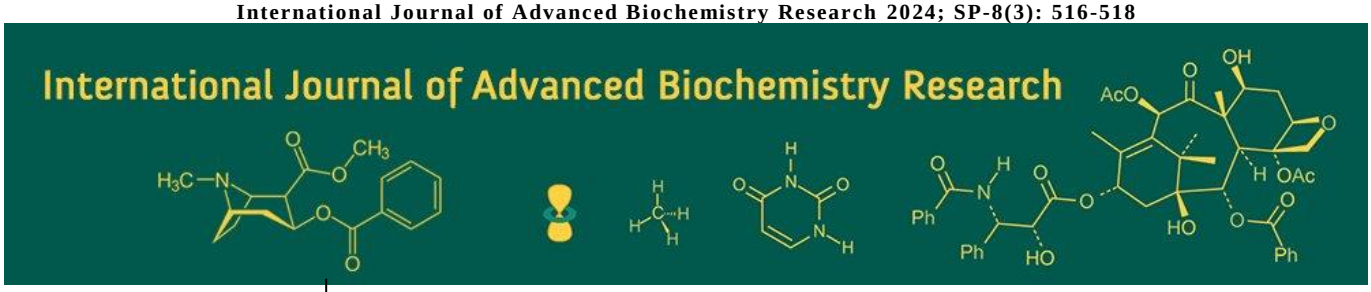

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Medicinal properties of *Emblica officinalis* and docking studies of its active components

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Abstract
Amla, also known as Indian gooseberry, has been revered in Ayurveda for its rejuvenating properties and extensive use in traditional formulations like Triphala and Chyavanaprasha. This fruit is rich in phytochemicals such as quercetin, gallic acid, tannins, flavonoids, and vitamin C, which have long been recognized for their medicinal properties. These compounds contribute to its diverse therapeutic potential, accumulated over centuries of ethnomedical use and documented in ancient texts. Contemporary pharmacological studies have corroborated its traditional uses, demonstrating Amla's antioxidant, anticarcinogenic, antitumor, antigenotoxic, and anti-inflammatory activities. These findings underscore its broader applicability in modern medicine. Moreover, research into Amla's phytochemical complexity, including terpenoids, alkaloids, flavonoids, and tannins, highlights its versatility in addressing various health concerns. Computational docking studies have delved into the molecular interactions between Amla's bioactive compounds and specific target proteins, revealing insights into its mechanisms of action at the molecular level. In this study, receptor proteins associated with metabolism were selected and interaction studies were performed with *Emblica officinalis* using Autodock Vina 1.5.6 software. Quercetin showed affinity for inflammatory mediators like cyclooxygenase (COX) and lipoxygenase (LOX), suggesting potential anti-inflammatory effects, gallic acid with cell cycle regulators like cyclin-dependent kinases (CDKs), indicating its potential antiproliferative effects on cancer cells. Tannins have been studied for their inhibitory effects on enzymes involved in carbohydrate metabolism, offering potential benefits for diabetes management. Overall, Amla emerges as a promising source of therapeutically valuable products, with its well-documented pharmacological properties and favorable safety profile. Continued research efforts will further unlock its potential applications in contemporary healthcare.

Keywords: Docking, amla, *Emblica officinalis*, drug discovery

Introduction
Natural products derived from plants, bacteria, and other organisms, either in their pure form or as crude extracts, play a pivotal role in pharmaceutical industries. Despite the focus of modern medicinal research on incurable and life-threatening diseases like diabetes and metastasis, there remains a growing challenge in addressing newly discovered diseases. In our pursuit of developing new synthetic molecules, the rich treasure of traditional medicines has often been overlooked. Numerous medicinal plants, often combined in herbal preparations within traditional healthcare systems like Ayurveda, Siddha, and Unani, are celebrated for their antioxidant properties. One such plant is *Emblica officinalis*, also known as Amla or Indian gooseberry, belonging to the Euphorbeaceae family. Amla, renowned for its medicinal and nutritional properties, is particularly valued for its high content of vitamin C and minerals compared to other citrus fruits (Maurya *et al*., 2011) [10]. While all parts of Amla are utilized for medicinal purposes, its fruits are especially prominent in Rasayana formulations, either alone or in combination with other herbs, for treating various infectious and non-infectious diseases (Udupa, 1985) [6]. In India, Amla fruits are commonly employed as anti-inflammatory and antipyretic agents, as well as tonics during the winter season.
Docking studies on the active components of Amla (*Emblica officinalis*) with receptors linked to metabolism offer valuable insights into how Amla's bioactive compounds interact with specific proteins involved in metabolic pathways. These findings help us understand the molecular mechanisms behind Amla's potential therapeutic effects on metabolic disorders

like diabetes and obesity.

Through computational simulations, these docking studies reveal that Amla's phytoconstituents have a tendency to bind to key receptors associated with carbohydrate and lipid metabolism. For example, compounds such as quercetin, gallic acid, and tannins present in Amla show a strong affinity for receptors like pancreatic alpha-amylase, aldose reductase, and peroxisome proliferator-activated receptors (PPARs) (Ramakanth *et al*., 2012) [14]. These receptors play critical roles in regulating glucose and lipid levels in the body (Oosterveer *et al*., 2012) [12]. Phytosterols present in Amla showed high affinity for PPARs (-15.0 kcal/mol). Other active components, namely Phyllaemblicin B, emblicanin, gallic, ellagic, chebulinic, chebulagic acids showed affinity towards Aldo-Keto reductase family 1 B10 receptor (-9. -7.3, -7.3, -6.6, -6.5, -5.4, -4.3 kcal/mol, respectively) and pancreatic alpha amylase (-10, -8.5, -8.8, -7.5, -6.7, -6.4, -5.5 kcal / mol, respectively) (Yokozawa *et al*., 2007) [16].

Materials and Methods

Preparation of ligand: List of ligands present in *Emblica officinalis* was obtained from IMPPAT, a database on medicinal Indian plants containing more than 9500 phytochemicals. Compound ID number for phytochemicals were collected from IMPPAT database along with their 3D structures (SDF and PDB) and canonical SMILE. Canonical SMILES obtained from IMPPAT were used for this purpose to evaluate the phytochemical properties of the obtained phytochemicals using SwissADME database.

Preparation of Binding Site

Canonical SMILES and 3D SDF files were utilized for the prediction of binding sites using 'Swiss Target Prediction' webserver (Gfeller *et al*., 2014) [3] and 'BindingDB' (Gilson *et al*., 2016) [4]. Target sites obtained from Swiss Target Prediction and Binding DB were compiled on an Excel worksheet. The target sites were individually studied and only those receptors that played a role in carbohydrate and lipid metabolism were selected. Uniprot DB was used to obtain information about 3D structures of selected binding sites, namely PDB files for these receptors were downloaded from RCSB protein data bank (Rose *et al*., 2016) [15] and prepared for molecular docking by removal of water molecules, heteroatoms, any side chains using Discovery Studio version 4.0.

Docking Simulation

AutoDock Vina (Version 1.5.6.) was used for molecular docking. Autodock tool was applied to build a complete pdbqt file name of ligands and receptors. Receptor preparation was carried out by four major steps, *viz.* addition of polar hydrogen, removal of water molecule, addition of Kollman charges and location of grid box. For setting the ligand, the 3D structure in PDB type file was loaded into Autodock tool to detect the root and convert it to pdbqt. Size of grid box was set in 60X60X60 points and number of modes were 10. Affinity scores were generated.

Analysis of docked complexes

The docked complexes were analysed using BIOVIA Discovery Studio version 4.0. The number and length of hydrogen bonds in the complexes and the interacting residues of proteins were analyzed.

Result and Discussion

Phytosterols present in Amla showed high affinity for PPARs (-15.0 kcal/mol). While the chemical discovery of plant sterols, also known as phytosterols, dates back to 1922, their significance in human and animal health has been overlooked for many years. It wasn't until 1983 that researchers began to recognize their potential role in controlling plasma cholesterol levels in individuals with hypercholesterolemia. This recognition came about due to the structural properties of phytosterols, which suggested that they could inhibit the absorption of cholesterol from dietary sources through steric hindrance (Ikeda *et al*., 1983) [5]. Consuming foods enriched with phytosterols is a common therapeutic approach aimed at reducing plasma cholesterol levels and lowering the risk of atherosclerotic disease. The mechanism behind the cholesterol-lowering action of phytosterols is believed to involve their competitive displacement of dietary and biliary cholesterol within mixed micelles (Mel'nikov *et al*., 2004) [11]. This interference with cholesterol absorption undermines its uptake, thereby contributing to the reduction of cholesterol levels in the bloodstream.

Other active components, namely Phyllaemblicin B, Emblicanin (Emblicanin-A and Emblicanin-B compounds fall under the class of hydrolyzable tannins), gallic, ellagic, chebulinic, chebulagic acids showed affinity towards aldo-keto reductase family 1 B10 receptor (-9. -7.3, -7.3, -6.6, -6.5, -5.4, -4.3 kcal/mol, respectively) and pancreatic alpha amylase (-10, -8.5, -8.8, -7.5, -6.7, -6.4, -5.5 kcal/mol, respectively). The AKR1B10 (aldo-keto reductase family 1, member B10) protein is predominantly expressed in the normal human small intestine and colon. However, its expression becomes aberrant in various types of human cancers, where it is often overexpressed. This abnormal expression pattern has led to AKR1B10 being considered as a potential tumor marker (Liu *et al*., 2022) [9]. The aldo-keto reductase (AKR) protein superfamily is expansive, encompassing numerous members categorized into 16 families. These enzymes are ubiquitous across different phyla and play a pivotal role in catalyzing the reduction of various carbonyl substrates (Jez *et al*., 1997) [7]. Among these substrates are sugar aldehydes, keto-steroids, keto-prostaglandins, retinals, quinones, and lipid peroxidation by-products. AKR enzymes are involved in diverse metabolic pathways, including carbohydrate metabolism, steroid metabolism, prostaglandin metabolism, retinoid metabolism, and detoxification processes (Pollak *et al*., 2007; Biason-Lauber *et al*., 2013) [13, 2]. Their broad substrate specificity enables them to participate in crucial cellular processes, such as biosynthesis, metabolism, and cellular defense mechanisms against oxidative stress (Jin and Penning, 2007) [7]. Amylase serves as a pivotal enzyme in the breakdown of carbohydrates, playing a vital role in converting complex starches and glycogen into simpler sugars like glucose and maltose. Its significance lies in facilitating the absorption and utilization of these sugars for energy within organisms. Amylase is naturally produced in humans by both the pancreas and the salivary glands, where it aids in the digestive processes occurring in the small intestine and mouth, respectively. Beyond humans, amylase is also present in various microbes, plants, and animals, contributing to carbohydrate digestion across different biological systems. This enzyme is broadly categorized into alpha (α), beta (β), and gamma (γ) subtypes, with alpha

amylase recognized for its faster action compared to beta amylase. Alpha amylase primarily targets α-1,4 glycosidic bonds in starch and glycogen molecules, while beta amylase acts more slowly, specifically cleaving these bonds at non-reducing ends to release maltose. This classification underscores amylase's role as a glycoside hydrolase, emphasizing its ability to break down glycosidic bonds in carbohydrates. Overall, amylase's multifaceted functions underscore its importance in carbohydrate metabolism and energy production across diverse biological systems (Akinfemiwa *et al*., 2023) [1].

Conclusion

While alternative forms of medicine are effective, they often come with unwanted side effects that present significant challenges. Herbal medicine addresses many of these issues, with amla playing a significant role in treating various diseases. Amla's high antioxidant content and biological properties help prevent numerous health problems by providing essential nutrients, particularly ascorbic acid.

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