



**IMPROVEMENT OF GAMMA-AMINOBUTYRIC ACID BIOSYNTHESIS FROM
Lactiplantibacillus plantarum B7 VIA OPTIMISATION, IMMOBILISATION
AND REPEATED-BATCH FERMENTATION METHODS AND ITS
POTENTIAL APPLICATIONS**

By

SANGKARAN A/L PANNERCHELVAN

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

December 2023

FBSB 2023 9

All material contained within the thesis, including without limitation text, logos, icons, photographs and all other artwork, is copyright material of Universiti Putra Malaysia unless otherwise stated. Use may be made of any material contained within the thesis for non-commercial purposes from the copyright holder. Commercial use of material may only be made with the express, prior, written permission of Universiti Putra Malaysia.

Copyright © Universiti Putra Malaysia



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

**IMPROVEMENT OF GAMMA-AMINOBUTYRIC ACID BIOSYNTHESIS FROM
Lactiplantibacillus plantarum B7 VIA OPTIMISATION, IMMOBILISATION
AND REPEATED-BATCH FERMENTATION METHODS AND ITS POTENTIAL
APPLICATIONS**

By

SANGKARAN A/L PANNERCHELVAN

December 2023

Chairman : Assoc. Prof. Murni Halim, PhD
Faculty : Biotechnology and Biomolecular Sciences

This study focuses on enhancing the production of gamma-aminobutyric acid (GABA), a non-protein amino acid with various physiological benefits, using *Lactiplantibacillus plantarum* B7 isolated from *Budu* (fermented anchovy sauce). Through a combined optimisation method, including one factor at a time, two-level factorial design, steepest ascent, and central composite design, the GABA production was improved from 11.68 g/L (unoptimised approach) to 32.18 g/L (equivalent to a 175.51% increment) along with increased cell growth. These improvements were achieved by developing an optimum fermentative medium (modified MRS medium containing 1% glucose, 2.5% yeast extract, 2 ppm each of tween 80, calcium carbonate, and potassium iodide together with 335.61 mM of initial MSG and 0.723 mM of PLP with an initial pH of 5.66) and conditions (at 35.6°C with 125 rpm for 63.66 h). Further enhancements were achieved through repeated batch fermentation using watermelon rind and apple immobilised cells, resulting in GABA productions of 218.48 g/L (equivalent to a 570.18% increment) and 195.44 g/L (equivalent to a 499.51% increment), respectively, compared to free cells GABA production (32.6 g/L) in single batch fermentation mode. Additionally, compared to free cells, *L. plantarum* B7 was able to maintain 50% of its cell viability when immobilised on both natural supports even after the 12th cycle of RBF. In fermented milk product, optimisation led to an increase GABA concentration from 1.29 g/L to 4.85 g/L (equivalent to a 275.97% increment) using a food-grade medium (10% of skim milk containing 50 mM of food-grade MSG and 0.3 mM of food-grade PLP, incubated at 35.6°C with 125 rpm for 48 h). The use of watermelon rind-immobilised *L. plantarum* B7 in a food-grade medium for fermented milk production exhibited superior GABA (5.98 g/L) and lactic acid (7.48 g/L) production, with a high viable cell count retained after 28 days of storage at 4°C. Overall, the study showcases the potential of *L. plantarum* B7 in combination with optimisation, whole-cell immobilisation, and

repeated batch fermentation for improved GABA production in functional food and pharmaceutical applications.



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

**PENINGKATAN BIOSINTESIS ASID GAMA-AMINOBUTIRIK DARI
LACTIPLANTIBACILLUS PLANTARUM B7 MELALUI KAEDAH
PENGOPTIMUMAN, IMMOBILISASI DAN FERMENTASI KELOMPOK
BERULANG SERTA APLIKASI POTENSINYA.**

Oleh

SANGKARAN A/L PANNERCHELVAN

Disember 2023

Pengerusi : Profesor Madya Murni Halim, PhD
Fakulti : Bioteknologi dan Sains Biomolekul

Kajian ini memberi tumpuan kepada peningkatan penghasilan asid gama-aminobutirik (GABA), sejenis asid amino bukan protein dengan pelbagai faedah fisiologi, menggunakan *Lactiplantibacillus plantarum* B7 yang diasingkan daripada Budu (sos ikan bilis). Melalui kaedah pengoptimuman gabungan, termasuk satu faktor pada satu masa, reka bentuk faktorial dua peringkat, pendakian paling curam, dan reka bentuk komposit pusat, penghasilan GABA telah dipertingkatkan daripada 11.68 g/L (pendekatan tidak dioptimumkan) kepada 32.18 g/L (bersamaan kenaikan 175.51%), bersama dengan peningkatan pertumbuhan sel. Peningkatan ini dicapai dengan membangunkan medium fermentasi optimum (medium MRS yang diubah suai mengandungi 1% glukosa, 2.5% ekstrak yis, 2 ppm setiap tween 80, kalsium karbonat, dan kalium iodida bersama dengan 335.61 mM MSG permulaan dan 0.723 mM PLP dengan pH permulaan 5.66) dan keadaan fermentasi optimum (pada suhu 35.6°C dengan 125 rpm selama 63.66 jam). Peningkatan selanjutnya dicapai melalui fermentasi kelompok berulang menggunakan sel yang diimobilisasi dengan kulit tembikai dan epal, yang telah menghasilkan pengeluaran GABA masing-masing sebanyak 218.48 g/L (bersamaan kenaikan 570.18%) dan 195.44 g/L (bersamaan kenaikan 499.51%), berbanding penghasilan GABA (32.6 g/L) daripada sel bebas dalam mod fermentasi sekelompok. Selain itu, berbanding dengan sel bebas, *L. plantarum* B7 dapat mengekalkan 50% kebolehhidupan selnya apabila diimobilisasi pada kedua-dua sokongan semula jadi walaupun selepas kitaran ke-12 RBF. Dalam produk susu fermentasi, pengoptimuman telah meningkatkan kepekatan GABA, daripada 1.29 g/L kepada 4.85 g/L (bersamaan kenaikan 275.97%) menggunakan medium gred makanan (10% susu skim yang mengandungi 50 mM MSG gred makanan dan 0.3 mM PLP gred makanan, diinkubasi pada 35.6°C dengan 125 rpm selama 48 jam). Penggunaan *L. plantarum* B7 yang diimobilisasi dengan kulit tembikai dalam medium gred

makanan untuk penghasilan susu fermentasi menunjukkan penghasilan GABA (5.98 g/L) dan asid laktik (7.48 g/L) yang lebih baik, dengan kadar sel yang tinggi dikekalkan selepas 28 hari penyimpanan pada 4°C. Keseluruhannya, kajian ini menunjukkan potensi *L. plantarum* B7 dalam kombinasi pengoptimuman, imobilisasi sel sepenuhnya, dan fermentasi kelompok berulang untuk meningkatkan pengeluaran GABA dalam aplikasi makanan fungsian dan farmaseutikal.



ACKNOWLEDGEMENTS

First of all, I would like to express my appreciation and gratitude to my supervisor, Associate Professor Dr. Murni Halim, for her guidance, support, motivation and immense knowledge. Her continuous support and guidance throughout this journey have helped me a lot to complete the research. Moreover, I would like to extend my appreciation and gratitude to my co-supervisors, Professor Dr. Rosfarizan Mohamad, Dr. Mohd Shamzi Mohamed, and Dr. Fadzlie Wong Faizal Wong, for their insights, ideas, and suggestions throughout this study that improved the research a lot. I also would like to express my gratitude to Universiti Putra Malaysia for the scholarship (Geran Universiti Putra Malaysia) and financial aid (Graduate Research Fellowship) that have supported me in completing my study.

Besides that, I would like to thank all the lecturers and staff at Laboratory 1.6: Associate Professor Dr. Helmi Wasoh, Associate Professor Dr. Nor'Aini Abdul Rahman, Dr. Mohamad Zulfazli Mohd Sobri, Dr. Khairul Basyar Baharudin, Mrs. Renuga Panjamurti, Mrs. Aluyah Marzuki, Mrs. Norazlina Mohammad, Ms. Ainnatul Mardiah Idris, Mr. Firoz Mohd Irwan and Ms Siti Noraishah Abdul Rahman. Also, my sincere gratitude to fellow staff at Biomanufacturing and Bioprocessing Research Centre (BBRC), Universiti Putra Malaysia: Mr. Mohd. Rizal Kapri, Mrs. Zainon Sidik, Mr. Sobri Mohd Akhir and Mrs. Liyana Ithnin for their help. Furthermore, I would also like to thank my fellow post-graduate colleagues: Mr. Tan Shang Wei, Ms. Gan Zixuen, Ms. Amalia, Mrs. Imanina, Ms. Nadirah, Ms. Hidayah, Dr. Hidayat, Dr. Aidil and Mr. Fakhri, who gave me their hands when I needed them. I also would like to sincerely thank Mr. Faiz and Ms. Lanne, undergraduate students from the department of Bioprocess Technology at Universiti Putra Malaysia, who helped me with my work.

Last but not least, I would sincerely like to thank my beloved parents, Mr. Pannerchelvan and Mrs. Kalathevi and my siblings, Mr. Murugan, Ms. Lalithambigai, and Mr. Suriya Kanthan, who helped me by giving their continuous support and encouragement for me to complete my studies. Moreover, I would like to express my special gratitude to my best friend, Ms. Komati, who directly and indirectly influenced my decision to pursue my PhD degree. Finally, a special thanks to my friends, Mr. Velan and Mr. Kumaravel, who were with me and supported me through thick and thin during this journey. I would like to thank all those who directly and indirectly supported me in completing my PhD degree successfully.

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

Murni binti Halim, PhD

Associate Professor

Faculty of Biotechnology and Biomolecular Sciences

Universiti Putra Malaysia

(Chairman)

Rosfarizan binti Abdul Rahman, PhD

Professor

Faculty of Biotechnology and Biomolecular Sciences

Universiti Putra Malaysia

(Member)

Mohd Shamzi bin Mohamed, PhD

Senior Lecturer

Faculty of Biotechnology and Biomolecular Sciences

Universiti Putra Malaysia

(Member)

Fadzlie Wong bin Faizal Wong, PhD

Senior Lecturer

Faculty of Biotechnology and Biomolecular Sciences

Universiti Putra Malaysia

(Member)

ZALILAH MOHD SHARIFF, PhD

Professor and Dean

School of Graduate studies

Universiti Putra Malaysia

Date: 14 March 2024

TABLE OF CONTENTS

ABSTRACT	i
ABSTRAK	iii
ACKNOWLEDGEMENTS	v
APPROVAL	vi
DECLARATION	viii
LIST OF TABLES	xiv
LIST OF FIGURES	xv
LIST OF APPENDICES	xix
LIST OF ABBREVIATIONS	xx

CHAPTER

1	INTRODUCTION	1
2	LITERATURE REVIEW	5
	2.1 Gamma-aminobutyric acid (GABA)	5
	2.2 GABA health benefits	5
	2.3 GABA dosage and side effects	7
	2.4 Sources of GABA	9
	2.4.1 GABA from animals and human	9
	2.4.2 GABA from plants	9
	2.4.3 GABA from microorganisms	10
	2.5 GABA-producing lactic acid bacteria	12
	2.6 Methods for GABA production	14
	2.6.1 Chemical synthesis of GABA	14
	2.6.2 Biosynthesis of GABA	15
	2.7 Fermentation factors affecting GABA production	16
	2.7.1 Fermentation modes	16
	2.7.2 Optimisation of fermentation parameters	18
	2.8 Whole-cell immobilisation strategy	25
	2.9 Repeated batch fermentation	28
	2.10 GABA enriched fermented foods	28
	2.11 Concluding remarks	33
3	ISOLATION, SCREENING AND IDENTIFICATION OF GABA-PRODUCING LACTIC ACID BACTERIA FROM FERMENTED FOODS.	35
	3.1 Introduction	35
	3.2 Materials and Methods	36
	3.2.1 Fermented food samples	36
	3.2.2 Isolation and Maintenance of lactic acid bacteria	37
	3.2.3 Qualitative analysis for LAB determination	37
	3.2.4 GABA production via fermentation using LAB	38
	3.2.5 Screening for GABA-producing LAB	38
	3.2.6 Molecular identification	39

3.2.7	<i>In-vitro</i> probiotic characterisation of GABA-producing LAB	40
3.2.8	Statistical Analysis	42
3.3	Results and Discussion	42
3.3.1	Screening of lactic acid bacteria	42
3.3.2	Qualitative and quantitative analysis of GABA	44
3.3.3	Identification of GABA-producing isolates using 16S rDNA gene analysis	46
3.3.4	<i>In-vitro</i> probiotic characterisation of GABA-producing LAB	49
3.5	Summary	56
4	MEDIUM FORMULATION AND OPTIMISATION OF FERMENTATION CONDITION FOR IMPROVEMENT OF γ-AMINOBUTYRIC ACID (GABA) PRODUCTION BY <i>Lactiplantibacillus plantarum</i> B7	58
4.1	Introduction	58
4.2	Materials and Methods	60
4.2.1	Samples	60
4.2.2	<i>L. plantarum</i> B7 growth and GABA production profile	60
4.2.3	Fermentation medium formulation (Single factor experiment design)	60
4.2.4	Two-level factorial design for screening	61
4.2.5	Steepest ascent experiment design	62
4.2.6	Central Composite Design (CCD) using RSM	63
4.2.7	Validation of optimised parameters	63
4.2.8	Statistical analysis	63
4.3	Results and Discussion	64
4.3.1	Growth profile of <i>Lactiplantibacillus plantarum</i> B7	64
4.3.2	Reducing sugar concentration, MSG depletion and GABA production profile	66
4.3.3	Effects of carbon, nitrogen and growth factors on GABA production and cell growth	67
4.3.4	Screening by two-level factorial design	71
4.3.5	Optimisation via steepest ascent method	75
4.3.6	Optimisation by CCD	75
4.3.7	Validation of quadratic optimisation model	84
4.4	Summary	85

5	IMPROVEMENT OF γ-AMINOBUTYRIC ACID PRODUCTION AND CELL VIABILITY OF <i>Lactiplantibacillus plantarum</i> B7 VIA WHOLE-CELL IMMOBILISATION IN REPEATED BATCH FERMENTATION SYSTEM	86
5.1	Introduction	86
5.2	Materials and Methods	88
5.2.1	Samples	88
5.2.2	Cell immobilisation	88
5.2.3	GABA fermentation using various biocatalysts	89
5.2.4	Successive fermentation batches of GABA	90
5.2.5	Biocatalyst and free cell viable count	90
5.2.6	pH, lactic acid and GABA analyses	91
5.2.7	Scanning electron microscopy (SEM)	91
5.2.8	Statistical Analysis	91
5.3	Results and Discussion	92
5.3.1	Screening of ideal natural supports for <i>L. plantarum</i> B7	92
5.3.2	Repeated batch fermentation (RBF) using immobilised <i>L. plantarum</i> B7	97
5.4	Summary	106
6	EVALUATION OF IMPROVED GABA PRODUCTION IN FERMENTED MILK USING NATURAL SUPPORT IMMOBILISED <i>Lactiplantibacillus plantarum</i> B7	107
6.1	Introduction	107
6.2	Materials and Methods	109
6.2.1	Samples	109
6.2.2	Strain activation	109
6.2.3	Optimisation of fermentation parameters to develop a GABA-enriched fermented milk via OFAT	109
6.2.4	Immobilisation of <i>L. plantarum</i> B7 on watermelon rinds and apple pieces	110
6.2.5	Production of GABA-enriched fermented milk via immobilisation technique	111
6.2.6	Storage stability test	111
6.2.7	Physicochemical analysis	111
6.2.8	Sensory evaluation	112
6.2.9	Statistical Analysis	113
6.3	Results and Discussion	113
6.3.1	Optimisation of fermentation conditions for producing GABA-enriched fermented milk using OFAT	113
6.3.2	Storage stability test on GABA-enriched fermented milk	119
6.3.3	Physicochemical characteristics of fermented milk	125
6.3.4	Sensory properties	129

6.4	Summary	131
7	CONCLUSIONS AND RECOMMENDATIONS FOR FUTURE RESEARCH	132
7.1	Conclusions	132
7.2	Recommendations for future research	133
	REFERENCES	136
	APPENDICES	172
	BIODATA OF STUDENT	184
	LIST OF PUBLICATIONS	185



LIST OF TABLES

Table	Page
2.1 GABA-producing LAB	13
2.2 Various LAB isolates from different sources produce GABA under optimised fermentation conditions	18
2.3 GABA-enriched foods	31
4.1 Two-level factorial design (coded) and response value	62
4.2 Regression analysis of two-level factorial design experiment	74
4.3 Experimental design and corresponding response of steepest ascent	75
4.4 Experimental design and the result of CCD	77
4.5 Regression analysis a reduced second-order polynomial model for GABA concentration and growth optimisation of <i>Lactiplantibacillus plantarum</i> B7	79
5.1 Numbers of <i>Lactiplantibacillus plantarum</i> B7 cells immobilised and retained on various fruit samples incubated for 63.66 h at 35.6°C	93
5.2 Numbers of <i>Lactiplantibacillus plantarum</i> B7 cells immobilised and retained on various fruit waste samples incubated for 63.66 h at 35.6 °C	95
5.3 Numbers of cells immobilised and retained at 12 th cycle of fermentation	100
5.4 Total successful GABA and lactic acid production from various samples in RBF	105
6.1 <i>Lactiplantibacillus plantarum</i> B7's GABA production and final pH of fermented milk using research-grade and food-grade MSG and PLP	119
6.2 Total mean score of free cells fermented milk (FCFM), watermelon rind biocatalyst fermented milk (WRBFM) and apple biocatalyst fermented milk (ABFM)	130

LIST OF FIGURES

Figure		Page
2.1	GABA synthesis mechanism in bacteria. GDH, L-glutamate dehydrogenase; GAD, glutamate decarboxylase; GABA-AT, GABA aminotransferase; SSADH, succinate semialdehyde dehydrogenase	11
3.1	An image of B7 isolate (from <i>Budu</i> food sample) surrounded by yellow zone on Bromocresol purple agar (BCP)	43
3.2	B7 isolate (from <i>Budu</i> food sample) observed as catalase negative (A) due to no bubble formation; oxidase negative (B), due to no blue colour ring formation around the colonies; Gram positive (C) due to stained purple colour under magnification of microscope at 10×	44
3.3	Isolates (d) B7, (e) B8, (f) B9, (g) B10, (h) B11 and (i) B12 from <i>Budu</i> food sample observed with reddish orange colour spot at the same level and colour of (c) 1% GABA standard spot. (a) MRS media and (b) 1% monosodium glutamate	45
3.4	GABA concentration (g/L) of 37 LAB isolates after 24 hours when inoculated into MRS medium supplied with 1% MSG. (K1-K14 isolates) isolated from <i>Kimchi</i> ; (B1-B13 isolates) isolated from <i>Budu</i> ; (C1-C12 isolates) isolated from <i>Cinca</i> lok	45
3.5	Neighbour-joining tree derived from 16S rDNA sequence data of potential GABA-producing isolate (B7) and other closely related species	47
3.6	Survival of <i>Lactiplantibacillus plantarum</i> B7 exposed to acid (A) and bile salts (B) for 4 h, and phenol (C) for 24 h	51
3.7	Cell surface hydrophobicity of <i>Lactiplantibacillus plantarum</i> B7 towards various solvent (A) and cell auto-aggregation at different incubation time (B)	52
3.8	<i>Lactiplantibacillus plantarum</i> B7 DPPH free radical scavenging activity after 24 h of incubation at 37°C	54
3.9	Antibacterial activity (inhibition zone diameter, mm) of <i>Lactiplantibacillus plantarum</i> B7 and 10 µg ampicillin (positive control) against various pathogenic bacteria	56

4.1	Cell density (OD 600nm), viable cell count (log CFU/mL), reducing sugar (g/L), MSG depletion (g/L) and GABA production by <i>Lactiplantibacillus plantarum</i> B7 in MRS medium containing 1% of MSG	65
4.2	(A) The effects of 1% (w/v) of carbon, (C) nitrogen sources and (E) 2 ppm of growth factors; (B) the effects of glucose and (D) yeast extract concentrations; (F) the effects of different combination of selected growth factors (at 2 ppm) on GABA production by <i>Lactiplantibacillus plantarum</i> B7 in MRS medium containing 1% of MSG for 24 h of fermentation	69
4.3	Response surface curve with corresponding contour plots for the interactions that affect GABA production significantly. (a and b) interaction between AB, (c and d) interaction between AC and (e and f) interaction between BC	81
4.4	Response surface curve with corresponding contour plots for the interactions that affect cell growth significantly. (a and b) interaction between AB, (c and d) interaction between AC and (e and f) interaction between AE	83
5.1	<i>Lactiplantibacillus plantarum</i> B7 immobilised on apple fruit pieces (a) and watermelon rind pieces (b)	89
5.2	The effects of <i>Lactiplantibacillus plantarum</i> B7 immobilised on various fruit samples on lactic acid, GABA concentration and final pH of the fermentation medium after incubating for 63.66 h at 35.6 °C with 125 rpm	93
5.3	The effects of <i>Lactiplantibacillus plantarum</i> B7 immobilised on various fruit waste samples on lactic acid, GABA concentration and final pH of the fermentation medium after incubating for 63.66 h at 35.6 °C with 125 rpm	94
5.4	GABA production at various cycles by whole-cell immobilised <i>Lactiplantibacillus plantarum</i> B7 on watermelon rind, apple and free cell as a control. Successful GABA production cycle is noticed above black line (free cell), green line (watermelon rind biocatalyst) and red line (apple biocatalyst)	98
5.5	Lactic acid concentration at various cycles by whole-cell immobilised <i>Lactiplantibacillus plantarum</i> B7 on watermelon rind, apple and free cell as a control. Successful lactic acid production cycle is noticed above	99

	black line (free cell), green line (watermelon rind biocatalyst) and red line (apple biocatalyst)	
5.6	Final pH of the sample containing whole-cell immobilised <i>Lactiplantibacillus plantarum</i> B7 on watermelon rind, apple and free cell as a control at various cycles	99
5.7	Free cell count within the fermentation medium for three different samples (free cell sample, watermelon rind biocatalyst sample and apple biocatalyst sample) at various cycles	100
5.8	Scanning electron microscopic image of whole-cell immobilised <i>Lactiplantibacillus plantarum</i> B7 on watermelon rind before the fermentation (a) and after the 12 th cycle of fermentation (b); whole-cell immobilised <i>Lactiplantibacillus plantarum</i> B7 on apple pieces before the fermentation (c) and after the 12 th cycle of fermentation (d)	101
5.9	Watermelon rind biocatalyst before fermentation (a) and after 12 th cycle fermentation (b). Apple fruit biocatalyst before fermentation (c) and after 12 th cycle fermentation (d)	103
6.1	(A) The effects of various skim milk concentrations and initial pH on GABA production and final pH by <i>Lactiplantibacillus plantarum</i> B7 incubated at 35.6°C for 24 h of fermentation	115
6.2	Final pH and GABA production (g/L) by <i>Lactiplantibacillus plantarum</i> B7 inoculated in (A) various food-grade MSG (<i>Ajinomoto</i>) and (B) various research-grade MSG concentration in 10% (w/v) of skim milk incubated for 24 h at 35.6°C with 125 rpm	116
6.3	Final pH and GABA production (g/L) by <i>Lactiplantibacillus plantarum</i> B7 inoculated in (A) various food-grade PLP (Vitamin B6) concentration (in 10% (w/v) of skim milk containing 50 mM of food-grade MSG) and (B) various research-grade PLP concentration (in 10% (w/v) of skim milk containing 50mM of research-grade MSG), incubated for 24 h at 35.6°C with 125 rpm	117
6.4	Final pH and GABA production (g/L) by <i>Lactiplantibacillus plantarum</i> B7 inoculated in (A) 10% of skim milk containing 50 mM of food-grade MSG and 0.3 mM of food-grade PLP; (B) 10% of skim milk containing 50 mM of research-grade MSG and 0.6mM research-grade PLP, incubated at 35.6°C with 125 rpm for various incubation periods	118

6.5	Various storage period at 4°C against GABA (A), lactic acid production (B), antioxidant activity (C), pH (D) and viable cell count (E) of <i>Lactiplantibacillus plantarum</i> B7 in different types of fermented milk produced using an optimised food-grade fermentative medium under optimised conditions	124
6.6	Titratable acidity (A), water-holding capacity (B), viscosity (C) of various types of GABA-enriched fermented milk produced by <i>Lactiplantibacillus plantarum</i> B7. Correlation of shear stress and shear rate (D) of various fermented milks	128
6.7	Sensory pattern of free cell fermented milk (FCFM), watermelon rind biocatalyst fermented milk (WRBFM) and apple biocatalyst fermented milk (ABFM)	130

LIST OF APPENDICES

Appendix		Page
A	Microscopic image of <i>Lactiplantibacillus plantarum</i> B7 under 100× resolution	172
B	Determination of GABA using colorimetric method	173
C	Determination of antibacterial activity of <i>Lactiplantibacillus plantarum</i> B7 using agar well diffusion method	175
D	Determination of reducing sugar using DNS method	176
E	Determination of glutamic acid concentration using glutamate assay kit	178
F	GABA-producing fermentation with whole-cell immobilisation technique using natural support	180
G	Determination of lactic acid concentration using spectrophotometric method	181
H	GABA production from free cell and natural support immobilised <i>Lactiplantibacillus plantarum</i> B7 using optimised medium and condition	182
I	GABA-enriched fermented milk from free cell and natural support immobilised <i>Lactiplantibacillus plantarum</i> B7 under optimum condition	183

LIST OF ABBREVIATIONS

%	Percentage
°C	Degree celcius
μL	Microliter
ABAL	4-aminobutyaldehyde
ACE	Angiotensin converting enzyme
Al (NO ₃) ₃ ·9H ₂ O	Aluminium nitrate nonahydrate
AMADH	Aminoaldehyde dehydrogenase
ANN	Artificial neural network
ANOVA	Analysis of variance
BBD	Box-Behnken design
BCP	Bromocresol purple agar
BLASTn	Basic local alignment search tool of nucleotide
Ca ²⁺	Calcium cation
CaCl ₂	Calcium chloride
CaCO ₃	Calcium carbonate
CCD	Central composite design
CFS	Cell-free supernatant
CFU/mL	Colony forming unit per milliliter
CGTase	Cyclodextrin glycosyltransferases
cm ³	Cubic centimeter
CuSO ₄ ·5H ₂ O	Copper sulphate pentahydrate
d	Day
DAO	Diamine oxidase

df	Degree of freedom.
DNA	Deoxyribonucleic acid
dNTP	Deoxynucleotides triphosphates
DPPH	2,2-diphenyl-1-picrylhydrazyl
FeCl ₃ ·6H ₂ O	Iron (III) chloride hexahydrate
g	Gram
<i>g</i>	<i>g</i> force
GABA	Gamma-aminobutyric acid
GABA-AT	GABA aminotransferase
GAD	Glutamic acid decarboxylase
GDH	L-glutamate dehydrogenase
gDNA	Genomic deoxyribonucleic acid
GIT	Gastrointestinal tract
GLA	Gamma-linolenic acid
Glu	Glutamate
GRAS	Generally Recognized as Safe
h	Hour
H ⁺	Hydrogen ion
H ₂ O	Water
H ₂ O ₂	Hydrogen peroxide
HCl	Hydrochloric acid
HEMA	2-hydroxyethyl methacrylate
HVZ	Hell-Volhard-Zelinsky
IgA	Immune globulin A
K ₂ HPO ₄	Dipotassium hydrogen phosphate

kg	Kilogram
KH_2PO_4	Monopotassium phosphate
KNO_3	Potassium nitrate
L	Liter
LAB	Lactic acid bacteria
M	Molar
mg	Milligram
$\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$	Magnesium sulphate heptahydrate
min	Minutes
mL	Milliliter
mM	Millimolar
mm	millimeter
MnSO_4	Manganese sulphate
$\text{MnSO}_4 \cdot \text{H}_2\text{O}$	Manganese (II) sulphate monohydrate
mol	Mole
MRS	Man, Rogosa, and Sharpe
MSG	Monosodium glutamate
NaCl	Sodium Chloride
NAD	Nicotinamide adenine dinucleotide
NADPNa_2	Nicotinamide adenine dinucleotide phosphate disodium
NaOH	Sodium hydroxide
NCBI	National Centre Biotechnology Information
NH_4NO_3	Ammonium nitrate
nm	Nanometer

O ₂	Oxygen
OD	Optical density
OFAT	One-factor-at-a-time
PA	Polyamine
PAO	Polyamine oxidase
PBS	Phosphate buffered saline
PCR	Polymerase chain reaction
PEGDA	Polyethylene glycol diacrylate
PLP	Pyridoxal-5'-phosphate
pmol	Picomoles
ppm	Parts per million
Put	Putrescine
R^2	Correlation determination
R^2_{Adj}	Adjusted coefficients of determination
RBF	Repeated batch fermentation
rDNA	Recombinant deoxyribonucleic acid
ROS	Reactive oxygen species
rpm	Revolutions per minute
RSM	Response surface methodology
sec	Second
SBH	Soybean hydrolysate
SEM	Standard error of mean
SEM	Scanning electron microscopy
Spd	Spermidine
Spm	Spermine

SSADH	Succinate semialdehyde dehydrogenase
TCA	Tricarboxylic acid cycle
TLC	Thin-layer chromatography
UHT	Ultra-high temperature
UNiCC	Microbial culture Collection Unit
v/v	Volume per volume
VB	Vitamin B
w/v	Weight per volume
WHC	Water-holding capacity
Zn (CH ₃ COO) ₂ ·2H ₂ O	Zinc acetate dihydrate
β-CD	Beta-Cyclodextrin
μg	Microgram
μM	Micromolar
μm	Micrometer

CHAPTER 1

INTRODUCTION

Gamma-aminobutyric acid (GABA), a non-protein amino acid where the amino group is attached to γ -carbon, is widely spread in nature (Guo *et al.*, 2023). The primary enzyme, glutamic acid decarboxylase (GAD), is responsible for catalysing the irreversible α -decarboxylation of L-glutamic acid to GABA in the presence of the coenzyme pyridoxal-5'-phosphate (PLP) (Yogeswara *et al.*, 2020; Wu *et al.*, 2018). The history of GABA began in the early 1880s; where the first chemical synthesis of GABA was reported, and it was recognised as a natural metabolite product of plants and microbes (Diez-Gutiérrez *et al.*, 2020; Wu *et al.*, 2018). Later, in 1950, GABA's role as a significant inhibitory neurotransmitter in the human brain system was recognised.

GABA is a well-known bioactive compound for its numerous physiological and pharmacological roles in humans (Guo *et al.*, 2023; Ochoa-de la Paz *et al.*, 2021). This has given rise to innovative ideas and ground-breaking approaches to develop more effective GABA-based medicinal interventions for various diseases, including diabetes, cancer, asthma, cardiovascular, nervous system, and brain disorders (Diez-Gutiérrez *et al.*, 2020; Grewal, 2020). Numerous organisms, including bacteria, yeasts, fungi, moulds, mammals, and plants have been studied as potential natural sources of GABA (Sahab *et al.*, 2020). However, GABA from microbes has received more attention because the factors influencing its production are easier to control compared to plants that have low concentrations of GABA and animals which have GABA that cannot cross the blood-brain barrier, thus limiting its function for the human body (Sahab *et al.*, 2020; Gasmi *et al.*, 2022).

Chemical and biosynthetic (enzymatic or whole-cell biocatalysis and microbial fermentation) methods are the two major approaches to produce GABA (Oketch-Rabah *et al.*, 2021; Yogeswara *et al.*, 2020). Although the chemical route is relatively simple and fast, the biosynthetic approach is preferred for the synthesis of GABA because the reaction process is easier and involves milder reaction conditions, high product yield and catalytic efficiency, as well as more sustainable and environmentally friendly (Lyu *et al.*, 2022). Additionally, the chemical synthesis approach is less effective for producing GABA, particularly in the food industry, due to the use of potentially hazardous or corrosive chemicals, low selectivity, producing unwanted byproducts, and potential environmental contamination issues (Oketch-Rabah *et al.*, 2021). Through enzymatic or whole-cell biocatalysis approaches, isolated GADs or recombinant host strains expressing GAD act as catalysts for the biotransformation of L-glutamate to GABA. The enzymatic properties of the chosen GADs contribute to the efficient GABA production in these systems. Although these approaches are able to produce mass GABA titers, the complexity and expensive operational processes favour microbial fermentation for GABA production (Grewal, 2020). Furthermore,

GABA produced through fermentation by naturally occurring microbes is preferred due to the growing demand for naturally-made nutritional supplies (Wan-Mohtar *et al.*, 2020), inexpensive, safe, and can be directly marketable as a functional food item (Diez-Gutiérrez *et al.*, 2020).

Lactic acid bacteria (LAB), *Streptococcus salivarius* and *Escherichia coli* are among the most studied microorganisms to produce GABA naturally (Kim *et al.*, 2022a; Yogeswara *et al.*, 2020). Among these, many researchers prefer LAB for GABA synthesis due to its readily available nature, distinct physiological characteristics, and generally recognized as safe (GRAS) status (Kim *et al.*, 2022a). Numerous LAB species from various sources, particularly those derived from fermented foods, have shown the ability to biosynthesise GABA at various levels (Cui *et al.*, 2020). However, it is still insufficient to meet the market demand for the production of GABA-related or GABA-enriched products by using the natural GABA production capabilities of LAB. Therefore, optimisation of the fermentation medium and fermentation parameters (temperature, initial pH, initial monosodium glutamate (MSG) concentration, initial pyridoxal-5'-phosphate (PLP) concentration, and incubation time) could be used to increase the GABA titer (Thuy *et al.*, 2021; Cai *et al.*, 2023). One-factor-at-a-time (OFAT), orthogonal design, artificial neural network (ANN) and response surface methodology (RSM) are some examples of the optimisation techniques that can be used to improve GABA production (Wu *et al.*, 2018). For instance, according to Wu *et al.* (2018) and Park *et al.* (2021), optimisation using the OFAT method produced a maximum GABA up to 62.523 g/L by *Levilactobacillus brevis* RK03 and 19.8 g/L by *Lactiplantibacillus plantarum* EJ2014, respectively. Also, various studies used RSM to improve GABA levels; for example, Sharafi and Nateghi (2020), produced the highest GABA (19.9 g/L) by *Levilactobacillus brevis* TD10 using Box-Behnken's RSM. Besides that, *Lactiplantibacillus plantarum* FRT7 produced the maximum GABA content (1158.6 ± 21.22 mg/L) after being optimised using the central composite design's RSM (Cai *et al.*, 2023).

Immobilisation techniques are widely used approaches to improve various metabolic productions and cell viability. Accordingly, various studies have been conducted to investigate GABA production employing whole cell and/or GAD enzyme immobilisation approaches (Dahiya *et al.*, 2021; Son *et al.*, 2022). Due to expensive purification procedures and rapid loss of function, whole-cell immobilisation is preferred over using immobilised GAD to produce GABA (Son *et al.*, 2022). For example, gellan gum-immobilised *Levilactobacillus brevis* GadA Δ C14 was found to produce up to 87.56 g/L of GABA under optimal experimental conditions for ten consecutive reaction cycles (Lyu *et al.*, 2019). However, due to the limitations of using both natural and synthetic polymers as whole-cell carriers, natural supports from plant-based materials as carriers have attracted more attention from researchers (Bisht *et al.*, 2023). Besides, plant sources are commonly used as whole-cell matrices due to their low cost, widespread nature, and sustainable agro-waste management. In particular, fruit and fruit waste, are among the most highly investigated plant sources to improve various targeted productions and cell stability (Budžaki *et al.*, 2022; Vitola *et al.*, 2020).

Repeated batch fermentation (RBF) is a technique that is frequently used in a variety of microbiological productions, particularly those derived from bacteria and yeast, such as ethanol, lipids, and organic acids (Sriputorn *et al.*, 2023; Rahman *et al.*, 2021; Luongo *et al.*, 2019). Its benefits over conventional batch fermentation include the preparation of a single inoculum for multiple batches, higher and sustained productivity in a short duration, and more user-friendly operational control than continuous mode (Sriputorn *et al.*, 2023). Numerous studies have employed RBF combined with an immobilisation strategy to further enhance various targeted production (Sriputorn *et al.*, 2023; Milessi *et al.*, 2020; Ng *et al.*, 2020; Chen *et al.*, 2019).

The synthesis of pure GABA or GABA-related products in various sectors, such as the pharmaceutical, agro-chemical, and food industries, has increased in demand due to its vast health benefits (Gramazio *et al.*, 2020; Xie *et al.*, 2019). However, due to the various challenges of developing pure GABA (as a supplement or medicine) from natural sources, simpler, cheaper, and more effective GABA-containing products such as GABA-enriched functional foods can be excellent alternative products. Among numerous GABA-enriched functional foods, GABA-enriched dairy products, particularly fermented milk, are in high demand. However, the quantity of GABA produced by natural bacteria in fermented milk is often very low (Santos-Espinosa *et al.*, 2020). This could be improved by optimisation of fermentation conditions and medium (Sharafi & Nateghi, 2020; Galli *et al.*, 2022) along with whole-cell immobilisation technique. Besides enhancing productivity, whole-cell immobilisation fruits and fruit wastes could also improve cell stability and the sensory qualities of the fermented milk (Kandyliis *et al.*, 2021; Ng *et al.*, 2020; Jasińska *et al.*, 2018).

The beneficial effects of GABA in humans are hindered by the presence of the blood-brain barrier, which restricts the flow of it beyond the central nervous system (CNS). To overcome this limitation, GABA requires uptake from external sources such as plants (vegetables and fruits), animals (meat), and microorganisms. However, most vegetables and fruits contain a relatively low amount of GABA and the efforts to enhance their GABA production levels are challenging. On the other hand, there is currently no substantial evidence or research supporting meat as a significant GABA source. Furthermore, GABA sourced from meat is not ideal for vegan and vegetarian communities. This brings the focus to microorganisms, particularly naturally occurring lactic acid bacteria, as a preferred and highly sought-after source of GABA. Nevertheless, the GABA generated spontaneously by these bacteria is insufficient to exhibit its advantageous benefits.

Therefore, this study was focused on improving GABA production by naturally GABA-producing lactic acid bacteria, *Lactiplantibacillus plantarum* B7, that have been isolated from fermented food (*Budu*). The production of GABA and the cell viability of *L. plantarum* B7 were improved via a combination of optimisation approaches, followed by further enhancement of the production of GABA and lactic acid using a whole-cell immobilisation strategy with repeated batch fermentation using natural supports (selected fruits and fruit wastes). The study

also describes an application of GABA by developing a novel GABA-enriched fermented milk using an optimisation and whole-cell immobilisation approaches using the ideal fruit and fruit waste supports. The specific objectives of this study were:

1. To screen, identify and characterise GABA-producing LAB from various fermented food sources.
2. To optimise the experimental conditions and fermentative medium to produce maximum GABA using selected LAB.
3. To characterise for the ideal natural supports for the immobilisation of *Lactiplantibacillus plantarum* B7 and further improve the GABA production via repeated batch fermentation using optimised experimental conditions.
4. To develop and analyse GABA-enriched fermented milks produced through selected natural supports immobilised *Lactiplantibacillus plantarum* B7 under optimised fermentation parameters.

REFERENCES

- Ab Kadir, S., Wan-Mohtar, W.A.A.Q.I., Mohammad, R., Abdul Halim Lim S., Mohammed, A.S. and Saari, S. (2016). Evaluation of commercial soy sauce koji strains of *Aspergillus oryzae* for γ -aminobutyric acid (GABA) production. *Journal of Industrial Microbiology and Biotechnology* 43(10):1387–1395.
- Abd El-Fattah, A., Sakr, S., El-Dieb, S. and Elkashef, H. (2018). Developing functional yogurt rich in bioactive peptides and gamma-aminobutyric acid related to cardiovascular health. *Food Science and Technology* 98:390–397.
- Abdel-Rahman, M.A., Hassan, S.E.D., Azab, M.S., Mahin, A.A. and Gaber, M.A. (2019). High improvement in lactic acid productivity by new alkaliphilic bacterium using repeated batch fermentation integrated with increased substrate concentration. *BioMed Research International* 1–13.
- Abdel Tawab, F.I., Abd Elkadr, M.H., Sultan, A.M., Hamed, E.O., El-Zayat, A.S. and Ahmed, M.N. (2023). Probiotic potentials of lactic acid bacteria isolated from Egyptian fermented food. *Scientific Reports* 13(1):16601.
- Abdualrahm, M.A.Y., Olayinka, B.U. and Etejere, E.O. (2018). Comparative study between local and imported apple (*Malus domestica*) fruits and their uses in juice production. *Science International* 3(2):1060–1066.
- Abdul Rahman, I., Mohd Lazim, M.I., Mohamad, S., Peng, K.S., Othaman, M.A., Abdul Manan, M. and Mohd Asri, M.A. (2018). The influence of lactobacilli in GABA and amino acid profile of fermented mature coconut water. *The Open Food Science Journal* 10:8–15.
- Abdullah, A., Winaningsih, I. and Hadiyanto, A. (2021). Lactic acid fermentation from durian seeds (*Durio zibethinus* Murr.) using *Lactobacillus plantarum*. *IOP Conference Series: Materials Science and Engineering* 1053(1):12032.
- Aeron, G. and Shiwangi, M. (2017). Immobilisation and microencapsulation. *Journal of Advanced Research in Biotechnologies* 2(3):1–4.
- Ahmad, F., Mahmud, M.F., Ali, N.S.C., Ayub, M.N.A., Mohamad, S.N., Ismail, N., Chilek, T. Z.T., Zamri, A.I. and Khalid, M.I. (2019). Determination of proximate composition and amino acid profile of *Budu* from Setiu, Terengganu and Tumpat, Kelantan. *Asian Journal of Agriculture and Biology* 7:61–68.
- Aidilfitri, M., Roslan, M., Sohedein, I., Ling, P.S., Sobri, Z.M., Tan, A., Zuan, K., Cheak, S.C., Aini, N. and Rahman, A. (2021). Sustainable agronomic valorization of unsulfured molasses and defatted soybean meal as an optimised formulation of bio-organic fertilizer enriched with high cell density *p*-solubilizing bacteria. *Agronomy* 11(5):996.

- Al-Sayed, H.M.A. and Ahmed, A.R. (2013). Utilisation of watermelon rinds and sharlyn melon peels as a natural source of dietary fiber and antioxidants in cake. *Annals of Agricultural Sciences* 58(1):83–95.
- Allgeyer, L.C., Miller, M.J. and Lee, S.Y. (2010). Sensory and microbiological quality of yogurt drinks with prebiotics and probiotics. *Journal of Dairy Sciences* 93(10):4471–4479.
- Almeida, D.P., Gíão, M.S., Pintado, M. and Gomes, M.H. (2017). Bioactive phytochemicals in apple cultivars from the Portuguese protected geographical indication “Maçã de Alcobaça:” Basis for market segmentation. *International Journal of Food Properties* 20(10):2206–2214.
- Altieri, C., Campaniello, D., Speranza, B., Sinigaglia, M., Corbo, M.R. and Bevilacqua, A. (2019). Immobilization of *Saccharomyces cerevisiae* on apple pieces to produce cider. *Fermentation* 5(3):74.
- Amenaghawon, N., Oiwoh, O. and Ebewe, O. (2015). Optimisation of solid-state fermentation of banana peels for citric acid production. *Nigerian Journal of Technology* 34(4):716.
- Ando, A. and Nakamura, T. (2016). Prevention of GABA reduction during dough fermentation using a baker's yeast dal81 mutant. *Journal of Bioscience and Bioengineering* 122:441–445.
- Anggraini, L., Marlida, Y., Mirzah, M., Wizna, W., Jamsari, A. and Huda, N. (2019). Isolation and characterisation of lactic acid bacteria producing GABA from indigenous West Sumatera fermented food. *International Journal on Advanced Science, Engineering and Information Technology* 9(3):855–860.
- Ariyajarearnwong, P., Laopaiboon, L., Jaisil, P. and Laopaiboon, P. (2011). Repeated-batch ethanol fermentation from sweet sorghum juice by free cells of *Saccharomyces* NP 01. *African Journal of Biotechnology* 10(63):13909–13918.
- Aroua, M., Ben Haj Koubaier, H., Bouacida, S., Ben Saïd, S., Mahouachi, M. and Salimei, E. (2023). Chemical, physicochemical, microbiological, bioactive, and sensory characteristics of cow and donkey milk kefir during storage. *Beverages* 9(1):2.
- Asma, U., Morozova, K., Ferrentino, G. and Scampicchio, M. (2023). Apples and apple by-products: antioxidant properties and food applications. *Antioxidants* 12(7):1–17.
- Asun, A.C., Lin, S.T., Ng, H.S. and Lan, J.C.W. (2022). Production of gamma-aminobutyric acid (GABA) by *Bacillus subtilis* BBEL02 fermentation using nitrogen-rich industrial wastes as crude feedstocks. *Biochemical Engineering Journal* 187:108654.

- Ayyash, M., Abdalla, A., Abu-Jdayil, B., Huppertz, T., Bhaskaracharya, R., Al-Mardeai, S., Mairpady, A., Ranasinghe, A. and Al-Nabulsi, A. (2022). Rheological properties of fermented milk from heated and high pressure-treated camel milk and bovine milk. *Food Science and Technology* 156:113029.
- Aziz, M., Anwar, M., Uddin, Z., Amanat, H., Ayub, H. and Jadoon, S. (2013). Nutrition comparison between genus of apple (*Malus sylvestris* and *Malus domestica*) to show which cultivars is best for the province of Balochistan. *Journal of Asian Scientific Research* 3(4):417–424.
- Balakrishnan, G. and Agrawal, R. (2014). Antioxidant activity and fatty acid profile of fermented milk prepared by *Pediococcus pentosaceus*. *Journal of Food Science and Technology* 51:4138–4142.
- Balasingham, K., Valli, C., Radhakrishnan, L. and Balasuramanyam, D. (2017). Probiotic characterisation of lactic acid bacteria isolated from swine intestine. *Veterinary World* 10(7):825.
- Barkema, H.W., von Keyserlingk, M.A., Kastelic, J.P., Lam, T.J., Luby, C., Roy, J.P., LeBlanc, S.J., Keefe, G.P. and Kelton, D.F. (2015). Invited review: Changes in the dairy industry affecting dairy cattle health and welfare. *Journal of dairy science* 98(11):7426-7445.
- Barla, F., Koyanagi, T., Tokuda, N., Matsui, H., Katayama, T., Kumagai, H., Michihata, T., Sasaki, T., Tsuji, A. and Enomoto, T. (2016). The γ -aminobutyric acid-producing ability under low pH conditions of lactic acid bacteria isolated from traditional fermented foods of Ishikawa Prefecture, Japan, with a strong ability to produce ACE-inhibitory peptides. *Biotechnology Reports* 10:105–110.
- Batra, V., Lomash, H. and Ganguli, A. (2018). Fermentation of groundnut brittle by *Lactococcus lactis* produces by γ -amino butyric acid and enhances nutritional quality and safety. *Food Quality and Safety* 2(2):83–87.
- Behbahani, B.A., Jooyandeh, H., Falah, R. and Vasiee, A. (2020). Gamma-aminobutyric acid production by *Lactobacillus brevis* A3: Optimisation of production, antioxidant potential, cell toxicity, and antimicrobial activity. *Food Science & Nutrition* 8(10):5330–5339.
- Benítez-Chao, D.F., León-Buitimea, A., Lerma-Escalera, J.A. and Morones-Ramírez, J.R. (2021). Bacteriocins: An overview of antimicrobial, toxicity, and biosafety assessment by *in-vivo* models. *Frontiers in Microbiology* 12:630695.
- Bhanwar, S., Bamnia, M., Chosh, M. and Ganguli, A. (2013). Use of *Lactococcus lactis* to enrich sourdough bread with γ -aminobutyric acid. *International Journal of Food Sciences and Nutrition* 64(1):77–81.
- Binh, T.T.T., Ju, W.T., Jung, W.J. and Park, R.D. (2014). Optimisation of γ -amino butyric acid production in a newly isolated *Lactobacillus brevis*.

- Biratsi, A., Athanasopoulos, A., Kouvelis, V.N., Gournas, C. and Sophianopoulou, V. (2021). A highly conserved mechanism for the detoxification and assimilation of the toxic phytoproduct L-azetidine-2-carboxylic acid in *Aspergillus nidulans*. *Science Reports* 11:7391.
- Bisht, M., Thayallath, S.K., Bharadwaj, P., Franklin, G. and Mondal, D. (2023). Biomass-derived functional materials as carriers for enzymes: Toward sustainable robust biocatalysts. *Green Chemistry* 25(12):4591-4624.
- Bolmanis, E., Dubencovs, K., Suleiko, A. and Vanags, J. (2023). Model predictive control—A stand out among competitors for fed-batch fermentation improvement. *Fermentation* 9(3):206.
- Bonet-Fernández, J.M., Tranque, P., Aroca-Aguilar, J.D., Muñoz, L.J., López, D.E., Escribano, J. and de Cabo, C. (2023). Seizures regulate the cation-Cl⁻ cotransporter NKCC1 in a hamster model of epilepsy: Implications for GABA neurotransmission. *Frontiers in Neurology* 14:1207616.
- Borshchevskaya, L.N., Gordeeva, T.L., Kalinina, A.N. and Sineokii, S.P. (2016). Spectrophotometric determination of lactic acid. *Journal of Analytical Chemistry* 71:755–758.
- Boyer, J.L. and Soroka, C.J. (2021). Bile formation and secretion: an update. *Journal of Hepatology* 75(1):190–201.
- Brzozowska, A., Burdan, F., Duma, D., Solski, J. and Mazurkiewicz, M. (2017). γ -amino butyric acid (GABA) level as an overall survival risk factor in breast cancer. *Annals of Agricultural and Environmental Medicine* 24(3):435–439.
- Budžaki, S., Velić, N., Ostojčić, M., Stjepanović, M., Rajs, B.B., Šereš, Z., Maravić, N., Stanojev, J., Hessel, V. and Strelec, I. (2022). Waste management in the agri-food industry: The conversion of eggshells, spent coffee grounds, and brown onion skins into carriers for Lipase immobilization. *Foods* 11(3):409.
- Buranakhajorn, S. and Chauvatcharin, S. (2016). Process development for γ -aminobutyric acid (GABA) production by biotransformation. *Suranaree Journal of Science and Technology* 23(3):367-378
- Burke, N., Zacharski, K.A., Southern, M., Hogan, P., Ryan, M.P. and Adley, C.C. (2018). The dairy industry: process, monitoring, standards, and quality. *Descriptive food science* 162: doi: 10.5772/intechopen.80398.
- Burnison, H., Granato, T., King, M., Peoples, H. and Hallidayschult, T. (2018). The effect of monosaccharides versus disaccharides on the rate of CO₂ production. *Journal of Undergraduate Biology Laboratory Investigations* 1(1):1–4.
- Cai, H., Li, X., Li, D., Liu, W., Han, Y., Xu, X., Yang, P. and Meng, K. (2023).

Optimisation of gamma-aminobutyric acid production by *Lactiplantibacillus plantarum* FRT7 from Chinese paocai. *Foods* 12(16):3034.

Campaniello, D., Bevilacqua, A., Speranza, B., Sinigaglia, M. and Corbo, M.R. (2020). Alginate-and gelatin-coated apple pieces as carriers for *Bifidobacterium animalis* subsp. *lactis* DSM 10140. *Frontiers in Microbiology* 11:566596.

Carafa, I., Stocco, G., Nardin, T., Larcher, R., Bittante, G., Tuohy, K. and Franciosi, E. (2019). Production of naturally γ -aminobutyric acid-enriched cheese using the dairy strains *Streptococcus thermophilus* 84C and *Lactobacillus brevis* DSM 32386. *Frontiers Microbiology* 10:19.

Cardoso, V.M., Campani, G., Santos, M.P., Silva, G.G., Pires, M.C., Gonçalves, V.M., de C. Giordano, R., Sargo, C.R., Horta, A.C.L. and Zangirolami, T.C. (2020). Cost analysis based on bioreactor cultivation conditions: Production of a soluble recombinant protein using *Escherichia coli* BL21. *Biotechnology Reports* 26:e00441.

Cataldo, P.G., Villena, J., Elean, M., Savoy de Giori, G., Saavedra, L. and Hebert, E.M. (2020a). Immunomodulatory properties of a γ -aminobutyric acid-enriched strawberry juice produced by *Levilactobacillus brevis* CRL 2013. *Frontiers Microbiology* 11:610016.

Cataldo, P.G., Villegas, J.M., Savoy de Giori, G., Saavedra, L. and Hebert, E.M. (2020b). Enhancement of γ -aminobutyric acid (GABA) production by *Lactobacillus brevis* CRL 2013 based on carbohydrate fermentation. *International Journal of Food Microbiology* 333:108792.

Cha, J.Y., Kim, Y.R., Beck, B.R., Park, J.H., Hwang, C.W. and Do, H.K. (2018). Production of γ -amino butyric acid by lactic acid bacteria in skim milk. *Journal of Life Science* 28(2):223–228.

Chandel, V., Biswas, D., Roy, S., Vaidya, D., Verma, A. and Gupta, A. (2022). Current advancements in pectin: Extraction, properties and multifunctional applications. *Foods* 11(17):2683.

Chen, C.C., Lan, C.C., Pan, C.L., Huang, M.Y., Chew, C.H., Hung, C.C., Chen, P.H. and Lin, H.T.V. (2019). Repeated-batch lactic acid fermentation using a novel bacterial immobilization technique based on a microtube array membrane. *Process Biochemistry* 87:25-32.

Chen, H.H., Cheng, P.W., Ho, W.Y., Lu, P.J., Lai, C.C., Tseng, Y.M., Fang, H.C., Sun, G.C., Hsiao, M., Liu, C.P. and Tseng, C.J. (2016). Renal denervation improves the baroreflex and GABA system in chronic kidney disease-induced hypertension. *Scientific Reports* 6:38447.

Chen, Y.S., Wu, H.C. and Yanagida, F. (2010). Isolation and characteristics of lactic acid bacteria isolated from ripe mulberries in Taiwan. *Brazilian Journal of Microbiology* 41:916–921.

- Chen, L., Alcazar, J., Yang, T., Lu, Z. and Lu, Y. (2018a). Optimised cultural conditions of functional yogurt for γ -aminobutyric acid augmentation using response surface methodology. *Journal of Dairy Science* 101(12):10685–10693.
- Chen, X., Wei, Z., Zhu, L., Yuan, X., Wei, D., Peng, W. and Wu, C. (2018b). Efficient approach for the extraction and identification of red pigment from *zanthoxylum bungeanum maxim* and its antioxidant activity. *Molecules* 23(5):1109.
- Cheng, F., Chen, H., Lei, N., Zhang, M. and Wan, H. (2019). Effects of carbon and nitrogen sources on activity of cell envelope proteinase produced by *Lactobacillus plantarum* LP69. *Acta Universitatis Cibiniensis. Series E: Food Technology* 23(1):11–18.
- China Agricultural University. (2015). Semicontinuous fermentation method for producing gamma-aminobutyric acid by lactic acid bacteria. (Patent No. CN102108370B).
- CODEX STAN 243. (2003). Codex Standard for fermented milks. (Adopted in 2003. Revised in 2008, 2010, 2018.). *International Foods Standards, Food and Agriculture Organization of the United Nations*. World Health Organization.
- Colakoglu, H. and Gursoy, O. (2011). Effect of lactic adjunct cultures on conjugated linoleic acid (CLA) concentration of yogurt drink. *Journal of Food, Agriculture and Environment* 9(1):60–64.
- Cui, L., Chang, S.K. and Nannapaneni, R. (2021). Comparative studies on the effect of probiotic additions on the physicochemical and microbiological properties of yoghurt made from soymilk and cow's milk during refrigeration storage (R2). *Food Control* 119:107474.
- Cui, Y., Miao, K., Niyaphorn, S. and Qu, X. (2020). Production of gamma-aminobutyric acid from lactic acid bacteria: A systematic review. *International Journal of Molecular Sciences* 21(3):1–21.
- Cuypers, K., Maes, C. and Swinnen, S.P. (2018). Aging and GABA. *Aging* 10(6):1186–1187.
- Dada, E.O., Alade, A.O., Adeniji, A.T. and Afolabi, T.J. (2023). Enhanced biohydrogen production through repeated-batch fermentation of rice-bran. *Scientific Study and Research. Chemistry and Chemical Engineering, Biotechnology, Food Industry* 24(1):25-40.
- Dagang, W.R.Z.W. and Zaidi, N.N. (2023). Isolation of biofilm-biofloculant producing bacteria from palm oil mill effluent. *Journal of Materials in Life Sciences (JOMALISC)* 2(1):115-122.
- Dahiya, D., Manuel, J. V. and Nigam, P. S. (2021). An overview of bioprocesses employing specifically selected microbial catalysts for γ -aminobutyric acid

- production. *Microorganisms* 9(12):2457.
- Dai, J., Fang, L., Zhang, M., Deng, H., Cheng, X., Yao, M. and Huang, L. (2022). Isolation and identification of new source of bacteriocin-producing *Lactobacillus plantarum* C010 and growth kinetics of its batch fermentation. *World Journal of Microbiology and Biotechnology* 38(4):67.
- Dantas, D.S., Lais, D., Viera, V.B., Soares, J.K.B., dos Santos, K.M.O., do Egito, A.S., de Figueirêdo, R.M.F., dos Santos Lima, M., Machado, N.A.F., de Souza, M.D.F.V., da Conceição, M.L. and do Egypto, R.D.C.R. (2022). *Pilosocereus gounellei* (xique-xique) flour: Improving the nutritional, bioactive, and technological properties of probiotic goat-milk yogurt. *Food Science and Technology* 158:113165.
- Darah, I., Nor-hawani, S., Hong, L., Rosma, A. and Haritharan, W. (2013). Pomelo peels as alternative substrate for extracellular pectinase production by *Aspergillus niger* HFM-8. *Malaysian Journal of Microbiology* 9(4):308–316.
- Das, K. and Roychoudhury, A. (2014). Reactive oxygen species (ROS) and response of antioxidants as ROS-scavengers during environmental stress in plants. *Frontiers in Environmental Science* 2:53.
- Dashti, M.G. and Abdesahian, P. (2016). Batch culture and repeated-batch culture of *Cunninghamella bainieri* 2A1 for lipid production as a comparative study. *Saudi journal of biological sciences* 23(2):172-180.
- Devi, P.B., Rajapuram, D.R., Jayamanohar, J., Verma, M., Kavitha, D., Avany, B.A.M., Rani, P.U., Ravi, R. and Shetty, P.H. (2023). Gamma-aminobutyric acid (GABA) production by potential probiotic strains of indigenous fermented foods origin and RSM based production optimization. *Food Science and Technology* 176:114511.
- Dhakar, R., Bajpai, V.K., Baek, K. and Korea, R. (2012). Production of GABA (γ -aminobutyric acid) by microorganisms: a review. *Brazilian Journal of Microbiology* 43:1230–1241.
- Diana, M., Rafecas, M., and Quílez, J. (2014a). Free amino acids, acrylamide and biogenic amines in gamma-aminobutyric acid enriched sourdough and commercial breads. *Journal of Cereal Science* 60(3):639–644.
- Diana, M., Quílez, J. and Rafecas, M. (2014b). Gamma-aminobutyric acid as a bioactive compound in foods: A review. *Journal of Functional Foods* 10:407–420.
- Diez-Gutiérrez, L., San Vicente, L., Luis, L.J., del Carmen Villarán, M. and Chávarri, M. (2020). Gamma-aminobutyric acid and probiotics: Multiple health benefits and their future in the global functional food and nutraceuticals market. *Journal of Functional Foods*, 64:103669.
- Diğrak, M., Bağci, E. and Alma, M.H. (2002). Antibiotic action of seed lipids from

- five tree species grown in Turkey. *Pharmaceutical Biology* 40(6):425–428.
- Dikshit, R. and Tallapragada, P. (2015). Screening and optimisation of γ -aminobutyric acid production from *Monascus sanguineus* under solid-state fermentation. *Frontiers in Life Science* 8(2):172–181.
- Dimitrellou, D., Kandyliis, P. and Kourkoutas, Y. (2019a). Assessment of freeze-dried immobilised *Lactobacillus casei* as probiotic adjunct culture in yogurts. *Foods* 8(9):374.
- Dimitrellou, D., Kandyliis, P., Petrović, T., Dimitrijević-Branković, S., Lević, S., Nedović, V. and Kourkoutas, Y. (2016). Survival of spray dried microencapsulated *Lactobacillus casei* ATCC 393 in simulated gastrointestinal conditions and fermented milk. *Food Science and Technology* 71:169–174.
- Dimitrellou, D., Salamoura, C., Kontogianni, A., Katsipi, D., Kandyliis, P., Zakyntinos, G. and Varzakas, T. (2019b). Effect of milk type on the microbiological, physicochemical and sensory characteristics of probiotic fermented milk. *Microorganisms* 7(9):1–8.
- Din, S.N., Mubarak, A., Lani, M.N., Yahaya, M.Z. and Wan Abdullah, W.Z. (2022). Development of pastilles from flesh and rind of watermelon. *Food Research* 6(3):288-297.
- Ding, T. and Li, Y. (2021). Beneficial effect and mechanism of walnut oligopeptide on *Lactobacillus plantarum* Z7. *Food Science and Nutrition* 9(2):672–681.
- El Bouchikhi, S., Pagès, P., El Alaoui, Y., Ibrahimi, A. and Bensouda, Y. (2019). Syneresis investigations of lacto-fermented sodium caseinate in a mixed model system. *BMC Biotechnology* 19:1-10.
- EL Moslamy, S.H. (2019). Application of fed-batch fermentation modes for industrial bioprocess development of microbial behaviour. *Annals of Biotechnology and Bioengineering* 1(1):1001.
- Fadzil, N.F. and Othman, S.A. (2021). The growing biorefinery of agricultural wastes: a short review. *Journal of Sustainable Natural Resources* 2(2):46–51.
- Falah, F., Vasiee, A., Alizadeh Behbahani, B., Tabatabaee Yazdi, F. and Mortazavi, S.A. (2021). Optimisation of gamma-aminobutyric acid production by *Lactobacillus brevis* PML1 in dairy sludge-based culture medium through response surface methodology. *Food Science and Nutrition* 9(6):3317–3326.
- Farvin, K.S., Baron, C.P., Nielsen, N.S., Otte, J. and Jacobsen, C. (2010). Antioxidant activity of yoghurt peptides: Part 2–Characterisation of peptide fractions. *Food Chemistry* 123(4):1090–1097.
- Fazilah, N.F., Hamidon, N.H., Ariff, A.B., Khayat, M.E., Wasoh, H. and Halim, M.

- (2019). Microencapsulation of *Lactococcus lactis* Gh1 with gum arabic and *Synsepalum dulcificum* via spray drying for potential inclusion in functional yogurt. *Molecules* 24:1422.
- Flores-Ramos, M., Salinas M., Carvajal-Lohr, A. and Rodríguez-Bores, L. (2017). The role of gamma-aminobutyric acid in female depression. *Gaceta Médica de México* 153:444-452.
- Galli, V., Venturi, M., Mari, E., Guerrini, S. and Granchi, L. (2022). Gamma-aminobutyric acid (GABA) production in fermented milk by lactic acid bacteria isolated from spontaneous raw milk fermentation. *International Dairy Journal* 127:105284.
- Ganjali Dashti, M., Abdesahian, P., Wan Yusoff, W.M., Kalil, M.S. and Abdul Hamid, A. (2014). Repeated batch fermentation biotechnology for the biosynthesis of lipid and gamma-linolenic acid by *Cunninghamella bainieri* 2A1. *BioMed Research International*: 831783.
- Gao, J., Lin, S., Gao, Y., Zou, X., Zhu, J., Chen, M., Wan, H. and Zhu, H. (2019). Pinocembrin inhibits the proliferation and migration and promotes the apoptosis of ovarian cancer cells through down-regulating the mRNA levels of N-cadherin and GABAB receptor. *Biomedicine and Pharmacotherapy* 120:109505.
- Gao, Q., Duan, Q., Wang, D., Zhang, Y. and Zheng, C. (2013). Separation and purification of γ -aminobutyric acid from fermentation broth by flocculation and chromatographic methodologies. *Journal of Agricultural and Food Chemistry* 61(8):1914–1919.
- García, A., Navarro, K., Sanhueza, E., Pineda, S., Pastene, E., Quezada, M., Henriquez, K., Karlyshev, A., Villena, J. and González, C. (2017). Characterisation of *Lactobacillus fermentum* UCO-979C, a probiotic strain with a potent anti-*Helicobacter pylori* activity. *Electronic Journal of Biotechnology* 25:75-83.
- Gardner-Fortier, C., St-Gelais, D., Champagne, C.P. and Vuilleumard, J.C. (2013). Determination of optimal conditions for γ -aminobutyric acid production by *Lactococcus lactis* ssp. *lactis*. *International Dairy Journal* 32(2):136–143.
- Gasmi, A., Nasreen, A., Menzel, A., Gasmi Benahmed, A., Pivina, L., Noor, S., Peana, M., Chirumbolo, S. and Bjørklund, G. (2022). neurotransmitters regulation and food intake: The role of dietary sources in neurotransmission. *Molecules* 28(1):210.
- Geethanjali, S. and Subash, A. (2013). Optimisation and Immobilisation of purified labeo rohita visceral protease by entrapment method. *Enzyme Research*:1–7.
- Genisheva, Z., Teixeira, J.A. and Oliveira, J.M. (2014). Immobilised cell systems for batch and continuous winemaking. *Trends in Food Science and Technology* 40(1):33–47.

- Gharehyakheh, S. (2021). Gamma aminobutyric acid (GABA) production using *Lactobacillus* sp. Makhdzir Naser-1 (GQ451633) in the cherry-kefir beverage. *Journal of Food Processing and Preservation* 45(6):15521.
- Ghosh, S., Nag, M., Lahiri, D., Sarkar, T., Pati, S., Kari, Z.A., Nirmal, N.P., Edinur, H.A. and Ray, R.R. (2022). Engineered biofilm: Innovative nextgen strategy for quality enhancement of fermented foods. *Frontiers in Nutrition* 9:808630.
- Girelli, A.M., Astolfi, M.L. and Scuto, F.R. (2020). Agro-industrial wastes as potential carriers for enzyme immobilisation: A review. *Chemosphere* 244:125368.
- Giri, S.S., Sen, S.S., Saha, S., Sukumaran, V. and Park, S.C. (2018). Use of a potential probiotic, *Lactobacillus plantarum* L7, for the preparation of a rice-based fermented beverage. *Frontiers in Microbiology* 9:473.
- Gomaa, E.Z. (2015). Enhancement of γ -aminobutyric acid production by co-culturing of two lactobacilli strains. *Asian Journal of Biotechnology* 7(3):108–118.
- Gramazio, P., Takayama, M. and Ezura, H. (2020). Challenges and prospects of new plant breeding techniques for GABA improvement in crops: Tomato as an example. *Frontiers in Plant Science* 11:1–16.
- Granier, A., Goulet, O. and Hoarau, C. (2013). Fermentation products: Immunological effects on human and animal models. *Pediatric Research* 74:238–244.
- Grażyna, C., Hanna, C., Adam, A. and Magdalena, B.M. (2017). Natural antioxidants in milk and dairy products. *International Journal of Dairy Technology* 70(2):165–178.
- Grendpina, N., Fitri, D., Julendra, H., Sofyan, A. and Damayanti, E. (2020). Enhancing anti-pathogenic bacteria activity of *Lactobacillus plantarum* AKK-30 cultured on the medium containing fructose-oligosaccharides. *16th ASEAN Food Conference*:205–209.
- Grewal, J. (2020). Gamma-aminobutyric acid (GABA): A versatile bioactive compound. *European Journal of Molecular and Clinical Medicine* 7(7):3068-3075.
- Gu, I., Balogun, O., Brownmiller, C., Kang, H.W. and Lee, S.O. (2023). Bioavailability of citrulline in watermelon flesh, rind, and skin using a human intestinal epithelial Caco-2 cell model. *Applied Sciences* 13(8):4882.
- Guantario, B., Zinno, P., Schifano, E., Roselli, M., Perozzi, G., Palleschi, C., Uccelletti, D. and Devirgiliis, C. (2018). *In-vitro* and *in-vivo* selection of potentially probiotic lactobacilli from nocellara del belice table olives. *Frontiers in Microbiology* 9:595.

- Guo, Z., Gong, J., Luo, S., Zuo, Y. and Shen, Y. (2023). Role of gamma-aminobutyric acid in plant defense response. *Metabolites* 13(6):741.
- Gupta, A. and Tiwari, S.K. (2014). Plantaricin LD1: A bacteriocin produced by food isolate of *Lactobacillus plantarum* LD1. *Applied Biochemistry and Biotechnology* 172(7):3354–3362.
- Hafiizha, A., Kayaputri, I.L., Tensiska, T. and Amalia, N.R. (2020). The effect of skim milk concentration on sensory quality and pH of probiotic yoghurt added with red dragon fruit (*Hylocereus polyrhizus*). *Jurnal Ilmu dan Teknologi Hasil Ternak (JITEK)* 15(1):52-60.
- Hajar-Azhari, S., Wan-Mohtar, W.A.A.Q.I., Ab Kadir, S., Rahim, M.H.A. and Saari, N. (2018). Evaluation of a Malaysian soy sauce koji strain *Aspergillus oryzae* NSK for γ -aminobutyric acid (GABA) production using different native sugars. *Food Science and Biotechnology* 27(2):479–488.
- Hajar, S. and Hamid, T.H.T.A. (2013). Isolation of lactic acid bacteria strain *Staphylococcus piscifermentans* from Malaysian traditional fermented shrimp *cincaluk*. *International Food Research Journal* 20(1):125–129.
- Halim, M., Mohd Mustafa, N.A., Othman, M., Wasoh, H., Kapri, M.R. and Ariff, A.B. (2017). Effect of encapsulant and cryoprotectant on the viability of probiotic *Pediococcus acidilactici* ATCC 8042 during freeze-drying and exposure to high acidity, bile salts and heat. *Food Science and Technology* 81:210–216.
- Halim, Y., Tantradjaja, S.F., Hardoko, H. and Handayani, R. (2021). Immobilisation of providencia stuartii cells in papaya trunk wood for n-acetylglucosamine production from penaeus vannamei shrimp shells. *Jurnal Ilmiah Perikanan Dan Kelautan* 13(2):88–101.
- Ham, S., Kim, H.J., Shin, N., Hwang, J.H., Oh, S.J., Park, J.Y., Joo, J.C., Kim, H.T., Bhatia, S.K. and Yang, Y.H. (2023). Continuous production of gamma aminobutyric acid by engineered and immobilised *Escherichia coli* whole-cells in a small-scale reactor system. *Enzyme and Microbial Technology* 168:110258.
- Hamdy, S.M., Abdelmontaleb, H.S., Mabrouk, A.M. and Abbas, K.A. (2021). Physicochemical, viability, microstructure, and sensory properties of whole and skimmed buffalo set-yogurts containing different levels of polydextrose during refrigerated storage. *Journal of Food Processing and Preservation* 45(7):e15643.
- Han, M., Liao, W.Y., Wu, S.M., Gong, X. and Bai, C. (2020). Use of *Streptococcus thermophilus* for the in situ production of γ -aminobutyric acid-enriched fermented milk. *Journal of Dairy Science* 103(1):98–105.
- Harnentis, H., Nurmiati, N., Marlida, Y., Adzitey, F. and Huda, N. (2019). γ -Aminobutyric acid production by selected lactic acid bacteria isolate of an

- Indonesian indigenous fermented buffalo milk (dadih) origin. *Veterinary World* 12(8):1352–1357.
- Hepsomali, P., Groeger, J.A, Nishihira, J. and Scholey, A. (2020). Effects of oral gamma-aminobutyric acid (GABA) administration on stress and sleep in humans: A systematic review. *Frontiers Neuroscience* 14:923.
- Hernández, A., Pérez-Nevado, F., Ruiz-Moyano, S., Serradilla, M.J., Villalobos, M.C., Martín, A. and Córdoba, M.G. (2018). Spoilage yeasts: What are the sources of contamination of foods and beverages?. *International Journal of Food Microbiology* 286:98–110.
- Hinton, T., Jelinek, H.F., Viengkhou, V., Johnston, G.A. and Matthews, S. (2019). Effect of GABA-fortified oolong tea on reducing stress in a university student cohort. *Frontiers Nutrition* 6:27.
- Ho, N.A.T., Hou, C.Y., Kim, W.H. and Kang, T.J. (2013). Expanding the active pH range of *Escherichia coli* glutamate decarboxylase by breaking the cooperativeness. *Journal of Bioscience and Bioengineering* 115(2):154–158.
- Heli, Z., Hongyu, C., Dapeng, B., Yee Shin, T., Yejun, Z., Xi, Z. and Yingying, W. (2022). Recent advances of γ -aminobutyric acid: Physiological and immunity function, enrichment, and metabolic pathway. *Frontiers in Nutrition* 9:1076223.
- Hong LE, P., Parmentier, N., Trung LE, T. and Raes, K. (2021). Evaluation of using a combination of enzymatic hydrolysis and lactic acid fermentation for γ -aminobutyric acid production from soymilk. *Food Science and Technology* 142:111044.
- How, Y.H., Teo, M.Y.M., In, L.L.A., Yeo, S.K. and Pui, L.P. (2022). Development of fermented milk using food-grade recombinant *Lactococcus lactis* NZ3900. *NFS Journal* 28:1–14.
- Hsueh, Y.H., Yang, J.H., Ou, S.F., Chen, S.T., Kuo, J.M. and Wu, C.H. (2021). Mass production of γ -Aminobutyric acid by semi-continuous fermentation. *Food Science and Technology* 140:110640.
- Hsueh Y.H., Liaw W.C., Kuo J.M., Deng C.S. and Wu, C.H. (2017). Hydrogel film-immobilised *Lactobacillus brevis* RK03 for γ -aminobutyric acid production. *International Journal of Molecular Sciences* 18:2324.
- Huang, C.Y., Kuo, W.W., Wang, H.F., Lin, C.J., Lin, Y.M., Chen, J.L., Kuo, C.H., Chen, P.K. and Lin, J.Y. (2014). GABA tea ameliorates cerebral cortex apoptosis and autophagy in streptozotocin-induced diabetic rats. *Journal of Functional Foods* 6(1):534–544.
- Huang, Y., Su, L. and Wu, J. (2016). Pyridoxine supplementation improves the activity of recombinant glutamate decarboxylase and the enzymatic production of gamma-aminobutyric acid. *PLoS ONE* 11(7):1–18.

- Hussin, F.S., Chay, S.Y., Hussin, A.S.M., Wan Ibadullah, W.Z., Muhialdin, B.J., Abd Ghani, M.S. and Saari, N. (2021). GABA enhancement by simple carbohydrates in yoghurt fermented using novel, self-cloned *Lactobacillus plantarum* Taj-Apis362 and metabolomics profiling. *Scientific Reports* 11(1):1–12.
- Ilyanie, H.Y., Huda-Faujan, N., Muryany, M.I. and Zuraida, J. (2022). Isolation and characterisation of probiotic lactic acid bacteria from Malaysian fermented fish products budu and bosou. *International Food Research Journal* 29(2):338-348.
- Iorizzo, M., Paventi, G. and Di Martino, C. (2023). Biosynthesis of gamma-aminobutyric acid (GABA) by *Lactiplantibacillus plantarum* in fermented food production. *Preprints* <https://doi.org/10.20944/preprints202311.1843.v1>.
- Iqbal, J., Siddiqui, R., Kazmi, S.U. and Khan, N.A. (2013). A simple assay to screen antimicrobial compounds potentiating the activity of current antibiotics. *BioMed Research International*: 927323.
- Iqbal, M. and Saeed, A. (2005). Novel method for cell immobilisation and its application for production of organic acid. *Letters in Applied Microbiology* 40(3):178–182.
- Jasińska, U.T., Skapska, S., Owczarek, L., Dekowska, A. and Lewińska, D. (2018). Immobilisation of *Bifidobacterium infantis* cells in selected hydrogels as a method of increasing their survival in fermented milkless beverages. *Journal of Food Quality*:1–12.
- Jawan, R., Abbasiliasi, S., Tan, J.S., Mustafa, S., Halim, M., & Ariff, A.B. (2020). Influence of culture conditions and medium compositions on the production of bacteriocin-like inhibitory substances by *Lactococcus lactis* GH1. *Microorganisms* 8(10):1–14.
- Jawan, R., Kasimin, M.E., Jalal, S.N., Faik, A.M., Abbasiliasi, S. and Ariff, A. (2019). Isolation, characterisation and in vitro evaluation of bacteriocins-producing lactic acid bacteria from fermented products of Northern Borneo for their beneficial roles in food industry. *Journal of Physics: Conference Series* 1358(1):12020.
- Jiang, Z., Nero, T., Mukherjee, S., Olson, R. and Yan, J. (2021). Searching for the secret of stickiness: How biofilms adhere to surfaces. *Frontiers in microbiology* 12:686793.
- Ju, S.Y., Kim, J.H. and Lee, P.C. (2016). Long-term adaptive evolution of *Leuconostoc mesenteroides* for enhancement of lactic acid tolerance and production. *Biotechnology for Biofuels* 9(1):1–12.
- Junter, G.A. and Jouenne, T. (2017). Immobilised viable cell biocatalysts: a paradoxical development. *Reference Module in Life Sciences*.

- Kaewman, P., Nudmamud-Thanoi, S., Amatyakul, P. and Thanoi, S. (2021). High mRNA expression of GABA receptors in human sperm with oligoasthenoteratozoospermia and teratozoospermia and its association with sperm parameters and intracytoplasmic sperm injection outcomes. *Clinical and Experimental Reproductive Medicine* 48(1):50–60.
- Kandyliis, P., Dimitrellou, D., Gousi, M., Kordouli, E. and Kanellaki, M. (2021). Effect of immobilization support and fermentation temperature on beer and fermented milk aroma profiles. *Beverages* 7(3):47.
- Kanklai, J., Somwong, T.C., Rungsirivanich, P. and Thongwai, N. (2021). Screening of GABA-producing lactic acid bacteria from thai fermented foods and probiotic potential of *Levilactobacillus brevis* F064A for GABA-fermented mulberry juice production. *Microorganisms* 9(1):1–17.
- Kanwal, S., Rasogi, R.P. and Incharoensakdi, A. (2014). Glutamate decarboxylase activity and gamma-aminobutyric acid content in *Synechocystis* sp. PCC 6803 under osmotic stress and different carbon sources. *Journal of Applied Phycology* 26:2327–2333.
- Karimian, E., Moayedi, A., Khomeiri, M., Aalami, M. and Mahoonak, A.S. (2020). Application of high-GABA-producing *Lactobacillus plantarum* isolated from traditional cabbage pickle in the production of functional fermented whey-based formulate. *Journal of Food Measurement and Characterisation* 14(6):3408–3416.
- Keerthi, T.R. (2018). Probiotic potency of *Lactobacillus plantarum* KX519413 and KX519414 isolated from honey bee gut. *FEMS Microbiology Letters* 365(4):285.
- Kempen, E., Kasambala, J., Christie, L., Symington, E., Jooste, L. and Van Eeden, T. (2017). Expectancy-value theory contributes to understanding consumer attitudes towards cow's milk alternatives and variants. *International Journal of Consumer Studies* 41(3):245-252.
- Kerry, R.G., Patra, J.K., Gouda, S., Park, Y., Shin, H.S. and Das, G. (2018). Benefaction of probiotics for human health: A review. *Journal of Food and Drug Analysis* 26(3):927–939.
- Keshani, S., Daud, W.R.W., Nourouzi, M.M., Namvar, F. and Ghasemi, M. (2015). Spray drying: An overview on wall deposition, process and modeling. *Journal of Food Engineering* 146:152-162.
- Keshavarz, T., Bucke, C. and Lilly, M.D. (1996). Problems in scale-up of immobilised cell cultures. *Progress in Biotechnology* 11:505-510.
- Khairina, R., Fitriani, Y., Satrio, H. and Rahmi, N. (2016). Physical, chemical, and microbiological properties of “ronto” a traditional fermented shrimp from South Borneo, Indonesia. *Aquatic Procedia* 7:214–220.

- Khalifa, K., brahim Al-Tabib, A.I., Kalil, M.S. and Nasser Al-Shorgani, N.K. (2018). High yield of butanol production in repeated batch culture fermentation by *Clostridium Acetobutylicum* YM1. *Jurnal Kejuruteraan* 1(4):7–14.
- Khan, W., Regmi, O., Hasan, M. and Panda, B.P. (2020). Response surface modeling for the enrichment of gamma-aminobutyric acid with a minimum content of citrinin in *Monascus*-fermented rice. *EFood* 1(2):181-187.
- Kim, J.A., Park, M.S., Kang, S.A. and Ji, G.E. (2014). Production of γ -aminobutyric acid during fermentation of *Gastrodia elata* Bl. by co-culture of *Lactobacillus brevis* GABA 100 with *Bifidobacterium bifidum* BGN4. *Food Science and Biotechnology* 23:459–466.
- Kim, J., Lee, M.H., Kim, M.S., Kim, G H. and Yoon, S.S. (2022a). Probiotic properties and optimisation of gamma-aminobutyric acid production by *Lactiplantibacillus plantarum* FBT215. *Journal of Microbiology and Biotechnology* 32(6):783–791.
- Kim S-Y., Kim K.J., Chung H-C. and Han, G.D. (2019). Use of rice bran for preparation of GABA (γ -aminobutyric acid)-rich sourdough. *Food Science and Technology Research* 25(3):399–404.
- Kim, S., Lee, J.Y., Jeong, Y. and Kang, C.H. (2022b). Antioxidant activity and probiotic properties of lactic acid bacteria. *Fermentation* 8(1):29.
- Ko, C.Y., Lin, H.T.V. and Tsai, G.J. (2013). Gamma-aminobutyric acid production in black soybean milk by *Lactobacillus brevis* FPA 3709 and the antidepressant effect of the fermented product on a forced swimming rat model. *Process Biochemistry* 48(4):559–568.
- Kok, C.R. and Hutkins, R. (2018). Yogurt and other fermented foods as sources of health-promoting bacteria. *Nutrition Reviews* 76:4–15.
- Kook, M.C., Seo, M.J., Cheigh, C.I., Lee, S.J., Pyun, Y.R. and Park, H. (2010a). Enhancement of γ -amminobutyric acid production by *Lactobacillus sakei* B2–16 expressing glutamate decarboxylase from *Lactobacillus plantarum* ATCC 14917. *Journal of the Korean Society for Applied Biological Chemistry* 53(6):816–820.
- Kook, M.C. and Cho, S.C. (2013). Production of GABA (gamma amino butyric acid) by lactic acid bacteria. *Korean Journal for Food Science of Animal Resources* 33(3):377–389.
- Kourkoutas, Y., Bosnea, L., Taboukos, S., Baras, C., Lambrou, D. and Kanellaki, M. (2006). Probiotic cheese production using *Lactobacillus casei* cells immobilised on fruit pieces. *Journal of Dairy Science* 89(5):1439–1451.
- Kourkoutas, Y., Komaitis, M., Koutinas, A.A. and Kanellaki, M. (2001). Wine

- production using yeast immobilised on apple pieces at low and room temperatures. *Journal of Agricultural and Food Chemistry* 49(3):1417–1425.
- Kourkoutas, Y., Xolias, V., Kallis, M., Bezirtzoglou, E. and Kanellaki, M. (2005). *Lactobacillus casei* cell immobilisation on fruit pieces for probiotic additive, fermented milk and lactic acid production. *Process Biochemistry* 40(1):411–416.
- Kriaa, M., Ayadi-Zouari, D., Sahnoun, M., Jemli, S., Bejar, S. and Kammoun, R. (2015). Improved stability and reusability of cotton-immobilized recombinant *Escherichia coli* producing US132 *Cyclodextrin Glucanotransferase*. *Annals of microbiology* 65(1):383-391.
- Kwon, H.Y., Choi, J.S., Kim, S.J., Kim, E.M., Uhm, J.H., Kim, B.K., Lee, J.Y., Kim, Y.D. and Hwang, K.T. (2022). Optimization of solid-phase *Lactobacillus* fermentation conditions to increase γ -aminobutyric acid (GABA) content in selected substrates. *Fermentation* 9(1):22.
- Lai, D.Q. and Pham, T.T. (2020). Refinery of gamma-aminobutyric acid (GABA) from the fermentation of rice bran extract by ultrafiltration. *CET Journal-Chemical Engineering Transactions* 78:463-468.
- Lapeña, D., Olsen, P.M., Arntzen, M.Ø., Kosa, G., Passoth, V., Eijsink, V.G. and Horn, S.J. (2020). Spruce sugars and poultry hydrolysate as growth medium in repeated fed-batch fermentation processes for production of yeast biomass. *Bioprocess and Biosystems Engineering* 43:723-736.
- Laroute, V., Yasaro, C., Narin, W., Mazzoli, R., Pessione, E., Coccagn-Bousquet, M. and Loubière, P. (2016). GABA production in *Lactococcus lactis* is enhanced by arginine and co-addition of malate. *Frontiers in Microbiology* 7:1–11.
- Latif, A., Shehzad, A., Niazi, S., Zahid, A., Ashraf, W., Iqbal, M.W., Rehman, A., Riaz, T., Aadil, R.M., Khan, I.M. and Özogul, F., (2023). Probiotics: mechanism of action, health benefits and their application in food industries. *Frontiers in Microbiology* 14:1216674.
- Lee, J.Y. and Jeon, S.J. (2014). Characterisation and immobilisation on nickel-chelated Sepharose of a glutamate decarboxylase A from *Lactobacillus brevis* BH2 and its application for production of GABA. *Bioscience, Biotechnology and Biochemistry* 78(10):1656–1661.
- Lee, S., Ahn, J., Kim, Y.G., Jung, J.K., Lee, H. and Lee, E.G. (2013). Gamma-aminobutyric acid production using immobilised glutamate decarboxylase followed by downstream processing with cation exchange chromatography. *International Journal of Molecular Sciences* 14(1):1728–1739.
- Lei, Z., Tian, J., Qiu, P., Wang, L., Long, X., Zhang, S. and Tian, Y. (2014). Biosynthesis of gamma-aminobutyric acid by induced resting cells of

Lactobacillus brevis SIIA11021. *Journal of Chemical and Pharmaceutical Research* 6(12):342–348.

- Li, H., Qiu, T., Chen, Y. and Cao, Y. (2011). Separation of gamma-aminobutyric acid from fermented broth. *Journal of Industrial Microbiology and Biotechnology* 38(12):1955–1959.
- Li, J., Zhang, Z., Liu, X., Wang, Y., Mao, F., Mao, J., Lu, X., Jiang, D., Wan, Y., Lv, J.Y. and Cao, G., (2015). Study of GABA in healthy volunteers: Pharmacokinetics and pharmacodynamics. *Frontiers in Pharmacology* 6:260.
- Li, N., Xu, X., Liu, D., Gao, J., Gao, Y., Wu, X., Sheng, H., Li, Q. and Mi, J. (2023a). The delta subunit of the GABAA receptor is necessary for the GPT2-promoted breast cancer metastasis. *Theranostics* 13(4):1355.
- Li, T.J., Jiang, J., Tang, Y.L. and Liang, X.H. (2023b). Insights into the leveraging of GABAergic signaling in cancer therapy. *Cancer Medicine* 12(13):14498–14510.
- Li, W., Wei, M., Wu, J., Rui, X. and Dong, M. (2016). Novel fermented chickpea milk with enhanced level of γ -aminobutyric acid and neuroprotective effect on PC12 cells. *PeerJ* 4:2292.
- Li, Y., Chen, X., Shu, G. and Ma, W. (2020a). Screening of gamma-aminobutyric acid-producing lactic acid bacteria and its application in monascus-fermented rice production. *Acta Scientiarum Polonorum Technologia Alimentaria* 19(4):387–394.
- Li, G., Chen, Z., Chen, N. and Xu, Q. (2020b). Enhancing the efficiency of L-tyrosine by repeated batch fermentation. *Bioengineered* 11(1):852–861.
- Li, H., Qiu, T., Gao, D. and Cao, Y. (2010a). Medium optimisation for production of gamma-aminobutyric acid by *Lactobacillus brevis* NCL912. *Amino Acids* 38:1439–1445.
- Li, H., Qiu, T., Huang, G. and Cao, Y. (2010b). Production of gamma-aminobutyric acid by *Lactobacillus brevis* NCL912 using fed-batch fermentation. *Microbial Cell Factories* 9(1):1–7.
- Liao, W.C., Wang, C.Y., Shyu, Y.T., Yu, R.C. and Ho, K.C. (2013). Influence of preprocessing methods and fermentation of adzuki beans on γ -aminobutyric acid (GABA) accumulation by lactic acid bacteria. *Journal of Functional Foods* 5(3):1108–1115.
- Lie, Y., Farmer, T.J. and Macquarrie, D.J. (2018). Facile and rapid decarboxylation of glutamic acid to γ -aminobutyric acid via microwave-assisted reaction: Towards valorisation of waste gluten. *Journal of Cleaner Production* 205:1102–1113.
- Lim, H.S., Seo, D.H., Cha, I.T., Lee, H., Nam, Y.D. and Seo, M.J. (2018).

Expression and characterisation of glutamate decarboxylase from *Lactobacillus brevis* HYE1 isolated from *Kimchi*. *World Journal of Microbiology and Biotechnology* 34(3):1–10.

- Lim, H.S., Cha, I.T., Roh, S.W., Shin, H.H. and Seo, M.J. (2017). Enhanced production of gamma-aminobutyric acid by optimising culture conditions of *Lactobacillus brevis* HYE1 isolated from *kimchi*, a Korean fermented food. *Journal of Microbiology and Biotechnology* 27(3):450–459.
- Lin, Q. (2013). Submerged fermentation of *Lactobacillus rhamnosus* YS9 for γ -aminobutyric acid (GABA) production. *Brazilian Journal of Microbiology* 44:183–187.
- Lin, Q., Li, D. and Qin, H. (2017). Molecular cloning, expression, and immobilisation of glutamate decarboxylase from *Lactobacillus fermentum* YS2. *Electronic Journal of Biotechnology* 27:8–13.
- Liong, M.T., Rosma, A., Azhar, M.E., Afiza, T.S. and Wan Nadiah, W.A. (2008). Vitamin-B contents of yeast extracts from yeasts grown on agrowastes. In *Proceedings of the International Conference on Environmental Research Technology* 197–201.
- Liu, Z., Ren, Z., Zhang, J., Chuang, C.C., Kandaswamy, E., Zhou, T. and Zuo, L. (2018). Role of ROS and nutritional antioxidants in human diseases. *Frontiers in Physiology* 9:477.
- Liu, H., Yuan, J., Tian, Q., Ji, N. and He, W. (2017). An efficient synthesis of enantiomerically pure γ -aminobutyric acid (GABA) derivatives. *Journal of Materials Science and Chemical Engineering* 5(8):25–32.
- Liwinski, T., Lang, U.E., Brühl, A.B. and Schneider, E. (2023). Exploring the therapeutic potential of gamma-aminobutyric acid in stress and depressive disorders through the gut–brain axis. *Biomedicines* 11(12):3128.
- Lobo, A.R., Satish, S. and Shabaraya, A.R. (2018). Review on pharmacological activities of *Malus Domestica*. *International Journal of Pharma and Chemical Research* 4(4):243–246.
- López-Gómez, J.P., Alexandri, M., Schneider, R. and Venus, J. (2019). A review on the current developments in continuous lactic acid fermentations and case studies utilising inexpensive raw materials. *Process Biochemistry* 79:1–10.
- Lou, W.-Y., Fernández-Lucas, J., Ge, J. and Wu, C. (2021). Editorial: Enzyme or whole cell immobilisation for efficient biocatalysis: Focusing on novel supporting platforms and immobilisation techniques. *Frontiers in Bioengineering and Biotechnology* 9:620292.
- Luongo, V., Policastro, G., Ghimire, A., Pirozzi, F. and Fabbicino, M. (2019). Repeated-batch fermentation of cheese whey for semi-continuous lactic acid production using mixed cultures at uncontrolled

pH. *Sustainability* 11(12):3330.

- Lye, H.S., The, S.S., Lim, T.J., Bhat, R., Ahmad, R., Wan-Abdullah, W.N. and Liong, M.T. (2012). Bioactive property of soymilk fermented by agrowastes-immobilised lactobacilli. *British Food Journal* 114(9):1339–1353.
- Lyu, C., Zhao, W., Peng, C., Hu, S., Fang, H., Hua, Y., Yao, S., Huang, J. and Mei, L. (2018). Exploring the contributions of two glutamate decarboxylase isozymes in *Lactobacillus brevis* to acid resistance and γ -aminobutyric acid production. *Microbial Cell Factories* 17:180.
- Lyu, C., Zhao, W., Hu, S., Huang, J., Lu, T., Jin, Z., Mei, L. and Yao, S. (2017). Physiology-oriented engineering strategy to improve gamma-aminobutyrate production in *Lactobacillus brevis*. *Journal of Agricultural and Food Chemistry* 65:858–866.
- Lyu, C.J., Liu, L., Huang, J., Zhao, W.R., Hu, S., Mei, L.H. and Yao, S.J. (2019). Biosynthesis of γ -aminobutyrate by engineered *Lactobacillus brevis* cells immobilised in gellan gum gel beads. *Journal of Bioscience and Bioengineering* 128(2):123–128.
- Lyu, J.F., Lyu, C.J., Cao, J.R., Mei, J.Q., Hu, S., Zhao, W.R., Xu, T.Y., Wang, Y.T., Wang, D.L., Huang, J. and Mei, L.H. (2022). High level production of γ -aminobutyric acid in engineered *Escherichia coli* by refactoring the glutamate decarboxylase. *Process Biochemistry* 118:243-251.
- Ma, W., Zhang, J., Shu, L., Tan, X., An, Y., Yang, X., Wang, D. and Gao, Q. (2020). Optimisation of spray drying conditions for the green manufacture of γ -aminobutyric acid-rich powder from *Lactobacillus brevis* fermentation broth. *Biochemical Engineering Journal* 156:107499.
- Mani-López, E., Palou, E. and López-Malo, A. (2014). Probiotic viability and storage stability of yogurts and fermented milks prepared with several mixtures of lactic acid bacteria. *Journal of Dairy Science* 97(5):2578–2590.
- Mantzourani, I., Terpou, A., Alexopoulos, A., Kimbaris, A., Bezirtzoglou, E. and Koutinas, A. A. (2019). Production of a potentially synbiotic pomegranate beverage by fermentation with *Lactobacillus plantarum* ATCC 14917 adsorbed on a prebiotic carrier. *Applied Biochemistry and Biotechnology* 188:1096–1107.
- Manzoor, A., Qazi, J.I., Haq, I.U., Mukhtar, H. and Rasool, A. (2017). Significantly enhanced biomass production of a novel bio-therapeutic strain *Lactobacillus plantarum* (AS-14) by developing low-cost media cultivation strategy. *Journal of biological engineering* 11:1-10.
- Marinelli, V., Lucera, A., Incoronato, A.L., Morcavallo, L., Del Nobile, M.A. and Conte, A. (2021). Strategies for fortified sustainable food: The case of watermelon-based candy. *Journal of Food Science and Technology* 58:894–901.

- Markowiak, P. and Ślizewska, K. (2017). Effects of probiotics, prebiotics, and synbiotics on human health. *Nutrients* 9(9):1021.
- Martins, S.C.S., Martins, C.M., Fiúza, L.M.C.G. and Santaella, S.T. (2013). Immobilization of microbial cells: A promising tool for treatment of toxic pollutants in industrial wastewater. *African journal of biotechnology* 12(28):4412-4418.
- Martinsen, T.C., Fossmark, R. and Waldum, H.L. (2019). The phylogeny and biological function of gastric juice—microbiological consequences of removing gastric acid. *International journal of molecular sciences* 20(23):6031.
- Md Sidek, N.L., Halim, M., Tan, J.S., Abbasiliasi, S., Mustafa, S. and Ariff, A.B. (2018). Stability of bacteriocin-like inhibitory substance (BLIS) produced by *Pediococcus acidilactici* kp10 at different extreme conditions. *BioMed Research International*:5973484.
- Medhammar, E., Wijesinha-Bettoni, R., Stadlmayr, B., Nilsson, E., Charrondiere, U.R. and Burlingame, B. (2012). Composition of milk from minor dairy animals and buffalo breeds: a biodiversity perspective. *Journal of the Science of Food and Agriculture* 92(3):445–474.
- Milessi, T.S., Perez, C.L., Zangirolami, T.C., Corradini, F.A., Sandri, J.P., Foulquié-Moreno, M.R., Giordano, R.C., Thevelein, J.M. and Giordano, R.L. (2020). Repeated batches as a strategy for high 2G ethanol production from undetoxified hemicellulose hydrolysate using immobilized cells of recombinant *Saccharomyces cerevisiae* in a fixed-bed reactor. *Biotechnology for biofuels* 13:1-12.
- Ming, L.C., Halim, M., Rahim, R.A., Wan, H.Y. and Ariff, A.B. (2016). Strategies in fed-batch cultivation on the production performance of *Lactobacillus salivarius* I 24 viable cells. *Food Science Biotechnology* 25:1393–1398.
- Mittler, R. (2017). ROS are good. *Trends in Plant Science* 22(1):11–19.
- Mohanty, B., Mahanty, A., Ganguly, S., Sankar, T.V., Chakraborty, K., Rangasamy, A., Paul, B., Sarma, D., Mathew, S., Asha, K.K. and Behera, B. (2014). Amino acid compositions of 27 food fishes and their importance in clinical nutrition. *Journal of Amino Acids*: 269797.
- Mohd Yusof, H., Mohamad, R., Zaidan, U.H. and Rahman, N.A. (2020). Sustainable microbial cell nanofactory for zinc oxide nanoparticles production by zinc-tolerant probiotic *Lactobacillus plantarum* strain TA4. *Microbial Cell Factories* 19(1):1–17.
- Mokoena, M. P. (2017). Lactic acid bacteria and their bacteriocins: classification, biosynthesis and applications against uropathogens: a mini-review. *Molecules* 22(8):1255.
- Moore, J.F., DuVivier, R. and Johanningsmeier, S.D. (2021). Formation of γ -

aminobutyric acid (GABA) during the natural lactic acid fermentation of cucumber. *Journal of Food Composition and Analysis* 96:103711.

Morales, B., Spadetto, L., Calvo, M.À., Yeste, M., Arosemena, L., Rigau, T. and Rivera del Alamo, M.M. (2022). Evaluation of the probiotic in vitro potential of lactic acid-producing bacteria from canine vagina: Possible role in vaginal health. *Animals* 12(6):796.

Mora-Villalobos, J.A., Montero-Zamora, J., Barboza, N., Rojas-Garbanzo, C., Usaga, J., Redondo-Solano, M., Schroedter, L., Olszewska-Widrat, A. and López-Gómez, J.P. (2020). Multi-product lactic acid bacteria fermentations: A Review. *Fermentation*. 6(1):23.

Moreno-García, J., García-Martínez, T., Mauricio, J.C. and Moreno, J. (2018). Yeast immobilization systems for alcoholic wine fermentations: Actual trends and future perspectives. *Frontiers in microbiology* 9:241.

Moreno Osorio, J.H., Pollio, A., Frunzo, L., Lens, P.N.L. and Esposito, G. (2021). A review of microalgal biofilm technologies: definition, applications, settings and analysis. *Frontiers in Chemical Engineering* 3:737710.

Mu, G., Gao, Y., Tuo, Y., Li, H., Zhang, Y., Qian, F. and Jiang, S. (2018). Assessing and comparing antioxidant activities of lactobacilli strains by using different chemical and cellular antioxidant methods. *Journal of Dairy Science* 101(12):10792–10806.

Mushtaq, M., Sultana, B., Bhatti, H.N. and Asghar, M. (2015). RSM based optimised enzyme-assisted extraction of antioxidant phenolics from underutilised watermelon (*Citrullus lanatus* Thunb.) rind. *Journal of Food Science and Technology* 52(8):5048–5056.

Nadiah, I., Khairi, B.M., Huda, N., Nadiah, W., Abdullah, W., Fadhl, A. and Al-Karkhi, M. (2014). Protein quality of fish fermented product: *Budu* and rusip. *Asia Pacific Journal of Sustainable Agriculture Food and Energy* 2(2):17–22.

Najib, T., Solgi, M., Farazmand, A., Heydarian, S.M. and Nasernejad, B. (2017). Optimisation of sulfate removal by sulfate reducing bacteria using response surface methodology and heavy metal removal in a sulfidogenic UASB reactor. *Journal of Environmental Chemical Engineering* 5(4):3256–3265.

Nath, S., Sikidar, J., Roy, M. and Deb, B. (2020). *In-vitro* screening of probiotic properties of *Lactobacillus plantarum* isolated from fermented milk product. *Food Quality and Safety* 4(4):213–223.

Nedović, V., Gibson, B., Mantzouridou, T.F., Bugarski, B., Djordjević, V., Kalušević, A., Paraskevopoulou, A., Sandell, M., Šmogrovičová, D. and Yilmaztekin, M. (2015). Aroma formation by immobilized yeast cells in fermentation processes. *Yeast* 32(1):173-216.

Nedzlek, C.D. and Michaelis, A. (2022). An unusual presentation of an

- uncommon drug: A case report on phenibut overdose. *Cureus* 14:4.
- Negash, A.W. and Tsehai, B.A. (2020). Current applications of bacteriocin. *International Journal of Microbiology*:4374891.
- Nejati, F., Rizzello, C., Di Cagno, R., Sheikh-Zeinoddin, M., Diviccaro, A., Minervini, F. and Gobetti, M. (2013). Manufacture of a functional fermented milk enriched of angiotensin-I converting enzyme (ACE)-inhibitory peptides and gamma-amino butyric acid (GABA). *Food Sciences and Technology* 51(1):183–189.
- Nezbedova, L., McGhie, T., Christensen, M., Heyes, J., Nasef, N.A. and Mehta, S. (2021). Onco-preventive and chemo-protective effects of apple bioactive compounds. *Nutrients* 13(11):1–29.
- Ng, K.S., Wang, S.Y. and Chen, M.J. (2020). A novel immobilised cell system involving Taiwanese kefir microorganisms and sugar cane pieces for fermented milk production. *Journal of Dairy Science* 103(1):141–149.
- Nguyen, T.A. and Vandamme, P. (2022). Isolation, screening, identification and optimization of culture parameters to produce γ -aminobutyric acid by *Lactiplantibacillus pentosus* R13, an isolate from ruoc (Fermented shrimp paste). *Applied Food Biotechnology* 9(1)1-8.
- Ngo, D.H. and Vo, T.S. (2019). An updated review on pharmaceutical properties of gamma-aminobutyric acid. *Molecules* 24(15):2678.
- Novarina, I., Dinoto, A., Julistiono, H., Handayani, R. and Saputra, S. (2020). Assessment of potential probiotic lactic acid bacteria from tempe and tape. *IOP Conference Series: Earth and Environmental Science* 572(1):12026.
- Nursini, N.W., Antara, N.S., Sugitha, I.M. and Sujaya, I.N. (2022). Screening of *Lactobacillus rhamnosus*-producing gamma aminobutyric acid (GABA) isolated from Sumbawa mare milk and its potential application to increase GABA content in fermented milk. *Food Research* 6(3):187–195.
- Ochoa-de la Paz, L.D., Gulas-Cañizo, R., Ruíz-Leyja, E.D., Sánchez-Castillo, H. and Parodí, J. (2021). The role of GABA neurotransmitter in the human central nervous system, physiology, and pathophysiology. *Revista Mexicana de Neurociencia* 22(2):67–76.
- Ogando, F.I.B., Santos, C.B., Nouer, P.A., Alves, M.E. and Aguiar, C.L. (2022). Control of reducing sugars in sugarcane bioenergy industries by colorimetric methods: Is it always possible?. *Revista Brasileira de Tecnologia Agroindustrial* 16(2):3936-3953.
- Ohmori, T., Tahara, M. and Ohshima, T. (2018). Mechanism of gamma-aminobutyric acid (GABA) production by a lactic acid bacterium in yogurt-sake. *Process Biochemistry* 74:21–27.
- Oketch-Rabah, H.A., Madden, E.F., Roe, A.L. and Betz, J.M. (2021). United States Pharmacopeia (USP) safety review of gamma-aminobutyric acid

(GABA). *Nutrients* 13(8):1–21.

- Olayinka, B.U. and Etejere, E.O. (2018). Proximate and chemical compositions of watermelon (*Citrullus lanatus* (Thunb.) Matsum and Nakai cv red and cucumber (*Cucumis sativus* L. cv Pipino). *International Food Research Journal* 25(3):1060–1066.
- Othman, M., Ariff, A.B., Kapri, M.R., Rios-Solis, L. and Halim, M. (2018). Growth enhancement of probiotic *Pediococcus acidilactici* by extractive fermentation of lactic acid exploiting anion-exchange resin. *Frontiers Microbiology* 9:2554.
- Othman, M., Ariff, A.B., Rios-Solis, L. and Halim, M. (2017). Extractive fermentation of lactic acid in lactic acid bacteria cultivation: A review. *Frontiers Microbiology* 8:2285.
- Palachum, W., Chisti, Y. and Choorit, W. (2018). *In-vitro* assessment of probiotic potential of *Lactobacillus plantarum* WU-P19 isolated from a traditional fermented herb. *Annals of Microbiology* 68:79-91.
- Palaniswamy, S.K. and Govindaswamy, V. (2016). *In-vitro* probiotic characteristics assessment of feruloyl esterase and glutamate decarboxylase producing *Lactobacillus* spp. isolated from traditional fermented millet porridge (kambu koozh). *Food Science and Technology* 68:208–216.
- Papadimitriou, K., Alegría, Á., Bron, P.A., De Angelis, M., Gobbetti, M., Kleerebezem, M., Lemos, J.A., Linares, D.M., Ross, P., Stanton, C. and Turroni, F. (2016). Stress physiology of lactic acid bacteria. *Microbiology and Molecular Biology Reviews* 80(3): 837-890.
- Papadimitriou, K., Zoumpopoulou, G., Foligné, B., Alexandraki, V., Kazou, M., Pot, B. and Tsakalidou, E. (2015). Discovering probiotic microorganisms: *In-vitro*, *in-vivo*, genetic and omics approaches. *Frontiers in Microbiology* 6:1–28.
- Park, S.J., Kim, D.H., Kang, H.J., Shin, M., Yang, S.Y., Yang, J. and Jung, Y.H. (2021). Enhanced production of γ -aminobutyric acid (GABA) using lactobacillus. *Food Science and Technology* 137:110443.
- Park, S., Kim, K., Lee, M. and Lim, S. (2013). Physiological characteristics and GABA production of *Lactobacillus plantarum* K255 isolated from kimchi. *Korean Journal for Food Science of Animal Resources* 33(5):595–602.
- Patel, P., Patel, V. and Subhash, R. (2015). Milk fermentation efficacy of immobilised *L.paracasei* cells on selected fresh fruit pieces. *Journal of Pure and Applied Sciences* 22&23:52–58.
- Peng, C., Huang, J., Hu, S., Zhao, W., Yao, S. and Mei, L. (2013). A two-stage pH and temperature control with substrate feeding strategy for production of gamma-aminobutyric acid by *Lactobacillus brevis* CGMCC 1306.

- Pereira, J.A.M., Berenguer, C.V., Andrade, C.F.P. and Câmara, J.S. (2022). Unveiling the bioactive potential of fresh fruit and vegetable waste in human health from a consumer perspective. *Applied Sciences* 12(5):2747.
- Phuengjayaem, S., Kuncharoen, N., Booncharoen, A., Ongpipattanakul, B. and Tanasupawat, S. (2021). Genome analysis and optimization of γ -aminobutyric acid (GABA) production by lactic acid bacteria from plant materials. *The Journal of General and Applied Microbiology* 67(4):150-161.
- Pisol, B., Abdullah, N., Khalil, K. A. and Nuraida, L. (2015). Isolation and identification of lactic acid bacteria from different stages of traditional Malaysian tempeh production. *Malaysian Journal of Microbiology*:358-364.
- Plessas, S., Bekatorou, A., Koutinas, A.A., Soupioni, M., Banat, I.M. and Marchant, R. (2007). Use of *Saccharomyces cerevisiae* cells immobilised on orange peel as biocatalyst for alcoholic fermentation. *Bioresource Technology* 98(4):860–865.
- Pouliot-Mathieu, K., Gardner-Fortier, C., Lemieux, S., St-Gelais, D., Champagne, C.P. and Vuilleumard, J.C. (2013). Effect of cheese containing gamma-aminobutyric acid-producing lactic acid bacteria on blood pressure in men. *Pharma Nutrition* 1(4):148.
- Prabhurajeshwar, C. and Chandrakanth, R.K. (2017). Probiotic potential of lactobacilli with antagonistic activity against pathogenic strains: An *in-vitro* validation for the production of inhibitory substances. *Biomedical Journal* 40(5):270–283.
- Pribadhi, A.N., Kusdiyantini, E. and Ferniah, R.S. (2021). Isolation and characterisation of lactic acid bacteria from cincaok fermentation as a production of gamma-aminobutyric acid. *Jurnal Bioteknologi dan Biosains Indonesia* 8(1):25-32.
- Quílez, J. and Diana, M. (2017). Gamma-aminobutyric acid-enriched fermented foods. In *Fermented foods in health and disease prevention* (pp. 85-103). Academic Press.
- Ragab, E.S., Zhang, S., Korma, S.A., Buniowska-olejnik, M., Abd, S., Nasser, A., Esatbeyoglu, T., Lv, J. and Nassar, K.S. (2023). Physicochemical and rheological properties of stirred yoghurt during storage induced from high-intensity thermosonicated goat and cow milk. *Fermentation* 9(1):42.
- Rahman, S.N.S.A., Kalil, M.S. and Hamid, A.A. (2021). Production of docosahexaenoic acid, DHA using different modes of cultivation by *Aurantiochytrium* sp. SW1. *Sains Malaysiana* 50(7):1947-1957.
- Rajoka, M.S.R., Mehwish, H.M., Siddiq, M., Haobin, Z., Zhu, J., Yan, L., Shao, D., Xu, X. and Shi, J. (2017). Identification, characterisation, and probiotic potential of *Lactobacillus rhamnosus* isolated from human milk. *Food*

- Ramos-Ruiz, R., Martinez, F. and Knauf-Beiter, G. (2019). The effects of GABA in plants. *Cogent Food and Agriculture* 5(1):1670553.
- Ramos, I.M. and Poveda, J.M. (2022). Fermented sheep's milk enriched in gamma-amino butyric acid (GABA) by the addition of lactobacilli strains isolated from different food environments. *Food Science and Technology* 163:113581.
- Rashmi, D., Zanan, R., John, S. and Khandagale, K. (2018). γ -Aminobutyric acid (GABA): Biosynthesis, role, commercial production, and applications. *Studies in Natural Products Chemistry* 57:413–452.
- Ratanaburee, A., Kantachote, D., Charernjiratrakul, W. and Sukhoom, A. (2013). Enhancement of γ -aminobutyric acid (GABA) in Nham (Thai fermented pork sausage) using starter cultures of *Lactobacillus namurensis* NH2 and *Pediococcus pentosaceus* HN8. *International Journal of Food Microbiology* 167(2):170–176.
- Rayavarapu, B., Tallapragada, P. and Usha, M. S. (2021). Optimisation and comparison of γ -aminobutyric acid (GABA) production by LAB in soymilk using RSM and ANN models. *Beni-Suef University Journal of Basic and Applied Sciences* 10(1):14.
- Reddy, L.V.A., Reddy, Y.H.K. and Reddy, O.V.S. (2006). Wine production by guava piece immobilised yeast from Indian cultivar grapes and its volatile composition. *Biotechnology* 5(4):449–454.
- Reddy, L.V., Kumar, Y.H., Anjaneya, L.P. and Sarathi, O.V. (2008). Wine production by novel yeast biocatalyst prepared by immobilisation on watermelon (*Citrullus vulgaris*) rind pieces and characterisation of volatile compounds. *Process Biochemistry* 43(7):748–752.
- Redruello, B., Saidi, Y., Sampedro, L., Ladero, V., del Rio, B. and Alvarez, M.A. (2021). GABA-producing *Lactococcus lactis* strains isolated from camel's milk as starters for the production of GABA-enriched cheese. *Foods* 10:633.
- Reyes, E., Ladero, V., Tornadijo, M.E. and Fresno, J.M. (2019). Production of sheep milk cheese with high γ -aminobutyric acid and ornithine concentration and with reduced biogenic amines level using autochthonous lactic acid bacteria strains. *Food Microbiology* 78:1–10.
- Rezaei, Z., Khanzadi, S. and Salari, A. (2021). Biofilm formation and antagonistic activity of *Lactocaseibacillus rhamnosus* (PTCC1712) and *Lactiplantibacillus plantarum* (PTCC1745). *AMB Express* 11(1):1-7.
- Ribeiro, S., Domingos-Lopes, M.F.P., Stanton, C., Ross, R.P. and Silva, C.C.G. (2018). Production of γ -aminobutyric acid (GABA) by *Lactobacillus otakiensis* and other *Lactobacillus* sp. isolated from traditional Pico cheese.

- Ridlon, J.M., Harris, S.C., Bhowmik, S., Kang, D.J. and Hylemon, P.B. (2016). Consequences of bile salt biotransformations by intestinal bacteria. *Gut microbes* 7(1):22-39.
- Ridza, P.M., Ya'Acob, A., Zainol, N. and Mortan, S.H. (2020). Application of two level factorial design to study the microbe growth inhibition by pineapple leaves juice. *In IOP Conference Series: Materials Science and Engineering* 736:022011.
- Rolfe, M.D., Rice, C.J., Lucchini, S., Pin, C., Thompson, A., Cameron, A.D., Alston, M., Stringer, M.F., Betts, R.P., Baranyi, J. and Peck, M.W. (2012). Lag phase is a distinct growth phase that prepares bacteria for exponential growth and involves transient metal accumulation. *Journal of Bacteriology* 194(3):686–701.
- Sahab, N.R.M., Subroto, E., Balia, R.L. and Utama, G.L. (2020). γ -Aminobutyric acid found in fermented foods and beverages: current trends. *Heliyon* 6(11):e05526.
- Salas-Tovar, J.A., Escobedo-García, S., Olivas, G.I., Acosta-Muñiz, C.H., Harte, F. and Sepulveda, D.R. (2021). Method-induced variation in the bacterial cell surface hydrophobicity MATH test. *Journal of Microbiological Methods* 185:106234.
- Sanchart, C., Watthanasakphuban, N., Boonseng, O., Nguyen, T.H., Haltrich, D. and Maneerat, S. (2018). Tuna condensate as a promising low-cost substrate for glutamic acid and GABA formation using *Candida rugosa* and *Lactobacillus futsaii*. *Process Biochemistry* 70:29–35.
- Sanchart, C., Rattanaporn, O., Haltrich, D., Phukpattaranont, P. and Maneerat, S. (2017). *Lactobacillus futsaii* CS3, a new GABA-producing strain isolated from Thai fermented shrimp (Kung-Som). *Indian Journal of Microbiology* 57(2):211–217.
- Santillo, M.F. and Sprando, R.L. (2023). Picamilon, a γ -aminobutyric acid (GABA) analogue and marketed nootropic, is inactive against 50 biological targets. *Basic & Clinical Pharmacology and Toxicology* 132(4):352-355.
- Santoso, I., Fadhilah, Q.G., Maryanto, A.E., Dwiranti, A., Wang, P., Al-Rais, M.F. and Sigar, I.M. (2023). Characteristics of isolated lactic acid bacilli bacteria from black glutinous rice (*Oryza sativa* L.) tapai and its antimicrobial activity in mung bean (*Vigna radiata* L.) milk. *Kuwait Journal of Science* <https://doi.org/10.1016/j.kjs.2023.12.001>.
- Santos-Espinosa, A., Beltrán-Barrientos, L.M., Reyes-Díaz, R., Mazorra-Manzano, M.Á., Hernández-Mendoza, A., González-Aguilar, G.A., Sáyo-Ayerdi, S.G., Vallejo-Cordoba, B. and González-Córdova, A.F. (2020). Gamma-aminobutyric acid (GABA) production in milk fermented by specific wild lactic acid bacteria strains isolated from artisanal Mexican

- cheeses. *Annals of Microbiology* 70(1):12.
- Saraphanchotiwitthaya, A. and Sripalakit, P. (2018). Production of γ -aminobutyric acid from red kidney bean and barley grain fermentation by *Lactobacillus brevis* TISTR 860. *Biocatalysis and Agricultural Biotechnology* 16:49–53.
- Sarasa, S.B., Mahendran, R., Muthusamy, G. Thankappan, B., Selta, D.R.F. and Angayarkanni, J. (2020). A brief review on the non-protein amino acid, gamma-amino butyric acid (GABA): Its production and role in microbes. *Current Microbiology* 77:534–544.
- Sarawagi, A., Soni, N.D. and Patel, A.B. (2021). Neurometabolism in major depressive disorder. *Frontiers in Psychiatry* 12:637863.
- Sarwar, A., Aziz, T., Al-Dalali, S., Zhao, X., Zhang, J., ud Din, J., Chen, C., Cao, Y. and Yang, Z. (2019). Physicochemical and microbiological properties of synbiotic yogurt made with probiotic yeast *Saccharomyces boulardii* in combination with inulin. *Foods* 8(10):468.
- Savedboworn, W., Riansa-ngawong, W., Sinlapacharoen, W., Pajakang, S., Patcharajarukit, B. and Tipkanon, S. (2014). Assessment of probiotic properties in lactic acid bacteria isolated from fermented vegetables. *KMUTNB International Journal of Applied Science and Technology* 7(4):53–65.
- Schmidt, A., Schreiner, M.G. and Mayer, H.K. (2017). Rapid determination of the various native forms of vitamin B6 and B2 in cow's milk using ultra-high performance liquid chromatography. *Journal of Chromatography A* 1500:89-95.
- Schür, R.R., Draisma, L.W.R., Wijnen, J.P., Boks, M.P., Koevoets, M.G.J.C., Joels, M., Klomp, D.W., Kahn, R.S. and Vinkers, C.H. (2016). Brain GABA levels across psychiatric disorders: A systematic literature review and meta-analysis of IH-MRS studies. *Human Brain Mapping* 37:3337–3352.
- Seo, M.J., Nam, Y.D., Lee, S.Y., Park, S.L., Yi, S.H. and Lim, S.I. (2013a). Expression and characterisation of a glutamate decarboxylase from *Lactobacillus brevis* 877G producing γ -aminobutyric acid. *Bioscience, Biotechnology and Biochemistry* 77(4):853–856.
- Seo, M.J., Nam, Y.D., Park, S.L., Lee, S.Y., Yi, S.H. and Lim, S.I. (2013b). γ -Aminobutyric acid production in skim milk co-fermented with *Lactobacillus brevis* 877G and *Lactobacillus sakei* 795. *Food Science and Biotechnology* 22:751–755.
- Setyawardani, T. and Sumarmono, J. (2015). Chemical and microbiological characteristics of goat milk kefir during storage under different temperatures. *Journal of the Indonesian Tropical Animal Agriculture* 40(3):183–188.

- Setyawardani, T., Widayaka, K. and Astuti, T.Y. (2014). Antimicrobial activity of indigenous probiotic *L. plantarum* TW 14 from goat milk as natural preservative candidate. *The 16 Th AAAP Animal Science Congress* 2:1273–1275.
- Shah, A.M., Tarfeen, N., Mohamed, H. and Song, Y. (2023). Fermented foods: their health-promoting components and potential effects on gut microbiota. *Fermentation* 9(2):118.
- Shan, Y., Man, C.X., Han, X., Li, L., Guo, Y., Deng, Y., Li, T., Zhang, L.W. and Jiang, Y. J. (2015). Evaluation of improved γ -aminobutyric acid production in yogurt using *Lactobacillus plantarum* NDC75017. *Journal of Dairy Science* 98(4):2138–2149.
- Sharafi, S. and Nateghi, L. (2020). Optimisation of gamma-aminobutyric acid production by probiotic bacteria through response surface methodology. *Iranian Journal of Microbiology* 12(6):584–591.
- Shi, F. and Li, Y. (2011). Synthesis of γ -aminobutyric acid by expressing *Lactobacillus brevis*-derived glutamate decarboxylase in the *Corynebacterium glutamicum* strain ATCC 13032. *Biotechnology Letter* 33:2469–2674.
- Shi, X., Chang, C., Ma, S., Cheng, Y., Zhang, J. and Gao, Q. (2017). Efficient bioconversion of L-glutamate to γ -aminobutyric acid by *Lactobacillus brevis* resting cells. *Journal of Industrial Microbiology and Biotechnology* 44(4–5):697–704.
- Shibdawa, M.A., Ushie, O., Ogah, E. and Longbap, B. (2018). Physiochemical analysis of local (Fulani) yoghurt syrup sold in Bauchi metropolis. *International Journal of Advanced Research in Chemical Science* 5(4):17-22.
- Śliżewska, K. and Chlebicz-Wójcik, A. (2020). Growth kinetics of probiotic *Lactobacillus* strains in the alternative, cost-efficient semi-solid fermentation medium. *Biology* 9(12):423.
- Somasundaram, S., Jeong, J. and Hong, S.H. (2021). Cell surface display of *Neurospora crassa* glutamate decarboxylase on *Escherichia coli* for extracellular Gamma-aminobutyric acid production from high cell density culture. *Biochemical Engineering Journal* 176:108196.
- Son, J., Baritugo, K.A., Sohn, Y.J., Kang, K.H., Kim, H.T., Joo, J.C. and Park, S.J. (2022). Production of γ -aminobutyrate (GABA) in recombinant *Corynebacterium glutamicum* by expression of glutamate decarboxylase active at neutral pH. *ACS Omega* 7(33):29106–29115.
- Spiering, M. J. (2018). The discovery of GABA in the brain. *Journal of Biological Chemistry* 293(49):19159-19160.
- Sriputorn, B., Laopaiboon, L. and Laopaiboon, P. (2023). Repeated-batch

ethanol fermentation from sweet sorghum stem juice under a very high gravity condition using a stirred tank bioreactor coupled with a column bioreactor by immobilised *Saccharomyces cerevisiae*. *Fermentation* 9(2):159.

Stephens, I. (2017). Medical yoga therapy. *Children* 4(2):12.

Sun, L., Bai, Y., Zhang, X., Zhou, C., Zhang, J., Su, X., Luo, H., Yao, B., Wang, Y. and Tu, T. (2021). Characterization of three glutamate decarboxylases from *Bacillus* spp. for efficient γ -aminobutyric acid production. *Microbial cell factories* 20(1):1-12.

Tajabadi, N., Ebrahimpour, A., Baradaran, A., Rahim, R.A., Mahyudin, N.A., Manap, M.Y. A., Bakar, F.A. and Saari, N. (2015). Optimisation of γ -aminobutyric acid production by *Lactobacillus plantarum* Taj-Apis362 from honeybees. *Molecules* 20(4):6654–6669.

Tanamool, V., Hongsachart, P. and Soemphol, W. (2020). Screening and characterisation of gamma-aminobutyric acid (GABA) producing lactic acid bacteria isolated from Thai fermented fish (Pla-som) in Nong Khai and its application in Thai fermented vegetables (Som-pak). *Food Science and Technology* 40(2):483–490.

Taoka, Y., Nakamura, M., Nagai, S., Nagasaka, N., Tanaka, R. and Uchida, K. (2019). Production of anserine-rich fish sauce from giant masu salmon, *oncorhynchus masou masou* and γ -aminobutyric acid (GABA)-enrichment by *Lactobacillus plantarum* train N10. *Fermentation* 5(2):45.

Teh, S.S., Bhat, R., Ahmad, R., Wan-Abdullah, W.N. and Liong, M.T. (2010). Growth characteristics of agrowaste-immobilised lactobacilli in soymilk during refrigerated storage. *International Journal of Food Science and Technology* 45(10):2089–2095.

Thuy, D.T.B., Nguyen, A.T., Khoo, K.S., Chew, K.W., Cnockaert, M., Vandamme, P., Ho, Y.C., Huy, N.D., Cocolletzi, H.H. and Show, P.L. (2021). Optimisation of culture conditions for gamma-aminobutyric acid production by newly identified *Pediococcus pentosaceus* MN12 isolated from 'mam nem', a fermented fish sauce. *Bioengineered* 12(1):54–62.

Tofalo, R., Fusco, V., Böhnlein, C., Kabisch, J., Logrieco, A.F., Habermann, D., Cho, G.S., Benomar, N., Abriouel, H., Schmidt-Heydt, M., Neve, H., Bockelmann, W. and Franz, C.M.A.P. (2020). The life and times of yeasts in traditional food fermentations. *Critical Reviews in Food Science and Nutrition* 60:3103–3132.

Tong, Z., Zheng, X., Tong, Y., Shi, Y.C. and Sun, J. (2019). Systems metabolic engineering for citric acid production by *Aspergillus niger* in the post-genomic era. *Microbial Cell Factories* 18:28.

Toro, G. and Pinto, M. (2015). Plant respiration under low oxygen. *Chilean Journal of Agricultural Research* 75(1):57–70.

- Tripathi, M.K. and Giri, S.K. (2014). Probiotic functional foods: Survival of probiotics during processing and storage. *Journal of Functional Foods* 9:225–241.
- Tung, Y.T., Lee, B.H., Liu, C.F. and Pan, T.M. (2011). Optimisation of culture condition for ACEI and GABA production by lactic acid bacteria. *Journal of Food Science* 76(9):585–591.
- Van Zyl, W.F., Deane, S.M. and Dicks, L.M. (2020). Molecular insights into probiotic mechanisms of action employed against intestinal pathogenic bacteria. *Gut microbes* 12(1):1831339.
- Vangpikul, S., Vichitphan, K. and Leelavatcharamas, V. (2022). *In-vitro* assessment of probiotic properties and gamma-aminobutyric acid production of selected lactic acid bacteria strains. *Food Research* 6(5):199–214.
- Venturi, M., Galli, V., Pini, N., Guerrini, S. and Granchi, L. (2019). Use of selected lactobacilli to increase γ -aminobutyric acid (GABA) content in sourdough bread enriched with amaranth flour. *Foods* 8(6):218.
- Verni, M., Vekka, A., Immonen, M., Katina, K., Rizzello, C.G. and Coda, R. (2022). Biosynthesis of γ -aminobutyric acid by lactic acid bacteria in surplus bread and its use in bread making. *Journal of Applied Microbiology* 133(1):76-90.
- Vickers, N.J. (2017). Animal communication: when i'm calling you, will you answer too?. *Current Biology* 27(14):713-715.
- Villalba, M., Verdasco-Martín, C.M., dos Santos, J.C.S., Fernandez-Lafuente, R. and Otero, C. (2016). Operational stabilities of different chemical derivatives of Novozym 435 in an alcoholysis reaction. *Enzyme and Microbial Technology* 90:35–44.
- Villegas, J.M., Brown, L., Savoy de Giori, G. and Hebert, E.M. (2016). Optimisation of batch culture conditions for GABA production by *Lactobacillus brevis* CRL 1942, isolated from quinoa sourdough. *Food Science and Technology* 67:22–26.
- Vitola, H.R.S., dos Santos Cruxen, C.E., da Silva, F.T., Thiel, P.R., de Lima Marques, J., da Silva, W.P. and Fiorentini, Â.M. (2020). *Lactobacillus casei* CSL3: Evaluation of supports for cell immobilisation, viability during storage in Petit Suisse cheese and passage through gastrointestinal transit *In-vitro*. *Food Science and Technology* 127:109381.
- Vo, T.T.T. and Park, J.H. (2019). Characteristics of potential gamma-aminobutyric acid-producing bacteria isolated from Korean and Vietnamese fermented fish products. *Journal of Microbiology and Biotechnology* 29(2):209–221.

- Voss, C.M., Arildsen, L., Nissen, J.D., Waagepetersen, H.S., Schousboe, A., Maechler, P., Ott, P., Vilstrup, H. and Walls, A.B. (2021). Glutamate dehydrogenase is important for ammonia fixation and amino acid homeostasis in brain during hyperammonemia. *Frontiers in Neuroscience* 15:646291.
- Wan-Mohtar, W.A.A.Q.I., Sohedein, M.N.A., Ibrahim, M.F., Ab Kadir, S., Suan, O.P., Weng Loen, A.W., Sassi, S. and Ilham, Z. (2020). Isolation, identification, and optimization of γ -aminobutyric acid (GABA)-producing *Bacillus cereus* strain KBC from a commercial soy sauce moromi in submerged-liquid fermentation. *Processes* 8(6):652.
- Wang, C., Cui, Y.H. and Qu, X.J. (2018a). Mechanisms and improvement of acid resistance in lactic acid bacteria. *Archives of Microbiology* 200:195–201.
- Wang, D., Wang, X., Luo, M.T., Wang, H. and Li, Y.H. (2019). Gamma-aminobutyric acid levels in the anterior cingulate cortex of perimenopausal women with depression: A magnetic resonance spectroscopy study. *Frontiers in Neuroscience* 13:785.
- Wang, D., Wang Y., Lan, H., Wang, K., Zhao, L. and Hu, Z. (2021). Enhanced production of γ -aminobutyric acid in litchi juice fermented by *Lactobacillus plantarum* HU-C2W. *Food Science* 42:101155.
- Wang, J., Hu, Y., Qiu, C., Fan, H., Yue, Y., Jiao, A., Xu, X. and Jin, Z. (2018b). Immobilised cells of *Bacillus circulans* ATCC 21783 on palm curtain for fermentation in 5 L fermentation tanks. *Molecules* 23(11):2888.
- Wang, L., Zhang, M., Li, Y., Cui, Y., Zhang, Y., Wang, Z., Wang, M. and Huang, Y. (2017). Application of response surface methodology to optimise the production of antimicrobial metabolites by *Micromonospora* Y15. *Biotechnology and Biotechnological Equipment* 31(5):1016–1025.
- Wang, Q., Liu, X., Fu, J., Wang, S., Chen, Y., Chang, K. and Li, H. (2018c). Substrate sustained release-based high efficacy biosynthesis of GABA by *Lactobacillus brevis* NCL912. *Microbial Cell Factories* 17(1):1–8.
- Wang, Y., Zhang, Z., Jiang, C. and Xu, T. (2016). Recovery of gamma-aminobutyric acid (GABA) from reaction mixtures containing salt by electrodialysis. *Separation and Purification Technology* 170:353–359.
- Watanabe, M., Maemura, K., Kanbara, K., Tamayama, T. and Hayasaki, H. (2002). GABA and GABA receptors in the central nervous system and other organs. *International Review of Cytology* 213:1–47.
- Widodo, Handaka, R., Wahyuni, E. and Taufiq, T.T. (2017). The quality of fermented milk produced using intestinal-origin lactic acid bacteria as starters. *International Food Research Journal* 24(6):2371–2376.
- Wike, N.Y., Kelechi, M.S., Onyeso, G., Amadi, O. and Krukru, E.E. (2021). Preliminary study on the effect of methanolic extract of watermelon

(*Citrullus lanatus*) rind on prednisolone suppressed immunity in male Wistar rats. *Journal of Advances in Medical and Pharmaceutical Sciences* 23(2):1–6.

- Woraharn, S., Lailerd, N., Sivamaruthi, B.S., Wangcharoen, W., Sirisattha, S., Peerajan, S. and Chaiyasut, C. (2016). Evaluation of factors that influence the L-glutamic and γ -aminobutyric acid production during *Hericium erinaceus* fermentation by lactic acid bacteria. *CyTA - Journal of Food* 14(1):47–54.
- Wu, Q., Law, Y.S. and Shah, N.P. (2015). Dairy *Streptococcus thermophilus* improves cell viability of *Lactobacillus brevis* NPS-QW-145 and its gamma-aminobutyric acid biosynthesis ability in milk. *Scientific Reports* 2:12885.
- Wu, C.H., Hsueh, Y.H., Kuo, J.M. and Liu, S.J. (2018). Characterisation of a potential probiotic *Lactobacillus brevis* RK03 and efficient production of γ -aminobutyric acid in batch fermentation. *International Journal of Molecular Sciences* 19(1):143.
- Xie, W., Ashraf, U., Zhong, D., Lin, R., Xian, P., Zhao, T., Feng, H., Wang, S., Duan, M., Tang, X. and Mo, Z. (2019). Application of γ -aminobutyric acid (GABA) and nitrogen regulates aroma biochemistry in fragrant rice. *Food Science and Nutrition* 7(11):3784–3796.
- Xiudong, X., Ying, W., Xiaoli, L., Ying, L. and Jianzhong, Z. (2016). Soymilk residue (okara) as a natural immobilisation carrier for *Lactobacillus plantarum* cells enhances soymilk fermentation, glucosidic isoflavone bioconversion, and cell survival under simulated gastric and intestinal conditions. *PeerJ* 4(11):e2701.
- Xu, B., Long, Y., Feng, X., Zhu, X., Sai, N., Chirkova, L., Betts, A., Herrmann, J., Edwards, E. J., Okamoto, M., Hedrich, R. and Gilliam, M. (2021). GABA signalling modulates stomatal opening to enhance plant water use efficiency and drought resilience. *Nature Communications* 12:1952.
- Xu, M., Zhao, J., Yu, L. and Yang, S.T. (2017a). Comparative genomic analysis of *Clostridium acetobutylicum* for understanding the mutations contributing to enhanced butanol tolerance and production. *Journal of Biotechnology* 263:36–44.
- Xu, N., Wei, L. and Liu, J. (2017b). Biotechnological advances and perspectives of gamma-aminobutyric acid production. *World Journal of Microbiology and Biotechnology* 33(3):64.
- Yadav, R., Puniya, A.K. and Shukla, P. (2016). Probiotic properties of *Lactobacillus plantarum* RYPR1 from an indigenous fermented beverage Raabadi. *Frontiers in Microbiology*, 7(10):1–9.
- Yang, T., Rao, Z., Kimani, B.G., Xu, M., Zhang, X. and Yang, S.T. (2015). Two-step production of gamma-aminobutyric acid from cassava powder using *Corynebacterium glutamicum* and *Lactobacillus plantarum*. *Journal of*

- Yang, Y., Ren, L., Li, W., Zhang, Y., Zhang, S., Ge, B., Yang, H., Du, G., Tang, B., Wang, H. and Wang, J. (2023). GABAergic signaling as a potential therapeutic target in cancers. *Biomedicine & Pharmacotherapy* 161:114410.
- Yao, J., He, Y., Su, N., Bharath, S.R., Tao, Y., Jin, J. M., Chen, W., Song, H. and Tang, S.Y. (2020). Developing a highly efficient hydroxytyrosol whole-cell catalyst by de-bottlenecking rate-limiting steps. *Nature Communications* 11(1):1515.
- Yi, G., Liu, Q., Lin, J., Wang, W., Huang, H. and Li, S. (2017). Repeated batch fermentation for surfactin production with immobilised *Bacillus subtilis* BS-37: Two-stage pH control and foam fractionation. *Journal of Chemical Technology and Biotechnology* 92(3):530–535.
- Yilmaz, M.T., Dertli, E., Toker, O.S., Tatlisu, N.B., Sagdic, O. and Arici, M. (2015). Effect of in situ exopolysaccharide production on physicochemical, rheological, sensory, and microstructural properties of the yogurt drink ayran: An optimisation study based on fermentation kinetics. *Journal of Dairy Science* 98(3):1604–1624.
- Yogeswara, I.B.A., Kittibunchakul, S., Rahayu, E.S., Domig, K.J., Haltrich, D. and Nguyen, T.H. (2021). Microbial production and enzymatic biosynthesis of γ -aminobutyric acid (GABA) using *Lactobacillus plantarum* FNCC 260 isolated from indonesian fermented foods. *Processes* 9(1):1–17.
- Yogeswara, I.B.A., Maneerat, S. and Haltrich, D. (2020). Glutamate decarboxylase from lactic acid bacteria—a key enzyme in GABA synthesis. *Microorganisms* 8(12):1–24.
- Youssef, H.A.I., Vitaglione, P., Ferracane, R., Abuqwider, J. and Mauriello, G. (2023). Evaluation of GABA production by alginate-microencapsulated fresh and freeze-dried bacteria enriched with monosodium glutamate during storage in chocolate milk. *Microorganisms* 11(11):2648.
- Yu, A.O., Wei, L. and Marco, M.L. (2022). Calcium determines *Lactiplantibacillus plantarum* intraspecies competitive fitness. *Applied and Environmental Microbiology* 88(15):e00666-22.
- Yu, H.H., Yoon, G.H., Choi, J.H., Kang, K.M. and Hwang, H.J. (2017). Application of baechu-*kimchi* powder and GABA-producing lactic acid bacteria for the production of functional fermented sausages. *Food Science of Animal Resources* 37(6):804–812.
- Yu, K., Lin, L., Hu, S., Huang, J. and Mei, L. (2012). C-terminal truncation of glutamate decarboxylase from *Lactobacillus brevis* CGMCC 1306 extends its activity toward near-neutral pH. *Enzyme and Microbial Technology* 50(4–5):263–269.

- Yu, L., Han, X., Cen, S., Duan, H., Feng, S., Xue, Y., Tian, F., Zhao, J., Zhang, H., Zhai, Q. and Chen, W. (2020). Beneficial effect of GABA-rich fermented milk on insomnia involving regulation of gut microbiota. *Microbiological Research* 233:126409.
- Yuan, D., Wu, X., Gong, B., Huo, R., Zhao, L., Li, J., Lü, G. and Gao, H. (2023). GABA metabolism, transport and their roles and mechanisms in the regulation of abiotic stress (hypoxia, salt, drought) resistance in plants. *Metabolites* 13(3):347.
- Yuan, H., Wang, H., Fidan, O., Qin, Y., Xiao, G. and Zhan, J. (2019). Identification of new glutamate decarboxylases from streptomyces for efficient production of γ -aminobutyric acid in engineered *Escherichia coli*. *Journal of Biological Engineering* 13:24.
- Yun, Y.R., Lee, J.J., Lee, H.J., Choi, Y.J., Lee, J.H., Park, S.J., Park, S.H., Seo, H.Y. and Min, S.G. (2021). Comparison of quality characteristics of commercial kimchi manufactured in Korea, China, and the United States. *Foods* 10(10):2488.
- Yuvadetkun, P. and Boonmee, M. (2018). Comparison between free cells and immobilised cells of *Candida shehatae* in ethanol production from rice straw hydrolysate using repeated batch cultivation. *Renewable Energy* 115:634–640.
- Zarei, F., Nateghi, L., Eshaghi, M.R. and Taj Abadi, M.E. (2018). Optimisation of gamma-aminobutyric acid production in probiotics extracted from local dairy products in west region of Iran using MRS broth and whey protein media. *Applied Food Biotechnology* 5(4):233–242.
- Zarei, O., Dastmalchi, S. and Hamzeh-Mivehroud, M. (2016). A simple and rapid protocol for producing yeast extract from *Saccharomyces cerevisiae* suitable for preparing bacterial culture media. *Iranian Journal of Pharmaceutical Research* 15(4):907.
- Zareian, M., Ebrahimpour, A., Bakar, F.A., Mohamed, A K.S., Forghani, B., Ab-Kadir, M.S.B. and Saari, N. (2012). A glutamic acid-producing lactic acid bacteria isolated from malaysian fermented foods. *International Journal of Molecular Sciences* 13(5):5482–5497.
- Zareian, M., Ebrahimpour, A., Mohamed, A.K.S. and Saari, N. (2013). Modeling of glutamic acid production by *Lactobacillus plantarum* MNZ. *Electronic Journal of Biotechnology* 16(4):12-12.
- Zhang, J., Bu, Y., Zhang, C., Yi, H., Liu, D. and Jiao, J. (2020a). Development of a low-cost and high-efficiency culture medium for bacteriocin Lac-B23 production by *Lactobacillus plantarum* J23. *Biology* 9(7):171.
- Zhang, J., Wang, L., Guo, Z., Sun, Z., Gesudu, Q., Kwok, L., Menghebilige and Zhang, H. (2014). 454 pyrosequencing reveals changes in the faecal microbiota of adults consuming *Lactobacillus casei* Zhang. *FEMS*

- Zhang, Q., Sun, Q., Tan, X., Zhang, S., Zeng, L., Tang, J. and Xiang, W. (2020b). Characterisation of γ -aminobutyric acid (GABA)-producing *Saccharomyces cerevisiae* and coculture with *Lactobacillus plantarum* for mulberry beverage brewing. *Journal of Bioscience and Bioengineering* 129(4):447–453.
- Zhang, Q., Zeng, L., Tan, X., Tang, J. and Xiang, W. (2017). An efficient γ -aminobutyric acid (GABA) producing and nitrite reducing ability of *Lactobacillus plantarum* BC114 isolated from Chinese Paocai. *Food Science and Technology Research* 23(5):749-755.
- Zhang, T., Geng, S., Cheng, T., Mao, K., Chitrakar, B., Gao, J. and Sang, Y. (2023). From the past to the future: Fermented milks and their health effects against human diseases. *Food Frontiers* 4:1747–1777.
- Zhao, A., Hu, X., Li, Y., Chen, C. and Wang, X. (2016). Extracellular expression of glutamate decarboxylase B in *Escherichia coli* to improve gamma-aminobutyric acid production. *AMB Express* 6(1):55.
- Zhao, A., Hu, X., Pan, L. and Wang, X. (2015). Isolation and characterisation of a gamma-aminobutyric acid producing strain *Lactobacillus buchneri* WPZ001 that could efficiently utilise xylose and corn cob hydrolysate. *Applied Microbiology and Biotechnology* 99(7):3191–3200.
- Zheng, H., Hao, M., Liu, W., Zheng, W., Fan, S. and Wu, Z. (2019). Foam fractionation for the concentration of exopolysaccharides produced by repeated batch fermentation of *Cordyceps militaris*. *Separation and Purification Technology* 210:682-689.
- Zheng, Z.Y., Cao, F.W., Wang, W.J., Yu, J., Chen, C., Chen, B., Liu, J.X., Firman, J., Renye, J. and Ren, D.X. (2020). Probiotic characteristics of *Lactobacillus plantarum* E680 and its effect on hypercholesterolemic mice. *BMC Microbiology* 20(1):1–9.
- Zhong, Y., Wu, S., Chen, F., He, M. and Lin, J. (2019). Isolation of high γ -aminobutyric acid-producing lactic acid bacteria and fermentation in mulberry leaf powders. *Experimental and Therapeutic Medicine* 18(1):147–153.
- Zhou, Y., Gong, W., Xu, C., Zhu, Z., Peng, Y. and Xie, C. (2022). Probiotic assessment and antioxidant characterisation of *Lactobacillus plantarum* GXL94 isolated from fermented chili. *Frontiers in Microbiology* 13:1–12.
- Zhu, N., Wang, T., Ge, L., Li, Y., Zhang, X. and Bao, H. (2017). γ -Amino butyric acid (GABA) synthesis enabled by copper-catalyzed carboamination of alkenes. *Organic Letters* 19(18):4718–4721.
- Zielińska, D., Marciniak-Lukasiak, K., Karbowski, M. and Lukasiak, P. (2021). Effects of fructose and oligofructose addition on milk fermentation using

novel *Lactobacillus* cultures to obtain high-quality yogurt-like products. *Molecules* 26(19):5730.

Zolgharnein, J., Shahmoradi, A. and Ghasemi, J.B. (2013). Comparative study of Box–Behnken, central composite, and Doehlert matrix for multivariate optimisation of Pb (II) adsorption onto Robinia tree leaves. *Journal of Chemometrics* 27(1–2):12–20.

Zotta, T., Faraone, I., Giavalisco, M., Parente, E., Lela, L., Storti, L.V. and Ricciardi, A. (2022). The production of γ -aminobutyric acid from free and immobilised cells of *Levilactobacillus brevis* cultivated in anaerobic and aerobic conditions. *Microorganisms* 10(11):2184.

Zur, J., Wojcieszynska, D. and Guzik, U. (2016). Metabolic responses of bacterial cells to immobilisation. *Molecules* 21(7):958.

Zuriana S.A. and Sakinah A.M. (2017). Production of sorbitol by repeated batch fermentation using immobilised of *Lactobacillus plantarum* strain (BAA-793) via solid state fermentation. *Food Research* 1(5):176–182.