Investigating the comparative effect of gemcitabine and capecitabine drugs on alpha –fetoprotein (AFP) by molecular docking method

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ABSTRACT

The aim of this study was to investigate the comparative effect of these drugs, Capecitabine and Gemcitabine, on their protein Alpha-fetoprotein (AFP) in Liver cancer. This was done by the method of Docking molecular, which was done using Pyrex and Chimera software. The positions of these drugs on the target protein were examined, and according to the RMSD and Binding affinity obtained from the placement of these drugs on AFP, it was concluded of Capecitabine that the binding affinity was more negative (-6.9) and the RMSD higher,(RMSD Lower case :21.327),(RMSD Upper case :22.401) has a better and greater effect on Alpha-feto protein .

Keywords: Alpha -fetoprotein, Gemcitabine and Capecitabine ,Liver cancer , PyRx, Chimera .

1. *INTRODUCTION*

Alph fetoprotein (AFP) is one of the proteins in the blood. This protein is produced during the embryonic peeriod in the yolksac and liver of the fetus,and it is the embryonic form of albumin, and this protein binds to copper,nickel,fatty acids, an d bilirubin. Alpha –fetoprotein has a glycoprotein structure and consists of 591 amino acids [1].
Visible froms of this protein exists in the blood in the form of three monomer forms ,dimeric and trimeric. Alpha –fetoprotein is not normally found in the blood of healthy men and non-pregnant women or its amount is very small ,except in some diseases such as liver cancer and germ cell tumors[2].

***Fig 1**. The structure of Alpha – fetoprotein (AFP)*

Gemcitabine (brand name Gemzar) is injected into the body and is used to treat certain types of cancer , including breast ,lung ,ovarian , pancreatic , and liver cancer. Gemcitabine is a chemotherapy drug that slows down or stops the growth of cancer cells . The does and amount of Gemcitabine different from person to person .Therefore,the medicine exactly use as prescribed by your doctor.

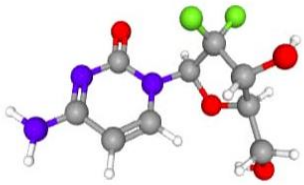

Fig 2. *Three – dimensional structure of Gemcitabine*

Capecitabine (brand name Xeloda) belongs to a group of drugs called cytotoxic drugs that stop the growth of cancer cells . Zelorak contains capecitabine , which is not a cytostatic drug by itself , and after being absorbed by the body , it become an active anti –cancer drug . This drug is used to treat breast , colon,rectal (anal) and liver cancer . This drug is avaliable in the tablet from in doses of 150 and 500mg .

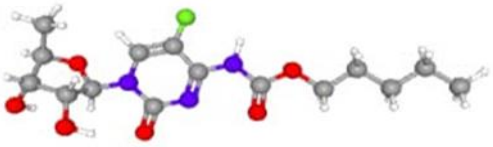

Fig 3*. Three – dimensional structure of Capecitabine*

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2. *HOW TO DO THE WORK:*

To campare the effects of Gemcitabine and Capcetabine drugs on (AFP) protein .the causative agent of liver cancer, first we downloaded the structural form of alpha-fetoprotein from Uniprot website in PDB format , then using Chimera software for determinded the number of chains of this protein and among the chains we chose the big chain,since (AFP) has two chains , one very small and the other very big . We chose the big chain as the desired chain , then checked and saved the final protein title in PDB format.

After that using Pubchem site for save the three –dimensional structure of Gemcitabine and Capecitabine drugs in SDF format , we saved the form of the file , and in the last step using PyRx software and checked the possibility of connecting the drug to the protein.

How to work with PyRx software : For this first we selected the structure of the protein stored in PDB format from the file section of the Molecular load option after doing this by right –clicking on the protein file , we converted it into a micromolecule to place the drug on the protein on the part we clicked file and selected the Import option and selected the three –dimensional shape of the drug in SDF format , then to change the drug format click convert to PDB qt and then choose the Minimize for change from SDF to PDB. After this we selected Vina wizard and then click on Forward and check the Gemcitabine drug in terms of the drug in different parts of the protein.

In the last step of this work , we selected the Forward option and waited to do the docking of the drug . After the complection of the docking operation ,we compared the resulting data table.

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Table1. *Data obtained from the docking of Capecitabine drug on alpha-fetoprotein of the causative agent*

Ligand	*Bonding Affinity(kcal.mol)*	*Mode*	*RMSD Lower bound*	*RMSD Upper bound*
Final-AFP-60953-uff-E341.24-	*-6.9*	*0*	*0.0*	*0.0*
Final-AFP-60953-uff-E341.24-	*-6.8*	*1*	*16.1*	*17.773*
Final-AFP-60953-uff-E341.24-	*-6.7*	*2*	*15.8*	*17.301*
Final-AFP-60953-uff-E341.24-	*-6.6*	*3*	*20.337*	*22.775*
Final-AFP-60953-uff-E341.24-	*-6.5*	*4*	*19.921*	*21.199*
Final-AFP-60953-uff-E341.24-	*-6.4*	*5*	*2.25*	*2.511*
Final-AFP-60953-uff-E341.24-	*-6.4*	*6*	*19.934*	*22.381*
Final-AFP-60953-uff-E341.24-	*-6.2*	*7*	*16.451*	*19.089*
Final-AFP-60953-uff-E341.24-	*-6.1*	*8*	*21.397*	*22.401*

Table2. *.Data obtained from the docking of Gemcitabine drug on Alpha –fetoprotein of the causative agent*

Ligand	*Bonding Affinity(kcal.mol)*	*Mode*	*RMSD Lower bound*	*RMSD Upper bound*
Final-AFP-60750-uff-E341.24-	*-6.0*	*0*	*0.0*	*0.0*
Final-AFP-60750-uff-E341.24-	*-6.0*	*1*	*23.011*	*24.194*
Final-AFP-60750-uff-E341.24-	*-5.9*	*2*	*15.555*	*16.624*
Final-AFP-60750-uff-E341.24-	*-5.8*	*3*	*23.036*	*24.027*
Final-AFP-60750-uff-E341.24-	*-5.8*	*4*	*22.651*	*24.079*
Final-AFP-60750-uff-E341.24-	*-5.6*	*5*	*2.309*	*3.506*
Final-AFP-60750-uff-E341.24-	*-5.6*	*6*	*2.902*	*5.499*
Final-AFP-60750-uff-E341.24-	*-5.6*	*7*	*21.405*	*22.627*
Final-AFP-60750-uff-E341.24-	*-5.5*	*8*	*23.294*	*24.414*

3. CONCLUSION

*According to the docking results , it was found that Capecitabine has a more negative binding affinity and better RMSD compared to Gemcitabine and has a better effect on (AFP) target protein and a better effect for contro*l ,*Capecitabine has (Binding Affinity: -6.9) and Gemcitabine has (Binding Affinity : -6.0).*

REFERENCES:

[1] *Drug information was collected from the following site:* https://arvin-center.com/cancer-medicine/.

[2] *Uniprot – P02771AFP – Homo sapiens (Human):* https://www.uniprot.org/uniprotkb/P02771/entry.

[3] *Pubchem- structures of Gemcitabine :* https://pubchem.ncbi.nlm.nih.gov/compound/60750#section=3D-Conformer.

[4] *Pubchem- structure of Capecitabine*: https://pubchem.ncbi.nlm.nih.gov/compound/60953#section=3D-Conformer.