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A STUDY OF ANTICANCER PROPERTIES OF TEA (*CAMELLIA SINENSIS*) AGAINST LUNG AND BREAST CANCER: AN IN-SILICO APPROACH OF DRUG DESIGN

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ABSTRACT

Tea (*Camellia sinensis (L.) Kuntze*) is a popular beverage, a part of many cultures, and a valuable source of medicine for a variety of ailments. Tea contains bioactive compounds that can be used to formulate drug compounds. An effort has been made to characterise the chemopreventive efficacy of some previously reported bioactive compounds from Tea against some important target enzymes and proteins such as human 17 beta-hydroxysteroid dehydrogenase type 1 (17-HSDs), aspartate aminotransferase (AAT), vascular endothelial growth factor (VEGF), and human epidermal growth factor receptor 2 (HER2), all of which play important roles in the development of breast and lung cancer.It is an in-silico approach to characterise the chemopreventive efficacy of some previously reported bioactive compounds from Tea (*Camellia sinensis* (L.) Kuntze). In Molegro Virtual Docker 6.0, the selected bioactive compounds isolated from Tea (*Camellia sinensis* (L.) Kuntze) were docked with some important target enzymes and proteins that play important roles in the development of breast and lung cancer. The results were analysed using the docking score, H-Bond interaction and the ADME study performed in admetSAR1. Ligands Thearubigin (1), Theaflavin-3-gallate (2), and

Theaflavin (5) have been shown to be nontoxic, have better interaction with the selected targets, and have good ADME properties. Thearubigin (1), Theaflavin-3-gallate (2), and Theaflavin (5) have the potential to be anticancer lead molecules for the treatment of breast and lung cancer and should be investigated further.

Keywords: *Camellia sinensis*, Chemopreventive activity, breast and lung cancer, Molecular docking

INTRODUCTION

The two most commonly diagnosed types of cancer are the breast and lung cancer, and are the leading cause of mortality around the world. According to GLOBOCAN 2020, breast cancer is now the most common cancer diagnosed type with an estimated 2,261419 (11.7%) new cases followed by lung cancer of 2,206771 (11.4%) new cases. The report also stated the maximum number death due to lung cancer and breast cancer was 1796144 (18%) and 684996 (6.9%) respectively **[1]**. Despite the fact that there are numerous FDA-approved drugs for lung and breast cancer, their use is limited due to high costs and severe side effects **[2, 3, 4]**. Therefore a trend of screening out new drug candidates of natural origin has been growing. In regard, we have conducted an in-silico method to screen some previously isolated compounds from Tea (*Camellia sinensis*) (1 to 10) **(Figure 1)** against some important drug targets of both breast and lung cancer therapy. Laptinib, an anti-cancer drug used for breast and lung cancer has been selected as reference drug **[5]**. It suppresses the tyrosine kinase activity of two oncogenes, EGFR (epidermal growth factor receptor) and HER2/neu (Human EGFR type 2) **[6]**. During treatment Lapatinib has shown some side effects like diarrhoea, fatigue, nausea, and rashes **[7]**.

Tea is an extremely nutritious beverage that contains various bioactive chemicals that provide a many health benefits. The major bioactive compounds are alkaloid, flavonoids, steroids, and terpenoids. These phytochemicals are convenient source to develop drugs for various illnesses, including cancer **[8]**. Several studies reveals that polyphenols and flavonoid compounds derived from tea, such as Epicatechin, epigallocatechin-3 gallate, epicatechin gallate, and epicatechin gallate, have the ability to prevent cancer cell survival **[9]**. Tea contains catechins, which can protect the skin from UV rays and improve photo stability. Among catechins, EGCG accounts for the greatest proportion of catechin compounds **[10]**. They have the power to impact the initiation, development, and promotion of

tumours **[11]**. Epicatechin induces apoptosis in cells of breast cancer, which slows their proliferation **[12]**. ECG alters the expression of numerous genes involved in apoptosis, angiogenesis and cell cycle arrest **[13]**. Tea contains theaflavins, a type of polyphenolic substance which can be utilised to treat oestrogen receptor positive breast cancer, lung cancer, leukaemia and ovarian cancer **[14]**. In animal and cultured cell line models, another major component of tea, caffeine has been shown to suppress cancer cell proliferation. Caffeine is also effective with a number of anticancer medicines to boost their cytotoxic effects **[15]**. Procyanidin has the potential as a chemopreventive drug which can change gene expression in animal models **[16]**.

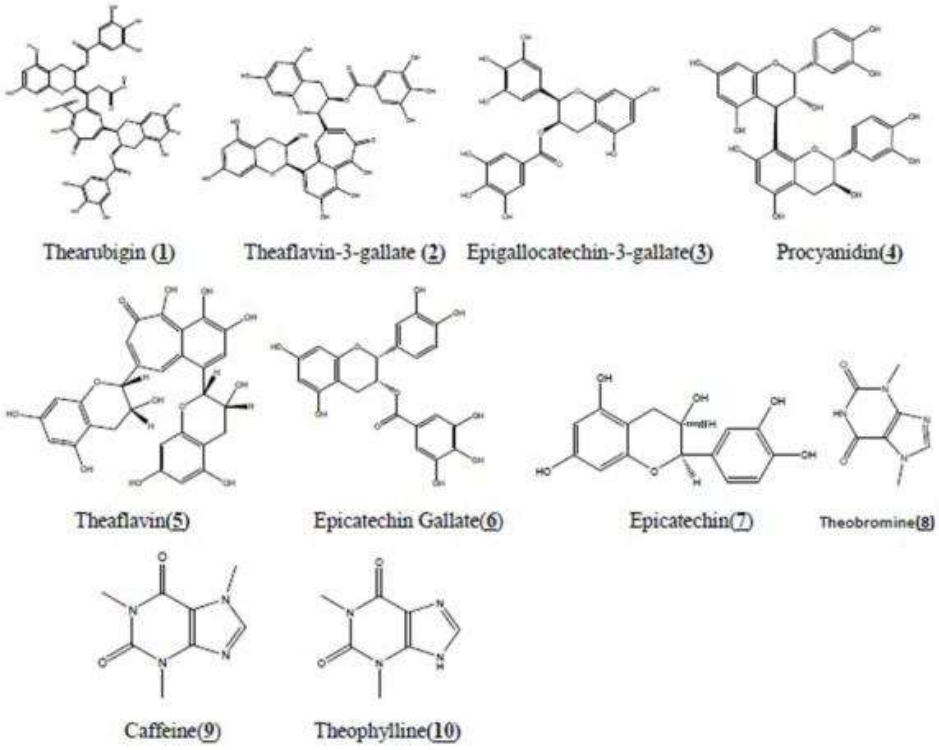

Figure 1: Structure of selected compound

Human 17-hydroxysteroid dehydrogenases type 1 (17-HSDs) is a steroid-converting enzyme that catalyses the final step in oestrogen activation and thus plays a critical role in the development of breast cancer. It is also thought to be an important prognostic factor 1in patients with non-small cell lung cancer (NSCLC) **[17, 18]**. 17-HSD produces active oestrogen, estradiol, and other estrogens such 5-androstene-3 and 17-diol, and inactivates androgen, dihydrotestosterone (DHT), all of which

stimulates and contribute in the progression of breast tumours **[19]**. 17HSD1 is regarded to be an important prognostic factor in patients with oestrogen-responsive NSCLC **[20]**.

Aspartate aminotransferase (AAT) is a prospective molecular target for the formulation of anti-cancer medicines because it works with malate dehydrogenase to transfer electrons from NADH through the inner mitochondrial membrane **[21]** VEGF, a crucial angiogenic factor can affects a number of endothelial cell processes, including mitogenesis. VEGF increases tumour angiogenesis, and high VEGF levels in tumour tissue were linked to bigger tumour size in a study of 574 individuals with node-negative breast cancer **[22-25]**.

The EGFR/ErbB family of receptors includes human epidermal growth factor receptor 2 (HER2). HER2 overexpression is identified in around 20 – 30 percent of breast cancer tumours. **[26, 27]**. By aggregating in cell membranes, HER2 proteins act upon tumour genesis **[28, 29]** and disruption of HER-mediated signalling pathways leads to cancer cell growth and dissemination. **[30]**. HER2 proteins also responsible for survival of NSCLC **[31]**.

The present study aims to look the anticancer capabilities of tea phytochemicals in order to find new chemotherapeutic drugs for the aforementioned breast and lung cancer targets. The select compounds were docked, and the findings were analysed on the basis of docking score and hydrogen bond interaction **[32, 33]**. The Absorption, distribution, metabolism, and excretion (ADME) properties of the substances and their toxicity were examined.

MATERIAL AND METHODS

Protein Preparation and Calculation of Protein Parameters

17-HSD1 (PDB ID: 1FDV), AM (PDB ID: 1IVR), VEGF (PDB ID: 2C7W), and HER2 (PDB ID: 2C7W) crystal structures were acquired from the Protein Data Bank and imported one at a time into the Molegro Virtual Docker (MVD). The associated ligand, water, and co-factors were removed using the MVD Protein preparation tab. Hybridization state, bond order, and explicit hydrogen were assigned in the automatic preparation mode, and according to the scoring algorithm charges were assigned (MolDock Scoring Function).

To find the binding sites of the selected proteins, grid-based cavity prediction methods with resolution of 0.8 covering the proteins were used in MVD. The accessibility of the grid points was tested by placing spheres of radius 1.4 determined by

the Van der Waals method for overlap analysis and choosing random directions from the accessible grid point to see if any inaccessible grid points were encountered along the way. This was repeated for 16 different directions, with the accessibility of the grid points being determined if 12 or more of these lines intersected an inaccessible volume. Volumes less than 10.0 3 were deleted as useless after connecting the neighbouring grid points **[34]**. Based on their volumes, the projected cavities were scored and ranked, with the highest scoring one being picked. The binding cavity for 17-HSD1 was set at X: 49.730 Y: -0.971 Z: 55.62 with Volume: 528.38 (A2), X: 45.58 Y: 12.76 Z: 39.96 with Volume 125.44 (A2), X: 31.35Y:-32.27 Z: 9.70 with Volume 24.064 (A2), and X: 177.17Y: 8.53 Z:1.90 with Volume 10842.2.

Ligand Preparation

ChemDraw Ultra 12.0.2.1076 (Cambridge Soft) was utilized to create the ligands. The 2D structures of the ligands were sketched and subsequently transformed to 3D **[35]**. ChemDraw 3D was applied to optimise the 3D chemical structure and energy of the selected compounds and reference medicinal compounds, using a 0.1 RMS gradient for geometry optimization.

Molecular Docking and Interaction Analysis

To finish docking processes, Molegro Virtual Docker (MVD) was employed. The optimized ligands were permitted to dock to the 17-HSD1, AAT, VEGF, and HER2 predicted active sites. MolDock Score [GRID] was employed as the scoring function, and tri-linear interpolation was applied to evaluate energy potentials for grid points. MolDock SE (Simplex Evolution) was utilized as the scoring function, with a maximum repetition of 1500 for a population size of 50 and 5 runs. Following docking, the best poses were selected for further investigation using Moldock or docking scores, a statistical scoring tool that translates interaction energy into numerical values **[36]**. The best postures were translated into hydrogen bonds and ligands and interactions between the ligands and proteins were discovered one at a time.

ADME and toxicity prediction

In admetSAR1, the toxicity and ADME properties of selected ligands and reference drugs were studied. Nearly 2 lakh quantitative structure-activity relationship (QSAR) models are included in admetSAR1, including 22 qualitative classification and 5 quantitative regression models. For ADMET prediction, annotated data points from the

scientific literature for over 96 thousand different compounds are obtained **[37]**.

RESULTS AND DISCUSSION

Molecular docking

Natural products are a great source of lead compounds, and studying them can help to find new drug candidates for various cellular targets, activities, and therapeutic changes. Through molecular docking study and taking Lapatinib as a reference, eleven anticancer compounds were extracted from Tea and studied for their anticancer potential against lung and breast cancer.

The MolDock score was used to examine the data from the docking study, which is a statistical scoring tool that converts contact energy into numerical values **[38, 39]**. **Table 1** show that all of the chosen compounds had high MolDock scores with each target protein, implying that they possessed anticancer properties. Thearubigin outperformed the reference medicine Lapatinib over docking scores with each target.

H-Bond interaction

In drug design hydrogen bonds are very important because they not only control the direction in which an inhibitor binds to a receptor, but they also influence binding affinity **[40]**. The interactions of H-Bond with the involved residues were found when the best docking poses were translated into ligands **(Figures. 1 and 2 and supplemental material S1 to S9)**. Weak H-Bonds serve an important role in the interaction between proteins and ligands. These connections are easily disrupted, but they're important because they help keep the ligand in the target protein stable **[41, 42]**. With the 17-HSDs, HER2 Protein, AAT, and VEGF, compound 1 has the greatest H-Bond, followed by compounds 5, 4, 2, 3, 6, 7, 8, 10, and 9 **(Figures 2, 3, 4 and supplementary Figures S1-S8)**. In terms of H-Bond interaction, all the chosen compounds outperformed the reference drug Lapatinib **(Table 2)**. **Figures 2-4** and supplemental **Figure S1 to S9** show residues interacting with selected ligands and proteins forming hydrogen bonds.

ADME and toxicity study

The features of absorption, distribution, metabolism, excretion, and toxicity (ADMET) are crucial in the identification or development of pharmacological candidates. The top seven docking compounds in PreADME were projected to penetrate the Blood-Brain Barrier (BBB), Human Intestinal Absorption (HIA), Plasma Protein Binding (PPB), Caco-2 Permeability (Caco-2), CYP metabolism, AMES toxicity, and Carcinogens **(Table 3)**.

The therapeutic effectiveness of oral medicine administration is depends on efficient absorption and transport to the circulation. The relevant aspects of drugs are bioavailability, plasma solubility, membrane permeability, protein binding, transport properties and diffusion kinetics **[43]**. In **Table 3**, these values were calculated using preADMET for chemicals 1-10 and the reference drug.

The principal barrier of bioavailability **[44, 45]** is referred to as HIA (Human Intestinal Absorption), it is the sum of bioavailability and absorption as indicated by the excretion ratio or cumulative excretion in urine, bile and faeces. PreADMET at pH 7.4 revealed that ligands 7, 8, 9, 10, and the reference drug Lapatinib are well absorbed molecules, with higher than 60% of absorption percentages. In addition, in vitro approaches such as Human colon adenocarcinoma (Caco-2) and Madin-Darby canine kidney cell (MDCK), which are two highly recommended and trustworthy in vitro models for predicting oral medication absorption **[46, 47]**, are utilised to analyse the properties of intestinal absorption. Caco-2 cells, which are generated from human colon cancer, contain various drug transport pathways that traverse the intestinal epithelium. Permeability is low in compounds with Pcaco-2 (nm/sec) values less than 4. Permeability is moderate when Caco-2 levels are in between 4 and 70, while compounds with values more than 70 are extremely permeable.

The Blood Brain Barrier (BBB), which is mostly made up of densely connected brain capillaries, astrocytes, and other cells, keeps drug-like substances out of the brain. The BBB's permeability is a fundamental criteria for CNS function. BBB values more than 2.0 percent indicate good absorption, 2.0 percent to 0.1 percent indicate medium absorption, and less than 0.1 percent indicate low absorption to CNS **[47]**. With the exception of Certonardosterol C (3), which exhibits BBB impermeability, ligands 6–10 have intermediate CNS absorption, whilst others have poor absorption.

PPB (Plasma Protein Binding) is an important pharmacokinetic characteristic that affects the distribution of a drug. Pharmacokinetically and pharmacodynamically, the drug molecule combines with plasma protein are inactive. Low PPB binding, on the other hand, has a very small volume of distribution that is quickly removed, preventing the therapeutic action. Compounds with PPB values greater than 90% are firmly bound, whereas those with PPB values less than 90% are weekly

bound **[48]**. Ligands 1 to 7 are tightly bonded and permeability is 100%.

The enzyme CYP3A4 plays a crucial role in drug metabolism **[49]**. CYP3A4 inhibitors 1–7 were found, but non-inhibitors 8–10 were found. CYP3A4 substrates are ligands 1, 2, 4, 5, and 9, while ligands 3, 6, 7, and 10 are weakly substrates. We found that ligands 1–6 were non-mutagenic and non-carcinogenic in a toxicity study, while ligands 7–10 were mutagen but not carcinogenic **(Table 3)**.

Table 1: Results of docking between the selected compounds and targets

17β-HSDs (1FDV)		AAT (1 IVR)		VEGF (2C7W)		HER2 (3WSQ)	
Ligand	MolDock Score (kcal/mol)	Ligand	MolDock Score (kcal/mol)	Ligand	MolDock Score (kcal/mol)	Ligand	MolDock Score (kcal/mol)
Thearubigin(1)	-208.66	Thearubigin	-209.16	Thearubigin	-187.49	Thearubigin	-206.16
*Lapatinib	-161.70	*Lapatinib	-166.27	*LapatinibL	-159.55	Theaflavin-3-gallate	-163.99
Theaflavin-3-gallate (2)	-161.53	Procyanidin	-155.42	Theaflavin-3-gallate	-144.32	*Lapatinib	-163.06
Epigallocatechin-3-gallate(3)	-142.97	Theaflavin-3-gallate	-149.36	Procyanidin	-132.90	Procyanidin	-151.87
Procyanidin(4)	-142.89	Epigallocatechin-3-gallate	-140.00	Epigallocatechin-3-gallate	-118.86	Theaflavin	-132.96
Theaflavin(5)	-125.92	EpicatechinGallate	-135.40	Theaflavin.	-117.62	Epigallocatechin-3-gallate	-130.91
EpicatechinGallate(6)	-121.42	Theaflavin	-119.26	EpicatechinGallate	-115.11	EpicatechinGallate	-122.62
Epicatechin(7)	-85.26	Epicatechin	-98.97	Epicatechin	-82.84	Epicatechin	-93.89
Theobromine(8)	-78.70	Theobromine	-75.15	Theobromine	-68.31	Theobromine	-74.41
Caffeine(9)	-65.34	Theophylline.	-72.22	Caffeine	-61.72	Caffeine	-71.66
Theophylline(10)	-61.23	Caffeine	-71.50	Theophylline.	-61.18	Theophylline	-67.02
*reference drug							

Table 2: Hydrogen bonding pattern at the binding sites of the targets

Compound	H-bond with 17β-HSDs (1FDV)	H-bond with 1 AAT (1 IVR)	H-bond with VEGF (2C7W)	H-bond with HER2 (3WSQ)
Thearubigin (1)	N(Asn 152)-H-O N(Gly 94)-H-O O(Gly 186)-H-O O(Gly 92)-H-O O(Asn 90)-H-O O(Tyr 218)-H-O O(Ser 142)-H-O O(Tyr 155)-H-O O(Asn 90)-H-O O(Ser 12)-H-O O(Gly 9)-H-O	O(Ser 247)-H-O O(Asp 13)-H-O O(Leu 16)-H-O O(Tyr 255)-H-O N(Lys 250)-H-O N(Gly 36)-H-O N(Lys 23)-H-O	O(Glu 92)-H-O N(Glu 920-H-O O(lle 80)-H-O N(Gly 41)-H-O O(Glu 38)-H-O N(Leu 39)-H-O N(Thr 36)-H-O	N(Gly 42)-H-O O(Gln 39)-H-O O(Tyr 95)-H-O O(Val 114)-H-O O(Leu 40)-H-O O(Val 164)-H-O O(Glu 162)-H-O O(Arg 143)-H-O N(Arg 86)-H-O
*Lapatinib	O(Tyr 218)-H-O O(Ser 222)-H-O N(Asn 152)-H-O O(Tyr 155)-H-O O(Ser 142)-H-O	N(Arg 258)-H-N ;N(Arg 258)-H-O	N(Leu 39)-H-O N(Thr 36)-H-O	O(Thr 115)-H-O O(Tyr 88)-H-O N(Gln 39)-H-O
Theaflavin-3-gallate (2)	O(Thr 190)-H-O S(Cys 185)-H-O O(Tyr 155)-H-O O(Lys 2230-H-O O(Ser 222)-H-O; N(Leu 95)-H-O N(Asn 152)-H-O O(Tyr 218)-H-O	O(Asp 214)-H-O O(Tyr 217)-H-O O(Gly 36)-H-O N(Arg 378)-H-O O(Leu 16)-H-O N(Lys 23)-H-O N(Arg 258)-H-O	O(Thr 42)-H-O N(Thr 36)-H-O N(Gly 41)-H-O N(Gln 75)-H-O O(Pro 34)-H-O O(Glu 96)-H-O N(Arg 56)-H-O N(Arg 56)-H-O	O(Gly 42)-H-O O(Gln 43)-H-O N(Gly 42)-H-O N(Val 164)-H-O O(Ala 173)-H-O N(Gln 167)-H-O O(Ala 40)-H-O N(Gln 39)-H-O

Epigallocatechin-3-gallate(3)	**O(Tyr 155)-H-O N(Lys 159)-H-O O(Gly 141)-H-O S(Cys 185)-H-O O(Val 188)-H-O N(lle 14)-H-O O(Gly 9)-H-O O(Gly 186)-H-O**	**O(Asn 186)-H-O N(Asn 186)-H-O O(Tyr 217)-H-O N(Ala 216)-H-O N(Arg 258)-H-O O(Ser 247)-H-O O(Thr 106)-H-O**	**O(Ser 94)-H-O O(Pro 34)-H-O O(Arg 56)-H-O O(Thr 42)-H-O N(Thr 36)-H-O**	**N(Asp 86)-H-O O(Asp 86)-H-O O(Gln 43)-H-O O(Gln 39)-H-O O(Tyr 95)-H-O N(Gly 42)-H-O N(Gln 39)-H-O N(Arg 143)-H-O**
Procyanidin(4)	**O(Ser 12)-H-O O(Gly 9)-H-O O(Asn 90)-H-O O(Asn 90)-H-O S(Cys 185)-H-O O(Gly 141)-H-O O(Thr 190)-H-O O(Gly 186)-H-O N(Val 188)-H-O**	**N(Trp 133)-H-O N(Arg 258)-H-O N(Thr 106)-H-O O(Tyr 217)-H-O N(Arg 378)-H-O**	**O(Leu 39)-H-O O(Ser 94)-H-O O(Glu 92)-H-O N(Glu 92)-H-O O(IIe 80)-H-O O(Thr 42)-H-O O(Thr 42)-H-O**	**N(Gly 42)-H-O N(Arg 143)-H-O O(Val 164)-H-O O(Tyr 95)-H-O N(Gly 42)-H-O O(Tyr 88)-H-O O(Tyr 1740-H-O**
Theaflavin(5)	**O(Val 188)-H-O O(Thr 190)-H-O O(Tyr 218)-H-O O(Leu 95)-H-O N (Asn 152)-H-O O(Ser 142)-H-O N(Val 143)-H-O**	**N(Gly 105)-H-O O(Ser 104)-H-O O(Tyr 217)-H-O N(Asn 186)-H-O N(Ala 216)-H-O N(Lys 250)-H-O O(Asp 13)-H-O**	**O(Leu 39)-H-O O(Thr 42)-H-O N(Gln 75)-H-O N(Arg 56)-H-O N(Thr 36)-H-O N(Glu 38)-H-O N(Gly 41)-H-O**	**N(Gly 42)-H-O O(Gly 42)-H-O O(Gln 43)-H-O N(Gln 39)-H-O N(Arg 143)-H-O N(Val 164)-H-O N(Gln 167)-H-O O(Ala 173)-H-O**
Epicatechin Gallate(6)	**O(Tyr 155)-H-O S(Cys 185)-H-O O(Thr 140)-H-O N(Lys 159)-H-O O(Val 188)-H-O N(Val 188)-H-O**	**O(Ser 247)-H-O N(Arg 258)-H-O N(Lys 250)-H-O N(Ala 216)-H-O N(Asn 186)-H-O O(Tyr 217)-H-O**	**O(Ser 94)-H-O N(Arg 56)-H-O O(Pro 34)-H-O O(Thr 42)-H-O N(Thr 36)-H-O**	**O(Pro 8)-H-O N(Arg 143)-H-O N(Arg 143)-H-O O(Gln 43)-H-O N(Leu 45)-H-O O(Gly 42)-H-O**
Epicatechin(7)	**N(Arg 37)-H-O N(Ser 11)-H-O O(Ser 12)-H-O N(Gly 92)-H-O N(Lys 159)-H-O**	**O(Thr 106)-H-O O(Asp 214)-H-O O(Ala 184)-H-O O(Tyr 217)-H-O N(Asn 186)-H-O**	**N(Gln 75)-H-O O(Gln 75)-H-O N(Leu 39)-H-O N(Arg 56)-H-O O(Thr 42)-H-O N(Thr 36)-H-O N(Val 37)-H-O O(Pro 34)-H-O**	**O(Leu 45)-H-O O(Asp 86)-H-O O(Gly 102)-H-O**
Theobromine(8)	**N(Asn 90)-H-O N(Gly 15)-H-O N(Ser 11)-H-O O(Ser 12)-H-O O(Ser 12)-H-O**	**N(Asn 1860-H-O O(Tyr 217)-H-O**	**O(Pro 34)-H-O N(Thr 36)-H-O N(Leu 39)-H-O O(Leu 39)-H-N O(Gly 41)-H-N**	**O(Val 100)-H-O O(Ser 99)-H-O O(Tyr 88)-H-O N(Gly 44)-H-O**
Caffeine(9)	**O(Ser 142)-H-O N(Val 188)-H-O**	**O(Tyr 217)-H-O N(Asn 186)-H-O**	**N(Leu 39)-H-O N(Thr 36)-H-O**	**N(Gln 167)-H-O O(Tyr 174)-H-O**
Theophylline(10)	**N(Val 188)-H-O O(Ser 142)-H-O Val(Val 143)-H-O**	**N(Asn 186)-H-O O(Tyr 217)-H-O**	**N(Leu 39)-H-O N(Glu 38)-H-O N(Thr 36)-H-O**	**N(Arg 143)-H-O O(Tyr 174)-H-O N(Gln 167)-H-O**

***reference drug**

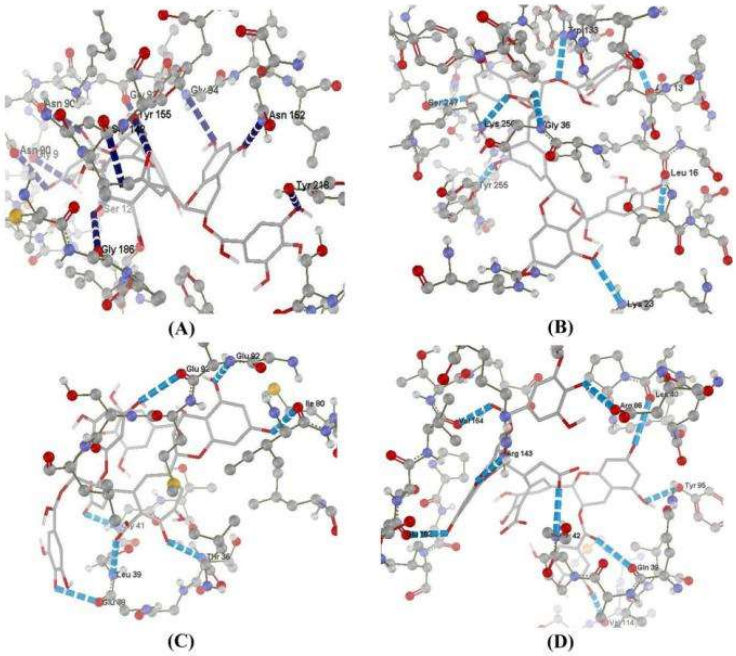

Figure 2: Residues interacting with Thearubigin (1) forming Hydrogen bonds (blue dash lines) in (a) 17β-HSDs (b) AAT (c) VEGF (d) HER2

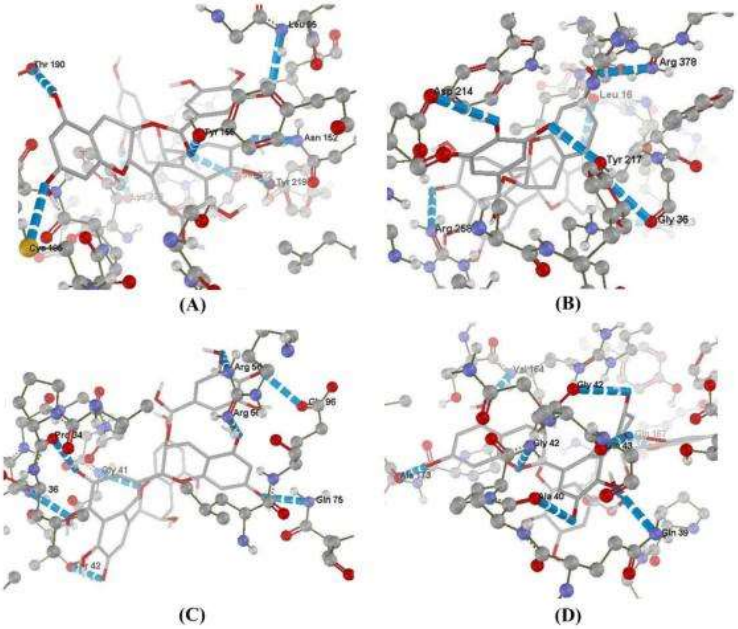

Figure 3: Residues interacting with Theaflavin-3-gallate (2) forming Hydrogen bonds (blue dash lines) in (a) 17β-HSDs (b) AAT (c) VEGF (d) HER2

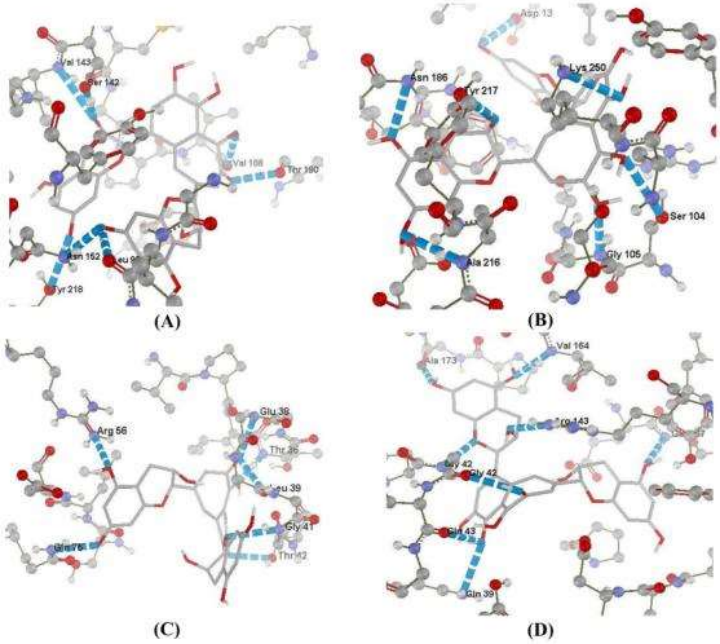

Figure 4: Residues interacting with Theaflavin (5) forming Hydrogen bonds (blue dash lines) in (a) 17β-HSDs (b) AAT (c) VEGF (d) HER2

Table 3: ADMET (absorption, distribution, metabolism , excretion and toxicity) properties of the best ligands

Ligand	HIA[a] (%)	CaCo-2[b] (nm/sec)	MDCK[c] (nm/sec)	PPB[d] (%)	BBB[e] (C.brain/ C.blood)	CYP_3A4 inhibition	CYP_3A4 Substrate	Ames_test	Carcino_ Mouse
Thearubigin	1.029	17.43	0.043	100	0.029	Inhibitor	Substrate	non-mutagen	Negative
*Lapatinib	96.86	17.99	0.052	97.56	0.031	Non Inhibitor	Substrate	non-mutagen	Negative
Theaflavin-3-gallate	10.66	16.011	0.043	100	0.032	Inhibitor	Substrate	non-mutagen	Negative
Epigallocatechin-3-gallate	20.71	12.04	0.044	100	0.0875	Inhibitor	Weakly	non-mutagen	Negative
Procyanidin	19.51	13.67	0.044	100.	0.0649	Inhibitor	Substrate	non-mutagen	Negative
Theaflavin	26.22	14.87	0.044	100.	0.035	Inhibitor	Substrate	non-mutagen	Negative
Epicatechin Gallate	40.58	13.21	0.046	100.	0.141	Inhibitor	Weakly	non-mutagen	Negative
Epicatechin	66.70	0.65	44.38	100.	0.394	Inhibitor	Weakly	mutagen	Negative
Theobromine	87.95	20.98	1.610	17.28	0.272	Non Inhibitor	Weakly	mutagen	Negative
Caffeine	93.82	21.25	2.953	14.07	0.331	Non Inhibitor	Substrate	mutagen	Negative
Theophylline	85.54	20.64	1.743	12.53	0.278	Non Inhibitor	Non	mutagen	Negative

[a] HIA = Human Intestinal Absorption.
[b] CaCo-2 = Human colon adenocarcinoma cells.
[c] MDCK = Madin-Darby canine kidney cells.
[d] PPB = Plasma Protein Binding.
[e] BBB = Blood Brain Barrier

CONCLUSION

According to the study's findings, tea compounds have anticancer potential since they have a high Moldock score and H-Bond interaction with multiple target enzymes and proteins involved in lung and breast cancer. Thearubigin (1), Theaflavin-3-gallate (2), and Theaflavin(5) have been proven to be nontoxic, have better target interaction, and have good ADME properties. According to the findings, tea has anticancer properties, and Thearubigin (1), Theaflavin-3-gallate (2), and Theaflavin (5) are prospective anticancer medicine options for breast and lung cancer that should be investigated further.

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Conflicts of interest

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