Computational Biology and Chemistry 35 (2011) 34–39

Contents lists available at ScienceDirect

Computational Biology and Chemistry

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

Research Article

Interaction of zervamicin IIB with lipid bilayers. Molecular dynamics study

Olga V. Levtsova*, Mikhail Yu. Antonov, Tatsina V. Naumenkova, Olga S. Sokolova

MSU, Faculty of Biology, 119991 Moscow, 1-12 Leninskie Gory, Russia

ARTICLE INFO

Article history:
Received 22 October 2010
Accepted 23 December 2010

Keywords:
Molecular dynamics simulation
Peptaibols
Zervamicin
Ion channels
Lipid bilayers

ABSTRACT

In this work we have studied the interaction of zervamicin IIB (ZrvIIB) with the model membranes of eukaryotes and prokaryotes using all-atom molecular dynamics. In all our simulations zervamicin molecule interacted only with lipid headgroups but did not penetrate the hydrophobic core of the bilayers. During the interaction with the prokaryotic membrane zervamicin placed by its N-termini towards the lipids and rotated at an angle of 40° relatively to the bilayer surface. In the case of eukaryotic membrane zervamicin stayed in the water and located parallel to the membrane surface. We compared hydrogen bonds between peptide and lipids and concluded that interactions of ZrvIIB with prokaryotic membrane are stronger than those with eukaryotic one. Also it was shown that two zervamicin molecules formed dimer and penetrated deeper in the area of lipid headgroups.

1. Introduction

Zervamicin IIB is an antimicrobial peptide that interacts with the cell membrane and increases ion permeability. ZrvIIB, isolated from cultures of *Emericellopsis salmosynnemata*, is a member of the antibiotics peptaibol family. Peptaibols usually have activity against Gram-positive bacteria and lack of toxicity towards eucariotic cells (Argoudelis et al., 1974). Also they are known to be potentially useful for chemotherapeutic applications in oncology (Oh et al., 2002). Zervamicin IIA and zervamicin IIB appear to inhibit the locomotors activity of test mice, probably via their effect on the brain. These effects of zervamicin IIA become apparent at lower dosages (0.05–2.0 mg/kg) as compared to zervamicin IIB (0.5–12.0 mg/kg). ZrvIIB consists of 16 amino acid residues and, like other peptaibols, contains a high proportion of helix-promoting α,α-dialkylated amino acids. The N-terminus of the peptide forms an alpha-helix, whereas C-terminus has 3(10)-helical structure (Shenkarev et al., 2004). ZrvIIB, as opposed to long peptaibols such as alamethicin, possesses helical structure in mixed solvents of different polarity ranging from $CDCl_3/CD_3OH$ (9:1, v/v) to CD_3OH/H_2O (1:1, v/v) (Balashova et al., 2000). In planar lipid bilayer ZrvIIB forms voltage-dependent ion channels with multilevel conductance state (Balaram et al., 1992). The exact channel structure is still unclear. But the conventional model for

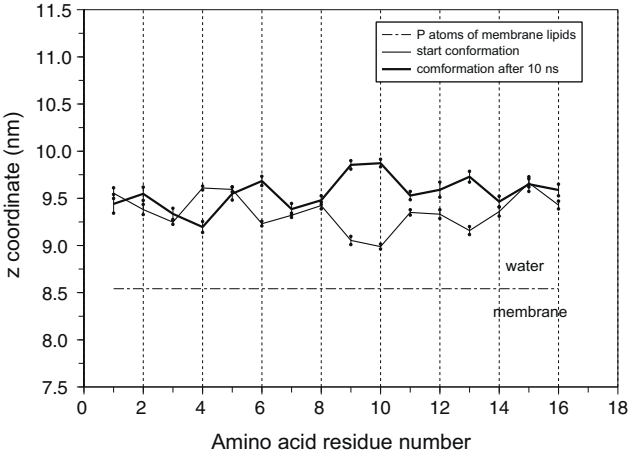

Fig. 1. Position of Ca-atoms relatively to the membrane surface in the starting conformation and after 10 ns of dynamics (POPC lipid bilayer).

* Corresponding author.
E-mail address: sunely@yandex.ru (O.V. Levtsova).

1476-9271/$ – see front matter © 2011 Elsevier Ltd. All rights reserved.
doi:10.1016/j.compbiolchem.2010.12.005

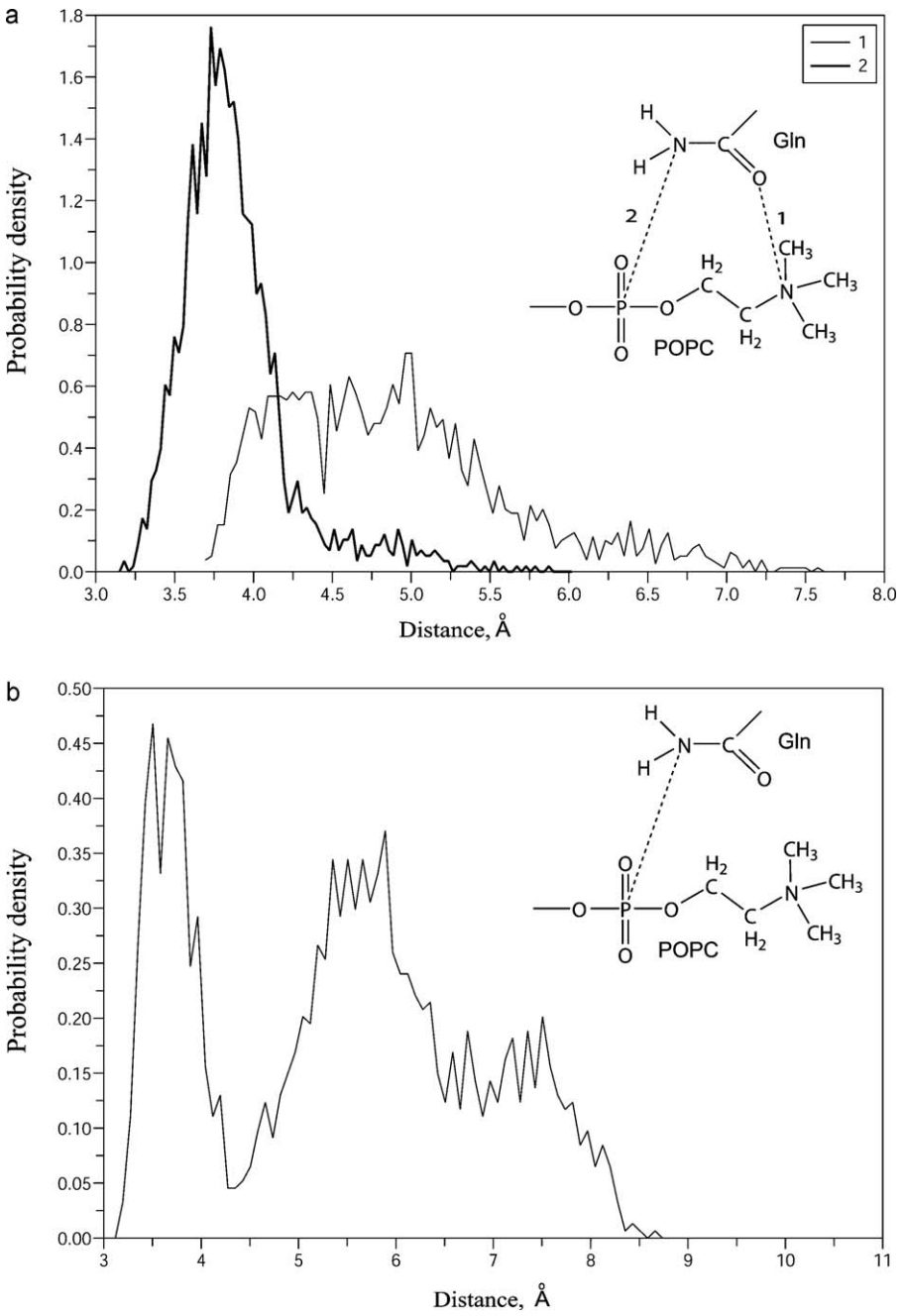

Fig. 2. (A) Distance between carboxyl oxygen of Gln11 side chain and nitrogen atom of POPC (1), between nitrogen atom of Gln3 side chain and phosphorus atom of POPC (2). (B) Distance between nitrogen of Gln3 side chain and phosphorus atom of POPC.

voltage-gated peptaibol channel action involves the formation of the water-filled pore by a bundle of parallel helices (Laver, 1994). Different conductance levels are thought to correspond to different numbers of helices in a bundle (Agarwalla et al., 1992). According to barrel-stave model (BS-model) of peptaibol action, peptaibol adsorbs on the membrane surface and embeds into the lipid bilayer under the transmembrane potential. In this article we have studied the interaction of zervamicin IIB with the model membranes of eukaryotes and prokaryotes using all-atom molecular dynamics. Also the ability of zervamicin molecules to aggregate with each other on the membrane surface has been investigated.

2. Methods

POPC lipid bilayer was used as model of eukaryotic membrane and POPE/POPG (in a proportion of 4:1) bilayer as prokaryotic one. Each monolayer of the membranes consisted of 32 lipids and