INTRODUCTION

1.1. Background

In the evolving world of medical research, finding novel strategies in treating diseases has led scientists to explore different aspects of medication. Natural products have emerged as an alternative way to synthetic drugs, and this has drawn attention in the research world as a potential therapy option for a wide range of diseases. This shift in focus towards alternative therapies is supported by the will to discover other methods that could enhance the efficacy of existing medications or to even unveil new therapeutic approaches for disease that remain enigmatic, such as chronic granulomatous disease, a rare genetic disorder that affects the neutrophil function (Leliefeld et al., 2016).

Neutrophils are the primary cells that play a significant role in the innate immune defense system. They act as the first responders in the innate immune system (Malech et al., 2014). During a pathogenic invasion, these cells are recruited to the site of infection and perform many different functions, such as phagocytosis, respiratory burst, degranulation, and formation of NETs (Gierlikowska et al., 2021). Nonetheless, researchers have discovered that neutrophils have various functions in the immune system (Gretchen et al., 2017). They respond to different signaling particles by the secretion of cytokines and various mediators that regulate the immune system and the inflammatory response (Scapini & Cassatella, 2014). Consequently, neutrophil activation is crucial in defending the host from bacteria infections (Lehman & Segal, 2020). A few potential drug candidates have yet to be investigated in solving this medical problem.

Regardless of their function in immune defense, targeting the neutrophils for therapeutic interventions has been challenging due to their signaling pathway and mechanism complexity. Therefore, the search for potential drug candidates that regulate or even enhance neutrophil function remains a big question in science. In this research, DX23 has been chosen to be investigated as a drug candidate to improve neutrophils' regulation of function. DX23 is a type of drug that is used to treat cystic fibrosis, which is a genetic disorder that correlates to the digestive system and lungs (Kapoor et al., 2014). It is classified as one of a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator that targets defective CFTR proteins and to enhance its function (Condren & Bradshaw, 2013). It works by binding to the CFTR protein on the surface of the cell and will assist the protein to have longer duration in opening, which enhances the modulation of the transport of chloride and water across the membrane (Fohner et al., 2017). In the pursuit of an existing solution towards cystic fibrosis (CF) patients, the urgency to harness the therapeutic potential of DX23 unfolds

as a compelling investigation. At the core of this scientific attempt lies the need to address not only the primary manifestations of CF, pointed by the dysfunction of the CFTR protein in the respiratory system, but also the interplay between the immune response, specifically the role of neutrophils. As previous research has been delving into the mechanism of CF, DX23 sheds as an alternative medication, a CFTR modulator portraying remarkable efficacy in improving the functions of the respiratory system. However, it does not end right here. Acknowledging the interconnected ways of CF and the inflammatory challenges it has, researchers are propelled by an urgent need to further investigate DX23's secondary effects, specifically its influence on neutrophil activity. Therefore, further research and studies of this drug must be continued to find innovative therapeutic strategies for treating infectious diseases.

1.2. Research Aims

This research is aimed to elucidate the potential of DX23 as a candidate drug for enhancing neutrophil activity and regulating the immune response.

1.3. Scope of Research

This project's scope consisted of but was not limited to, human neutrophil isolation, which will analyze and examine the immune response and neutrophil function towards the drug being tested. Moreover, This research also analyzes superoxide anion generation along with luminol chemiluminescence assay for detection of ROS, examining the enzymatic activity of elastase, assessing the formation of NETs, as well as CD marker detection to identify granules released by the neutrophil.

1.4. Research Hypothesis

Drug DX23 could be a potential alternative therapy in treating infectious diseases, mainly conditions involving inflammatory responses. Furthermore, it would also enhance the neutrophil functions and regulate the immune system.