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Molecular docking studies using garlic metabolites - a peek into the apoptotic pathway

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Abstract: The organosulfur compounds derived from Garlic employ cytotoxic effects via (ROS) reactive oxygen species production for signaling, by activating cysteine proteases and stress kinases for apoptosis in human cancerous cell. With the increase in mitochondrial membrane permeability due to stress, the intracellular free [Ca^{2+}] level increases. Thus, the activation of caspase-4 alongwith the expression of calreticulin indicates the involvement of (ER) endoplasmic reticulum stress in the process of apoptosis. Down-regulation of some BIRC proteins and Bcl-2, activation of Caspase3, Caspase-9 and Calpain, mitochondrial release of cytochrome *c* and Smac into the cytosol and overexpression of Bax are the related events included in apoptosis. In this work, homology modeling approach was employed in order to develop structures for these proteins. Some protein structures were readily available in the PDB database. Expasy's Prot-param server were used for functional and physico-chemical characterization of the protein. Chemsketch was used for drawing molecules and ligands. Babel is the software used to convert .mol files to .pdb files for docking. Autodock software was used to dock ligands with their respective proteins, Patchdock and Firedock was also used to determine Protein-Protein interaction. Docking was performed to evaluate the binding constants of the different interactions mediated by garlic in the apoptotic pathway.

Keywords: Docking, apoptosis, apoptotic pathways, Reactive oxygen species, protein structures.

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1. Introduction: The organosulfur compounds derived from Garlic like (DATS) diallyltrisulfide, (DADS) diallyl disulfide and (DAS) diallyl sulfide deliver significant defense counter to carcinogenesis. Treating the cancerous cells with garlic compounds elicited the production of (ROS) reactive oxygen species which encouraged apoptosis. In multicellular organisms, Apoptosis is a process of programmed cell death. As per Ancient Greek term Apoptosis means "falling off". There is a series of biochemical events which results in characteristic cell changes (morphology) and death **[1].** Caspases are the classes of proteolytic enzymes which mediates apoptosis by cleaving specific proteins in the nucleus and cytoplasm **[2].**

Apoptosis is the process of programmed cell death. In the course of development of multicellular organisms, some cells need to die. Undesirable cells are removed during metamorphosis, embryogenesis and tissue turnover. All cells retain the pathways which can cause demise by apoptosis. The pathway

causing cell death gets activated by an appropriate stimuli, which requires protein and RNA synthesis by the dying cells **[3].**

Apoptosis is essential not only in the elimination of cancerous cells but also in tissue development and promoting the immune defense **[4, 5].** Neurodegenerative diseases are the consequences of inappropriate stimulation of apoptosis. The key defense against cancer is the ability of the tumor suppressor p53 to activate apoptosis **[6].** Fas consists of a cytoplasmic domain called "death domain" which is involved in protein-protein interaction **[4, 7]**. Fas is a trimer that aggregates upon interaction with FasL. A tumor cell is distinguished from a normal cell by its immortality, morphological transformation, and (sometimes) ability to metastasize. The cancerous cells are characterized morphologically by the presence of a large nucleus, having an irregular shape and size, the cytoplasm is scarce and intensely colored, the nucleoli are prominent. In case of neoplastic cells, the nucleus changes are concerned to its shape, density, volume, surface, the nucleus/cytoplasm ratio as well as structure and homogeneity **[10].** Some oncoproteins are cytoplasmic tyrosine kinases and their targets are mostly unidentified. Their activation may be a result of autophosphorylation of tyrosine kinase receptors.

Cancer: Cancer is defined as a disease in which abnormal cells divides in an uncontrolled manner **[1].** It starts when cells grow out of control and crowd out normal cells. It can start at any place in the body. Thus effecting the normal functioning of the body. Cancerous cells form lumps. These lumps are also called tumors. These lumps may be cancerous(malignant) or non-cancerous[benign (be-NINE)].The changes in the morphological characters occur at the metabolic level in relation to the augmented structures related to cell division and the attenuation of the structures which are associated with other metabolisms. These tumors are intensely classified by the presence of gigantic nuclei and multinucleate cell expression in abnormal divisions **[1]**. Mostly cancer is treated by chemotherapy, radiation and surgery.

Various research activities have been done in order to identify the etiology and prevention of cancer. It is a concern of the public health policy. Dietary intake and nutritional profiling contributes to the risk of cancer. Significant results have been obtained upon dietary modification while reducing the incidence of cancer. In order to obtain the effective proof of relationship between cancer and dietary intake patterns, different epidemiological designs have been established. This deals with the viewpoint for originating various primary and secondary prevention measures for prevention and control of cancers **[9].**

Garlic and garlic-derived compounds: The organosulfur compounds from garlic target many pathways, like the angiogenic pathway, intrinsic and extrinsic pathways. It also plays a major role in regulating cell cycle machinery, which may all subsidize to their anticancer activities **[6].** Preclinical data have shown that organosulphur compounds analogues are highly effective in providing defense against cancer brought by diversity in chemical carcinogens **[7].**

Garlic is also known as Allium sativum. Organosulfur compounds (allin), enzymatically produced compound from allin (allicin) and enzymes (allinase) are the active ingredients found in garlic. These compounds synergistically influence each other to show different effects. From antiquity, it is used for treating major health issues. It is one of the best-selling herbal ingredients and one of the burning research topic of concern **[8, 9].** Garlic oil contains Diallyl sulfide, an organosulfur compound & has anticarcinogenic property **[7].**

Pathways of Apoptosis: Garlic derived organosulfur compounds detoxify carcinogens and control the activity of several metabolizing enzymes that either inhibit or activates the formation of DNA adducts in numerous target tissues. These compounds were suspected as cancer preventive agents and the toxicity level of the dosage will be determined by numerous clinical trial data outputs. Alterations in the cell cycle and induction of apoptosis are achieved on induction of these compounds in tumor cell lines. This

is also known as Antiproliferative activity. Lack of oxygen or hypoxia, severe genetic damages, presence of some viral proteins, very high concentration of cytosolic Ca^{+2} ions, free radicals mediated severe oxidative stress acts as stimuli to oxidative stress. Intrinsic pathways of apoptosis are facilitated by the Bcl-2 family proteins. This protein consists of one or more BH domains. The gene which codes for Bcl-2 protein was overexpressed in the cancer cells due to translocation.

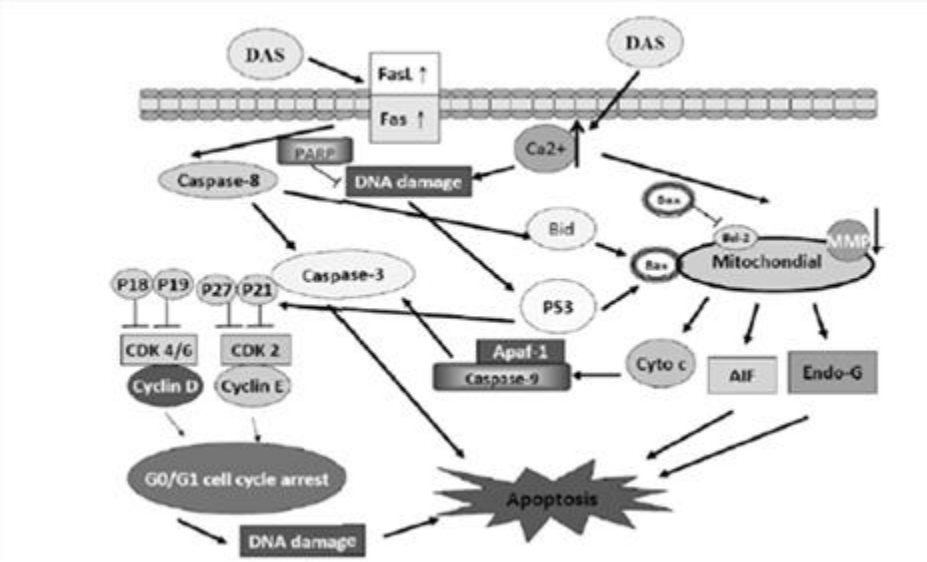


Figure (1): This figure shows DAS-interceded cell cycle arrest and apoptosis in cells. DAS encouraged G0/G1 phase arrest through the Fas and FasL activation of caspase-3 and caspase-8. Increase in intracellular Ca^{2+} and reduction in *ΔΨm(permeability)* of mitochondria. Release in AIF, Endo G and cytochrome c and promotion of caspase-3 and caspase-9 activation results in programmed cell death.

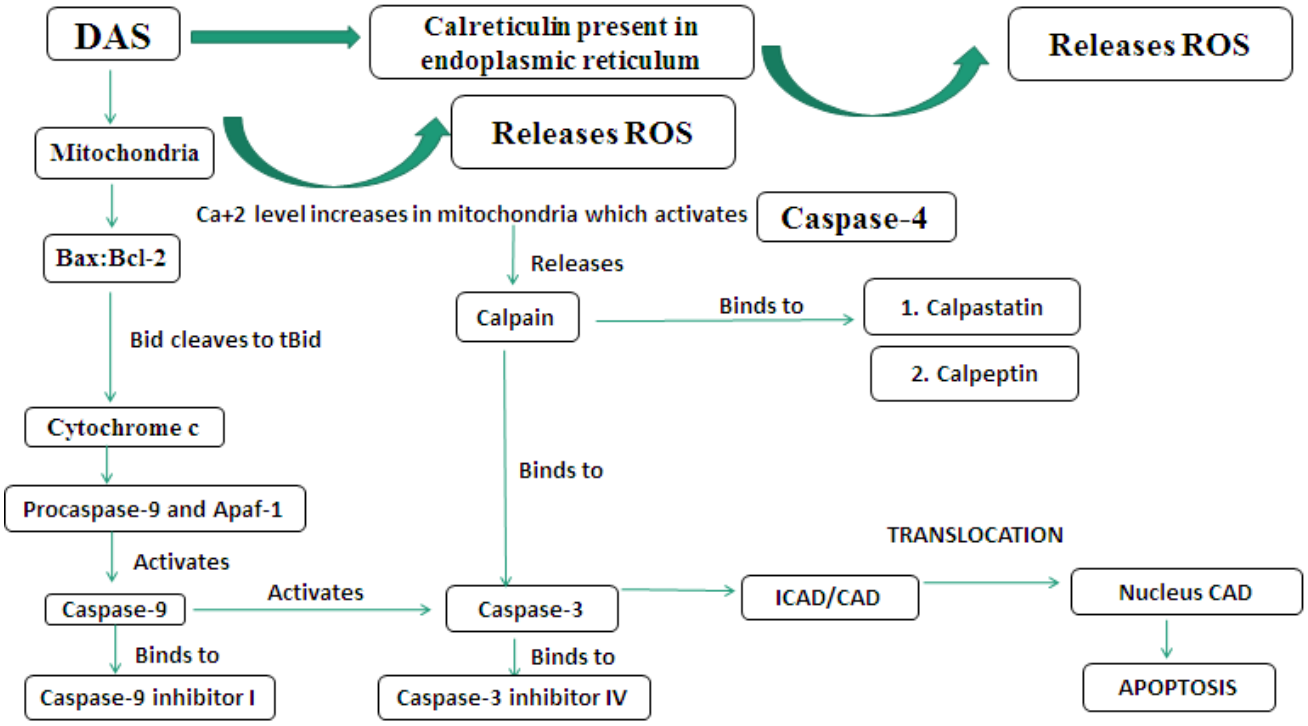


Figure (2): Intrinsic pathway involving organosulfur compound (DAS) present in Garlic.

In some human lymphomas, Bcl-2 has been identified as the first cancer triggering oncogene. It promotes the subsistence of the cancerous cells that otherwise would die by apoptosis.

Cytokines induce Extrinsic pathway of apoptosis with the help of an extracellular messenger protein called TNF. Exposure to elevated temperature, radiation, or other toxic substances/ Introduction of viral proteins provokes the immune cell to produce TNF.

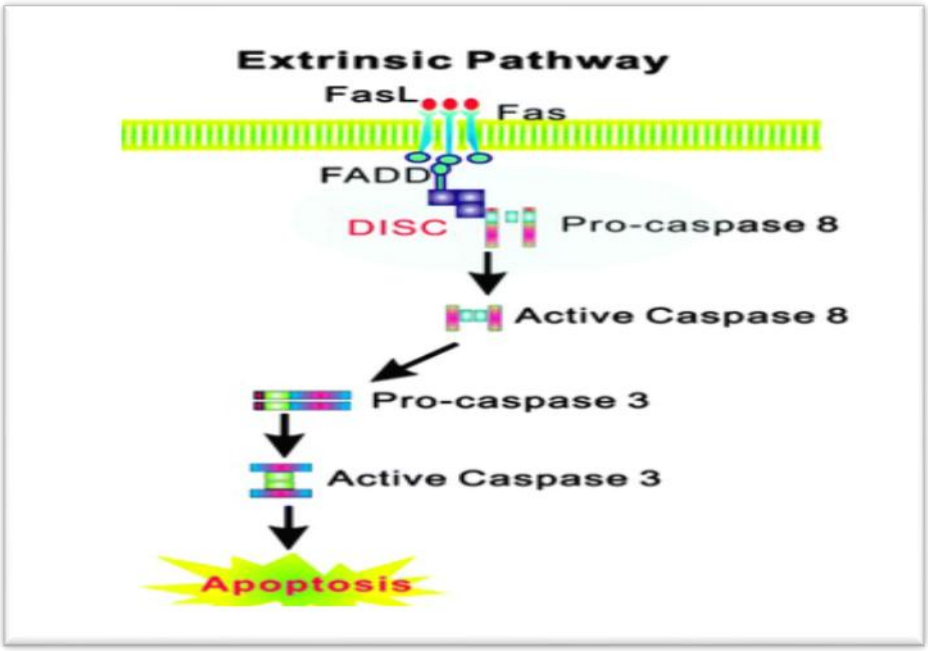


Figure (3). Extrinsic pathway of apoptosis.

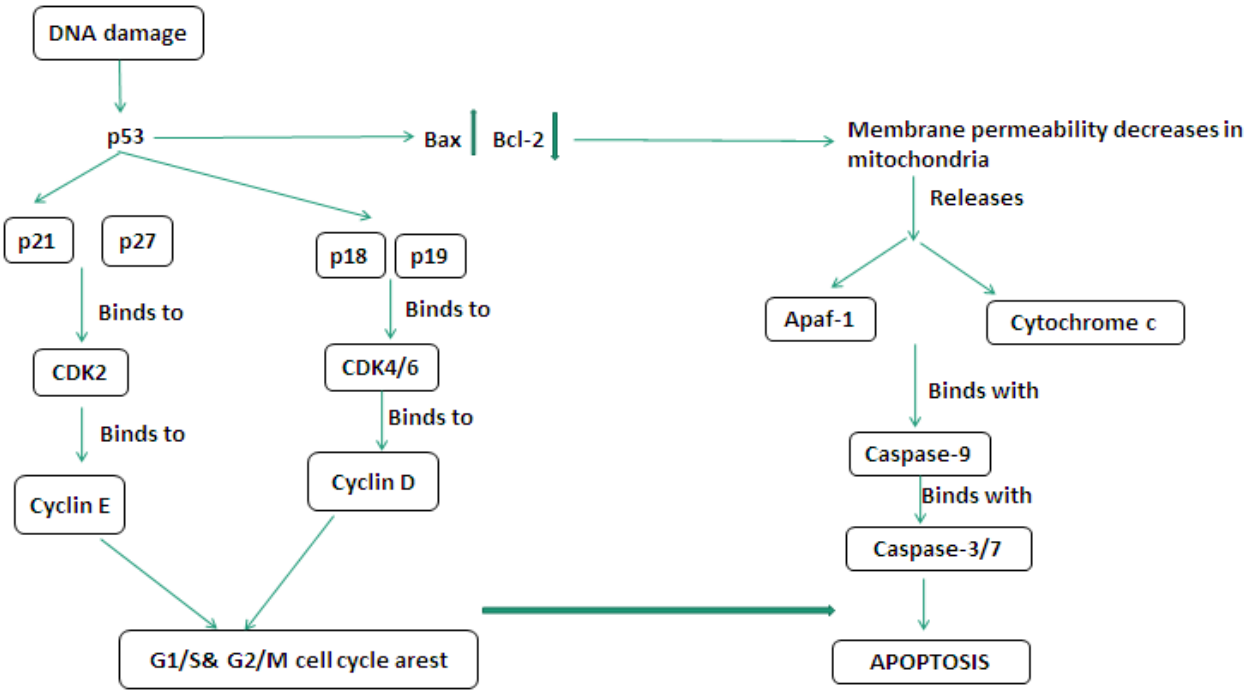


Figure (4): p53 pathway of apoptosis.

Symbols, units, and abbreviations: ROS (Reactive Oxygen Species), ER (Endoplasmic Reticulum), DAS (diallyl sulfide), DADS (diallyl disulfide), DATS (diallyl trisulfide), PDB (Protein Data Bank),

DNA (Deoxyribonucleic acid), FADD (Fas-associated protein with death domain), DISC (death-inducing signaling complex), FasL (Fas Ligand), CDK (Cyclin Dependent Kinase), Apaf-1 (Apoptotic protease activating factor1), NMR (Nuclear magnetic reasonance), Upregulation (↑), Downregulation (↓), ACE (Atomic Contact Energy), HB (Hydrogen Bond), kI (Inhibition constant value in Autodock), Endo G (Endonuclease G), AIF (Apoptosis Inducing factor),TNF (Tumour Necrosis Factor), *Ψm (mitochondrial membrane permeability),* mM, μM, VdW, e- value.

2. Experimental

2.1 Searching the protein targets involved from Protein Data Bank and characterization using online servers:

The proteins involved in these pathways can be directly downloaded from Protein Data Bank (PDB). The macromolecular structural data obtained from NMR and X-ray diffraction were represented in a standard format in the Protein Data Bank (PDB). This representation was formed in the 1970's and a large amount of software using it has been noted. ProtParam is the program which is used for protein characterization and ExpaSy is the server.

2.2 Docking the ligand with receptors to find the e value & docked sites:

For Protein-Ligand interaction, Autodock is the software which is used for docking. For Protein-Protein interaction, PatchDock is the software used. Structure refinement is done by using FireDock. In case of Autodock the best results were obtained considering the Binding energy, e value and the number of hydrogen bonds. Shape complementarity principles are the basis of Molecular docking algorithm. Input, output and user interface were the main entities of the PatchDock web server. Smaller number of results indicates higher value. 1.5 A° for protein-small molecule docking and 4A° for protein-protein docking were the acclaimed standard values. Complex Type: Always default complex type can be used but PatchDock consists of variable parameters sets, which can be optimized for variable complexes being analyzed.

2. Results and discussion:

Recent findings show that DAS is first activated through Fas and FasL. Downstream activation is done by caspase-8 and then caspase-3 induces apoptosis, mitochondrial membrane potential is disrupted by increase in Bid and Bax. The activation of mitochondria-facilitated downstream molecular proceedings which includes release in cytochrome c, the release of Endo G and AIF and consecutive activation of caspase-3 and caspase-9 results in apoptosis. Our molecular docking studies completely agreed with these findings. The single docking experiments also provided binding energies which suggested that the pathway is energetically favourable. The precise binding sites could also be ascertained for all the components of the pathway.

Table (1): Best results obtained using AutoDock.

Sl. no	Macromolecule	Ligand	Docking Results
1	Diallyl Sulfide	FADD (Fas Associated Death Domain)	Rank: 1_1 Binding Energy: -3.5 kI: 2.74mM Intermolecular Energy: -4.69 Internal Energy: -0.08 Torsional Energy: 1.19

			Unbound Extended Energy: -0.08 Cluster RMS: 0.0 Ref RMS: 5.43
2	Diallyl Sulfide	Calreticulin	Rank: 1_1 Binding Energy: -2.36 kI: 35.29mM Intermolecular Energy: -3.55 Internal Energy: -0.08 Torsional Energy: 1.19 Unbound Extended Energy: -0.08 Cluster RMS: 0.0 Ref RMS: 27.01
3	Bax	Bcl-2	Rank: 1_1 Binding Energy: -0.32 kI: 582.15mM Intermolecular Energy: -2.41 Internal Energy: 143.34 Torsional Energy: 2.09 Unbound Extended Energy: 143.34 Cluster RMS: 0.0 Ref RMS: 3.45
4	Bid	Bax	Rank: 1_1 Binding Energy: -0.06 kI: 899.41mM Intermolecular Energy: -0.96 Internal Energy: 3.39 Torsional Energy: 0.89 Unbound Extended Energy: 3.39 Cluster RMS: 0.0 Ref RMS: 6.98
5	Calpain	Bid	Rank: 1_1 Binding Energy: -5.87 kI: 50.07uM Intermolecular Energy: -6.76 Internal Energy: -0.53 Torsional Energy: 0.89 Unbound Extended Energy: -0.53 Cluster RMS: 0.0 Ref RMS: 9.06
6	Calpain	Calpastatin	Rank: 1_1 Binding Energy: -7.12 kI: 6.08uM Intermolecular Energy: -8.91 Internal Energy: 66.57 Torsional Energy: 1.79 Unbound Extended Energy: 66.57 Cluster RMS: 0.0 Ref RMS: 4.51
7	Calpain	Calpeptin	Rank: 1_1 Binding Energy: -3.59

			kI: 2.34mM Intermolecular Energy: -6.57 Internal Energy: 145.82 Torsional Energy: 2.98 Unbound Extended Energy: 145.82 Cluster RMS: 0.0 Ref RMS: 4.74
8	Cdk2 cyclinE	Imantinib	Rank: 1_1 Binding Energy: -6.93 kI: 8.39uM Intermolecular Energy: -9.01 Internal Energy: -0.02 Torsional Energy: 2.09 Unbound Extended Energy: -0.02 Cluster RMS: 0.0 Ref RMS: 22.49
9	p19	Abemaciclib (CDK 4/6)	Rank: 1_1 Binding Energy: -5.02 kI: 210.02uM Intermolecular Energy: -7.11 Internal Energy: 4.23 Torsional Energy: 2.09 Unbound Extended Energy: 4.23 Cluster RMS: 0.0 Ref RMS: 12.79
10	p53	Bax	Rank: 1_1 Binding Energy: -1.5 kI: 78.97mM Intermolecular Energy: -2.4 Internal Energy: 3.48 Torsional Energy: 0.89 Unbound Extended Energy: 3.48 Cluster RMS: 0.0 Ref RMS: 19.27
11	p53	Bcl-2	Rank: 1_1 Binding Energy: -3.63 kI: 2.19mM Intermolecular Energy: -5.72 Internal Energy: 143.44 Torsional Energy: 2.09 Unbound Extended Energy: 143.44 Cluster RMS: 0.0 Ref RMS: 16.11

Table (2): Best Results obtained using PatchDock.

Sl. No	Receptor	Ligand	Solution no	Score	Area	ACE	Transformation
1	Procaspase-9 and Apaf-	Cytochrome c	1	5278	636.10	19.65	-2.83 0.36 2.71 51.17 26.21 71.30

	1		2	5178	669.60	-17.74	0.26 -0.24 0.24 50.40 26.36 76.74
			3	5162	630.20	-15.06	-1.05 -0.75 0.38 52.44 33.80 78.91
			4	5140	628.10	-7.03	-1.46 0.20 -2.89 55.50 30.90 77.47
			5	5100	631.10	-49.36	-1.07 -0.87 0.47 54.16 31.37 81.64
2	Bid	Bax	1	964	106.70	23.00	3.07 0.03 2.64 16.43 -12.11 3.81
			2	872	94.40	20.27	-2.99 -0.08 -0.09 6.07 -10.17 4.45
			3	664	70.50	13.34	3.08 -0.07 2.81 12.63 -10.29 4.44
3	Calpain	Bid	1	1836	193.70	-226.26	3.03 0.22 0.87 1.20 -6.64 -1.47
			2	1770	188.10	-214.70	2.91 -0.16 0.52 1.24 -2.98 1.61
			3	1768	193.70	-212.00	3.14 -0.12 1.89 9.39 -5.58 1.16
			4	1746	179.30	-205.05	-0.09 0.04 1.17 4.74 -5.31 -0.80
			5	1720	177.80	-212.25	3.09 0.01 -2.07 9.66 6.49 0.70
4	Calpain	Calpastatin	1	1332	145.20	-252.53	2.99 0.09 -0.30 0.63 4.23 -0.24
			2	1280	138.10	-247.98	0.09 0.17 -2.13 9.58 8.24 6.03
			3	1228	126.40	-251.18	3.07 0.06 -2.69 12.34 1.98 -7.87
			4	1148	118.10	-240.25	0.02 -0.08 3.04 10.65 0.24 7.90
			5	1144	130.30	-197.47	2.82 -0.02 2.80 13.14 1.35 -6.89
5	Calpain	Calpeptin	1	1470	153.70	-271.53	-3.05 0.23 -2.16 10.85 6.08 -1.30
			2	1422	145.40	-230.04	-3.05 -0.17 0.89 1.11 -3.75 1.74
			3	1326	133.10	-219.70	-0.26 -0.00 -2.51 11.04 2.99 7.93
			4	1312	135.40	-215.72	2.90 -0.30 -1.82 8.55 9.85 -5.27
			5	1226	139.60	-203.76	-0.66 -0.30 0.48 2.31 1.22 8.89
6	Caspase-3	Caspase-3 inhibitor IV	1	4508	527.30	28.07	-2.00 1.38 2.16 141.64 88.29 122.64
			2	4498	529.60	24.66	-2.97 -0.18 -0.21 151.71 96.42 111.64

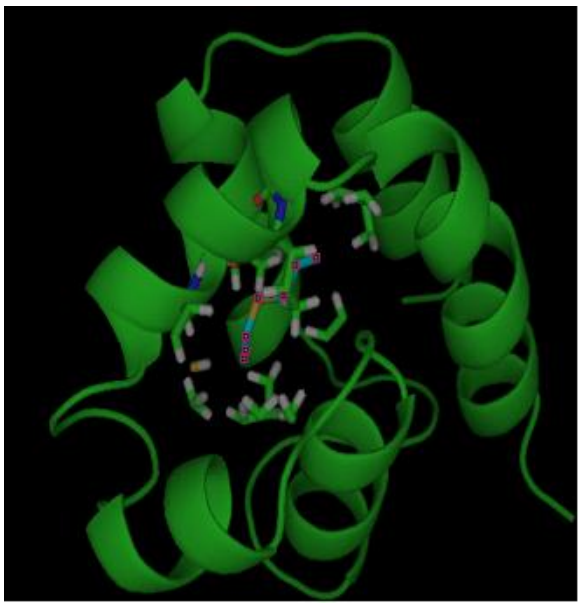
			3	4042	473.30	35.45	0.07 0.53 2.54 167.28 87.90 134.41
			4	3846	442.20	11.48	-2.86 -0.28 -2.57 163.85 93.00 119.58
			5	3816	469.00	-23.20	0.98 0.94 2.30 168.09 96.49 129.70
7	CDK2 Cyclin E	Imantinib	1	6290	804.60	-347.60	-1.18 0.78 1.06 -0.24 8.41 -30.32
			2	5972	820.60	-413.27	0.90 0.29 -2.00 7.50 26.29 -28.45
			3	5906	843.50	-335.40	0.35 -0.96 2.34 15.93 19.60 -17.26
			4	5790	782.30	-355.61	1.65 -0.93 1.55 24.07 5.76 -27.17
			5	5740	714.00	-294.51	0.10 -0.16 2.88 22.06 -0.62 2.24
8	p19	Abemaciclib	1	5182	673.10	-137.07	-1.40 -0.42 2.27 19.00 -12.36 43.21
			2	4872	641.20	-166.34	1.59 0.17 2.41 19.33 -14.93 24.96
			3	4850	560.80	-130.69	1.31 -0.17 2.66 17.82 -10.31 21.16
			4	4826	706.80	-116.26	-1.50 -1.17 -3.08 0.66 -10.15 22.49
			5	4786	691.90	-191.52	-2.88 -0.57 -1.30 22.20 -4.62 39.76
9	p18	Abemaciclib	1	5168	652.20	31.94	-2.78 -0.75 -1.65 26.77 9.09 40.69
			2	5134	685.00	120.69	-1.39 -0.22 0.42 27.64 46.77 37.95
			3	5090	765.40	56.73	0.57 -0.62 -2.45 32.54 60.03 29.50
			4	5062	701.50	50.64	0.52 -0.13 -1.65 22.67 53.30 26.48
			5	5050	693.50	96.13	-2.77 1.28 -1.14 32.38 53.80 23.26
10	p53	Bax	1	2242	273.20	97.80	2.99 -0.08 -0.61 -20.69 10.36 -61.44
			2	2238	247.00	93.47	-0.98 1.08 -3.11 -43.64 -3.51 -54.19
			3	2182	276.00	60.88	1.98 -0.09 -2.98 -35.00 28.87 -44.03
			4	2164	246.90	72.05	-2.89 1.22 -1.33 -22.76 -9.50 -31.98
			5	2096	226.90	101.81	2.71 -0.55 2.60 -36.07 19.98 -60.16
11	p53	Bcl-2	1	3086	334.10	-88.68	1.80 -0.69 -0.80 -53.50

							13.66 -59.12
			2	3058	344.80	-201.55	2.37 0.42 -2.97 -42.48 2.40 -43.66
			3	2996	336.70	-155.91	-3.06 -0.01 1.83 -65.19 10.53 -73.18
			4	2986	324.20	-106.06	-2.63 0.54 -2.90 -47.81 -1.17 -44.56
			5	2958	341.80	-149.73	1.35 0.57 2.26 -46.14 27.49 -68.52

Table (3): Best Results obtained from FireDock.

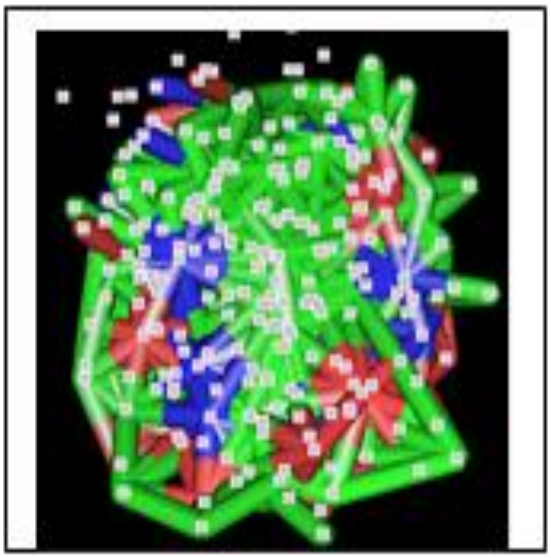
Receptor	**Ligand**	**Rank**	**Solution no**	**Global Energy**	**Attractive VdW**	**Repulsive VdW**	**ACE**	**HB**
Procaspase-9 and Apaf-1	Cytochrome c	1	2	-46.40	-32.67	12.97	-7.60	0.00
		2	8	-44.33	-27.69	14.00	-10.64	0.00
		3	10	-35.89	-25.10	18.67	-9.52	0.00
		4	7	-30.85	-22.93	16.47	-8.15	0.00
		5	6	-30.71	-21.45	10.46	-5.75	0.00
Bid	Bax	1	1	-4.16	-9.18	0.86	1.25	0.00
		2	2	-3.87	-9.21	0.05	1.17	0.00
		3	3	-1.27	-8.17	0.11	1.05	0.00
Calpain	Bid	1	10	-40.91	-19.20	2.50	-12.59	0.00
		2	1	-39.82	-18.50	4.27	-12.95	0.00
		3	3	-38.56	-19.66	5.60	-12.42	0.00
		4	5	-37.60	-18.06	3.52	-11.96	0.00
		5	9	-37.43	-17.31	1.33	-12.11	0.00
Calpain	Calpastatin	1	3	-54.61	-24.76	1.29	-15.33	0.00
		2	10	-50.87	-24.87	3.29	-14.19	0.00
		3	4	-50.06	-23.47	2.62	-14.62	0.00
		4	6	-49.86	-23.08	1.84	-14.29	0.00
		5	5	-47.03	-23.05	6.41	-15.05	0.00
Calpain	Calpeptin	1	3	-38.42	-19.29	4.63	-12.76	0.00
		2	5	-38.24	-19.26	3.13	-12.84	0.00
		3	1	-35.65	-19.17	6.99	-13.36	0.00
		4	2	-35.45	-17.82	4.45	-13.29	0.00
		5	4	-31.75	-17.15	5.25	-11.87	0.00
Caspase-3	Caspase-3 inhibitor IV	1	2	-21.14	-20.94	4.87	0.75	-1.17
		2	9	-17.44	-13.45	7.23	-5.89	-0.79
		3	3	-12.20	-22.60	15.16	1.63	-0.91
		4	8	-6.84	-12.19	5.25	1.62	0.00
		5	1	-2.45	-8.26	2.12	-0.72	0.00
p19	Abemaciclib	1	3	-19.77	-12.62	2.47	-5.57	0.00
		2	4	-14.27	-11.92	6.94	-4.20	0.00
		3	2	-11.18	-13.17	5.76	-2.13	0.00
		4	10	-7.70	-8.39	1.51	-0.63	0.00
		5	7	-6.39	-10.50	7.65	-2.41	0.00

CDK2 Cyclin E	Imantinib	1	2	-52.41	-25.00	12.58	-16.37	0.00
		2	4	-47.82	-20.28	4.44	-14.48	0.00
		3	10	-41.14	-20.85	4.27	-9.58	0.00
		4	5	-39.30	-17.49	6.25	-13.11	0.00
		5	1	-33.41	-15.00	10.50	-12.79	0.00
p18	Abemaciclib	1	7	-15.29	-17.07	8.66	-0.38	0.00
		2	4	-12.20	-11.45	3.71	-1.46	0.00
		3	10	-11.30	-15.60	8.02	1.88	0.00
		4	6	-10.69	-12.64	5.02	-0.88	0.00
		5	1	-6.73	-11.60	4.95	1.36	0.00
p53	Bax	1	2	-5.05	-10.78	0.70	5.76	0.00
		2	4	-1.11	-7.08	0.54	5.01	0.00
		3	8	-0.81	-7.46	1.39	3.78	0.00
		4	9	-0.33	-5.85	2.08	3.18	0.00
		5	1	1.13	-4.79	1.05	4.20	0.00
p53	Bcl2	1	6	-29.97	-16.84	5.01	-6.23	0.00
		2	3	-26.36	-14.59	6.28	-6.65	0.00
		3	2	-23.98	-11.95	2.50	-6.26	0.00
		4	10	-23.53	-14.23	5.56	-5.29	0.00
		5	7	-14.50	-7.09	1.14	-3.57	0.00

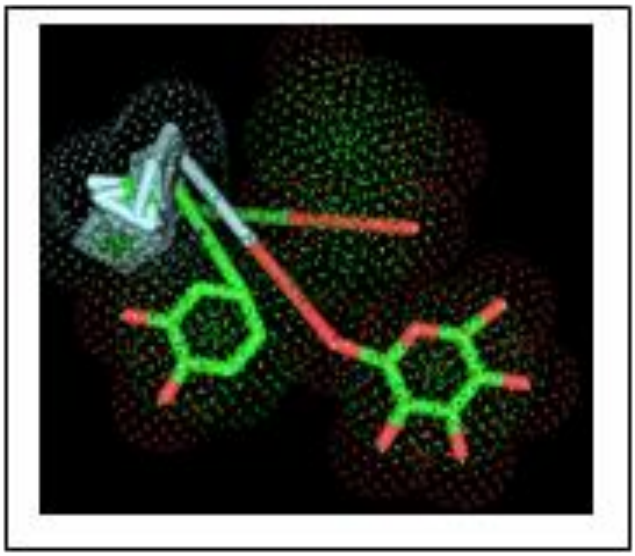


(1) FADD with DAS

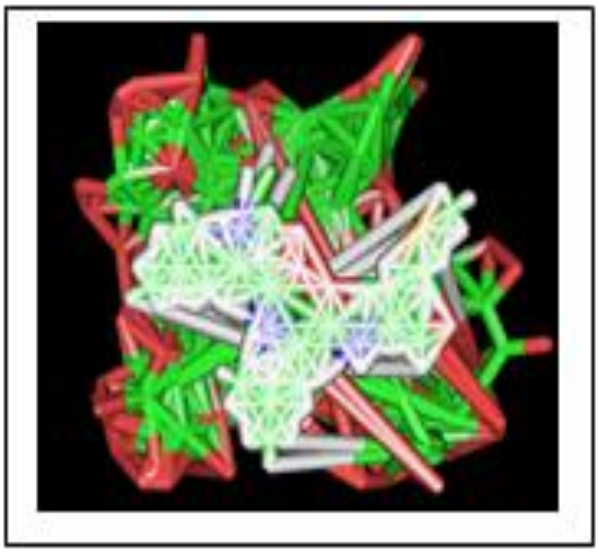
(2) DAS with calreticulin



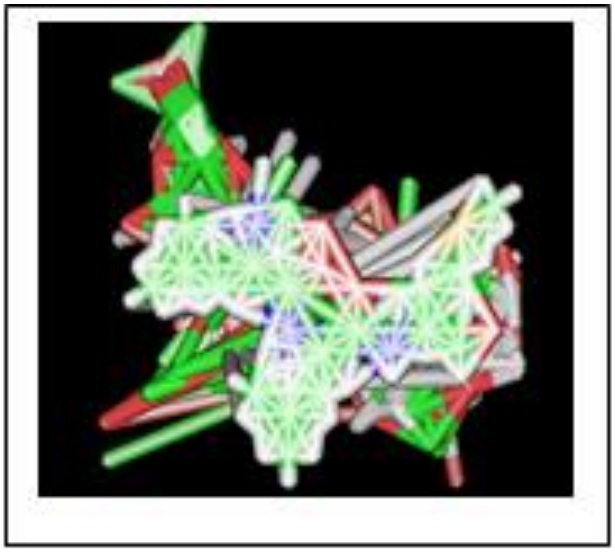
(3) Bax with Bcl-2



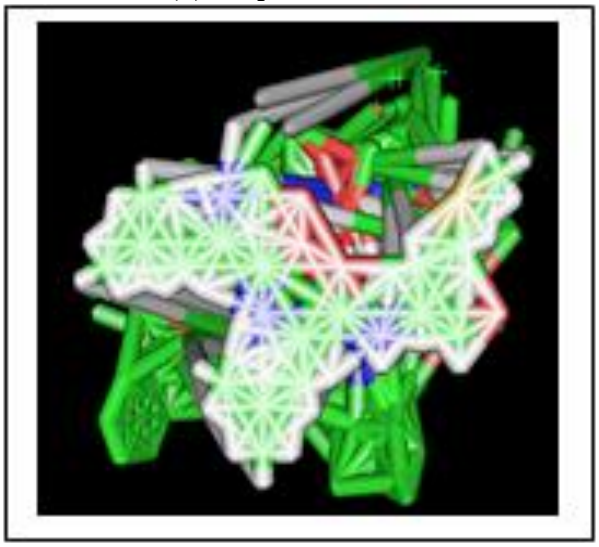
(4) Bid with Bax



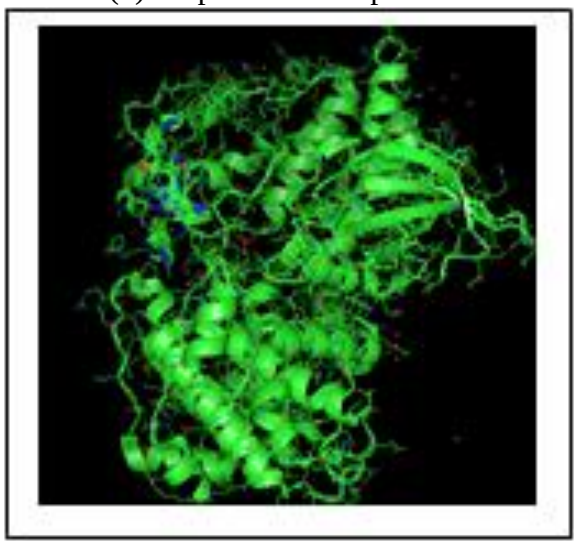
(5) Calpain with Bid



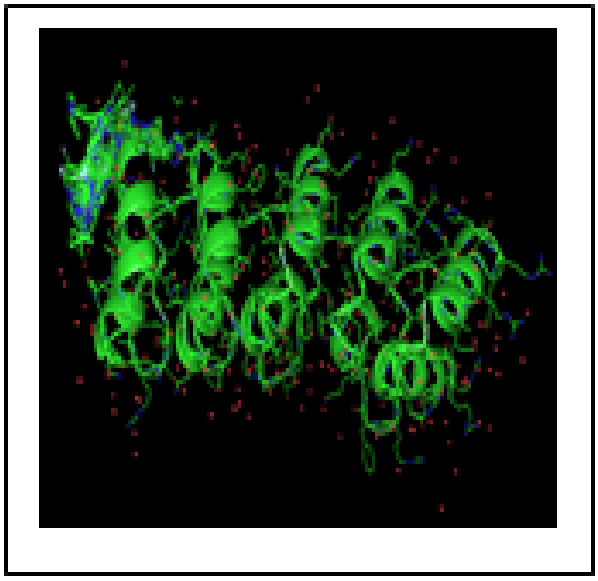
(6) Calpain with Calpastatin



(7) Calpain with Calpeptin

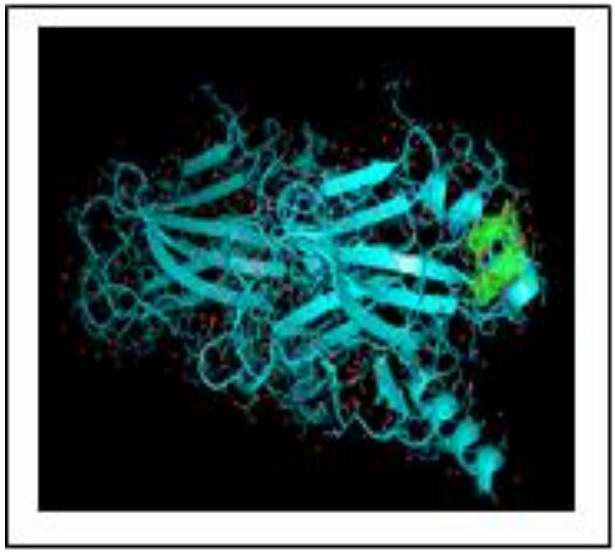


(8) CDK2 Cyclin E with Imantinib



(9) p19 with Abemaciclib

(10) p53 with Bax



(11) p53 with Bcl-2

Figure (5): Best results obtained using AutoDock.

The term "molecular docking" covers computational methods used for predicting binding conformations of a given pair of receptor and ligand. For the sake of computational feasibility, a common approximation in docking approaches, among others, is to restrict the conformational flexibility of both, ligand and receptor, and to disregard the impact of explicit solvent molecules on intermolecular interactions. Docking procedures are basically the combination of search algorithms and scoring functions. Search algorithms predict the ligand binding orientation and conformations commonly referred to as posing. Firstly, AutoDock uses Lamarkian Genetic Algorithm and sometimes these ligands present too many degrees of freedom and docking methods are not able to search the accessible conformational space. Second, the protein targets often show significant conformational flexibility, which is not modeled in the AutoDock suite, apart from the selective side-chain motion. Thus Autodock has been substituted by PatchDock and the structure refinement was done by FireDock.

Molecular docking of the elements involved in Intrinsic, Extrinsic was performed using AutoDock and all the binding energies were found negative which means there is a stable binding between them. Protein molecules could not be docked by using AutoDock so PatchDock was used for this purpose and the structures obtained were refined by FireDock. Perceiving the results of the intrinsic pathway with garlic metabolites, we are interested to know whether there is a similar effect on the other pathways namely extrinsic and p53 pathway.

3. Conclusions:

Computational docking is widely used for the study of protein–ligand interactions and for drug discovery and development. Typically, the process starts with a target of known structure, such as a crystallographic structure of an enzyme of medicinal interest. Docking is then used to predict the bound conformation and binding free energy of small molecules to the target. Literature survey shows that till date no work has been done on the molecular docking studies of the garlic mediated apoptotic pathway. Our findings are unique in that respect.

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