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Advances in Bioresearch

## ORIGINAL ARTICLE

# Metabolites of Docosahexaenoic Acid Produced by Probiotic *Bacillus cereus* able to Inhibit 2BX4 and 6LU7 Receptors of SARS-COV-2

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**ABSTRACT**

*Inflammatory properties of omega-3 fatty acids have been shown to play a pivotal role in attenuation of uncontrolled immune response in the lungs secondary to bacterial or viral infections which could be useful against COVID-19. In this study, metabolites of docosahexaenoic acid were evaluated against SARS-CoV-2 Main protease (Mpro). GC–MS analysis of docosahexaenoic acid shown that 51 compounds produced by Bacillus cereus. They were docked against three SARS-CoV-2 proteins (receptors), namely Mpro using Epic, LigPrep and Glide module of Schrödinger. Among 51 compounds, Hexadecanoic acid, 2-hydroxy-1 (hydroxymethyl) ethyl ester (MW-330.5g/ moL), Monoelaidin (MW-356.5g/ moL), (Z)-3-(Heptadec-10-en-1-yl) phenol (MW-330.5g/ moL), Decanedioic acid, bis(2-ethylhexyl) ester.1(MW-426.7g/ moL), Glycidyl palmitate (MW-312.5g/ moL) and Phenol,2,4-Bis(1,1-Dimethylethyl)(MW-278.5) were found to have an ability to bind with both the candidate receptor proteins, 2BX4 and 6LU7.Thus, these compounds could be chosen for further research and assessment in the context of targeted medicinal therapy approach for the virulent SARS-CoV-2 virus.*

**Keywords:** Docosahexaenoic acid, Bioconversion, Metabolites, Molecular docking, SARS-CoV-2.

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## INTRODUCTION

Several notable viral diseases, including influenza, chikunguniya, Nipah, Zika, and Ebola, have caused global outbreaks in recent decades [1,2]**.** The sudden emergence of COVID-19 has become a life-threatening threat for millions of people throughout the world. The upsurge of COVID-19 caused by SARS-CoV-2 had put the world on a standstill, within a short span of time. The epidemic had its repercussions on every walk of life, affecting the global economy, transportation and healthcare systems. Besides, there are difference in opinion about the credibility and safety of the drugs available in the market [3]**.** Discovering the immunizing agent, the community of researchers uses different strategies focusing to develop an anti-viral drug by targeting either of many structural and non-structural proteins with an agenda for developing inhibitors **(i)** to impede infectious agent passage into the host cells, and **(ii)** to forestall infectious agent replication [4]**.** Several drugs are being repurposed to treat COVID-19, including ritonavir, lopinavir, hydroxychloroquine, chloroquine, azithromycin, remdesivir and clinical trials are underway [5]**.** However, a potential COVID-19 medication has still a long way to come. In this context, it is

a timely requisite that we should consider natural compounds as a substitute for the synthetic molecules for tackling this disease.

Several SARS-CoV-2 macromolecules have been chosen for designing and developing anti-Covid-19 medicines, including 3-chymotrypsin-like protease (3CL pro), endoribonuclease, RNA-dependent RNA polymerase, and 2-O methyltransferase. 3CLpro protein is involved in all stages of the virus life cycle, including viral entry, viral protein maturation, and viral infection pathogenesis [6]. (3CLpro/Mpro), the viral 3 C–like protease or major protease encoded by Non-Structural Protein, is one of the best-characterized therapeutic targets among Covid and it produces NSPs such as RNA dependent RNA polymerase and helicase which play an essential role in viral replication, and its inhibition interrupts the viral life cycle [7]. The 3CLpro/Mpro or main proteases namely, $M^{Cov1}$Pro (PDB code 2BX4) from SARS-CoV and $M^{Cov2}$Pro (PDB code 6LU7) from SARS-CoV-2 were used in this study.

Now-a-days, *in-silico* techniques have become an inevitable part in the domain of drug discovery, especially when we arrive at the question of target identification [8,9]. For short-listing the probable hits from the huge data of candidate molecules and identification of the lead compound, computational tools are a boon, since they save the cost both in terms of time and money. Target identification is the first step in any drug designing process [10]. Cellular structures, especially proteins which are suspected to play a pivotal role in the pathogenicity of the microbe are identified as the target for drug delivery [8,10]. An ideal target should be effective, safe and should be specific to the selected ligand/drug molecule. Lead identification and optimization is the next phase in the hierarchy of drug development [10]. Optimized lead molecule will then go through pre-clinical trials to test its safety and efficacy [9,11].

In this study, we are employing *in-silico* drug designing techniques by focusing on structure-based computational modeling of ligand-receptor interactions, to identify potential targets for SARS-CoV-2. Molecular docking is a widely used technique in the domain of drug designing [12]. It helps in understanding how macromolecules, usually proteins interact with small molecules called ligands to form a stable complex [8,10]. The particulars we could gain from the favoured orientations could be used to predict the best pose/conformer of the ligand-receptor interactions [12,13]. This could be achieved from the scoring function of the molecular docking software [14]. Through docking, we aim to arrive at a confirmation of ligand-receptor complex with minimum free energy and maximum stability [13]. If we could figure out the general principles underlying the stability and energy of the ligand-receptor complex formation, we might be able to forecast the variables that influence the docking of the molecules [12]. Docking could also be employed to understand protein-protein interactions [8,14], binding site identification [14], hit identification [14] and lead optimization [10] in the drug discovery process [14,15]. In the case of protein-ligand interaction, molecular docking techniques provide us with distinct docked conformers and orientation of ligand molecule, so as to be compatible with the active site of the receptor protein [14]. The prospective candidate compounds capable of reducing viral replication, infection and thus acting as an effective treatment against SARS-CoV-2 may be identified based on the affinity shown by the ligands.

DHA (Docosahexaenoic acid) is a vital component for immunity and critical life stages (such as postpartum) and it's crucial during pregnancy and childhood because it's play important role in brain development [16,17]. DHA makes up approximately 90% of the omega-3 fatty acids in the human brain, as well as up to 25% of the total fat content. It is largely found in cell membranes, where it enhances membrane fluidity and cell-to-cell gaps. This makes it easier for nerve cells to send and receive electrical impulses [18]. In addition to its documented antimicrobial and antiviral properties, DHA possesses anti-inflammatory activity and inhibit tumorigenesis [19,20,5,21]. The microbicidal activity of selected Long Chain Unsaturated Fattyacid's and their derivatives has been reported on various enveloped viruses, parasites and pathogenic bacteria such as *Pseudomonas aeruginosa, Bacillus subtilis, Listeria monocytogenes, Helicobacter pylori, Staphylococcus aureus* and *Neisseria gonorrhea* [19,22]. Fish oil inhibits tumor cell proliferation, whereas arachidonic acid, a long-chain n-6 fatty acid, promotes cancer cell proliferation [23]. Bristrian has suggested using parenteral supplementation of fish-oil emulsions containing significant levels of EPA (Eicosapentaenoic acid) and DHA (4–6 gram/day) to treat patients with severe SARS-CoV-2 in order to limit cytokine release and moderate the inflammatory response [24]. In our study, we focused on structure-based computational modelling of ligand-receptor interactions and deals with the *in-silico* study of various bioconverted docosahexaenoic acid metabolites as potential bioactive components (to be used as drugs) against COVID-19 enzyme (A) $M^{Cov1}$Pro (PDB code 2BX4) from SARS-CoV and (B) $M^{Cov2}$Pro (PDB code 6LU7) from SARS-CoV-2 as the receptors.

## MATERIAL AND METHODS

### BIOCONVERSION OF DHA USING PROBIOTIC *BACILLUS CEREUS*

Bioconversion was described previously [22] and carried out in five set of 50 mL SM broth with supplement of 200mg of DHA were added to 24 hrs old culture of *Bacillus cereus* to the five set of SM broth individually and followed by continued incubation for an 24 hrs to 120 hrs at 37°C and bioconversion was allowed to proceed.

### EXTRACTION OF FATTYACIDS FROM BIOCONVERTED BROTH

Bio-converted broth were suspended in 3mL of 4 $moL^{-1}$ sodium hydroxide, and incubated at 90°C for 90 min. After cooling, the pH of the sample was adjusted to 2 with hydrochloric acid. Fatty acids were then extracted by adding 2 mL anhydrous diethyl ether and separated by centrifugation at 5500×g for 10 min. The upper phase was removed and dehydrated by adding anhydrous sodium sulfate. The dehydrated fatty acids were collected and dried under a stream of nitrogen. Next, 50 µL bistrimethylsilyltrifluoroacetamide (BSTFA) was added, and the mixture was incubated at 70°C for 30 min and dried under a stream of nitrogen. The fatty acids were dissolved in 100 µL hexane for GC/MS analysis [25]**.**

### CHARACTERIZATION OF BIOCONVERTED METABOLITES BY GC-MS ANALYSIS

Fatty acid composition analysis was performed on the Shimadzu GCMS QP 2020 that employed a fused silica column, packed with SH-Rxi-%Sil MS (30 m × 0.25 mm ID × 250µmdf) and the components were separated using Helium as carrier gas at a constant flow of 1 ml/min. The injector temperature was set at 280°C during the chromatographic run.1µL of extract sample injected into the instrument the oven temperature was as follows: 40°C (2 min); followed by 280°C at the rate of 10°C min−1 and 280°C, where it was held for 3 min. The mass detector conditions were: transfer line temperature 280°C; ion source temperature 230°C; and ionization mode electron impact at 70 eV, a scan time 0.2 s and scan interval of 0.1 s, fragments from 40 to 550 Da. The spectrums of the components were compared with the database of spectrum of known components stored in the GC-MS NIST (2017) library.

### LIGAND PREPARATION

From the GC-MS analysis, 53 compounds were downloaded in SDF (Spatial Data File) two-dimensional (2D) format from the PubChem database (https:/pubchem.ncbi.nlm.nih.gov/, accessed on March 2021). Ligand was prepared using LigPrep tool of Maestro v 11.1. The pH 7.0 ± 2.0 was used for the generation of ionization states of the compounds with Epik 2.2 (Force field: OPLS4) in Schrödinger ver.11.1. Up to 32 possible stereoisomers per ligand were retained.

### PROTEIN PREPARATION

The three-dimensional (3D) structure of the (A) $M^{Cov1}$Pro (PDB code 2BX4) from SARS-CoV and (B) $M^{Cov2}$Pro (PDB code 6LU7) from SARS-CoV-2 were retrieved from the RCSB Protein Data Bank (https://www.rcsb.org/structure/, accessed on 12 March 2021) in PDB format. The Protein Preparation Wizard (Schrödinger ver.11.1) was used to prepare the 6LU7 and 2BX4 receptor using the following processes: optimization, removal of water molecules, and minimization (Force field: OPLS4).

### RECEPTOR GRID GENERATION AND GLIDE BASED MOLECULAR DOCKING

The grid generation (Schrödinger Maestro ver.11.1) for the selected receptor was performed using the default parameters (Force field: OPLS4). Receptor grids were calculated for the prepared proteins for the observation of poses by various ligands bound within the active predicted site during the docking procedure. The vander Waals radius scaling factor and the partial atomic charge were 1.00 and 0.25, respectively. A cubic box of specific dimensions centered on the centroid of the active site residues was obtained for the receptor. The bounding box was set to 14 × 14 × 14 Å for docking experiments. Ligand docking was followed by the flexible standard precision (Schrödinger ver.11.1), and the docking score and the interactions of the receptor-ligand docking were recorded using Glide.

## RESULTS AND DISCUSSION

Coronaviruses are single stranded RNA viruses with a length of about 26,000-32,000 base pairs [26]**.** As of now, 39 coronavirus species have been identified in 27 sub-genera, 5 genera and 2 sub-families that belong to the family Coronaviridae of the order Nidovirales [27]**.** Even though the rate of mutation of SARS-CoV-2 has been estimated to be about 1-2 mutations per month, the mode of infection and transmission still remains unchanged [28]**.** This makes it prone to drug ability. By focusing on its mode of entry into the host system, it is possible to sort out the proteins that are crucial for its virulence and thus effective anti-viral drugs could be developed against this fatal disease.

In the present study, structure-based computational modeling of ligand-receptor interactions has been performed, focusing on the ligand molecules which were derived from the bioconversion of DHA. A total of 82 compounds were identified from the bioconverted DHA using GC-MS, which are listed in (**Fig.1-5)**

and (Table S1-S6) along with their medicinal properties. The total ionic chromatogram (TIC) is shown in (Fig 1-5). Fifty-one compounds were selected for molecular docking analyses based on their medicinal properties. DHA has been shown to possess anti-viral, anti-cancerous and anti-microbial properties [29,30]. It has also demonstrated therapeutic effect in reducing cardio metabolic risk factors [31]. Besides, independent studies by researchers substantiates the role of DHA in inhibiting viral replication and infection [32,33]. One of the best-characterized and distinguished drug targets among CoVs is 3CLpro also called Mpro, a viral 3 C–like protease or main protease. 3CLpro along with PLpro (papain–like protease) cleaves the polyprotein pp1ab and pp1a to produce non-structural proteins (NSPs) such as RNA dependent RNA polymerase and helicase [34, 35, 36]. They play an essential role in viral replication and hence its inhibition interrupts the viral life cycle. Mpro is highly conserved among CoVs, sharing over 90% sequence identity, differing only 12 residues between $M^{Cov1}$Pro from SARS-CoV and $M^{Cov2}$Pro from SARS-CoV-2 [7]. The crystal structure of SARS-CoV-2 main protease in complex with an inhibitor N3 (PDB ID 6LU7) and the crystal structure of SARS Coronavirus Main Proteinase (P21212) (PDB ID 2BX4) were considered as the receptors for the present study. Nelfinavir, a protease inhibitor (PI) [37] has been used as the control for molecular docking throughout our experiment. It is widely used in the treatment of HIV (human immunodeficiency virus) infection and the AIDS (acquired immunodeficiency syndrome) [38]. Nelfinavir selectively binds to the HIV protease and inhibits it by interfering in its replication machinery [38]. Both experimental and computational evidences suggest the ability of nelfinavir in inhibiting the cytopathic effect caused by SARS-CoV-2 [39].

Molecular Docking was carried out using bioconverted DHA metabolites against COVID-19 enzyme receptors, 6LU7 and 2BX4 with Nelfinavir as the control. Docking was done using Glide module (Maestro software) of Schrodinger ver.11.1. The strength of the receptor-ligand interactions was determined based on the Glide score. The higher the Glide score value in the negative scale, the better the interaction between the protein and the ligand [40]. In other words, the lower the Glide scores the better the affinity between the protein and the ligand. Potential ligands were shortlisted based on the ligand efficiency, Glide score and docking score. The receptors, 2BX4 and 6LU7 were docked with 51 ligands which were derived from the bioconversion of DHA, whose results are displayed in (Table 1-2) respectively. In the docking experiment, four ligands were shown to possess considerable docking score against 2BX4 (Table-1). Among them, Hexadecanoic acid, 2-hydroxy-1 (hydroxymethyl) ethyl ester displayed the highest predicted binding affinity with a Glide score of -5.118. The next in line was Monoelaidin (Gscore: -4.515), (Z)-3-(Heptadec-10-en-1-yl) phenol (Gscore: -4.376) and Decanedioic acid, bis(2-ethylhexyl) ester.1(Gscore: -4.085). In the case of 6LU7, two ligands exhibited appreciable binding efficiency (Table-2). They were (Z)-3-(Heptadec-10-en-1-yl) phenol with a Glide score of -3.872 and Phenol, 2,4-Bis(1,1-Dimethylethyl), Oxime with a Gscore of -3.672.

The docking interaction between the control and 2BX4 was appreciably high with a Glide score of -4.687. Molecular docking revealed that 3 ligand atoms of the control, interacted with various aminoacid residues of the protein at position 108(proline), 110(glutamine) and 294 (phenylalanine) respectively. Proline made a hydrophobic interaction with the 'OH' atom of nelfinavir, whereas glutamine made a polar hydrogen bond interaction with the functional group, 'NH' and phenylalanine made a hydrophobic interaction with 'N+H' group of the ligand (Fig.6a). 51 metabolites derived from the bioconversion of DHA were docked against 2BX4. Among them, Hexadecanoic acid, 2-hydroxy-1 (hydroxymethyl) ethyl ester displayed the highest binding efficiency with a Glide score of -5.118. Docking results revealed that 2 ligand atoms of Hexadecanoic acid, 2-hydroxy-1 (hydroxymethyl) ethyl, interacted with amino acid residues of the protein at positions 111 and 295 with threonine and aspartic acid respectively. Threonine makes a polar hydrogen bond interaction with the 'OH' atom of the ligand, whereas aspartic acid makes a negatively charged hydrogen bond interaction with OH (Fig.6b). The next interacting molecule with 2BX4 with a higher Glide score was monoelaidin (Gscore: -4.515). Monoelaidin made an OH bond interaction with threonine and aspartate at positions 111 and 295 respectively, similar to that of hexadecanoic acid, 2-hydroxy-1 (hydroxymethyl) ethyl ester (Fig.6c). (Z)-3-(Heptadec-10-en-1-yl) phenol comes in the next position with a Glide score of -4.376. It made an OH bond interaction with asparagine at 203th position (Fig.6D). Decanedioic acid, bis(2-ethylhexyl) ester.1(Gscore: -4.085) interacted with the histidine amino acid residue of 2BX4 at 246th position. It made a polar hydrogen bond interaction with the 'O' atom of the protein (Fig.6e).

6LU7 is a key enzyme in SARS-Cov-2, which was illustrated as playing a crucial role in the viral replication and infection [5].The docking interaction between the control (nelfinavir) and 6LU7 was considerably high with a Glide score of -4.009, as in the case of 2BX4. Molecular docking revealed that 4 ligand atoms of the control, interacted with different amino acid residues of 2BX4 at positions 105,110 and 294 with arginine, glutamine and phenylalanine respectively (Fig.7a). Arginine made a positively charged hydrogen

bond interaction with the 'OH' atom of nelfinavir, whereas glutamine made hydrogen bond interactions with the functional groups, 'NH' and 'OH'. Phenylalanine made a hydrophobic pi-pi stacking with the benzene ring as shown in (Fig.7a). 51 bioconverted metabolites of DHA were docked against 6LU7 and the docking images and the bonding interactions were analysed. In the case of 6LU7, two ligands exhibited appreciable binding efficiency (Table-2).They were (Z)-3-(Heptadec-10-en-1-yl) phenol with a Gscore of -3.872 and phenol, 2,4-Bis(1,1-Dimethylethyl) with a Gscore of -3.672. Docking results revealed that 2 ligand atoms of (Z)-3-(Heptadec-10-en-1-yl) phenol, interacted with the amino acid residues of the protein at position 108 and 246 with proline and histidine respectively. Proline made a hydrophobic interaction with 'OH' atom of the ligand, whereas histidine makes a polar pi-pi stacking with the benzene ring as shown in (Fig.7b). In the case of phenol, 2,4-Bis(1,1-Dimethylethyl), 2 ligand atoms interacted with the amino acid residues of 6LU7 at position 110 and 294 with glutamine and phenyl alanine respectively. Glutamine made a polar hydrogen bonding interaction with the 'OH' atom of the ligand, whereas phenylalanine made a hydrophobic pi-pi stacking with the benzene ring (Fig.7c).

Thus, in this study, the SARS-CoV-2 proteins namely, 6LU7 and 2BX4 were considered as targets to screen the bioconverted metabolites of DHA and identify potential drugs against SARS-CoV-2 that have appreciable binding affinity towards these receptor proteins which play essential role in viral replication. In the docking experiments, four ligands showed considerable docking score against 2BX4 (Table-1). Among them, Hexadecanoic acid, 2-hydroxy-1 (hydroxymethyl) ethyl ester displayed the highest Glide score (-5.118), greater than even that of the control (nelfinavir) (Gscore: -4.687). Hence, Hexadecanoic acid, 2-hydroxy-1 (hydroxymethyl) ethyl ester is proposed to possess better inhibitory property towards 2BX4 than that of the control. Thus, Hexadecanoic acid, 2-hydroxy-1 (hydroxymethyl) ethyl ester is strongly recommended as a potential drug candidate for SARS-CoV-2 ($M^{Cov1}Pro$). Interestingly, in the case of 6LU7, the standard inhibitor, nelfinavir (Gscore: -4.009) showed the highest docking score compared to the analysed compounds. Next in line was (Z)-3-(Heptadec-10-en-1-yl) phenol, which depicted a Glide score of -3.872. Hence, (Z)-3-(Heptadec-10-en-1-yl) phenol could also be considered as a drug candidate for SARS-CoV-2 ($M^{Cov2}Pro$). This study recommended that Hexadecanoic acid, 2-hydroxy-1 (hydroxymethyl) ethyl ester(MW-330.5g/moL), Monoelaidin (MW-356.5g/moL), (Z)-3-(Heptadec-10-en-1-yl) phenol(MW-330.5g/moL), Decanedioic acid, bis(2-ethylhexyl) ester.1(MW-426.7g/moL), Glycidyl palmitate(MW-312.5g/moL) and Phenol,2,4-Bis(1,1-Dimethylethyl)(MW-278.5) have the ability to bind to both the candidate receptor proteins, 2BX4 and 6LU7 (Table-3). Hence, these identified compounds could be selected for further study and evaluation with respect to the targeted drug treatment approach for the noxious SARS-CoV-2.

**Fig. 1. GC-MS Chromatogram of Docosahexaenoic acid bioconverted metabolites at 24 hrs**

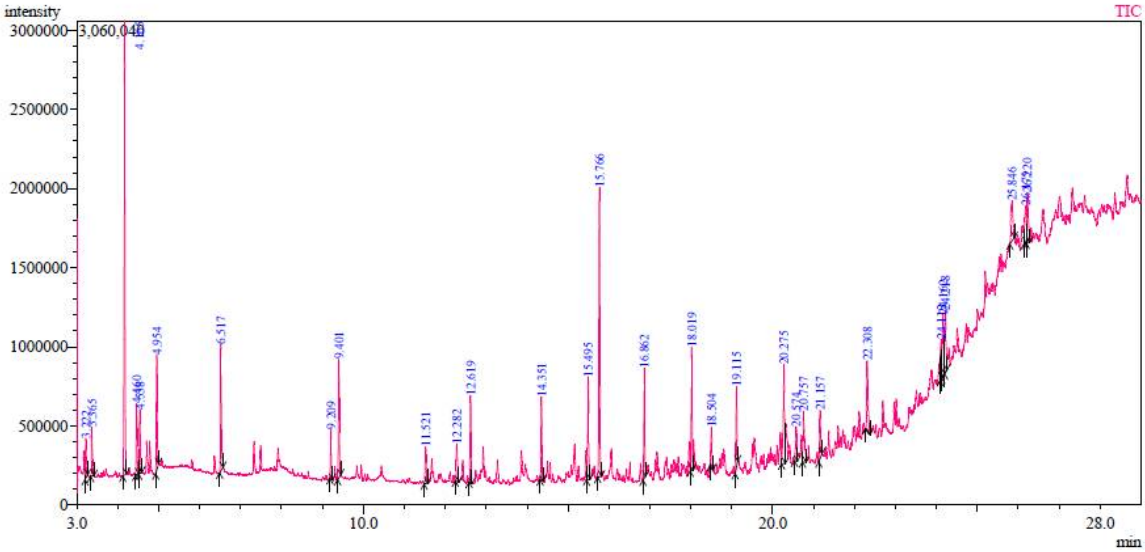


**Fig. 2. GC-MS Chromatogram of Docosahexaenoic acid bioconverted metabolites at 48 hrs**

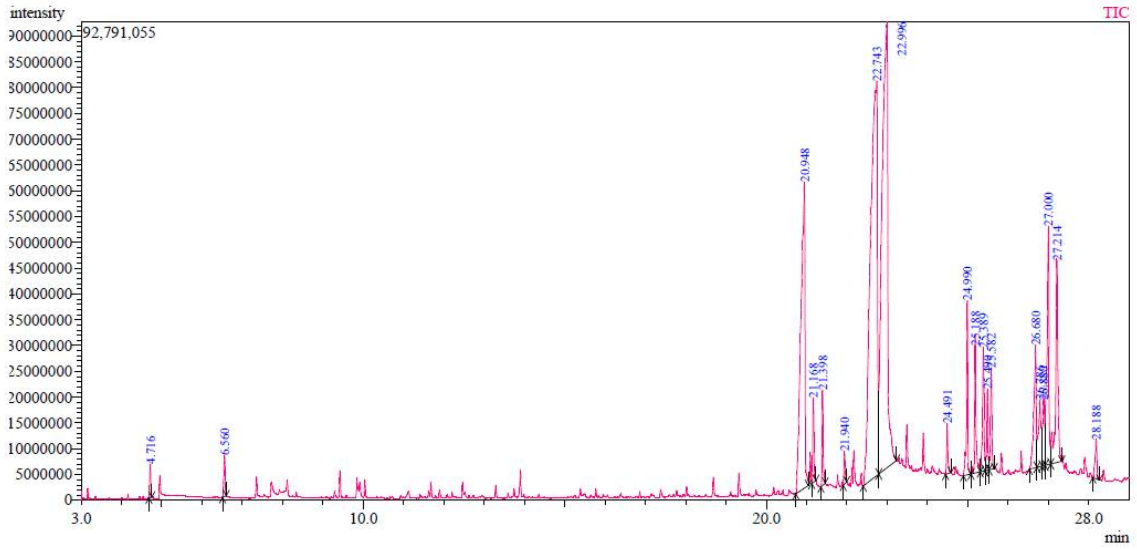



**Fig. 3. GC-MS Chromatogram of Docosahexaenoic acid bioconverted metabolites at 72 hrs**

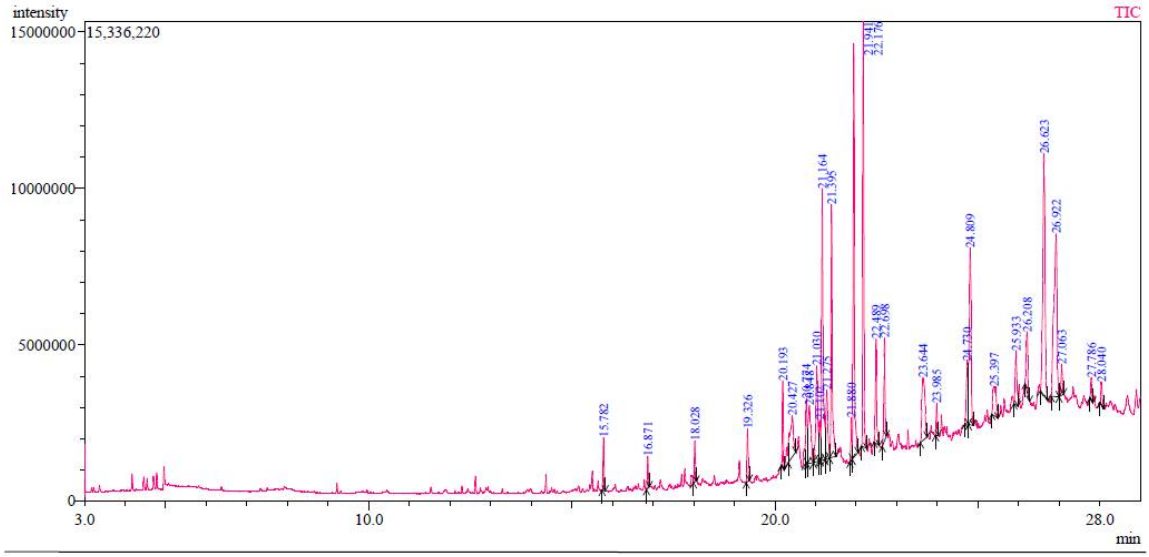



**Fig. 4. GC-MS Chromatogram of Docosahexaenoic acid bioconverted metabolites at 96 hrs**

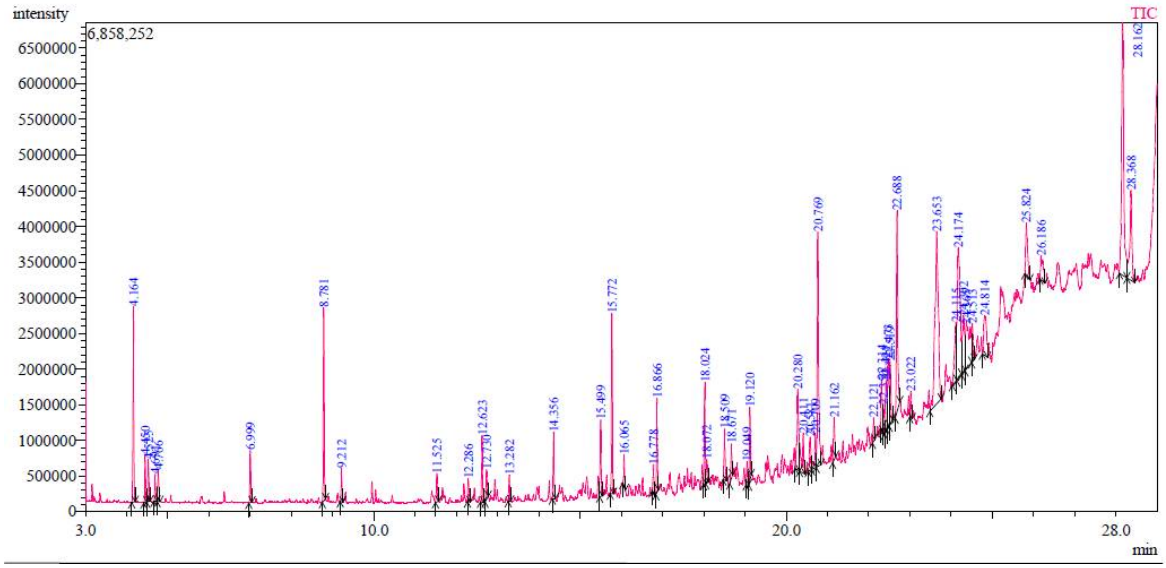


**Fig. 5. GC-MS Chromatogram of Docosahexaenoic acid bioconverted metabolites at 120 hrs**

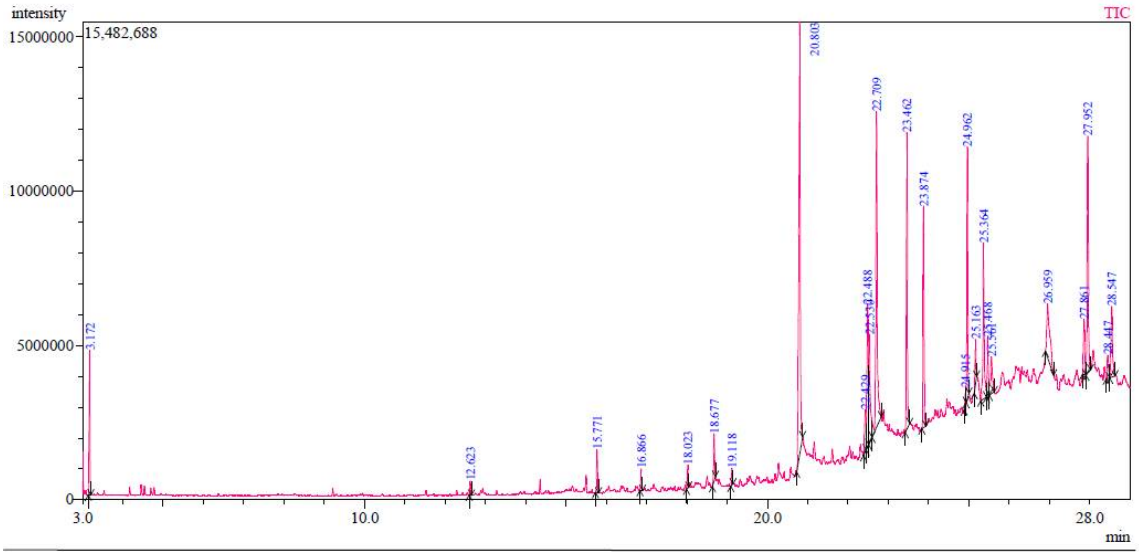
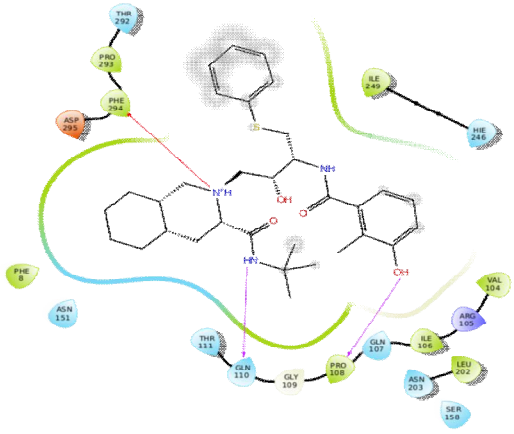
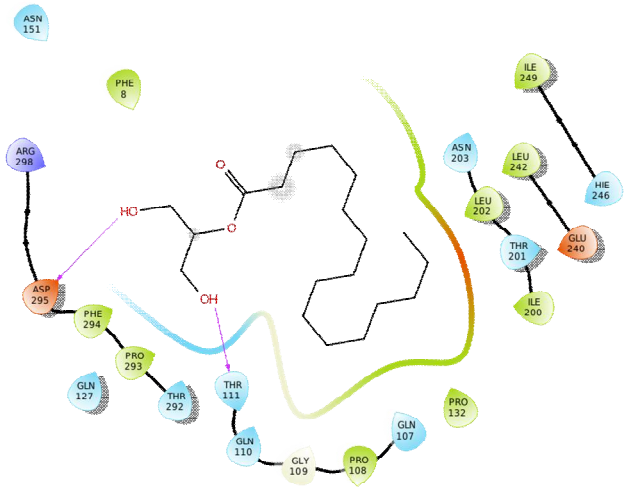



**Fig. 6. Interaction diagram with H-bonds and other interactions of a 2BX4 with (a)** Nelfinavir, with **(b)** Hexadecanoic acid 2-hydroxy-1-(hydroxymethyl)ethyl ester, with **(c)** Monoelaidin, **(d)** (Z)-3-(Heptadec-10-en-1-yl)phenol, with **(e)** Decanedioic acid, bis(2-ethylhexyl) ester, and with **(f)** Glycidyl palmitate showing different polar and non-polar interactions and bonds

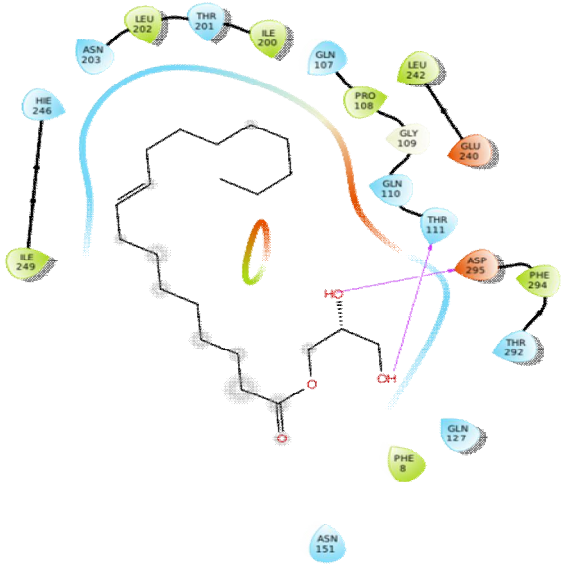


**(a): Nelfinavir (Control)**

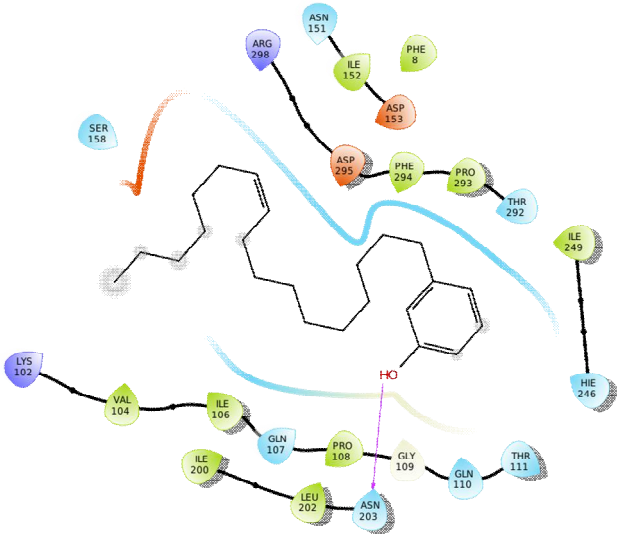


**(b): Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester**

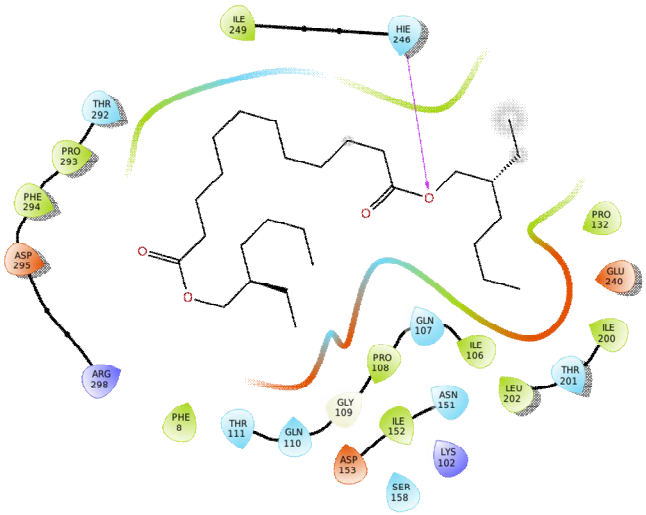
 




**(c): Monoelaidin**



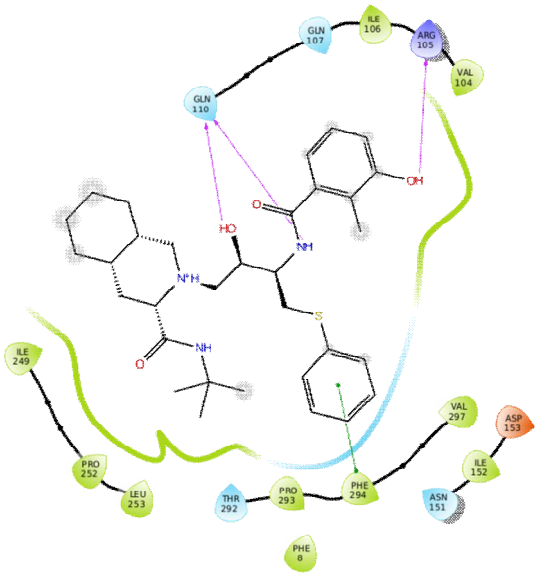

**(d): (Z)-3-(Heptadec-10-en-1-yl)phenol**



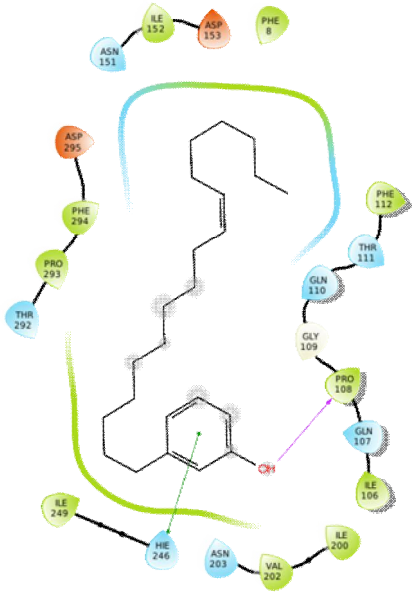

**(e): Decanedioic acid, bis(2-ethylhexyl) ester**

**Fig. 7. Interaction diagram with H-bonds and other interactions of a 6LU7 with (a**) Nelfinavir, with **(b)** (Z)-3-(Heptadec-10-en-1-yl)phenol, with **(c)** Phenol, 2,4-Bis(1,1-Dimethylethyl)-, **(d)** Oxime-, methoxy-phenyl- (3), **(e)** with Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl) ethyl ester **(f)** 9-Octadecenoic Acid (9Z)-, Oxiranylmethyl Ester, **(g)** Decanedioic Acid, Bis(2-Ethylhexyl) Ester, **(h)** Squalene, **(i)** 2-Pentacosanone, **(j)** Z,Z-6,27-Hexatriactontadien-2-One, **(k)** Glycidyl Palmitate, **(l)** Propyl Stearate, **(m)** Benzene, 1,3-Bis(1,1-Dimethylethyl)-, **(n)** Monoelaidin, **(o)** 1-Hexanol, 2-Ethyl-, **(p)** Z,Z-6,28-Heptatriactontadien-2-One, **(q)** Arachidic Acid showing diferent polar and non-polar interactions and bonds

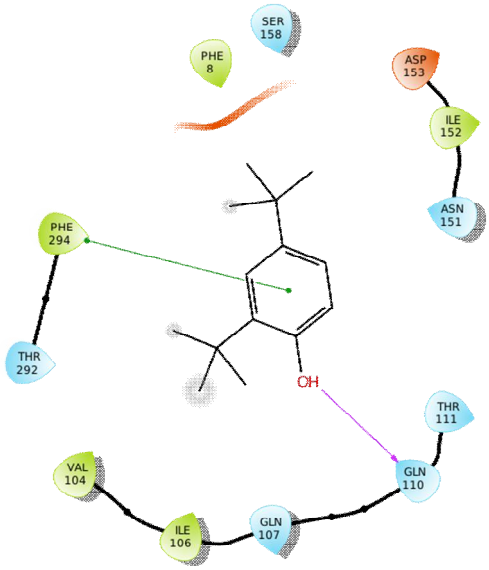



**(a): Nelfinavir (Control)**

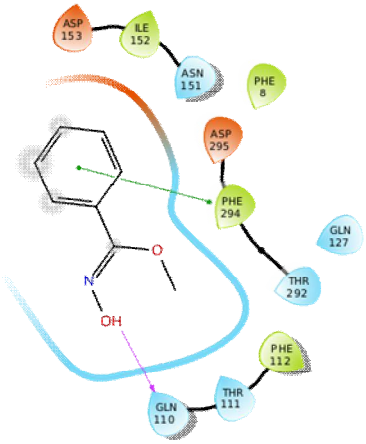



**(b): (Z)-3-(Heptadec-10-en-1-yl)phenol**

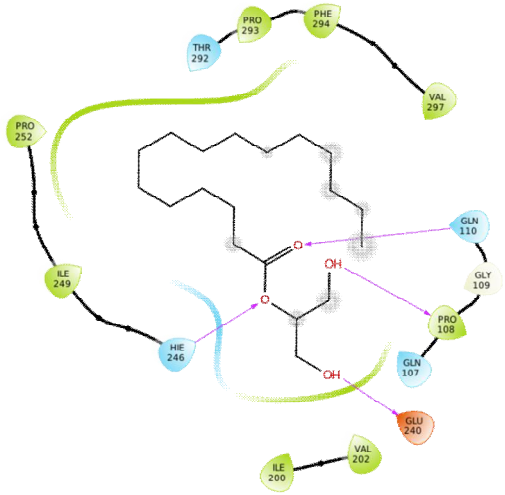
 




**(c): Phenol, 2,4-Bis(1,1-Dimethylethyl)-**

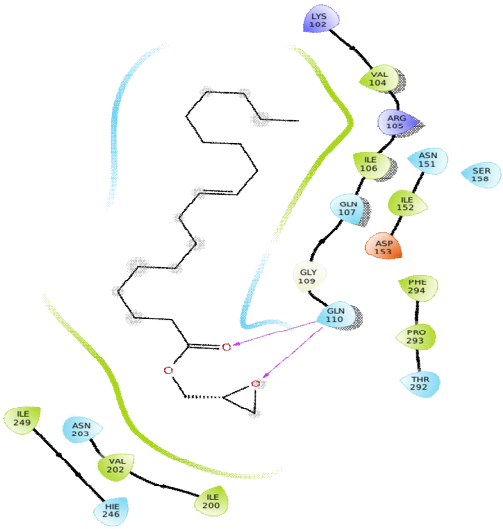



**(d): Oxime-, methoxy-phenyl- (3)**

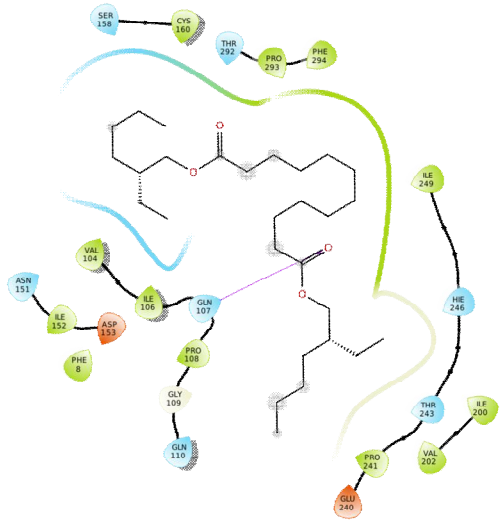



**(e): Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester**

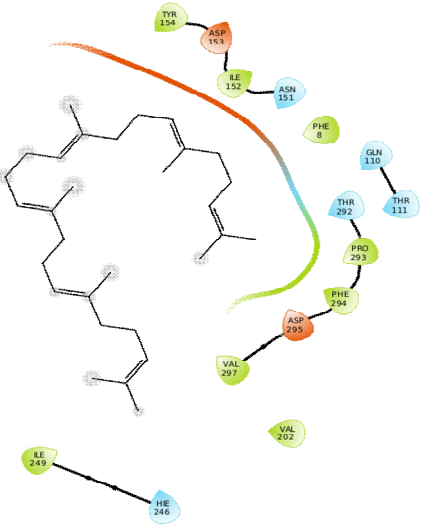
 




**(f): 9-Octadecenoic acid (9Z)-, oxiranylmethyl ester**

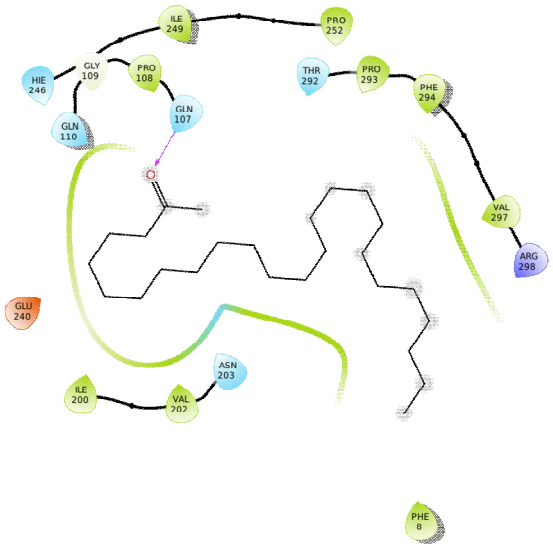



**(g): Decanedioic acid, bis(2-ethylhexyl) ester**

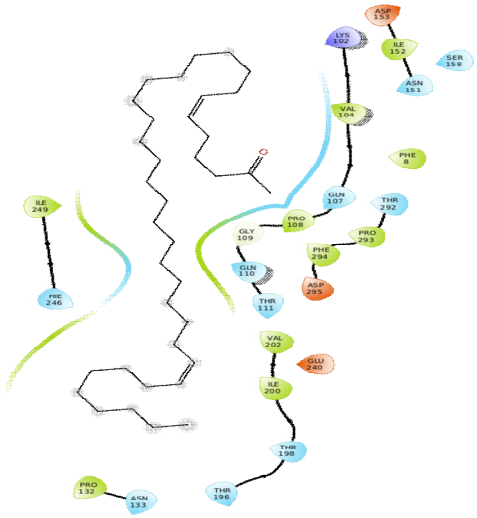



**(h): Squalene**

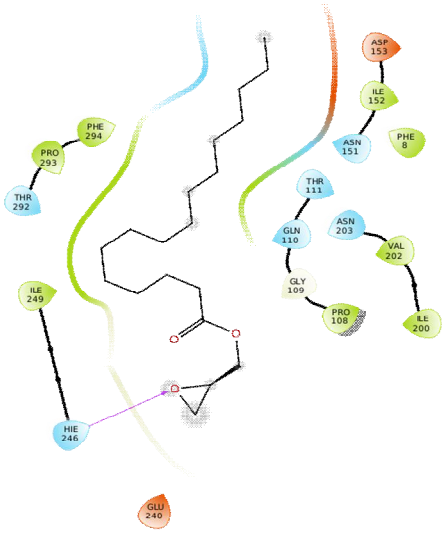
 




**(i): 2-Pentacosanone**

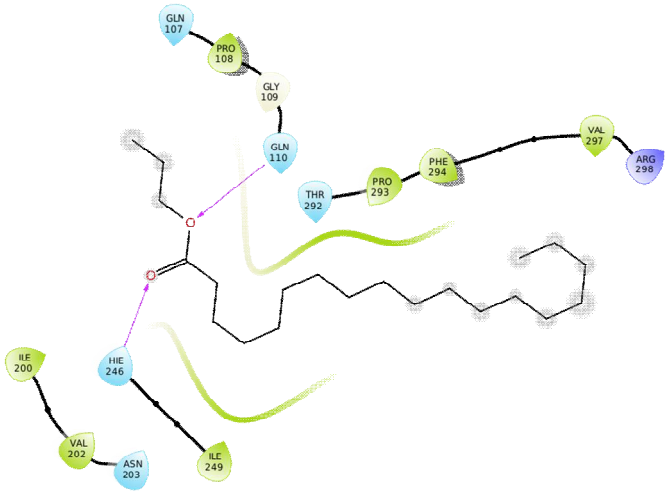



**(j): Z,Z-6,27-Hexatriactontadien-2-one**

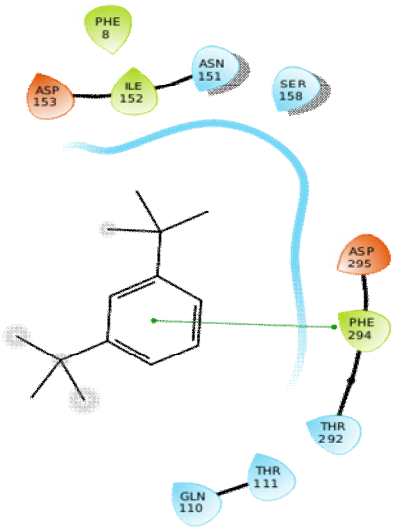



**(k): Glycidyl palmitate**

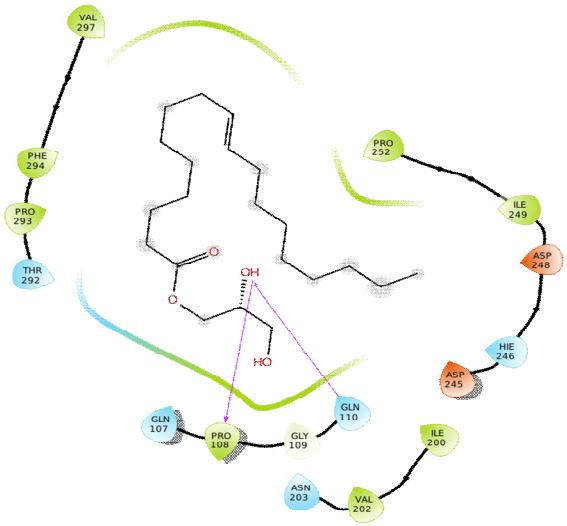
 




**(l): Propyl stearate**

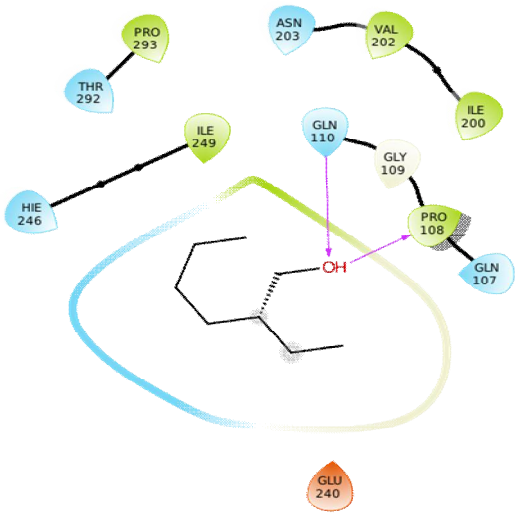



**(m): Benzene, 1,3-Bis(1,1-Dimethylethyl)-**

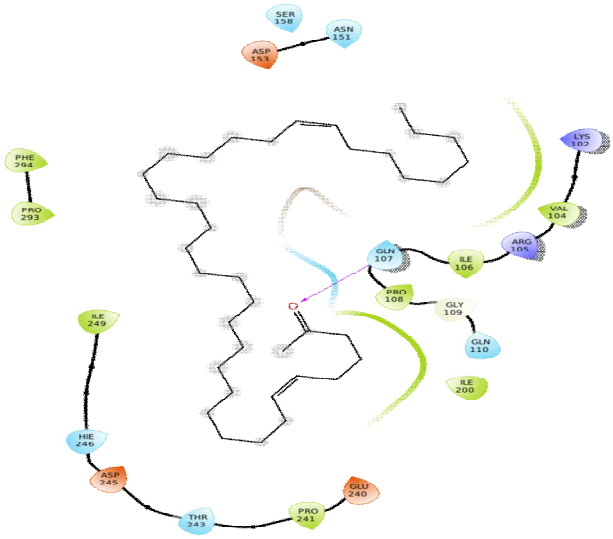



**(n): Monoelaidin**

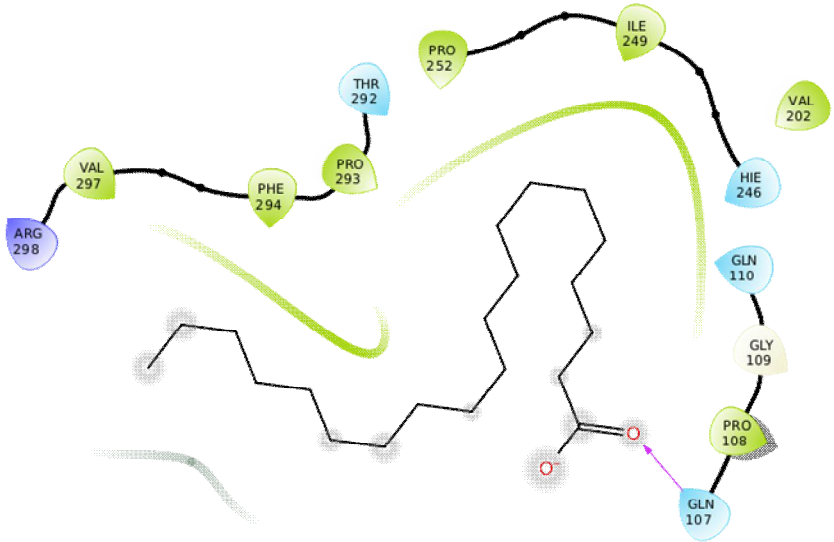
 




**(o): 1-Hexanol, 2-Ethyl-**




**(p): Z,Z-6,28-Heptatriactontadien-2-one**




**(q): Arachidic acid**

**Table 1 - Result of the docking experiment performed between the receptor (2BX4) and the ligands (Compounds)**

| S.N | Receptor | Ligand | Glide Ligand Efficiency | Docking Score | Glide G score | RMSD |
|---|---|---|---|---|---|---|
| 1 | The 3CLpro/ Mpro or mains proteases (PDB code 6LU7) from SARS-CoV | Nelfinavir (Control) | -0.1 | -3.995 | -4.009 | 1.4 |
| 2 | | (Z)-3-(Heptadec-10-En-1-Yl)Phenol | -0.161 | -3.871 | -3.872 | 1.6 |
| 3 | | Phenol, 2,4-Bis(1,1-Dimethylethyl)- | -0.245 | -3.672 | -3.672 | 0.6 |
| 4 | | Oxime-, Methoxy-Phenyl- (3) | -0.303 | -3.334 | -3.334 | 0.4 |
| 5 | | Hexadecanoic Acid, 2-Hydroxy-1-(Hydroxymethyl)Ethyl Ester | -0.144 | -3.314 | -3.314 | - |
| 6 | | 9-Octadecenoic Acid (9Z)-, Oxiranylmethyl Ester | -0.136 | -3.272 | -3.272 | - |
| 7 | | Decanedioic Acid, Bis(2-Ethylhexyl) Ester | -0.1 | -3.206 | -3.206 | - |
| 8 | | Squalene | -0.104 | -3.133 | -3.133 | 1.8 |
| 9 | | 2-Pentacosanone | -0.12 | -3.124 | -3.124 | - |
| 10 | | Z,Z-6,27-Hexatriactontadien-2-One | -0.084 | -3.119 | -3.119 | - |
| 11 | | Glycidyl Palmitate | -0.14 | -3.09 | -3.09 | - |
| 12 | | Propyl Stearate | -0.127 | -2.922 | -2.922 | - |
| 13 | | Benzene, 1,3-Bis(1,1-Dimethylethyl)- | -0.207 | -2.891 | -2.891 | 0.6 |
| 14 | | Monoelaidin | -0.11 | -2.746 | -2.746 | - |
| 15 | | 1-Hexanol, 2-Ethyl- | -0.289 | -2.604 | -2.604 | 0.6 |
| 16 | | Z,Z-6,28-Heptatriactontadien-2-One | -0.067 | -2.556 | -2.556 | - |
| 17 | | Arachidic Acid | -0.114 | -2.518 | -2.521 | - |
| 18 | | Stigmast-5-En-3-Ol,Oleate | -0.047 | -2.286 | -2.286 | - |
| 19 | | Stigmasta-5,22-Dien-3-Ol, Acetat, (3-Beta,2 | -0.069 | -2.276 | -2.276 | - |
| 20 | | Ergosta-5,7,9(11),22-Tetraen-3-Ol, (3.Beta.,22E)- | -0.077 | -2.235 | -2.235 | 0.8 |
| 21 | | Furan, Tetrahydro-2,5-Dimethyl- | -0.263 | -1.844 | -1.844 | 0.4 |
| 22 | | Hexamethylcyclotrisiloxane | -0.148 | -1.776 | -1.776 | 0.4 |
| 23 | | 2,3-Diacetoxypropyl Stearate | -0.054 | -1.665 | -1.665 | - |
| 24 | | Octane, 6-Ethyl-2-Methyl- | -0.146 | -1.604 | -1.604 | 0.6 |
| 25 | | Hexanal | -0.225 | -1.573 | -1.573 | 0.6 |
| 26 | | 2,6,11-Trimethyldodecane | -0.099 | -1.491 | -1.491 | 0.8 |
| 27 | | 9,17-Octadecadienal, (Z)- | -0.078 | -1.474 | -1.474 | 1.4 |
| 28 | | 4-Pentyl-Cyclohexanecarboxylic Acid | -0.077 | -1.377 | -1.377 | 0.8 |
| 29 | | 3-Hexanone | -0.077 | -1.377 | -1.377 | 0.4 |
| 30 | | (8Z,11Z)-Heptadecadienal | -0.077 | -1.377 | -1.377 | 1.2 |
| 31 | | Oleic Acid | -0.066 | -1.325 | -1.329 | 1.4 |
| 32 | | 1-Propene, 3,3-Dichloro- | -0.259 | -1.297 | -1.297 | 0.4 |
| 33 | | Butyl Isodecyl Phthalate | -0.05 | -1.291 | -1.291 | 1.2 |
| 34 | | Cyclodecasiloxane, Eicosamethyl- | -0.029 | -1.179 | -1.179 | 0.8 |
| 35 | | 10(E),12(Z)-Conjugated Linoleic Acid | -0.059 | -1.171 | -1.174 | 1.4 |
| 36 | | Hexadecane, 2,6,10,14-Tetramethyl- | -0.058 | -1.162 | -1.162 | 1.6 |
| 37 | | 2 Nonadecanone | -0.051 | -1.028 | -1.028 | - |
| 38 | | Heneicosane | -0.041 | -0.858 | -0.858 | - |
| 39 | | Stearic Acid | -0.041 | -0.815 | -0.819 | - |
| 40 | | Palmitic Acid | -0.029 | -0.522 | -0.526 | 1.4 |
| 41 | | Hexadecanal | -0.028 | -0.479 | -0.479 | 1.2 |
| 42 | | Cis-9-Hexadecenal | -0.02 | -0.344 | -0.344 | 1.2 |
| 43 | | 2-Heptodecanone | -0.011 | -0.207 | -0.207 | 1.4 |
| 44 | | 9-Heptadecanone | -0.01 | -0.173 | -0.173 | 1.4 |
| 45 | | 1-Cyclohexyldimethylsilyloxybutane | 0 | 0.007 | 0.007 | 0.6 |
| 46 | | Icosanal | 0.005 | 0.097 | 0.097 | - |
| 47 | | Hexadecane | 0.006 | 0.1 | 0.1 | 1.4 |
| 48 | | Dodecane | 0.027 | 0.319 | 0.319 | 0.8 |
| 49 | | Eicosane | 0.034 | 0.677 | 0.677 | - |
| 50 | | 8-Octadecanone | 0.038 | 0.725 | 0.725 | 1.4 |
| 51 | | Dotriacontane | 0.08 | 2.575 | 2.575 | - |

**Table 2 - Result of the docking experiment performed between the receptor (6LU7) and the ligands (Compounds)**

| S.No | Receptor | Ligand | Docking Score | Glide Ligand Efficiency | Glide G score | RMSD |
|---|---|---|---|---|---|---|
| 1 | The 3CLpro/Mpro or mains proteases: $M^{Cov2_{Pro}}$ (PDB code 6LU7) 7) from SARS-CoV-2. | Nelfinavir (Control) | -4.673 | -0.117 | -4.687 | 1.4 |
| 2 | | Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester | -5.118 | -0.223 | -5.118 | - |
| 3 | | Monoelaidin | -4.515 | -0.181 | -4.515 | - |
| 4 | | (Z)-3-(Heptadec-10-en-1-yl)phenol | -4.375 | -0.182 | -4.376 | 1.6 |
| 5 | | Decanedioic acid, bis(2-ethylhexyl) ester | -4.085 | -0.128 | -4.085 | - |
| 6 | | Glycidyl palmitate | -3.837 | -0.174 | -3.837 | - |
| 7 | | Phenol, 2,4-Bis(1,1-Dimethylethyl)- | -3.754 | -0.25 | -3.754 | 0.6 |
| 8 | | Squalene | -3.747 | -0.125 | -3.747 | 1.8 |
| 9 | | Butyl isodecyl phthalate | -3.741 | -0.144 | -3.741 | - |
| 10 | | Propyl stearate | -3.611 | -0.157 | -3.611 | - |
| 11 | | Oxime-, methoxy-phenyl- (3) | -3.561 | -0.324 | -3.562 | 0.4 |
| 12 | | 9-Octadecenoic acid (9Z)-, oxiranylmethyl ester | -3.512 | -0.146 | -3.512 | - |
| 13 | | Ergosta-5,7,9(11),22-tetraen-3-ol, (3.beta.,22E)- | -3.282 | -0.113 | -3.282 | 0.8 |
| 14 | | Furan, tetrahydro-2,5-dimethyl-.1 | -3.268 | -0.467 | -3.268 | 0.4 |
| 15 | | 4-Pentyl-Cyclohexanecarboxylic Acid | -3.239 | -0.231 | -3.242 | 0.8 |
| 16 | | Stigmasta-5,22-Dien-3-Ol, Acetat, (3-Beta,2 | -3.201 | -0.097 | -3.201 | - |
| 17 | | 2 Nonadecanone | -3.161 | -0.158 | -3.161 | - |
| 18 | | Z,Z-6,27-Hexatriactontadien-2-one | -3.104 | -0.084 | -3.104 | - |
| 19 | | 2-Pentacosanone | -3.039 | -0.117 | -3.039 | - |
| 20 | | 1-Hexanol, 2-Ethyl- | -2.885 | -0.321 | -2.885 | 0.6 |
| 21 | | Octane, 6-Ethyl-2-Methyl- | -2.794 | -0.254 | -2.794 | 0.6 |
| 22 | | Oleic acid | -2.776 | -0.139 | -2.78 | 1.4 |
| 23 | | 9,17-Octadecadienal, (Z)- | -2.759 | -0.145 | -2.759 | 1.4 |
| 24 | | 1-Cyclohexyldimethylsilyloxybutane | -2.756 | -0.197 | -2.756 | 0.6 |
| 25 | | 3-Hexanone | -2.728 | -0.39 | -2.728 | 0.4 |
| 26 | | Benzene, 1,3-Bis(1,1-Dimethylethyl)- | -2.503 | -0.179 | -2.503 | 0.6 |
| 27 | | Hexanal | -2.442 | -0.349 | -2.442 | 0.6 |
| 28 | | Hexadecane, 2,6,10,14-Tetramethyl- | -2.42 | -0.121 | -2.42 | 1.6 |
| 29 | | 10(E),12(Z)-Conjugated linoleic acid | -2.318 | -0.116 | -2.321 | 1.4 |
| 30 | | Z,Z-6,28-Heptatriactontadien-2-one | -2.252 | -0.059 | -2.252 | - |
| 31 | | Arachidic acid | -2.236 | -0.102 | -2.239 | - |
| 32 | | cis-9-hexadecenal | -2.218 | -0.13 | -2.218 | 1.2 |
| 33 | | Icosanal | -2.211 | -0.105 | -2.211 | - |
| 34 | | Hexadecanal | -2.131 | -0.125 | -2.131 | 1.2 |
| 35 | | 2-Heptodecanone | -2.121 | -0.118 | -2.121 | 1.4 |
| 36 | | (8Z,11Z)-Heptadecadienal | -2.024 | -0.112 | -2.024 | 1.2 |
| 37 | | 2,6,11-Trimethyldodecane | -1.999 | -0.133 | -1.999 | 0.8 |
| 38 | | Hexamethylcyclotrisiloxane | -1.992 | -0.166 | -1.992 | 0.4 |
| 39 | | 9-Heptadecanone | -1.982 | -0.11 | -1.982 | 1.4 |
| 40 | | Stearic acid | -1.97 | -0.098 | -1.973 | - |
| 41 | | Palmitic acid | -1.71 | -0.095 | -1.714 | 1.4 |
| 42 | | 2,3-Diacetoxypropyl stearate | -1.669 | -0.054 | -1.669 | - |
| 43 | | 8-Octadecanone | -1.559 | -0.082 | -1.559 | 1.4 |
| 44 | | 1-Propene, 3,3-Dichloro- | -1.5 | -0.3 | -1.5 | 0.4 |
| 45 | | Cyclodecasiloxane, eicosamethyl- | -1.289 | -0.032 | -1.289 | 0.8 |
| 46 | | Heneicosane | -1.284 | -0.061 | -1.284 | - |
| 47 | | Tetradecane | -1.125 | -0.08 | -1.125 | 1.2 |
| 48 | | Eicosane | -0.831 | -0.042 | -0.831 | - |
| 49 | | Hexadecane | -0.751 | -0.047 | -0.751 | 1.4 |
| 50 | | Dodecane | -0.62 | -0.052 | -0.62 | 0.8 |
| 51 | | Stigmast-5-en-3-ol,oleate | -0.27 | -0.006 | -0.27 | - |

**Table 3 - Potential candidates for targeted drug treatment approach for SARS-CoV-2 ($M^{Cov1}_{Pro}$ and $M^{Cov2}_{Pro}$)**

| S. No. | Compound | G score with 2BX4 | G score with 6LU7 |
|---|---|---|---|
| 1 | Hexadecanoic acid, 2-hydroxy-1 (hydroxymethyl) ethyl ester | -5.118 | -3.314 |
| 2 | Monoelaidin | -4.515 | -2.746 |
| 3 | (Z)-3-(Heptadec-10-en-1-yl) phenol | -4.376 | -3.872 |
| 4 | Decanedioic acid, bis(2-ethylhexyl) ester.1 | -4.085 | -3.206 |
| 5 | Glycidyl palmitate | -3.837 | -3.09 |
| 6 | Phenol,2,4-Bis(1,1-Dimethylethyl) | -3.754 | -3.672 |

**Table S1 - Metabolites from bioconverted Docosahexaenoic acid at 24 hrs**

| S. No. | Retention Time (min) | Percentage (%) | Compound Name | Medicinal Properties |
|---|---|---|---|---|
| 1 | 22.176 | 13.27 | 2-Nonadecanone | Anti-depression<br>Anti-bacterial<br>Anti-tumor |
| 2 | 21.941 | 12.91 | Z,Z-6,27-Hexatriactontadien-2-one | - |
| 3 | 21.164 | 8.47 | cis-9-Hexadecenal | Anti-biofilm<br>Anti-melanogenic<br>Anti-fungal |
| 4 | 21.395 | 7.89 | Eicosanal- | Anti-depressant<br>Anxiolytic effect<br>Anti-oxidant |
| 5 | 26.623 | 7.54 | Stigmast-5-En-3-Ol, Oleat | Anti-obesity |
| 6 | 26.922 | 5.07 | Tetrapentacontane | Anti-microbial<br>Anti-Oxidant |
| 7 | 22.489 | 3.26 | Oleic Acid | Anti-tumor<br>Anti-Microbial |
| 8 | 22.698 | 3.20 | Octadecanoic acid | Anti-bacterial<br>Anti-oxidant |
| 9 | 21.275 | 2.15 | (Z)-3-(Heptadec-10-en-1-yl)phenol | Anti-bacterial<br>Anti-diarrheal<br>Anti-oxidant |
| 10 | 20.193 | 2.69 | 2-Heptadecanone | |
| 11 | 20.774 | 2.05 | n-Hexadecanoic acid | Anti-bacterial<br>Anti-fungal<br>Anti-biofilm<br>Anti-cancer |
| 12 | 24.730 | 1.95 | Heneicosane | Anti-inflammatory |
| 13 | 15.782 | 1.65 | Phenol, 2,4-Bis(1,1-Dimethylethyl)- | Anti-fungal<br>Anti-oxidant |
| 14 | 19.326 | 1.64 | Hexadecanal | - |
| 15 | 21.880 | 1.34 | 8,11-Heptadecadienal, (8Z,11Z)- | - |
| 16 | 21.102 | 1.28 | 9,17-Octadecadienal, (Z)- | Antimicrobial |
| 17 | 23.985 | 0.99 | 2-Pentacosanone | - |
| 18 | 16.871 | 0.99 | Hexadecane | - |
| 19 | 27.063 | 0.97 | 8-Octadecanone | Antimicrobial |
| 20 | 25.397 | 0.89 | Stigmasta-5,22-Dien-3-Ol, Acetat, (3-Beta,2 | Antimicrobial |
| 21 | 28.040 | 0.72 | 9-Heptadecanone | - |
| 22 | 27.786 | 0.70 | Z,Z-6,28-Heptatriactontadien-2-one | Alpha-amylase Inhibition Antioxidant Activity |

**Table S2 - Metabolites from bioconverted Docosahexaenoic acid at 48 hrs**

| S. No. | Retention Time (min) | Percentage (%) | Compound Name | Medicinal Properties |
|---|---|---|---|---|
| 1 | 22.996 | 15.86 | Octadecanoic acid | Anti-bacterial<br>Anti-oxidant |
| 2 | 22.743 | 13.93 | 6-Octadecenoic acid | Anti-bacterial |
| 3 | 20.948 | 10.92 | n-Hexadecanoic acid | Anti-bacterial<br>Anti-fungal<br>Anti-biofilm<br>Anti-cancer |
| 4 | 27.000 | 8.34 | 9-Octadecenoic acid (Z)-, 2,3-dihydroxypropyl ester | Anti-microbial<br>Anti-Fungal |
| 5 | 27.214 | 7.11 | Octadecanoic acid, 2,3-dihydroxypropyl ester | Anti-microbial<br>Anti-oxidant |
| 6 | 25.389 | 4.40 | 9-Octadecenoic acid (Z)-, oxiranylmethyl ester | - |
| 7 | 26.680 | 4.30 | n-Propyl 9-octadecenoate | - |
| 8 | 25.582 | 3.50 | Glycidyl palmitate | Anti-staphylococcal activity |
| 9 | 21.398 | 11.29 | Eicosanal- | Anti-depressant<br>Anxiolytic effect<br>Anti-oxidant |
| 10 | 21.168 | 3.01 | cis-9-Hexadecenal | Anti-biofilm<br>Anti-melanogenic<br>Anti-fungal |
| 11 | 25.490 | 2.83 | Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethy | Anti-fungal<br>Anti-microbial |
| 12 | 26.786 | 2.31 | 1-Cyclohexyldimethylsilyloxybutane | - |
| 13 | 26.880 | 2.26 | Octadecanoic acid, propyl ester | - |
| 14 | 24.491 | 1.75 | Eicosanoic acid | Anti-bacterial |
| 15 | 6.560 | 1.43 | Oxime-, methoxy-phenyl- | Pancreatic lipase inhibitory activity |
| 16 | 28.188 | 1.41 | Dotriacontane | Anti-fungal |
| 17 | 4.716 | 1.18 | Hexanal | Anti-fungal |
| 18 | 21.940 | 1.15 | Z,Z-6,27-Hexatriactontadien-2-one | - |

**Table S3 - Metabolites from bioconverted Docosahexaenoic acid at 72 hrs**

| S. No. | Retention Time (min) | Percentage (%) | Compound Name | Medicinal Properties |
|---|---|---|---|---|
| 1 | 4.165 | 17.03 | Benzene, Methyl- | - |
| 2 | 15.766 | 10.84 | Phenol, 2,4-Bis(1,1-Dimethylethyl | Anti-fungal<br>Anti-oxidant |
| 3 | 6.517 | 4.75 | Oxime-, methoxy-phenyl- | Pancreatic lipase inhibitory activity |
| 4 | 18.019 | 4.61 | Eicosane | Anti-microbial |
| 5 | 9.401 | 4.43 | Cyclotrisiloxane, hexamethyl- | Anti-oxidant<br>Anti-biofilm |
| 6 | 16.862 | 4.11 | Hexadecane | - |
| 7 | 12.619 | 3.28 | Dodecane, 2,6,11-trimethyl- | Anti-microbial<br>Anti-oxidant |
| 8 | 14.351 | 3.12 | Tetradecane | - |
| 9 | 19.115 | 3.03 | Heneicosane | Anti-inflammatory |
| 10 | 4.460 | 2.65 | 3-Hexanone | - |
| 11 | 22.308 | 2.62 | Octadecane | - |
| 12 | 4.538 | 2.39 | 2-Hexanone | - |
| 13 | 24.218 | 2.32 | 1H,5H-Cyclopropa[G][1,2,4]Triazolo[1,2-A] | - |
| 14 | 24.162 | 2.31 | Hexatriacontane | Anti-oxidant<br>Anti-microbial |
| 15 | 20.757 | 1.90 | 1-Butyl 2-(8-Methylnonyl) Phthalate # | - |
| 16 | 26.220 | 1.90 | Silikonfett Se30 (Grevels) | - |
| 17 | 9.209 | 1.86 | Octane, 6-Ethyl-2-Methyl- | - |
| 18 | 3.365 | 1.82 | Furan, tetrahydro-2,5-dimethyl- | - |
| 19 | 24.112 | 1.50 | Cyclodecasiloxane, eicosamethyl- | Immunotherapeutic agent |
| 20 | 25.846 | 1.48 | Tetrapentacontane | Anti-microbial<br>Anti-Oxidant |
| 21 | 12.282 | 1.41 | Benzene, 1,3-Bis(1,1-Dimethylethyl)- | Anti-cancer |
| 22 | 11.521 | 1.38 | Dodecane | - |
| 23 | 20.574 | 1.29 | 4-Pentyl-Cyclohexanecarboxylic Acid | - |

**Table S4 - Metabolites from bioconverted Docosahexaenoic acid at 96 hrs**

| S. No. | Retention Time (min) | Percentage (%) | Compound Name | Medicinal Properties |
|---|---|---|---|---|
| 1 | 28.162 | 7.18 | Decanedioic acid, bis(2-ethylhexyl) ester | Anti-fungal |
| 2 | 20.769 | 6.67 | n-Hexadecanoic acid | Anti-bacterial<br>Anti-fungal<br>Anti-biofilm<br>Anti-cancer |
| 3 | 22.688 | 5.70 | Octadecanoic acid | Anti-bacterial<br>Anti-oxidant |
| 4 | 4.164 | 5.56 | Benzene, Methyl- | - |
| 5 | 8.781 | 5.49 | 1-Hexanol, 2-Ethyl- | - |
| 6 | 15.772 | 5.11 | Phenol, 2,4-Bis(1,1-Dimethylethyl)- | Anti-fungal<br>Anti-oxidant |
| 7 | 23.653 | 4.90 | Ergosta-5,7,9(11),22-tetraen-3-ol, (3.beta.,22E)- | - |
| 8 | 24.174 | 3.72 | Tetrapentacontane | Anti-microbial<br>Antioxidant |
| 9 | 18.024 | 2.88 | Eicosane | Anti-microbial |
| 10 | 16.866 | 2.68 | Hexadecane | - |
| 11 | 28.368 | 2.56 | Squalene | - |
| 12 | 15.499 | 2.17 | Hexadecane, 2,6,10,14-Tetramethyl- | - |
| 13 | 19.120 | 2.06 | Heneicosane | Anti-inflammatory |
| 14 | 22.473 | 1.96 | Oleic Acid | Anti-tumor<br>Anti-microbial |
| 15 | 12.623 | 1.90 | Dodecane, 2,6,11-trimethyl- | Anti-microbial<br>Anti-oxidant |
| 16 | 14.356 | 1.88 | Tetradecane | - |
| 17 | 24.115 | 1.67 | Cyclodecasiloxane, eicosamethyl- | Immunotherapeutic agent |
| 18 | 6.999 | 1.48 | 1-Propene, 3,3-Dichloro- | - |
| 19 | 25.824 | 1.48 | Bis(2-ethylhexyl) phthalate | - |
| 20 | 22.314 | 1.44 | Hexatriacontane | Anti-microbial |
| 21 | 22.421 | 1.44 | 10(E),12(Z)-Conjugated linoleic acid | Anti-carcinogen<br>Anti-inflammatory |
| 22 | 4.450 | 1.36 | 3-Hexanone | Anti-microbial<br>Anti-oxidant |
| 23 | 4.525 | 1.20 | 2-Hexanone | - |
| 24 | 20.411 | 1.15 | Hexadecanoic acid, methyl ester | Anti-oxidant |
| 25 | 24.814 | 1.13 | 1,16-Dibromohexadecane | - |
| 26 | 18.671 | 0.99 | Tetradecanoic acid | Anti-oxidant<br>Anti-bacterial |
| 27 | 20.709 | 0.98 | 2,6,10,15,19,23-Hexamethyltetracosane | - |
| 28 | 9.212 | 0.95 | Octane, 6-Ethyl-2-Methyl- | Anti-cancer |
| 29 | 20.581 | 0.94 | 4-Pentyl-Cyclohexanecarboxylic Acid | - |
| 30 | 4.766 | 0.90 | 2-Hexanol | Antimicrobial<br>Anti-inflammatory |
| 31 | 16.065 | 0.88 | Hexadecane, 2,6,10,14-Tetramethyl | - |
| 32 | 12.730 | 0.85 | 4-Propylbenzaldehyde | - |
| 33 | 11.525 | 0.81 | Dodecane | - |
| 34 | 16.778 | 0.81 | 1-Hexadecanol | - |
| 35 | 4.691 | 0.76 | 3-Hexanol | Anti-bacterial |
| 36 | 13.282 | 0.75 | Dodecane, 4,6-dimethyl- | - |

**Table S5 - Metabolites from bioconverted Docosahexaenoic acid at 120 hrs**

| S. No. | Retention Time (min) | Percentage (%) | Compound Name | Medicinal Properties |
|---|---|---|---|---|
| 1 | 20.803 | 15.04 | n-Hexadecanoic acid | Anti-bacterial<br>Anti-fungal<br>Anti-biofilm<br>Anti-cancer |
| 2 | 22.709 | 10.97 | Octadecanoic acid | Anti-bacterial<br>Anti-oxidant |
| 3 | 23.462 | 10.31 | Palmitoyl chloride | - |
| 4 | 24.962 | 8.77 | 9-Octadecenoic acid (Z)-, 2,3-dihydroxypropyl ester | Anti-microbial<br>Anti-fungal |
| 5 | 27.952 | 10.69 | Butyl 4,7,10,13,16,19-docosahexaenoate | - |
| 6 | 23.874 | 7.70 | Glycidyl palmitate | - |
| 7 | 25.364 | 5.43 | 9-Octadecenoic acid (Z)-, oxiranylmethyl ester | - |
| 8 | 3.172 | 5.02 | Heptane | - |
| 9 | 22.488 | 8.71 | Oleic Acid | Anti-tumor<br>Anti-microbial |
| 10 | 25.468 | 2.07 | Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethy | Anti-fungal<br>Anti-microbial |
| 11 | 27.861 | 2.73 | Methyl 4,7,10,13,16-docosapentaenoate | - |
| 12 | 26.959 | 1.87 | cis-10-Pentadecenoic acid, isobutyl ester | - |
| 13 | 18.677 | 1.65 | Tetradecanoic acid | Anti-oxidant<br>Anti-bacterial |
| 14 | 25.163 | 1.59 | Octadecanoic acid, 2,3-dihydroxypropyl ester | Anti-microbial<br>Anti-oxidant |
| 15 | 15.771 | 1.50 | Phenol, 2,4-Bis(1,1-Dimethylethyl)- | Anti-fungal<br>Anti-oxidant |
| 16 | 22.429 | 1.46 | 9,12-Octadecadienoic Acid (Z,Z)- | Anti-bacterial |
| 17 | 25.561 | 1.28 | Myristic acid glycidyl ester | - |
| 19 | 18.023 | 0.80 | Eicosane | Anti-microbial |
| 20 | 16.866 | 0.75 | Hexadecane | - |
| 21 | 24.915 | 0.61 | 3-({[2-(4-Fluorophenyl)Ethyl]Amino}Methyl | - |
| 22 | 19.118 | 0.59 | Heneicosane | Anti-inflammatory |
| 23 | 12.623 | 0.48 | Dodecane, 4,6-dimethyl- | - |

**Table S6 - Metabolites from bioconverted Docosahexaenoic acid using *Bacillus cereus***

| S. No. | Retention Time (min) | Percentage (%) | Compound Name | Medicinal Properties |
|---|---|---|---|---|
| 1 | 22.176 | 13.27 | 2-Nonadecanone | Anti-depression<br>Anti-bacterial<br>Anti-tumor |
| 2 | 21.941 | 12.91 | Z,Z-6,27-Hexatriactontadien-2-one | - |
| 3 | 43.881 | 11.48 | cis-9-Hexadecenal | Anti-biofilm<br>Anti-melanogenic<br>Anti-fungal |
| 4 | 21.395 | 7.89 | Eicosanal- | Anti-depressant<br>Anxiolytic effect<br>Anti-oxidant |
| 5 | 26.623 | 7.54 | Stigmast-5-En-3-Ol, Oleat | Anti-obesity |
| 6 | 26.922 | 10.27 | Tetrapentacontane | Anti-microbial<br>Anti-oxidant |
| 7 | 22.489 | 13.93 | Oleic Acid | Anti-tumor<br>Anti-microbial |
| 8 | 22.698 | 32.53 | Octadecanoic acid | Anti-bacterial<br>Anti-oxidant |
| 9 | 21.275 | 2.15 | (Z)-3-(Heptadec-10-en-1-yl)phenol | Anti-bacterial<br>Anti-diarrheal<br>Anti-oxidant |
| 10 | 20.193 | 2.69 | 2-Heptadecanone | - |
| 11 | 20.774 | 34.68 | n-Hexadecanoic acid | Anti-bacterial<br>Anti-fungal |

| | | | | |
|---|---|---|---|---|
| | | | | Anti-biofilm<br>Anti-cancer |
| 12 | 24.730 | 7.63 | Heneicosane | Anti-inflammatory |
| 13 | 15.782 | 31.59 | Phenol, 2,4-Bis(1,1-Dimethylethyl)- | Anti-fungal<br>Anti-oxidant |
| 14 | 19.326 | 1.64 | Hexadecanal | - |
| 15 | 21.880 | 1.34 | 8,11-Heptadecadienal, (8Z,11Z)- | - |
| 16 | 21.102 | 1.28 | 9,17-Octadecadienal, (Z)- | Antimicrobial agent |
| 17 | 23.985 | 0.99 | 2-Pentacosanone | - |
| 18 | 16.871 | 8.53 | Hexadecane | - |
| 19 | 27.063 | 0.97 | 8-Octadecanone | Antimicrobial metabolite |
| 20 | 25.397 | 0.89 | Stigmasta-5,22-Dien-3-Ol, Acetat, (3-Beta,2 | Antimicrobial |
| 21 | 28.040 | 0.72 | 9-Heptadecanone | - |
| 22 | 27.786 | 0.70 | Z,Z-6,28-Heptatriactontadien-2-one | Alpha-amylase inhibition<br>Antioxidant activity |
| 23 | 27.000 | 17.11 | 9-Octadecenoic acid (Z)-, 2,3-dihydroxypropyl ester | Anti-microbial<br>Anti-fungal |
| 24 | 27.214 | 8.7 | Octadecanoic acid, 2,3-dihydroxypropyl ester | Anti-microbial<br>Anti-oxidant |
| 25 | 25.389 | 9.83 | 9-Octadecenoic acid (Z)-, oxiranylmethyl ester | - |
| 26 | 26.680 | 4.30 | n-Propyl 9-octadecenoate | - |
| 27 | 25.582 | 3.50 | Glycidyl palmitate | Anti-staphylococcal activity |
| 28 | 25.490 | 4.9 | Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethy | Anti-fungal<br>Anti-microbial |
| 29 | 26.786 | 2.31 | 1-Cyclohexyldimethylsilyloxybutane | - |
| 30 | 26.880 | 2.26 | Octadecanoic acid, propyl ester | - |
| 31 | 24.491 | 1.75 | Eicosanoic acid | Anti-bacterial |
| 32 | 6.560 | 6.18 | Oxime-, methoxy-phenyl- | Pancreatic lipase inhibitory activity |
| 33 | 28.188 | 1.41 | Dotriacontane | Anti-fungal |
| 34 | 4.716 | 1.18 | Hexanal | Anti-fungal |
| 35 | 4.165 | 22.59 | Benzene, Methyl- | - |
| 36 | 18.019 | 8.29 | Eicosane | Anti-microbial |
| 37 | 9.401 | 4.43 | Cyclotrisiloxane, hexamethyl- | Anti-oxidant<br>Anti-biofilm |
| 38 | 12.619 | 5.18 | Dodecane, 2,6,11-trimethyl- | Anti-microbial<br>Anti-oxidant |
| 39 | 14.351 | 5.0 | Tetradecane | - |
| 40 | 4.460 | 4.01 | 3-Hexanone | Anti-microbial<br>Anti-oxidant |
| 41 | 22.308 | 2.62 | Octadecane | - |
| 42 | 4.538 | 3.59 | 2-Hexanone | - |
| 43 | 24.218 | 2.32 | 1H,5H-Cyclopropa[G][1,2,4]Triazolo[1,2-A] | - |
| 44 | 24.162 | 3.75 | Hexatriacontane | Anti-oxidant<br>Anti-microbial |
| 45 | 20.757 | 1.90 | 1-Butyl 2-(8-Methylnonyl) Phthalate # | - |
| 46 | 26.220 | 1.90 | Silikonfett Se30 (Grevels) | - |
| 47 | 9.209 | 1.86 | Octane, 6-Ethyl-2-Methyl- | - |
| 48 | 3.365 | 1.82 | Furan, tetrahydro-2,5-dimethyl- | - |
| 49 | 24.112 | 1.50 | Cyclodecasiloxane, eicosamethyl- | Immunotherapeutic agent |
| 50 | 12.282 | 1.41 | Benzene, 1,3-Bis(1,1-Dimethylethyl)- | Anti-cancer |
| 51 | 11.521 | 2.19 | Dodecane | - |
| 52 | 20.574 | 1.29 | 4-Pentyl-Cyclohexanecarboxylic Acid | - |
| 53 | 28.162 | 7.18 | Decanedioic acid, bis(2-ethylhexyl) ester | Anti-fungal |
| 54 | 8.781 | 5.49 | 1-Hexanol, 2-Ethyl- | - |
| 55 | 23.653 | 4.90 | Ergosta-5,7,9(11),22-tetraen-3-ol, (3.beta.,22E)- | - |
| 56 | 28.368 | 2.56 | Squalene | - |
| 57 | 15.499 | 3.05 | Hexadecane, 2,6,10,14-Tetramethyl- | - |

| | | | | |
|---|---|---|---|---|
| 58 | 24.115 | 1.67 | Cyclodecasiloxane, eicosamethyl- | Immunotherapeutic agent |
| 59 | 6.999 | 1.48 | 1-Propene, 3,3-Dichloro- | - |
| 60 | 25.824 | 1.48 | Bis(2-ethylhexyl) phthalate | - |
| 61 | 22.421 | 1.44 | 10(E),12(Z)-Conjugated linoleic acid | Anti-carcinogen Anti-inflammatory |
| 62 | 20.411 | 1.15 | Hexadecanoic acid, methyl ester | Anti-oxidant |
| 63 | 24.814 | 1.13 | 1,16-Dibromohexadecane | - |
| 64 | 18.671 | 5.89 | Tetradecanoic acid | Anti-oxidant Anti-bacterial |
| 65 | 20.709 | 0.98 | 2,6,10,15,19,23-Hexamethyltetracosane | - |
| 66 | 9.212 | 0.95 | Octane, 6-Ethyl-2-Methyl- | Anti-cancer |
| 67 | 20.581 | 0.94 | 4-Pentyl-Cyclohexanecarboxylic Acid | - |
| 68 | 4.766 | 0.90 | 2-Hexanol | Anti-microbial Anti-inflammatory |
| 69 | 12.730 | 0.85 | 4-Propylbenzaldehyde | - |
| 70 | 16.778 | 0.81 | 1-Hexadecanol | - |
| 71 | 4.691 | 0.76 | 3-Hexanol | Anti-bacterial |
| 72 | 13.282 | 0.75 | Dodecane, 4,6-dimethyl- | - |
| 73 | 23.462 | 10.31 | Palmitoyl chloride | - |
| 74 | 27.952 | 10.69 | Butyl 4,7,10,13,16,19-docosahexaenoate | - |
| 75 | 23.874 | 7.70 | Glycidyl palmitate | - |
| 76 | 3.172 | 5.02 | Heptane | - |
| 77 | 27.861 | 2.73 | Methyl 4,7,10,13,16-docosapentaenoate | - |
| 78 | 26.959 | 1.87 | cis-10-Pentadecenoic acid, isobutyl ester | - |
| 79 | 22.429 | 1.46 | 9,12-Octadecadienoic Acid (Z,Z)- | Anti-bacterial |
| 80 | 25.561 | 1.28 | Myristic acid glycidyl ester | - |
| 81 | 24.915 | 0.61 | 3-({[2-(4-Fluorophenyl)Ethyl]Amino}Methyl | - |
| 82 | 12.623 | 0.48 | Dodecane, 4,6-dimethyl- | - |

**Table S7 - Result of the docking experiment performed between the receptor (2BX4) and the ligands (Compounds)**

| S. No. | Ligands | Glide Ligand Efficiency | Docking Score | Glide Score | Amino acid | Amino acid Residue position | Type of Interactions |
|---|---|---|---|---|---|---|---|
| 1. | Nelfinavir (Control) | -0.117 | -4.673 | -4.687 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Valine | Val 104 | Hydrophobic |
| | | | | | Arginine | Arg 105 | Positively charged |
| | | | | | Isoleucine | Ile 106 | Hydrophobic |
| | | | | | Glutamine | Gln 107 | Polar |
| | | | | | Proline | Pro 108 | Hydrophobic Hydrogen Bond with "OH" |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar Hydrogen Bond with "NH" |
| | | | | | Threonine | Thr 111 | Polar |
| | | | | | Asparagine | Asx 151 | Polar |
| | | | | | Histidine | His 246 | Polar |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic Hydrogen bond with "N+H" |
| | | | | | Aspartate | Asp 295 | Negatively charged |
| 2. | Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester | -0.223 | -5.118 | -5.118 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Glutamine | Gln 107 | Polar |
| | | | | | Proline | Pro 108 | Hydrophobic |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | Threonine | Thr 111 | Polar **Hydrogen Bond with "OH"(Distance-2.05)** |
| | | | | | Glutamine | Gln 127 | Polar |
| | | | | | Proline | Pro 132 | Hydrophobic |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Threonine | Thr 201 | Polar |
| | | | | | Leucine | Leu 202 | Hydrophobic |
| | | | | | Asparagine | Asn 203 | Polar |
| | | | | | Glutamate | Glu 240 | Negatively charged |
| | | | | | Leucine | Leu 242 | Hydrophobic |
| | | | | | Histidine | His 246 | Polar |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| | | | | | Aspartate | Asp 295 | Negatively charged **Hydrogen Bond with "OH"(Distance-1.72)** |
| | | | | | Arginine | Arg 298 | Positively charged |
| 3. | Monoelaidin | -4.515 | -0.181 | -4.515 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Glutamine | Gln 107 | Polar |
| | | | | | Proline | Pro 108 | Proline |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar |
| | | | | | Threonine | Thr 111 | Polar Hydrogen Bond with "OH"(Distance-1.84) |
| | | | | | Glutamine | Gln 127 | Polar |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Threonine | Thr 201 | Polar |
| | | | | | Leucine | Leu 202 | Hydrophobic |
| | | | | | Asparagine | Asn 203 | Polar |
| | | | | | Glutamate | Glu 240 | Negatively charged |
| | | | | | Leucine | Leu 242 | Hydrophobic |
| | | | | | Histidine | His 246 | Polar |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| | | | | | Aspartate | Asp 295 | Negatively charged Hydrogen Bond with "OH"(Distance-1.72) |
| 4. | (Z)-3-(Heptadec-10-en-1-yl)phenol | -0.182 | -4.375 | -4.376 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Lysine | Lys 102 | Positively charged |
| | | | | | Valine | Val 104 | Hydrophobic |
| | | | | | Isoleucine | Ile 106 | Hydrophobic |
| | | | | | Glutamine | Gln 107 | Polar |
| | | | | | Proline | Pro 108 | Hydrophobic |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar |
| | | | | | Threonine | Thr 111 | Polar |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 152 | Hydrophobic |
| | | | | | Aspartate | Asp 153 | Negatively |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | | | charged |
| | | | | | Serine | Ser 158 | Polar |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Leucine | Leu 202 | Hydrophobic |
| | | | | | Asparagine | Asn 203 | Polar Hydrogen Bond with "OH"(Distance-2.01) |
| | | | | | Histidine | His 246 | Polar |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| | | | | | Aspartate | Asp 295 | Negatively charged |
| | | | | | Arginine | Arg 298 | Positively charged |
| 5. | Decanedioic acid, bis(2-ethylhexyl) ester.1 | -0.128 | -4.085 | -4.085 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Lysine | Lys 102 | Positively charged |
| | | | | | Isoleucine | Ile 106 | Hydrophobic |
| | | | | | Glutamine | Gln 107 | Polar |
| | | | | | Proline | Pro 108 | Hydrophobic |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar |
| | | | | | Threonine | Thr 111 | Polar |
| | | | | | Proline | Pro 132 | Hydrophobic |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 152 | Hydrophobic |
| | | | | | Aspartate | Asp 153 | Negatively charged |
| | | | | | Serine | Ser 158 | Polar |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Threonine | Thr 201 | Polar |
| | | | | | Leucine | Leu 202 | Hydrophobic |
| | | | | | Glutamate | Glu 240 | Negatively charged |
| | | | | | Histidine | His 246 | Polar Hydrogen Bond with"O"(Distance-2.51) |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| | | | | | Aspartate | Asp 295 | Negatively charged |
| | | | | | Arginine | Arg 298 | Positively charged |
| 6. | Glycidyl palmitate | -0.174 | -3.837 | -3.837 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Lysine | Lys 102 | Positively charged |
| | | | | | Isoleucine | Ile 106 | Hydrophobic |
| | | | | | Glutamine | Gln 107 | Polar |
| | | | | | Proline | Pro 108 | Hydrophobic |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar |
| | | | | | Threonine | Thr 111 | Polar |
| | | | | | Proline | Pro 132 | Hydrophobic |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 152 | Hydrophobic |
| | | | | | Aspartate | Asp 153 | Negatively charged |
| | | | | | Serine | Ser 158 | Polar |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Threonine | Thr 201 | Polar |
| | | | | | Leucine | Leu 202 | Hydrophobic Hydrogen Bond with |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | | | "O"(Distance-2.18) |
| | | | | | Asparagine | Asn 203 | Polar |
| | | | | | Glutamate | Glu 240 | Negatively charged |
| | | | | | Leucine | Leu 242 | Hydrophobic |
| | | | | | Histidine | His 246 | Polar |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |

**Table S8 - Result of the docking experiment performed between the receptor (6LU7) and the ligands (Compounds)**

| S.No | Ligands | Glide Ligand Efficiency | Docking Score | Glide Score | Amino acid | Amino acid Residue | Type of Interactions |
|---|---|---|---|---|---|---|---|
| 1. | Nelfinavir (Control) | -0.1 | -3.995 | -4.009 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Valine | Val 104 | Hydrophobic |
| | | | | | Arginine | Arg 105 | Positively charged Hydrogen Bond with OH(Distance-2.43) |
| | | | | | Isoleucine | Ile 106 | Hydrophobic |
| | | | | | Glutamine | Gln 107 | Polar |
| | | | | | Glutamine | Gln 110 | Hydrogen Bonding with NH(Distance-1.85) and OH(Distance-2.07) |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 152 | Hydrophobic |
| | | | | | Aspartate | Asp 153 | Negatively Charged |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Proline | Pro 252 | Hydrophobic |
| | | | | | Leucine | Leu 253 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic Pi-Pi Stacking (Distance-3.75) |
| | | | | | Valine | Val 297 | Hydrophobic |
| 2. | (Z)-3-(Heptadec-10-en-1-yl)phenol | -0.161 | -3.871 | -3.872 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Isoleucine | Ile 106 | Hydrophobic |
| | | | | | Glutamine | Gln 107 | Polar |
| | | | | | Proline | Pro 108 | Hydrophobic Hydrogen Bond with OH(Distance-1.84) |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar |
| | | | | | Threonine | Thr 111 | Polar |
| | | | | | Phenylalanine | Phe 112 | Hydrophobic |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 152 | Hydrophobic |
| | | | | | Aspartate | Asp 153 | Negatively Charged |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Valine | Val 202 | Hydrophobic |
| | | | | | Asparagine | Asn 203 | Polar |
| | | | | | Histidine | His 246 | Polar Pi-Pi Stacking (Distance-5.19) |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |

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| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| | | | | | Aspartate | Asp 295 | Negatively charged |
| 3. | Phenol, 2,4-Bis(1,1-Dimethylethyl)- | -0.245 | -3.672 | -3.672 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Valine | Val 104 | Hydrophobic |
| | | | | | Isoleucine | Ile 106 | Hydrophobic |
| | | | | | Glutamine | Gln 107 | Polar |
| | | | | | Glutamine | Gln 110 | Polar<br>Hydrogen Bond with OH (Distance-1.70) |
| | | | | | Threonine | Thr 111 | Polar |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 152 | Hydrophobic |
| | | | | | Aspartate | Asp 153 | Negatively charged |
| | | | | | Serine | Ser 158 | Polar |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic<br>Pi-Pi stacking (Distance-4.99) |
| 4. | Oxime-, methoxy-phenyl- (3) | -0.303 | -3.334 | -3.334 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 152 | Hydrophobic |
| | | | | | Aspartate | Asp 153 | Negatively charged |
| | | | | | Glutamine | Gln 110 | Polar<br>Hydrogen Bond (Distance-1.59) |
| | | | | | Threonine | Thr 111 | Polar |
| | | | | | Phenylalanine | Phe 112 | Hydrophobic |
| | | | | | Glutamine | Gln 127 | Polar |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic<br>Pi-Pi stacking (Distance-3.95) |
| | | | | | Aspartate | Asp 295 | Negatively charged |
| 5. | Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl) ethyl ester | -0.144 | -3.314 | -3.314 | | | |
| | | | | | Glutamine | Gln 107 | Polar |
| | | | | | Proline | Pro 108 | Hydrophobic<br>Hydrogen Bond with OH (Distance-1.81) |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar<br>Hydrogen Bond with O (Distance-2.64) |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Valine | Val 202 | Hydrophobic |
| | | | | | Glutamate | Glu 240 | Negatively charged<br>Hydrogen Bond with OH **(**Distance-1.78) |
| | | | | | Histidine | His 246 | Polar<br>Hydrogen Bond with O (Distance-1.94) |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Proline | Pro 252 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| | | | | | Valine | Val 297 | Hydrophobic |
| 6. | 9-Octadecenoic acid | -0.136 | -3.272 | - | Lysine | Lys 102 | Positively charged |

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|---|---|---|---|---|---|---|---|
| | (9Z)-, oxiranylmethyl ester | | | 3.272 | Valine | Val 104 | Hydrophobic |
| | | | | | Arginine | Arg 105 | Positively charged |
| | | | | | Isoleucine | Ile 106 | Hydrophobic |
| | | | | | Glutamine | Gln 107 | Polar |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar Hydrogen Bond with O **(**Distance-2.00) and O (Distance-2.05) |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 152 | Hydrophobic |
| | | | | | Aspartate | Asp 153 | Negatively charged |
| | | | | | Serine | Ser 158 | Polar |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Valine | Val 202 | Hydrophobic |
| | | | | | Asparagine | Asn 203 | Polar |
| | | | | | Histidine | His 246 | Polar |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| 7. | Decanedioic acid, bis(2-ethylhexyl) ester | -0.1 | -3.206 | -3.206 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Valine | Val 104 | Hydrophobic |
| | | | | | Isoleucine | Ile 106 | Hydrophobic |
| | | | | | Glutamine | Gln 107 | Polar Hydrogen Bonding with O (Distance-1.78) |
| | | | | | Proline | Pro 108 | Hydrophobic |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 152 | Hydrophobic |
| | | | | | Aspartate | Asp 153 | Negatively charged |
| | | | | | Serine | Ser 158 | Polar |
| | | | | | Cysteine | Cys 160 | Hydrophobic |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Valine | Val 202 | Hydrophobic |
| | | | | | Glutamate | Glu 240 | Negatively charged |
| | | | | | Proline | Pro 241 | Hydrophobic |
| | | | | | Threonine | Thr 243 | Polar |
| | | | | | Histidine | His 246 | Polar |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| 8. | Squalene | -0.104 | -3.133 | -3.133 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Glutamine | Gln 110 | Polar |
| | | | | | Threonine | Thr 111 | Polar |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 152 | Hydrophobic |
| | | | | | Aspartate | Asp 153 | Negatively charged |
| | | | | | Tyrosine | Tyr 154 | Hydrophobic |
| | | | | | Valine | Val 202 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| | | | | | Aspartate | Asp 295 | Negatively charged |
| | | | | | Valine | Val 297 | Hydrophobic |

 

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| | | | | | Histidine | His 246 | Polar |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| 9. | 2-Pentacosanone | -0.12 | -3.124 | -3.124 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Glutamine | Gln 107 | Polar Hydrogen Bond with "O"(Distance-1.79) |
| | | | | | Proline | Pro 108 | Hydrophobic |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Glu 110 | Polar |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Valine | Val 202 | Hydrophobic |
| | | | | | Asparagine | Asn 203 | Polar |
| | | | | | Glutamate | Glu 240 | Negatively charged |
| | | | | | Histidine | His 246 | Polar |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Proline | Pro 252 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| | | | | | Valine | Val 297 | Hydrophobic |
| | | | | | Arginine | Arg 298 | Positively charged |
| 10. | Z,Z-6,27-Hexatriactontadien-2-one | -0.084 | -3.119 | -3.119 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Lysine | Lys 102 | Positively charged |
| | | | | | Valine | Val 104 | Hydrophobic |
| | | | | | Glutamine | Gln 107 | Polar |
| | | | | | Proline | Pro 108 | Hydrophobic |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | |
| | | | | | Threonine | Thr 111 | Polar |
| | | | | | Proline | Pro 132 | Hydrophobic |
| | | | | | Asparagine | Asn 133 | Polar |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Aspartate | Asp 153 | Negatively charged |
| | | | | | Serine | Ser 158 | Polar |
| | | | | | Threonine | Thr 196 | Polar |
| | | | | | Threonine | Thr 198 | Polar |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Valine | Val 202 | Hydrophobic |
| | | | | | Glutamate | Glu 240 | Negatively charged |
| | | | | | Histidine | His 246 | Polar |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| | | | | | Aspartate | Asp 295 | Negatively charged |
| 11. | Glycidyl palmitate | -0.14 | -3.09 | -3.09 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Proline | Pro 108 | Hydrophobic |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar |
| | | | | | Threonine | Thr 111 | Polar |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 152 | Hydrophobic |
| | | | | | Aspartate | Asp 153 | Negatively charged |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Valine | Val 202 | Hydrophobic |
| | | | | | Asparagine | Asn 203 | Polar |
| | | | | | Glutamate | Glu 240 | Negatively charged |
| | | | | | Histidine | His 246 | Polar Hydrogen Bond with "O"(Distance-2.24) |

 

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|---|---|---|---|---|---|---|---|
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| 12. | Propyl stearate | -0.127 | -2.922 | -2.922 | Glutamine | Gln 107 | Polar |
| | | | | | Proline | Pro 108 | Hydrophobic |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar Hydrogen Bond with "O"(Distance-2.73) |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Valine | Val 202 | Hydrophobic |
| | | | | | Asparagine | Asn 203 | Polar |
| | | | | | Histidine | His 246 | Polar Hydrogen Bond with"O"(Distance-1.97) |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| | | | | | Valine | Val 297 | Hydrophobic |
| | | | | | Arginine | Arg 298 | Positively charged |
| 13. | Benzene, 1,3-Bis(1,1-Dimethylethyl)- | -0.207 | -2.891 | -2.891 | Phenylalanine | Phe 8 | Hydrophobic |
| | | | | | Glutamine | Gln 110 | Polar |
| | | | | | Threonine | Thr 111 | Polar |
| | | | | | Asparagine | Asn 151 | Polar |
| | | | | | Isoleucine | Ile 152 | Hydrophobic |
| | | | | | Aspartate | Asp 153 | Negatively charged |
| | | | | | Serine | Ser 158 | Polar |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic Pi-Pi stacking **(Distance-3.93)** |
| | | | | | Asparagine | Asn 295 | Negatively charged |
| 14. | Monoelaidin | -0.11 | -2.746 | -2.746 | Glutamine | Gln 107 | Polar |
| | | | | | Proline | Pro 108 | Hydrophobic Hydrogen Bond with "OH"**(Distance-1.82)** |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar Hydrogen Bond with "OH"**(Distance-1.90)** |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Valine | Val 202 | Hydrophobic |
| | | | | | Asparagine | Asn 203 | Polar |
| | | | | | Aspartate | Asp 245 | Negatively charged |
| | | | | | Histidine | His 246 | Polar |
| | | | | | Aspartate | Asp 248 | Negatively charged |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Proline | Pro 252 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| | | | | | Valine | Val 297 | Hydrophobic |
| 15. | 1-Hexanol, 2-Ethyl- | -0.289 | -2.604 | -2.604 | Glutamine | Gln 107 | Polar |
| | | | | | Proline | Pro 108 | Hydrophobic |

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|---|---|---|---|---|---|---|---|
| | | | | | | | Hydrogen Bond with "OH" **(Distance-1.98)** |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar Hydrogen Bond with "OH" **(Distance-1.96)** |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Valine | Val 202 | Hydrophobic |
| | | | | | Asparagine | Asn 203 | Polar |
| | | | | | Glutamate | Glu 240 | Negatively charged |
| | | | | | Histidine | His 246 | Polar |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| 16. | Z,Z-6,28-Heptatriactontadien-2-one | -0.067 | -2.556 | -2.556 | Lysine | Lys 102 | Positively charged |
| | | | | | Valine | Val 104 | Hydrophobic |
| | | | | | Arginine | Arg 105 | Positively charged |
| | | | | | Isoleucine | Ile 106 | Hydrophobic |
| | | | | | Glutamine | Glu 107 | Polar Hydrogen Bond with "O"**(Distance-2.22)** |
| | | | | | Proline | Pro 108 | Hydrophobic |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar |
| | | | | | Asparagine | Arg 151 | Polar |
| | | | | | Aspartate | Asp 153 | Negatively charged |
| | | | | | Serine | Ser 158 | Polar |
| | | | | | Isoleucine | Ile 200 | Hydrophobic |
| | | | | | Glutamate | Glu 240 | Negatively charged |
| | | | | | Proline | Pro 241 | Hydrophobic |
| | | | | | Threonine | Thr 243 | Polar |
| | | | | | Aspartate | Asp 245 | Negatively charged |
| | | | | | Histidine | His 246 | Polar |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| 17. | Arachidic acid | -0.114 | -2.518 | -2.521 | Glutamine | Gln 107 | Polar Hydrogen Bond with "O"**(Distance-1.78)** |
| | | | | | Proline | Pro 108 | Hydrophobic |
| | | | | | Glycine | Gly 109 | Glycine |
| | | | | | Glutamine | Gln 110 | Polar |
| | | | | | Valine | Val 202 | Hydrophobic |
| | | | | | Histidine | His 246 | Polar |
| | | | | | Isoleucine | Ile 249 | Hydrophobic |
| | | | | | Proline | Pro 252 | Hydrophobic |
| | | | | | Threonine | Thr 292 | Polar |
| | | | | | Proline | Pro 293 | Hydrophobic |
| | | | | | Phenylalanine | Phe 294 | Hydrophobic |
| | | | | | Valine | Val 297 | Hydrophobic |
| | | | | | Arginine | Arg 298 | Positively charged |

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**COMPETING INTERESTS**

The authors have declared that no competing interest exists.

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