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Evaluating the Binding Affinity of Juglone on 1kms- An *In Silico* Approach

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Abstract

Cancer is one of the major causes of deaths seen in the humans. This is one of the major problems which have to be addressed with priority. There are many naturally available drugs for cancer. Juglone is a naturally available plant component which has a host of biological roles. This also has proven to be an anticancer drug. In the present article Juglone and Juglone compounds were docked with 1 KMS to evaluate their binding affinities.

Keywords: 1KMS, cancer, cancer drugs, Juglone, naturally available cancer drugs.

Introduction

Napthoquinone derivatives are known to have antibacterial, antifungal and antiviral properties besides exhibiting anticancer properties (1-5). Quinones represent a broad category of quinoid compounds in nature (6). One of the important quinone found in walnut trees is Juglone (5-hydroxy- 1, 4- naphthaquinone (7, 8). It is produced in roots, leaves and bark of walnut (7, 9). The immature exocarp of the walnut is used in the treatment of certain cancers like gastric cancer, liver cancer etc. (10). In 1998 Sugie reported that Juglone could inhibit the intestinal carcinogenesis in rats (11). In the year 2009, Ji Y-B, et al reported that Juglone could induce apoptosis in human gastric cancer (12). Juglone is a natural compound found in the roots, leaves, nut-hulls, bark and wool of Manchurian walnut (Juglands mandshurica), black walnut (Juglans nigra), walnut (Juglans regia) and butternut (Junglans cinerea) trees (13).

The objective of the present paper is to dock the Juglone with 1 KMS, a validate drug target for cancer and to access the binding affinities of the Juglone with 1 KMS.

Dihydrofolate Reductase (PDB ID: 1KMS), EC 1.5.1.3 is an enzyme with the molecular weight of 21.3 KDa. It bears 187 amino acids and is found in the q 11-q22 region of the chromosome 5 (14). DHFR also aids in the maintains the intracellular folate pool and thus maintains the one carbon transfer reactions. (15)

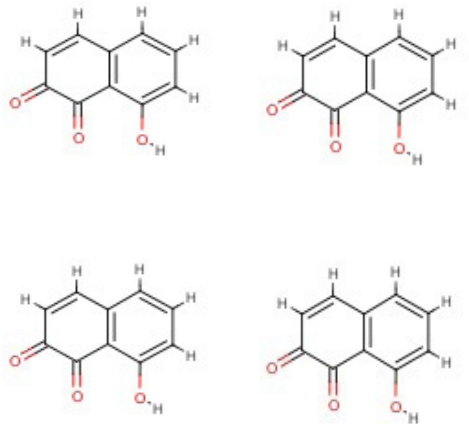
Materials and Methods:

Protein Selection:

The protein for the present study was selected from the Protein Data Bank (PDB). The protein was then downloaded and is imported onto the Molegro Virtual Docker (MDV).

Ligand Selection:

Juglone and similar compounds, the ligands for the present study is downloaded from PubChem compounds. They were then imported onto the Molegro.



Docking

Molegro virtual docker was used for the establishing the binding affinities of the Juglone compound with the 1KMS.

Results

The protein ligand docking showed the following results. The docking produced 20 poses.

Name	Ligand	MolDock Score	Rerank Score	HBond
[00]3806	3806	-98.6508	-81.1867	-9.64939
[01]3806	3806	-95.945	-78.9918	-9.52759
[02]3806	3806	-89.2107	-72.6325	-6.67935
[03]3806	3806	-89.0832	-52.2483	-8.12859
[04]3806	3806	-86.0643	-71.6499	-3.68512
[00]6011...	60116266	-95.425	-76.3107	-11.5137
[03]6011...	60116266	-92.5376	-74.723	-6.11936
[01]6011...	60116266	-92.2303	-71.6597	-11.4488
[04]6011...	60116266	-91.3136	-75.0891	-8.16302
[02]6011...	60116266	-90.7974	-73.9528	-5.95359
[00]6669...	66695376	-95.9152	-78.9919	-9.51146
[01]6669...	66695376	-92.0449	-61.2628	-8.37486
[02]6669...	66695376	Name: [00]66695376	-69.49	-8.60455
[04]6669...	66695376	Rank: 11	76.3062	-2.14545
[03]6669...	66695376	-86.0697	-71.6516	-3.69247
[00]7054...	70541023	-119.851	-95.2737	-9.86631
[02]7054...	70541023	-112.906	-87.6043	-8.83126
[01]7054...	70541023	-112.564	-90.8961	-4.08946
[04]7054...	70541023	-106.328	-86.6605	-4.28728
[03]7054...	70541023	-105.795	-86.202	-1.66524

Table 1: Dock Score

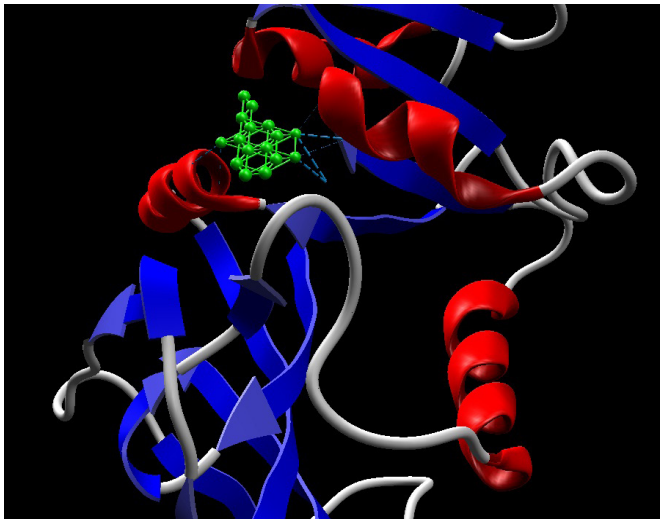


Figure 1: Protein – Ligand Docking

The compound 4 showed the highest MolDock score of -119.851.The results showed hydrogen bond interactions between the amino acids Serine 118, Serine 119, Threonine 56, Lysine 55.

Conclusion

Juglone is a naturally available plant compound which is reported to have anticancer property. It acts against gastric cancer, lung cancer and also against intestinal cancer. The present article could successfully prove the anticancer ability of the Juglone. It also concludes that among the four ligands taken, ligand fourth could be the potential drug for cancer.

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