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Molecular Docking for chitosan, salicylaldoxime and 3-Chloro aniline act as an Estrogen Receptor (β) in MCF-7 Cell line.

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KEYWORDS

Bio-composite, FT-IR, Estrogen Receptor, Molecular Docking, In-vitro studies.

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ABSTRACT

Computational modeling of the structure created by multiple interacting molecules is known as molecular docking. Molecular docking software is mostly utilized for new drug confirmation and medication enhancement. Salicylaldoxime already functions as an estrogen receptor, and the anti-cancer properties were enhanced by the combination of pure chitosan and 3-chloro aniline. A new one (E)(2R, 3R, 4S, and 6R) -2-hydroxybenzaldehyde O-(3-amino -6-(E)-(imino)methyl(3-chloropheyl)-2H-pyran-4-yl -2-5-dimethoxytetrahydroTo assess anticancer efficacy against the MCF-7 breast cancer cell line, oxime (CS-ClA) was produced. Domine (PDB ID: 1QKM, 1X7R, 1X78, 2nV7, 3ERT, 7KBS, 3UUD, 3BQT, 5TOA, 6PRD) is bound by the CS-ClA estrogen receptor ligand. The docking capacity in binding affinities for new compounds is impacted by the interaction between the sampling and scoring functions in the Docking Assessment.

INTRODUCTION

According to statistics, breast cancer accounts for 28.2% of all female cancers in India. Here are some stsstistics about bosom malignant growth in India. The Bosom Disease in India expanded by 39.1%from 1990 to 2019. In India, the death rate from breast cancer is 12.7% per 100,000 women. The majority of breast cancer patients in India are under 50 years old, which is the primary risk factor.

Telangana has the highest incidence of breast cancer, followed by Karnataka and Tamilnadu. According to WHO data, India has the highest estimated number of female breast cancer deaths—98,337—for the year 2022.

By moving the OH (salicylaldehyde) and oxime groups to different positions, salicylaldoxime-based compounds were made. Since chitosan Schiff base derivatives contain carbonyl groups, they are regarded as one of the best options for enhancing chitosan's antibacterial properties. Salicylaldoxime is a bio isosteric substitution of the phenol ring, which is a characteristic functional group of the majority of estrogen receptor (ER) ligands. [1] The effects of estrogen receptor subtypes alpha and beta, which are ligand-regulated transcription factors, are mediated by [2] reported chitosan Schiff base with the imine characteristic group (-RC=N-). An amino group and a phenyl group make up the chemical molecule known as aniline, which has good antibacterial and antimicrobial activity [3]. The structure was found [4], and the effects of common ions, particularly salicylaldoxime and carbonate as a collector for hydroxyl ion functional group, were investigated. Estrogen receptors (ER¤) are atomic transcriptional controllers of the physiological elements of estrogenic mixtures. These receptors apply a large number of their activities in the core, where they tie to related DNA administrative groupings and tweak the record of explicit objective qualities. [Two subtypes of ER (ER and ER¤)]

The molecular docking method approaches an interaction between a ligand and a protein, making it useful for predicting compounds' bioactive poses and prioritizing compounds for experimental evaluation[5]. The main finding these limiting measure ments is the affirmation of our underlying speculation got from the PC helped drug design.[6] The mixtures (CS-ClA) showing the most elevated levels of ¤-selectivity in the receptor restricting. The PDB ID: 1QKM,1X7R, 1X78, 2nV7, 3ERT, 7KBS, 3UUD, 3BQT, 5TOA, 6PRD this ¤-receptors.

2. EXPERIMENTAL SECTION

2.1 Materials and methods:

The compound salicylaldoxime,chitosan and 3-Chloro aniline with an immaculateness of close to 100% were from Sigma-Aldrich. The Analytical Reagent is 99 percent pure when used as a solvent in the synthesis with acetic acid and DMSO. Without additional purification, they were utilized subsequent to being acquired from Sigma-Aldrich.

2.2 Synthesis

The purified chitosan (1.004 g mmol) was dissolved in 25 ml of acetic acid and stirred for two hours at 45°C. After that, salicylaldoxime (1.006 g mmol) dissolved in 20 milliliters of DMSO was added to the viscous solution and agitated for 12 hours. After adding 1.005 g mmol of 3-chloro aniline and stirring continuously for three hours at 45°C, an exact solution was obtained on the chitosan matrix, resulting in the formation of a Schiff base with a

slight brownish hue. HPLC analysis, UV-Visible spectroscopy, FT-IR spectroscopy, NMR, GC-mass spectroscopy, in vitro studies, and molecular docking-in silico analysis are used to control its purity. Thermogravimetric analysis (TG/DSC) was used to determine the effects of chitosan and aniline oxidation on the thermal durability of CS-ClA in order to evaluate the salicylaldoxime.

3.RESULT AND DISCUSSION (Structure Confirmation)

3.1 FT-IR Spectral data

The functional groups were identified by FT-IR analysis. 3398 band with (N-H) Stretching of imine in intermolecular bonding,3009 (C-H) in vibrational bonding of Chitosan and, 1248 (C-O-C) linkage of chitosan.[7] 2600 and 1399 O-H Stretching of chitosan hydrogen bonded inter molecular bonding.[8]1707 C=N stretching of salicylaldoxime 1248 C-N stretching of 3-chloro aniline were confirmed.

3.2 NMR Spectroscopy

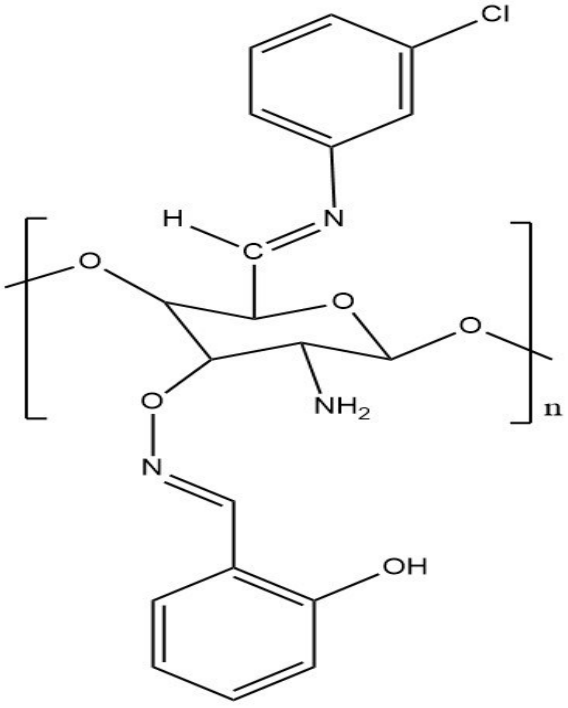
^{1}H-NMR and ^{13}C- NMR spectral studies

The structure of this compound was confirmed by ^{1}H NMR and ^{13}C NMR spectroscopy analysis.[9] The solution ^{1}H-NMR (H-2 in 8.583 and H-6 in 4.881) and ^{13}C-NMR (C-3 C=N-OH and C-6 C=N) is a confirmed structure of the Bio-composite.

The signal from 153.38ppm to 154.72ppm confirmed the C=N-OH with H+ anions turned assays co-ordination of H+ anions turned assays co-ordination of H+ anion and NH_2 co-ordinates with chitosan in CS- ClA bio-composite. The multiples from 111.79ppm to 152.17ppm due to the aromatic carbons in the new CS-ClA bio-composite of 3-Chloro aniline and salicylaldoxime. There are doublet, triplet, and quadruplets 21.45ppm to 40.35ppm due to amine NH_2 in the ring structure.[10] The structure was confirmed by NMR spectrum.

4.3Bio activity of the Bio-composite (CS-ClA)

4.3.1 In vitro studies



(*E*)-2-hydroxybenzaldehyde *O*-((2*R*,3*R*,4*S*,6*R*)-3-amino-6-((*E*)-((3-chlorophenyl)imino)methyl)-2,5-dimethoxytetrahydro-2*H*-pyran-4-yl) oxime

Fig (1)

The cytotoxic effect of different concentrations of the CS-ClA scaffold was obtained by MCF-7 231 A cell line from human breast cancer. The concentration increases the % of cell viability decreases cancer activity tested by in-vitro studies shown in table 1. If dead cells are abundantly seen, the compounds have more active toward cancer cells.[11] concentration control and compound treated. Table1. Shown %cell viability and concentration.

Table 1. Anticancer activity of CS-ClA

CS-ClA	Optical density		% of cell viability	
Control	0.79	1.212	500	500
5	0.782	0.991	98.9873	81.7657
50	0.75	0.826	90.9367	52.9703
100	0.716	0.642	78.3544	32.9402
300	0.682	0.517	12.1519	3.4653
500	0.619	0.399	2.78481	0.9901

3.2Molecular docking-In silico analysis

Docking analysis was carried out using PyRx docking programs. Chemical structure ligand 2-(((3S,5S,6R)-5-methoxy-6-((E)-(phenylimino)tetrahydro-2H-pyran-3-yl)1□□□-diazenyl)phenol using Chem-Draw Ultra 21.0 and Chem 3D Ultra 21.0 (www.cambridgeSoft.com). Target protein's three-dimensional shapes;
1QMK,1X7R,1X78,2Nv7,3ERT,7KBS,3UUD,3BQT,5TOA,6PRD (http://www.pdb.org). Using the trial edition of Discovery Studio 2021 Client, docked ligand-receptor interactions were visualised and analysed.

According to the docking results. The compound CS-ClA was performed in-vitro anticancer activity against the Breast cancer cell line[12]. The binding energy of CS-ClA with PDB:1QMK is highest level in -5.7. the binding group of 1QMK is strong OH bond the particular values of this compound affinity is LEU477, TYR488. Molecular docking were analysis in various proteins [13]. Docking results shown in table 2.

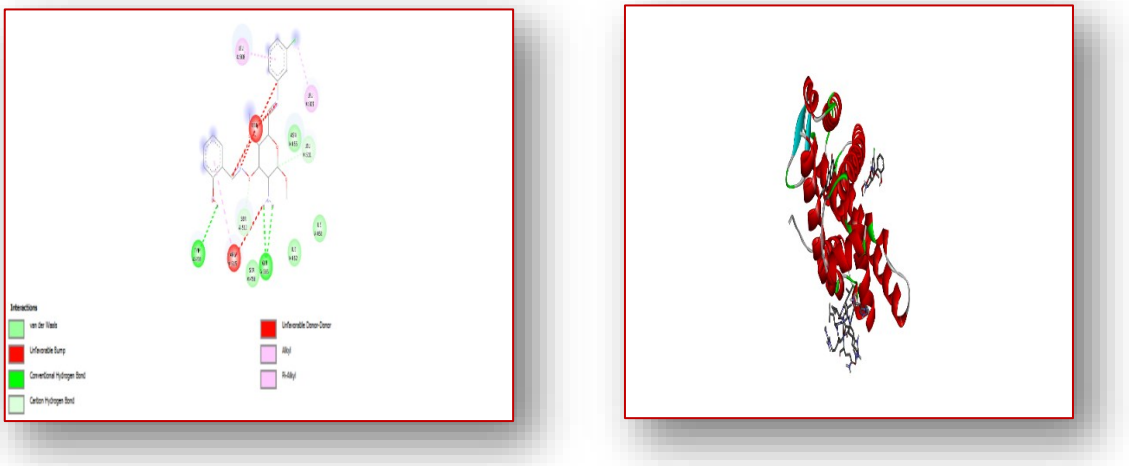


Fig (2)

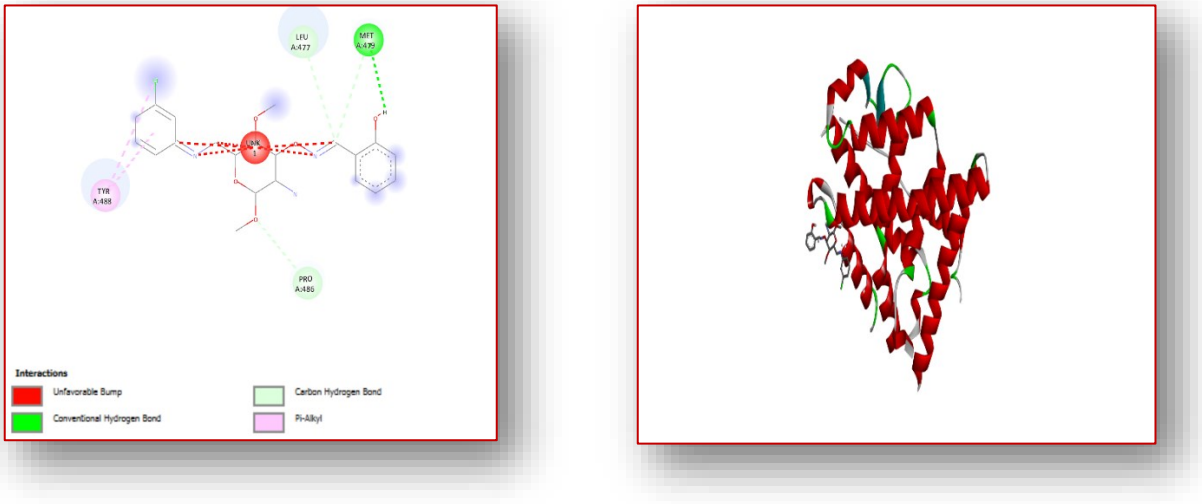
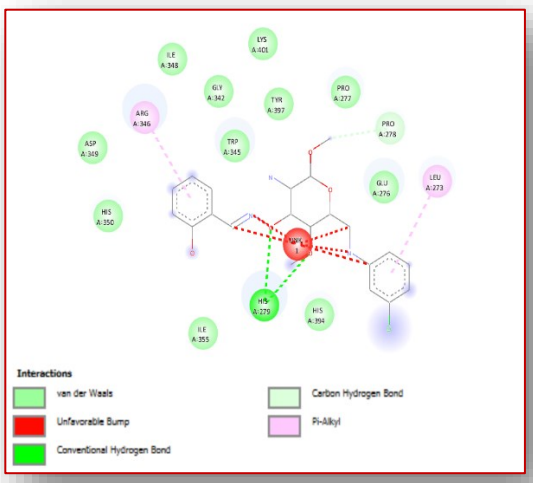


Fig (3)



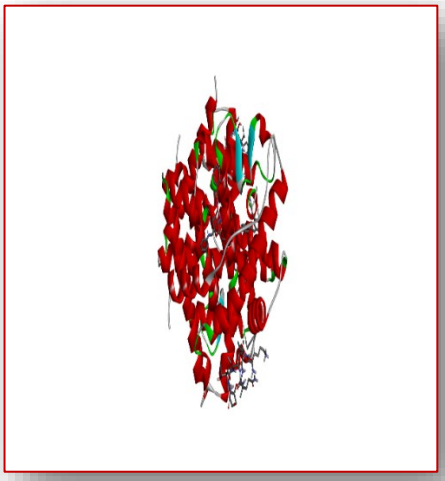
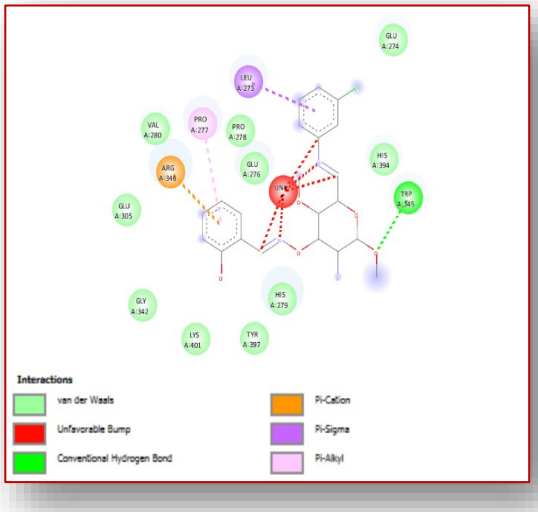


Fig (4)



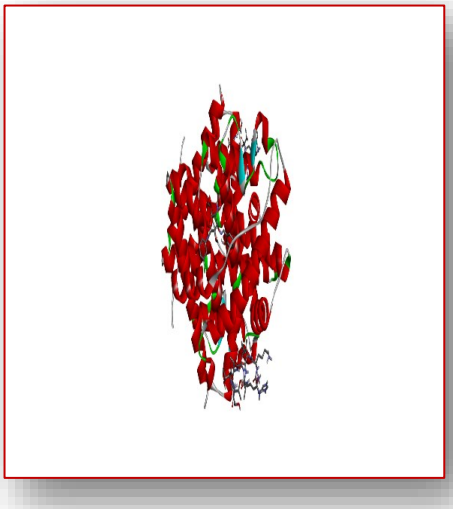
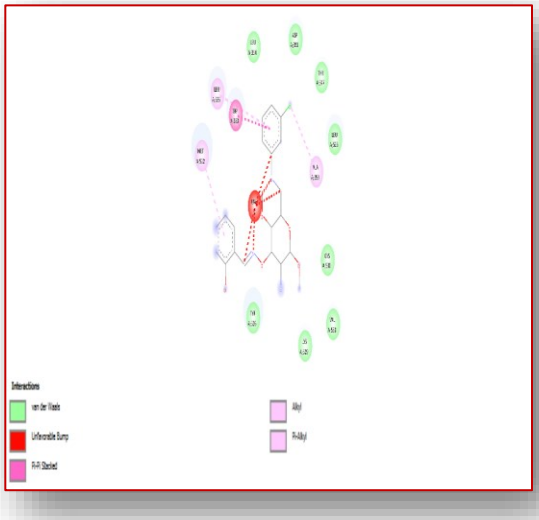


Fig (5)



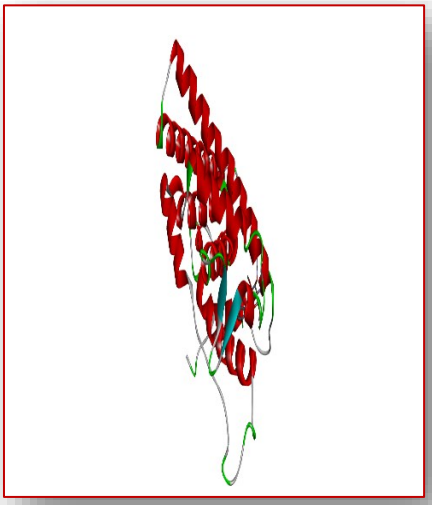
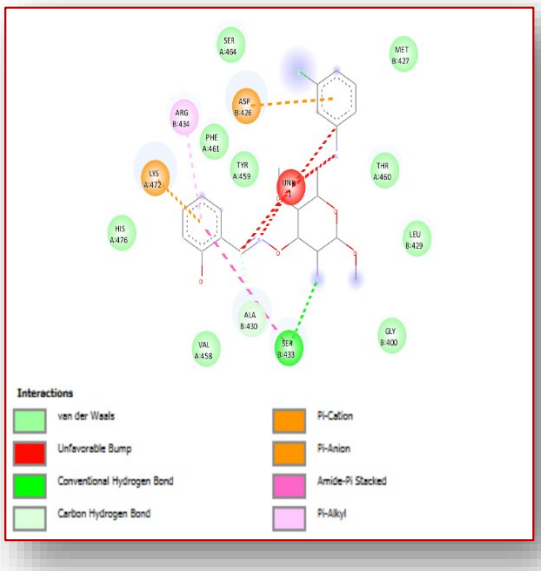


Fig (6)



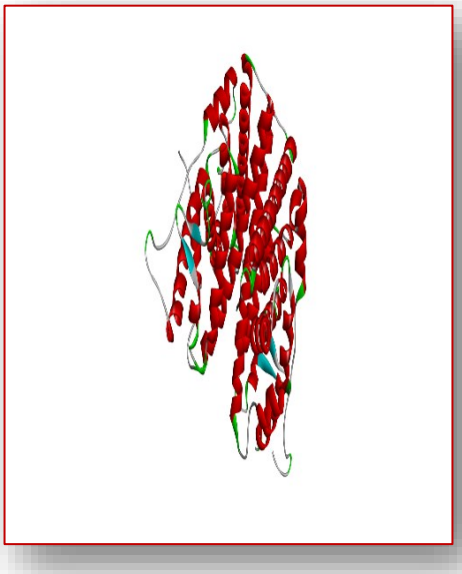
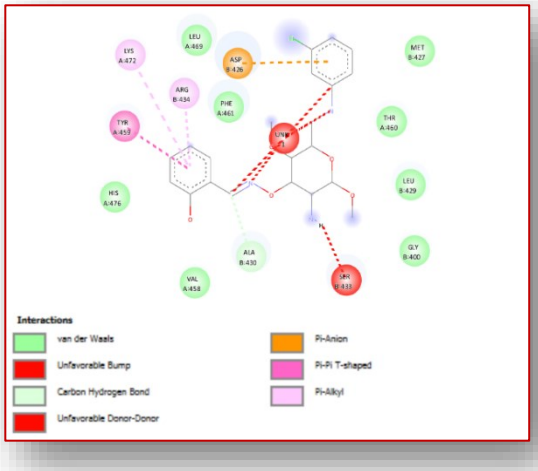


Fig (7)



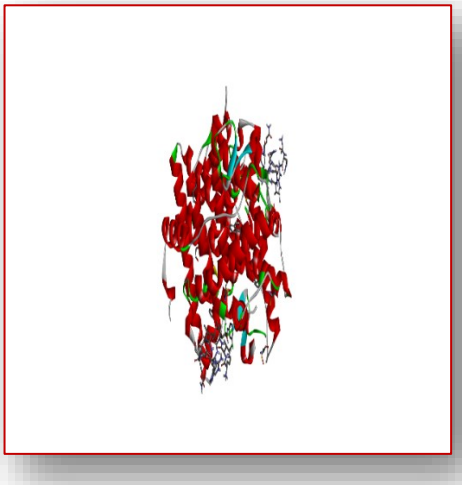


Fig (8)

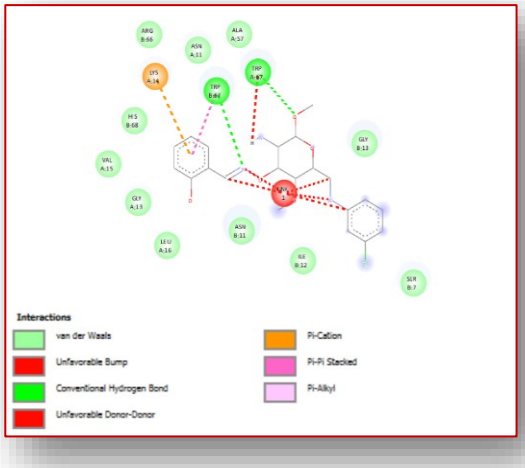


Fig (9)

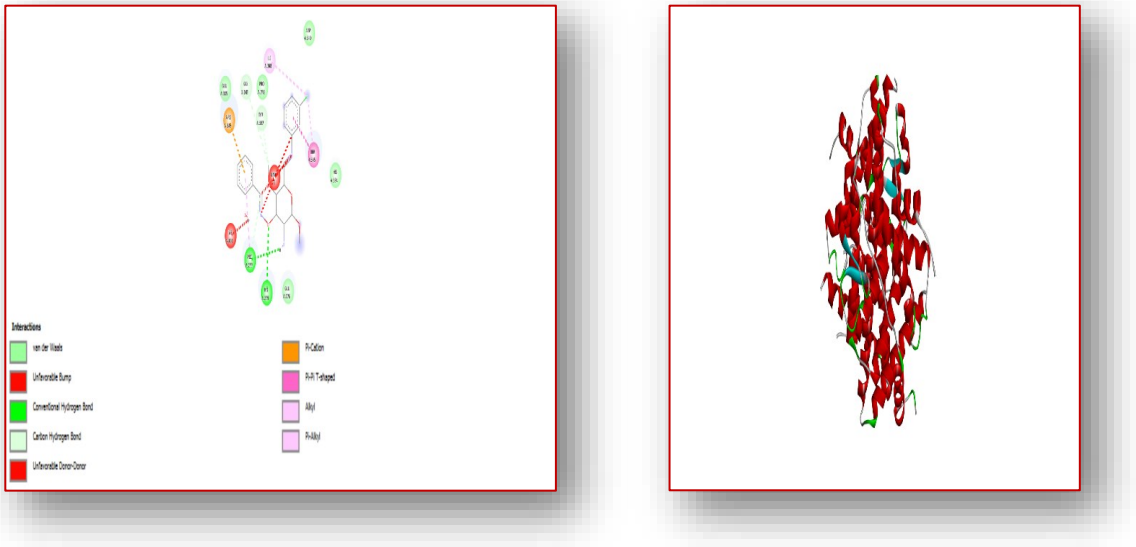


Fig (10)

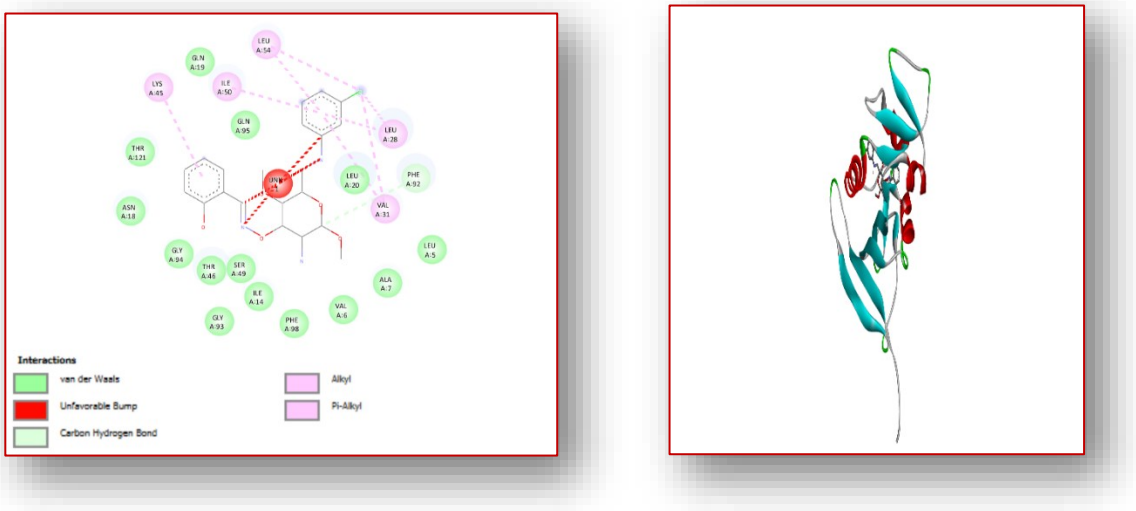


Fig (11)

Table 2

Ligand	PDB id Enzyme	Amino acid involved in interaction	Types of hydrogen bond	Binding affinity (Kcal/mol)
CS-ClA	1QKM	LEU477 TYR488	O-H	-5.7
	1X7R	ILE 451 GLU 385 TYR 459	O-H H-N-H	-6.1
	1X78	HIS 279 ARG 348	O-H-N	-6.6
	2nV7	TRP 345 LEU 273	O-H	-6.8
	3ERT	LYS529 ALA 350 CYS530	O-H	-6.8
	7KBS	SER 433 ASP 426 VAL 430	N-H	-6.9

	3UUD	ALA 430 SER 433 ARG 434	C=N-OH N-H	-6.9
	3BQT	TRP B.67 GYL 432	O-H N-H	-7.1
	5TOA	HIS 279 PRO 277 ARG 346	N-H O-H	-7.2
	6PRD	PHE 93 THR 121	C=N-OH	-8.9

CONCLUSION

Target-ligand interaction screening is followed by the probable docking approach. The compound CS-ClAsubstances in particular demonstrated full agonist activity on the ER¤ and activated transcription of reporter genes and endogenous genes, demonstrating their extremely high potency selectivity for the ER¤, as demonstrated by the in vitro and docking results. In conclusion, we were able to demonstrate through in vitro studies that one of these salicylaldoxime compounds effectively promoted the growth of human breast cancer cells that expressed ER¤. Results with ER¤ selective agonists have a greater therapeutic potential.

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