

**ANTICANCER POTENTIAL OF ISOLATED PHYTOCHEMICALS  
FROM *TERMINALIA BELLERICA* AGAINST BREAST CANCER: *IN  
SILICO* MOLECULAR DOCKING APPROACH.**

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**ABSTRACT**

Breast cancer is an increasing public health problem. One of the main causes of breast cancer is estrogen receptor alpha. Over expression of estrogen receptor is seen in number of cases of breast cancer. The aim of this study was to screen out the effective bioactive compounds from *Terminalia bellerica* namely Anolignan B, Gallic acid, Termilignan, Thannilignan, which may be potential inhibitors of estrogen receptor alpha (ER- $\alpha$ ) for searching a drug against the breast cancer. A wide range of docking score found during molecular docking by Schrodinger. Anolignan B, Gallic acid, Termilignan, Thannilignan showed the docking score -8.004, -6.351, -

7.875 and -7.774 respectively. Among all the compounds Anolignan B showed best docking score towards estrogen receptor alpha. So, Anolignan B is the best compounds for selective inhibitors of estrogen receptor alpha, as it possessed the best value in Molecular docking. Further *in vitro* and *in vivo* investigation need to identify estrogen receptor alpha inhibitory activity of isolated compounds from *Terminalia bellerica*.

**KEYWORDS:** *Terminalia bellerica*, estrogen receptor alpha, Breast cancer, Anolignan B.

## INTRODUCTION

Breast cancer incidence is rising worldwide with a rise in aggressive neoplasias in young women.<sup>[1]</sup> and a significant public health problem. The incidence is rising in most countries and is projected to rise any over future twenty years despite current efforts to prevent the illness.<sup>[2-5]</sup> The enhanced incidence is not shocking since there has been, in most countries, an increase in numbers of women with major breast cancer risk factors, as well as lower age of start, late age of first maternity, fewer pregnancies, shorter or no periods of breastfeeding, and a later menopause. Alternative risk factors which boost the burden of carcinoma are the rise in obesity, alcohol consumption, inactivity, and hormone replacement therapy (HRT).<sup>[5]</sup> Breast cancer most typically develops in cells from the lining of milk ducts and therefore the lobules that provide the ducts with milk. Cancers developing from the ducts area unit referred to as ductal carcinomas, whereas those developing from lobules area unit referred to as lobe carcinomas.<sup>[6]</sup> The designation of carcinoma is confirmed by taking a biopsy of the regarding lump. Once the designation is created, any tests ar done to see if cancer has unfolded on the far side the breast and that treatments it should reply to.<sup>[6]</sup>

*Terminalia bellerica* (Combretaceae), known as belleric myrobalan, is a large deciduous tree and exhibits several pharmacological effects including anti-bacterial, anti-malarial, anti-fungal, anti-HIV, anti-oxidant, and anti-mutagenic effects.<sup>[7-10]</sup> A decoction of the green fruit is used for cough. The pulp of the fruit is useful in dysenteric-diarrhoea, dropsy, piles and leprosy. Half ripe fruit is used as purgative. Kernel of the fruit is narcotic. Fruits are used in menstrual disorder. Seed oil is used in rheumatism. Gum of the bark is demulcent and purgative. The triterpenoid present in the fruits possesses significant antimicrobial activity.<sup>[11]</sup>

*In silico* is an expression meaning "performed on the computer or via computer simulation". *It* is a scientific research journal aiming to advance the use of computational models and simulations in studies applied to advanced biological phenomena. *In silico* computer-based modeling technologies have also been applied in: Whole cell analysis of prokaryotic and eukaryotic hosts, Bioprocess development and improvement e.g. improvement of product yields. Besides it have also applied in Analysis, interpretation and visualization of heterologous information sets from numerous sources e.g. genome, transcriptome or proteome data, Protein design.<sup>[12-14]</sup>

The aim of the study to find the mechanism of action of the isolated compounds from *Terminalia bellerica* was explored the potential inhibitors of estrogen receptor alpha (ER- $\alpha$ ) for searching a drug against the breast cancer by molecular docking analysis.

## MATERIALS AND METHODS

### *In silico* analysis

#### Molecular docking analysis of isolated compounds

##### Protein Preparation

Three-dimensional crystal Structure of estrogen receptor alpha (PDB id: 3ERT) was downloaded in pdb format from the protein data bank. After that, the structure was prepared and refined using the Protein Preparation Wizard of Schrödinger-Maestro v10.1. Charges and bond orders were assigned, hydrogens were added to the heavy atoms, selenomethionines were converted to methionines, and all waters were deleted. Using force field OPLS\_2005, minimization was carried out setting maximum heavy atom RMSD (root-mean-square-deviation) to 0.30 Å.<sup>[15, 16]</sup>

##### Ligand Preparation

Compounds were retrieved from PubChem databases, i.e. Anolignan B, Gallic acid, Termilignan, Thannilignan.<sup>[17-19]</sup>

##### Glide Standard Precision (SP) ligand docking

SP flexible ligand docking was carried out in Glide of Schrödinger-Maestro v 10.1 within which penalties were applied to non-cis/trans amide bonds. Van der Waals scaling factor and partial charge cutoff were selected to be 0.80 and 0.15, respectively for ligand atoms. Final scoring was performed on energy-minimized poses and displayed as Glide score. The best-docked pose with lowest Glide score value was recorded for each ligand.<sup>[20][21][22]</sup>

## RESULTS AND DISCUSSIONS

### *In silico* analysis

#### Molecular docking analysis

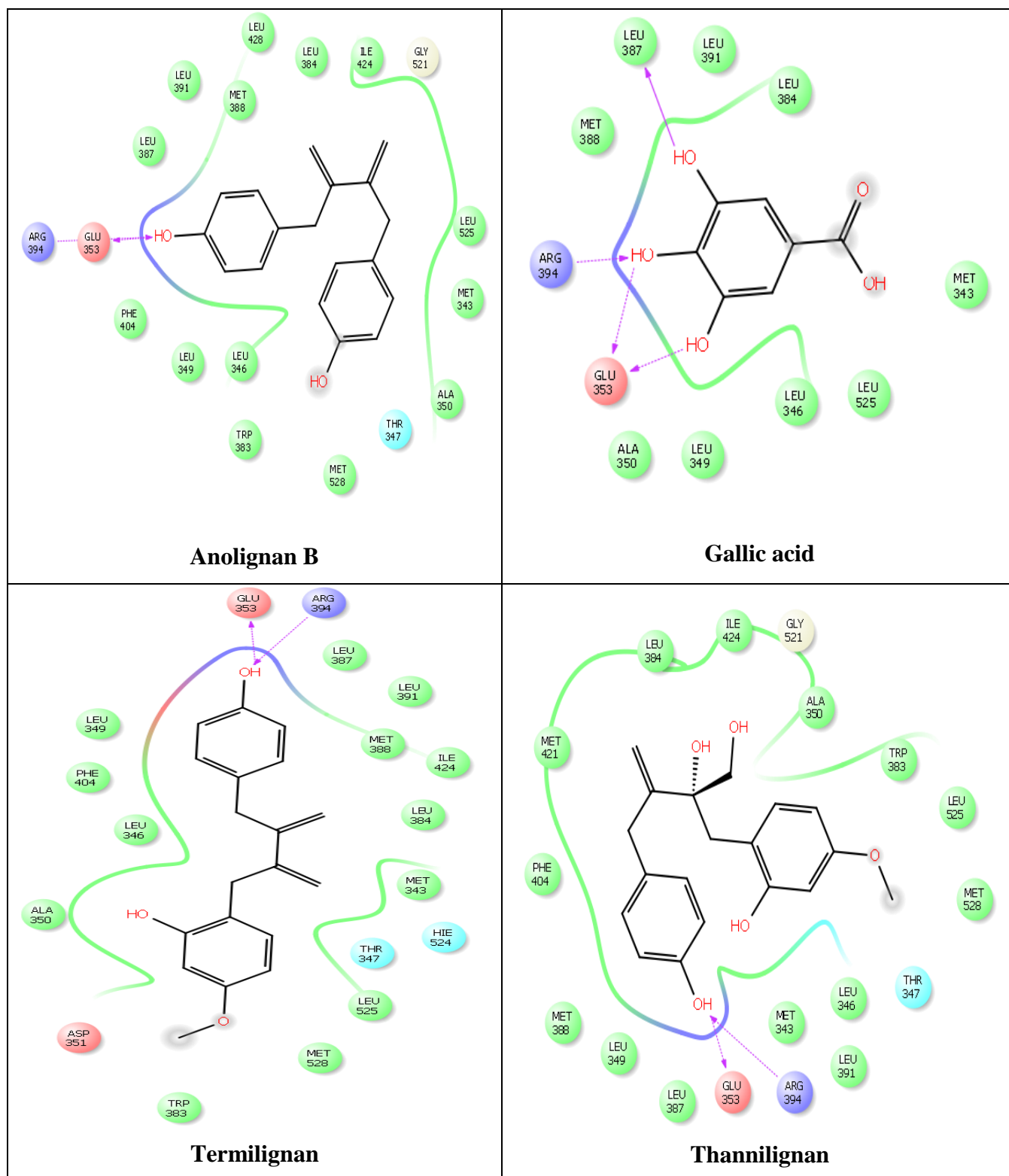
Various scientific studies show that aberrance in redox balance with an elevated level of oxygen-free radicals, reactive oxygen species (ROS), and reactive nitrogen species (RNS) plays an important role in the origin and progression of most human diseases including cancer.<sup>[23, 24]</sup> Reactive oxygen species (ROS) act as a secondary messenger in intracellular signaling cascades and elevated level of ROS associated with carcinogenesis by promoting

initiation, progression, and metastasis of cancer cells. It also induced DNA damage leading to genetic lesions that initiate tumorigenicity and subsequent tumor progression.<sup>[25]</sup>

Extracts of medicinal plants have been used for the treatment of various diseases, including cancer all over the globe, as they are easily prepared, standardized, and stored. Herbal extracts are also cost effective which increase their accessibility to the patients of all economic status.<sup>[26, 27]</sup> Global health policies promote the therapeutic use of herbal extract. World Health Organization (WHO) also encourages the use of medicinal plants in the treatment of disease.<sup>[28]</sup> Medicinal plants use for health benefit are not taken under the appropriate instruction and consultant of physician. The modern approach to discover a new drug molecule involves either isolation from a natural source or the synthesis of a particular compound responsible for a therapeutic effect.<sup>[29]</sup> And *in silico* way of finding new potential compounds from the isolated compounds of the plant becoming more popular over the years. In this study, the binding mode of estrogen receptor was investigated by doing computational analysis, glide docking. Both glide standard (SP) and extra precision (XP) mode had been introduced, where extra precision mode used for cross-validation purpose. The results of docking analysis were described in Table 1 and the docking figure showed in Figure 1. Binding energy is the primary parameter which is generated as a result of molecular docking. It gives us the idea of strength and affinity of the interaction between the ligand and the receptor. The greater the binding energy is, the weaker the interaction is and vice versa. Thus during any docking study, we intend to look for the ligand which displays the least binding energy, thus the best affinity among the test molecules.<sup>[30]</sup> Among all the compounds, Anolignan B showed the good docking score.

**Table 1: Docking results of Anolignan B, Gallic acid, Termilignan, Thannilignan with estrogen receptor alpha (PDB: 3ERT).**

Compound Name	Docking Score
Anolignan B	-8.004
Gallic acid	-6.351
Termilignan	-7.875
Thannilignan	-7.774



**Figure 1: Docking results of A. Anolignan B, B. Gallic acid, C. Termilignan and D. Thannilignan with estrogen receptor alpha (PDB: 3ERT).**

## CONCLUSION

Among all the compounds Anolignan B showed best docking score towards estrogen receptor alpha. So, Anolignan B is the best compounds for selective inhibitors of estrogen receptor

alpha, as it possessed best value in Molecular docking. Further *in vitro* and *in vivo* investigation need to identify estrogen receptor alpha inhibitory activity of isolated compounds from *Terminalia bellerica*.

### COMPETING INTERESTS

The authors declare that they have no competing interests.

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