MANUSCRIPT

THE SYNERGISTIC EFFECT OF *CLITORIA TERNATEA* AND *GANONERMA LUCIDUM* EXTRACT ON WOUND HEALING

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ABSTRACT: Wound healing can be one of the most complex processes in the human body. Years ago, plants and their extracts have been utilized for therapeutic purposes. The present study aimed to investigate the wound healing effect of *Clitoria ternatea* and *Ganoderma lucidum* extract on zebrafish tail regeneration. Zebrafish embryo toxicity testing was done to determine the lethal concentration (50%). Zebrafish model was used for wound healing treatment grouping. Tail amputation had been done and tail regeneration was recorded. The treatment dose of *C. ternatea*, *G. lucidum*, and both extracts were given for 15 days. Histological studies were also performed. Scanning electron microscopy had been done for *C. ternatea.* LC_{50} of *G. lucidum* was determined (10.57 µg/mL). The growth of the zebrafish model tails had demonstrated substantial results. Histological findings demonstrated a significant presence of inflammatory cells. SEM detected the presence of few elements in *G. lucidum.* The embryo toxicity investigation revealed the toxicity levels of *G. lucidum* were quite low. When the two extracts were combined, there was a noticeable growth in a shorter amount of time. Histological finding of tail regeneration showed that the inflammatory cells are particularly distinctive. To conclude, the advantages of *C. ternatea* and *G. lucidum* extracts on the healing of wounds have been demonstrated.

Keywords: Wound healing, *Clitoria ternatea, Ganoderma lucidum*, Zebrafish tail regeneration, Synergistic effect

INTRODUCTION

The skin is the largest organ by surface area in the human. It is the essential structure that aids in protecting the internal tissues from microbial infection, mechanical damage, extreme temperature, and ultraviolet radiation (Rodrigues et al., 2019). Due to this, this makes it more susceptible to injury. Wounds are the result of injuries or disruption of cellular and functional continuity of living tissue. Wound healing can be one of the most complex processes in the human body. This can prove when it involves with the spatial and temporal synchronisation of various cell types with specific roles in the phases of haemostasis, inflammation, growth, re-epithelialisation, and remodelling.

Clitoria ternatea, also known as butterfly pea, is a perennial herbaceous plant that comes from the Fabaceae family. They are native to tropical Asian countries especially in Malaysia and Indonesia. It has been widely used in traditional medicine, specifically as a supplement to enhance cognitive functions and alleviate symptoms of numerous ailments which include inflammation, pain, fever, and diabetes (Oguis et al., 2019). Pharmacologically, this flower is also an anxiolytic, anti-inflammatory, analgesic, and anti-carcinogenic.

Furthermore, *C. ternatea* possesses vibrant blue flowers in which in commonly known to be anthocyanins. Anthocyanins are a group of dietary flavonoids where it is known as a natural bioactive compound (Limsitthichaikoon et al., 2018). The abundance of unique anthocyanins alongside other secondary metabolites in *C. ternatea,* makes the plant an ideal source of natural additives that can enhance the nutritive values of consumer products (Oguis et al., 2019). There have been new studies suggest its potential applications in both modern medicine and agriculture, as well as for antioxidants.

Ganoderma lucidum or commonly known to the public as “Ling Zhi” is an annual or perennial fungus. This fungus is the family of *Ganodermataceae* (Yang et al., 2019). In nature, it can be found mostly growing in subtropical and temperate climate regions such as Africa, Europe, Asia, and America. Pharmaceutically active chemicals are abundant in medicinal mushrooms. Based on recent research, it has been confirmed that this fungus contains over 400 bioactive compounds. This includes polysaccharides, triterpenoids, steroids, fatty acids, amino acids, nucleosides, proteins, and alkaloids (Lu et al., 2020). For *G. lucidum*, the active components and relative pharmacological activity vary depending on the stage of growth.