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RESEARCH ARTICLE

MOLECULAR DYNAMICS SIMULATION OF PALMITOYEL – CO A HYDROLASE INTERACTION WITH FMN ، CLOFIBRATE و 2,4- DICHLOROPHENOXY ACETIC ACID LIGANDS

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ABSTRACT

In the enzymology, the palmitoyl – co a hydrolase is said to the enzyme that hydrolase the fatty acid. For this enzyme polmitoyl – coa and water are considered. According to available reports this enzymes are effective in regulating of intracellular concentration of acyl coa, fatty acid and co ezyme. Beside the design and construction of effective inhibitors for disabling of enzyme, the study of interaction of enzyme on the inhibitor by using of computational methods in presenting the acceptance model for performance. In the present study the effectiveness of inhibitors named Ibuprofen, Niacin, FMN. On the palmitoyl – co a hydrolase by codes of 3.1.2.2 and by using of dynamics. Molecular computational were simulated and were studied. Simulation in the condition that was similar to the physiological condition in the aquatic environment the temperature of 37 and the pressure of 1 atmosphere was conducted. Then doing the required parameters molecular dynamic from trajectory and extraction simulation and analyzing of results were done. FMN by reducing of irregular rate of RMSD and increasing of accessible level of solvent, regular structures of alpha and Beta are weakest inhibitor were recognized.

INTRODUCTION

Molecular modeling is a way to follow the behavior of one molecule or a set of molecules. Molecular modeling is a strong tool to consider molecular behaviors in such scale inavailable by experimental studies (1). Proteins almost do all of biological processes. Knowing proteins exactly need to know about thermodynamical, operational and structural properties, and also it is required to have some technologies available to appoint the properties. Since Palmitoyel – Co A hydrolase uses long chain acyl Co A sters a sobestra, it is considered to be severe effective on molecular concentration of these compounds and is intended to connect to the long chain of acyl Co A 12-22 carbonate fat acids; and acts for it more particular. Also it plays an essential role in processes such as restoring and transferring the long chain of acyl Co A (2). Oxidation the fat acids is continued inter Mythocondries after passing through the Mythocondry membrane and so any interface in transferring the long chain of acyl Co As leads to severe default in operation of methabolizing tissues of the fat acids in body. Interface of fat methabolysm by diabetes in body may be established by intermolecular concentration of these compounds (2 & 3). It is considerable to investigate inhibitors of Palmitoyel – Co enxyme A hydralase and setting value and carrying the intercellular of acyl CoA long chains has an improved role protecting the tissue operation.

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Planning and making more effective inhibitors to inactivate the enzyme by using computational methods, so presenting acceptable model for the operation and justifying the action reaching the inhibitors will be more effective. Idea microscopic behavior simulation a set of atoms by using molecular dynamics simulation method in computer was presented by Fermi in 1940. But the first applied simulation with this method was done by Elder and Vineryte in 1957. The next effective step was done by Raman studying liquid Argon gas utilizing more real potential. Possibility of simulation of more complicated systems extendingnumbers and authority development during 70th decade was prepared. Nowadays, protein complexes DNA, protein compounds and Nocleid lipid acids,…are found too much (4 & 5).

(2,4-Dichlorophenoxy) acetic Acid [2,4-D]

On May 16, 2008, Health Canada's Pest Management Regulatory Agency (PMRA) concluded its re-evaluation of 2,4-dichlorophenoxyacetic acid (2,4-D), RE-EVALUATION DECISION, determining that the herbicide can be used safely according to label directions for a variety of lawn, turf, industrial, forestry and agricultural applications. After a thorough re-evaluation of the herbicide (2,4-dichloro phenoxy)acetic acid [2,4-D], Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the Pest Control Products Act and Regulations, has decided to allow continued registration for the sale and use in Canada of certain products containing 2,4-D.

Products containing 2,4-D do not pose unacceptable risks to human health or the environment. They also have value for lawn and turf, agriculture, forestry and industrial uses when used according to the label directions proposed in previous consultation documents. As a condition of the continued registration of these 2,4-D products, new risk-reduction measures must be included on product labels. In addition, registrants must submit additional confirmatory scientific information, identified in this document. Some products and uses of 2,4-D are being phased out because the risks exceed current health and environmental standards or there was a lack of adequate data for assessment. This includes all products containing the diethanolamine (DEA) form of 2,4-D and products for aquatic uses. The regulatory approach for the re-evaluation of 2,4-D was proposed in two consultation documents. Proposed Acceptability for Continuing Registration PACR2005-01, Re-evaluation of the Lawn and Turf Uses of (2,4-Dichlorophenoxy)acetic Acid[2,4-D] Proposed Acceptability for Continuing Registration PACR2007-06, Re-evaluation of the Agricultural, Forestry, Aquatic and Industrial Site Uses of (2,4-Dichlorophenoxy)acetic Acid [2,4-D].

A summary of the comments received in response to the consultation on lawn and turf uses, and PMRA's responses to those comments is presented in Re-evaluation Note REV2006-11, Lawn and Turf Uses of (2,4-Dichlorophenoxy)acetic Acid [2,4-D]: Interim Measures. This Re-evaluation Decision document2 describes this final stage of the PMRA's re-evaluation of 2,4-D and summarizes the Agency's decision and the reasons for it. Appendix I includes a summary of comments received during the consultation process for non-turf uses, and the PMRA's response to these comments. This decision is consistent with the proposed re-evaluation decisions stated in Proposed Acceptability for Continuing Registration documents PACR2005-01 and PACR2007-06 and Re-evaluation Note REV2006-11. To comply with this decision, registrants of products containing 2,4-D will be informed of the specific requirements affecting their product registrations and of the regulatory options available to them. Two types of explants, leaf and pith, and two auxins, 2,4-dichlorophenoxy acetic acid and indole-3-acetic acid, were tested to optimize callogenesis for root establishment. Leaves as explants with 3.0 mg/L 2,4-dichlorophenoxy acetic acid gave the best results, both for callus induction and proliferation. Half-strength Murashige and Skoog medium with 1.5 mg/L indole-3-butyric acid proved to be the best for rooting. Red rot-resistant somaclones of the R2 generation along with the parent were assessed for genetic variability at the molecular level using RAPD and SSR markers. Polymorphism based on RAPD and SSR was 32 and 67%, respectively. Polymorphic information content ranged from 0.06-0.45 for RAPD and 0.06-0.47 for SSR. We conclude that somaclonal variation of sugarcane varieties is sufficient to allow selection.

MATERIALS AND METHODS

1- Palmitoyel – co A hydrolase enzyme:

In enzymology, Palmitoyel – co A hydrolase 2 is such enzyme to catalyze the following chemical reaction (7).

$$CoA + palmitate \rightleftharpoons palmtoyl - CoA + H_2O$$

This enzyme is called systematically, palmitoyl-CoA hydrolase. The most value of this enzyme is found in sitozul, mythocondry, proxim 1 and Endoplasm net of heart and brain – different animals, bacteries and plants (8). The most rich source of this enzyme is mouse s brain (6 & 9). Enzyme inhibitors:

1) 2&4 Dichlorophenoxy acetic acid formulated by:$C_8H_6Cl_2O_3$
2) Clofibrate formulated by :$C12H_{15}ClO_3$
3) Flavin mononucleotide (FMN) formulated by;$C_8H_6Cl_2O_3$

The case study research stages

At first, structural file of enzyme was found from database (www.rscb.org) in pdb after opening in word pad and cancelling water molecules and others (HETATM), we restore it for doing next stages by hex software. A suppose dyking was done to recognize locations of the palmytoyl CoA enzyme connected to it which are connected to the enzyme having energies of the ligands, we restore the most stable state for doing next stage in pdb. We add drug structural file to protein structural file and then minimize to obtain the dtug and enzyme optimized structure. In this stage we apply location limitation for 20ps considering to rest time of 10ps. Here to apply temperature and pressure in Brendsen method, we use algorithm of linear limitation for all of joints to remain fixed. To simulate molecular dynamics without any location limitation, we prepare file for mdrun command in this stage (full. Mdp) and set its time 2000ps and time step 0.001ps, we get radius of the section as 1.4nm.

CONCLUSION AND DISCUSSION

The main result obtained from simulation of considering irregular structure of the enzyme is as the following diagram.

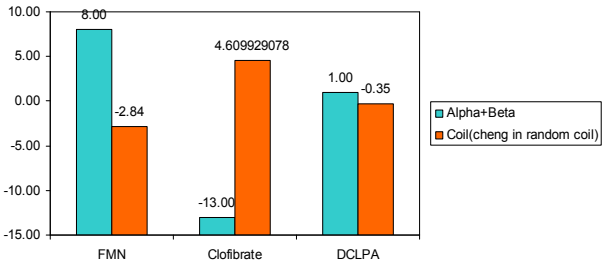

Fig. 1 Statistics of regular and irregular structure of simulated enzyme

Effect of inhibitors on the second structure of α co chains and β co planes what having increasing trend associated to the inhibitor weakening. The above figure shows effect value in irregular structure (coil) of protein after and before simulation. The main result obtained from considering RMSD variations of inhibitors in simulated system are as the following figures.

As it is observed in the above figure, variations of strong inhibitors RMSD is more than weak ones and we could conclude more fastened movement of these inhibitors. We could conclude from the two diagrams that the strongest inhibitor, Clofibrate, includes less accessible surface rather than weak ones like Fmn. In the other words, it causes cancelling hydrofub forces and increasing folding of protein while effects on accessible surface is similar to strong inhibitors like DCLPA.

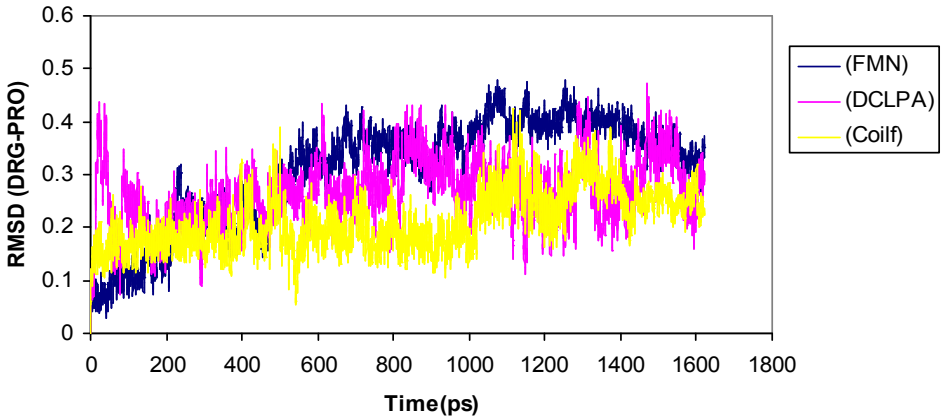

Fig. 2. RMSD variations of inhibitors in simulated system

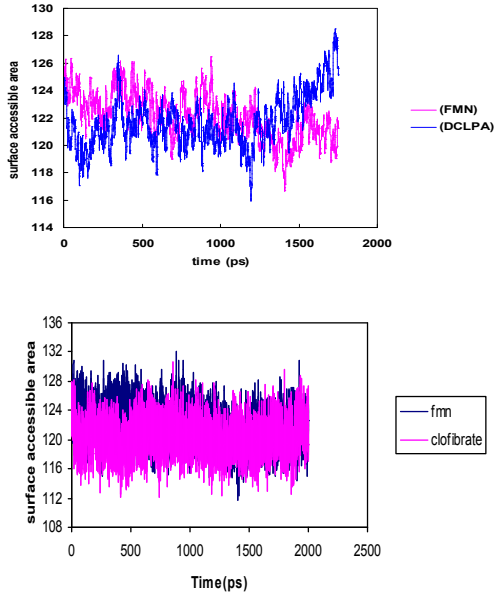

Fig.3. Accessible surface of the simulated enzyme

REFERENCES

[1 Leach, A. (2001) Molecular modeling, Principle and Application, Scond edition. Prentice Hall.

[2] Diego FG,Vallejo J,Marcelo D.2007.A hydrophobic loop in acyl-coa binding protein is functionally important for binding to palmitoyl – coenzyme a :amolecular dynamics study. *Journal of Biological Macromolecules,* 42:271-277

[3] Yamada J, Kuramochi Y,Takoda M,Takagi M, Suga T ,2003.Hepatic induction of mitochondrial and cytosolic acyl- coa thioestterasees / hydrolases in rats under conditions of diabetes and fasting. *Journal of Metabolism Clinical and Experimental,* 52:1527-1529

[4] http://en. Wikipedia.org/wiki/template

[5] Wilfred E van Gunsteren , Herman J. C. Berendsen,1990. Computer Simulation of Molecular Dynamics: Methodology, applications, and aerspectives in chemistry. *Journal of AnRFn,. Chem. hi. Ed. Engr.*, 28:992-1023.

[6]]http://www.ch.embnet.org/MD_tutorial/pages/MD.Part1.html

[7] Hunt M,Alexson S, 2002. The role Acyl-CoA thioesterases play in mediatingintracellular lipid metabolism. *Journal of Progress in Lipid Research,* 41:99-130.

[8] Kirkby B, Roman N, Kobe B, Kellie S, Forwood K. [8] 2011,Functional and structural properties of mammalian acyl-coenzyme A thioesterases, *Journal of Progress in Lipid Research,* doi:10.1016/j.plipres.2010.04.001

[9] Knauer T , 1978. Factors Affecting the activity and stability of the palmitoyl- coenzyme A hydrolase of rat brain. *Journal of Biochem.,*179,515-523.

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