

# Molecular docking analysis of beta-catenin with compounds derived from *Lycopersicon esculentum*

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#### Abstract:

Beta-catenin is linked with colorectal cancer (CRC). Therefore, it is of interest to design and develop novel compounds to combat CRC. Hence, we document compounds (chlorogenic acid, gallic acid, protocatechuic acid, quercetin and vanillic acid) from *Lycopersicon esculentum* with optimal binding features for further consideration.

**Key words:** Colon Cancer, *Lycopersicon esculentum*, Beta-catenin, Molecular docking

**Background:**

Colon and rectum carcinoma is a significant health concern globally, with more than 700,000 deaths each year [1]. Nearly 30% of CRC patients develop recurrences despite curative surgery [2]. Infections in various sites or remote lymph nodes (remote recurrences) have a serious impact on the CRC prognosis. Wnt signal pathways regulate cell proliferation, migration and destiny during embryonic development. It is known that Wnt signalling pathways, Wnt / b-catenin (canonical pathway) is mutated in nearly 90% of colorectal cancers (CRCs) [3]. The vast majority of colorectal cancers have mutations in Wnt pathway genes like adenomatous polyposis coli (APC) and  $\beta$ -catenin (CTNNB1) genes. The APC gene was previously identified as causative of family adeno matous polyposis (FAP) syndrome [4,5] and often mutated in sporadic colo-rectal cancers. APC mutations occur similarly in replication error (RER) positive and negative colorectal cancers [6,7] and are the earliest genetic event in the so-called ade-noma-carcinoma sequence. Therefore, it is of interest to design and develop novel compounds to combat CRC.

**Materials and Methods:****Preparation of Receptor for docking:**

The three-dimensional structure of Beta-catenin from Homo sapiens PDB: ID 1JDH downloaded from the protein databank (PDB) was used in this study [8].

**Preparation of Ligands:**

10 known compounds from the tomato plant have been selected from the literature for this Study (Table 1). The structures of these compounds were obtained from the PubChem Compound Database in the Spatial Data File (.SDF) format and converted to the PDB file format using the Online Smile Translator. Energy minimization of ligands was completed with ChemBio 3D Ultra 12.0 using standard procedure.

**Molecular Docking of ligands with Beta-catenin:**

Molecular docking analysis of beta-catenin with compounds derived from *Lycopersicon esculentum* was completed using the Hex 8.0.0. Docking software [9].

**Results and Discussion:**

The HEX docking results of selected compounds with beta catenin showed that they would have a great docking score (E-total value) as shown in Table 2. The more negative the value, the more stable the complex is and the more binding affinity. According to energy funnel theory, less energy represents extremely reliable conformation. More negative Etotal value indicates that there must be a substantial relationship between ligand and receptor, leading

to the activation of receptor activity [10]. The molecular docking findings of the selected five compounds (chlorogenic acid, gallic acid, protocatechuic acid, quercetin & vanillic acid) with beta-catenin were shown in Figure 1. We selected the best five of the 12 compounds. All the five compounds have good docking score and E-total value. The molecules that bind to the receptor inhibit its function for further consideration. HEX 8.0 has shown that the selected five compounds have a binding value of -170.22 to -255.21 kJ/mol. Molecular docking data shows that these five compounds are potent beta-catenin inhibitor.

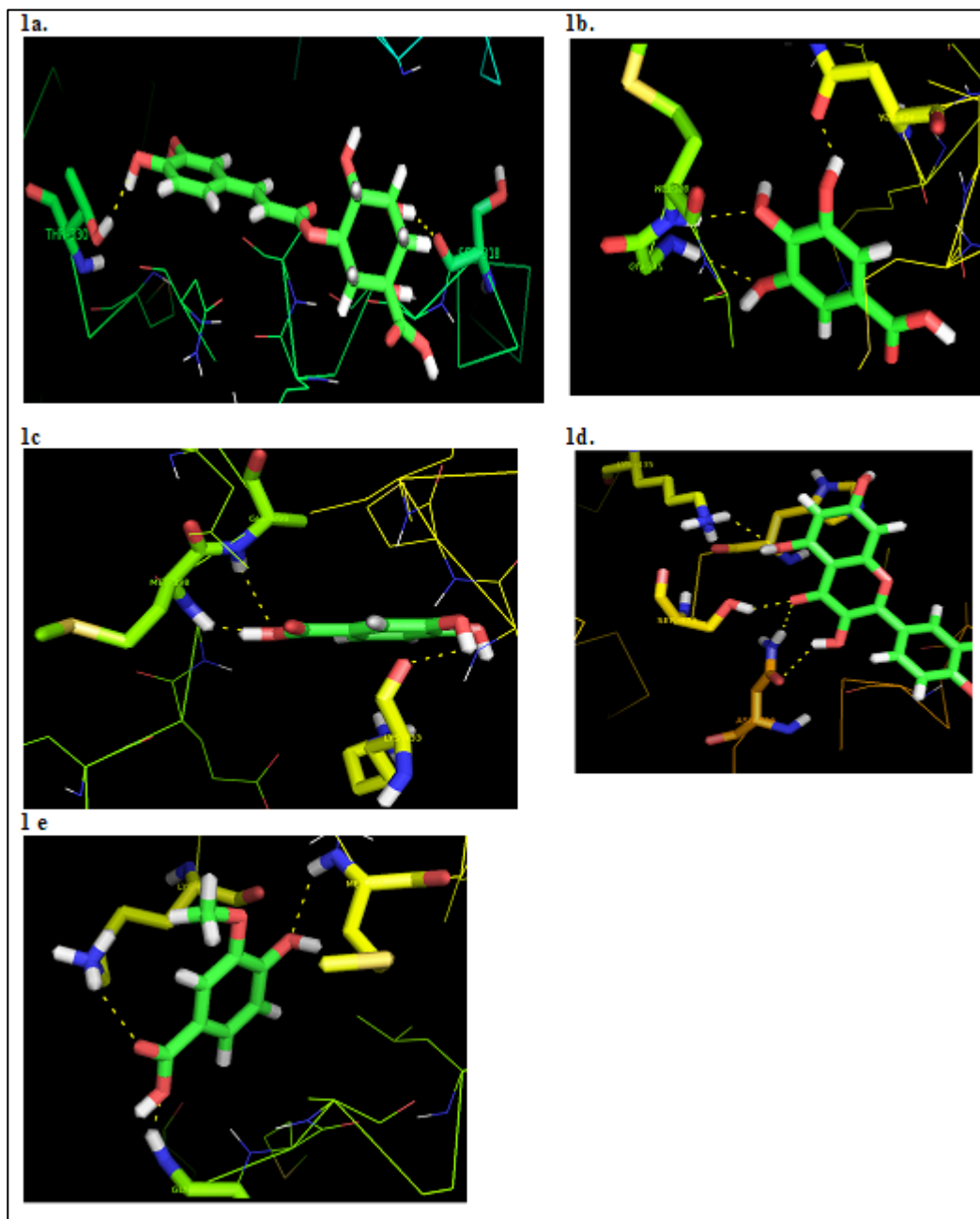
**Table 1:** Selected compounds from tomato (*Lycopersicon esculentum*)

S.No	Compound Name
1	Benzoic acid
2	Chloregenic acid
3	Cinnamic acid
4	Gallic acid
5	Glucoside
6	Kaempferol
7	Naringenin
8	Protocatechuic acid
9	Quecetin
10	Rutin

**Table 2:** Molecular docking results obtained from HEX

S.No	Compound Name	E-Total	H-bond Interaction
1	Chlorogenic acid	-243.48	SER-318 THR-330
2	Gallic acid	-183.25	GLY-397 MET-398 ASN-434 GLU-399
3	Protocatechuic acid	-173.62	MET-398 LYS-433
4	Quercetin	-255.21	LYS-435 SER-473 ASN-516
5	Vanillic acid	-170.22	GLY-397 LYS-433 MET-437

The resultant docked complexes were further examined with pymol to show the H-bond interactions between the selected compounds and the beta-catenin protein. The findings showed that many of the compounds displayed significant H-bonding interactions with beta-catenin through the amino acids SER-318, THR-330, GLY-397, MET-398, ASN-434, GLU-399, LYS-433, LYS-435, SER-473, ASN-516 and MET-437 (Figure 1). Higher binding molecular docking scores and strong molecular interactions recommended that such compounds are effective candidate for inhibition of beta catenin for further consideration.



**Figure 1:** Molecular Interaction of  $\beta$ -catenin with (a) Chlorogenic acid b) Gallic acid, (c) Protocatechuic acid; (d) Quercetin and (e) Vanillic acid is shown

**Conclusion:**

We document compounds (chlorogenic acid, gallic acid, protocatechuic acid, quercetin and vanillic acid) from *Lycopersicon esculentum* with optimal binding features for further consideration to combat CRC.

**Conflict of interests:** None declared.

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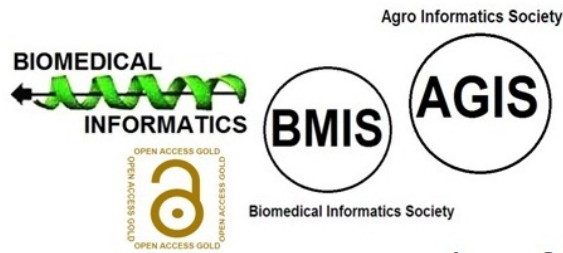
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