INTERLEUKIN-2 PRODUCTION BY PERIPHERAL BLOOD MONONUCLEAR CELL (PBMC) TREATED WITH *Gynura procumbens* ETHANOLIC EXTRACT

By

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Thesis Submitted in Partial Fulfilment of the Requirements for Bachelor of Medical Laboratory Technology (Hons)
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2016

ACKNOWLEDGEMENT

I am grateful to Allah SWT, for the blessed gave to me and also the strength and health to complete the study and the thesis. Huge gratitude and appreciation for everyone who involved directly or indirectly from the beginning until the completion of this study.

First of all, I would like to thanks my supervisor, Mr Wan Shahriman Wan Yushdie and co-supervisor, Mr Mohd Nazri Abu for a very helpful guidance, advice, ideas, motivation and all the patience in during assisting us from the start until the end of the research.

Special thanks to my beloved family members, especially Mr Rahim Omar and (parents) and my siblings on their moral support, understanding, prays and encouragement for me to successfully complete this research.

I would like to express my gratitude to all the laboratory staff of Medical Laboratory Department, Faculty of health Sciences especially for their helpful assistance in making our study to run smoothly.

I am also greatly thankful to Mdm Rohana, phlebotomist in Unit Kesihatan UiTM Puncak Alam, Mdm Fahanah Misripin and Mdm Mastura Maad, laboratory staff of Faculty of Pharmacy and also the postgraduate students of Faculty of Health Sciences for the big help during and before the lab work process.

Last but not least, to all my supportive group member for their commitment, assistance and opinions for me to complete this research.

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ABSTRACT

Gynura procumbens from the family of Compositae are widely distributed through South East Asia particularly in Indonesia, Thailand, and Malaysia. It is routinely used by folk as traditional medicine to treat various diseases such as cancer, eruptive fever, diabetes mellitus and hypertension. Previous study on *G. procumbens* shows it immunomodulatory activity on proliferation of T-cell and B-cell but lack study done on its ability to modulate the cytokine production particularly interleukin-2. Thus the aim of this study is investigate the effect of *G.procumbens* ethanolic extract (GPEE) on the expression of interleukin-2 (IL-2). Phytochemical screening was first done on the GPEE to detect the presence of flavonoid, saponins, tannins, terpenoids and anthraquinones. Peripheral blood mononuclear cell (PBMC) was used to study the effect of GPEE on the expression of IL-2. The production of IL-2 were evaluated in the cell with or without treatment of GPEE. CLI-095, a specific Toll-Like Receptor 4 (TLR4) inhibitor were used to determine whether the activity of GPEE are through TLR4 signaling pathway or not. The present of endotoxin in the extract that contributes to its immunomodullatory activity were evaluated by polymixin-B (PMB), an endotoxin inhibitor. GPEE were found to contain flavonoid, saponins, tannins, and terpenoids but lack in anthraquinones. It also increased the production IL-2 by PBMC. The co-treatment of PBMC with CLI-095 and PMB do not inhibit the production of IL-2 by PBMC. *G. procumbens* shows imunomodulltory activity by enhancing the expression of IL-2 independent of TLR4 pathway and contamination of endotoxin. This finding provide an insight to the role of *G.procumbens* in stimulating immune system which could be potential as a new therapeutic strategy.

Keywords: *Gynura procumbens*, peripheral blood mononuclear cell, interleukin-2, toll-like receptor 4, immunomodulation, Luminex

CHAPTER 1

INTRODUCTION

1.1 Background

Gynura procumbens from the Family of Compositae is an evergreen perennial herbaceous plant. It is fast growing, a decumbent shrub with a fleshy stem that widely distributed in South East Asia country particularly in Indonesia, Thailand, and Malaysia. *G. procumbens* have medicinal value where folks routinely use it as traditional medicine to treat various diseases such as cancer, eruptive fever, rash, hypertension, diabetes mellitus, kidney disease, migraine, constipation, inflammation, rheumatism and viral infection. The local names for *G. procumbens* are Sambung Nyawa in Malay or Jian Wei Feng in Chinese (Perry, 1980). *G. procumbens* proved to possessed immunomodulatory activities and act as immunomodulators based on the test done on mice splenic cells. It appears to be both immunostimulant and immunosuppressant which show an increasing effect on the proliferation of Tcells and decreasing effect on the proliferation of B cells (Dwijayanti and Rifa'i, 2014).

Immunomodulation is the modulation or regulation of immune system either by increasing or suppressing the immune response. Immunomodulators can be either biological or synthetic substances which are able to modulate, stimulate or suppress the immune system in any aspect including the innate and adaptive immune system (Kumar et al., 2012). Strategies used for the development of immunomodulators in various immune diseases includes; transcription factor modulation, T_H subset balance, cell surface molecules, gene activation, signalling sequences, Toll-like receptor-4 agonist, cytokines, and cytokines receptor (Ballas, 2008).

Interleukin-2 (IL-2)is a type of cytokine that primarily being produced by activated $CD4^+$ T cell upon stimulation with antigen (Leonard, 2001). It also produce by $CD8^+$ cells in lesser extends (Paliard et al., 1988), activated dendritic cells (DCs) (Granucci, Vizzardelli, Pavelka, & Feau, 2001) , NK T cells (Yui, Sharp, & Havran, 2004), and mast cells (Hershko, Suzuki, Charles, & Alvarez-Errico, 2011). IL-2 act as