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Microbiological and *in silico* evaluation of triazole and bi-triazole derivatives

Avaliação microbiológica e *in silico* de derivados de triazol e bi-triazol

Evaluación microbiológica e *in silico* de derivados de triazol y bi-triazol

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ABSTRACT

Objective: To determine the antibacterial activity of triazole and bi-triazole compounds against the pathogens *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and methicillin-resistant *Staphylococcus aureus* (MRSA). **Methods:** This targeted research was combined with *in silico* predictions aimed at the rational and safe screening of these compounds. For this purpose, the virtual programs Osiris, Molinspiration, and ADMETlab were used. The inhibitory potential of the compounds was evaluated by the agar dilution method and by determining the Minimum Inhibitory Concentration (MIC). **Results:** The results showed that none of the nine compounds exhibited promising levels of bacterial inhibition at the maximum concentration of 500 µg/mL in both tests. These results suggest the need to add other radicals to the pharmacophoric group of triazoles and bi-triazoles to achieve antibacterial action against these species. Although the triazoles and bi-triazoles tested were not effective in bacterial inhibition, the *in silico* predictions for physicochemical properties revealed that all compounds met Lipinski's and Veber's rules in the development of a potential oral drug. **Conclusion:** These *in silico* results indicate that both chemical classes have potential for developing a possible prototype, provided that their relevant bioactivity against other diseases can be confirmed.

Keywords: Bi-Triazoles, Triazoles, Antimicrobial, *In silico.*

RESUMO

Objetivo: Determinar a atividade antibacteriana dos compostos triazóis e bi-triazóis contra os patógenos *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* e *Staphylococcus aureus* resistente à meticilina (MRSA). **Métodos:** Esta pesquisa direcionada foi combinada com previsões *in silico*, visando a triagem racional e segura desses compostos, para tanto, foi utilizado os programas virtuais Osiris,

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Molinspiration e ADMETlab. O potencial inibitório dos compostos foi avaliado pelo método de diluição em ágar e pela determinação da Concentração Inibitória Mínima (CIM). **Resultados:** Os resultados mostraram que nenhum dos 9 compostos apresentou níveis promissores de inibição bacteriana na concentração máxima de 500 µg/mL em ambos os testes. Esses resultados sugerem a necessidade de adicionar outros radicais ao grupo farmacofórico dos triazóis e bi-triazóis para obter ação antibacteriana contra essas espécies. Apesar de os triazóis e bi-triazóis testados não terem sido eficazes na inibição bacteriana, as previsões *in silico* para as propriedades físico-químicas revelaram que todos os compostos atenderam às regras de Lipinski e Veber no desenvolvimento de um eventual medicamento oral. **Conclusão:** Esses resultados *in silico* indicam que ambas as classes químicas têm potencial para desenvolver um possível protótipo, desde que sua bioatividade relevante contra outras doenças possam ser confirmada.

Palavras-chave: Bi-triazóis, Triazóis, Antimicrobiano, *In sílico*.

RESUMEN

Objetivo: Determinar la actividad antibacteriana de los compuestos triazoles y bi-triazoles contra los patógenos *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa* y *Staphylococcus aureus* resistente a la meticilina (MRSA). **Métodos:** Esta investigación dirigida se combinó con predicciones *in silico*, con el objetivo de realizar un cribado racional y seguro de estos compuestos. Para ello, se utilizaron los programas virtuales Osiris, Molinspiration y ADMETlab. El potencial inhibidor de los compuestos se evaluó mediante el método de dilución en agar y la determinación de la Concentración Inhibitoria Mínima (CIM). **Resultados:** Los resultados mostraron que ninguno de los nueve compuestos presentó niveles prometedores de inhibición bacteriana en la concentración máxima de 500 µg/mL en ambas pruebas. Estos resultados sugieren la necesidad de añadir otros radicales al grupo farmacóforo de los triazoles y bi-triazoles para lograr una acción antibacteriana contra estas especies. Aunque los triazoles y bi-triazoles probados no fueron eficaces en la inhibición bacteriana, las predicciones *in silico* para las propiedades fisicoquímicas revelaron que todos los compuestos cumplieron con las reglas de Lipinski y Veber en el desarrollo de un posible medicamento oral. **Conclusión:** Estos resultados *in silico* indican que ambas clases químicas tienen potencial para desarrollar un posible prototipo, siempre que su bioactividad relevante contra otras enfermedades pueda ser confirmada.

Palabras-clave: Bi-triazoles, Triazoles, Antimicrobiano, *In silico*.

INTRODUCTION

The current scenario of antimicrobial resistance constitutes a serious threat to global health (EL MALAH T, et al., 2020). In this sense, the inappropriate and excessive use of antibiotics accelerates and contributes to the spread of bacterial resistance, and multidrug resistance has caused a worsening of infections, an increase in periods of hospital stays and an increase in mortality (LLOR C e BJERRUM L, 2014).

The World Health Organization (WHO, 2017), aiming to promote research on and development of new antibiotics, has catalogued 12 bacterial families that need greater medical attention and that represent the greatest threat to human health. Within this list, Gram-negative bacteria that are resistant to various drugs making them able to transmit their genetic material, consequently propagating resistant strains, stand out.

The group containing *Acinetobacter*, *Pseudomonas* along with some bacteria from the *Enterobacteriaceae* family (including *Klebsiella*, *E. coli*, *Serratia* and *Proteus*), was the most critical listed by the Who. The damages caused range from infections in the bloodstream, pneumonia to serious infections, which can lead to patient death. These bacteria mainly pose a threat to hospitals, nursing homes and patients who need more intensive care, such as the use of ventilators and blood catheters.

Other bacteria were classified as high priority (*Enterococcus faecium*, *Staphylococcus aureus*, *Helicobacter pylori*, *Campylobacter* spp., *Salmonella* spp., *Neisseria gonorrhoeae*) and others as medical priority (*Streptococcus pneumoniae*, *Haemophilus influenzae*, *Shigella* spp.) (WHO, 2017; WHO, 2021).

The MRSA strain (methicillin-resistant *Staphylococcus*) causes 60-70% of nosocomial infections (Negi et al. 2016). Some MRSA infections are acute and can cause metastatic foci in different tissues. In more severe cases this strain can cause pneumonia, bacteremia, osteomyelitis, endocarditis, myocarditis, pericarditis, meningitis, muscle and brain abscesses. *P. aeruginosa*, in addition to causing the same diseases as MRSA

and others, also has the ability to form biofilms, making it highly resistant to conventional drugs (LOWY FD, 1998; MESAROS N, et al. 2007; GELATTI LN, et al., 2009; FERRIS RA, et al., 2017).

The clinical complications attributed to *K. pneumoniae* are also associated with urinary infections, gastrointestinal infections, pneumonia and endocarditis and are distinguished by the ability to cause post-surgical infections and septicemia (NAVON-VENEZIA, S, et al. 2017). The bacterium *A. baumannii* is more commonly associated with infections in the blood, in the urinary system, in the abdominal region and pneumonia (ASIF M, et al. 2018; WANG X e QIN L, 2019).

Faced with both clinical and economic complications, the present study focuses on molecules belonging to the chemical classes of triazoles and bi-triazoles. Using the keyword “triazole and antibacterial”, in the PubMed (National Library of Medicine) database, in the last 10 years (2012-2022) 2,734 studies were found. However, when searching the same database using the keyword “bi-triazole and antibacterial”, no studies were found. This demonstrates the importance of continuing to seek out new alternatives for treatment not only for the bacteria targeted in this study, but also for other bacterial families of clinical importance that are harmful to human health.

Currently, with the advancement of computer technology, numerous programs have been created to assist in the virtual screening (*in silico*) of potential molecules; with this it was possible to measure their pharmacokinetics (absorption, distribution, metabolism and excretion), pharmacodynamics (mechanism of action) and physicochemical properties.

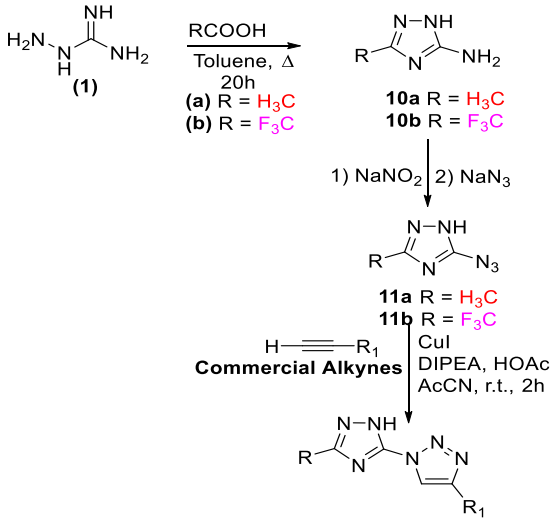
From this perspective, these results can guide and assist in improving the bioactivity of molecules in *in vitro* and *in vivo* experiments before reaching clinical trials (LOMBARDO F, et al., 2017). In this context, this study aims to determine the physicochemical and pharmacokinetic properties of triazole and bi-triazole compounds through *in silico* tests, as well as to evaluate the antibacterial activity *in vitro* of these chemical classes

METHODS

The proposed synthesis of bi-triazoles was initiated via the synthesis of the amino triazoles (**10a** and **10b**) which were then used as starting material. The preparation of 2-amino-1,2,4-1*H*-triazoles substituted in position 5 involved the condensation and cyclization reaction of aminoguanidine bicarbonate (**1**) with acetic or trifluoroacetic acid, as reported by (LOPYREV VA e RAKHMATULINA TN, 1984) in 1983.

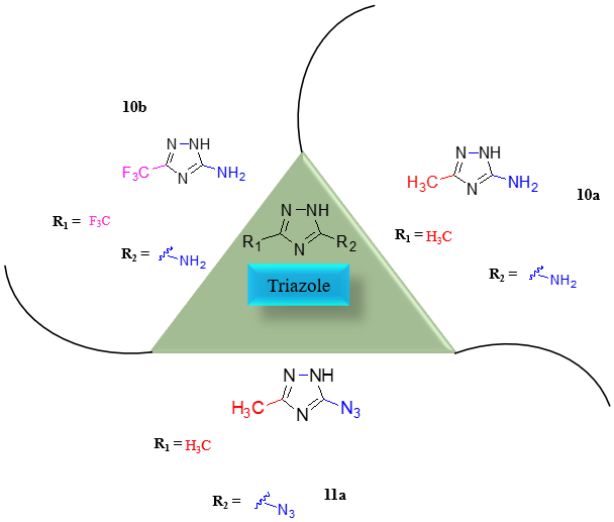
Then, the azides 11**a** and 1**1b** were synthesized in a diazotization reaction, and bi-triazoles were obtained through a Huisgen 1,3-dipolar cycloaddition reaction between azide derivatives and commercial terminal alkynes, catalyzed by Cu (I) through diisopropylethylamine, acetonitrile and acetic acid (**Figure 1**, **2** and **3**).

Figure 1 - Synthesis of substituted bi-triazoles.



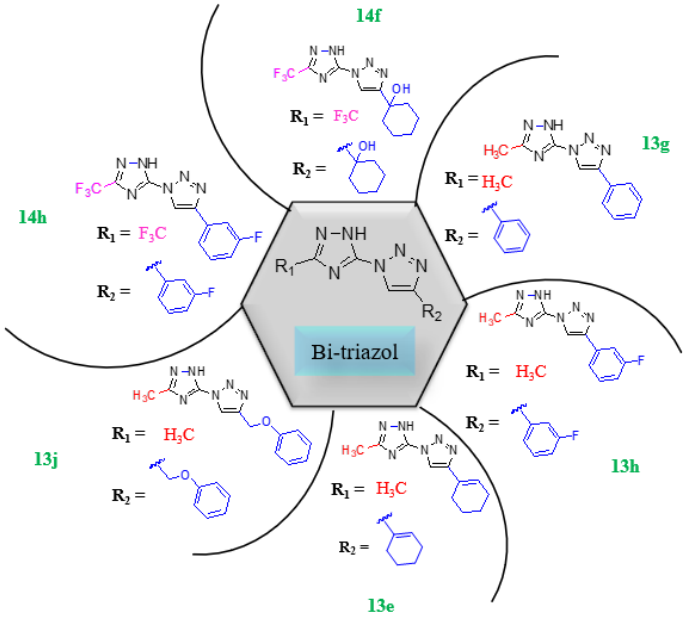
Source: Matinez LN, et al., 2024.

Figure 2 - Structure of the 1,2,3-triazoles 10b, 10a and 11a using a conventional heating process. Schematic representation of the structures of the triazole compounds with their respective radicals 1 (R1) and 2 (R2).



Source: Matinez LN, et al., 2024.

Figure 3 - Structure of the Bi-triazoles 14f, 13g, 13h, 13e, 13j, 14h derived from 1,2,3-triazoles through a conventional heating process. Schematic representation of the structures of the bi-triazole compounds with their respective radicals 1 (R1) and 2 (R2).



Source: Matinez LN, et al., 2024.

2.2 Compound solubilization

Samples were solubilized in 10% dimethylsulfoxide (DMSO) (Sigma-Aldrich) (EL MALAH T, et al., 2020). The initial concentration of samples was 1mg/mL (BASTOS I, 2016).

2.3 *In silico* prediction

2.3.1 OSIRIS property explorer, Molinspiration and ADMETlab

After screening the compounds to assess their antibacterial activity, a virtual screening of all triazole (10a, 10b, 11a) and bi-triazole compounds (14h, 14f, 13g, 13h, 13e, 13j) was performed. These predictions are relevant because they assess the theoretical prediction of parameters related to the physicochemical and pharmacokinetic properties of each molecule.

In this study, warnings of toxicity and/or adverse effects were generated, along with estimations of physicochemical and pharmacokinetic properties that are relevant to oral bioavailability. *In silico* predictions were predicted using OSIRIS property explorer (https://www.organic-chemistry.org/prog/peo/), Molinspiration (http://www.molinspiration.com) and ADMETlab (http://admet.scbdd.com/).

2.3.2 OSIRIS

The OSIRIS platform was used to predict the degree of solubility in an aqueous medium (LogS); the parameters used for the LogS value were: insoluble, for values lower than -10; poorly soluble ≤ -6; moderately soluble ≤ -4; soluble ≤ -2; highly soluble ≤ 0 (DAINA A, et al., 2017). Drug-score and drug-likeness were predicted, which are described in the literature as parameters that should be considered in the selection of new compounds with potential use in new medications.

Drug-likeness values can be negative or positive, where positive values indicate that the compound is similar to commercially available compounds, while negative values indicate the opposite. Drug-score values, on the other hand, range from 0 to 1; values close to 1 indicate that the compound qualifies as a drug, since the drug-score is a final parameter that is calculated based on physicochemical characteristics, toxicity and drug-likeness (https://www.organic-chemistry.org/prog/peo/).

The software **OSIRIS** property explorer supports a list in its database with approximately 5,300 different compounds. These fragments, in turn, are obtained from 3,300 commercial drugs and 15,000 chemicals that are made available by the company Fluka®.

2.3.3 Molinspiration

Predictions on the Molinspiration platform (http://www.molinspiration.com) permitted the evaluation of some physicochemical parameters, such as: PSA: polar surface area; HBA: hydrogen acceptors; HBD: hydrogen donors; VIO: number of violations; ROT: number of rotatable bonds; VOL: volume.

The software Molinspiration uses the following parameters: number of violations (molecules with values greater than 1 may present problems in oral bioavailability) and Lipinski's rule of five for the classification of a compound as a possible drug; among these characteristics, the molecule must have values for four parameters that are multiples of 5: logP less than or equal to 5, Molecular Mass less than or equal to 500 daltons; number of hydrogen bond acceptors less than or equal to 10 (expressed by the sum of Nitrogen (N) and Oxygen (O) atoms in the molecule); number of hydrogen bond donors less than or equal to 5 (bonds expressed by the sum of OH and NH in the molecule) (LIPINSKI C, 2004).

Other parameters were also considered in this study, such as: polar surface area (PSA) less than or equal to 140 $Å^2$ and the number of rotatable bonds (nrotb) less than or equal to 10; both parameters are related to oral bioavailability according to (VEBER D, et al., 2002).

2.4 *In vitro* experiments

2.4.1 *In vitro* culture of bacterial inoculum and strains used

The strains used had been previously cultured in Brain Heart Infusion (BHI) broth (HIMEDIA). The microbial cultures were then diluted in culture medium according to the 0.5 McFarland scale (1.5×10^8 CFU mL) and incubated at 35 ± 2 °C for 16 to 24 hours (CLSI, 2012). All assays were performed in triplicate.

The bacterial strains used in this study were *Klebsiella pneumoniae* (ATCC 4352-083); *Acinetobacter baumannii* (ATCC 19606-143); *Pseudomonas aeruginosa* (ATCC 29336); and Methicillin-resistant *Staphylococcus* (ATCC 33591) (MRSA), all belonging to the bacteriometry library of the Biotechnology Bioassay Platform (RPT11H), of Instituto Leônidas and Maria Deane (ILMD) – Fundação Oswaldo Cruz (Fiocruz), Manaus-AM, Brazil.

2.4.2 Antibacterial activity with the *in vitro* agar diffusion method

Antibacterial activity was determined using the agar diffusion method, with the well technique, according to (GROVE C e RANDALL W, 1955), with modifications. Initially, the Agar Müeller Hinton culture medium (AMH)

(HIMEDIA) was used to perform all tests. In this assay, the drug TIENAM (imipenem + cilastatin sodium) was used at a concentration of 500 µg/mL as a positive control; all compounds were added at a concentration of 1 mg/mL. Then, the plates were incubated at 37 °C for a period of 24 hours, after which, triphenyl tetrazolium chloride (CTT), a dye at a concentration of 0.01%, plus 0.1% bacteriological agar, was added to the plates; the culture was then incubated again for 30 minutes.

After color conversion in the overlay, inhibition halos were measured with the aid of a millimeter ruler as described by (NEGI B, et al., 2016). The criteria for determining bacterial activity by measuring the halo were defined according to (AL-HEBSHI N, et al., 2006), and (OSTROSKY E, et al., 2008): ≥ 20 mm good activity; between 15 and 20 mm moderate activity; between 10 and 15 mm little activity; ≤ 10 mm no halo/inactive. After this test, only the molecules that showed some inhibition according to halo size were submitted to the minimum inhibitory concentration test (MICs).

2.4.3 Determination of the Minimum Inhibitory Concentration (MIC) by microdilution in broth

The minimum inhibitory concentration (MIC) values of the samples capable of forming halos in the agar diffusion test were determined using the microdilution method in a 96-well plate, according to (Clinical and Laboratory Standards Institute (CLSI), with some modifications. Each well received the standardized bacterial inoculum, and in this test, the concentration ranged from 500 to 1.95 µg/mL, and 20 µL of resazurin at a concentration of 0.01%, totaling a final volume of 100 µL/well. A

s a negative control, 10% DMSO was used, and as a positive control, bacterial inoculum was used as a growth control. As a death control, the drug (TIENAM) was used at the same concentration as the samples. Subsequently, the plates were incubated at 37 °C for 24 h. The MIC was defined as the lowest concentration of the samples capable of inhibiting bacterial growth, indicated by the permanence of the blue color of resazurin. The criteria for determining bacterial activity by means of the MIC test were defined according to (HOLETZ FB, et al., 2002), with an MIC ≤ 100 µg/mL being considered good activity; between 100 and 500 µg/mL moderate activity; ≥ 500 µg/mL inactive.

RESULT and DISCUSSION

In this study, antibacterial activity was evaluated for three triazole compounds (10a, 10b, 11a) and 7 bi-triazole compounds (14h, 14f, 13g, 13h, 13e and 13j) (**Figure 2** and **3**). The bi-triazole compounds named 14f and 14h have trifluoromethyl groups on radical 1 (R1), the compounds named 13g, 13h and 13e and 13j have a methyl group on R1. All compounds within this class had different groups on radical 2 (R2), 14h had a fluorophenyl group, 14f cyclohexanol; while 13g had a phenyl group, 13h fluorophenyl, 13e phenoxymethyl and 13j cyclohexane (**Figure 3**).

Regarding the triazoles used in this study, on radical 1, **Table 1** Osiris calculations on physicochemical properties and toxicity prediction of triazoles and bi-triazoles. compound 10b had a trifluoromethyl group, 10a and 11a had a methyl group. On radical 2, compounds 10b and 10a had an amine, while 11a had an azide (**Figure 2**). In view of the results obtained, all compounds tested were inactive against the four strains of bacteria used, *K. pneumoniae*, *A. baumannii*, *P. aeruginosa* (Gram-negative) and Methicillin-resistant *Staphylococcus* (Gram-positive). Only compounds 10b and 13j were able to form a small inhibition halo of 7.33 ± 0.0 mm and 7 ± 0.0 mm, respectively, for *P. aeruginosa bacteria*.

In this context, compounds 10b and 13j were submitted to testing in order to determine their minimum inhibitory concentrations against *P. aeruginosa bacteria*, but neither compound was active in this assay. Although none of the compounds tested here showed promising bacterial inhibition, previous reports have been published focused on antibacterial activity for compounds of the triazole chemical class for the four strains of bacteria in this study (NEGI B, et al., 2016; ANEJA B, et al., 2018; WANG X; QIN L, 2019; EL MALAH T, et al., 2020; SU Z, et al., 2011) and only 2 strains have been studied (*Klebsiella pneumoniae*, *Pseudomonas aeruginosa*) against bi-triazoles (ARAFA W e MOHAMED A, 2011; DEMIRCI S, et al., 2013). Both chemical classes showed promising activity against the respective strains according to the literature; this study is one of the first that investigated *Acinetobacter baumannii* and methicillin-resistant *Staphylococcus* (MRSA).

In this sense, even though none of the compounds showed promising inhibition, the search for new drugs with bactericidal action must continue, since reports of resistance represent a threat to the treatment of bacterial diseases. Along with the antimicrobial tests performed with triazole and bi-triazole compounds, their physicochemical and pharmacokinetic properties were also predicted.

The characterization of physicochemical properties and ADMETox (administration, distribution, metabolism, toxicity and excretion) are essential in the search for a new drug, allowing for the exclusion of or promoting modifications of molecules seeking to meet the desired parameters. The results for mutagenicity, tumorigenicity, reproductive toxicity and the irritant effect were promising, presenting parameters from non-toxic to slightly toxic, attesting that none of the compounds from either chemical class will cause eventual toxicities (**Table 1**).

Table 1 - Osiris calculations on physicochemical properties and toxicity prediction of triazoles and bi-triazoles.

	Toxicity alert					Physicochemical characteristics			
Compounds	**MW**	**MUT**	**TUM**	**IRRI**	**REP**	**DL**	**DS**	**cLogP**	**cLogS**
10b	152.08	NT	NT	NT	LV	-10.18	0.39	-0.07	-0.98
10a	98.06	NT	NT	NT	LV	1.56	0.72	-0.78	-0.54
11a	124.05	NT	NT	NT	LV	-0.38	0.55	0.57	-0.20
14h	298.20	NT	NT	NT	LV	-14.25	0.38	1.7	0.090
14f	302.26	NT	NT	NT	LV	-16.74	0.38	1.5	0.72
13g	226.10	NT	NT	NT	LV	-0.88	0.50	0.87	0.66
13h	244.09	NT	NT	NT	LV	-3.64	0.40	1.0	0.35
13e	256.11	NT	NT	NT	LV	-1.04	0.49	0.79	1.0
13j	248.14	NT	NT	NT	LV	-6.92	0.39	1.1	1.15

Note: NT: non-toxic; MT: moderately toxic; T: toxic; MUT: mutagenic; TUM: tumorigenic; IRR: irritant; REP: reproductive toxicity; VL: slightly toxic; MW: molecular weight; DL: drug-likeness; DS: drug-score; cLogP: lipophilicity; cLogS: solubility. **Source:** Matinez LN, et al., 2024.

Among the drug-likeness values, only compound 10a showed a positive value, which means that only this compound has fragments similar to those found in commercially available drugs, and therefore, it has structural similarity with these compounds, unlike the other compounds in this study (MAGALHÃES U, 2009). This lack of similarity may mean that these compounds have a pharmacophore rarely found in molecules already used in clinical medicine.

For the drug-score parameters, once again, compounds of the triazole chemical class stood out with the highest values close to 1, which indicates that these compounds can qualify as a medication. The toxicity prediction showed that none of the compounds from either chemical class generated alerts for mutagenicity, tumorgenicity or irritant effect (**Table 1**). In relation to physicochemical properties, all the compounds met the criteria of (LIPINSKI CA, 2004) and (VEBER D, et al. 2002) in relation to their physicochemical properties. When these characteristics are met, the chances of developing a possible drug increase (**Table 2**).

Table 2 – *In silico* prediction of the physicochemical properties and possible biological activities of triazoles and bi-triazoles.

PHYSICOCHEMICAL PROPERTIES						
Compound	**TPSA**	**HBA**	**HBD**	**VIOL**	**ROTB**	**VOL**
Triazole						
10b	67.59	2	3	0	4	103.30
10a	72.29	3	1	0	0	88.57
11a	91.33	3	1	0	1	102.17
Bi-triazole						
14h	72.29	5	1	0	3	216.92
14f	92.52	6	2	0	3	238.16
13g	72.29	5	1	0	2	197.15
13h	72.29	5	1	0	2	202.08

13e	81.53	6	1	0	4	222. 94
13j	72.29	5	1	0	2	209.52

Note: TPSA: polar surface area; HBA: hydrogen acceptors; HBD: hydrogen donors; VIOL: number of violations; ROTB: number of rotatable bonds; VOL: volume. **Source:** Matinez LN, et al., 2024.

The compounds, in addition to having slightly toxic and non-toxic properties, also meet the criteria of (LIPINSKI CA, 2004) and (VEBER D, et al., 2002), who consider the following necessary characteristics for a compound to have adequate oral bioavailability: a LogP less than or equal to 5, molecular mass less than 500 daltons, number of Hydrogen binding acceptors less than or equal to 10, number of Hydrogen binding donors less than or equal to 5 (Table 2) [17] a TPSA ≤ 140 $Å^2$, and the number of rotatable bonds ≤ 10 (Table 2) [18].

The first theoretical *in silico* prediction of pharmacokinetics was performed to predict solubility (cLogS), and equilibrium solubility and permeability of compounds (partition coefficient - cLogP), in which only compounds 10a and 10b showed low permeability in the lipid bilayer (cLogP), the others were classified as having moderate permeability and solubility (balance of permeability and solubility). The aqueous solubility prediction results (cLogS) demonstrated that all compounds were classified as highly soluble (**Table 1**).

Were considered to be at the equilibrium of permeability and solubility threshold, which characterized them as potential compounds for the development of oral drugs (KERNS E e DI L, 2008a). The results show that only compounds 10a and 10b are considered hydrophilic, and the others were classified as having balanced permeability and solubility in the lipid bilayer according to the criteria of (KERNS E e DI L, 2008a), indicating that these compounds present no potential problems regarding their oral bioavailability. Another fact that supports this statement is that all compounds are highly soluble.

Regarding structure activity, the data obtained can also inform new synthesis strategies involving this pharmacophoric nucleus, with the goal of retaining its structure while incorporating other substituents to enhance antimalarial activity. In this context, adding a methyl group (-CH3) can increase a compound's lipophilicity, making it less water-soluble, or in some cases, enhance solubility through mechanisms such as intermoleculares interactions, including hydrophobic interactions and changes in ionization (BAZZINI P e WERMUTH DL, 2008).

Another notable characteristic of fluorine is the greater stability of the C-F (carbon-fluorine) bond compared to the C-H (carbon-hydrogen) bond. The C-F bond is more resistant to metabolic oxidation [68] and increases lipophilicity relative to hydrogen. Moreover, fluorine's high electronegativity strongly affects the acidity or alkalinity of nearby functional groups. As a result, the molecule's bioavailability is improved, facilitating membrane permeation (SHAH P e WESTWELL AD, 2007).

CONCLUSION

The present study describes the microbiological evaluation of two chemical classes of compounds; none of the ten compounds evaluated were able to inhibit the bacteria tested. However, although the results regarding bacterial inhibition are promising, the predictions made in this study show that the compounds have the potential for the development of a possible drug with pharmacokinetic parameters favorable to its use.

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