of *Lactobacillus fermentum* DR9 on the longevity of AD flies and to study the effect of *Lactobacillus fermentum* DR9 on the mobility of AD flies. Longevity test and climbing test were conducted in triplicates to determine the effect of treatment using *Lactobacillus fermentum* DR9 in alleviating the lifespan shortening and mobility impairment of AD flies respectively. Based on the results, the survival rate of Actin5C-Aβ42.DR9 had showed a slower decreasing trend that deviated from that of Actin5C-Aβ42.nf from Day 11 onwards. At Day 23, the survival rate of Actin5C-Aβ42.DR9 was 23% higher than that of Actin5C-Aβ42.nf. Most climbing parameters presented appealing results inferring that Actin5C-Aβ42.DR9 had good improvement after receiving probiotic treatment from Day 5 to Day 20. The correlations among climbing parameters even supported that probiotic treatment can be put into consideration to alleviate the mobility degeneration. It was shown that the decrease in climbing speed of Actin5C-Aβ42.DR9 was significantly attenuated, consequently resulting in shorter time required to cross the centre line and more height climbed than Actin5C-Aβ42.nf. We believed that probiotic treatment using *L. fermentum* DR9 has the potential to rescue the shortening of lifespan and mobility impairment of AD model.