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Molecular Docking Study of α-Cyclodextrin With Psoralen: MDA-MB-231 Cancer Cell

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ABSTRACT

Psoralen is an important bioactive component, isolated from the leaves of Ficus carica (Fig). Psoralen is proved to inhibit breast cancer cell growth and in tumor bearing mice the function of osteoblasts and osteoclasts is regulated. It is difficult to treat Triple-Negative Breast Cancer, a sub type of breast cancer. On treating Fig leaf extract, it is found that the leaf extract inhibits the proliferation of MDA-MB-231, which is a TNBC cell line, but not MCF10A cells, which is normal breast epithelial cell line. To increase the stability, solubility, volatility, it is beneficial to encapsulate natural products with α-Cyclodextrin (α-CD). Cyclodextrin constituted by 6 glucose units are termed as α-Cyclodextrin. Compared to host molecule guest: host inclusion complexes exhibit improved chemical or biological properties. Main aim of the study is interaction of Psoralen with α-CD and MDA-MB-231 Cancer cell with α-CD: Psoralen inclusion complex by molecular docking studies. 3D structures of Psoralen, α-CD and MDA-MB-231 cancer cell are obtained and docking is carried out using PatchDock server. Model which is highly favorable will have a high score. Energetically favorable and most probable structures of α-CD: Psoralen and MDA-MB-231 cancer cell: α-CD Psoralen inclusion complex has a score of 1762 and 6230 respectively.

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INTRODUCTION

Bioactive component, Psoralen is isolated from the leaves of ficus carica (fig) (Rashid *et al.*, 2017). Breast cancer cell, MDA-MB-231, growth is found to be inhibited by Psoralen, without affecting normal breast cell, MCF10A (Zhang *et al.*, 2018). Encapsulation of natural products leads to increase in stability volatility etc., encapsulation has various applications including core material is protected from degradation, modification of physical characteristics, mask unwanted flavor or taste (Sebaaly *et al.*, 2018). In cyclodextrin because of presence of pyranose ring, it has an internal hydrophobic cavity. External surface is hydrophilic due to presence of primary and secondary hydroxyl groups of glucose unit. CDs composed of 6 glucose units are called α-cyclodextrin. CDs composed of 7 glucose units are called β-cyclodextrin and CDs composed of 8 glucose units are called γ-cyclodextrin (Carneiro *et al.*, 2019). Inclusion complexes with α-CD improves solubility, physicochemical stability, shelf life of drugs, eliminate unpleasant taste and smell (Kfoury *et al.*, 2016). Docking studies implies the best association of molecular interaction if their structures are given separately. Last 3 decades provides many docking algorithms like Z-Dock (Chen *et al.*, 2002),

GRAMM (Vakser *et al.*, 1999), CAPRI (Inbar *et al.*, 2005) and GOLD (Jones *et al.*, 1997). The few web services are available for free nowadays (Comeau *et al.*, 2004). For protein protein docking efficient algorithm PatchDock has been developed. The best geometry based molecular docking algorithm is PatchDock, which gives good shape and molecular complementarity (Duhovny *et al.*, 2002). The evaluation is done by scoring function, which involves atomic desolvation energy and clear geometric fit (Zhang *et al.*, 1997).

Root mean square deviation value is applied to minimize the redundant solutions. PatchDock is highly efficient due to its run time less than 10 minutes.

The input is given in Protein Data Bank (PDB) file format. For result notification user e-mail is mandatory. Some non-mandatory fields are also present (Schneidman-Duhovny *et al.*, 2005).

Clustering RMSD

Proves that the distance between any two output solutions will be specified. The default value is 4s.

Complex Type

For different type of complexes, different parameters are optimized. The parameter set is optimized for small size molecules in case of protein-small ligand docking.

MATERIALS AND METHODS

Molecular docking study of α-cyclodextrin with Psoralen and MDA-MB-231 cancer cells with α-CD: Psoralen complex

Using PatchDock server the molecular docking studies were carried out for Psoralen; α-CD; MDA-MB-231 cancer cells and determined the most favorable structure. ChemSpider database enable us to obtain the structure of α-CD (Roselet *et al.*, 2017). The 3D structural data of Psoralen was obtained by translating its SDF format into PDB using PYMOL software. The 3D structural data of MDA-MB-231 cancer cell is obtained from Protein Data Bank using the search interface. PatchDock is used for docking the 3D structure of guest Psoralen into the host α-CD.

This server analyse the receptor (α-CD) and the ligand (Psoralen) and ranks them with a score. Similarly, MDA-MB-231 cancer cells acts as a receptor and the inclusion complex (Psoralen with α-CD) acts as ligand. The model with a high score is the best model and it is the energetically stable model.

RESULTS AND DISCUSSION

Docking of α-CD with Psoralen

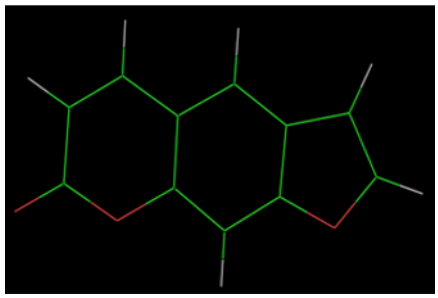

Figure 1: Structure of Psoralen

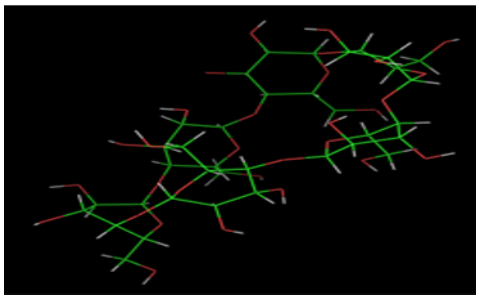

Figure 2: Structure of α-CD

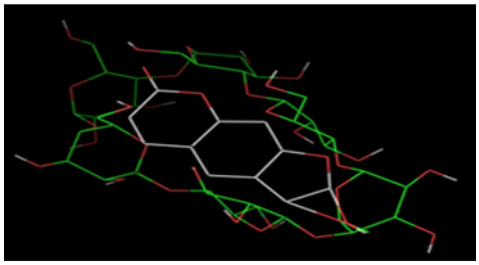

Figure 3: Structure of α-CD Psoralen inclusion complex

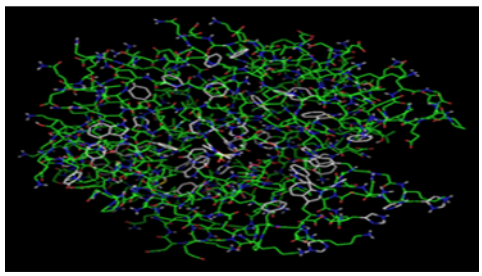

Figure 4: Structure of MDA-MB-231 cancer cell

The 3D structure of Psoralen is taken from PubChem server and is shown in Figure 1. The 3D structure of α-CD is taken from ChemSpider and it is shown in Figure 2. Psoralen, the guest molecule is docked into α-CD, the host cavity by PatchDock server. The docked structure is viewed by PyMol software. On taking into account the score, interacting area, atomic contact energy and transformation value, various structures are obtained. These values are given in Table 1. Out of which 8 values are chosen. The model with high score value of 1762 is shown in Figure 3 and the lowest score is 756.

Table 1: Set of Patch Dock results showing the docking structures of α-CD with Psoralen

Solution No	Score	Area	ACE	Transformation
1	1762	179.60	-105.41	-1.88 0.71 -1.02 -3.40 -4.77 0.16
2	1698	183.30	-105.25	1.67 -0.10 2.04 -2.29 -6.50 0.68
3	1590	171.90	-85.72	-1.98 -0.51 -1.22 -3.84 -3.49 2.43
4	1540	158.10	-91.67	1.43 -0.63 2.39 -4.59 -3.55 -0.74
5	1334	149.80	-76.96	-2.40 -0.98 -1.90 -2.32 -6.74 1.63
6	1226	128.60	-64.67	1.65 1.01 2.04 -4.68 -3.35 1.78
7	1176	120.20	-76.85	-1.15 1.20 -1.27 -4.95 -2.78 -3.21
8	756	82.10	-42.22	3.02 1.08 -1.15 -2.72 -7.72 2.84

*ACE: Atomic Contact Energy.

Table 2: Set of Patch Dock results showing the docking structures of MDA-MB-231 cancer cell with α-CD Psoralen inclusion complex

Solution No	Score	Area	ACE	Transformation
1	6230	707.40	-21.62	-2.74 -0.81 1.04 31.83 -6.10 3.04
2	5806	684.60	-36.61	2.10 0.89 -1.19 31.40 -5.08 4.29
3	5794	748.90	-20.16	1.38 1.07 2.37 31.07 -6.40 5.26
4	5790	670.90	-237.70	-1.48 -1.14 -0.16 24.63 6.38 7.95
5	5690	706.40	-211.08	-1.19 0.49 -3.08 25.08 -14.91 11.74
6	5658	691.00	-173.69	-1.82 0.40 1.55 26.73 -13.40 12.24
7	5652	729.70	-84.18	-2.83 0.51 -2.86 8.31 9.17 33.18
8	5648	669.90	-163.60	2.39 -0.03 0.87 12.06 5.86 35.56
9	5648	688.10	-39.24	-0.61 0.26 -0.42 31.25 -2.70 2.34
10	5630	677.30	-149.38	1.32 0.95 2.60 8.74 7.09 34.84

*ACE: Atomic Contact Energy.

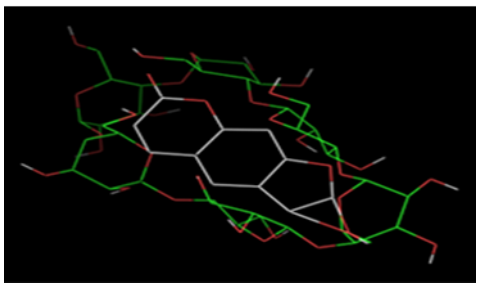

Figure 5: Structure of α-CD Psoralen inclusion complex

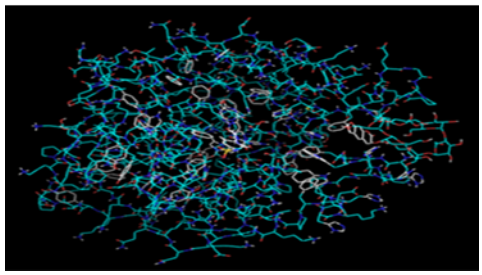

Figure 6: Structure of α-CD Psoralen inclusion complex with MDA-MB-231 cancer cell

Docking of MDA-MB-231 cancer cell with α-CD Psoralen inclusion complex

Figure 4 shows the 3D structure of MDA-MB-231 cancer cell obtained from Protein Data Bank. α-CD: Psoralen inclusion complex, Figure 5 is docked into MDA-MB-231 cancer cell, by PatchDock server.

The docked structure is viewed by PyMol software. Considering the score value, interacting area, atomic contact energy and transformation value, various structures are obtained and the values are provided in Table 2. Out of which 10 values are chosen. A

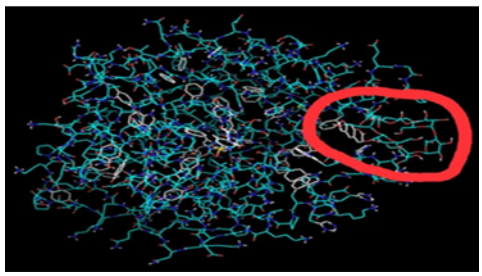

Figure 7: α– CD Psoralen inclusion complex docked with MDA-MB-231 cancer cell

score value of 6230 is taken as preferred model and is shown Figure 6 and Figure 7. 5630 is the lowest score value and is considered as the least favorable model.

CONCLUSIONS

The present study reveals the docking of α-CD with Psoralen and MDA-MB-231 cancer cell with α-CD: Psoralen complex. The study results are evaluated from score, interacting area, atomic contact energy values. The score value for α-CD: Psoralen complex is 1762, corresponding interaction area and atomic energies are 179.60Å and -105.41KJ/mol respectively. So this model is taken as the favored model. Similarly, the score value, interacting area and atomic energies of MDA-MB-231 cancer cell: α-CD Psoralen inclusion complex is 6230,707.40Å and -21.62KJ/mol respectively. Based on these values this model is considered as the preferred model.

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The authors declare that they have no funding support for this study.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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