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MICROWAVE-ASSISTED SYNTHESIS AND *IN-SILICO* SCREENING OF NOVEL SUBSTITUTED 1, 3, 4-THIADIAZOLE DERIVATIVES FOR TREATING ANTIVIRAL AGENTS

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ABSTRACT: Background: Cancer is one of the deadly diseases, accounting for nearly 10 million deaths every year. Cancer is one of the leading dreadful conditions which most people. Cancer is may due to genetic change, which interferes with normal growth mechanisms. A mutant cell divides and produces abnormal masses. Cancer cells can break away from the mass (or tumour) and travel via the bloodstream or lymphatic system to different body parts. These cells can settle in other body parts to form secondary cancer or metastasis. Various approaches have been introduced to eradicate cancer. **Objective:** In this literature, we aim to study the *In Silico* molecular docking for Thiadiazole derivative with an anti-tumor receptor. **Methodology:** We have used Argus lab software for molecular docking. Ligand is prepared using Chemsketch software and proteins are prepared using Chimera software. **Main Observation:** our study shows that the binding value lies between -9.7 to -7, and hydrogen bonds are formed. **Conclusion:** Our study concludes that the Thiadiazole derivative forms good binding affinity with chosen receptors and suggests it can be further developed in future studies.

INTRODUCTION: The use of present commodities to meet anticipated medical requirements and the investigation of novel chemical entities are all part of drug development. Cancer is a disease marked by uncontrolled cell development that can spread to other sections of the body. Hepatic carcinoma is the most frequent kind of primary liver cancer in persons with cirrhosis, and it is the leading cause of mortality [1]. Cancer is a disease in which one or more cells develop uncontrollably and frequently metastasis. This affects older. Lung and liver tumours account for the majority of disease-related fatalities [2]. Developing efficient and safe chemotherapeutic drugs in cancer treatment is extremely difficult for medicinal chemists. These efforts are aimed at a variety of metabolic mechanisms involved in the development of various malignancies [3]. In many pharmaceutical formulations, nitrogen and sulphur heterocycles (especially five-membered heterocycles with two or three heteroatoms) constitute structural units [4].

QUICK RESPONSE CODE

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The thiadiazole ring is a flexible scaffold that has been extensively researched in medicinal chemistry. Thiadiazole-containing compounds can permeate the cellular membrane and interact strongly with biological targets because of the ring's mesoionic nature. As a result, these chemicals have a wide range of biological effects [10]. In addition, 1,3,4-thiadiazole derivatives are notable for their broad biological actions, which

include antibacterial, anticonvulsant, anti-tuberculosis, antiviral, anti-inflammatory, antioxidant and anticancer properties [5]. Computational biology and bioinformatics have the potential to change not just the way pharmaceuticals are developed but also to speed up the drug development process and reduce costs [9]. Molecular docking is a computational tool that uses a genetic algorithm as a search strategy and a rapid scoring function to allow users with little or no expertise in protein-ligand simulations to do docking simulations [6]. The docking was done utilizing multiple enzymes and receptor proteins involved in the cell cycle, cell development, and DNA replication to examine possible molecular targets and corroborate the experimental activity testing for these anticancer drugs [7]. Additionally, utilizing Argus lab, molecular docking of the new chemical entities revealed their binding mechanisms inside the active site [8].

***In-silico* Molecular Docking Study:** *In-silico* molecular docking studies were done with the help of ArgusLab.exe software. We select the random amino acid. The grid box is created with the dimension (X, Y, Z) of 15 X 15 x15. Allowing the ligand to attach to the receptor enables more flexible molecular docking. The molecular docking calculation made by the software and the final docking energy was found [11].

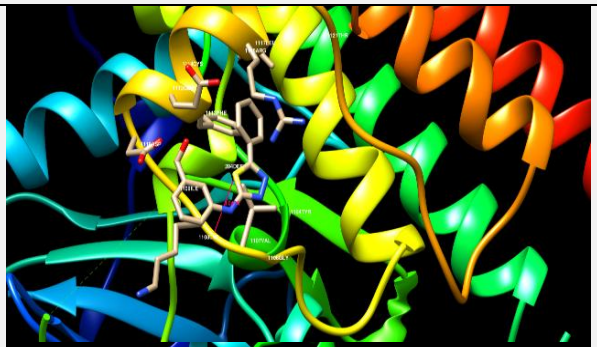
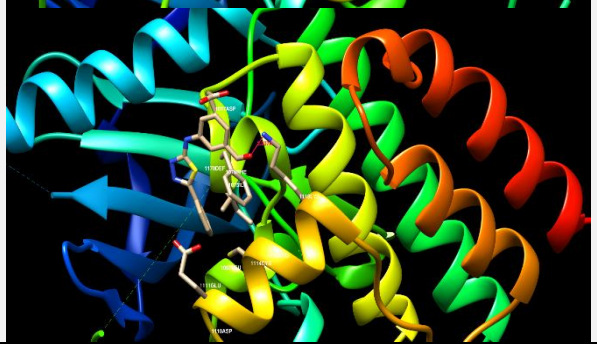
Preparation of Protein: PDB code 1YWN [12], 5NQR [13], 2KCE [14] is downloaded from the RCSB protein databank. Further, the complex structure and solvents that binds with protein are removed with the help of chimera software, and hydrogen is added to the protein with the help of Argus Lab. exe software. The receptors are thus made ready for docking.

Ligand Preparation: Using the ACD/ Chemsketch software, the three-dimensional structure of 3-[(5-phenyl-1, 3, 4-thiadiazol-2-yl)amino] benzaldehyde is sketched. The molecular description is investigated further [15].

Molecular Docking: The prepared protein binding site is collected with the help of the Computed Atlas of Surface Topography of the protein web server and allowed to bind with ligand in ArgusLab.exe software.

RESULT AND DISCUSSION:

TABLE 1: PDB CODE: 1YWN

S. no.	Binding Active Site	Docking Score (kcal/mol)	Image	Hydrogen Bond
01	1110ASP	-8.6558 kcal/mol		1
02	1077ASP	-7.94817 kcal/mol		1

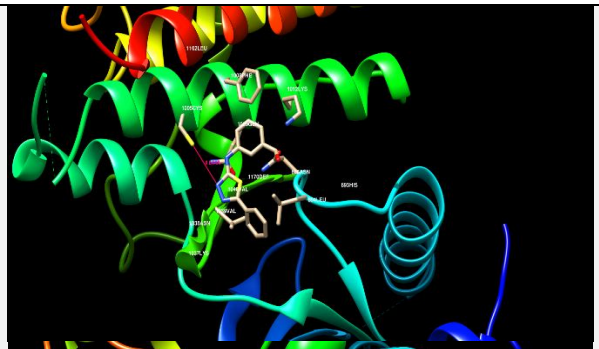
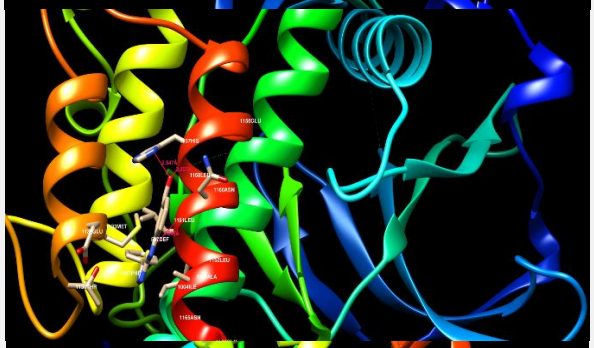
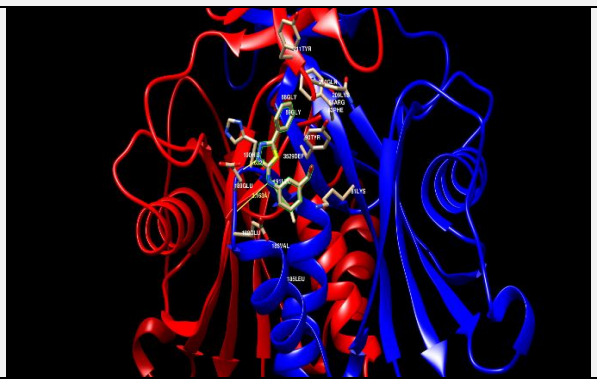
03	895ASN	-8.48709 kcal/mol		1
04	1160ASN	-8.80813 kcal/mol		3
05	1114CYS	-9.77682 kcal/mol		1
06	873THR	-8.94091 kcal/mol		2

TABLE 2: PDB CODE: 5 NQR

S. no.	Binding Site	Docking Score (kcal/mol)	Image	Hydrogen Bond
01	189GLU	-9.42535 kcal/mol		2

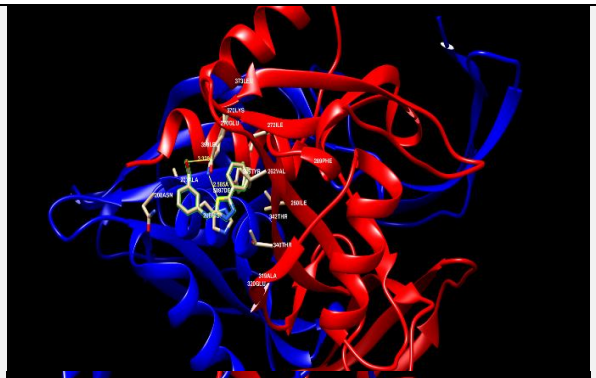
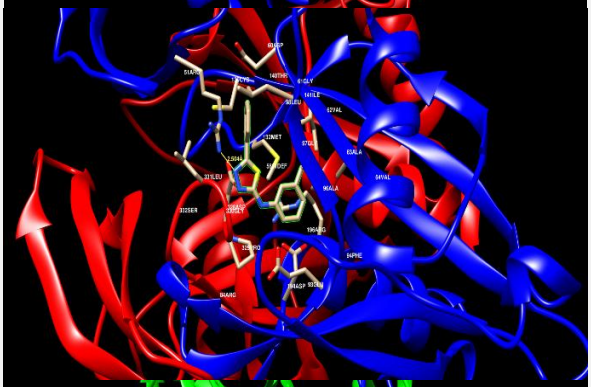
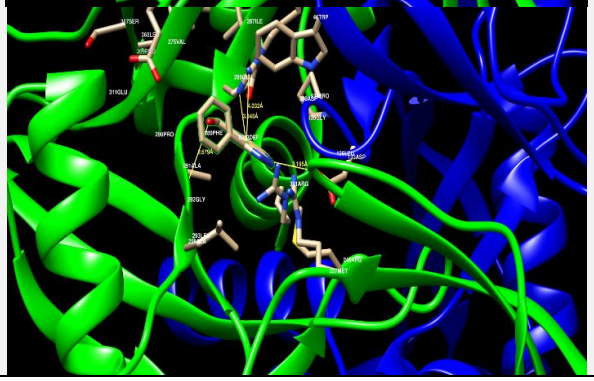
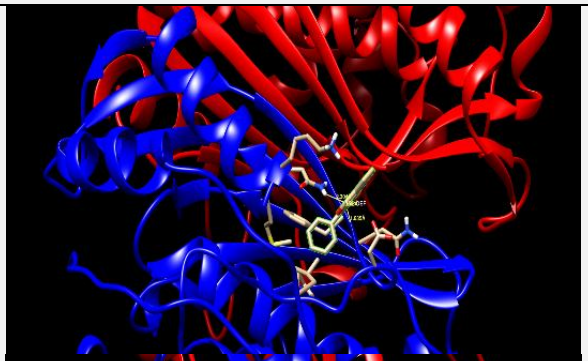
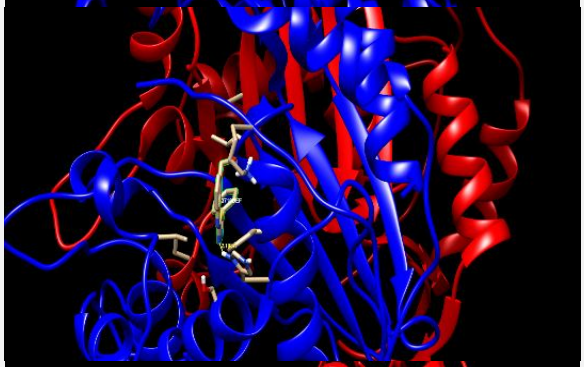
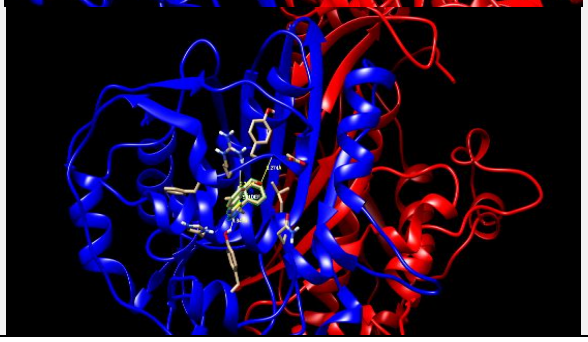
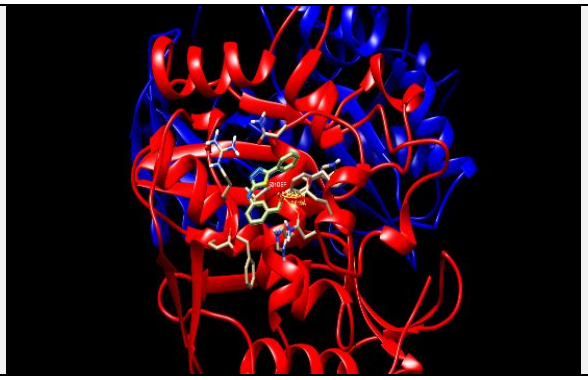
02	206HIS	-8.14212 kcal/mol		2
03	143ILE	-8.71524 kcal/mol		1
04	204LEU	-7.42225 kcal/mol		4
05	316GLY	-8.1046 kcal/mol		4
06	368LEU	-8.12398 kcal/mol		4

TABLE 3: PDB CODE: 2KCE

S. no.	Binding Site	Docking Score (kcal/mol)	Image	Hydrogen Bond
01	37ASN	-7.72229 kcal/mol		2
02	51HIS	-8.51315 kcal/mol		1
03	154VAL	-7.70015 kcal/mol		2
04	193ASP	-7.97719 kcal/mol		1
05	243ARG	-7.4427 kcal/mol		3

06	507ARG	-9.04196 kcal/mol		1

DISCUSSION: The study shows that the 1, 3, 4 thiadiazole derivative has good binding affinity with the three receptors, namely binding of the anticancer drug.

CONCLUSION: Thiadozle derivative binds with PDB: 1YWN shows the best docking score of -9.77682 kcal/mol, while 5NQR and 2KCE show -9.42535 kcal/mol and -9.04196 kcal/mol, respectively. The hydrogen bonds are viewed with Chimera software and their distance is calculated.

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CONFLICTS OF INTEREST: The author has no conflicts of interest regarding this investigation.

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