Research Article

Molecular Docking and Dynamic Studies on the Bioactive Principles of *Solanum nigrum* and Synthetic Drugs against Triple Negative Breast Cancer Targets

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ABSTRACT

Triple negative breast cancer (TNBC) is a heterogeneous cluster categorized by the lack of expression of hormonal receptors and also the absence of HER2 over expression. Most of the cancers are treated with chemotherapy but it has a lot of side effects. TNBC lacks receptors and hence cannot be treated using targeted therapies. Drugs from herbal sources are easily available, less toxic and less expensive. *Solanum nigrum* commonly used plant has lot of medicinal properties including anticancer activity. The active compounds of *S.nigrum* regallic acid, kaempherol, usnic acid, catechin, caffeic acid, epicatechin, rutin, and PCA. The scope of the present study is to identify the drug lead bioactive principles present in *S.nigrum* that can be exploited to find triple negative breast cancer targets. The Wnt and notch signaling pathway are mainly involved in triple negative breast cancer and were identified with help of pathway enrichment. There are several genes involved in these two pathways and among these genes with top hit p-value were selected as targets for the present study. The identified compounds *S.nigrum* were checked for pharmacokinetic properties. Hence *in silico* screenings including docking and molecular dynamics methods were used for the identification of potential drug lead compound. The results of the present study revealed that the active compound of *S.nigrum* namely epicatechin was found to be equally effective with good docking scores when compared to standard chemotherapeutic drugs. Lower RMSD and small fluctuations in RMSF of docking complex and contacts are good indications of system stability. Hence can be exploited as an alternative to chemotherapeutic drugs in order to minimize the side effects of these agents.

Keywords: Triple negative breast cancer, Phyto compounds, Dynamics, *S.nigrum, in silico* screening.

INTRODUCTION

Cancer is defined as a group of diseases categorized by uncontrolled growth, and also the spread of abnormal cells that if left untreated might cause death. Cancer continues to be a serious pathological state Worldwide and over ten million new cancer cases occur annually, roughly half of that is prevalent within the developed countries, and also the disease causes over six million deaths a year.[1] Breast cancer is the most typical form of cancer in women worldwide. Many patients are diagnosed with a group of breast cancers outlined by the lack of expression of and/or amplification of targetable biomarkers.

Four major intrinsic subtypes are known by genomic studies: the Luminal subtypes A and B, that express hormone receptor-related genes, basal-like (BL) breast cancer, and HER2-positive breast cancer.[2]Triple-negative Breast cancer (TNBC) is characterized by the lack of expression of hormonal receptors and also the absence of HER2 overexpression.[3]At present, no approved targeted therapy exists and therefore the cytotoxic chemotherapy remains as the treatment modality. The identification of TNBC subtypes has provided a basis for distinctive possible targeted therapeutic options[4]. There are various types of cancer therapy employed that includes surgery, radiotherapy and chemotherapy. Most cancers are treated with chemotherapy but it has a lot of side effects. TNBC lacks receptors and hence cannot be treated using targeted therapies. Medicinal herbs are incorporated into the historical medicine of virtually all human cultures. The plants are a rich supply of the secondary metabolites with interesting biological activities.[5] *Solanum nigrum* (black nightshade) is commonly used as green leafy vegetable with lots of medicinal values. The family *Solanaceae* has been screened by researchers for their medicinal values. It is proved that herbal drugs are effective in the treatment of the many diseases.[6]*Solanum nigrum* is extensively used to treat severe diseases like inflammation, pain and fever, as well as used as an anti tumorigenic, antioxidant, anti-inflammatory, anti-cancer, diuretic, and antipyretic agent.[7] Pathway analysis also called functional enrichment analysis, is quickly becoming one amongst the foremost tools of Omics research. Pathway analysis strategies possess a broad range of applications in physiological and biomedical analysis.[8] Molecular docking may be a method that anticipates the favored orientation of ligand against receptor (Protein) to form a stable complex. Therefore, docking plays an important role within the drug design and discovery method.[9] Modern drug discovery is especially primarily based *in-silico* chemico biological approach. Use of computer aided techniques in drug discovery and development method is quickly gaining popularity, implementation and appreciation.[10] Molecular dynamics (MD) simulations predict how each atom in a protein or different molecular system can give way to time based general

model of the physics governing inter atomic interactions. MD simulations are typically utilized in combination with a large kind of experimental structural biology techniques, including X-ray crystallography, nuclear magnetic resonance (NMR), electron paramagnetic resonance.[11] A number of synthetic anticancer drugs are available for triple negative breast cancer in the market but they have lots of side effects. As chemotherapy has lots of side effects so plants products are gaining more importance.[12] Hence the need for alternative sources from natural products is crucial. Recent advances in the *in vitro* screening of phyto compounds have the broadened the range of new therapeutic drug targets. The aim of the study was to identify small molecules as hit against the target protein that may potentially have anticancer activity.

In the present study, homology modeling, molecular docking and molecular dynamics studies were carried out against the modeled and selected target proteins have been performed and phyto compounds in order to find small hits as anticancer agents.

METHODS

GEO database

GEO2R is an interactive web tool. In the present study, we have analyzed the datasets GSE27447 gene expression profiles of TNBC were downloaded from Gene Expression Omnibus of the National Centre for Biotechnology Information based on the GLP6244 platform data. The datasets were analysed with GEO2R tool and the data were grouped such as TNBC and non-TNBC and top 250 hits were obtained. From this up-regulated and down-regulated genes are obtained from adjusted the p-value criteria.[13]

Network analyst

Pathway Analysis also referred to as functional enrichment analysis, is becoming one among the foremost tools of Omics analysis. Network analyst is a web-based platform for gene expression profiling and biological network analysis (Pathway enrichment).[14] Network Analyst is often applied to three different types of input data: gene lists, a single gene expression knowledge set or multiple gene expression datasets. In the present study the gene lists were obtained from the Gene Expression Omnibus (GEO) database and were analyzed with GEO2R and the up regulated and down-regulated genes were obtained which were given as input.

Molecular docking maestro

Ligand Preparation

The phyto-compounds present in *Solanum nigrum* were used as ligand molecules for the present study. In addition, the commercially available anti-cancer drugs were also selected to compare with new lead compound. The structure of ligand molecule of the phyto compounds in *S.nigrum* and synthetic drug were collected from the small databases viz., Pub Chem databases to screen new potent anticancer molecule and all those molecules were loaded. The geometries were optimized and molecular charges were assigned using OPLS_2005 force field using LigPrep the output file was *Jobname_ligprep.out*[15] (Table 1).

Pharmacokinetic property prediction

ADME describes the disposition of a pharmaceutical compound within an organism. There are several algorithms that evaluate the drug-like character of a molecule on the basis of chemical and physical properties. The phyto-compounds in *S.nigrum* should obey the drug like properties. In this study ADME property for all the ligands were calculated using QikPropin Maestro.[16] The *Jobname_Ligprep.out file* was given as input, Output file for Qikprop was *Jobname_qikprop.out.*

Target Protein Preparation

The target proteins selected for the present study were CREB-binding protein (CREBBP), Catenin Beta 1 (CTNNB1), Tumor Protein P53 (TP53), Cyclin D2(CCND2) as shown in Table 1. The Three Dimensional structure of the target protein CCND2 was modelled using 2W9Z.pdb as template using Prime.[17] Then the quality of the modelled structures were validated using Ramachandran plot.

Protein Preparation

The protein preparation wizard accepts a protein from its raw state to a state in which it is properly prepared for calculations. The selected target proteins (Table 2) were prepared using protein preparation wizard and the output file was *Jobname.impref_ref.out.*

Receptor grid generation

Receptor was defined and the co-crystallized ligands were differentiated from the active site of receptor using receptor grid generation window of Glide module. The Grid was generated at the centroid of selected residues. This was done using Receptor grid generation option in the Glide. The output file generated was *glide_grid.zip.*

Active site prediction

The active site of the target protein: CREBBP, CTNNB1, TP53 were obtained from the PDB Sum database, whereas, for the modelled structures of CCND2 the active site was predicted using SiteMap[18] (Table 3).

Ligand docking

The ligand docking was carried out with the SP mode of Glide. The output file was generated with extension *glide. SP_pv.mae.* The docking results were viewed using the pose viewer panel in the Glide.[19]

Molecular Dynamics

Molecular dynamic simulations were performed to docking complex to evaluate the conformational changes, stability and to get insights into the natural dynamics on different timescales in solution. Simulations were carried out using Desmond v5.6 implemented in Maestro v11.8 graphical user interface.[20]

Table 1: List of the ligands

LIGANDS	PUBCHEM ID	LIGANDS	PUBCHEM ID
Active compounds of *S.nigrum*		**Synthetic anticancer drugs**	
Catechin	9064	Tamoxifen	2733526
Caffeic acid	689043	Zoledronic acid	68740
Epicatechin	72276	Gefitinib	123631
Kaempferol	5280863	Palbociclib	5330286
Gallic acid	370	Epirubicin	41867
M-Coumaric acid	637541	Doxorubicin	31703
Naringenin	932	Fulvestrant	104741
PCA	72	Ixabepilone	6445540
Rutin	5280805	Letrozole	3902
Usnic acid	633552	Capecitabine	60953

Table 2: List of the Target Proteins

S. No	Target	PDB ID	Experimental Method	Resolution
1	CREBBP	4A9K	X-raydiffraction	1.81 Å
2	CCND2	Modeled with template2w9z	-	-
3	CTNNB1	3SLA	X-raydiffraction	2.5 Å
5	TP53	4LOE	X-raydiffraction	1.85 Å

Table 3: Active site residues of the Target Proteins

Target	PDB ID	Active Site Residues
CREBBP	4A9K	PRO1114,ASN1168,PRO1110, MET1133, ASN1168, GLN1113, LEU1120 TYR 1125
CCND2	Modelled with template 2w9z	GLU65,GLU68,ASP264, ASP191, GLN260, THR 190, TYR 54, ARG57
CTNNB1	3SLA	LYS170,ASP27,GLN203, GLU209, GLN177, ALA272, ASP272, SER234, LYS180, ARG212
TP53	4LOE	ASP184,LYS139,LEU137,TYR150,TYR 239, TYR107,SER260,PRO153, LEU 264,SER106, MET243, HIS178, THR239, THR107, HIP 179, ALA139, LYS 139.

RESULTS AND DISSCUSION

Triple negative breast cancer is characterized by the absence of estrogens receptor(ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2). So patients with TNBC do not benefit from hormonal or *trastuzumab* based therapies. The present study is mainly focused to identify the potent bioactive principles of *S.nigrum* that has the ability to inhibit the triple negative breast cancer targets using molecular docking and dynamics studies.

Network analyst

The GSE27447 gene expression profiles of TNBC were downloaded from Gene Expression Omnibus of the National Center for Biotechnology Information based on the GLP6244 platform data. In total, 19 specimens, including 5 TNBC and 14 non-TNBC samples, were used in the present study. From this data 172 up-regulated genes and 55 down-regulated genes were identified and were used as input for Network analyst. Notch and Wnt signaling pathways play an important role in maintaining normal cell fate and these signaling pathways are also involved in a number of cancers. The results obtained from the network analyst showed that the differentially expressed genes (DEGs) are collected from the GEO datasets and network analyst explicated that the Wnt pathway and Notch signaling pathway have significant P-value (figure 1). These results were compared with KEGG database, and two of these pathways are mainly involved

in the triple negative breast cancer progenies. In the present study, the genes which were in top 5 hits were chosen as target for the molecular docking studies (fig 2).

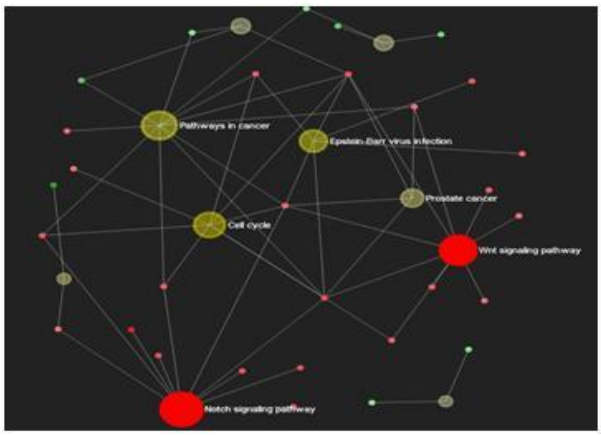

Figure 1: Red colour shows Wnt and Notch signalling pathway that have top most P-value

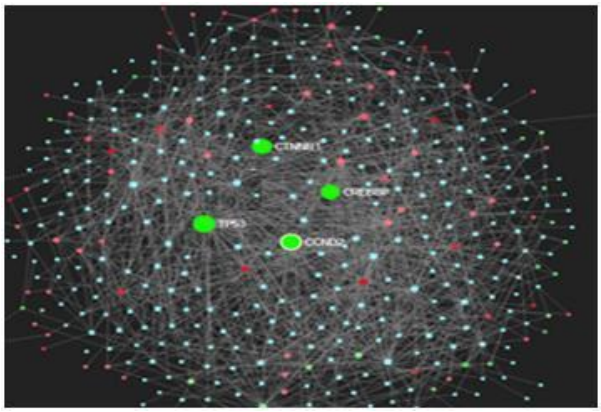

Figure 2: Green colour indicates genes that have top hits P-value

Among the genes of Wnt and notch signalling pathway the genes having highest P-value were selected namely CREB-binding protein (CREBBP), Catenin Beta 1 (CTNNB1), Tumor Protein P53 (TP53), Cyclin D2(CCND2). Since no structure was available for CCND2 modeling studies were done for these two genes.

Molecular modeling

The homology modeling is based on the observation that structure is more conserved than sequence, such that a known protein structure can be used to construct a model of a homologous protein. There is no binding or docking study done for CyclinD2 (CCND2). This is due to lack of an appropriate crystal structure. Therefore, the 3D structures of target proteins CyclinD2 (CCND2) was predicted by comparative modeling identity between a target sequence of interest and the template sequence. The first step in molecular modeling is Structure Prediction using Prime

Structure Prediction using Prime

Prime was used to generate three-dimensional model of the CyclinD2 (CCND2). The 3D structure of target CCND2 was modeled using 2W9Z.pdb as template using Prime. Then the quality of modeled structures was validated using Ramachandran Plot.

CyclinD2 (CCND2)

>EAW88851.1 Cyclic D2 [Homo sapiens]

MELLCHEVDPVRRAVRDRNLLRDDRVLQNLLTIEERYLPQCSYF
KCVQKDIQPYMRRMVATWMLEVCEEQKCEEEVFPLAMNYLD
RFLAGVPTPKSHLQLLGAVCMFLASKLKETSPLTAEKLCIYTDNS
IKPQELLEWELVVLGKLKWNLAAVTPHDFIEHILRKLPQQREKL
SLIRKHAQTFIALCATDFKFAMYPPSMIATGSVGAAICGLQQDE
EVSSLTCDALTELLAKITNTDVDCLKACQEQIEAVLLNSLQQYRQ
DQRDGSKSEDELDQASTPTDVRDIDL

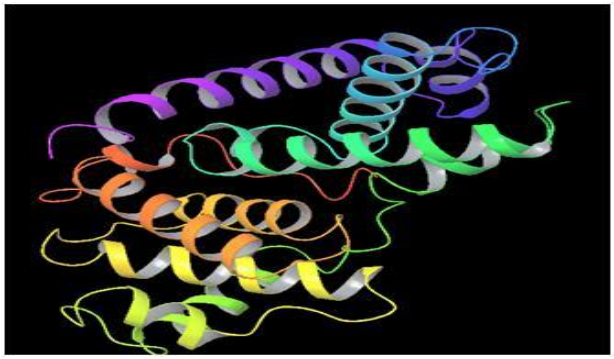

Figure 3: Structure of CCND2

For the modeled protein structure CCND2, PDB-BLAST was performed for identifying an appropriate template for homology modeling (PDB ID: 2W9Z). The template sequence displayed highest matching score having 66%identity with that of target sequence. The selected model showed 90.6% of residues in favored regions, 9.4% of residues in allowed regions and none of the of residues were in the disallowed regions of Ramachandran plot as shown in figure 4**.**

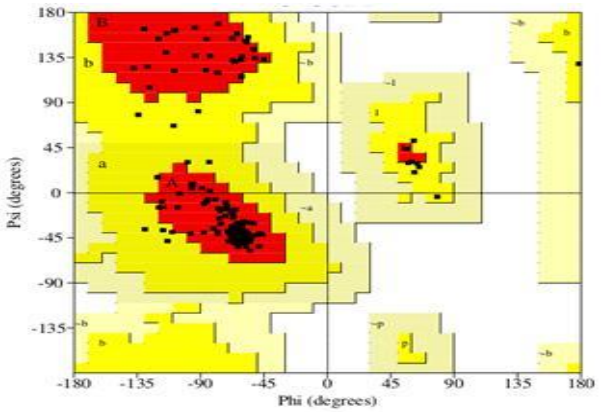

Figure 4: Ramachandran plot of CCND2

Similarly Sheikh *et al.,*(2018) [21], performed the BLAST search coupled with Clustal W alignment and identified the template structure. The template sequence displayed highest matching score having 71% identity with that of target sequence. The selected model showed 90% of residues in favored regions, 8.7% of residues in allowed regions and 0.2% of residues in disallowed regions of Ramachandran plot.

Pharmacokinetics properties

Our aim was to identify the bioactive principles in *Solanum nigrum* which had good drug like properties. As a first step to this attempt, we carried out pharmacokinetic studies using QikProp3.4. The compounds selected for docking were gallic acid, kaempherol, usnic acid, catechin, caffeic acid, epicatechin, rutin, narigenin, M-coumaric acid and PCA. The compounds were screened for their pharmacokinetics properties using Qik Prop 3.4 and the results are shown in Table 4.

The results of study showed that all the pharmacokinetic parameters were within the acceptable range defined for human use, thereby indicating their potential as drug-like molecules. The selected compounds show good cell permeability and oral absorption which indicated that all the selected compounds were orally active.

Makala *et al*., (2017)[22] reported that the biphenyl-4-sulfonamide (B4S) and pyridazine analogs showed physical signifiers and pharmacologically relevant properties of the top hits including molecular weight, log P (o/w), QP log S, percentage of human oral absorption. Predicted octanol/water coefficient was in the range of 5.9–6.8 and it is in allowed region. All the compounds exhibited 100% human oral absorption (QP). Identified molecules all were within the acceptable range of Lipinski rule of five.

Table 4: ADME results of active compounds of *Solanum nigrum*

Ligand Name	Molecular weight (Da)	Donor H-Bond	Acceptor H-Bond	Octal water	%Human Oral Absorption	Rule Of Five
Catechin	290.272	5	5.45	0.481	60.671	0
Caffeic acid	180.16	3	3.5	0.543	54.272	0
Epicatechin	290.272	5	5.45	0.494	61.023	0
Kaempferol	286.24	3	4.5	1.059	64.74	0
Gallic acid	170.121	4	4.25	-0.571	41.179	0
M-Coumaric acid	164.16	2	2.75	1.429	67.502	0
Naringenin	272.257	2	4	1.658	74.476	0
PCA	154.122	3	3.5	0.027	52.533	0
Rutin	610.524	9	20.55	-2.394	0	3
Usnic acid	386.357	0	10.75	0.106	65.104	0

Our results were also in accordance with the reported studies where the compounds from *Solanum nigrum* namely catechin, caffeicacid, epicatechin, gallic acid, kaempherol, usnic acid, narigenin, M-coumaric acid, and PCA which showed better human oral absorption expect rutin alone which violated the Lipinski rule of 5 and its has no human oral absorption. Hence it cannot be exploited as a pharmacokinetic compound.

Molecular docking

Based on our ADME results molecular docking studies were done with the selected triple negative breast cancer targets, namely CREB-binding protein (CREBBP), Catenin Beta 1 (CTNNB1), Tumor Protein P53 (TP53), Cyclin D2(CCND2). Molecular Docking is an efficient technique to predict modes of the ligand with the protein of known three dimensional structures. Studies on binding modes are essential to elucidate key structural characteristic and interactions and they provide helpful data for designing effective inhibitors. Molecular docking studies of the target proteins, namely CREB-binding protein (CREBBP), Catenin Beta 1 (CTNNB1), Tumor Protein P53 (TP53), Cyclin D2(CCND2) with library of collected active compounds of *Solanum nigrum* and the existing drug molecules were done. The docking results of catechin, caffeic acid, epicatechin, gallic acid, kaempherol, usnic acid, narigenin, M-coumaric acid and PCA are depicted in table 5. Glide score and H-bond are depicted for the active compounds of *Solanum nigrum.*

Docking results with CREBBP, TP53, CCND2 and CTNNB1 with the drug which are used as to treat triple negative breast cancer is shown in table 6.

Liu *et al* (2019)[23] have reported the glide results of series of PI3Kδ inhibitors. They have compared the docking score of inhibitors and the one having minimum glide score and energy was selected.

Our results clearly validate the fact that from the docking results among the various phyto compounds tested epicatechin showed a high glide score of -9.419 with CREBBP compared to others. In order to identify the best drug molecule docking was done with a series of synthetic drugs commonly employed to treat breast cancer. Among those tested capecitabine showed a glide score of -7.52 with CREBBP compared to other protein targets. Hence, we studied the stability of interaction of CREBBP by molecular dynamics.

Table 5: Docking results with active compounds of *Solanum nigrum*

COMPOUNDS	CREBBP		TP53		CCND2		CTNNB1	
	Glide Score	H-Bond	Glide Score	H-Bond	Glide Score	H-Bond	Glide Score	H-Bond
Epicatechin	-9.419	4	-8.258	4	-7.87	5	-8.229	4
Rutin	-9.042	2	-8.358	5	-7.847	6	-7.528	7
Narigenin	-6.485	2	-5.477	2	-4.899	2	-6.096	2
Gallic acid	-5.16	2	-5.779	4	-5.098	3	-5.333	1
PCA	-6.017	3	-4.688	2	-4.816	2	-6.294	2
Catechin	-6.207	3	-5.865	5	-5.298	3	-5.161	2
Caffeic acid	-6.263	3	-4.763	3	-4.924	3	-5.235	1
Kaempferol	-6.042	1	-5.892	2	-5.024	3	-5.739	2
M-Coumaric acid	-5.79	3	-4.499	2	-5.05	2	-4.865	4
Usnic acid	-4.146	1	-5.111	1	-2.788	1	-6.151	3

Table 6: Docking results for existing drug Molecules

COMPOUNDS	CREBBP		TP53		CCND2		CTNNB1	
	Glide Score	H-Bond	Glide Score	H-Bond	Glide Score	H-Bond	Glide Score	H-Bond
Zoledronic acid	-5.039	3	-7.423	7	-7.276	4	-5.57	4
Capecitabine	-7.52	4	-6.15	2	-3.278	2	-5.684	3
Doxorubicin	-4.467	3	-3.902	3	-4.197	2	-7.03	4
Tamoxifen	-4.707	0	-4.437	1	-2.789	0	-5.854	1
Gefitinib	-5.475	1	-4.415	2	-3.572	2	-4.915	1
Palbociclib	-4.96	1	-4.088	1	-3.958	1	-5.117	0
Epirubicin	-5.264	3	-4.509	2	-4.256	2	-6.577	5
Fulvestrant	-3.148	1	-5.128	2	-3.896	2	-4.273	2
Ixabepilone	-3.321	1	-3.733	2	-3.703	1	-4.632	2
Letrozole	-5.543	2	-4.714	1	-3.544	0	-4.787	1

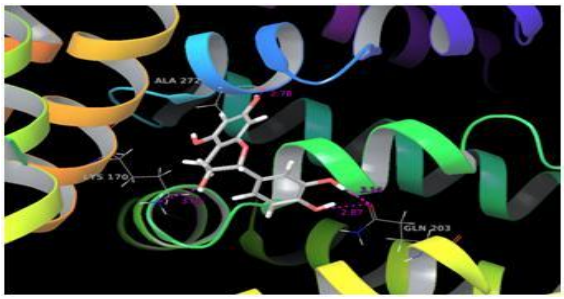

Figure 5: H-bond interaction between active compound Epicatechin and CREBBP

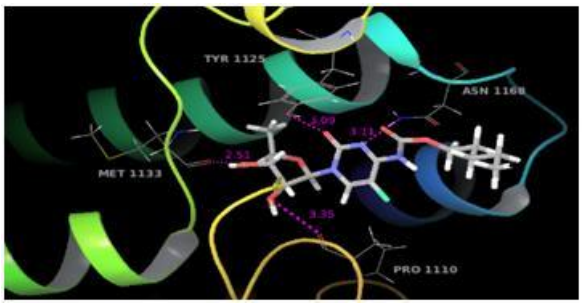

Figure 7: H-bond interaction between existing drug capecitabine and CREBBP

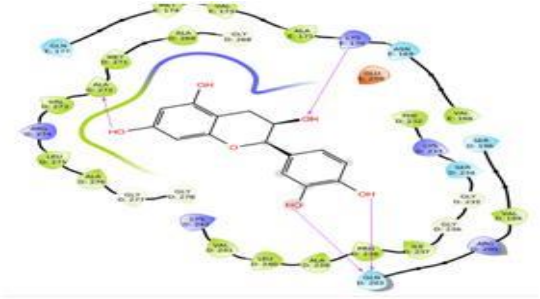

Figure 6: Ligand interaction diagram of active compound Epicatechin and CREBBP

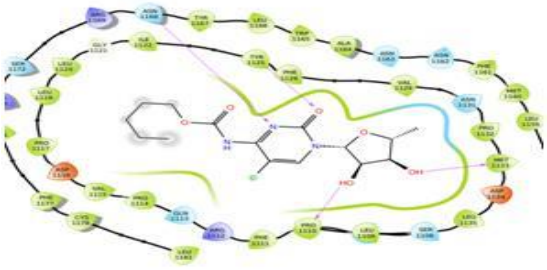

Figure 8: Ligand interaction diagram of capecitabine and CREBBP

Molecular dynamics simulation

Molecular dynamics (MD) simulation was performed using Desmond software with the simulation period of 10ns.

Protein and Ligand RMSD

The Cα atoms and side chain atoms of the CREBBP protein was within the range of 0.67-2.25 Å, when it was in complex with the lead molecule – epicatechin. Ligand RMSD indicates how stable the ligand is fit with respect to protein. When it was in complex with the lead molecule – epicatechin and the simulation of protein and ligand RMSD are within the acceptable range. The RMSD plots reveals that the system got equilibrated by 8 ns.RMSD plot is shown in figure 9.

Protein RMSF

RMSF is useful for characterizing local changes along the protein chain. Its helps to find which protein residues come into contact with ligand. The Cα and side chain atoms of the CREBBP residues fluctuate in a range of 0.4 – 3.2 Å respectively, which ensures that the interactions are stable. The lesser fluctuation of Cα atoms and side chain atoms ensure that the complex is less flexible or rigid in nature. The protein RMSF plot was shown in figure 10.

Ligand RMSF

The ligand RMSF gives an insight on how ligand fragments interact with the protein and their entropic role in the binding event. The ligand RMSF was measured for all the atoms in the lead molecule-epicatechin. The ligand atoms fluctuate in a range of 2 - 3.5Å. This shows that the ligand is more stable in the binding pocket. Both the RMSD and RMSF analysis authenticates that the conformation of the CREBBP and epicatechin complex is stable and lesser flexible. The ligand RMSF plot was shown in figure 11.

In the present study, the results of dynamics revealed that the simulation of CREBBP and epicatechin RMSD are within the acceptable range. The RMSD plots revealed that the system got equilibrated by 8 ns. The lesser RMSF fluctuations ensure that the interactions are stable. Both the protein and ligand RMSD and RMSF values ensure that the lead molecules are stable in the active site of the protein. Lower RMSD and small fluctuations in RMSF of docking complex and contacts are good indications of system stability.

Vats *et al.*,(2014)[24] have reported that the dynamic behaviour of the ligand– AChE complexes.

From the results discussed it is clear that, the ADME showed all active compounds selected exhibited 100% human oral absorption and acceptable range of Lipinski rule of five. Docking studies showed epicatechin possessed high glide score and energy. Among the synthetic drugs tested capecitabine showed high glide score and energy with CREBBP. Epicatechin also showed better H-bond interaction with CREBBP. Molecular dynamics study revealed that Cα atoms and side chain atoms of the CREBBP protein was within the range and it formed a complex with lead molecule epicatechin and simulation of protein and ligand RMSD were within the acceptable range.

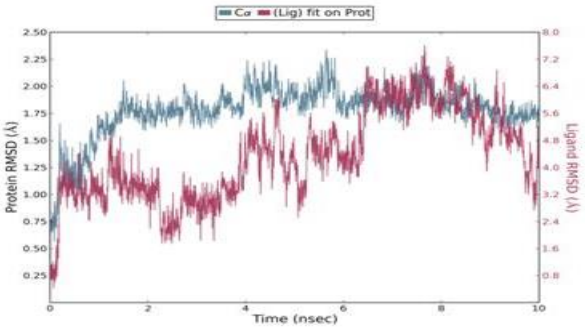

Figure 9: The Protein and Ligand RMSD

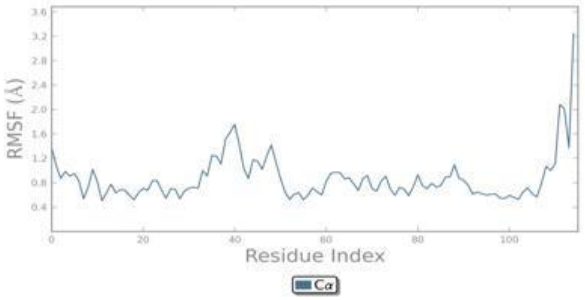

Figure 10: Protein RMSF

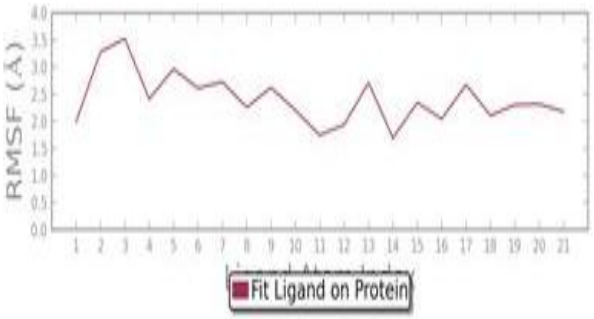

Figure 11: Ligand RMSF

CONCLUSION

Solanum nigrum, a commonly used plant has lots of medicinal properties including anticancer property. There are numerous active compounds in *Solanum nigrum* namely, gallic acid, kaempherol, usnic acid, catechin, caffeicacid, epicatechin, rutin, narigenin, M-coumaric acid and PCA. It is a potent anticancer agent which exhibits its anticancer activity through several mechanisms including inhibition of proliferation of cancer cells, transformation of normal cells; inhibit the synthesis of protein responsible for tumor growth. The present study aimed to identify the drug lead bioactive principles present in *Solanum nigrum* that can be exploited for the treatment of triple negative breast cancer. As Wnt and notch signalling pathway are mainly involved in triple negative breast cancer, we identified

several genes involved in Wnt and notch signalling pathway and among these genes with top hit p-value were selected as targets for the present study. The selected targets were CREBBP, CTNNB1, TP53 and CCND2. There are various synthetic anticancer drugs which are available for breast cancer treatment but they have side effects. Among the various anticancer drugs chosen for docking studies, Capecitabine showed good interaction with CREBBP and among the various active compounds docked epicatechin showed good interaction with CREBBP and was chosen for further analysis and molecular dynamics.

Molecular Dynamics simulations proved that epicatechin and CREBBP were having better binding orientations, RMSD, RMSF and has good pharmacological properties. The RMSD of the CREBBP protein was within the range when it was in complex with the lead molecule epicatechin. The ligand RMSF was measured for all the atoms in the lead molecule epicatechin which showed that the ligand was more stable in the binding pocket. Both the RMSF and RMSD analysis depicted that the conformation of the CREBBP and epicatechin complex was stable and lesser flexible. The results of the present study revealed that the active compound of *Solanum nigrum* namely epicatechin was found to be equally effective with good docking scores when compared to standard chemotherapeutic drugs. Hence can be exploited as an alternative to chemotherapeutic drugs in order to minimize the side effects of these agents.

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