RESEARCH
O&G Forum 2024; 34 – 2s: 623 - 627

DETERMINATION OF ALPHA GLUCOSIDASE INHIBITION ACTIVITY OF ODINA WODIER BARK

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Abstract

INTRODUCTION *:* Diabetes is a global health concern affecting millions of people worldwide.It is a chronic metabolic disorder characterized by high blood sugar levels (hyperglycemia) resulting from the body's inability to produce enough insulin or effectively utilize it. alpha glucosidase is an enzyme found in the small intestine that breaks down complex carbohydrates into simple sugars, which are then absorbed into the bloodstream. Inhibition of this enzyme can help regulate blood sugar levels and manage conditions like diabetes.Odina wodier, commonly known as the Indian silver oak, is a tree species found in various parts of Asia, including India. It is known for its medicinal properties and has been traditionally used in Ayurvedic and folk medicine for the treatment of various ailments.

AIM: The Aim of this study is to examine the alpha glucosidase inhibitory activity of Odina wodier bark and evaluate its potential as a natural inhibitor for treating metabolic illnesses such as diabetes.

OBJECTIVES: The objective of this study is to examine the alpha-glucosidase inhibitory activity of Odina wodier bark in order to determine its potential as a complementary treatment for controlling blood sugar.

MATERIAL AND METHODS: To determine the binding energy of putative MMP8 inhibitors, docking analysis was used. Based on a thorough review of the literature, phytochemicals were chosen, and the PubChem database was used to retrieve their chemical compositions. As a reference, the three-dimensional structure of glucosidase (PDB ID: 3L4Y) was used. Rigid docking analysis was performed using Hex 8.0.0, and Pymol was used to display the docked complexes. A greater connection between the ligand and receptor, potentially increasing receptor activity, was indicated by a more negative E-total value.

DISCUSSION: The strong alpha-glucosidase inhibition found in the bark of Odina wodier suggests that it may be used as a natural diabetes treatment to slow the digestion of carbohydrates and lower blood sugar levels.

RESULTS: The study found that the bark of Odina wodier has considerable alpha-glucosidase inhibitory activity, suggesting that it may be useful as a natural diabetes treatment by controlling blood sugar levels by blocking the digestion of carbohydrates.

CONCLUSION: Odina wordier bark exhibited inhibitory effects. Visualizing the protein-ligand interaction using PyMOL revealed strong interactions with a more negative E-total value in Hexdocking server 8.0, suggesting receptor activation.

KEYWORDS: Citronella essential oil, in vitro study, in silico study, multi-drug resistant, gram-negative pathogens.

INTRODUCTION:

A persistent global health issue is diabetes mellitus, a chronic metabolic condition marked by high blood glucose levels. The prevalence of the illness is constantly increasing, resulting in significant financial and medical difficulties.The persistent metabolic condition Diabetes mellitus is a rapidly spreading global issue (1)with serious social, health, and economic ramifications. According to estimates(2), this condition affected 285 million people worldwide in 2010—roughly 6.4% of the adult population. In the absence of effective prevention or treatment, this figure is projected to rise to 430 million. (3)The two main causes of the growth are an aging population and obesity Traditional and alternative medicine, with a focus on natural goods, has seen increased attention as people look for effective therapeutic agents to manage diabetes. (4,5)As a result of its possible alpha-glucosidase inhibitory action, the bark of Odina wodier has emerged as a prospective contender.

The two main kinds of diabetes are Type 1, which is defined by inadequate insulin production, and Type 2,(6,7) which is characterized by insulin resistance. Inhibiting the small intestine's carbohydrate-digestion and -absorption enzymes in Type 2 (6)diabetes is an essential part of controlling blood glucose levels. One such enzyme, alpha-glucosidase, is essential for converting complex carbs into simple sugars and consequently affecting postprandial blood glucose levels.

Odina wodier, also referred to as the Wodier tree, is a species of the Rhamnaceae family that is found throughout Asia and Africa. Several parts of this plant, especially the bark, have historically been used in indigenous medical systems due to its healing qualities.(4) The bark of Odina wodier has been utilized in traditional medicine for a variety of medical purposes. It has been used to treat a number of diseases and health issues.it has been used to lessen inflammation and treat inflammatory-related illnesses.(6–8)The bark of Odina wodier is helpful in preventing oxidative stress since it contains antioxidants. Antioxidants aid in the body's defense against dangerous free radicals, which can speed up aging and cause a number of ailments(9).Odina wodier's bark is rich in a variety of phytochemicals, including flavonoids, alkaloids, tannins, and phenolic compounds. Its alpha-glucosidase inhibitory activity is thought to be caused by one or more of these chemicals. These substances may work by attaching to the alpha-glucosidase enzyme and preventing it from converting complex carbs into glucose. As a result of this interference, the release of glucose into the bloodstream after meals is slower and more controlled. Recent studies have suggested that the bark of Odina wodier contains bioactive substances with potential health advantages, including alpha-glucosidase inhibitory action.

Certain substances can slow down or prevent the absorption of glucose into the bloodstream from the small intestine by inhibiting the enzyme alpha-glucosidase. By doing this, they assist in controlling postprandial blood sugar rises, an important part of managing diabetes. The capacity of natural products to control alpha-glucosidase activity, such as the bark of the Odina wodier plant, has drawn attention. The bark of Odina wodier has important implications for the management of diabetes because of its alpha-glucosidase inhibitory activity. Natural goods like (10)Odina wodier offer a possibly safer and more sustainable alternative to conventional treatments like synthetic medications, which frequently have adverse effects and can contribute to drug resistance. If beneficial in clinical studies, Odina wodier bark extracts or its bioactive substances could be included in dietary supplements or functional meals made to assist people with diabetes in controlling their blood sugar levels.

MATERIAL AND METHODS:

α-glucosidase inhibitory activity of extract and fractions was carried out according to the standard method with minor modification.[Yamaki and Mori (2006)]

In a 96-well plate, reaction mixture containing 50 µl phosphate buffer (100 mM, pH = 6. 8), 10 µl alpha-glucosidase (1 U/ml), and 20 µl of varying concentrations of extract and fractions (2,4,6,8 and 10 mg/ml) was pre- incubated at 37°C for 15 min.

Then, 20 µl P-NPG (5 mM) was added as a substrate and incubated further at 37°C for 20 min. The reaction was stopped by adding 50 µl Na2co3 (0.1 M). The absorbance of the released p-nitrophenol was measured at 405 nm using Multiplate Reader. Acarbose at various concentrations (0.1–0.5 mg/ml) was included as a standard. Without test substance was set up in parallel as a control

Cell viability assay on Odina wodier

Biosafety assessments of plant extracts and cytotoxicity of ethanol The biologically safe or noncytotoxic concentration of plant extracts and cytotoxicity of ethanol were identified using 3-(4,5-dimethylthiazol-2- yl)-2,5-diphenyltetrazolium bromide (MTT) and neutral red uptake (NRU) assays.

HepG2 cells were exposed to various concentrations (10–1000 mg/ml) of plant extracts for 24 h. For the cytotoxicity of ethanol, HepG2 cells were exposed to various concentrations (50–1000 mM) for 24 h.

MTT assay Percentage cell viability was assessed using MTT assay as described (Siddiqui et al., 2008).

Briefly, cells (1 104) were allowed to adhere for 24 h in CO2 incubator at 37C in 96-well culture plates. After the respective exposure, MTT (5 mg/ml of stock in phosphate-buffered saline; PBS) was added (10 ml/ well in 100 ml of cell suspension) and the plates were incubated for 4 h. Then the supernatants were discarded and 200 ml of DMSO were added to each well and mixed gently. The developed color was read at 550 nm using a multiwell microplate reader (Thermo Scientific, Vantaa, Finland). Untreated sets were also run under identical conditions and served as control.

Methodology of MOLECULAR DOCKING

The docked molecules were screened according to highest binding energy. To calculate the binding energy of the interaction between the target enzyme and substrate, docking was done, and the results of the study were used to find prospective inhibitors. Plant phytochemicals were chosen after a thorough literature search to develop ligands that would work against MMP8. From the PubChem-NCBI database, their corresponding two-dimensional chemical structures in structured data format (SDF) were obtained. SDF format was then transformed into Protein data bank (PDB) format using OpenBabel 2.3.1 version. Control is provided by the chemical composition of glucosidase. Glucosidase's three-dimensional structure (PDB ID: 3L4Y) was retrieved from the Protein Data Bank.. The receptor crystallographic water molecules were removed from the protein. The retrieved phytocompounds were individually using Hex 8.0.0. Protein docking program (http://hex.loria.fr), the Hex server is a first Fourier Transform (FFT) based analytics. In this method, rigid docking is undertaken taking into consideration different orientations through 6D analysis. The HEX program carries out a complete search over all six rigid-body degrees of freedom by rotating and

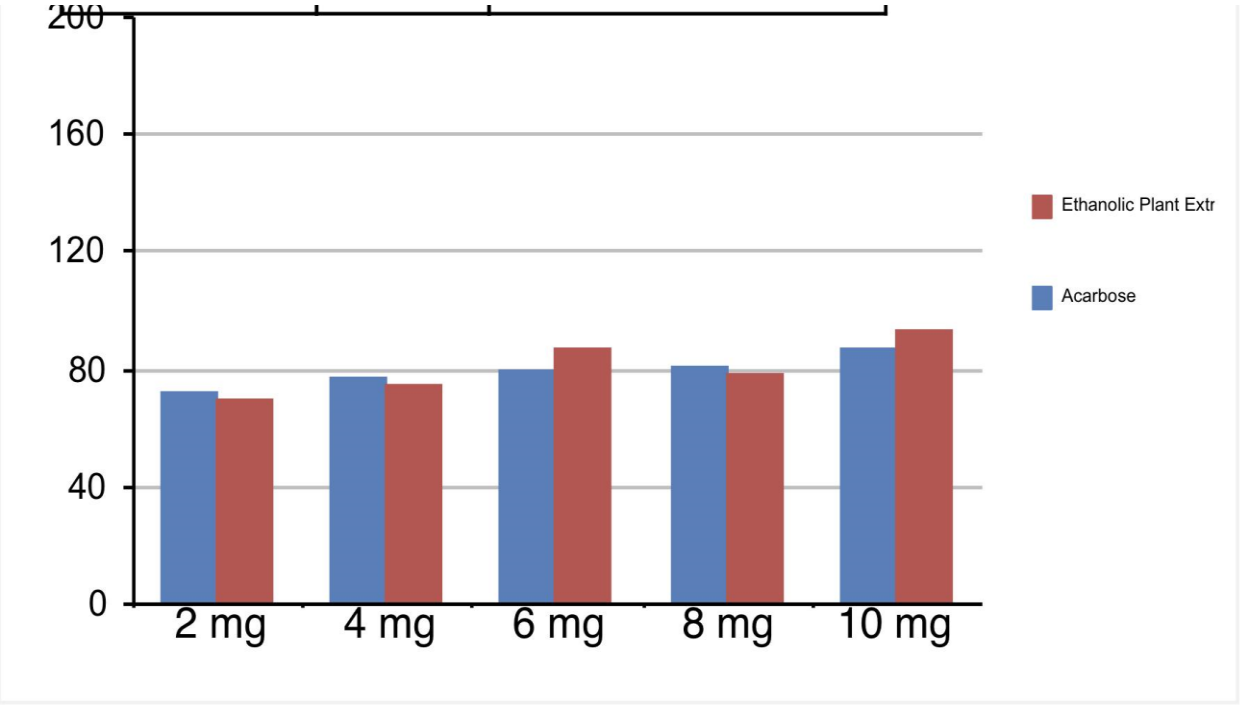
translating the expansion coefficients. This was carried out by maintaining suitable parameters such as FFT mode-3D fast lite, grid dimension-0.6, receptor range-180, ligand range-180, twist range-360 and distance range-40. Docked complex of protein and ligand interaction were visualized in Pymol.In the Hexdocking server 8.0 versions, more negative E-total value implied that there exists a strong interaction between ligand and receptor and that leads to activation of receptor activity

RESULTS:

Alpha amylase inhibition activity of Odina wodier

Concentration	Acarbose	Ethanolic Plant Extract
2 mg	72	69
4 mg	77	74
6 mg	79	87
8 mg	81	78
10 mg	87	93

Fig 1 : Alpha amylase inhibition activity of Odina wodier



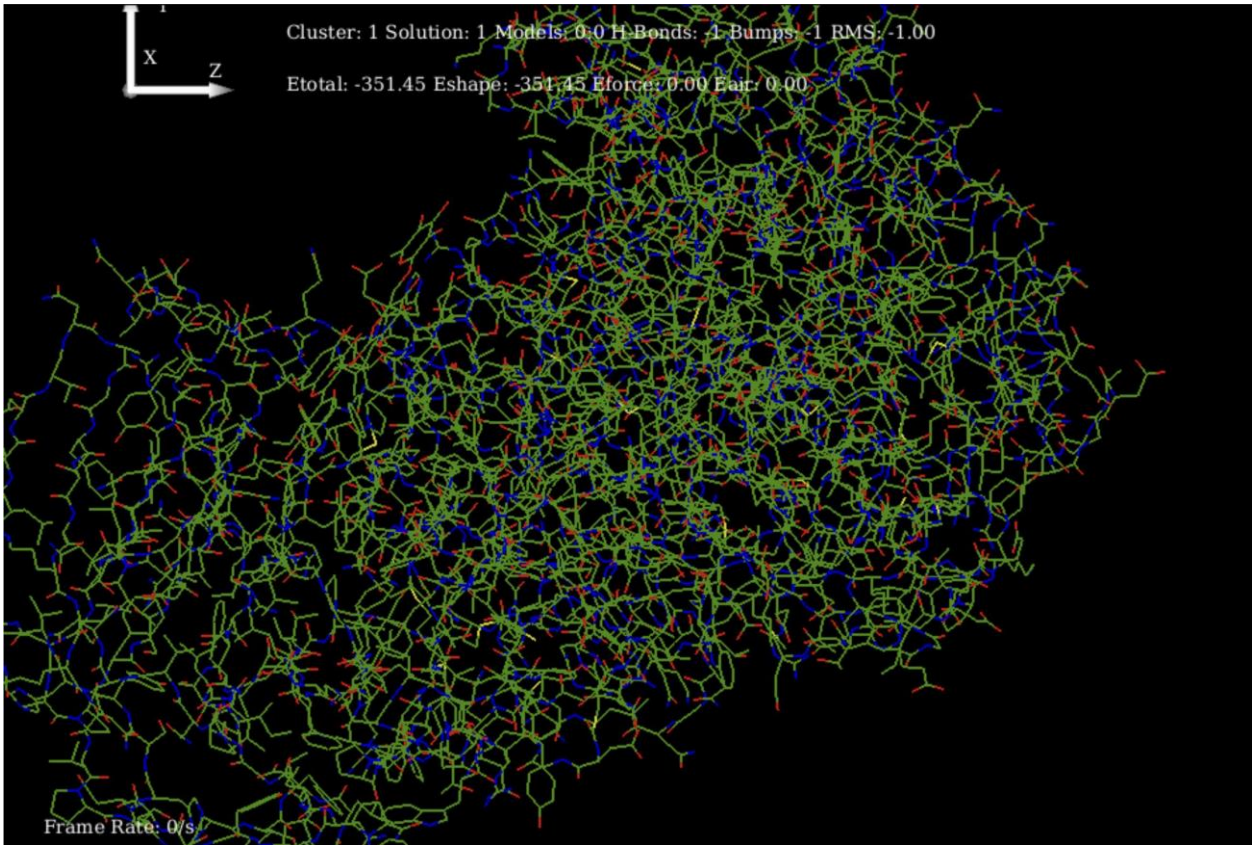
Graph 1: Alpha amylase inhibition activity of Odina wodier

Graph 1: The ethanolic plant extract of odina wodier plant is taken and compared with different concentrations of Acarbose which is standard drug used for diabetics and it was found that when increase in concentration of both standard drug and ethanolic extract there was similar effect of inhibition activity

CONCENTRATION		CELL VIABILITY IN (%)
CONTROL (WITHOUT EXTRACT)		100
10		99
25		98
50		95
100		92
250		87
500		85
1000		80

Fig 2 : Cell viability assay on Odina wodier

Fig2: when the concentration of extract is increased there is decrease in cell viability this shows that extract have alpha glucosidase inhibitor activity



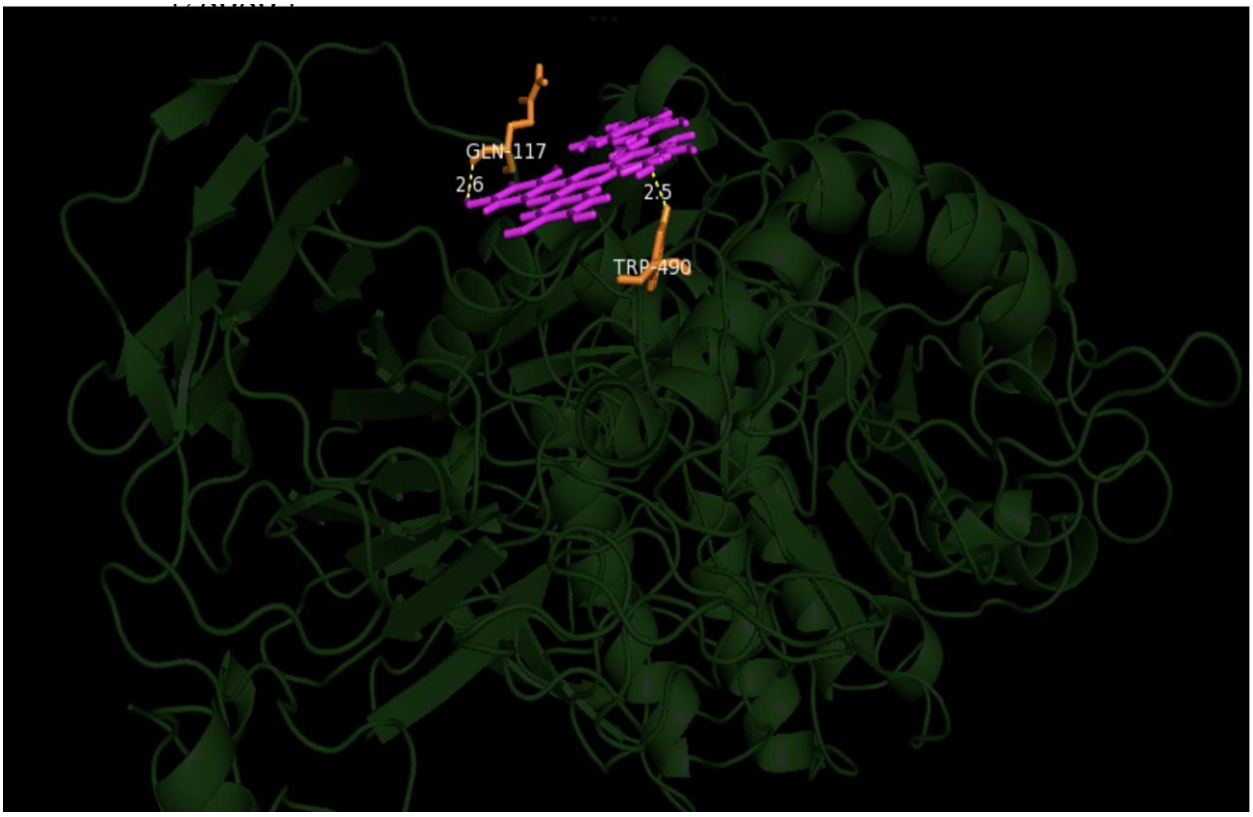


Fig 3: Glucosidase(PDB ID:3L4Y with Pubchem ID: RUTIN : 5280805

Fig3: Molecular docking was done in this protein and ligand are made to interact with each other And it was found that the glucose molecule strongly binded to protein molecule

The results were expressed as percentage inhibition, which was calculated using the formula,

Inhibitory activity (%) = (1 − As/Ac) ×100

DISCUSSION:

An enzyme called alpha-glucosidase converts complex carbohydrates in the digestive tract into less complicated sugars like glucose. The glycemic control can be improved by inhibiting alpha-glucosidase, which delays the absorption of glucose.

The evergreen Odina wodier, often called the Indian Marrygold tree, is native to areas of Asia and Africa. The possible health advantages of this tree's many sections have led to their usage in traditional medicine.

According to studies, alpha-glucosidase is significantly inhibited by extracts or compounds made from the bark of the Odina wodier tree. Particular phytochemicals discovered in the bark have been linked to this function(11). Odina have more beneficial activity such as anti inflammatory (12)The alpha-glucosidase enzyme's capacity to break down complex carbohydrates is thought to be decreased by these substances because they interact with the enzyme's active site.

Diabetes is typically treated with alpha-glucosidase inhibitors like acarbose. To evaluate the effectiveness and safety of Odina wodier bark, its inhibitory action could be compared to those of these common medicines.

The bark of the Odina wodier tree exhibits alpha-glucosidase inhibitory activity, which may be beneficial for diabetics. It can help avoid sharp rises in blood sugar levels after meals by reducing the digestion and absorption of carbs. For those who have type 2 diabetes, in which impaired glucose regulation is a major concern, this may be very helpful. A class of medications called alpha-glucosidase inhibitors is frequently recommended for the treatment of diabetes. (13)Natural substitutes, such as extracts of the Odina wodier bark, however, offer a number of benefits. (14)Compared to synthetic medications, they frequently have better tolerance, fewer adverse effects, and a lower risk of causing hypoglycemia.Compared to synthetic medications, using natural items like the bark of the odina wodier tree has various benefits. It frequently has less negative side effects, is more widely available, and is an environmentally friendly choice.

CONCLUSION:

The investigation on the bark of Odina wodier found considerable alpha-glucosidase inhibitory activity, suggesting its potential as a natural diabetes treatment. This inhibition suggests that it has the capacity to slow down carbohydrate digestion, potentially assisting in blood sugar regulation. In order to study the efficacy and safety of this effect in clinical settings, additional research is required to isolate and identify the active chemicals responsible for it. Nevertheless, these findings highlight the need of researching traditional medicinal plants like Odina wodier for their therapeutic potential in contemporary medicine, particularly for illnesses like diabetes where novel treatments are continually sought.

CONFLICT OF INTEREST

The author declare that there are no conflicts of interest

ACKNOWLEDGMENT

We extend our gratitude to saveetha Dental College and Hospital for their constant support and encouragement in helping in successful completion of this research project.

FUNDING
The present study was funded by
DR. Vijayakanth SLV
Panimalar medical college and hospital
Saveetha institute of medical and technical sciences
Saveetha dental college and hospital
Saveetha university

ETHICAL CLEARANCE:
Since it is an in Vitro study ethical clearance is not required

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