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CHROMATOGRAPHIC MASS SPECTROMETRIC ANALYSIS AND IN-SILICO SCREENING FOR ANTI-DIABETIC ACTION OF SIGNIFICANT PHYTOCHEMICALS IN THE ALCOHOLIC EXTRACT OF *Morinda Citrifolia. L*

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ABSTRACT

An endocrine condition that deteriorates over time, diabetes mellitus can cause significant health problems, including heart, kidney, eye, and nerve issues. The majority of oral anti-diabetic medications are made of synthetic chemicals and have potential negative effects after extended use. With fewer adverse effects, phytochemicals with anti-diabetic properties are becoming more and more significant in anti-diabetic treatment. An attempt was made to identify the main phytochemicals from the ethanolic extract of the *Morinda Citrifolia L*, also known as the Noni plant. The main phytocompounds identified by GCMS were n-Tridecanoic acid, n-Decanoic acid, Methyl Hexadecanoate, N-(3,4,5,6-tetrahydroxy-1-nitrohexan-2-yl) acetamide, and Hexaldehyde. The phytocompounds were analyzed in-silico using PyRX docking with the auto dock Vina tool. The human SGLT2-MAP17 complex bound with empagliflozin PDBID 7VSI receptor was selected to dock ligands. The standard drugs used to validate the processes were empagliflozin (-10.7) and sotagliflozin (-7.5). Potential candidates were selected for further investigation by comparing (N-(3,4,5,6-tetrahydroxy-1-nitrohexan-2-yl) acetamide) (-6.8), methyl hexadecanoate (-6.5), and n-Tridecanoic acid (-6.2). The Swiss-ADME settings were suitable. They followed the Lipinski rule. More synthetic, pharmacological, and structure-activity relationship (SAR) studies are needed to confirm their effectiveness in treating maturity-onset diabetes and elucidate their therapeutic utility further to enhance medicinal chemistry's hunt for life-saving medications.

KEYWORDS: Diabetes PyRX, *Morinda citrifolia*, Docking, Gas chromatography.

INTRODUCTION

Morinda citrifolia L., popularly called "noni," has been used for over two millennia in traditional Polynesian medicine. The ripe fruit of this evergreen shrub, a member of the Rubiaceous family, is characterized by a strong smell and flavor similar to butyric acid. Different portions of the plant are consumed by different groups worldwide, especially in Polynesia. The most commonly consumed parts are the leaves and fruit, while the roots are used to dye. Validating the plant's medicinal qualities has become more critical as "noni juice" has grown in popularity.[1] There is no scientific evidence about noni fruit's nutritional and medical benefits in people despite recent in vitro research demonstrating its antioxidant and antibacterial qualities. The fruit and anthraquinone chemical called damnacanthal was taken from noni. Type 2 diabetes (T2D) and other chronic inflammatory metabolic diseases are becoming more commonplace worldwide. Although exercise and diet are essential for managing type 2 diabetes, many people also need pharmaceutical therapies. These could include glucagon-like peptide-1 agonists, thiazolidinediones, sulfonylureas, or metformin. However, weight gain, hypoglycemia, and the possibility of treatment failure are some of the unfavorable side effects that these anti-diabetic medications frequently cause. As a result, there is now more interest in complementary and alternative therapies. Natural products have become increasingly popular in the pharmaceutical sector, bringing in over $28 billion worldwide. However, there is currently a lack of information about pharmacokinetics, long-term safety, bioactive chemicals, molecular targets, mechanisms of action, effective dosages, and unanticipated side effects. The human sodium-glucose cotransporter 2 (hSGLT2) significantly influences the renal reabsorption of glucose.[2,3] Oral inhibitors like empagliflozin, which pharmacologically block hSGLT2, improve glucose excretion and are frequently used in clinical practice to control blood glucose levels in people with type 2 diabetes. Morinda citrifolia L. has long been used to treat diarrhea, constipation, fungal infections, boils, abscesses, and inflammations. Natural red and yellow dyes have also been made from the anthraquinone-rich roots and bark. Polyphenols, flavonoids, tannins, carotenoids, ascorbic acid, nitrate, oxalate, and phytate are noteworthy phytoconstituents identified in noni.[4,5] Small-molecule libraries can be docked to macromolecules using virtual molecular screening to find lead compounds with particular biological activity. A typical method in computer-aided drug design is this in silico approach. As a research method, molecular docking is known for being successful and economical.[6,7]

AIMS AND OBJECTIVES

The aim of the present study is to profile the phytoconstituents, to predict the antidiabetic activity of major phytoconstituents of *Morinda citrifolia* by molecular docking technique.

MATERIALS AND METHODS

Figure 1: Fresh fruits of *Morinda Citrifolia L.*

Collection and preparation of the Noni fruit (Figure: 1)

Fresh fruits of *Morinda Citrifolia. L* was collected from the botany department's garden; the professor of botany department CMS College Kottayam Kerala, India authenticated the collected sample.. Fruits were peeled, chopped, dried, and powdered and used for preliminary phytochemical analysis and methanol Soxhlet extraction.[8]

Soxhlet Extraction

The Soxhlet apparatus consisted of a round-bottom flask, a condenser, and a thimble. The thimble contained the powdered fruit stuff. The circular-bottomed flask was filled with the solvent ethanol. The apparatus was heated to begin the extraction process. The solvent was cycled through the system to effectively dissolve the desired chemicals from the plant material and collect them in the round-bottom flask. The extraction process was carried out for a predetermined time or until there was no noticeable color change in the solvent in the siphon, indicating that not much more extraction had occurred.[9]

GCMS analysis

Five significant analytes were identified by the GC-MS analysis of the plant extract using an Agilent Technologies 7890 GC system with a 5975C inert MSD and helium as the carrier gas. The NIST11 and RTLPEST3 libraries were used to compare the data. Molecules are separated based on their chemical characteristics using the chromatographic method for mass detection. Five significant analytes were identified by the GC-MS analysis of the plant extract using an Agilent Technologies 7890 GC system with a 5975C inert MSD and helium as the carrier gas. The NIST11 and RTLPEST3 libraries were used to compare the data. Molecules are separated based on their chemical characteristics using the chromatographic method for mass detection. [10]

Molecular docking

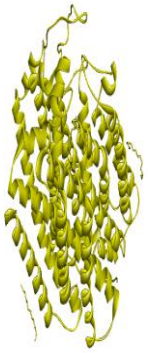

Figure 2: Human SGLT2-MAP17 complex bound with empagliflozin PDBID 7VSI receptor.

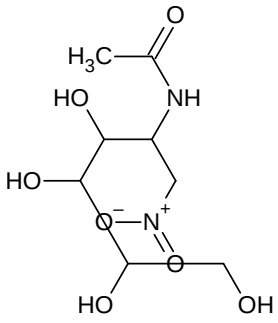

Figure 3: (N-(3,4,5,6-tetrahydroxy-1-nitrohexan-2-yl) acetamide) (Chem sketch).

PUBCHEM ID-2969 (n-Decanoic acid), 6184 (Hexanal), 8181 (methyl hexadecanoate), 12530 (tridecanoic acid) 536755 (N-(3,4,5,6-tetrahydroxy-1-nitrohexan-2-yl) acetamide),11949646 (empagliflozin) 24831714 (sotagliflozin) were downloaded from the PubChem database in sdf format, and their structures were accurately constructed using Chem Sketch software. The system was successfully opened, and using Bio via Drug Discovery Studio visualizer n, polar hydrogens, and charges were systematically incorporated, with torsions precisely configured before saving in PDBQT format. The target human SGLT2-MAP17 complex bound with empagliflozin PDBID 7VSI was downloaded in PDB format from the RCSB and maintained in PDB format (Fig:2). Then water molecules and heteroatoms were removed added polar hydrogens and Kollman charges, and saved the results in PDBQT format.[10-16] The control empagliflozin was extracted from the enzyme and stored in a separate molecular window in PDB format, which, along with sotagliflozin, was utilized for redocking and validation.[17] The drug-likeness RADAR for the compounds demonstrating substantial activity was generated, and thorough ADME predictions were made using Swiss ADME software.[18]

RESULTS

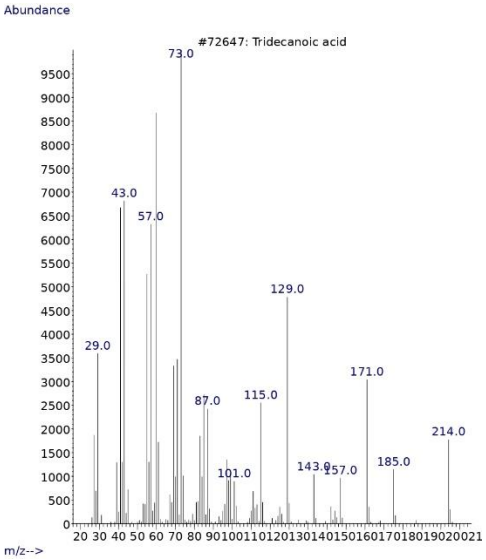

Figure 4: GCMS spectra of ethanol extract of *Morinda Citrifolia. L* (Agilent Technologies 7890 GC system, SAIF, CUSAT).

Table 1: Molecular docking results of significant ethanol phytocompounds extract of Morinda Citrifolia. L using PyRX 0.8n.

Ligands with pub chem ID	*LigandBinding Affinity	rmsd/ub
2969 (n-Decanoic acid)	-5.4	0
6184 (Hexanal)	-4.2	0
8181 (methyl hexadecanoate)	-6.5	0
12530 (tridecanoic acid)	-6.2	0
536755 (N-(3,4,5,6-tetrahydroxy-1-nitrohexan-2-yl) acetamide)	-6.8	0
11949646 (empagliflozin)	-10.7	0
24831714 (sotagliflozin)	-7.5	0
*Lesser binding energy denotes favourable binding, and more predicted biological activity, *n=9		

DISCUSSION

By binding to the Human SGLT2-MAP17 complex that is associated with the empagliflozin PDBID 7VSI receptor, the phytochemicals found in Morinda Citrifolia L fruit, specifically N-(3,4,5,6-tetrahydroxy-1-nitrohexan-2-yl) acetamide (Figure: 3), are predicted to show promising anti-diabetic activity. The effectiveness of these phytochemicals was confirmed by similar outcomes from molecular docking simulations of other noni-fruit phytocompounds utilizing Pyrex. The dependability of the docking results was further validated by redocking empagliflozin. These results demonstrate the potential of noni-fruit components as anti-diabetic agents and offer a strong basis for further investigation into plant-based compounds for treating maturity-onset diabetes. The main phytocompounds identified by GCMS were n-tridecanoic acid, n-decanoic acid, Methyl Hexadecanoate, N-(3,4,5,6-tetrahydroxy-1-nitrohexan-2-yl) acetamide, and Hexaldehyde. (Figure: 4) The phytocompound N-(3,4,5,6-tetrahydroxy-1-nitrohexan-2-yl) acetamide has demonstrated encouraging anti-diabetic activity, as indicated by its high docking score. (-6.8) Docking scores were compared using empagliflozin (-10.7) and sotagliflozin (-7.5) as reference medications. (Table) The binding energies of the other Phyto ligands were all comparable. Swiss-ADME parameters proved effective in examining the interactions between various proteins and ligands. One of the key targets for the fight against type II diabetes mellitus is sodium-glucose cotransporter 2 (SGLT2). Typically, an SGLT2 inhibitor lowers blood glucose levels by preventing glucose reabsorption.[19-20]

CONCLUSION

Recent advances in computational biology have enabled in-silico testing with various computer algorithms that predict a compound's biological action. The primary foundation of this prediction modelling is the examination of the chemical binding energies with their corresponding biological receptors. The anti-diabetic qualities of many vital compounds that were separated from Morinda citrifolia were assessed in this study using the PyRX 0.8 in-silico docking software suite. In-silico research to prevent diabetes uses the human SGLT2-MAP17 complex bound with empagliflozin as its objective.

The sodium-glucose cotransporter 2 (SGLT2) receptor is extensively distributed, according to literature data, and lowers blood glucose levels by blocking glucose reabsorption. Current medications for diabetes mellitus aim to control and return blood glucose levels in the vessels to normal. Nevertheless, most modern drugs have several side effects that might cause serious health problems while they are being taken. Traditional treatments are, therefore, beneficial complementary therapies that have been practiced for a long time. By continuing to research and evaluate the therapeutic properties of compounds derived from plants, we are accessing a multitude of potential new drugs, ultimately leading to innovative solutions for a range of health problems.

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