SYNTHESIS AND CHARACTERIZATION OF BIOGENIC MAGNESIUM OXIDE NANOPARTICLES AS ANTIDIABETIC AGENTS

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Abstract. The -application of nanoparticles for accurate diagnosis and ample treatment to various human diseases. Despite the use of diverse polymers in nanoparticle synthesis, biosynthesis of these particles in viable, metal-tolerant microorganisms is preferred over all other prevalent procedures including chemical methods, because of its cost-effectiveness, and eco-friendliness. Diabetes is the most fifth growing trend prevalent diseases worldwide due to the lifestyle changes, physical inactivity, aging, nutrition and lack of diet nutrition. The disease spread is influenced by numerous hereditary facts, environmental causes, temporal and additional behaviour. The study purpose by using in-silico approach identify inhibitors binding with α- glucosidase against DM. The α-glucosidase protein sequence from *Saccharomycescerevisiae* was retrieved using NCBI and utilizing software molecular docking and AdmetSAR were perormed. AdmetSAR utilized for the identification of properties of (ligand) MgONPs associate brain blood 0.9827% barrier and human intestinal 0.9848% absorption. MgONPs biodegradation 0.77% percentage was calculated with acute oral toxicity 0.589%. Total positive and negative charged residues Arg + Lys:73, Asp + Glu: 87 were also calculated. MgONPs exhibited super hydrogen bond formation interaction with polar amino acids, including ASP 37,SER 30, and LYS 39 residues of α-glucosidase.64.28 aliphatic index with -0.670 (GRAVY) grand average hydropathicity. The 100 µg /mL specimen cytotoxic concentration would be safe to ship. The α-glucosidase amino acids (ASP 46, VAL 325 and GLU 286) have a strong binding infinity with MgONPs. The amino acids of α-glucosidase (ASP 46, GLU 286 and VAL 325) have a strong binding interaction with MgONPs.
Keywords: *diabetes mellitus, nanoparticles, MgO, α-glucosidase*

Introduction

In the quest for knowledge, man is developing the most beautiful physical world. The components of this world are in biggest as well as in smallest size. This difference is in the view of many dimensions like length mass and times (Mohanraj and Chen, 2006). The importance of the smallest physical structures was unknown until the discovery of the nanoparticles. Nanotechnology is a very important and vast field of science. Bio-nanotechnology which is the combination of biotechnology and nanotechnology for the

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development of biosynthetic and environmentally friendly nanomaterial synthesis technology is emerging day by day. Nanotechnology and nanoscience have been burgeoned as on the most exciting and vast field of study with remarkable revolution in the current century by exploring this mysterious area of research due to its plenty of awesome opportunities. One of a lecture entitled" There is plenty of room at the bottom" was credited with discovering nanotechnology. Some researchers contemplate that Nanotechnology is implemented in all disciplines of science including engineering, information technology, material science and life science along with clarifying astonishing facts regarding human health, specifically in cancer treatment. (Naveed et al., 2024; Naveed et al., 2022a,b; Saleem et al., 2022; Shabbir et al., 2023; Waseem et al., 2023; Zawar et al., 2023; Hayat et al., 2023; Hussain et al., 2023; Nageen et al., 2023;). This field deals with the development and synthesis of various types of nanoparticles. These are the objects which have a size ranging from 1-100 nm (Shang et al., 2014) and these array of atoms on a 1-100 nm scale, nanodevices and structures makes them feasible in their search area (Iqbal et al., 2022). Keeping in view the size of these important particles, these are far different from bulk materials. Another unique feature of nanoparticles is their biomolecule nature such as polynucleic acid and proteins. They also have unique physio-chemical properties (Rampino et al., 2013).

In the present times, nanoparticles are being used in a lot of the world for different purposes (Adame et al., 2024). They are being used in the medical field as treatment and have a lot of applications in industry such as oxide fuel batteries and solar systems. They are also being used in wide incorporations such as into the diverse material thing of everyday use like clothes and cosmetics (Stark et al., 2015). In the present era, different types of nanoparticles are being produced by using different materials like copper, titanium, zinc, magnesium, alginate, gold, and silver. The growth and development of nanoparticles are complex enough processes. It depends upon many conditions like viscosity, temperature, the concentration of the medium, etc (Rajput, 2015). This review article will depict various methods for nanoparticle production and their applications.

Diabetes mellitus is characterized by an increase in blood glucose levels caused by an imbalance in the secretion of the hormone insulin. Increase in blood glucose levels and cytokine synthesis, improper carbohydrate metabolism, immunological reactions, leads to organ and pancreatic beta cell destruction and insulin resistance (Mazhar et al., 2021). Despite numerous therapeutic improvements, diabetes remains the fifth biggest cause of mortality globally and consistently battling against diabetes worldwide. Increasing rates of diabetes can be attributed to modern lifestyles, unhealthy eating habits, lack of exercise, and other lifestyle changes. The transmission of this disease may be influenced by a number of factors, including genetics as well as behavioral, environmental, and temporal aspects (Mazhar et al., 2021; Rodriguez-Saldana, 2023). Diabetes, as determined by the Global Systematic Search of published data, is an endocrine system illness. Type II diabetes affects 500 million people globally. While the predicted timeframe would see an increase in the prevalence rate across all countries, the developing and underdeveloped world would accepted for the greatest ratio of people with diabetes (Kaiser et al., 2018). Its global frequency among adults is considerable, rising from 4.7% in 2014 to 8.8% in 2017 and expected to reach 9.9% in 2045 (Bokolia et al., 2024). According to the International Diabetes Federation (IDF), Pakistan is projected to have 11.5 million individuals affected by diabetes by 2025, placing it as the fifth most affected country in terms of the diabetic population (Mohammad and Nanji, 2018). Recent developments in nanotechnology have shed light on its potential for the

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treatment of a wide range of disorders, including diabetes mellitus (Balsells et al., 2015).The manufacture nanoparticles manufacturing that may vary in size, shape, and chemical composition, while also being dispersed in a controlled manner, is an intriguing area of research that falls under the umbrella of nanotechnology (Chandrakala et al., 2022). The synthesis of nanoparticles is being carried out via physical, chemical, and biological methods (Apriliani et al., 2020). The biological approach to nanoparticle synthesis uses yeast extracts, which are environmental friendly and harmless then chemical and physical approach (Ahmad et al., 2023). Scientific progress has led to the development of yeast-based nanoparticles with anti-diabetic action and target specificity for the treatment of diabetes mellitus and to be more effective with fewer adverse effects (Saka and Chella, 2021). Nanotechnology made it possible to create silver nanoparticles from organic substances, which were effective in treating diabetes mellitus by inhibiting α-glucosidase enzymes (Telrandhe et al., 2017). The antidiabetic activity was enhanced due to the inhibition of the glucose metabolizing enzymes α-glucosidase and α-amylase by the silver nanoparticles that were generated from Allium cepa (Jini and Sharmila, 2020). Advancement in nanotechnology indicated as friendly and safer potential for utilizing MgO NPs materials are currently being evaluated for biological applications and disease-modifying treatments. This research suggests that MgO NPs can address a variety of DM symptoms. Therefore, additional research and clinical expertise are needed to fully understand the potential of MgO NPs as an anti-diabetic drug (San Tang, 2020). Synthesizing the more stable and mono dispersed MgO NPs utilizing the industrial yeast Saccharomyces cerevisiae was the goal of this effort. Various nanoparticles that are involved in the treatment of diabetes mellitus are mentioned in *Table 1*.

Table 1. *Different nanoparticles that are involved in the treatment of diabetes mellitus (inhibition of α-glucosidase and α-amylase)*

Sr. No	Source	Family	Size (nm)	Nanoparticles	Inhibition of enzyme	References
1	*Halymeniaporyphyroides*	*Halymeniaceae*	34 to 80	Ag NPs	α-glucosidase and α-amylase	(Manam and Murugesan, 2021)
2	*Tephrosiatinctoria*	*Fabaceae*	73	Ag NPs	α-glucosidase and α-amylase	(Nguyen et al., 2023)
3	*Aspergillus niger*	*Trichocomaceae*	5 to 100	CuO NPs	α-glucosidase	(Takcı et al., 2023)
4	*Padinaboergesenii*	*Dictyotaceae*	80	Au NPs	α-glucosidase	(Rokkarukala et al., 2023)
5	*Nigella sativa*	*Ranunculaceae*	20 to 30	Au NPs	α-glucosidase and α-amylase	(Mazhar et al.)
6	*Cladosporium species*	*Davidiellaceae*	24	Ag NPs	α-glucosidase and α-amylase	(Asam Raza et al., 2023)
7	*Capsicumfrutescens*	*Solanaceae*	25 to 35	CuO NPs	*α-Amylase*	(Asif et al., 2023)
8	*Silybummarianum*	*Asteraceae*	33.6	ZnO NPs	*In-vivo studies*	(Raja et al., 2023)

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Methodology

Retrieving protein sequences

The NCBI was used to get the *Saccharomyces cerevisiae* protein sequence of α-glucosidase. The α-glucosidase protein sequence from *Saccharomyces cerevisiae* was obtained through NCBI https://www.ncbi.nlm.nih.gov/ by searching the navigation bar, choose all databases, and then type α-glucosidase protein into the search bar. The 584 amino acid sequence of the α-glucosidase protein was saved under the accession number GAX66902.1.

α-glucosidaseenzyme (3D structuralprediction)

For α-glucosidase 3D structure prediction the homology modelling method was employed. The query sequence was utilised for BlastP analysis against pdb in order to identify an appropriate template. A query coverage of 92% with 72% identity was the best for the detected template sequence. The offline software MODELLER was used to predict the three-dimensional structure of α-glucosidase. The query sequence, which had a length of 584 aminoacids, was put into the Wint1.ali file before stearic. Using Notepad++, we changed the name of the Align2d.py file to match the target pdb file that we had received, which was 3a47. In row 17, the file name of the modified Get-model.py was changed to "3a74" using Notepad++. Rows 20 and 21 were used to edit the beginning and finishing models, with 1 and 5 correspondingly. Modeller was opened, and the first command that was put was cd space. After that, the path of the Modeller files was pasted. Enter these command, which was mod 9.25 align2d.py, after the modeller is able to determine the path. wnt1-3a47 and wnt1-3a47.pap two files were produced as process out come then a third command was executed, which was mod 9.25 get-model.py, which was generated after wards.

Visualisation of protein structures

Using chimaera https://www.cgl.ucsf.edu/chimera/., the protein structure was visualised and the α and β-sheets of the (α-glucosidase) protein were determined by Chimaera, and the results were recorded in the pdb format.

Refinement of thestructure of proteins

Using Galaxy WEB, five protein models were refined. The Galaxy WEB https://bio.tools/galaxyweb#! server uses template-based modelling to refine loop or terminal sections and evaluate the structure of proteins from sequence.

Model evaluation for α-glucosidase

Using the online SAVES server, the five α-glucosidase models' were evaluated. Thevarious characteristics were compared using the tools available under the SAVES server, specifically ERRAT and RAMPAGE. The quality factor of the proteins that were predicted was identified with the assistance of ERRAT.

The preparation of ligands

Downloading the ligand (MgONPs) was done through PubChem, which may be found at https://pubchem.ncbi.nlm.nih.gov/. The MgONPs' structure was subsequently saved in

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pdb format after being opened in chimaera. The ligand molecule's energy was minimised using ChemDraw 3D ultra.

Characteristics of admetSAR

The ligand's (MgO NP) characteristics were determined using the admetSAR programme (http://lmmd.ecust.edu.cn/admetsar2). This tool was useful for identifying several ligand features, such as its ability to cross the blood-brain barrier, its rate of biodegradation, its acute oral toxicity, its molecular weight in g/mol, and its role as a hydrogen bond acceptoror donor.

Molecular docking procedure

MgO NPs were docked with the α-glucosidase protein. The site https://bioinfo3d.cs.tau.ac.il/PatchDock/ was used to conduct the molecular docking analysis, which aided in verifying the interactions between α-glucosidase and MgO NPs. The protein (α-glucosidase) and ligand (MgO NPs) were added to the database using the default parameters, specifically under the ligand molecule and receptor molecule, respectively.

Results

3D model evaluation and prediction

A three-dimensional model of the α-glucosidase protein was created with the help of Modeller. The atomic composition of α-glucosidase protein described in *Table 2*. Following the identification of the quality factor, which was 93.22% through ERRAT, the molprobity score was 1.46 percent, and the physiochemical properties were predicted by utilising protparam, which predicted 68127.34 molecular weight with 5.59 theoretical PI, the α-glucosidase protein demonstrated significant results. Total number of positive and negative charged residues were determined like Arg + Lys:73, Asp + Glu: 87 approximately. The stability of the α-glucosidase protein was also confirmed by Protparam. (GRAVY) grand average hydropathicity -0.670 with Aliphatic index 64.28 were calculated. We also measured atoms and amino acids together with their compositions. Also, the 3D structure of α-glucosidase was assessed using the verify 3D method, which evaluated 92.22% score (*Figure 1 and Figure 2*).

Table 2. *Atomic composition of α-glucosidase protein*

Atoms	Composition
Carbon (C)	3105
Hydrogen (H)	4605
Nitrogen (N)	803
Oxygen (O)	908
Sulphur (S)	13
Total no. of atoms	**9434**

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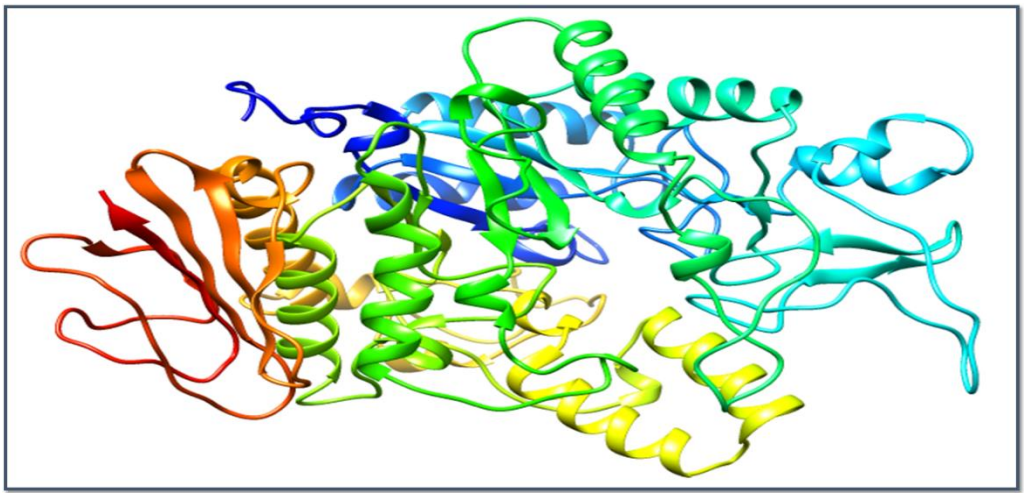

Figure 1. *3D Structure of α-glucosidase protein predicted through modeller*

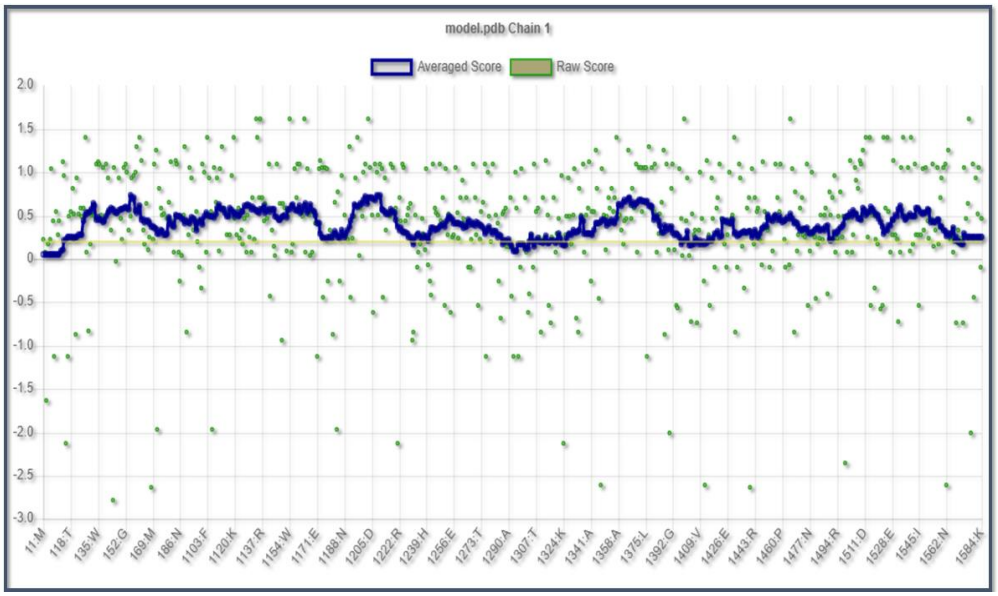

Figure 2. *Evaluation of α-glucosidase by using verify 3D. The blue color in the graph representing the average score and green color represent the raw score*

Assessment of α-glucosidase by rampage

Aminoacids (581) 99.45 % in (favored region), (3) aminoacids in (allowed region), eg ALA 278, PHE 177, GLU 530 no aminoacids in disallowed region were identified by RAMPAGE (*Figure 3*).

ADmetSAR characteristics of MgONPs

The characteristics of (ligand) MgONPs were determined using AdmetSAR; these included intestine absorption rate of 0.98 38% in individual brain blood barrier 0.98 37%. MgONPs biodegradation 0.78 % with acute oral toxicity 0.5742%, (MgONPs) ligand 40.3 g/mol molecular weight with 4 acceptor hydrogen bond and no donor hydrogen bond see in *Table 3*.

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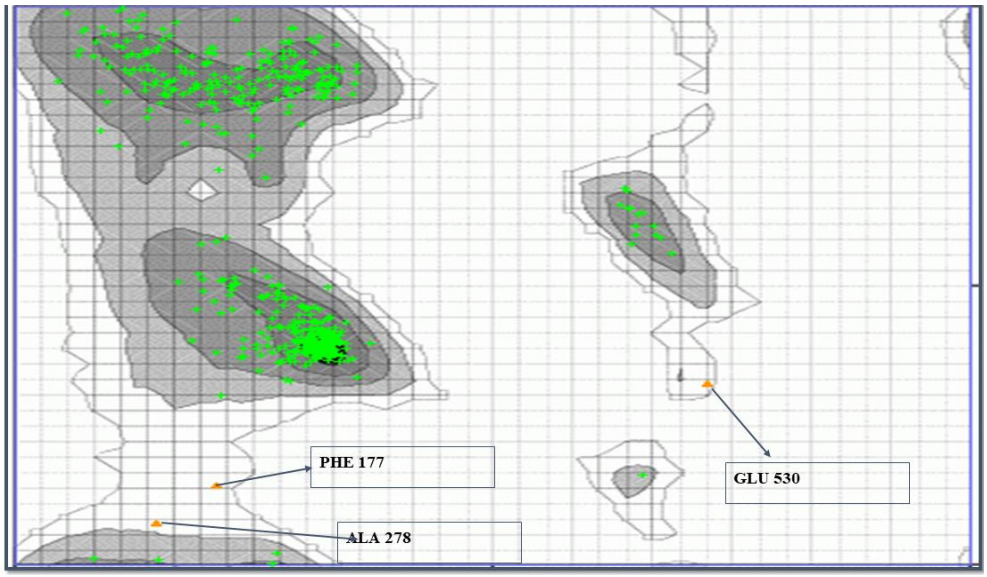

Figure 3. *α-glucosidase protein evaluation by using RAMPAGE. The green color in figure represents the aminoacid in favored region and orange color represents the aminoacids in allowed region*

Table 3. *Evaluation of α –glucosidase protein and physiochemical properties of MgONPs*

Protein							
Ramachandran Favored (%)	**Ramachandran Outliers (%)**	**MolProbity Score (%)**	**Quality Factor (%)**				
99.51 %	0.00	1.47	92.9897				
Ligand							
Brain Blood Barrier (%)	**Human Intestinal Absorption (%)**	**Biodegradation (%)**	**Acute Oral Toxicity (%)**	**Aqueos Solubility (IogS)**	**Molecular Weight (g/Mol)**	**Hydrogen Bond Acceptor**	**Hydrogen Bond Donor**
0.9746	0.9791	0.78	0.5742	-0.1968	39.9	4	0
MgO NP-α –glucosidase Interaction							
RMSD Value (Å)	**Binding Energy (Kcal/Mol)**	**VdW Forces (Kcal/Mol)**	**Bond Distance (Å)**				
1.7897	-2.81	-2.02	3.534				

Molecular docking study of MgONPs α-glucosidase

A-Glucosidase protein was attached to MgONPs by docking. Applying docking methodology, the binding sites and size impact of MgONPs on the association with α-glucosidase were discovered. The docking out comes of MgONPs associated α-glucosidase, which demonstrated a conserved binding pocket, are shown in *Figure 4*. A good score was achieved by the docking complex, which had the maximum RMSD value of 1.7897 Å. The binding energy of this interaction is the lowest at -2.81 kcal/mol. The bond distance and attractive VdW were determined to be 3.534 Å and -2.02 (kcal/mol) respectively. Based on these findings, the interaction is the easiest. Protein residues that conserved, including Serine (SER 30), Lysine (LYS 39), and Aspartic acid (ASP 37), were identified and found to greater interact with MgONPs primarily (*Figure 4*).

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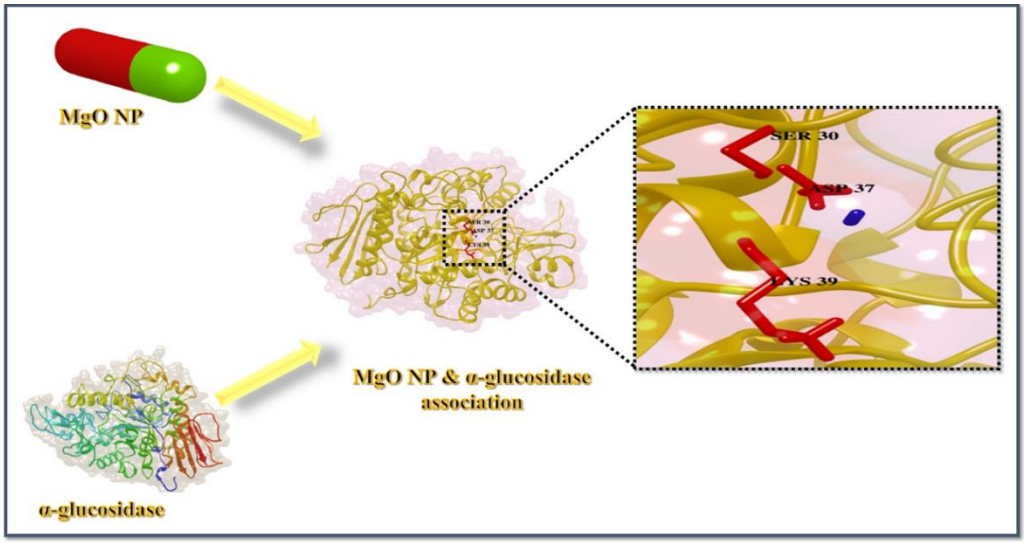

Figure 4. *Molecular docking analysis of α-glucosidase with MgO NPs by using patchDock. The golden color represent the protein and blue color represents the ligand*

Discussion

It is possible to synthesize nanoparticles using either chemical or biological processes but Biological approaches are quickly becoming the preferred choice for synthesizing nanoparticles due to their numerous advantages, including their low cost, reliability, environmental friendly, and ease of use (Gahlawat and Choudhury, 2019) Nanoparticle size, shape, and crystallinity are the primary determinants of biological interaction. In contrast, calcination temperatures altered nanoparticle size and crystallinity. The production of nanoparticles was reported by Shah et alas having been accomplished through the utilisation of biological organisms such as bacteria, actinobacteria, yeasts, moulds, algae, and plants, in addition to other goods. Plant and microbial molecules that synthesize nanoparticles through reduction include proteins, phenolic compounds, amines, enzymes, pigments and alkaloids (Aziz et al., 2024; Li et al., 2022). The purpose of this study was to produced MgO NPs and MgO NPs by using industrial *Saccharomyces cerevisiae* yeast. Biogenic synthesis from the yeast strain *Saccharomyces cerevisiae* yeast has not been recorded yet, while reports of MgO NPs production from the fungus *Aspergillus niger* have been published. Several additional benefits have been noted in various functional groups conjugated of MgO NPs surface, which makes it appropriate for a variety of biomedical applications (Ammulu et al., 2021; Kurhade et al., 2022).

It is possible to determine nanoparticles physical confirmation using a variety of ways. The yeast culture color intensity rose in metal nanoparticles surface of plasmon vibrations (Furletov et al., 2023). According to significant recorded finding Mg2+ ions reduction takes happen extracellularly. The use of a UV-spectrophotometer was employed in order to evaluate the generation of decreased MgO nanoparticles in the colloidal solution as well as their stability. Multiple approaches are applied in order find a number of functional groups, morphology, shape, elements, and size of the metal nanoparticles (Faye et al., 2022).

The action of these nanoparticles may be better understood if in-vitro anti-diabetic assays and in-silico molecular docking activities were carried out. The optimal particle size of 32 nm for the optimal hole size of the(α-glucosidase) enzyme is suggested by in-

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silico molecular docking experiments, which evaluate the best action for MgONPs. Negative complex binding energy in docked models suggests that nanoparticles and proteins associate easily and favourably. MgO NPs associated polar amino acids indicated strong interaction like SER 30, LYS 39 and ASP 37, α-glucosidase residues with hydrogen bonds formation. The specimen would be sent safely and effectively with less than 100 μg /mL cytotoxic concentration. The MgO NPs that were shown in this work are promising newcomers for inhibiting α-glucosidase with limited selectivity. Different studies conducted by Suresh et al. (2018) that found that ZnO NPs have a strong binding affinity of α-glucosidase for the amino acids (ASP 46, GLU 286, and VAL 325).

Data Availability Statement. The data generated during this study has been included in the manuscript.

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