ANTI-INFLAMMATORY AND ANTI-GLYCOLYTIC EFFECT OF MOMORDICA CHARANTIA AQUEOUS EXTRACT AND CHARANTIN IN LIPOPOLYSACCHARIDE INDUCED RAW264.7 CELLS

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ABSTRACT

Inflammation is a response of immune system towards cell injury caused by trauma or infection. In laboratory, inflammation can be studied by using macrophage cell models activated with lipopolysaccharide (LPS). *Momordica charantia* (*M. charantia*) or bitter gourds is known for its anti-diabetic activity and but its anti-inflammatory activity is not established. In addition, the connection between inflammation with perturbed glucose metabolism has not been fully elucidated. The aim of this project is to implement a combined cell-based assay, gene expression analysis, and metabolomics approach to investigate the anti-inflammatory and anti-glycolytic activities of *M. charantia*, and to characterise the metabolic changes associated with its anti-inflammatory action using a murine macrophage cell model. The results showed that *M. charantia* treatment inhibited the LPS-induced NF-κB nuclear translocation and downregulated pro-inflammatory *IL6* (-84.7 %), *TNF-α* (-85.1 %), *IL1β* (-94.2 %), *COX2* (-89.5 %), and *iNOS* (-28.8 %) genes. In addition, *M. charantia* treatment suppressed LPS-induced *GLUT1* expression (-94.3 %) and lactate production (-28 %), supporting a potential role of glucose metabolism in inflammation. The findings suggested that the anti-inflammatory effect of *M. charantia* may be associated with the regulation of glycolysis and the tricarboxylic acid (TCA) cycle, modulation of amino acid metabolism, and the action of potential anti-inflammatory metabolites in *M. charantia*. In addition, the present study also provided new findings showing anti-inflammatory and anti-glycolytic effect of charantin. Charantin is a key bioactive compound in *M. charantia* known for its hypoglycemic property but the anti-inflammatory potential of charantin has yet to be elucidated. It is a 1:1 mixture of two compounds including sitosterol glucoside and stigmasterol glucoside. In this study, charantin and each of its components were found to exert anti-inflammatory activities by suppressing the *IL6, TNF-α, iNOS, TLR4, MCP1, GLUT1* and *HK2* genes expression. Both components also showed synergistic inhibitory effect on *IL1β* nd COX2 genes expression. Furthermore, charantin and stigmasterol glucoside were found to partially inhibited NF-κB translocation, significantly inhibited p-38 MAPK phosphorylation, and reduced lactate production in the LPS-induced RAW264.7 cells. In this study, the anti-inflammatory and anti-glycolytic activities of aqueous *M. charantia* extract and charantin were found to share consistent results. To further investigate the link between the anti-inflammatory effect and perturbed glucose metabolism, an experiment was performed to study the potential anti-inflammatory strategy by targeting GLUT1 using WZB117, a specific GLUT1 inhibitor. WZB117 downregulated the expressions of *IL6* (-93.3 %), *TNF-α* (-63.2 %), *IL1β* (-76.1 %), *COX2* (-41.34 %), *iNOS* (-98.48 %), *MCP1* (-85.59 %), and *GLUT1* (-85.51 %) in the LPS-induced RAW264.7 cells. In addition, WZB117 also reduced LPS-induced lactate production by 11.16 %. Taken together, The present study highlighted anti-inflammatory and anti-glycolytic effects of *M. charantia* and charantin, and provided evidence showing perturbed glucose metabolism in inflammatory response. The current results supported a therapeutic strategy against inflammation by targeting glucose metabolism.

ABSTRAK

Keradangan merupakan tindak balas sistem imun terhadap kecederaan sel yang disebabkan oleh trauma atau jangkitan. Di makmal, keradangan boleh dikaji dengan menggunakan model sel makrofag yang diaktifkan dengan lipopolisakarida (LPS). *Momordica charantia* (*M. charantia*) atau peria katak, adalah terkenal dengan aktiviti anti-diabetes. Namun, aktiviti anti-radang *M. charantia* masih belum dikaji sepenuhnya. Selain itu, hubungan antara keradangan dengan gangguan dalam metabolism glukosa belum dapat dijelaskan sepenuhnya. Objektif projek ini adalah untuk menjalankan ujikaji menggunakan kaedah gabungan sel, analisa ekspresi gen, dan analisa metabolomik bagi mengkaji aktiviti-aktiviti anti-radang dan anti-glikolitik *M. charantia*, dan untuk mencirikan perubahan metabolik yang boleh dikaitkan dengan tindakan anti-radangnya dengan menggunakan sel makrofag murine. Hasil kajian menunjukkan bahawa rawatan *M. charantia* merencat translokasi NF-κB dan menyekat peningkatan ekspresi gen pro-keradangan yang dirangsang oleh LPS termasuk IL6 (-84.7 %), TNF-α (-85.1 %), IL1β (-94.2 %), COX2 (-89.5 %), dan iNOS (-28.8 %). *M. charantia* juga menurunkan ekspresi GLUT1 (-94.3 %) dan penghasilan laktat (-28 %) yang dirangsang oleh LPS. Data ini menyokong potensi peranan metabolisme glukosa dalam keradangan. Hasil kajian menunjukkan bahawa kesan anti-radang *M. charantia* boleh dikaitkan dengan pengawal aturan glikolisis dan kitaran asid trikarbosilik (TCA), modulasi metabolisme asid amino, dan tindakan metabolit anti-radang berpotensi dalam *M. charantia*. Di samping itu, kajian ini juga menghasilkan penemuan baharu yang menunjukkan kesan anti-radang dan anti-glikolitik charantin. Charantin merupakan sebatian bioaktif utama dalam *M. charantia* yang terkenal dengan sifat hipoglisemiknya tetapi sifat anti-radangnya belum dapat dijelaskan sepenuhnya. Ia adalah campuran 1:1 dua komponen termasuk sitosterol glukosida dan stigmasterol glukosida. Dalam kajian ini, charantin dan setiap komponennya didapati memaparkan aktiviti anti-radang dengan menyekat ekspresi gen IL6, TNF-α, iNOS, TLR4, MCP1, GLUT1 dan HK2. Kedua-dua komponen tersebut juga menyebabkan perencatan sinergistik terhadap ekspresi gen IL1β dan COX2. Selanjutnya, charantin dan stigmasterol glukosida didapati menyebabkan perencatan separa translokasi NF-κB, mengurangkan pemfosforilan p-38 MAPK secara signifikan, dan mengurangkan penghasilan laktat dalam makrofag sel RAW264.7 yang diaktifkan LPS. Dalam kajian ini, aktiviti-aktiviti anti-radang dan anti-glikolitik *M. charantia* dan charantin didapati menghasilkan keputusan kajian yang setanding. Untuk mengkaji lebih lanjut tentang hubungan antara kesan anti-radang dan gangguan metabolisme glukosa, satu ujikaji telah dilakukan untuk mengkaji potensi strategi anti-radang dengan menyasarkan GLUT1 menggunakan WZB117, sejenis perencat spesifik GLUT1. WZB117 didapati menurunkan ekspresi gen pro-radang *IL6* (-93.3 %), *TNF-α* (-63.2 %), *IL1β* (-76.1 %), *COX2* (-41.34 %), *iNOS* (-98.48 %), *MCP1* (-85.59 %) dan *GLUT1* (-85.51 %) dalam sel RAW264.7 yang diaktifkan LPS. Selain itu, WXB117 juga mengurangkan pengeluaran laktat yang ditingkatkan oleh LPS sebanyak 11.16 %. Secara keseluruhannya, kajian ini menunjukkan kesan anti-radang dan anti-glikolitik *M. charantia* dan charantin, dan memberikan bukti yang menunjukkan gangguan metabolisme glukosa dalam tindak balas keradangan. Hasil kajian ini menyokong strategi terapi melawan penyakit keradangan menyasarkan metabolisme glukosa.

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LIST OF ABBREVIATIONS

AKT	-	Protein kinase B
AOAC	-	Association of Official Agricultural Chemists
ATCC	-	American Type Culture Collection
ATP	-	Adenosine triphosphate
BMI	-	Body mass index
BSA	-	Bovine serum albumin
CARKL	-	Carbohydrate kinase-like protein
CE-MS	-	Capillary electrophoresis mass spectrometry
CSF	-	Colony-stimulating factor
COX	-	Cyclooxygenase
CPPD	-	calcium pyrophosphate dihydrate
CPT	-	Carnitine palmitoyl transferase
CRP	-	C-reactive protein
DMEM	-	Dulbecco's Modified Eagle's medium
DMSO	-	Dimethyl sulfoxide
DRG	-	dorsal root ganglion
ERK	-	Extracellular-signal-regulated kinases
ETC	-	Electron transport chain
eNOS	-	endothelial nitric oxide synthase
FADH	-	Flavin adenine dinucleotide
FAO	-	Fatty acid oxidation
FBS	-	Fetal bovine serum
FDA	-	Food and Drug Administration
FFA	-	Free fatty acid
FID	-	Free induction decay
FT-IR	-	Fourier transform infrared
GC-MS	-	Gas chromatography-mass spectrometry
GLUT	-	Glucose transporter
GM	-	Granulocyte macrophage
G6PD	-	Glucose-6-phosphate dehydrogenase

HCA	-	Hierarchical cluster analysis
HIF	-	Hypoxia-inducible factor
HIV	-	Human immunodeficiency viruses
HK	-	Hexokinase
HMDB	-	Human metabolome database
HOMA	-	Homeostatic model assessment
ICP-MS	-	Inductively coupled plasma mass spectrometry
IKKβ	-	IκB kinase
IFN	-	Interferon
IL	-	Interleukin
iNOS	-	inducible nitric oxide synthase
IR	-	Insulin resistance
IRS	-	Insulin receptor substrate
JNK	-	Jun amino-terminal kinases
KO	-	Knockout
LAL	-	Lysosomal acid lipase
LC-MS	-	Liquid chromatography mass spectrometry
LDH	-	Lactate dehydrogenase
LPS	-	Lipopolysaccharide
MAPK	-	Mitogen-activated protein kinases
MAPKK	-	MAPK kinase
MAPKKK	-	MAPK kinase kinase
MC	-	*Momordica charantia*
MCP	-	Monocyte chemotactic protein
MCT	-	Monocarboxylate transporter
MIF	-	Migration inhibitory factor
MLR	-	Multiple linear regression
MPP	-	1-methyl-4-phenylpyridinium
MSU	-	Monosodium urate
MTT	-	4,5-dimethylthiazol-2-yl-2,5-diphenyltetrazoliumbromide
NADH	-	Nicotinamide adenine dinucleotide $(NAD)^{+}$ hydrogen(H)
NF-κB	-	Nuclear factor-kappa B
NIPALS	-	Non-linear iterative partial least squares

NMR	-	Nuclear magnetic resonance
NO	-	Nitric oxide
NSAID	-	Non-steroidal anti-inflammatory drugs
nNOS	-	neuro nitric oxide synthase
ODC	-	Ornithine decarboxylase
OE	-	Over expression
OXPHOS	-	Oxidative phosphorylation
PBS	-	Phosphate-buffered saline
PC	-	Principal components
PCA	-	Principal components analysis
PDK	-	Pyruate degydrogenase kinase
PFK2	-	Phosphofructo-2-kinase
PFKFB3	-	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3
PGE_2	-	Prostaglandin E2
PKC	-	Protein kinase C
PKM2	-	Pyruvate kinase M2
PL	-	Phospholipase
PLS	-	Partial least squares
PLS-DA	-	Partial least squares discriminant analysis
PMSF	-	Phenylmethyl sulfonyl fluoride
PPP	-	Pentose phosphate pathway
PVDF	-	Polyvinylidene difluoride
p38	-	Stress-activated protein kinases
RNA	-	Ribonucleic acid
ROS	-	Reactive oxygen species
RT-PCR	-	Real time polymerase chain reaction
SLE	-	Self-organizing maps
SOTA	-	Self-organising tree algorithm
SPC	-	Standard plate count
TAM	-	Tumour-associated macrophage
TCA	-	Tricarboxylic acid cycle
TFRC	-	Transferrin receptor
TGF-β	-	Transforming growth factor- β

Th	-	T helper
TLR	-	Toll like receptor
TNF-α	-	Tumour necrosis factor- α
TOF	-	Time of flight
TSP	-	Trimethylsilylpropanoic acid
T2DM	-	Type 2 diabetes mellitus
VCAM	-	Vascular cell adhesion molecule
VEGF	-	Vascular endothelial growth factor
VIP	-	Variable important for the projection
2-DG	-	2- deoxyglucose

LIST OF SYMBOLS

µg	-	microgram
µL		microliter
mL	-	milliliter
rpm	-	Revolution per minute
kDa	-	kilo Dalton

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CHAPTER 1

INTRODUCTION

1.1 Background

Inflammation is an immune response of a biological system towards harmful stimuli such as toxic chemicals, infections or physical injury (Chen *et al.*, 2018). The signs of inflammation include pain, heat, swelling, and redness (Huo et al., 2013). Inflammation can be classified as either acute or chronic. Acute inflammation refers to short-term biological protective mechanism of organism towards an injury, irritation or surgery (Huo et al., 2013). If acute inflammation is left unresolved, it will lead to chronic inflammation, which may last for a prolonged periods(Zhou *et al.*, 2016). Notably, there are increasing reports showing association between chronic inflammation and diseases including cardiovascular diseases, type 2 diabetes mellitus, cancer, neurological diseases, and arthritis. (Oishi and Manabe, 2018).

Macrophages play a crucial role in regulating inflammatory events and immune responses (Gordon and Martinez-Pomares, 2017). They are responsible in initiating and resolving the inflammatory events. The classically-activated macrophages initiate inflammatory events by releasing pro-inflammatory cytokines to clear pathogens and damaged or dead cells, while the alternatively-activated macrophages support the repair process of damaged tissue (Freemerman *et al.*, 2014a). In laboratory, murine RAW264.7 macrophages have been recognized as an established model to study inflammation (Xu *et al.*, 2017; Yu *et al.*, 2017; Dong *et al.*, 2018; Xuehong Wang *et al.*, 2019; Q. Guo *et al.*, 2020).

The macrophages can be activated by treatment with lipopolysaccharide (LPS), a potent innate immune-activating stimuli (Rodriguez *et al.*, 2019). LPS is a prototypical endotoxin found in the outer membrane of Gram-negative bacteria. When treated with LPS, the macrophages showed production of measurable inflammatory mediators such as leukotrienes, TNF-α and interleukins (ILs) (Fan et al., 2013).

Momordica charantia (MC) is also known as bitter melon, bitter gourd and karela. It is climber plant that is widely cultivated and used as food in Asia, Africa and South America. MC is known for its therapeutic roles in traditional medicine (Dandawate *et al.*, 2016). The anti-inflammatory activities of 5β,19-epoxycucurbitane triterpenoids extracted from MC was reported to inhibit nitric oxide production in LPS-induced RAW264.7 cells. (Liaw *et al.*, 2015). In another study, ethanol extract of MC reduced LPS-induced nitric oxide, inducible nitric oxide synthase (iNOS), prostaglandin E2 (PGE_2) and pro-interleukin-1 beta expression (Dandawate et al., 2016). In mouse model, administration of freeze-dried MC powder also significantly decreases the protein levels of NF-κB, c-Jun N-terminal kinase (JNK), cyclooxygenase-2 (COX2), and inducible nitric oxide synthase (Yang et al., 2015). Furthermore, MC supplementation also found to improve inflammatory responses in sepsis mouse (Chao *et al.*, 2014).

The anti-diabetic mechanisms of MC reported in previous studies were contributed by its cucurbitane-type compounds, saponins, proteins and polysaccharides. These bioactives in MC were reported in in-vivo and in-vitro studies to exert anti-diabetic properties though different mechanism such as molecular docking activity on glycolytic enzymes, regulating energy metabolism and anti-oxidant activity that protect and repair pancreatic β cells (Poovitha and Parani, 2017; Yunos *et al.*, 2017; C. Zhang *et al.*, 2018; Abdel-Rahman *et al.*, 2019; Q. Wang *et al.*, 2019; Shivanagoudra *et al.*, 2019).

Previous studies of MC confirmed the anti-diabetic and anti-inflammatory effect of MC. However, they did not look into the possible link between the two. In addition, the effect of MC on glucose metabolism in macrophages has yet to be established. The study aimed to investigate the glycolytic effect of MC and the possible link between the anti-inflammatory effect of MC and the glycolytic effect of MC.

During inflammatory response, macrophages undergo reprogramming of their cellular metabolism (Ip et al., 2017). Notably, the activated macrophages preferentially metabolize glucose as an energy source and rely on glycolysis for their energy needs, in a manner similar to the Warburg effect in cancer cells (Ubanako *et al.*, 2019). In a previous study, high glucose was found to induce inflammatory response (Freemerman *et al.*, 2014a). The researchers also showed that the capacity of inflammation depends on glucose transporter (GLUT)-1 mediated glucose uptake and enhanced glucose metabolism (Freemerman *et al.*, 2014b). The changes in cellular metabolism of activated macrophages make it a suitable model to study the role of glucose metabolism in inflammatory events.

Metabolomics is a comprehensive and holistic characterization and quantification of intracellular and extracellular metabolites in a biological system. It could identify significant changes and perturbations happen as a result of cell adaptation (Emwas, 2015). The technology has been applied in many fields such as mechanism and diagnosis of human diseases, drug and biomarker discovery, plant biotechnology, food technology, toxicology, and environmental studies (Alonso *et al.*, 2016; Rattigan *et al.*, 2018; Mendes *et al.*, 2019; Ye *et al.*, 2020). Metabolomics will help to uncover the perturbed metabolism in inflammation and metabolic regulatory effects of MC.

Charantin is one of the key bioactive compounds of MC, known for its anti-diabetic activity (Wang et al., 2014; Desai and Tatke, 2015; Ahamad, Mir and Amin, 2019). To date, the anti-inflammatory potential of charantin has yet to be elucidated. Therefore, investigation on the potential regulatory effects of charantin on inflammation and metabolism in may provide new insight into their anti-inflammatory potential.

As differential cellular metabolism is closely related to the activation of immune cells, the research field was named “immunometabolism” and are now gaining more and more research interest with the hope to understand the complex immunity system better and to possibly provide clinical intervention through modulating the cellular metabolism in the treatment of inflammation associated diseases (Pålsson-McDermott and O’Neill, 2020). Therefore, perturbed metabolism may be a therapeutic target for inflammation. This study explored the possible link between the anti-inflammatory effect of MC with the effect of MC on perturbed glucose metabolism in activated macrophages.

1.2 Problem Statement

A number of studies showed anti-inflammatory activity of MC. However, there is a need of a comprehensive study on a aqueous extract of MC which is similar to the typical administration form of MC as a traditional herbal supplement such as dried MC powder capsules and MC-infused tea. The anti-inflammatory effect of aqueous MC extract and the effect of the extract on glucose metabolism of macrophages has yet to be established.

There are increasing studies associating inflammation with perturbed glucose metabolism (Van den Bossche *et al.*, 2017). To date, there is no answer to the question of whether the anti-inflammatory effect of MC can be linked to the effect of MC on glucose metabolism. Furthermore, the perturbation in cellular metabolism associated with inflammation and MC treatment in RAW264.7 cells are not established.

In addition, it has not been reported whether the anti-diabetic compound in MC, charantin, may exert ant-inflammatory action in activated macrophages. By targeting glucose metabolism, the potential of using specific GLUT1 inhibitor as an anti-inflammatory strategy is not fully understood. These research problems may be investigated using a combination of cell-based study, gene expression analysis, and metabolomics approach.

1.3 Objectives

The aim of this project is to implement a combined cell-based assay, gene expression analysis, and metabolomics approach to investigate the anti-inflammatory and anti-glycolytic activities of *Momordica charantia* and to characterise the metabolic changes associated with its anti-inflammatory action using a murine macrophage cell model. The main objectives are:

a) To characterize freeze-dried *Momordica charantia* and its aqueous extract.

b) To examine the anti-inflammatory and anti-glycolytic activities of *Momordica charantia* on LPS-induced RAW264.7 cells.

c) To characterize the metabolic perturbation associated with LPS induction and *Momordica charantia* treatment on RAW264.7 cells.

d) To investigate the potential anti-inflammatory and anti-glycolytic effect of charantin on the LPS-induced RAW264.7 cells.

e) To elucidate the potential of anti-inflammatory strategy by targeting GLUT1.

1.4 Scopes of The Study

The present study used LPS-induced murine RAW264.7 macrophages as a cell model of inflammation. Gene expression analysis was used to investigate the effects of LPS and MC treatments on twelve selected pro-inflammatory genes (including *IL6, TNF-α, IL-1β, COX2, iNOS, IL10, AKT1, AKT2, COX1, LOX5, LOX15* and *IFNβ*) and fifteen genes involved in glucose metabolism (including *GLUT1, HK2, LDHA, PFK1, ALDOA, PGK1, PGM1, ENO1, PGAM2, TPI1, PDK4, GPI1, IDH1, IDH3A* and *MDH2*).

In addition, the effects of LPS and MC on translocation of NF-κB from cytoplasm into nucleus was studied using immunofluorescence-staining method and observed under confocal microscope. Furthermore, the glucose consumption and lactate production in macrophages treated with LPS and MC were quantified using commercial assay kits.

Furthermore, a proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy based metabolomics study was carried out to characterize the metabolic perturbation associated with LPS-induced inflammation and the anti-inflammatory effect of *Momordica charantia*. The analysis was done by 850MHz Bruker NMR system and both intracellular and extracellular metabolome were analysed to provide a comprehensive overview for the perturbed metabolism associated with the event of LPS-induced inflammation and the anti-inflammatory activity of MC treatment in the RAW264.7 macrophages. Multivariate data analysis was performed to analysed the metabolomics data.

Next, the potential anti-inflammatory effect of charantin was investigated using the LPS-induced RAW264.7 macrophages. Charantin is an 1:1 mixture of two components, including sitosterol glucoside and stigmasterol glucoside (Satya Vani Chekka and Naresh Kumar Mantipelly, 2020). Charantin is known for its hypoglycemic activities. In this study, the LPS-induced RAW264.7 macrophages were treated with charantin, as well as each of its components (sitosterol glucoside and stigmasterol glucoside). Gene expression analysis was conducted which included nine selected proinflammatory (including *IL6, TNF-α, IL1β, COX2, iNOS, TLR4* and *MCP1*) and glycolytic genes (including *GLUT1* and *HK2*). Immunofluorescence-staining followed by observation using confocal microscope was also carried out to examine the effects of charantin and its components on NF-κB translocation. In addition, their effects on the inflammatory mitogen-activated protein kinase (MAPK) and JNK pathways were evaluated using Western blot. The relative protein expression of total p38 MAPK protein, phosphorylated-p38 MAPK protein, total JNK and phosphorylated-JNK protein were evaluated from cell lysate. The glucose and lactate concentrations in extracellular medium were also quantified to study their potential anti-glycolytic effect.

Then, an experiment was performed to study the anti-inflammatory potential of WZB117 (a specific GLUT1 inhibitor) using the LPS-induced macrophages. The study focused on the ability of WZB117 to suppress inflammation and glycolysis in macrophages. The study was carried out through RT-PCR analysis to examine the changes in the transcription of inflammatory and glycolytic genes (including *IL6, TNF-α, IL1β COX2, iNOS, TLR4, MCP1* and *GLUT1*), as well as the end-point glucose and lactate concentration.

1.5 Significance of The Study

The present study focused on the anti-inflammatory activities of *Momordica charantia*. This study provided new evidences showing the effect of LPS induction on the expression of glycolytic genes in the activated macrophages. In addition, the anti-inflammatory and anti-glycolytic activities of MC were also established using the RAW-264.7 cell model. The ^{1}H-NMR based experiment also provided new findings that associated perturbed cellular metabolism with the LPS-induced inflammation and the anti-inflammatory bioactivity of MC treatment.

The current results also uncover the anti-inflammatory potential of charantin, which has not been reported before. Furthermore, the effects of each of the components of charantin (including sitosterol glucoside and stigmasterol glucoside) on inflammation were also presented, showing the bioactivity of each component and their synergistic effects on suppression of inflammatory response. The finding reported the effect of charantin on glucose metabolism in RAW264.7 cells.

By targeting GLUT1 inhibition in LPS-induced RAW264.7 cells, the anti-inflammatory activity of WZB117 provided evidences for the link between glucose metabolism and macrophage activation. Together, the current study provided new insight into the anti-inflammatory potential of MC and charantin via their effects on glucose metabolism in macrophages. The findings also support a therapeutic strategy against inflammation by targeting glucose metabolism.

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LIST OF PUBLICATIONS

Journal with Impact Factor

1. **Lee, S. Y.**, Wong, W. F., Dong, J. & Cheng, K. K. (2020). *Momordica charantia* Suppresses Inflammation and Glycolysis in Lipopolysaccharide-Activated RAW264.7 Macrophages. *Molecules*, 25, 3783. http://doi:10.3390/molecules25173783. **(Q2, IF: 3.267)**

Indexed Conference Proceeding

1. **Lee, S. Y.**, Wong, W. F., & Cheng, K. K. (2018). Effect of *Momordica charantia* Treatment on Inflammatory Responses in RAW264.7 34 Cells. In *7th International Conference On Biotechnology For The Wellness Industry (7th ICBWI 2018)* (pp 34-37). IBD. **(Indexed by SCOPUS)**