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Insilico Evaluation Of Phytoconstitents From Mangifera Indica By Using Protein In Breast Cancer

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ABSTRACT:

In India, cancer ranks as the second most deadly disease. India is home to a wide variety of cancers, including lung, pancreatic, breast, and prostate cancers. In India, breast cancer is the most prevalent type of cancer across all age categories. There are three common forms of breast cancer, with triple-negative breast cancer having the greatest death rate. Lasers, chemotherapy, and replacement are treatment options for breast cancer. Although all of these therapy approaches are successful in curing this illness, they are too costly and have numerous adverse effects. Indians have practiced Ayurveda for centuries. Ayurvedic practitioners use many ayurvedic plants to cure a variety of illnesses, including cancer, diabetes, and inflammation. Ayurveda utilizes Mangifera indica as one such plant. veda. The flowering plant Mangifera indica is a member of the Anacardiaceae family. People use it to treat conditions such as stomach and skin issues, among others. Here, we used molecular docking and bioinformatic methods to investigate the various components of Mangifera indica's anti-cancer properties. Therefore, using a variety of bioinformatic approaches, we have investigated the potential of all the phytochemicals in mango plants to prevent breast cancer. The best phytochemical breast cancer candidate is mugiferin.

***KEYWORD**: Breast Cancer, Anticancer, Mangiferin, Phytochemical, Mangifera Indica*

INTRODUCTION

Globally, cancer is the largest cause of death from non-communicable diseases. It also causes a tremendous deal of morbidity and costs healthcare systems a lot of money [1]. The incidence and death of cancer have been rising faster than the rate at which population expansion alone could explain the various forms of cancer. Breast cancer is the most frequent cause of cancer in women, affecting around 2.1 million women annually and accounting for the largest number of female cancer-related deaths [2]. Breast cancer is a serious medical condition and one of the main causes of women's tumor growth-related deaths. The most common way for a breast tumor to grow is through metastatic phenotype, which means that cancerous cells split off from the main tumor and travel to other parts of the body, like the bone, brain, lymph nodes around the tumor, liver, and lungs [3]. The intricate and multi-step process of breast tumor metastasis involves morphological alterations, dissociation from the cellular layer, increased adaptability and invasion into surrounding tissues, intravasation, flow, bond, extravasation, and development at remote destinations [4]. The prevalence of major depression, a significant side effect of breast cancer, might reach 9.3% in this population [5]. Patients with breast cancer are particularly vulnerable to depression within the first year following diagnosis, especially if they are premenopausal, under 65, have a history of depression, or have undergone chemotherapy. Regrettably, the disorder of significant depression among patients with breast cancer remains poorly understood and inadequately addressed. Furthermore, only 27% of these patients received a mental health practitioner's consultation or antidepressant medication [6]. Research suggests that mangiferin could be an effective and affordable substance for maintaining and improving health, significantly improving the prognosis for individuals with specific cancers such as breast cancer, and reducing the risk of developing cancer [7]. Studies have demonstrated the anticancer potential of fruits and vegetables due to their bioactive chemicals [8]. One of the flowering plant species in the Anacardiaceae family is the mango tree, or *Mangifera indica*. About thirty tropical fruiting trees belonging to the genus Mangifera are members of this family [9]. India has grown Mangifera indica for over 4,000 years. Between the fourth and fifth centuries BC, it is believed to have made its way to East Asia. East Africa grew it, followed by Brazil, the West Indies, China, the United States, the Caribbean, and Mexico, all of which provided favorable environments for its development. Since the majority of the produce is consumed domestically, India is the world's top producer of mangoes, with relatively little exported [10]. Based on the phytochemicals essential for promoting good health, every part of the plant serves a variety of purposes. They function as antioxidants, stimulate the human system, and produce protective enzymes in the liver to prevent damage to genetic materials. They also have a number of other activities, such as antiviral, anticancer, antidiabetic, immunomodulatory, and analgesic effects [11]. Anthocyanins, isomangiferin, tannins, gallic acid derivatives, and mangiferin (a xanthone glycoside) are some of the phytochemicals that can be found in the plant. Bark contains mangiferin, catechin, and protocatechic acid [12]. These substances are significant antioxidants and may have potential medicinal applications [13]. By blocking efflux transporters, natural substances can make cancer cells more susceptible to anticancer medications, according to a number of recent studies. Mangiferin is one of the potential natural substances that may have chemosensitizing and anticancer properties [14]. There is evidence that prooxidant activity is linked to the anticancer potential of substances derived from plants, but most people now agree that antioxidant activity is a better indicator of how well these compounds will fight cancer. Therefore, the chemopreventive action of natural substances depends on their capacity to affect the generation of reactive oxygen species.

Mangiferin's strong antioxidant activity makes it abundantly evident that additional mechanistic research is required to completely understand its anti-cancer potential [15]. Mangiferin is a powerful anti-cancer drug that comes from naturally occurring glucosylxanthones. It is used to treat cancers like ovarian, breast, lung, prostate, and nasophageal [16]. Researchers think that mangiferin may kill cancer cells and even cause them to die by blocking and lowering NF-kB and NF-κB-inducing kinase. Several publications have also reported Mangiferin-induced apoptosis and carcinogenesis through altered gene expression, particularly with Bcl-2 and Bax. This bioactive phytochemical has demonstrated a definitive effect on the programmed cell death of HL-60 cells by inhibiting the NF-kB pathway and suppressing Bcl-xL and XIAP expression [17]. We investigated the anticancer characteristics of mgiferin using a bioinformatics technique. Docking is a bioinformatic method that predicts the shapes of the receptor and ligand when they are bound. It does this by giving information on the binding energy, hydrogen bonding, and amino acid residues that the ligand binds to, as well as the bond distance. This makes the complex more stable. Both the two molecules' binding affinities and the amino acid residues they bind to alter as the conformation does. As a result, docking helps forecast how medication molecules will connect to their target proteins [18]. Here, we utilize PBcl-2 as the targeted protein. Therefore, our goal is to give a concise overview of mangiferin's therapeutic potential against breast cancer [19].

MATERIALS AND METHODS

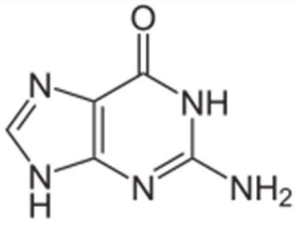
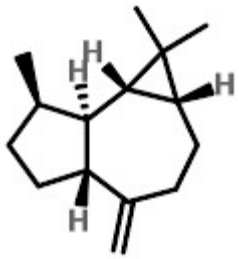
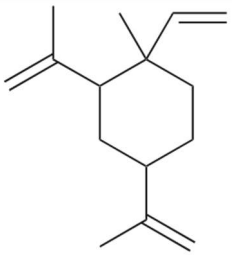
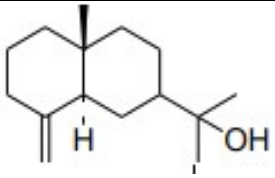
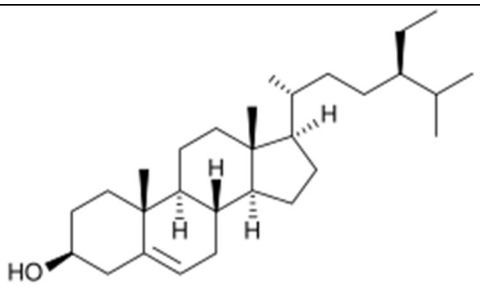
We used Autodock Vina software for molecular docking [20]. We used Chemdraw software to draw the various components of *Mangiferin Indica*, and an internet program named 3D Corina transformed the smilie file into a PDB file [21]. After placing the PDB files of various constituents into separate folders, we used the MGL Tools 1.5.4 software to further convert them into PDBQT files. We obtained the PDB file for the breast cancer protein BCL2 from the RCSPDB depository and cleaned it in the Discovery Studio [22]. We then used MGL Tools 1.5.4 to convert the cleaned PDB file into a PDBQT file [23]. The Autodock Vina software docked the protein and ligand files, producing an output file with multiple conformations [24]. The Pymol program displayed the output, providing pictures of the protein and ligand [25-28].

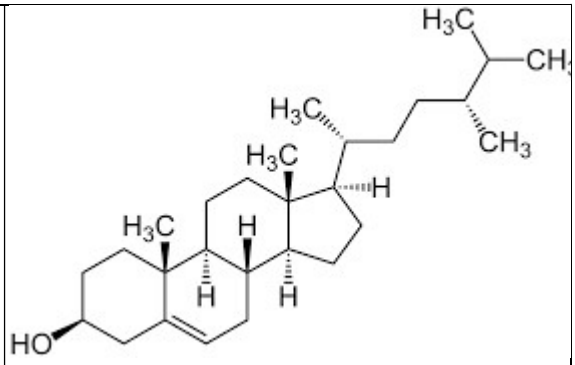
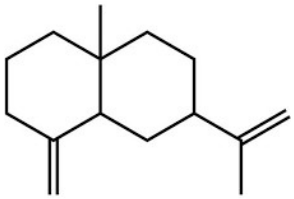
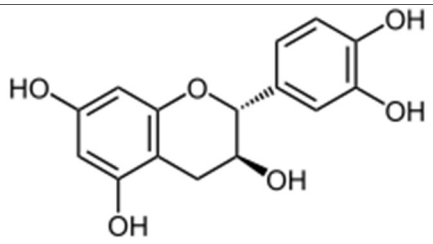
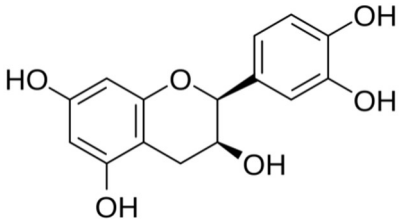
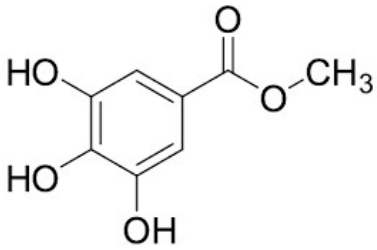
RESULTS AND DISCUSSION

Almost every part of the country grows the tropical plant *Mangifera indica*. Ayurveda has used the herb for centuries to treat skin and stomach disorders [15, 16]. This herb contains a variety of chemical components that combine to help treat ailments. The literature has identified and documented several components. Breast cancer is the second-leading cause of death in India. Several proteins are involved in the initiation and progression of breast cancer. Triple-negative breast cancer is associated with an up regulation of several proteins, including BCL2. Inhibiting BCL2 over expression can prevent triple-negative breast cancer. In this instance, we selected the BCL2 protein and made an effort to look at the different parts of its cavity. We have identified the binding characteristics and affinity of these chemical compounds and have tried to integrate them into the triple-negative breast cancer-causing protein. Table 1 lists the structures of each ingredient. Table 2 lists the protein's structurally stabilizing amino acid residues, hydrogen bond count, and binding energy. The results show that most of the components in mango plants inhibit the BCL2 protein, whereas M14 and M13 show -6.0 and -6.8

Kcal/mol, respectively (Figure 1 and 2).

Table 1: Different chemical constituents of *Mangifera Indica*

Sr. No.	Code	Name of Phytoconstituents	Structure
1	M1	A- guanine	
2	M2	Aromandrene	
3	M3	B –Eleman	
4	M4	B –Eudesmpl	
5	M5	B- Sitosterol	

6	M6	B-Campesterol	
7	M7	B-salinene	
8	M8	Catechin	
9	M9	Epicatechin	
10	M10	Gallic acid methyl ester	

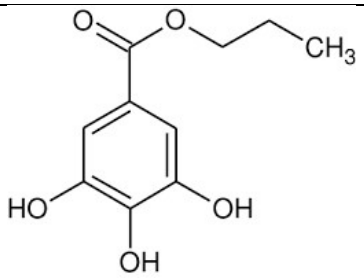
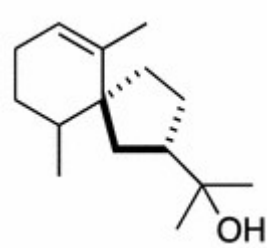
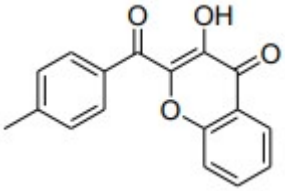
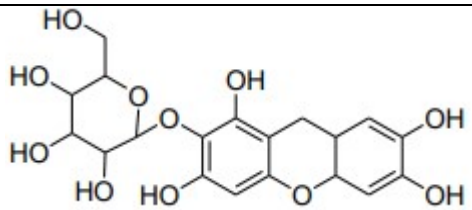
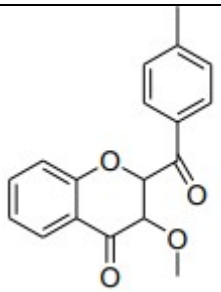
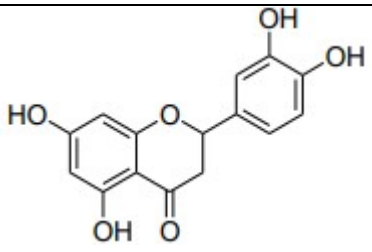
11	M11	Gallic acid propyl ester	
12	M12	Hinesol	
13	M13	Hydroxy chromone	
14	M14	Mangiferin	
15	M15	Methoxy chromone	
16	M16	Quercetin	

Table 2: Docking results of all the different chemical constituents of *Mangifera Indica*

Sr. No.	Code	Binding energy	No. of hydrogen bonds	Amino acid with which H bond is made	Bond distance [Ă]
1	M1	-6.2	-	-	-
2	M2	-6.8	-	-	-
3	M3	-5.9	-	-	-
4	M4	-6.0	2	ASN58, PHE62	1.3, 1.0
5	M5	-6.2	1	ARG67	2.9
6	M6	-6.7	1	ALA68	1.5
7	M7	-6.4	-	-	-
8	M8	-5.9	1	ASP191	2.1
9	M9	-5.5	2	ASP191, TYR180	2.0, 2.4
10	M10	-4.4	2	ALA100, ARG107	2.3Ă, 3.1
11	M11	-4.8	4	ARG107, TYR108, TYR63, PHE62	3.2, 2.0, 3.4, 1.2
12	M12	-6.0	1	ALA100	2.8
13	M13	-6.8	6	ARG107, TYR63, TYR63, PHE62, TYR108, ASN58	3.2, 3.4, 2.9, 1.4, 3.3, 1.1
14	M14	-6.0	3	THR187, THR187, THR187	2.0, 2.4, 2.6
15	M15	-6.5	2	ASN58, ALA57	3.1Aº, 2.2
16	M16	-5.8	6	LEU55, GLY59, ILE65, PHE62, LEU66, LEU66	1.4, 1.5, 3.0, 1.9, 2.3, 2.8

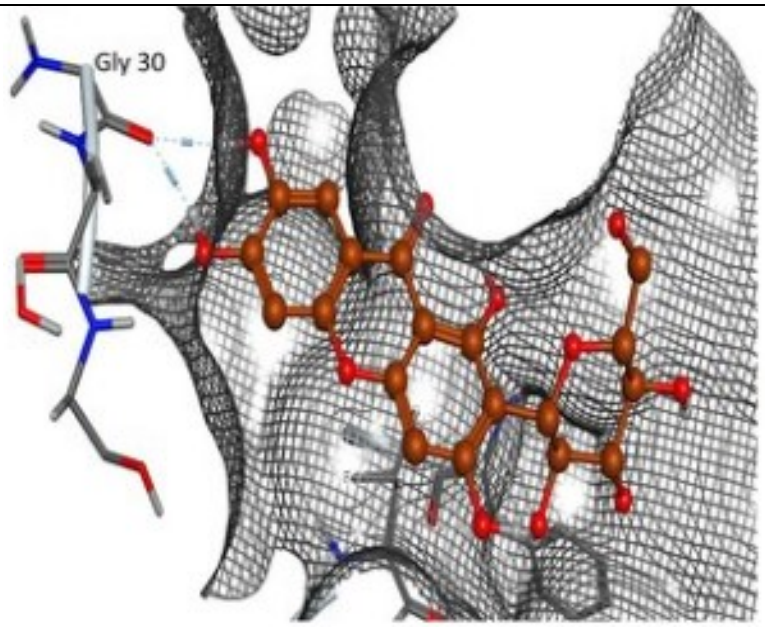


Figure 1: Ligand Interaction diagram of M14 Molecule Mangiferin with receptor by Ball and Stick model

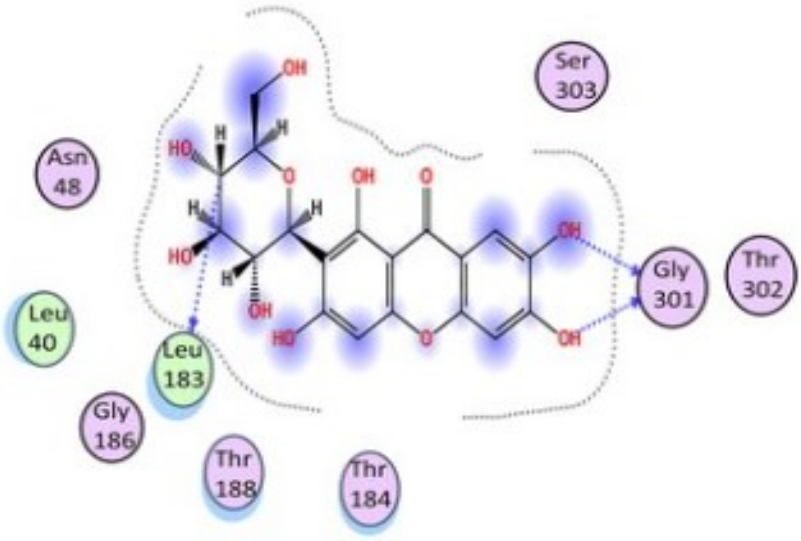


Figure 2: Ligand Interaction diagram of M14 Molecule Mangiferin with receptor by hide receptor model

CONCLUSION

Using molecular docking techniques, we have attempted to explore the many phytochemicals found in Mangifera indica and clarify their anticancer capabilities against breast cancer. The average binding energy of the 16 phytochemicals found in Mangiferin Indica is -5.99 Kcal/mol. M2 and M13 have the highest binding energies (-6.8 Kcal/mol) in the BCL2 protein out of the 16 phytochemicals. The

binding energy of mangiferin, a substance used in traditional medicine, is -6.0 Kcal/mol. A high binding energy signifies the phytochemical's stability within the protein's cavity and its enhanced inhibition of the protein. The presence of hydrogen bonds in the molecule aids in its distribution to the site of action, hence enhancing the drug's anticancer properties. Hydrogen bond distance also controls the delivery method; molecules with an average bond distance of 2.5 to 3.5 A show greater stability during transportation, while molecules with a lower or higher bond distance end up in the wrong places.

DECLARATIONS:

Ethics approval and consent to participate:

Not applicable.

Consent for publication:

All the authors approved the manuscript for publication.

Availability of data and material:

All required data is available.

Competing interests:

All authors declare no competing interests.

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