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Effect of a Liposome Model on the Ligand-Target Interactions in Chlamydophila Abortus

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Abstract – *In silico* drug design is a state-of-the-art tool in medicinal chemistry that uses molecular docking to determine the optimal interaction pose of a ligand with a macromolecule, such as a protein. This approach employs computer simulations to efficiently identify potential drug candidates, reducing testing and development time, costs, and resource consumption. *Chlamydophila abortus* is an obligate intracellular bacterial parasite that causes abortions in several mammals, particularly in livestock, leading to significant economic losses and posing a risk to human health as a zoonotic disease. In this study, we present the results of molecular docking experiments to evaluate a new treatment option using encapsulated liposomes. Our findings suggest that ligand efficiency indicates the use of liposomes can promote controlled drug delivery.

***Keywords*:** Liposome, *Chlamydophila*, abortion, nanomedicine, docking

1. Introduction

Molecular docking is a tool that helps optimize resources in drug discovery and the elucidation of drug-target interactions, as well as in studying the effects of certain molecules, such as nanoparticles, on these interactions. This method can reduce the number of experiments needed and provide a rational approach before conducting in vitro or in vivo assays [1].

Moreover, in the veterinary field, in-silico assays are less commonly used compared to human medicine, perhaps due to a lack of awareness or the smaller number of computational chemists involved in this area. However, in the present work, this tool is used to evaluate the effect of a liposome fragment on the interaction between a triazole and a *Chlamydophila abortus* target. This pathogen is an intracellular bacterium, whose only effective treatment is the bacteriostatic antibiotic tetracycline, used prophylactically. However, this drug has lower efficacy and poses a risk of bacterial resistance [2].

The liposomes are known to be an important nano-sized drug delivery system with a lipid bilayer structure assembling the cellular membrane, that is easy-to-prepare and has high biocompatibility. Drug candidates have been encapsulated in liposomes, demonstrating reduced toxicity and extended duration of therapeutic effect [3].

Lecithin derived from soybeans has had some auspicious accomplishments to the drug carrying aspect, like effectual encapsulation, controlled release and successful delivery of the curative factors to intracellular regions. The recent applications of soy lecithin-derived liposome are currently focusing on cancer treatment, brain target and vaccinology [4].

2. Computational methods

Based on the state-of-the-art in computational chemistry, the current work was conducted using molecular docking to evaluate the effect of a liposome fragment on triazole-target interactions, considering as the target a protein (ChlaDUB) present in *Chlamydophila abortus*, which was downloaded from the protein data bank with the PDB code: 6GZU. [5]. The evaluated triazole, tetracycline, and liposome fragment were modeled with Avogadro software [6], and the ligand-target interactions were analyzed with the Molegro Virtual Docker (MVD) package [7].

3. Results and discussion

To evaluate the effect of the liposome on triazole-target interactions, four **types** of interactions were proposed:

1. When the triazole interacts alone with the bacterium target
2. When the liposome fragment interacts alone with the target.
3. When first the triazole interacts with the target, and then the liposome fragment interacts with the triazole-target complex.
4. When first the liposome fragment interacts with the target, and then the triazole interacts with the liposome-target complex.

On Table 1, results have been filtered to the lowest ligand efficiency (LE) value as it is the preferential parameter for the best option. This is a way to compare their average link energy for every heavy atom (non-hydrogens) it has and what produces. Quantifies the efficacy of the molecule to use its structural characteristics to link with its target. The energy it produces measures the stability of the molecular structures and their capacity to react or interact under different conditions. As for the Van der Waals (VdW) energy, it describes the repulsion or attraction between atoms that are not directly linked. It describes the energy of the nonlinked molecules interaction.

Table 1. Energy and LE comparison between types

Molecule	Energy	LE	VdW	**Type**
“86e” Triazole	-195.57	-5.93	-35.99	1
Tetracyclines	-139.02	-4.34	92.32	1
“86e” Triazole	-116.30	-3.52	-14.17	4
Lecithin	-129.74	-2.45	-16.82	3
Lecithin	-112.70	-2.13	421.86	2
Tetracyclines	-51.25	-1.60	11.73	4

LE = Ligand Efficiency, VdW = Van der Waals Energy

The best interaction regarding the use of liposomes is presented on the type 4 interaction. The link happens on a lipidic setting; however, the protein presents hydrophilic and hydrophobic areas on which the liposome docks to strengthen the interaction (see Figure 1). The liposome gets ahold of both the triazole and the protein, allowing more stability on the docking.

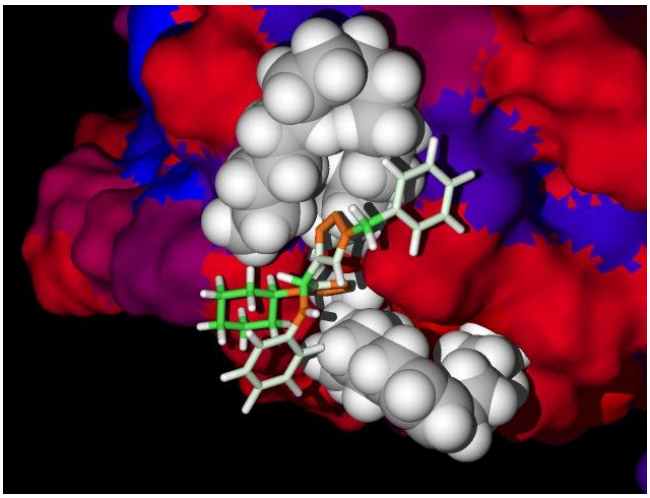

Figure 1: Hydrophobicity map, triazole interaction over lecithin (type 4).

In cancer therapy, liposomes have been successfully used to carry the anticancer drug paclitaxel, with a long-lasting release of up to 96 hours, while also demonstrating biocompatibility as nanocarriers and reducing the drug's toxicity [8]. Another example of the efficiency of liposomes can be seen in dermal drug delivery, where wound healing in rats was enhanced by liposomes through free radical scavenging and other medicinal properties [9]. A review of soy lecithin-derived liposomal delivery systems explores in greater depth the medicinal applications of lecithin, including antimicrobial, antiprotozoal, and antimalarial effects, among others.

Ligand-targeted liposomes have already been studied by several authors, showing effective results in terms of high specificity for targeting diseased cells [10, 11, 12]. The obtained results indicate lower interaction when the liposome enters first compared to when the drug enters freely into the target. However, this behavior may suggest that drug delivery is promoted more slowly due to the use of liposomes, creating a controlled-release system.

5. Conclusion

Due to the main characteristics of encapsulated liposomes, using this technique in conjunction with molecular docking to enhance specificity for target proteins is one of the best options currently available against C. abortus. The nature of this bacterium requires a continuous release of the drug to combat it, as well as facilitating its entry into the host cells where it resides. Ligand efficiency suggests that the use of liposomes can promote a controlled delivery of the drug.

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