Research Article

In Silico Approach of Apoptosis Induing Ability of Different Indole Derivatives by Interaction with Caspase9

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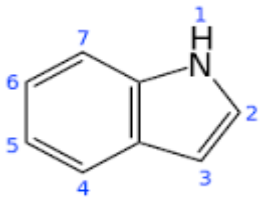
ABSTRACT

Indole compounds are well known for their wide variety of pharmacological activities. It is the combination of benzene with pyrrole ring. Compounds having indole group are biologically important. They are used as antimicrobial, antiviral, antituberular, anti-inflammatory, anticancer, ant-diabetic and anticonvulsant agents. Because of the wide variety of biological application, several substituted indole derivatives are studied for their molecular structure, molecular docking and bioavailability. The purpose of the study is to carry out the docking studies of indole derivatives containing electrophilic substitution and nucleophilic substitution with the anticancer target casp9. Fifty compounds were designed and by using Argus lab version 4.0.1. Their docking score was calculated and compared with the standard drug casodex. The drug likeness of compounds was performed using Lipinski rule of five. Result showed that 1,1'-(1H-indole-5,6-diyl)diethanone and 5-(trichloromethyl)-1H-indole and the phytoconstituent curcumin showed better docking score than that of the standard drug casodex. It is concluded that certain indole derivatives show greater affinity with casp9 protein. These compounds may be helpful in studying anticancer targets for casp9 protein.

Keywords: Prostate cancer, CASP9, apoptosis, indole compounds, docking.

INTRODUCTION

Prostate cancer is a disease condition in which the prostatic cell starts to divide uncontrollably that lead to tumor. It is the second most common cancer among men and the leading cause of death due to cancer in men. It is classified under adenocarcinoma and this is the malignancy affected to one of the major male gland.



Most common sites for prostatic metastasis are lymph node, lungs, various bone etc. It is the most commonly seen malignancy in adult male. The causes include family history, exposure to carcinogenic agents (cadmium, rubber etc.) and high fat diet. Symptoms of the disease include difficulty in maturation, pain or burning sensation during urination, blood in urine, pain in lower back etc. peripheral region is the most common site of adenocarcinoma.

The apoptosis activity of the caspases is based on two pathways mainly intrinsic and extrinsic path[1]. The intrinsic pathway is characterized by mitochondrial dysfunctioning release of cytochrome c activation of caspase9 and caspase3. The extrinsic pathway is activated through death receptor mediated activation of caspase8, caspase10, and activation of caspase3. These pathways are amplified by caspase9. Therefore it is the major initiator caspase[2]. GSTP1 (Glutathione-s-transferase) is involved in the detoxification of harmful electrophilic molecules hence protect prostate from carcinoma. Cell of prostatic intraepithelial neoplasia is devoid of GSTP1 so it undergoes genomic damage mediated by carcinogens. NKX3.1, PTEN, and P27 regulate the growth and differentiation of normal healthy prostate. NKX3.1, PTEN is tumor suppresser genes whereas p27 control cell cycle progression. The genomic damage leads to inadequate level of NKX3.1, PTEN, and P27. This condition leads to inhibition of apoptotic initiation property of casp9[3,4]. That causes increase in proliferation and decrease in apoptosis[5]. Majority of the cytotoxic drug initiate cell death by triggering the cytochromC/Apaf-1/Caspase dependent pathway through the mitochondria[6]. Studies state that more than 94% of the cell died of apoptosis is triggered mainly by the caspase9[7].

Indole compounds are well known for their anti-cancer activity[8]. I3C and its relative compounds are widely studied for their anti-cancerous activity. They are effective inducers of apoptosis. Induction of apoptosis is highly attributed to their anti-cancerous activity and also these compounds sensitize cancerous cell to standard chemotherapeutic agents[9]. This non-toxic compounds can reduce the toxic effects of chemotherapeutic agents. Also synthetic derivatives of indole showed the same anti-cancerous activity by inducing apoptosis[10,11]. Our aim is to analyze the interaction of different indole derivatives with the anti-cancer target casp9. The capability of a drug depends on its bioavailability, protein binding capacity and absorption. Molinspiration enable to calculate these factors along with their log p, molecular weight, number of hydrogen bond acceptors, number of hydrogen bond

donors, number of rotatable bonds and total polar surface area (TPSA). This will help to check whether the compounds follow Lipinski rule of five and any compound which disobey the rule is not considered as a lead molecule.

MATERIALS AND METHODS

The structure of CASP9 protein is obtained from RCSB protein data bank (crystallographic database for three dimensional structural of proteins or nucleic acid). Water molecules, ligands, and other hetero atoms were removed from the protein. The structure of different indole derivatives were developed through chemskecth software (10.1) and the 3D structure of the following are developed through corina, saved under PDB format. A standard drug Casodex, an FDA approved prostate cancer drug was used as reference. phytoconstituent curcumin was also docked with the same protein and compared the score with indole derivatives[12]. Drug-likeness property or Lipinski's rule of five formulated by Christopher Lipinski is aided to determine the molecular properties and the pharmacokinetic activity of the compounds. He postulated that the compounds should meet the following criteria such as molecular mass less than 500Da, lipophylicity clog p not greater than 5, hydrogen bond donor less than 5 and hydrogen bond acceptor less than 10. Molinspiration is a cheminformatic tool that helps in calculation of bioavailability and chemical properties of the compounds such as GPCR ligand, ion channel modulator, kinase inhibitor, nuclear receptor ligand, protease inhibitor and enzyme inhibitor. Ligand structure of indole compounds were opened in Argus lab 4.0.1 and binding sites for each of the compound was developed. Finally docking was conducted in Argus lab. Docking score for each of the compound is calculated.

RESULTS AND DISCUSSION

The properties are calculated by total polar surface area (TPSA), number of atoms, molecular weight, number of hydrogen bond acceptors, number of hydrogen bond donors, n number of violations and number of rotatable bonds (Table 1). The bioactivity scores were studied using parameters GPCR ligand, ion channel modulators, kinase inhibitor, nuclear receptor ligands, protease inhibitor and other enzyme targets (Table 2). Also the compounds are compared with the drug likeness and bioactivity score of phytoconstituent. After the initial analysis the ligands were opened in Argus lab 4.0.1 (Argus lab is a molecular modeling, drug designing software). The docking scores (Table 3) were compared with the standard drug (Table 4). The result shows that the values of fifty compounds and the phytoconstituent based on molecular weight is less than 500 dalton, number of hydrogen bond donors and number of hydrogen bond acceptors are below 5 and 10, partition coefficient lies within the limits of 5. This shows that there is no violation of Lipinski rule of five and the compounds has pharmacological or biological activity.

Table 1: Drug Likeness Calculation on Indole Ligand Molecules.

S. No.	Structure	Milogp	TPSA	Natoms	Mw	nON	nOHNH	nviolations	Nrotb	Volume
1	5-nitro-1-H-indole	2.10	61.62	12	162.1	4	1	0	1	136.3
2	5-chloro-1*H*-indole	2.81	15.79	10	151.6	1	1	0	0	126.5
3	1,1'-(1*H*-indole-5,6-diyl)diethanone	1.86	49.93	15	201.2	3	1	0	2	184.1
4	1*H*-indole-5-sulfonic acid	-0.87	70.16	13	197.2	4	2	0	1	152.4
5	5,6-dinitro-1*H*-indole	1.98	107.44	15	107.1	7	1	0	2	159.6
6	1*H*-indole-6-carbaldehyde	1.93	32.86	11	145.1	2	1	0	1	132
7	1*H*-indole-5,6-dicarbaldehyde	1.64	49.93	13	173.1	3	1	0	2	150.9
8	1*H*-indole-5-carbonyl chloride	2.59	32.86	12	179.6	2	1	0	1	145.5
9	5-(trichloromethyl)-1*H*-indole	3.96	15.79	13	234.5	1	1	0	1	170.1
10	1*H*-indole-5-sulfonyl chloride	2.02	49.93	13	215.6	3	1	0	1	157.9
11	1*H*-indole-5-carbonitrile	1.89	39.58	11	142.1	2	1	0	0	129.8
12	1*H*-indole-5-carboxamide	0.95	58.88	12	160.1	3	3	0	1	143.2
13	5-methoxy-1*H*-indole	2.19	25.02	11	147.1	2	1	0	1	138.5
14	5-(trifluoromethyl)-1*H*-indole	3.03	15.79	13	185.1	1	1	0	1	144.3
15	1*H*-indol-5-yl hydrogen sulfate	-0.75	79.39	14	213.2	5	2	0	2	161.4
16	1*H*-indol-5-yl cyanate	1.97	48.82	12	158.1	3	1	0	1	138.8
17	1*H*-indol-6-yl nitrite	1.99	54.46	12	162.1	4	1	0	2	136.8
18	1*H*-indol-6-yl acetate	1.69	42.10	13	175.1	3	1	0	2	157.5
19	1*H*-indole-5,6-diyl bis(thiocyanate)	2.48	63.38	15	231.3	3	1	0	2	183
20	*N*-(1*H*-indol-5-yl)acetamide	1.35	44.89	13	174.2	3	2	0	1	160.9
21	5-fluoro-1*H*-indole	1.33	15.79	10	135.1	1	1	0	0	117.9
22	1*H*-indole-5-thiol	2.37	15.79	10	149.2	1	1	0	0	130.6

23	6-chloro-1*H*-indole-5-carboxylic acid	2.31	53.09	13	195.6	3	2	0	1	153.5
24	6-fluoro-1*H*-indole-5-carbaldehyde	2.02	32.86	12	163.1	2	1	0	1	136.9
25	5-methyl-1*H*-indole	2.58	15.79	10	131.1	1	1	0	0	129.5
26	6-methyl-1*H*-indole	2.58	15.79	10	131.	1	1	0	0	129.5
27	(6-chloro-1*H*-indol-5-yl)acetic acid	2.17	53.09	14	209.6	3	2	0	2	170.3
28	(5-chloro-1*H*-indol-6-yl)acetaldehyde	2.74	32.86	13	193.63	2	1	0	2	162.3
29	(6-fluoro-1*H*-indol-5-yl)acetaldehyde	2.23	32.86	13	177.1	2	1	0	2	153.7
30	(6-chloro-1*H*-indol-5-yl)methyl acetate	2.78	42.10	15	223.6	3	1	0	3	187.8
31	(5-chloro-1*H*-indol-6-yl)methyl acetate	2.78	42.10	15	223.6	3	1	0	3	187.8
32	6-methyl-1H-indol-5-ol	2.50	36.02	11	147.1	2	2	0	0	137.6
33	5-methyl-1H-indol-6-ol	2.50	36.02	11	147.1	2	2	0	0	137.6
34	6-chloro-5-methyl-1H-indol	3.19	15.79	11	165.6	1	1	0	0	143.1
35	5-chloro-6-methyl-1H-indol	3.19	15.79	11	155.6	1	1	0	0	143.1
36	5,6-dichloro-1H-indol	3.42	15.79	11	185.0	1	1	0	0	140.0
37	5-methyl-6-(nitromethyl)-1H-indole	2.07	61.62	14	190.2	4	1	0	2	169.7
38	5-chloro-6-(nitromethyl)-1H-indole	2.30	61.62	14	210.6	4	1	0	2	166.6
39	1H-indol-5-ylacetaldehyde	2.13	32.86	12	159.1	2	1	0	2	148.8
40	1H-indol-5ylacetic acid	1.56	53.09	13	175.1	3	2	0	2	156.8
41	5-(nitro methyl)-1H-indole	1.69	61.62	13	176.1	4	1	0	2	153.1
42	1H-indol-6-carboxylic acid	2.05	53.09	12	161.1	3	2	0	1	140.0
43	1H-indol-5,6-diol	1.17	56.25	11	149.1	3	3	0	0	129.0
44	5,6-difluro-1H-indole	1.42	15.79	11	153.1	1	1	0	0	122.8
45	1H-indol-5,6-dithiol	2.52	15.79	11	181.2	1	1	0	0	148.3
46	6-sulfanyl-1H-indol-5-ol	2.07	36.02	11	165.2	2	2	0	0	138.7
47	5-sulfanyl-1H-indol-6-ol	2.07	36.02	11	165.2	2	2	0	0	138.7
48	6-chloro-1H-indol-5-thiol	2.97	15.79	11	183.6	1	1	0	0	144.2
49	5,6-bis(nitrosomethyl)-1H-indole	1.26	74.66	15	203.2	5	1	0	4	176.2
50	1H-indol-5-methanesulfonic acid	-0.81	70.16	14	211.2	4	2	0	2	169.2

Phytoconstituent

1	Curcumin	2.30	93.0	27	368.3	6	2	0	8	332.1

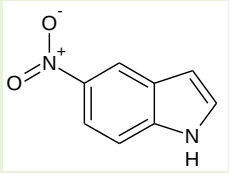
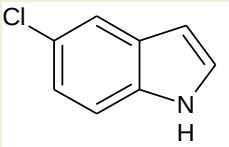
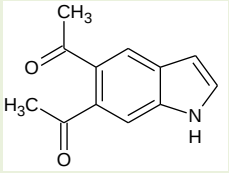
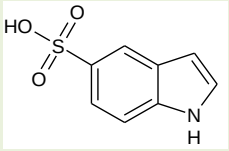
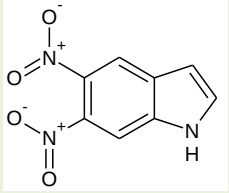
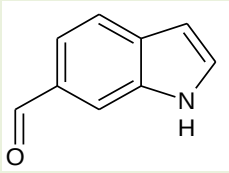
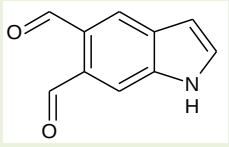
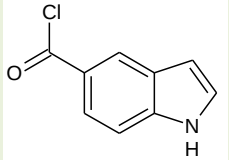
TPSA: total polar surface area, natoms: number of atoms, MW: molecular weight, Non: number of hydrogen bond acceptors, nOHNH: number of hydrogen bond donors, nrotb: number of rotatable bonds

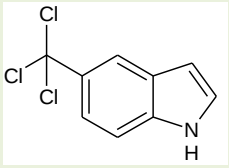
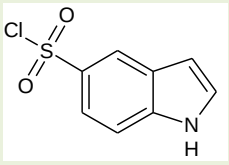
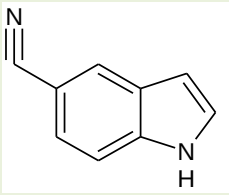
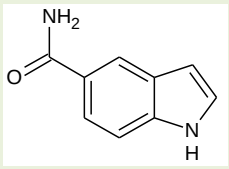
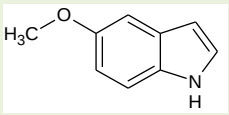
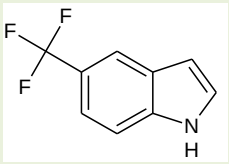
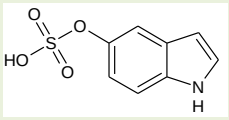
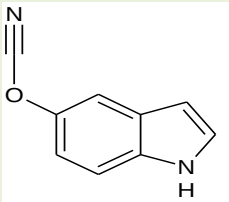
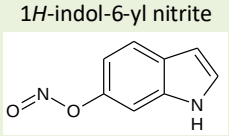
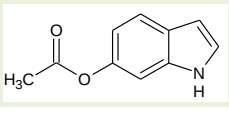
Table 2: Bioactivity Calculation of Indole Ligand Molecules

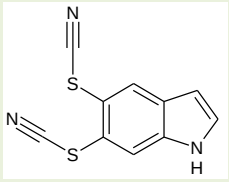
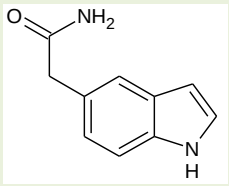
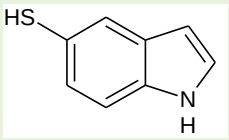
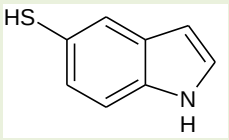
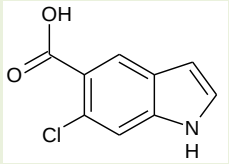
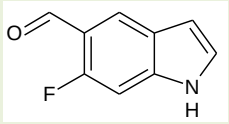
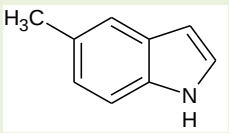
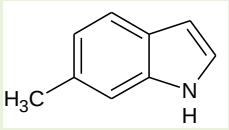
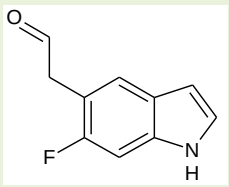
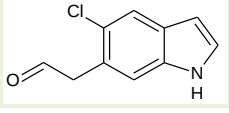
S. No	Structure	GPCR Ligand	Ion Channel Modulator	Kinase Inhibitor	Nuclear Receptor Ligand	Protease Inhibitor	Enzyme Inhibitor
1	5-nitro-1*H*-indole	-0.66	0	-0.37	-0.84	-1.08	-0.31
2	5-chloro-1*H*-indole	-0.56	0	-0.33	-0.95	-1.11	-0.30
3	1,1'-(1*H*-indole-5,6-diyl)diethanone	-0.21	0.11	-0.17	-0.40	-0.54	0
4	1*H*-indole-5-sulfonic acid	-0.06	0.26	-0.28	-1.03	-0.21	0.25
5	5,6-dinitro-1*H*-indole	-0.34	0.12	-0.13	-0.60	-0.75	-0.09
6	1*H*-indole-6-carbaldehyde	-0.67	0.01	-0.31	-0.62	-1.23	-0.24
7	1*H*-indole-5,6-dicarbaldehyde	-0.27	0.11	0	-0.27	-0.87	0.01
8	1*H*-indole-5-carbonyl chloride	-0.84	-0.44	-0.62	-1.08	-1.24	-0.57

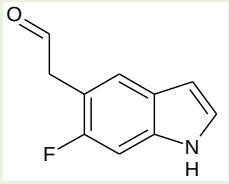
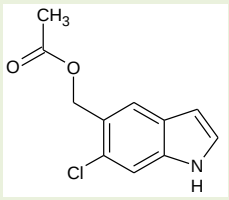
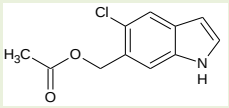
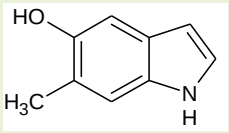
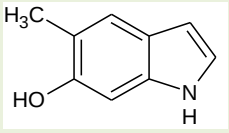
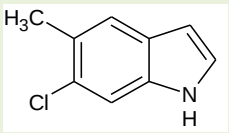
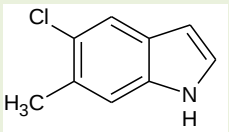
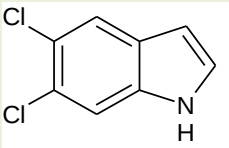
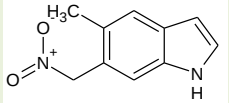
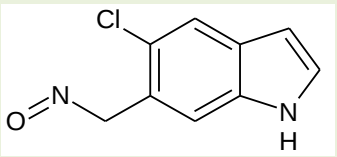
9	5-(trichloromethyl)-1*H*-indole	-0.37	0	-0.15	-0.58	-0.76	0.19
10	1*H*-indole-5-sulfonyl chloride	0.13	0.01	-0.15	-0.59	-0.52	-0.04
11	1*H*-indole-5-carbonitrile	-0.41	0.03	-0.02	-0.53	-0.86	-0.05
12	1*H*-indole-5-carboxamide	-0.34	-0.10	0.07	-0.85	-0.61	-0.01
13	5-methoxy-1*H*-indole	-0.55	-0.11	-0.24	-0.75	-1.07	-0.23
14	5-(trifluoromethyl)-1*H*-indole	-0.14	0.29	0.04	-0.21	-0.60	-0.02
15	1*H*-indol-5-yl hydrogen sulfate	0.33	0.18	-0.03	-0.28	0.24	0.94
16	1*H*-indol-5-yl cyanate	-0.04	0.29	-0.11	-0.52	-0.82	0.07
17	1*H*-indol-6-yl nitrite	-0.29	-0.05	0.08	-0.56	-0.62	0.04
18	1*H*-indol-6-yl acetate	-0.45	0	-0.26	-0.34	-0.73	0.06
19	1*H*-indole-5,6-diyl bis(thiocyanate)	-0.63	-0.13	-0.44	-0.61	-0.80	0.13
20	*N*-(1*H*-indol-5-yl)acetamide	-0.41	-0.10	-0.10	-0.85	-0.76	-0.22
21	5-fluoro-1*H*-indole	-0.49	0	-0.22	-0.81	-1.12	-0.22
22	1*H*-indole-5-thiol	-0.66	-0.37	-0.60	-1.29	-0.78	-0.14
23	6-chloro-1*H*-indole-5-carboxylic acid	-0.29	0.10	-0.23	-0.30	-0.71	0.02
24	6-fluoro-1*H*-indole-5-carbaldehyde	-0.41	0.09	-0.16	-0.48	-1.00	-0.17
25	5-methyl-1*H*-indole	-0.65	-0.20	-0.42	-0.95	-1.18	-0.36
26	6-methyl-1*H*-indole	0.66	-0.13	-0.39	-0.94	-1.16	-0.35
27	(6-chloro-1*H*-indol-5-yl)acetic acid	0.10	0.36	-0.10	0.09	-0.31	0.24
28	(5-chloro-1*H*-indol-6-yl)acetaldehyde	-0.24	0.23	-0.09	-0.34	-0.32	0.01
29	(6-fluoro-1*H*-indol-5-yl)acetaldehyde	-0.17	0.25	-0.03	-0.27	-0.18	0.07
30	(6-chloro-1*H*-indol-5-yl)methyl acetate	-0.10	0.24	-0.19	-0.26	-0.35	0.11
31	(5-chloro-1*H*-indol-6-yl)methyl acetate	-0.14	0.22	-0.16	-0.24	-0.32	0.10
32	6-methyl-1H-indol-5-ol	-0.53	-0.04	-0.12	-0.43	-1.02	-0.12
33	5-methyl-1H-indol-6-ol	-0.53	-0.04	-0.12	-0.43	-1.01	-0.13
34	6-chloro-5-methyl-1H-indol	-0.59	-0.09	-0.46	-0.85	-1.20	-0.34
35	5-chloro-6-methyl-1H-indol	-0.65	-0.13	-0.41	-0.84	-1.16	-0.36
36	5,6-dichloro-1H-indol	-0.41	0.17	-0.24	-0.79	-0.94	-0.17
37	5-methyl-6-(nitromethyl)-1H-indole	-0.35	0.05	-0.13	-0.46	-0.72	-0.09
38	5-chloro-6-(nitromethyl)-1H-indole	-0.35	0.15	-0.09	-0.41	-0.69	-0.12
39	1H-indol-5-ylacetaldehyde	-0.30	0.16	-0.18	-0.40	-0.33	0.06
40	1H-indol-5ylacetic acid	0.02	0.28	-0.14	0.07	-0.30	0.29
41	5-(nitro methyl)-1H-indole	-0.39	0.12	-0.16	-0.54	-0.75	-0.06
42	1H-indol-6-carboxylic acid	-0.34	0.10	-0.22	-0.30	-0.69	0.05
43	1H-indol-5,6-diol	-0.35	0.17	0.04	-0.45	-0.91	0.05
44	5,6-difluro-1H-indole	-0.31	0.17	-0.13	-0.65	-0.84	-0.08
45	1H-indol-5,6-dithiol	-0.57	-0.29	-0.44	-1	-0.71	-0.01
46	6-sulfanyl-1H-indol-5-ol	-0.55	-0.14	-0.25	-0.62	-0.66	0
47	5-sulfanyl-1H-indol-6-ol	-0.53	-0.07	-0.17	-0.67	-0.50	.1
48	6-chloro-1H-indol-5-thiol	-0.53	-0.09	-0.40	-1.03	-0.80	-0.12
49	5,6-bis(nitrosomethyl)-1H-indole	-0.31	0	-0.14	-0.52	-0.63	-0.12
50	1H-indol-5-ylmethanesulfonic acid	-0.18	-0.06	0.13	-0.30	-0.15	0.29

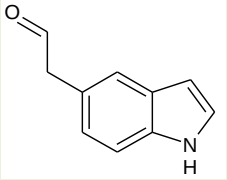
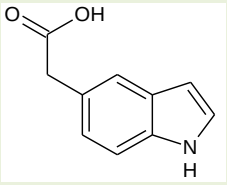
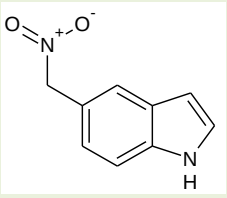
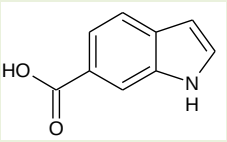
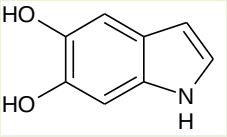
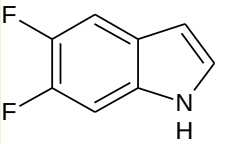
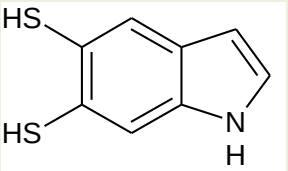
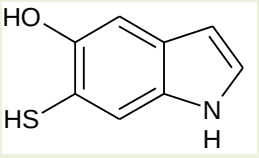
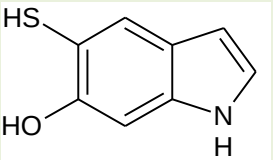
Table 3: Docking Score of Indole Ligand Molecules

S. No.	Docking Score kcal/mol	Structure
1	-7.6957	5-nitro-1-H-indole 
2	-8.3353	5-chloro-1*H*-indole 
3	-9.4755	1,1'-(1*H*-indole-5,6-diyl)diethanone 
4	-8.3832	1*H*-indole-5-sulfonic acid 
5	-7.2692	5,6-dinitro-1*H*-indole 
6	-8.1408	1*H*-indole-6-carbaldehyde 
7	-8.5118	1*H*-indole-5,6-dicarbaldehyde 
8	-8.9132	1*H*-indole-5-carbonyl chloride 

9	-9.4125	5-(trichloromethyl)-1*H*-indole 
10	-8.9429	1H-indole-5-sulfonylchloride 
11	-7.7115	1*H*-indole-5-carbonitrile 
12	-8.3189	1*H*-indole-5-carboxamide 
13	-8.3189	5-methoxy-1*H*-indole 
14	-7.8064	5-(trifluoromethyl)-1*H*-indole 
15	-5.9831	1*H*-indol-5-yl hydrogen sulfate 
16	-7.3126	1*H*-indol-5-yl cyanate 
17	-7.4149	1*H*-indol-6-yl nitrite 
18	-7.812	1*H*-indol-6-yl acetate 

19	-8.0722	1*H*-indole-5,6-diyl bis(thiocyanate) 
20	-7.0817	*2*-(1*H*-indol-5-yl)acetamide 
21	-7.7954	5-fluoro-1*H*-indole 
22	-7.7125	1*H*-indole-5-thiol 
23	-8.7737	6-chloro-1*H*-indole-5-carboxylic acid 
24	-8.0302	6-fluoro-1*H*-indole-5-carbaldehyde 
25	-8.1376	5-methyl-1*H*-indole 
26	-8.0112	6-methyl-1*H*-indole 
27	-8.8881	(6-chloro-1*H*-indol-5-yl)acetic acid 
28	-8.4737	(5-chloro-1*H*-indol-6-yl)acetaldehyde 

29	-7.9001	(6-fluoro-1*H*-indol-5-yl)acetaldehyde 
30	-8.2540	(6-chloro-1*H*-indol-5-yl)methyl acetate 
31	-8.3570	(5-chloro-1*H*-indol-6-yl)methyl acetate 
32	-5.3778	6-methyl-1H-indol-5-ol 
33	-8.0430	5-methyl-1H-indol-6-ol 
34	-8.5560	6-chloro-5-methyl-1H-indol 
35	-8.6779	5-chloro-6-methyl-1H-indol 
36	-8.6382	5,6-dichloro-1H-indole 
37	-9.0185	5-methyl-6-(nitromethyl)-1H-indole 
38	-8.8416	5-chloro-6-(nitromethyl)-1H-indole 

39	-7.9659	1H-indol-5-ylacetaldehyde 
40	-8.4907	1H-indol-5ylacetic acid 
41	-7.7583	5-(nitro methyl)-1H-indole 
42	-8.2346	1H-indol-6-carboxylic acid 
43	-7.4890	1H-indol-5,6-diol 
44	-7.8401	5,6-difluro-1H-indole 
45	-7.6019	1H-indol-5,6-dithiol 
46	-7.4473	6-sulfanyl-1H-indol-5-ol 
47	-7.8871	5-sulfanyl-1H-indol-6-ol 

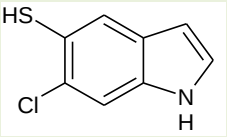
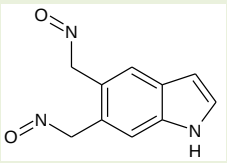
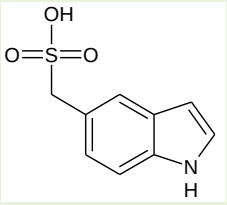
48	-8.173	6-chloro-1H-indol-5-thiol 
49	-8.459	5,6-bis(nitrosomethyl)-1H-indole 
50	-8.434	1H-indol-5-ylmethanesulfonic acid 

Table 4: Docking Scores of the Standard Drug and Phytoconstituent

Docking Score	Standard Drug
-9.074	Casodex
Docking Score	Phytoconstituent
-10.466	Curcumin

CONCLUSION

The docking study conducted in indole nucleus for its anti cancer activity was successful from which we came to a conclusion that indole derivative with ethanone substitution (Fig. 1) and trichloro substitution (Fig. 2) showed good docking score compared to that of the standard drug casodex.

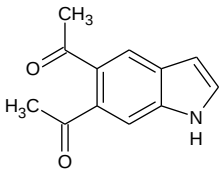


Figure 1: 1, 1-(1H-indole-5,6-diyl)diethanone

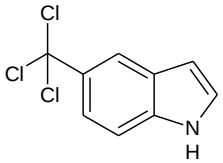


Figure 2: 5-(trichloromethyl)-1H-indole

Also 5, 6-bis (nitrosomethyl)-1H-indole (Fig-3) showed higher number of rotatable bond thus this compound is having higher flexibility.

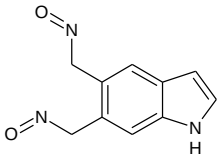


Figure 3: 5, 6-(bisnitrosomethyl)-1H-indole

From the present study we could also finalise that the electron withdrawing groups such as nitro group, carboxyl group, aldehydes, ketons, chlorine, amide, nitrile groups and electron releasing group such as methyl group, at the fifth and sixth position demonstrate greater affinity with casp9.

Phytoconstituent curcumin showed better docking score than that of the standard drug casodex and fifty indole compounds.

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