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SCHOOL OF CHEMICAL ENGINEERING

COLLEGE OF ENGINEERING

TITLE:

**MOLECULAR DOCKING OF AILANTHONE AND ITS DERIVATIVES
AS INHIBITORS TOWARDS HUMAN PANCREATIC ALPHA-
AMYLASE FOR THE TREATMENT OF DIABETES MELLITUS**

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AUTHOR'S DECLARATION

“ I hereby declare that this report is the result of my own work except for quotations and summaries which have been duly acknowledged.”

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ABSTRACT

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by high blood glucose levels either due to insufficient insulin production or improper insulin action. Effective management of Type 2 diabetes includes inhibiting enzymes involved in carbohydrate digestion, particularly human pancreatic α -amylase (HPA) [1]. This study investigates the molecular docking interactions between HPA and four ligands— eurycomanone, eurycomalactone, ailanthone and longilactone. Molecular docking simulations were employed to analyze the binding affinity of these compounds, with the results suggesting that ailanthone exhibited the highest binding affinity, indicating its potential as a promising candidate for further development as an α -amylase inhibitor. These findings underscore the role of molecular docking in discovering natural compounds that could potentially contribute to the development of more effective treatments diabetes [2]. The study highlights how computational tools can aid in understanding protein-ligand interactions and facilitate the identification of bioactive compounds for therapeutic purposes. The results provide valuable insights that nature's medicinal compounds for better management of Type 2 diabetes (T2DM).

BACKGROUND

1.1 INTRODUCTION

Diabetes Mellitus (DM) is a chronic metabolic disorder affecting millions of people worldwide, recognized as one of the leading causes of morbidity and mortality. It is known to be one of the most common causes of death worldwide [3]. DM is a metabolic disease that arises when the body produces less insulin or has less insulin action [4]. According to The World Health (WHO) Global report on diabetes, the number of adults with diabetes has nearly triplet since 1980 to 422 million and it is predicted to reach 693 million by 2045 [5]. In India, diabetes is rapidly becoming an epidemic with over 62 million individuals currently diagnosed, placing a significant burden on healthcare systems and economies [2].

Enzymes that control glycogenolytic or gluconeogenic pathways are therefore important biological targets for therapeutic treatments [6]. Diabetes mellitus type 2 can be effectively treated with α -amylase inhibitors, which efficiently control and reduce postprandial hyperglycemia. Among these, human pancreatic α -amylase (HPA) is a protein enzyme that lies under the glycoside hydrolase family and is found in pancreatic saliva and juice, aids in initiating the breakdown of carbohydrates chemically by hydrolyzing the glycosidic bonds in starch and related substrate polysaccharides, converting them into simple absorbable sugars and oligosaccharides [7]. Inhibiting α -amylase can slow carbohydrate digestion, thereby reducing glucose absorption and helping to control blood sugar levels effectively.

The enzyme α -amylase is a crucial therapeutic target that has been used to create various synthetic drugs to treat diabetes such as sulfonylureas, α -glucosidase and biguanides. Even though there are many diabetic medications available, it is proved that other drug monotherapy has not been successful in adequately controlling blood glucose levels and other comorbidities. Thus, combination therapy with drugs that act with distinct mechanism of action is frequently used to accomplish therapeutic management. However, the undesirable , serious side effects like gas, bloating and diarrhea have become a concern [8].

In response to these challenges, natural compounds have gained attention for their potential as α -amylase inhibitors, offering both safety and efficacy because ancient people used natural remedies as medicine [8]. Both the public and healthcare institutions are looking at natural medical products as alternatives to synthetic drugs since it is widely acknowledged that plant cures have less side effects and less costly than contemporary pharmaceuticals. Several edible plants such as *Centaurea iberica*, *Cichorium endivia* and *Rhus coriaria* show