RESEARCH ARTICLE
Open Access

Journal of Veterinary and Animal Sciences
ISSN (Print): 0971-0701, (Online): 2582-0605
https://doi.org/10.51966/jvas.2023.54.4.875-881

Molecular docking approach to identify potential anticancer agents from *Sida cordifolia* and *Eupatorium triplinervis*

K. Priyanka Menon[1], Bibu John Kariyil [2*], S. Aparna Sivapriya[1] and S. Arundhathy Nair[1]
Department of Veterinary Pharmacology and Toxicology
College of Veterinary and Animal Sciences, Mannuthy, Thrissur- 680 651
Kerala Veterinary and Animal Sciences University
Kerala, India

Citation: Menon, K.P., Kariyil, B.J., Sivapriya and S.A., Nair,S.A. 2023. Molecular docking approach to identify potential anticancer agents from *Sida cordifolia* and *Eupatorium triplinervis*.
J. Vet. Anim. Sci. **54**(4):875-881
DOI: https://doi.org/10.51966/jvas.2023.54.4.875-881

Received: 18.03.2022 *Accepted: 27.10.2023* *Published: 31.12.2023*

Abstract

Sida cordifolia and Eupatorium triplinervis have been used traditionally for treatment of various ailments. An in-silico study was carried out to identify the interaction between the selected phytocompounds with B-cell lymphoma 2 (Bcl2). The crystal structure of the Bcl2 protein (PDB Id: 4LXD) of Homo sapiens was used as the receptor. The docking was done with AutoDock V 4.0 using twenty-one ligands from both plants and the binding energy was assessed. The binding energy of various phytocompounds were observed to range from -2.74 Kcal/mol to -7.47 Kcal/mol. The standard compound doxorubicin showed a binding energy of -6.95 Kcal/mol. The compound stigmasterol and sitosterol showed binding energies of -7.15 and -7.47 Kcal/mol respectively. Molecular binding of the compounds was strengthened by hydrogen bonds and hydrophobic interactions. Hence the plant extracts can be used to separate promising lead compounds with anticancer activity.

Key words: *Sida cordifolia, Eupatorium triplinervis, BCl2, autodock*

Chemotherapy, hormone therapy, immunotherapy, gene therapy, surgery, radiation therapy, laser therapy, targeted therapy and combination therapy are the main cancer treatment modalities. Chemotherapy is the most popular and promising option (Urruticoechea *et al.,* 2010). Despite advancements in cancer treatments, resistance to chemotherapeutic medications remains a significant issue, and account for the majority of patient relapses and low survival rates. Hence, novel drugs to evade the resistance is the need of the hour. Plants always remain a major source of potential chemotherapeutic agents. Chemotherapeutic drugs like vincristine, epipodophyllotoxins, taxanes etc., that are commonly used, are plant derived. Natural secondary metabolites produced by the plant kingdom are being studied for their potential anticancer properties, which might lead to the creation of brand-new pharmaceuticals.

1. *MVSc Scholar*
2. *Assistant Professor*
**Corresponding author: bibujohn@kvasu.ac.in, Ph. 9895297842*

Structure- and ligand-based molecular docking has developed into a potent and affordable tool for finding new lead compounds. Novel anticancer drugs have been discovered through molecular docking against a number of protein targets. It is important to keep in mind that when it comes to natural products, the screening and isolation of bioactive chemicals from natural sources is always time- and money-consuming. A computational molecular docking technique with the intended protein target can be used to focus on the type of compounds that need to be isolated, the type of phytochemicals that might be responsible for the pharmacological activities, and the type of compounds that have a specific target and specific inhibition mechanism (Zubair *et al.,* 2016).

AutoDock 1.5.6 (www. mgltools. scripps.edu) is a tool that combines a quick energy assessment using grids of affinity potentials that have been calculated in advance with a number of search methods to locate an appropriate binding location for a ligand on a specific macromolecule. This programme ensures the rigidity of the macromolecule while providing the ligand with torsional flexibility (Morris *et al.,* 1998).

The present study was conducted to analyse the interaction of phytocompounds of *Sida cordifolia* and *Eupatorium triplinervis* with Bcl2 which will help in the identification of lead compounds having anticancer activity.

Materials and methods

Softwares

Molecular Graphics Laboratory tools for AutoDock 1.5.6 (www. mgltools.scripps. edu) (Morris *et al.,* 2009) was used for the docking study. The ligands were modified using MarvinView 17.25.0 (www.chemaxon. com). OpenBabel 3.1.1 (O'Boyle *et al.,* 2011) was used for the chemical file format conversion. The docked conformations were visualized using Accelrys Discovery Studio® Visualizer 3.5.0.12158 (Copyright© 2005- 12, Accelrys Software Inc.) and LigPlot + version 2.2.4 (Laskowski and Swindells, 2011).

Preparation of macromolecule

From the RCSB protein data bank (http://www.rcsb.org) the crystal structure of the Bcl2 protein (PDB Id: 4LXD) was downloaded in pdb format. Using MarvinView, the structure was prepared (clean in 2D and 3D) for docking. The 3D structure of 4LXD is shown in Fig.1. For the preparation of ligand and receptor molecules, standard protocol and parameters recommended by AutoDock Tools tutorial were followed.

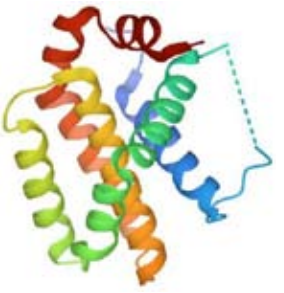

Fig. 1: 3D structure of Bcl2 protein (4LXD)

Preparation of ligands

Phytochemicals namely betaine, choline, coronaric acid, creptolepine, ephedrine, hypaphorine, malvalic acid, sitosterol, sterculic acid, stigmasterol, vascine, vascinol, vascinone and 4-methyl benzaldehyde from *S. cordifolia* were selected for the study. Herniarin, ayapin, borneol, cineol, α-phellandrene, sabinene, hexadecenoic acid from *E. triplinervis* were used for docking studies as ligands. From the PubChem Compound Database (National Centre for Biotechnology Information) (https://pubchem.ncbi.nlm.nih.gov/) chemical structures of selected phytochemicals were downloaded in the Spatial Data File (.SDF) format. The structures were modified in MarvinView and converted to Tripos Mol 2 file format. Ligand modifying tools of AutoDock Tool was used to prepare ligand structures in terms of root detection, the expansion of root as well as to choose the number of rotatable bonds. After the initial preparation, the ligands were converted to PDBQT format enabling its use with AutoDock4.

Docking methodology

For the docking studies, Autodock4 (Scripps Research Institute, La Jolla, CA: - www. autodock.scripps.edu) was used. Using AutoDock binding energy, ligand efficiency, inhibition constant, intermolecular energy, van der Waals interactions, electrostatic and

total internal energy were found. They were then used to analyze the relative strengths of the interactions. Binding energy and ligand efficiency were the most indicative of the overall strength of a given predicted interaction calculated by AutoDock. The grid map for docking studies was computed using AutoGrid4 that was included in the AutoDock4 package. The grid size was set at 54 × 46 × 44 (x, y, and z) points, and the grid centre was designated at x, y, and z dimensions of 20.143, 28.428 and -0.062, respectively, with a grid spacing of 0.631 Å, so that the already existing binding pockets, identified using LigPlot, were included in the grid. The prepared files were saved in the grid parameter file. The docking parameter files were generated with optimized parameters as recommended by the AutoDock Tool. The Lamarckian genetic algorithm was used for all docking runs, and the dock scores achieved were reported in Kcal/mol. The docking procedure used in the study included 10 independent genetic algorithm runs with an initial population of 150 randomly placed individuals, a maximum number of 250,000 energy evaluations, a crossover rate of 0.80 and mutation rate of 0.02.

Visualization of results

The post docking analysis was done with LigPlot and Discovery Studio Visualizer. Locations of binding sites, hydrogen-bond interactions, hydrophobic interactions, and bonding distances were analyzed. The conformation of ligands with least binding energy were chosen after observing their binding poses and characterizing their interactions with the protein.

Estimation of binding energy

The binding energy for the best docked confirmations for each molecule were obtained from the RMSD table in the docking log file and was expressed in Kcal /mol.

Results and discussion

In the present study, binding energies obtained from the docking studies of each compound is represented in Fig. 2. Table 1 represents the docking scores, their hydrogen bonds and hydrophobic interactions with corresponding amino acids in the receptor structure. The binding energy in KCal/mol (given in brackets) obtained for these compounds in the decreasing order were as follows: choline (-2.74), malvalic acid (-2.89), sterculic acid (-3.40), betaine (-3.47), coronaric acid (-3.59), hexadecenoic acid (-4.02), ephedrine (-4.44), 4-methyl benzaldehyde (-4.53), borneol (- 4.69), sabinene (-4.73), cineol (-5.08), herniarin (-5.11), α-phellandrene (-5.29), vascinone (-5.50), ayapin (-5.56), vascine (-5.57), vascinol (-5.69), hypaphorine (-6.11), creptolepine (-6.76), stigmasterol (-7.15), sitosterol (-7.47). The binding energy of standard drug, doxorubicin with Bcl2 (-6.92) is also displayed in Fig. 2.

Binding energy is defined as the sum of all intermolecular forces acting upon the receptor-ligand complex (Raj *et al.,* 2022). If the

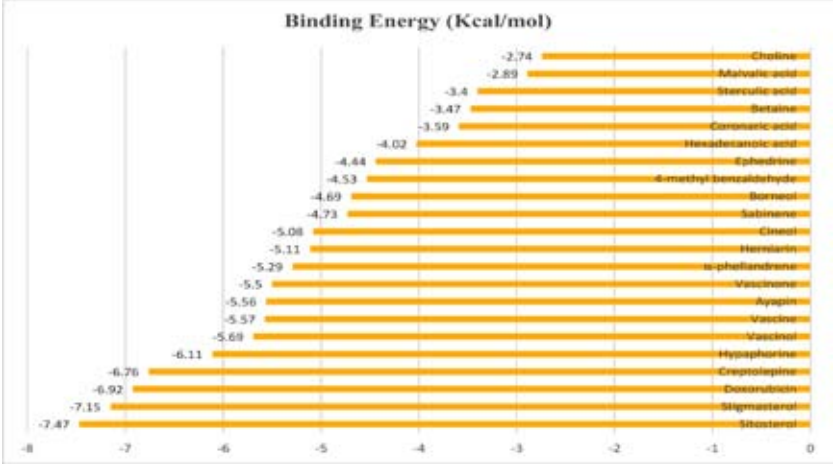

Fig. 2: Binding energies of various phytochemicals with Bcl2

Table 1 Docking score of phytochemicals with Bcl2 protein with the number of hydrogen bonds and hydrophobic interactions and the name and position of amino acid in the receptor.

Sl. No.	Phyto-chemicals	Pub Chem CID	Binding Energy	No. of Hydrogen bonds	Amino acids involved in Hydrogen bond	Amino acids with hydrophobic interaction
1	Betaine	247	-3.47	1	Arg 124 (A)	Ala 128 (A), Phe 127 (A), Tyr 177 (A), Trp 173 (A)
2	Choline	82143	-2.74	1	Tyr 105 (A)	Phe 109 (A), Glu 149 (A), Met 112 (A), Phe 150 (A), Ala 146 (A), Asp 108 (A), Phe 101 (A)
3	Coronaric acid	6246154	-3.59	1	Ala 146 (A)	Phe 150 (A), Phe 109 (A), Asp 108 (A), Met 112 (A), Gly 142 (A), Arg 143 (A), Leu 134 (A), Phe 101 (A), Glu 149 (A), Val 153 (A)
4	Creptolepine	82143	-6.76	0		Met 112 (A), Glu 133 (A), Phe 150 (A), Glu 149 (A), Phe 109 (A), Ala 146 (A), Ser 102 (A), Phe 101 (A), Asp 108 (A), Leu 134 (A), Val 130 (A)
5	Ephedrine	9294	-4.44	0		Val 153 (A), Phe 109 (A), Asp 108 (A), Phe 150 (A), Met 112 (A), Ala 146 (A), Phe 101 (A), Glu 149 (A), Ser 102 (A)
6	Hypaphorine	442106	-6.11	1	Ala 146(A)	Phe 150(A), Phe 101 (A), Glu 149 (A), Asp 108 (A), Phe 109(A), Val 130 (A), Glu 133 (A), Leu 134 (A), Met 112 (A)
7	Malvalic acid	10416	-2.89	1	Ala 146 (A)	Val 153 (A), Phe 150(A), Phe 109 (A), Met 112 (A), Arg 126 (A), Gln 115 (A), Glu 133 (A), Asp 108 (A), Phe 101 (A), Glu 149 (A)
8	Sitosterol	222284	-7.47	0		Met 112 (A), Gln 115 (A), Glu 133 (A), Leu 134 (A), Ala 146 (A), Val 153 (A), Glu 149 (A), Phe 109 (A), Phe 150 (A), Phe 101 (A), Asp 108 (A)
9	Sterculic acid	12921	-3.40	3	Leu 134 (A), Arg 143 (A)	Phe 150 (A), Phe 109 (A), Phe 101 (A), Glu 149 (A), Met 112 (A), Asp 108 (A), Glu 133 (A)
10	Stigmasterol	5280794	-7.15	1	Glu 149 (A)	Phe 150 (A), Val 153 (A), Asp 108 (A), Ala 146 (A), Leu 134 (A), Glu 133 (A), Glu 111 (A), Phe 101 (A), Met 112 (A), Phe 109 (A)
11	Vascine	387179541	-5.57	1	Ala 146 (A)	Phe 150 (A), Phe 101 (A), Phe 109 (A), Met 112 (A), Leu 134 (A), Val 130 (A), Asp 108 (A), Glu 149 (A)
12	Vascinol	442934	-5.69	2	Ala 146 (A), Val 130 (A)	Phe 150 (A), Phe 101 (A), Glu 149 (A), Phe 109 (A), Asp 108 (A), Met 112 (A), Leu 134 (A), Glu 133 (A)
13	Vascinone	442935	-5.50	1	Ala 146 (A)	Phe 150 (A), Val 130 (A), Leu 134 (A), Met 112 (A), Asp 108 (A), Glu 149 (A), Phe 109 (A), Phe 101 (A)
14	4-methyl benzaldehyde	193251	-4.53	0		Ala 146 (A), Phe 150 (A), Leu 134 (A), Val 130 (A), Phe 109 (A), Asp 108 (A), Ser 102(A), Phe 101 (A)
15	Herniarin	10748	-5.11	0		Leu 134 (A), Phe 150 (A), Glu 149 (A), Phe 109 (A), Phe 101 (A), Met 112 (A)
16	Ayapin	3083597	-5.56	0		Leu 134 (A), Val 130 (A), Met 112 (A), Phe 150 (A), Phe 101(A), Phe 109 (A)
17	Borneol	64685	-4.69	0		Val 153 (A), Tyr 105 (A), Phe 150 (A), Met 112 (A), Leu 134 (A), Ala 146 (A), Phe 109 (A), Asp 108 (A), Phe 101 (A), Glu 149 (A)
18	Cineol	2758	-5.08	0		Ser 102 (A), Glu 149 (A), Phe 101 (A), Phe 109 (A), Ala 146 (A), Leu 134 (A), Phe 150 (A), Met 112 (A), Asp 108 (A)
19	α-phellandrene	7460	-5.29	0		Glu 149 (A), Ala 146 (A), Phe 150 (A), Met 112 (A), Asp 108(A), Phe 109 (A), Tyr 105 (A), Ser 102 (A), Phe 101 (A)
20	Sabinene	18818	-4.73	0		Phe 101 (A), Val 153 (A), Ala 146 (A), Phe 150 (A), Met 112 (A), Phe 109 (A)
21	Hexadecenoic acid	985	-4.02	0		Asp 108 (A), Phe 150 (A), Glu 149 (A), Phe 109 (A), Phe 101 (A), Met 112 (A), Gly 142 (A), Arg 143 (A), Leu 134 (A), Ala 146 (A)

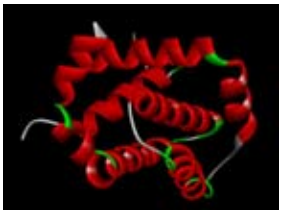

Fig. 3: Structure of Bcl2 (4LXD) in discovery studio

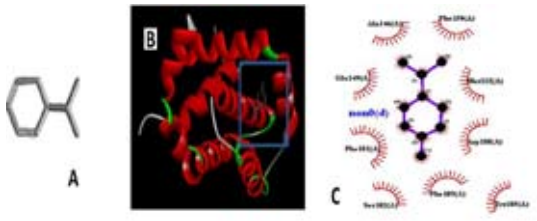

Fig. 4: A- α-phellandrene, B- Post docking interaction with Bcl2, C- Hydrophobic interaction

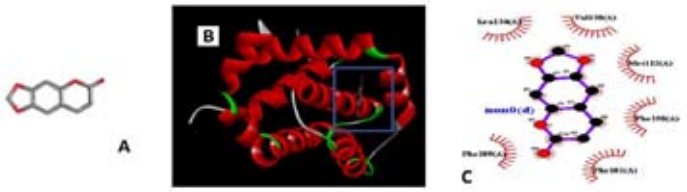

Fig. 5: A-Ayapin, B- Post docking interaction of ayapin with Bcl2, C- Hydrophobic interaction

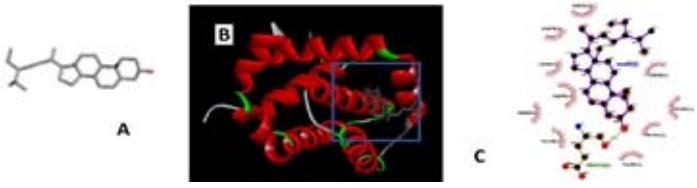

Fig. 6: A – Stigmasterol, B- Post docking interaction of stigmasterol with Bcl2, C- Hydrophobic interaction

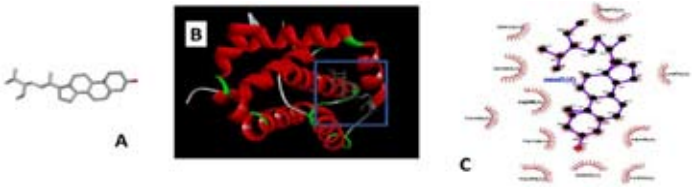

Fig. 7: A- Sitosterol, B- Post docking interaction of sitosterol with Bcl2, C- Hydrophobic interaction

binding energy is low for a docked compound, it indicates that those compounds have higher affinity. Doxorubicin, which was used as the standard compound, showed binding energy of -6.95 Kcal/mol with Bcl2. The compounds hypaphorine (-6.11 Kcal/mol) and creptolepine (-6.76 Kcal/mol) showed similar binding energies with that of doxorubicin. Stigmasterol and sitosterol showed better binding energies of -7.15 and -7.47 Kcal/mol when compared with doxorubicin. Hence it could be inferred that these compounds have more binding affinity to Bcl2 than doxorubicin. It has been reported that sitosterol have anticancer effects against MDA-MB-231 triple negative breast cancer (Awad *et al.,* 2003) and stigmasterol showed anticancer activity against ES2 and OV90 ovarian cancer cells (Bae *et al.,* 2020). Similarly, alkaloid cryptolepine possessed anticancer effects against non-melanoma skin cancer cell lines, SCC-13 and A431 (Pal and Katiyar, 2016). The results of the present study suggested that hypaphorine, creptolepine, stigmasterol and sitosterol from *S. cordifolia* could be further investigated for their anticancer potential. Among the various compounds from *E. triplinervis*, cineol, herniarin, α-phellandrene, ayapin showed binding energies ranging from -5.08 to -5.56 Kcal/mol. Gowtham *et al*. (2023) reported the binding energies of the docked compounds from *Wedelia trilobata* against Bcl2 protein ranged from -5.3 Kcal/mol

to -10.1 Kcal/mol. The previous studies had shown that herniarin from *E. triplinervis* and herniarin encapsulated solid lipid nanoparticles exhibited anticancer properties against mammary carcinoma in Sprague-Dawley rats and pancreatic cancer (Panc-1) cell lines respectively (Bose and Pattanayak, 2019; Delkhah *et al.*, 2023). Thus, it could be inferred that the compounds with binding energy of -5.0 Kcal/mol could be considered for their *in vitro* and *in vivo* evaluation for anticancer potential.

In silico tools have been used extensively in cancer drug discovery to identify compounds (hit and lead generation) which target different receptors in the Bcl2 family. The 3D structure of Bcl2 (Pubchem ID: 4LXD) is represented in Fig.3. The intrinsic or the mitochondrial pathway of apoptosis is regulated by the Bcl2 family of proteins which includes proapoptotic and anti-apoptotic proteins. The anti-apoptotic Bcl2 inhibit apoptosis through the inhibition of proapoptotic proteins. Molecular docking study conducted by Ismail *et al.* (2020) reported that sitosterol and stigmasterol had binding energies of -7.86 and -7.72 Kcal/mol respectively with Bcl2. While evaluating the effect of sitosterol on HepG2 cells Kim *et al.* (2014) reported that through the likely mitochondrial apoptosis signalling mechanism, stigmasterol had upregulated the expression of pro-apoptotic genes (Bax, p53), and downregulated the anti-apoptotic gene Bcl-2. According to the work conducted by Delkhah *et al.* (2023) the expression of Bcl2 was reduced in Panc-1 cell lines when treated with herniarin encapsulated solid lipid nanoparticles. Since the compounds creptolepine, hypaphorine, sitosterol and stigmasterol from *S. cordifolia* and cineol, herniarin, α-phellandrene and ayapin from *E. triplinervis* showed high binding affinity for Bcl2, it could be further interfered that these compounds could exhibit intrinsic or the mitochondrial pathway of apoptosis.

The results of hydrophobic interaction of α-phellandrene, ayapin, stigmasterol and sitosterol with Bcl2 is represented in Fig.4C, 5C, 6C and 7C respectively. All the compounds showed hydrophobic interaction with a range of 4 to 11 amino acids. Hydrophobic interactions increase the biological activity and binding affinity of complex molecules, as well as support the stabilisation of the target-drug complex biochemical surroundings (Patil *et al.,* 2010). Hence it could be inferred that these compounds may form stable complexes with Bcl2, thereby increasing the biological activity.

Among 21 different compounds docked, only 10 compounds formed H-bonds with Bcl2. Most of them formed H-bond with Ala 146 (A) of Bcl2. The H-bond is mainly an electrical interaction. The stabilisation of the ligands at the target site is facilitated by hydrogen bonds and enhanced hydrophobic interactions (Patil *et al.,* 2010). In the present study sterculic acid formed 3 H-bonds, vascinol formed 2 H-bonds, while others formed only 1 H-bond. Hence it could be inferred that all the compounds from *S. cordifolia* and *E. triplinervis* formed stable complexes at the target site.

Thus, the present molecular docking study revealed structural insights into the possible binding modes of major active compounds of *S. cordifolia* and *E. triplinervis* against Bcl2. Hence various solvent extracts from these two plants could be used to isolate these new leads for drug designing which would be useful in the management of cancer.

Conclusion

Over the past ten years, there has been a rise in the use of *in silico* techniques for natural product drug development. Numerous new avenues for research into the pharmacological action of plant preparations are now accessible owing to the development of chemo- and bioinformatics techniques and data on phytochemical structures. Bcl2 has a major role in the apoptosis of cancer. The present study on Bcl2 with 21 different compounds from two different plants, *S. cordifolia* and *E. triplinervis*, showed that most of the phytocompounds have good binding affinity to Bcl2. The compounds from *S. cordifolia* such as sitosterol and stigmasterol have lower binding energy than the standard doxorubicin which reveals the better association of these compounds with Bcl2. Among the compounds from *E. triplinervis,* α-phellandrene and ayapin had the lowest binding energy. *In silico* study revealed that these compounds might follow mitochondrial pathway of apoptosis. Hence, with this study we can conclude that phytochemicals from both

the plants can serve as new lead compounds for the development of novel drugs targeting Bcl2 protein. Also, further *in vitro* and *in vivo* studies are needed to validate the efficacy of these phytochemicals.

Conflict of interest

The authors declare that there are no conflicts of interest.

References

Awad, A.B., Roy, R. and Fink, C.S. 2003. β-sitosterol, a plant sterol, induces apoptosis and activates key caspases in MDA-MB-231 human breast cancer cells. *Oncol. Rep.* **2:** 497-500.

Bae, H., Song, G. and Lim, W. 2020. Stigmasterol causes ovarian cancer cell apoptosis by inducing endoplasmic reticulum and mitochondrial dysfunction. *Pharmcology,* **6:** 488-504.

Bose, P. and Pattanayak, S.P. 2019. Herniarin, a natural coumarin, inhibits mammary carcinogenesis by modulating liver X receptor-α/β-PI3K-Akt-Maf1 Pathway in Sprague-dawley rats. *Pharmacogn. Mag.* **3:** 510-519.

Delkhah, A.M.D., Karimi, E. and Farivar, S. 2023. Herniarin-loaded solid lipid nanoparticles: promising molecular mechanism and therapeutic potential against pancreatic cancer line. *Mol. Biol. Rep.* **50:** 6469-6479.

Gowtham, H.G., Ahmed, F., Anandan, S., Shivakumara, C.S., Bilagi, A., Pradeep, S., Shivamallu, C., Shati, A.A., Alfaifi, M.Y., Elbehairi, S.E.I. and Achar, R.R. 2023. In silico computational studies of bioactive secondary metabolites from wedelia trilobata against anti-apoptotic B-cell lymphoma-2 (Bcl-2) protein associated with cancer cell survival and resistance. *Molecules,* **28:** 1588-1597.

Ismail, N.Z., Annamalai, N., Zain, N.N.M. and Arsad, H. 2020. Molecular docking of selected compounds from *Clinacanthus nutans* with Bcl-2, p53, caspase-3 and caspase-8 proteins in the apoptosis pathway. *J. Bio. Sci. Opin.* **8:** 4-11.

Kim, Y.S., Li, X.F., Kang, K.H., Ryu, B. and Kim, S.K. 2014. Stigmasterol isolated from marine microalgae *Navicula incerta* induces apoptosis in human hepatoma HepG2 cells. *BMB Rep*. **8:** 433-438.

Laskowski, R.A. and Swindells, M.B. 2011. LigPlot+: multiple ligand–protein interaction diagrams for drug discovery. *J. Chem. Inf. Model*. **10:** 2778-2786.

Morris, G.M., Goodsell, D.S., Halliday, R.S., Huey, R., Hart, W.E., Belew, R.K. and Olson, A.J. 1998. Automated docking using a Lamarckian genetic algorithm and an empirical binding free energy function. *J Comput Chem* **19:**1639–1662.

Morris, G.M., Huey, R., Lindstrom, W., Sanner, M.F., Belew, R.K., Goodsell, D.S. and Olson, A.J. 2009. AutoDock4 and AutoDockTools4: Automated docking with selective receptor flexibility. *J. Comput. Chem.* **16:** 2785-2791.

O'Boyle, N.M., Banck, M., James, C.A., Morley, C., Vandermeersch, T. and Hutchison, G.R. 2011. Open Babel: An open chemical toolbox. *J. Cheminformatics*. **1:** 1-14.

Pal, H.C. and Katiyar, S.K. 2016. Cryptolepine, a plant alkaloid, inhibits the growth of non-melanoma skin cancer cells through inhibition of topoisomerase and induction of DNA damage. *Molecules*, **12:** 1758- 1776.

Patil, R., Das, S., Stanley, A., Yadav, L., Sudhakar, A. and Varma, A.K. 2010. Optimized hydrophobic interactions and hydrogen bonding at the target-ligand interface leads the pathways of drug-designing. *PloS one*. **8:** 12-29.

Raj, A., Nair, S.N., Abdulvahab, R. and Ittoop, G. 2022. In-silico modelling of interaction between environmental xenoestrogens and estrogen receptor of pacific oyster (*Magallana gigas* [Thunberg, 1793]) using auto dock. *Inform Studies*. **9:** 47-58.

Urruticoechea, A., Alemany, R., Balart, J., Villanueva, A., Vinals, F. and Capella, G. 2010. Recent advances in cancer therapy: an overview. *Curr. Pharm. Des.* **16:** 3–10.

Zubair, M.S., Anam, S., Khumaidi, A., Susanto, Y., Hidayat, M. and Ridhay, A. Molecular docking approach to identify potential anticancer compounds from Begonia (Begonia sp). In *AIP Conference Proceedings;* 2016, July. (Vol. 1755, No. 1, p. 080005). AIP Publishing LLC. ■