Computers in Biology and Medicine 43 (2013) 1732–1738

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/cbm

Computational evaluation on the binding affinity of non-specific lipid-transfer protein-2 with fatty acids

Mojtaba Tousheh [a], Mehran Miroliaei [a,*], Ali Asghar Rastegari [b], Kamran Ghaedi [a], Abolghasem Esmaeili [b], Adam Matkowski [c]

[a] Department of Biology, Faculty of Sciences, University of Isfahan, Isfahan, Iran
[b] Department of Molecular and Cell Biochemistry, Falavarjan Branch, Islamic Azad University, Isfahan, Iran
[c] Department of Pharmaceutical Biology and Botany, Medical University of Wroclaw, ul. Borowska 211, PL-50556 Wroclaw, Poland

ARTICLE INFO

Article history:
Received 24 April 2013
Accepted 18 August 2013

Keywords:
Lipid binding proteins
Fatty acids
Drug carriers
Protein Data Bank

ABSTRACT

A computational study was carried out to identify the structural determinant controlling the affinity, specificity and binding strength of several saturated and unsaturated fatty acids with *Oryza sativa (Indica group)* nonspecific lipid transfer protein (nsLTP2). Association between the number, position and conformation of hydrophobic patches and lipid binding properties of the protein was evidenced by docking analysis. Binding affinity is influenced by the number of carbon atoms, location of double bonds and hydroxyl group in the acyl chain. The results may direct at developing applications in LTP-mediated transport and controlled release of low molecular weight drugs.

© 2013 Elsevier Ltd. All rights reserved.

1. Introduction

Lipid transfer proteins (LTPs) are typically present in the majority of prokaryotic and eukaryotic cells [1] such as bacteria, yeasts, plants and animals [2]. Plant nsLTPs are basic (with pI 8–10) disulfide-rich proteins divided into two subfamilies; nsLTP1 (~9 kDa) and nsLTP2 (~7 kDa) [3,4]. While both proteins have comparable lipid transfer activity, greater stability of nsLTP2 has been proved [5]. Due to their main biological activity, lipid transportation across bio-membranes *in vitro*, nsLTPs have received much attention from pharmaceutical viewpoints. Owing to the ability of LTPs in promoting the movement of lipids other than phospholipids, clarification of the underlying mechanisms and specificities would be essential to development of LTP-mediated transport systems and controlled release of low molecular weight drugs. A potential role of LTPs in designing efficient drug delivery systems has been suggested [6,7]. Their actual biological roles are diverse, including participating in developmental processes and pathogen resistance [8]. Of the two main isoforms, plant nsLTP1 has been studied more frequently and its structure, function and binding properties are well characterized [9,10]. Computational studies on nsLTP1 revealed that the insertion of various lipids into the cavity does not necessarily induce significant structural changes with an exception of a prostaglandin. Proteins from various species also varied in terms of molecular surfaces and electrostatic potentials as well as the ability to bind negatively charged lipids. The lack of specificity of ligand binding is suggested to result from nonspecific character of van der Waals interactions [10].

Rice nsLTP2, builds of 69 amino acids and has smaller size, higher structural stability, different disulfide bond pattern and less than 30% sequence similarity with nsLTP1 [11]. Samuel et. al. have performed molecular docking of stearic acid into both LTP1 and LTP2 cavity, demonstrating marked differences between the two isoforms in accommodation of the fatty acid chain in the protein active site. These authors have also reported that there is a tunnel-like hydrophobic cavity running through the whole molecule of rice LTP2 [11]. Despite established beneficial capacities of nsLTP2 to drug delivery [12,13] it has not been identified how the plasticity of the protein cavity may help in fitting of diverse molecular shapes and sizes. The aim of the current study was to carry out a computational analysis to identify the binding strength, affinity and specificity of LTP2 from *Oryza sativa* with a number of saturated and unsaturated fatty acids which are known to be necessary substrates for the formation of cutin. Such structural model promotes our understanding of the nsLTP2 binding affinities in terms of specificity, binding site flexibility and preference towards various molecules containing acyl chains (phospholipids, fatty acids, acyl CoA or other acyl group containing molecules) and low molecular weight drugs.

2. Materials and methods

2.1. Three dimensional structure prediction

The amino acid sequences of *O. sativa* (Indica group) nsLTP2 (Accession no. A2XBN5.2) were obtained from SWISS-PROT database

* Corresponding author. Tel.: +98 311 793 2479; fax: +98 311 793 2456.
E-mail addresses: mmiroliaei@yahoo.com, mmiroliaei@sci.ui.ac.ir (M. Miroliaei).

0010-4825/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.compbiomed.2013.08.012

and verified in Protein Data Bank (PDB) (www.rcsb.org). The protein contains 96 amino acid residues, of them 27 residues in C-terminus that provide a signal peptide was removed from the mature protein structure. Due to the lack of crystal and three dimensional structure of *O. sativa* nsLTP2, M4T Server version 3.0 (http://manaslu.aecom.yu.edu/M4T/) was implemented. To prediction of three dimensional structure of nsLTP2, a comparative modeling was performed by utilizing combination of multiple templates and iterative optimization of alternative alignments [14]. The crystal and three dimensional structure of nsLTP2 (PDB ID: 1l6h) was applied as a similar template with minor differences in two amino acid residues. Higher the total energy, less stable the protein structure will be. To depict the *in vivo* interaction, we have minimized the energy of the target protein before performing the docking operations. Energy minimization for 3D structures was performed by Yet Another Scientific Artificial Reality Application (YASARA) [15]. Predicted three

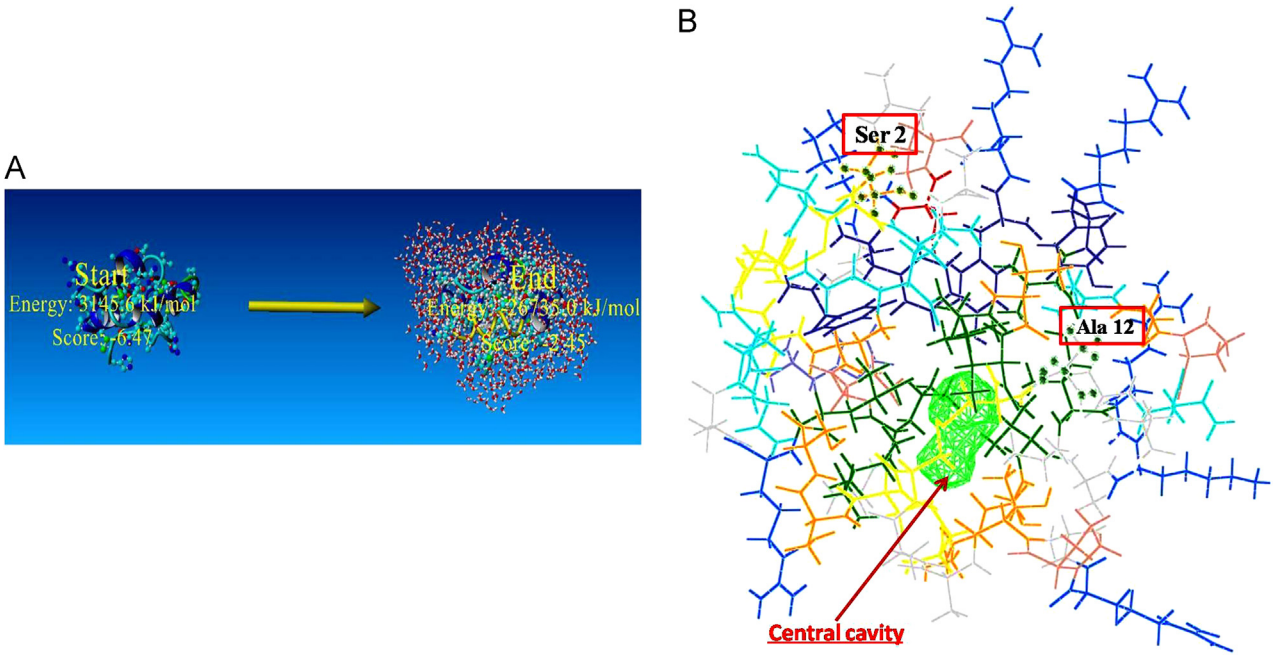

Fig. 1. Three dimensional structure of nsLTP2 before and after minimization with energy values (A). Wireframe model of rice nsLTP2 (indica variety). The hydrophobic central cavity is shown in the model in black color. Two amino acid residues, Ser2, Ala12, which are boxed, are different in nsLTP2 (Japonica variety) (B).

Table 1
Names and characteristics of fatty acids.

ChemSpider & Pubchem ID No.	Common name	Carbon atoms	Double bonds	Scientific name
259	Butyric acid	4	0	Butanoic acid
8552	Caproic acid	6	0	Hexanoic acid
370	Caprylic acid	8	0	Octanoic acid
2863	Capric acid	10	0	Decanoic acid
3756	Lauric acid	12	0	Dodecanoic acid
10539	Myristic acid	14	0	Tetradecanoic acid
960	Palmitic acid	16	0	hexadecanoic acid
CID 10466	16-Hydroxypalmitic acid	16	0	16-Hydroxy-, omega-Hydroxypalmitic acid
393216	Palmitoleic acid	16	1	9-Hexadecenoic acid
CID 445638	Cis-Palmitoleic acid	16	1	9-Cis-Hexadecenoic acid
CID 5282745	Trans-palmitoleic acid	16	1	9-Trans -hexadecenoic acid
CID 5312762	16-Hydroxy-9- trans-hexadecenoic acid	16	1	16-Hydroxy-9E-hexadecenoic acid
5091	Stearic Acid	18	0	Octadecanoic acid
393217	Oleic acid	18	1	9-Octadecenoic acid
558800	Ricinoleic acid	18	1	12-Hydroxy-9-octadecenoic acid
4444571	Vaccenic acid	18	1	11-Octadecenoic acid
4444105	Linoleic acid (*cis*,*cis*-Δ^{9},Δ^{12})	18	2	9,12-Octadecadienoic acid
4445609	Linoelaidic acid (*trans*,*trans*-Δ^{9},Δ^{12})	18	2	9E,12E-Octadecadienoic acid
4444437	Alpha-Linolenic Acid (ALA)	18	3	9,12,15-Octadecatrienoic acid
4444436	Gamma-Linolenic Acid (GLA)	18	3	6,9,12-Octadecatrienoic acid
CID 5282820	Beta-eleostearic acid	18	3	(9E,11E,13E)-9,11,13-Octadecatrienoic acid
10035	Arachidic Acid	20	0	Eicosanoic acid
4445894	Gadoleic Acid	20	1	9-Eicosenoic acid
392692	Arachidonic Acid (AA)	20	4	All-cis-5,8,11,14-eicosatetraenoic acid
CID 5312542	Eicosatetraenoic acid	20	4	All-trans -5,8,11,14-Eikosatetraensaeure
393682	EPA	20	5	5,8,11,14,17-Eicosapentaenoic acid
7923	Behenic acid	22	0	Docosanoic acid
4444561	Erucic acid	22	1	13-Docosenoic acid
393183	DHA	22	6	4,7,10,13,16,19-Docosahexaenoic acid
10724	Lignoceric acid	24	0	Tetracosanoic acid

Download English Version:

https://daneshyari.com/en/article/10351670

Download Persian Version:

https://daneshyari.com/article/10351670

Daneshyari.com