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Virtual Screening Of ADME Properties Of LAPDDAB – A Swissadme Study

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ABSTRACT

Lauramidopropyl dodecyl ammonium bromide (LAPDDAB) has been modelled and subjected to analyse the ADME properties using SwissADME web tool. It can be produced to operate as a medicine as it exhibits two promising factors, GI absorption and BBB permeability, along with a decent bioavailability score and worthy synthetic accessibility.

KEYWORDS: Quaternary ammonium salts, antimicrobial activity, ADME properties, SwissADME and drug discovery

I. INTRODUCTION

Quaternary ammonium salts (QASs) formulations are the disinfectants of choice for hospitals. The advantage of formulation containing QAS is the possibility of their usage as rinse free- solutions e.g. for hands. Long lasting and widespread industrial usage of (QAS) increase number of resistant pathogens not only to these but also other drugs. Thus, it is important to elucidate the chemical composition – activity relationships in order to create highly effective mixtures having synergistic activity. Material and Methods Antimicrobial activity of three different quaternary ammonium salts (cocamidopropyl betaine, dimethyl amine oxide and benzalkonium chloride) have been tested separately and as mixtures. Experiments were performed according to CSN PN-EN Standards on reference strains. Mixtures showed increased antimicrobial activity. There is positive correlation between critical micelle concentration and activity. Synergistic activity was found for mixture of compounds [1].

Dodecyl trimethyl ammonium sulphate inhibited growth of Salmonella Typhimurium and dimethylamino propyl glucosylamine showed a pronounced antifungal activity against Fusarium oxysporum cubens. The results revealed that at all concentrations used, DTA and DAPGA were effectiveness to inhibit the growth of F. oxysporum cubens. Furthermore, Dodecyl trimethyl ammonium (DTA) showed significant antibacterial activity against the growth of Salm. Typhimurium and Staph.aureus. The lack of significant antibacterial of N-(N,N-Dimethylamino) propyl glycosylamine against Staph. aureus and Salm. Typhimurium could be due to its remarked decomposition in D2O and research on its possible stabilization should be of interest. Through the findings, the reported antibacterial efficacy of ammonium compounds was confirmed: satisfying antimicrobial activity was obtained from small biodegradable molecule, dodecyl trimethyl ammonium sulphate. It is however to note that the toxicity assessment of this compound should be carefully realized before any application of this compound in various domains [2].

DDBA induced cross-resistance to multiple antibiotics in Salmonella while increasing sensitivity to colistin. Mutations and expression changes in genes to phoPQ, LPS, peptidoglycan and phospholipids resulted in collateral sensitivity to colistin. Changes in the expression of genes related to RND family, biofilm formation, bacterial flagella and oxidative stress led to cross resistance in the induced strain [3].

n-Alkyltrimethylammonium bromides possess antimicrobial activity and it was assessed as growth inhibitory activity towards representative strains of micro-organisms and as bacterial activity towards *Staphylococcus aureus* [4].

Furthermore, future effectiveness of antimicrobial therapy is somewhat in doubt since various microorganisms are becoming more resistant to the existing antimicrobial agents. Therefore, it is the responsibility of scientists to work hard and to find out environment friendly active compounds which can be used in this struggling. Previous reports indicated that amino sugars and ammonium compounds could be one of the good candidates to reach the goal [5-11].

Several attributes including disinfectant concentration, temperature, contact time and contaminated organic material account for the maximal efficiency of disinfectants; therefore, these attributes should be used as criteria for appropriate selection of disinfectants. It has been shown that, at room temperature, DDAB at 125 ppm was effective to inactivate Gram-negative bacteria (*SI* and *E. coli*) within 5 s; however, in AIV, inactivation at a higher concentration at 500 ppm was required to achieve similar efficacy. The efficacy of DDAB was still effective even in the presence of organic materials, indicating that contaminated organic materials commonly found in environment minimally impact the efficacy of DDAB; however, greater efficacy will be observed when organic contaminants are first removed. DDAB can inactivate bacteria and viruses, especially in the absence of organic material, and can be useful as a disinfectant for biosecurity enhancement on and around the animal farm [12].

The synthesized amidoamine based cationic surfactant, Lauramidopropyl dodecyl ammonium bromide (LAPDDAB) has a budding potential for industrial applications and exhibits an effective antibacterial spectrum against both Gram-positive as well as Gram-negative bacteria. It can be used as an antibacterial agent for treatment against infectious organisms [13].

Computational modelling techniques are becoming increasingly popular in designing formulation development of a drug because they can decrease time and save investments before experimental studies are done. Formulation development of drug can be a labor and time-consuming task if varying ratio of polymer development needs to be employed in case of CR tablet formulation. Thus, by applying computational models, prediction and optimization of better formulation profiles can be made possible. This way resource and time management efficiency can be improved markedly [14].

Based on the above references, the present study focuses on the Bio-availability radar, physicochemical properties, pharmacokinetics, druglikeness and medicinal chemistry of LAPDDAB by Swiss ADME web tool [15].

II. MATERIALS AND METHODS

Computational software and web-servers were utilized to study the physicochemical and pharmacokinetic properties of LAPDDEB. SwissADME, is publicly accessible web servers that suggest various properties of the active chemical entity by using accurate algorithms. Swiss ADME, free web tool was utilized to study the ADME properties of LAPDDAB in this present work.

Physicochemical properties

The physicochemical properties of the selected molecule such as canonical SMILES, molecular formula, molecular weight, number of such as canonical SMILES, formula, molecular weight, rotatable bonds, H-bond acceptors, H-bond donors, etc. were collected from web-based online server such as SwissADME.

Bioavailability Radar

Bioavailability radar for the Studied molecule has been obtained from SwissADME database. All the parameters in bioavailability radar have been analysed and the results were shown accordingly.

The bioavailability radar gives graphical interpretation of properties such as lipophilicity, compound size, insolubility, polarity, instaurations and flexibility in its six hexagonal vertices which help to evaluate scopes of improvement of bioavailability score.

For each feature anticipated to be orally accessible, the optimum physicochemical environment is illustrated by the pink area as LIPO: $-0.7 < XLOGP3 < +5.0$, SIZE (Molecular weight (MW)) $150 \text{ g/mol} < MW < 500 \text{ g/mol}$, POLAR (Polarity) $20 \text{ \AA}^2$ Molecular polar surface area (TPSA) $< 130 \text{ \AA}^2$, INSOLU

(Insolubility) $-6 < \text{Log S(ESOL)} < 0$, INSATU (Insaturation) $0.25 < \text{FractionCsp3} < 1$ and FLEX (Flexibility) $0 < \text{RP (Number of rotatable bonds)} < 9$ are the six physicochemical qualities that are taken into consideration.

Pharmacokinetics

The Pharmacokinetics study of the Selected molecule was performed by the utilization of Swiss ADME web server. In particular, Gastrointestinal absorption and Brain Blood Barrier permeation were studied.

Druglikeness

In this work, druglikeness was studied for the selected was molecules whether Lipinski rule was obeyed and bioavailability score was noted using web tool.

Medicinal Chemistry

The SWISS ADME web tool was very much useful to analyse the medicinal chemistry of the molecules in this work. Leadlikeness and Synthetic accessibility of the selected molecule have been noted for analysis.

III. RESULTS AND DISCUSSION

The Bio-availability radar, physicochemical properties, pharmacokinetics, druglikeness and medicinal chemistry of LAPDDAB (Figure 1.) have been analyzed by Swiss ADME web tool and all results are shown in Table 1. In the bio-availability radar shown in Figure 2., it is noted that two promising factors namely polarity and insaturation are within the pink area. The result indicates that the gastrointestinal (GI) absorption is high for the studied compound and it has blood brain barrier (BBB) permeation also. Therefore, it possesses good and promising effect on central nervous system. Even though the molecular weight of the compound is slightly higher than the limitation of Lipinski's rule (< 500) bioavailability score (0.55) and synthetic accessibility (4.09) of the studied compound is greater.

Two pharmacokinetic activities important for estimating at different stages of the drug development process are gastrointestinal absorption and brain access. To this end, as an effective predictive model that operates by measuring the lipophilicity and polarity of small molecules, the Brain or Intestinal Estimated permeation system (BOILED egg) is proposed [14].

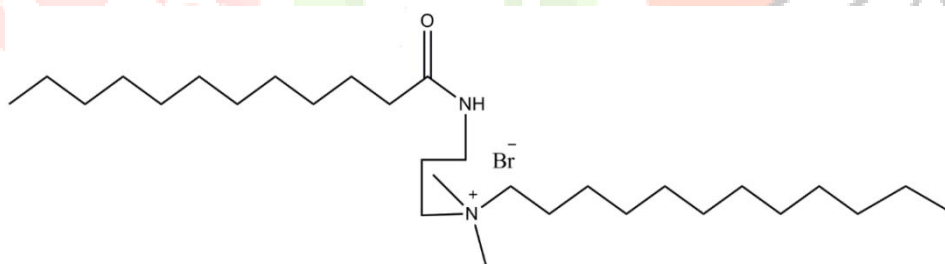


Figure 1. The structure of LAPDDAB

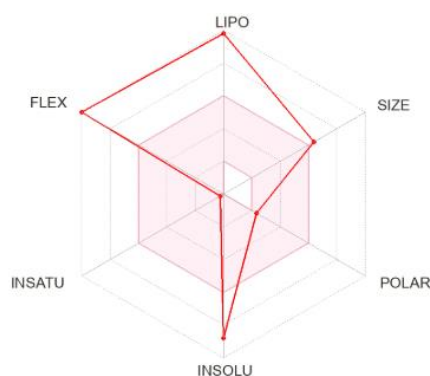
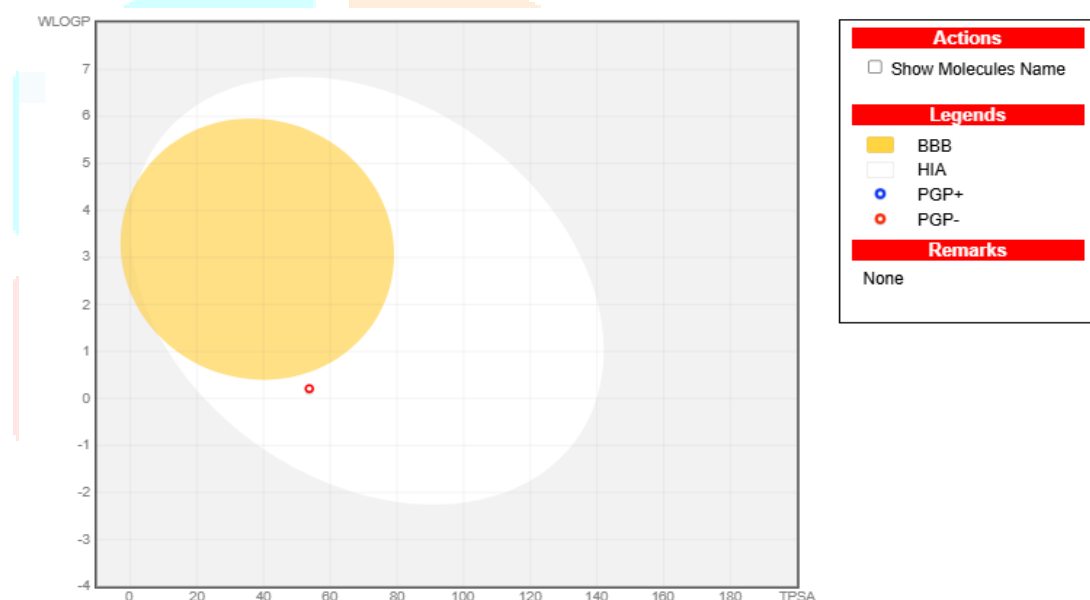


Figure 2. Bioavailability Radar of LAPDDAB using SwissADME web tool

Table 1. ADME properties of LAPDDAB by SwissADME web tool

SMILES	CCCCCCCCCCCC[N+](CCCNC(=O)CCCCCCCCCCC)C.[Br-]
Molecular Formula	C ₂₉ H ₆₁ BrN ₂ O
Molecular Weight	533.71 g/mol
Number of rotatable bonds	26
Number of Hydrogen bond acceptor	1
Number of Hydrogen bond donor	1
Molar Refractivity	155.82
TPSA	29.10 Å ²
Log P _{o/w}	5.13
Log S (ESOL)	-8.79 (poorly soluble)
GI absorption	High
BBB permeant	Yes
Log K _p (skin permeation)	-1.27 cm/s
Lipinski	Yes; 1 violation; MW > 500
Bioavailability Score	0.55
Leadlikeness	No; MW > 350
Synthetic accessibility	4.09

**Figure 3. BOILED Egg of LAPDDAB by SwissADME**

Due to the speed, accuracy, conceptual simplicity and consistent graphical performance of the model, concomitant predictions for both brain and intestinal permeation are derived from the same two physicochemical descriptors and directly converted through molecular architecture. From the filtering of chemical libraries at the early stages of drug research to the assessment of drug candidates for growth, BOILED Egg can be used in a number of settings. Boiled egg predicts the penetration of the drug through gastro intestinal and blood brain barrier (BBB). It is very useful for statistical method in drug designing. The white region shows the probability of passive absorption in the GI tract and yellow is the brain penetration. The studied molecule (shown in the white portion in Figure 3.) indicates that it has high intestinal absorption.

IV. CONCLUSION

LAPDDAB shows two promising factors namely GI absorption and BBB permeation with good bioavailability score and worthy synthetic accessibility which is the valuable result for a molecule to be synthesized for acting as a drug. This studied molecule has an insinuating role in drug discovery and a pronounced hope for the experimentalists.

V. REFERENCES

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