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Research Paper

The Study of Insilco Design and Biological Evaluation of Naphthalene Derivatives

Akshara Vinayakrishnan*, Malavika K., Aneesha Thomas, Aswagosh K.

College Of Pharmacy- Kannur Medical College Anjarakandy.

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ABSTRACT

Naphthalene is an aromatic compound that contain two fused benzene rings. Naphthalene derivatives has diverse biological activities and gained attention as potential therapeutic agents. In this study we applied Insilco drug design techniques to evaluate pharmacokinetic properties, biological activities and binding affinity of 2-(bromomethyl) naphthalene, 8-amino-2-naphthol and acenaphthalene. The molecular structures were created by using King Draw, followed by the prediction of key pharmacokinetic parameters (solubility, permeability, toxicity, etc.) using Swiss ADME. Biological activity predictions were performed with pass online, which identified potential activity (anticancer) of derivatives. To assess the binding potential of derivatives molecular docking were performed with One-dock, reveals strong binding affinity of compounds. Among these 2-(bromomethyl)naphthalene exhibit more anticancer activity.

INTRODUCTION

Drug Discovery and Development

Drug discovery is the process of finding new medicines that could help to treat diseases. It is a multi-step process that involves identification, design, testing and approval of new therapeutic agents to treat diseases. It takes several year and includes preclinical and clinical stages.

Drug Design

The process of creating new drugs by understanding a biological target is referred to as drug design, or simply rational design. Structure based drug design: Developing drugs by understanding the 3D structure of a biomolecular target, using computational techniques to optimize affinities and stabilities before clinical testing. Ligand based drug design: Focuses on designing compounds that bind to a biological target, typically used when the 3D structure of target is unavailable. In Silico Drug Design: Refers to the use of computational methods to aid in the discovery and development of new drugs. It

***Corresponding Author:** Akshara Vinayakrishnan
Address: *College Of Pharmacy- Kannur Medical College Anjarakandy.*
Email ✉: Aksharvin@gmail.com

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involves virtual screening, molecular docking, and quantitative structure-activity relationship (QSAR) modeling to predict the interaction of drug candidates with biological targets.

Naphthalene is an aromatic hydrocarbon Containing two fused benzene rings. Naphthalene has various pharmacological actions such as antimicrobial, antiviral, antidiabetic, anticancer, antiinflammatory,antiprotozoal,antihypertensive,antidepressant,anticonvulsant,antipsychotic and anti-neurodegenerative effects.

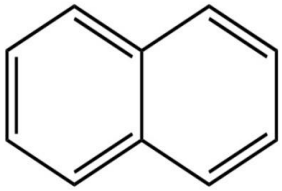

Figure 1 Structure of naphthalene

Plan Of Work

- **Overview**

To design new naphthalene derivatives that may possess therapeutic properties through insilico methods.

- **Selection Criteria**

Naphthalene derivatives are selected based on their structural variety, known pharmacological activity and the availability of chemical data. Molecular structure of naphthalene derivatives are obtained from data bases such as PubChem, ChEMBL, etc.

- **Preparation Of Molecular Structures**

Molecular structure of selected naphthalene derivatives can be drawn using KingDraw chemistry station software.

- **Prediction Of Properties**

Use software like molinspiration, Swiss ADME, pass online to predict pharmacological properties like lipophilicity, permeability, toxicity, solubility and metabolic stability. Evaluate the compliance with Lipinski's rule of five to filter out compounds that exhibit undesirable drug-like properties.

- **Molecular Docking**

Identify relevant biological targets like enzymes and receptors that are associated with the therapeutic potential of naphthalene derivatives.

Use docking software (eg.Auto dock, PyRx, One dock) to predict the interaction between each derivative and the target protein, assessing binding affinity and interactions at the binding site.

- **Analysis Of Docking Results**

Evaluate docking scores and binding energies to rank naphthalene derivatives based on their interaction strength.

Insilico Studies

In-silico drug design, computational techniques are used to model and predict the interaction between drug substances and biological targets. It helps in determining the properties of drug, lowering costs and reducing development time.

The softwares used for in-silico drug analysis are:

- **King Draw-chemistry station-**

It is a specialized chemical structure formula editor designed for chemists, researchers and students. Using the software chemical structure of naphthalene derivatives was drawn.

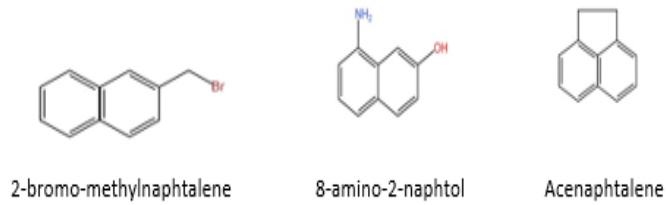

Figure 2 Structure of naphthalene derivatives

- **Molinspiration-**

It is used for computational chemistry and drug design as an online tool.It focuses on predicting

bioactivity and molecular properties. It provides a quick and efficient way to assess a molecule's suitability for further development in pharmaceutical research. The assessment is based on Lipinski rule of five affirms.The Lipinski Rule of Five states that most drug-like molecules have a log P value of 5 or less, a molecular weight of 500 or less, no more than 10 hydrogen bond acceptors, and no more than 5 hydrogen bond donors. Molecules that violate more than one of these criteria may face issues with bioavailability. This principle is referred to as the Lipinski Rule of Five.

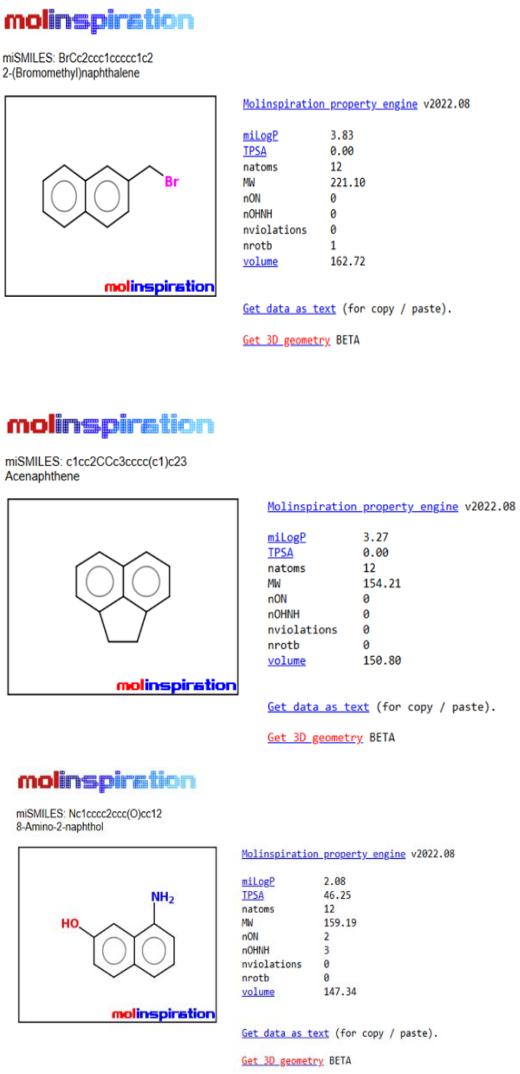

Figure 3 Calculation of molecular properties of naphthalene derivatives

- **Swiss Adme**

Swiss ADME is an online tool used in drug discovery process to predict the pharmacokinetic properties of molecules. The software helps the researchers to assess the drug potential of compounds before experimental testing by offering a range of predictions including lipophilicity, solubility and drug-likeness. Using this software pharmacokinetic Properties of derivatives were analyzed.

- **Prediction Of Activity Spectra (Pass)**

Pass software is a tool used to assess the biological potential of a molecule under investigation. The principle is that the activity is a function of structure (activity=f(structure)). It is possible to predict whether the compound exhibit activity by

comparing the structure of a new compound with a well- known biologically active substances. Pass contain data from thousands of substances that helps in objective evaluation of a compounds activity. It consist of around 16000 marketed drugs and 44000 drug candidates that are either in clinical or advanced pre-clinical stages. The results are displayed as list of activity with appropriate Pa and Pi values in an ordered by the descending difference (pa.pi)>0. If Pa <0.5 the compound is unlikely to exhibit activity in experiments. If activity is confirmed it may represent a new chemical entity. If 0.5<Pa<0.7 the compound has likely to reveal the activity in experiments, but its similarity to existing pharmaceutical agents is in less probability. If Pa>0.7 the compound is very likely to demonstrate activity in experiments, but in this case the chance of being the analogue of the known pharmaceutical agent is high.

- **Docking Software- One Dock**

It is an open source program for molecular docking, which uses a protein molecule and ligand to undergo binding.

s/no	Target	PDB ID
1	Thymidilate synthase	1AN5

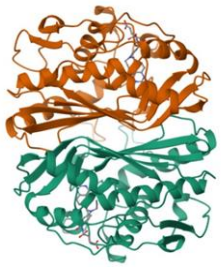

Figure 4 THymidilate synthase

RESULTS AND DISCUSSION

In-silico studies were carried out using molinspiration, Swiss ADME, pass and one dock softwares. Results are shown in the tables

Table.1 Molinspiration calculation of molecular properties

Compound	Log P	MW T	N o n	NOHN H	No Of Rotable Bonds	Violations
2(Bromomethyl)Naphthalene(Np1)	3.83	221.10	0	0	1	0
8-Amino-2-Naphthol(Np2)	2.08	159.19	2	3	0	0
Acenaphthalene(Np3)	3.27	154.21	0	0	0	0

Table.2 prediction of pharmacokinetic properties by Swiss ADME

Compound	Log P	Log S	GI absorption	BBB permeation	Log K_p(cm/s)	Bioavailability
NP1	3.54	-4.06	Low	Yes	-5.06	0.55
NP2	1.74	-2.46	High	Yes	-6.13	0.55
NP3	3.50	-3.88	Low	Yes	-4.46	0.55

Table.3 Analysis of drug using pass online

Compound	Activity	Pa	Pi
NP 1	Anticancer	0,595	0,004
NP 2	Anticancer	0,566	0,005
NP 3	Anticancer	0,541	0,009

Results of docking

Table.4 Result of docking

Compound	Glide Score
NP 1	-6.82
NP 2	-5.94
NP 3	-6.41

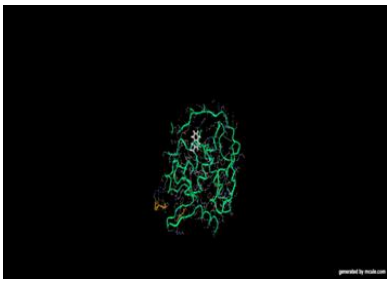

Figure 5 Docking image result

According to docking studies, compound 2-(bromomethyl) naphthalene shows more anticancer activity of glide score -6.82.

CONCLUSION

The present research titled "The study of insilico design and biological evaluation of naphthalene derivatives" examines the potential of naphthalene derivative through insilico analysis. The study mainly focuses on preliminary insilico designing of various naphthalene derivatives for their drug likeness, ADME properties and adherence with Lipinski's rule of five. It also predicts biological activities using software such as molinspiration, pass and one dock. Using pass software three derivatives were evaluated for their biological activity, it shows good anticancer activity. This lead to docking studies with the anticancer protein thymidylate synthase. The docking results reinforced by good glide scores highlight the promising anticancer potential of these derivatives. Predictions from swiss ADME suggest that these derivatives have the properties suitable for drug candidates. The derivative that complied with Lipinski's rule of five, without violations were selected for further evaluation. These derivatives showed significant anticancer activity.

Future research will be directed toward developing effective chemotherapeutic agent based on these findings.

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