

## 1. Introduction

Cancer refers to the uncontrolled proliferation of cells and represents a major category of illnesses that impact various organs of the body, contributing significantly to global mortality rates. The primary risk factors associated with cancer include a high body mass index, tobacco and alcohol consumption, insufficient physical activity, and a low intake of fruits and vegetables. By the end of the 20th century, the World Health Organization (WHO) projected that cancer would become the leading cause of death worldwide [1]. Cancer-related fatalities are frequently attributed to metastasis and disease recurrence, which often arise from the development of drug resistance. Between 2014 and 2019, the incidence of cancer rose by approximately 3% annually, with an estimated 1,665,540 new diagnoses and 585,720 deaths. As the global population continues to expand, the prevalence of cancer is expected to rise correspondingly [2].

Many cancer drugs have now been developed. One of the most commonly employed treatment methods is chemotherapy, which involves the use of pharmaceutical agents to destroy cancer cells [1]. Among the promising candidates for cancer therapy is the Matrix Metalloproteinase-9 (MMP-9) inhibitor, as MMP-9 functions as a biomolecule with potential utility in novel anticancer treatments. MMP inhibitors (MMPIs) exert their therapeutic effects by binding to zinc ions ( $Zn^{+2}$ ) located at the enzyme's catalytic site, thereby inhibiting the activity of MMPs, which contributes to their effectiveness as anticancer agents [3] [4]. However, the development of conventional therapeutic drugs is significantly constrained by the substantial financial burden it entails. It is estimated that the average cost of bringing a single new drug to market reaches approximately 403 million US dollars. Therefore, an alternative solution to overcome the problems of conventional methods in therapeutic drug development is Machine Learning [5].

Numerous studies have applied Machine Learning to anticancer drug development. Kurniawan et al. (2023) predicted indenopyrazole derivatives using ACO and ANN, achieving  $R^2$  test,  $R^2$  train, and  $Q^2$  train scores of 0.8822, 0.8495, and 0.8472, respectively [1]. Banerjee et al. (2023) modeled MMP-9 inhibitors using Bayesian, SARpy, and fragment-based RP classifiers, achieving accuracies of 0.87, 0.78, and 0.85, respectively [3]. In another study, Rizqi et al. (2021) investigated the anticancer activity of indenopyrazole derivatives using Simulated Annealing in combination with Support Vector Machine (SVM) algorithms. The SVM models employed Radial Basis Function (RBF), linear, and polynomial kernels, yielding  $R^2$  scores of 0.60, 0.63, and 0.50, respectively [6].

Research into machine learning approaches for MMP-9 inhibitor prediction has been previously examined, as previously mentioned. However, the performance outcomes of these studies still have room for improvement. One potential enhancement involves the integration of Deep Learning techniques, such as the one-dimensional Convolutional Neural Network (1-D CNN). The 1-D CNN model leverages a one-dimensional filtering mechanism specifically designed for sequential data, enabling it to effectively capture temporal patterns and extract relevant features from input sequences [7]. Further optimization of 1-D CNN performance can be achieved through the use of metaheuristic-based optimization algorithms, one of which is the Monarch Butterfly Optimization (MBO) method. The MBO algorithm offers several advantages, including a balanced approach to intensification and diversification, as well as suitability for parallel preprocessing, making it a promising choice for enhancing deep learning model efficiency [8].

This research aims to develop a model of MMP-9 inhibitors as a prediction of anticancer therapeutics using 1-D CNN optimized with the Monarch Butterfly algorithm. Monarch Butterfly algorithm is a swarm intelligence metaheuristic algorithm inspired by the migration behavior of monarch butterflies [9]. Combining the 1-D CNN method and MBO optimization is expected to predict MMP-9 inhibitors efficiently and accurately.