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Research Article

Molecular docking analysis of Bcl-2 with phyto-compounds

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Abstract:
The Bcl-2 protein is liked in several cancers and drug resistance to therapy is also known in this context. There are many Bcl-2 inhibitors under clinical trials. It is of further interest to design new Bcl2 inhibitors from phyto compounds such as artesunate, bruceantin, maytansin, Salvicine, indicine N-oxide, kamebanin and oxyacanthine. We report the optimal binding features of these compounds with Bcl-2 for further consideration towards *in vitro* and *in vivo* validation.

Keywords: Breast cancer, bioactive compounds, Bcl-2, molecular docking

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Background:
Cancer related issues **[1-6]** are linked to the BCL-2 family of proteins **[7-12].** BCL-2 is a known cancer target with several potential inhibitors under validation. Therefore, it is of interest to design and develop new compounds from plant source with improved binding features with the BCL-2 protein. Hence, we report the molecular docking analysis of Bcl-2 with phyto-compounds.

Methodology:
BCL-2 structure:
The structure data of Bcl-2 protein (PDB ID: 2W3L) was downloaded from the protein databank (PDB) **[13]** and processed for further analysis.

Ligand data:
The structures of phytocompounds such as artesunate, bruceantin, maytansin, Salvicine, indicine N-oxide, kamebanin, and oxyacanthine were downloaded from the pubchem database in SDF format and converted to PDB format using the Online Smiles Translator.

Active site prediction:
Binding site prediction of Bcl-2 was completed using MetaPocket 2.0 server **[14].**

Molecular docking:
PatchDock **[15, 16]** was used for the molecular docking analysis of BCL-2 with phytocompounds such as artesunate, bruceantin, maytansin, Salvicine, indicine N-oxide, kamebanin and oxyacanthine.

Results and Discussion:
BCL2 is a known cancer target. Therefore, it is of interest to design new Bcl2 inhibitors from phyto compounds such as artesunate, bruceantin, maytansin, Salvicine, indicine N-oxide, kamebanin and oxyacanthine. The predicted active site residues in BCL-2 are LYS 22, GLN 25, ARG 26, THR 55, ASP 62, SER 64, ARG 66, TYR 67, ARG 68, PHE 71, LEU 80, ARG 86, ASN 102, GLY 104, VAL 107 and GLU 111. The molecular docking analysis data of Bcl-2 with the phyto-compounds are given in **Table 1**. Detailed interaction between BCL-2 and the compounds are shown in **Figure 1**. The residues ARG 26, ARG 68, ARG 66, SER 64, ARG 86, ARG 68, GLY 104, LYS 22, SER 20, ASN 34, LYS 22, LYS 270, SER 351, ARG 469, and LYS 345 are found to be interacting with the phyto compounds (**Figure 1**). Thus, we report the optimal binding features of these compounds with Bcl-2 for further consideration towards *in vitro* and *in vivo* validation.

Conclusion:
We report compounds with improved binding features with Bcl-2 for further consideration towards *in vitro* and *in vivo* analysis.

Table 1: Molecular docking analysis of Bcl-2 with phyto-compounds

S. No	Compound Name	Score (kcal/mol)	ACE	Hydrogen bonds	Bond length	No of non-bonded interaction
1	Artesunate	4814	-211.33	ARG 26- NH-O	2.46	148
				ARG 68- NE-O	3.24	
				ARG 66- NH2-O	3.3	
2	Bruceantin	5714	-104.71	SER 64 OG-O	3.34	67
3	Maytansin	773.1	-110.4	ARG 86 NE-O	2.04	102
4	Salvicine	4946	-126.9	ARG 68 NE-O	2.17	131
				GLY 104 N-O	2.47	
5	Indicine N-oxide	4226	-130.62	LYS 22 NZ-O	1.75	37
				ARG 26 NH2-O	1.95	
6	Kamebanin	4002	-140.03	SER 64 OG-O	3.08	40
7	Oxyacanthine.	6368	-102	ARG 66 NE-O	2.79	31

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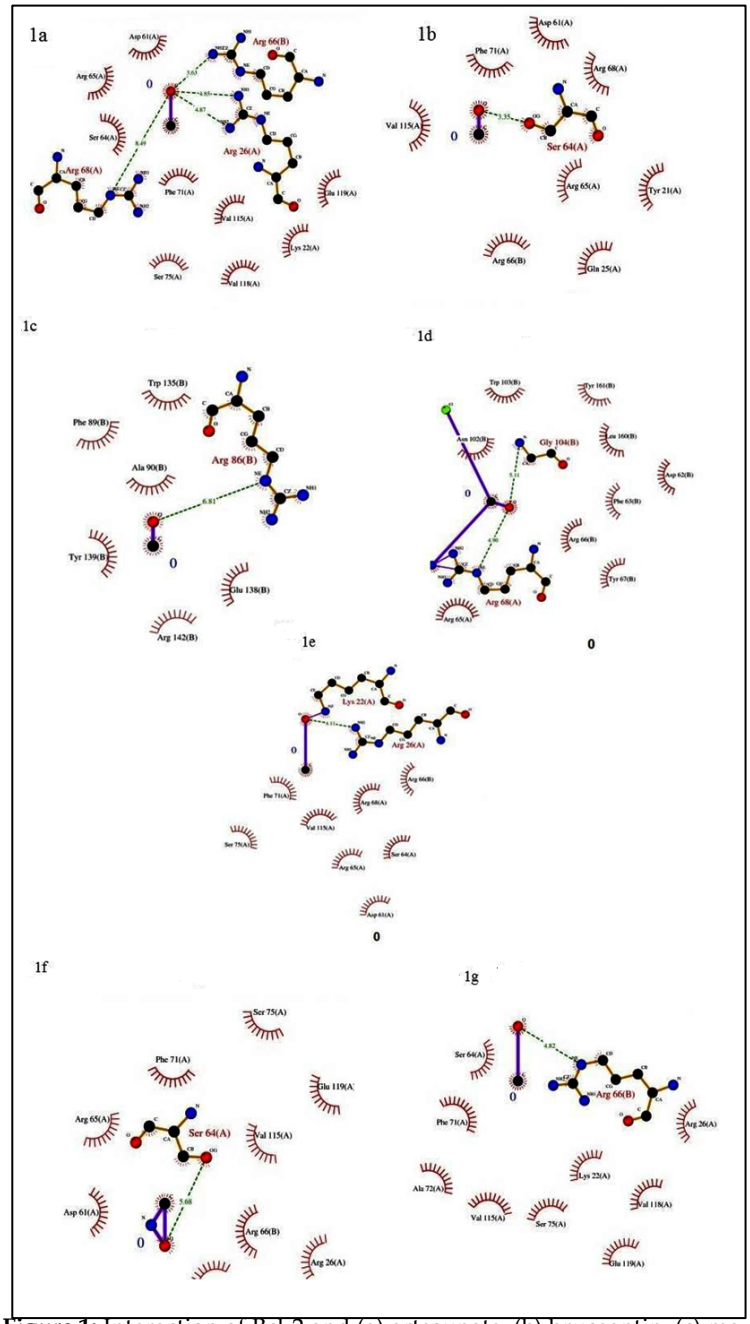

Figure 1: Interaction of Bcl-2 and (a) artesunate; (b) bruceantin; (c) maytansin; (d) salvicine; (e) indicine N-oxide; (f) kamebanin and (g) oxyacanthine is shown using ligplot.

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References:

[1] O'Shaughnessy J, *Oncologist.* 2005 10:20. [PMID: 16368868].
[2] Housman G, *Cancers (Basel).* 2014 6:1769. [PMID: 25198391].
[3] Rivera E *et al. Breast Cancer Res.* 2010 12:S2. [PMID: 21050423].
[4] Balunas MJ, *Life Sci.* 2005 78:431. [PMID: 16198377]
[5] Cragg GM *J Ethnopharmacol.* 2005 100:72. [PMID: 16009521]
[6] Newman DJ & Cragg GM, *J Nat Prod.* 2016 79:629. [PMID: 26852623].
[7] Roberts AW & Huang DCS, *Clin Pharmacol Ther.* 2017 101:89. [PMID: 27806433].
[8] Buolamwini JK Curr Opin Chem Biol. 1999 4:500. [PMID: 10419854]
[9] Lebedeva I *et al. Cancer Res.* 2000 60:6052. [PMID: 11085527]
[10] Kirkin V, *Biochim Biophys Acta* 2004 1644:229. [PMID: 14996506]
[11] Fernández Y *et al. Int J Cancer* 2002 101:317. [PMID: 12209955]
[12] Wang D *et al. Angew Chem Int Ed Engl* 2005 44:6525. [PMID: 16172999]
[13] Bernstein FC *et al. Arch Biochem Biophys* 1978 185:584. [PMID: 626512].
[14] Huang B, *OMICS* 2009 4:325. [PMID: 19645590].
[15] Schneidman-Duhovny D *et al. Proteins.* 2003 52:107. [PMID: 12784375]
[16] Schneidman-Duhovny D *et al. Nucleic Acids Res.* 2005 33:W363. [PMID: 15980490]

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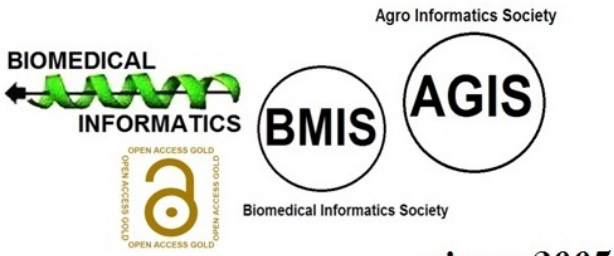

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