

Thesis Progression

Thesis title	: Effects of Chitosan on Human Neutrophil Functions Against <i>Acinetobacter baumannii</i> Infections
Student	: Dwi Khalimah, Student ID : 665070051-7
Advisor	: Dr. Arnone Nithichanon
Co-Advisor	: Asst. Prof. Dr.Sorujsiri Chareonsudjai
Date	: 31 st 2024

1.1 Background and Rationale

Acinetobacter baumannii is the most clinically significant bacterial infection that has become an increasing threat to human health worldwide related to multidrug resistance bacteria. World Health Organization (WHO) in 2023 listed that *A.baumannii* was the critical urgent pathogen which was estimated responsible for 1.27 million global deaths in 2019 and contributed to 4.95 million deaths. Colistin antibiotics are the last line of treatment that has resisted *A. baumannii*. Bacteria associate with some diseases such as bloodstream infections, pneumonia, meningitis, urinary tract infections, skin infections, and wound infections (Pogue et al., 2022). Important factors that cause patients to become infected with *A.baumannii* in the hospital are when the patient is hospitalized for a long time, receives treatment that requires the insertion of a tube into the body, and the patient's immune system reduced based on a research experiment of cancer patients receiving bone marrow transplants.

WHO in 2017 declared that development of antibiotics and immune promotion were one of urgent priorities to solve the problem. Many studies have been carried out on combination of certain antibiotics with biopolymers and most of their studies have succeeded in inhibiting or killing bacteria. However, in fact bacterial resistance is still quite common and many patients die. According to one report, the mortality rate did not depend on drug resistance however it depended on an impaired immune system (Nithichanon et al., 2022). Evaluating the immune system is something that must be considered after carrying out an antimicrobial test which is necessary for success in application. In past studies, it has been found that neutrophils are important white blood cells that are responsible for capturing and destroying *A. baumannii* through the mechanisms of phagocytosis, the generation of radical oxidative species (ROS) and the formation of neutrophil extracellular traps (NET) (Morris et al., 2019). However, *A. baumannii* still has the ability to evade immunity through a mechanism that inhibits the binding of white blood cells to the infection.

Chitosan is a promising polymer that has gotten a lot of attention in the last 10 years especially in medical formation. It is derived from chitin that is the main building blocks of the exoskeletons of insects, crustaceans, and fish, as well as the cell walls of fungi. It has great potential that encapsulates substances such as antimicrobial, anti-inflammatory, anti-oxidative (Hemmingsen et al., 2022) drug or active compounds, deliver them to specific places or sites, and provide a control release, a natural polysaccharide, cationic polymer, environmentally-benign, nontoxicity, biodegradability and physiological stability. Chitosan can also enhance the immune response to vaccine antigens to prevent infection *A. baumannii* from the creation of antibodies and responses from specific T helper 1 cells (Du et al., 2021).The aim of this research is to study effect of chitosan on neutrophil function against *A. baumannii*.

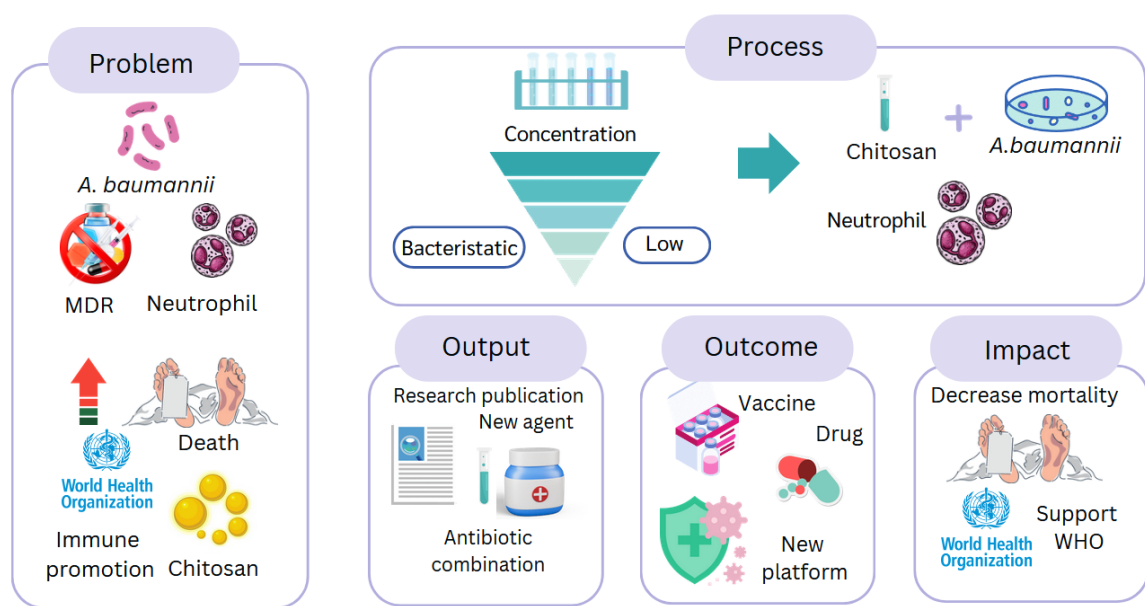
1.2 Objectives

- 1.2.1 To study the effect of chitosan against *A.baumannii*
- 1.2.2 To study the toxicity of chitosan against neutrophil.
- 1.2.3 To study the effect of chitosan on neutrophil function in *A.baumannii*.

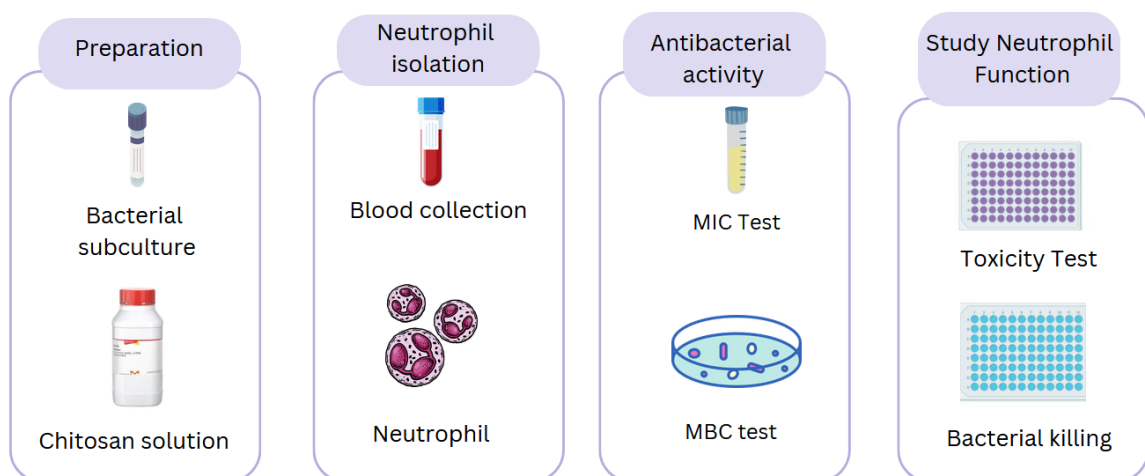
1.3 Hypothesis

- 1.3.1 Chitosan can inhibit on the growth of *Acinetobacter baumannii*
- 1.3.2 Chitosan can be optimized at the certain concentrations to enhance neutrophil function against *A. baumannii*.

1.4 Conceptual framework



1.5 Experimental design



MIC= Minimum Inhibitory Concentration

MIC= Minimum Bactericidal Concentration

1.6 Thesis Plan

No.	Activities	2023	2024	2025	
		Semester		Semester	
		1	2	3	4
1	Course work				
2	Literature review and planning				
3	Proposal presentation				
4	Bacterial preparation				
5	Data Collection and Evaluation				
6	Chitosan preparation				
7	MIC and MBC of Chitosan against <i>A. baumannii</i>				
8	Data Analysis and Evaluation				
9	Neutrophil Isolation				
10	Toxicity test of Chitosan against Neutrophil Function				
11	Data Analysis and Evaluation				
12	Studying Neutrophil Function				
13	Data Analysis and Evaluation				
14	Preparing a draft report of research result (revision)				
15	Submission and presentation research result (publication)				

Reference

- Du X., Xue J., Jiang M., Lin S., Huang Y., Deng K., Shu L., Xu H., Li Z., Yao J., Chen S., Shen Z., Feng G., (2021), A Multiepitope Peptide, rOmp22, Encapsulated in Chitosan-PLGA Nanoparticles as a Candidate Vaccine Against *Acinetobacter baumannii* Infection. PubMed. 16: 1819–1836. doi: 10.2147/IJN.S296527
- Hemmingsen L.M., Panchai P., Julin K., Basnet P., Nystad M., Johannessen M., Basnet S. N.,(2022), Chitosan-based delivery system enhances antimicrobial activity of chlorhexidine. *Frontier in Microbiology*. 13:1023083. doi: 10.3389/fmicb.2022.102308.
- Morris, F.C., Dexter, C., Kostoulias, X., Uddin, M.I., and Peleg, A.Y. (2019). The Mechanisms of Disease Caused by *Acinetobacter baumannii*. *Front Microbiol* 10, 1601.
- Nithichanon, A., Kewcharoenwong, C., Da-oh, H., Surajinda, S., Khongmee, A., Koosakunwat,S., Wren, B. W., Stabler, R. A., Brown, J. S., & Lertmemongkolchai, G. (2022).*Acinetobacter nosocomialis* Causes as Severe Disease as *Acinetobacter baumannii* in Northeast Thailand: Underestimated Role of *A. nosocomialis* in Infection. *Microbiology Spectrum*, 10(6). <https://doi.org/10.1128/spectrum.02836-22>
- Pogue, J. M., Zhou, Y., Kanakamedala, H., & Cai, B. (2022). Burden of illness in carbapenem-resistant *Acinetobacter baumannii* infections in US hospitals between 2014 and 2019.
- World Health Organization (WHO). November 21st, 2023. Antimicrobial resistance. January 27th, 2024, <https://www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance>.