World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

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In silico study of the therapeutic potential of nor-cucurbitacins from *Mareya micrantha* (Benth) Müll. Arg: An approach on DFT theory and ADME predication

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World Journal of Advanced Research and Reviews, 2025, 27(02), 963-971

Publication history: Received on 23 April 2025; revised on 31 May 2025; accepted on 03 June 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.27.2.2148

Abstract

In the context of the valorization of African medicinal resources, this study proposes a theoretical evaluation of the physicochemical, electronic, thermodynamic and pharmacokinetic properties of three nor-cucurbitacins (*Marmicranthine B glucoside*, *Marmicranthine A glucoside*, *Marmicranthine B*) isolated from *Mareya micrantha*, a medicinal plant commonly used in Ivory Coast. The analysis was carried out using density functional theory (DFT) with the base 6-31++G(d,p) and ADME prediction tools (SwissADME). The results show that the three compounds exhibit good thermodynamic stability, particularly enhanced in aqueous media for *Marmicranthine A glucoside* and *Marmicranthine B*, as well as a significant increase in their polarity (dipole moment) in this same medium, suggesting a better affinity for biological environments. The HOMO-LUMO gaps remained high and constant, reflecting good electronic stability. In terms of pharmacokinetics, *Marmicranthine B glucoside* and *Marmicranthine B* generally complied with Lipinski's rules and appeared to be good candidates for oral administration, while *Marmicranthine A glucoside* showed significant gaps limiting its bioavailability. These results indicate that *Marmicranthine B glucoside* and *Marmicranthine B* have promising potential for further therapeutic development as natural bioactive agents.

Keywords: Nor-cucurbitacins; DFT; SwissADME; Stability; Reactivity

1. Introduction

In Ivory Coast, as in many sub-Saharan African countries, medicinal plants represent not only a valuable source of treatment for various ailments, but also an important economic lever for local communities [1]. This is the case for *Mareya micrantha*, a Euphorbiaceae commonly used in traditional medicine to treat constipation, abdominal pain and certain infections caused by gastrointestinal disorders [2], such as intestinal worms [3], and hemorrhoids [4]. It is regularly used as a laxative [5]. This medicinal plant contains nor-cucurbitacin steroids, which have been shown to have antioxidant [6], muscle relaxant [7] and anticancer activity on the Hep3B chemo-resistant human hepatocarcinoma cell line [8].

In a global context where the search for new therapeutic agents of natural origin is intensifying, particularly for their antioxidant, anti-inflammatory and anticancer effects [9], it is becoming imperative to enhance the value of local medicinal heritage through rigorous studies. This is the background to the present study, which aims to examine in

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depth the properties of three nor-cucurbitacin steroid derivatives (*Marmicranthine B glucoside*, *Marmicranthine A glucoside*, *Marmicranthine B*) recently isolated from the hydroethanolic extract of *Mareya m*. leaves. The physicochemical, thermodynamic, electronic and pharmacokinetic characteristics of these compounds have not yet been fully evaluated. The general aim of this work was to evaluate, using theoretical approaches, the properties of these three nor-cucurbitacins mentioned above, with a view to determining their potential as candidates for drug development. More specifically, we analyzed their physicochemical, electronic and thermodynamic properties using density functional theory (DFT) with the 6-31++G(d,p) basis, a method recognized for its reliability in predicting electronic structure and stability [10, 11], and secondly, to assess the pharmacokinetic profile of these compounds using the online tool SwissADME, which allows rapid and reliable prediction of oral bioavailability according to Lipinski's rules [12, 13].

Thus, the first phase of the study will focus on:

- Calculating the standard enthalpy of formation ($\Delta_f H$), standard free energy ($\Delta G°$), total energy (E_T) and entropy (S), in order to assess the thermodynamic stability of these molecules;
- Determination of the dipole moment (μD), an indicator of molecular polarity;
- Analysis of the electronic properties by calculating the energies of the HOMO and LUMO frontier orbitals, as well as the energy gap (ΔE_{gap}), the latter providing indications of the chemical reactivity of these compounds;
- A comparison of the properties in two distinct environments (gaseous and aqueous) in order to better understand the influence of the medium on their stability.

The second phase will involve predicting the pharmacokinetic properties of *Marmicranthine B glucoside*, *Marmicranthine A glucoside* and *Marmicranthine B* using the SwissADME platform, based on Lipinski's rules, i.e. molecular weight, LogP, number of hydrogen bond donors and acceptors, with the aim of estimating their oral bioavailability potential [13].

In short, this study aims to provide a comprehensive and theoretically sound understanding of the therapeutic potential of nor-cucurbitacins from *Mareya micrantha.* Furthermore, this study contributes to the scientific development of a widely used and still under-exploited local natural resource.

2. Material and calculation methods

2.1. Material

In our work, we are interested in a set of three bioactive compounds (Figure 1) from the same structural family. These molecules were selected for their antioxidant biological properties and promising anticancer activity on the chemo-resistant human hepatocarcinoma cell line Hep3B.

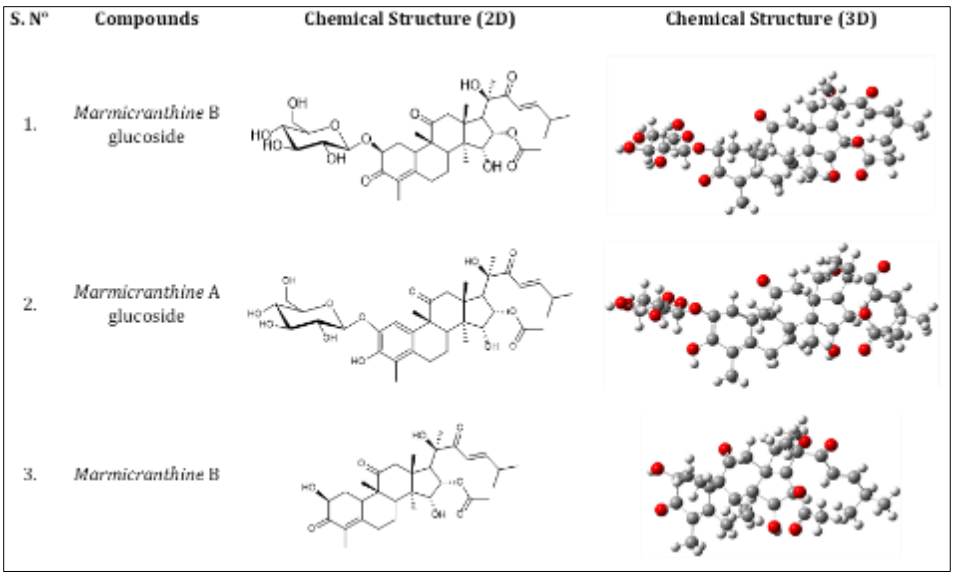

Figure 1 2D and 3D structures of the studied bioactive compounds from *Mareya micrantha*

2.2. Level of theory and calculation methodology

The calculations were carried out using Gaussian 09 software [14]. Density functional theory (DFT) method was used [15]. Previous theoretical work on the calculation of molecular properties has shown that hybrid functions such as B3LYP and others, combined with a broad base of functions, lead to values in good agreement with experimental results [16]. The level of theory chosen for this study is B3LYP/6-31++G(d,p).

First, the three-dimensional structures of these three nor-cucurbitacins, isolated from *Mareya m*., were modeled. Their optimized geometries were then subjected to density functional theory (DFT) quantum chemical calculations using Gaussian 09 software with the B3LYP functional and the 6-31++G(d,p) basis. These calculations were carried out both in the gas phase and in aqueous solution.

Several thermodynamic parameters, including global molecular descriptors, were extracted from the optimized geometries. These include: total energy (E_T), standard enthalpy of formation (Δ_fH), Gibbs free energy ($\Delta G°$) and entropy (S), all determined at room temperature (298.15 K). In parallel, the dipole moment, an indicator of molecular polarity, was also calculated in each of the media.

In addition, the electronic properties, including global molecular descriptors and molecular reactivity, were analyzed. This was made possible through the study of frontier orbitals, in particular the energy of the highest occupied orbital (HOMO), that of the lowest vacant orbital (LUMO), as well as the energy gap ($\Delta E_{gap} = E_{LUMO} - E_{HOMO}$), considered to be a determining parameter of chemical reactivity.

Finally, pharmacokinetic properties were assessed using SwissADME software. This analysis was used to predict ADME parameters (absorption, distribution, metabolism, excretion) and to check the compliance of compounds with Lipinski's rules, taking into account criteria such as molecular weight, LogP, number of hydrogen bond donors and acceptors, as well as topological polar surface area (TPSA).

3. Results and discussion

3.1. Analysis of thermodynamic parameters

The stability parameters examined in this series of compounds are: standard enthalpy of formation (Δ_fH), Gibbs free energy ($\Delta G°$), entropy (S) and total energy (E_T), all determined at room temperature (298.15 K). The calculated values of said parameters are reported in Table 1 below.

Table 1 Thermodynamic descriptors of the studied compounds in the gas and aqueous phases

SN.	Compounds	Environment	Δ_fH (kcal/mol)	$\Delta G°$(kcal/mol)	E_T (kcal/mol)	S (J/mol.k^{-1})
1	*Marmicranthine B glucoside*	Gaseous	-1 517 416.02	-1 517 505.55	-1 517 416.62	300.29
		Aqueous	-1 517 416.02	-1 517 505.55	-1 517 416.62	300.29
2	*Marmicranthine A glucoside*	Gaseous	-1 516 679.86	-1 516 766.94	-1 516 680.45	292.07
		Aqueous	-1 516 700.83	-1 516 789.52	-1 516 701.42	297.49
3	*Marmicranthine B*	Gaseous	-1 158 927.54	-1 159 001.54	-1 158 928.14	248.18
		Aqueous	-1 158 942.09	-1 159 016.67	-1 158 942.68	250.14

Analysis of the thermodynamic parameters of the compounds *Marmicranthine B glucoside*, *Marmicranthine A glucoside* and *Marmicranthine B*, both in the gas phase and in aqueous solution, reveals significant trends in stability, solvent-solute interactions and molecular organization.

Firstly, enthalpy of formation (Δ_fH) and standard free energy ($\Delta G°$) values are low for all compounds, indicating remarkable thermodynamic stability in both media [17]. However, *Marmicranthine A glucoside* and *Marmicranthine B* values are observed to become slightly lower in aqueous media, reflecting additional solvation-induced stabilization [18]. This improvement can be attributed to hydrophilic interactions such as hydrogen bonds or dipole-solvent forces [19]. This interaction is particularly favored in the case of glycosylated compounds, due to the presence of polar groups carried by the carbohydrate units, in particular the hydroxyl functions (-OH) of glucose. These functional groups

facilitate the establishment of hydrophilic interactions, such as hydrogen bonds, with the aqueous solvent. In contrast, *Marmicranthine B glucoside* showed identical values in the gas phase and in solution, suggesting relative inertia towards the aqueous solvent, probably due to a weakly polarizable structure or limited interaction with water.

In addition, the total energies follow the same pattern as the enthalpies, confirming the moderate influence of the solvent on *Marmicranthine A glucoside* and *Marmicranthine B*, while *Marmicranthine B glucoside* remains virtually unchanged. This consistency supports the hypothesis of high intrinsic stability for *Marmicranthine B glucoside*, independent of the environment.

Entropically, we note that *Marmicranthine B glucoside* maintains a stable entropy (≈ 300 J/mol.K^{-1}), suggesting a structure that is rigid or not very prone to reorganization in solution. Conversely, *Marmicranthine A glucoside* and *Marmicranthine B* show a slight increase in entropy in aqueous medium (+5.42 and +1.96 J/mol.K^{-1}, respectively). This variation can be explained by a conformational reorganization induced by the hydrophilic environment, or even by the release of water molecules organized around the solute, reflecting a moderate entropy gain.

In short, *Marmicranthine A glucoside* and *Marmicranthine B* benefit from a stabilizing effect of the aqueous solvent, both energetically and entropically, making them potentially more suitable for a physiological environment. On the other hand, the stability of *Marmicranthine B glucoside*, although remarkable, seems to result from a weak interaction with water, which could have a negative influence on its bioavailability in a biological environment. These results therefore provide valuable information for the pharmacochemical evaluation of these compounds, particularly with regard to their behavior in simulated biological environments.

3.2. Polarity analysis (dipole moment µD)

One of the reactivity parameters calculated for the studied compounds is the dipole moment. The results obtained are shown in Table 2.

Table 2 Dipole moment values of the studied compounds

SN.	Compounds	Dipole moment in the gas phase (Debye)	Dipole moment in aqueous phase (Debye)
1	*Marmicranthine B glucoside*	6.10	8.55
2	*Marmicranthine A glucoside*	5.72	8.68
3	*Marmicranthine B*	5.51	8.23

Evaluation of the dipole moment of *Marmicranthine B glucoside*, *Marmicranthine A glucoside* and *Marmicranthine B* revealed a significant increase in the dipole moment when moving from a gaseous to an aqueous environment. This increase in dipole moment, observed systematically for all three structures, reflects an electronic reorganisation induced by the solvent, which accentuates the intrinsic polarity of the molecules. Indeed, as a polar solvent, water promotes the stabilization of the most polarized molecular conformations, thus strengthening solute-solvent interactions. This phenomenon can be explained in particular by the solvent's ability to interact with the partial charges present on the surface of the molecules, leading to a preferential orientation of the dipoles [20].

Furthermore, *Marmicranthine A glucoside* is distinguished by a particularly high dipole moment in aqueous solution. This property suggests a high affinity of this compound for the hydrophilic medium, reflecting a more pronounced solvent-solute interaction. This high polarity is likely to improve both the solubility and thermodynamic stability of *Marmicranthine A glucoside* in the aqueous phase, in accordance with the principles of compatibility between solute and solvent polarity. Thus, dipole moment analysis highlights the structuring influence of the aqueous solvent on the electronic distribution and conformational dynamics of the compounds considered.

3.3. Analysis of Electronic Properties (HOMO, LUMO, ΔE_{gap})

The stability parameters examined in this series of compounds are: the energies of HOMO (E_{HOMO}), LUMO (E_{LUMO}) and the energy gap of the boundary orbitals (ΔE_{gap}) expressed in eV. The calculated values of the said parameters are reported in Table 3.

Table 3 Energy descriptors of the studied compounds

SN.	Compounds	Environment	E_{HOMO} (eV)	E_{LUMO} (eV)	ΔE_{gap} (eV)
1	*Marmicranthine B glucoside*	Gaseous	-5.79	-1.52	4.27
		Aqueous	-5.84	-1.59	4.25
2	*Marmicranthine A glucoside*	Gaseous	-5.59	-1.52	4.06
		Aqueous	-5.75	-1.67	4.08
3	*Marmicranthine B*	Gaseous	-5.81	-1.57	4.24
		Aqueous	-5.76	-1.72	4.04

In aqueous environment, a slight decrease in the energies of the HOMO and LUMO frontier orbitals was observed for all compounds. This moderate decrease suggests a stabilization of the electronic levels by the solvent, probably via dipole-dipole interactions or polarization effects induced by the electric field of the solvent. However, despite this influence, the gap between HOMO and LUMO remains relatively constant, indicating that the overall electronic reactivity of the compounds remains little altered in aqueous solution.

Consequently, all compounds retain good electronic stability, even in the presence of the solvent, reflecting a robustness of the electronic structures with respect to solvation effects. However, it should be noted that *Marmicranthine A glucoside* and *Marmicranthine B* have slightly lower gaps than *Marmicranthine B glucoside*, which may reflect marginally higher electronic reactivity for these two compounds. Thus, although water slightly modulates the energy levels, it only slightly affects the overall electronic behavior, maintaining the balance between stability and reactivity within the molecular systems studied [21].

3.4. Comparison between the gaseous and aqueous environments of the studied compounds

Table 4 summarizes the main thermodynamic and electronic parameters evaluated for the three studied compounds. These parameters were analyzed in two distinct environments: gaseous and aqueous, in order to better understand the impact of the solvent on their stability and reactivity. The results reveal trends that are broadly consistent with the physicochemical properties expected for polar bioactive molecules.

The very low enthalpies of formation ($\Delta_f H$) and standard free energies ($\Delta G°$) in both media reflect high thermodynamic stability, which becomes even more pronounced in the presence of water, suggesting a stabilizing effect of solvation. This stabilization is also corroborated by a slight increase in entropy, particularly for *Marmicranthine B glucoside*, possibly linked to a structured reorganization induced by the hydrated environment.

The dipole moment, an indicator of molecular polarity, showed a significant increase in aqueous solution, indicating a greater affinity of the compounds for the polar medium and an electronic reorientation favorable to the establishment of solute-solvent interactions. Finally, the values of the HOMO-LUMO energy gap (ΔE_{gap}), between 4.0 and 4.3 eV, confirm good electronic stability, with little variation between the two media, indicating an overall conserved chemical reactivity.

Table 4 thus provides an integrated overview of the effects of the solvent on the structural and electronic properties of the compounds, providing key elements for interpreting their behavior in a biological environment.

Table 4 Summary of results relating to the analysis of stability and reactivity parameters of the studied compounds in gaseous and aqueous media

Parameters	Gaseous Environment	Aqueous Environment
$\Delta_f H$ and $\Delta G°$	Very weak, stable compounds	Even lower, stabilization by solvatation
Entropy (J/mol.k^{-1})	Slightly higher (*Marmicranthine B glucoside*)	Molecular reorganization, possible structured solvatation
Dipole Moment (µD)	Moderately polar	Increased polarity, better affinity with water
ΔE_{gap} (HOMO-LUMO)	4.0 eV to 4.3 eV, good electronic stability	Almost identical, so responsiveness unchanged

The comparative evaluation in the gas and aqueous phases reveals that the studied compounds exhibit good thermodynamic stability in both environments. However, it is important to note that the presence of the aqueous solvent slightly improves this stability, as evidenced by the lower values of $\Delta_f H$ and $\Delta G°$. This increased stabilization can be attributed to specific solvation interactions, such as hydrogen bonds or dipole-dipole interactions, frequently observed in hydrophilic environments [22].

In addition, the transition to solution is accompanied by a marked increase in the dipole moment for all compounds, reflecting increased molecular polarization. This enhanced polarity is of particular interest in a pharmacological context, as it could promote the interaction of molecules with polar biological media, such as cytoplasm or blood plasma.

In terms of electronic reactivity, the HOMO-LUMO gap values remain virtually unchanged between the two media, suggesting that the electronic properties and chemical reactivity of the compounds are preserved in solution. This is a clear advantage in terms of chemical robustness in a variety of environments.

Finally, it should be noted that *Marmicranthine B glucoside* has the highest thermodynamic stability of the three analyzed structures, while *Marmicranthine A glucoside* has the highest dipole moment in aqueous media. This latter parameter suggests a stronger interaction with the biological environment, potentially giving *Marmicranthine A glucoside* greater efficacy in a therapeutic context.

3.5. Evaluation of pharmacokinetic properties

Lipinski's rules (Table 5), also known as the Rule of Five, are a set of criteria for assessing whether a compound has a good profile for oral administration, taking into account its ability to cross biological membranes. According to these rules, good oral bioavailability is likely if at least three of the following four criteria are met.

Table 5 Lipinski Rule criteria for assessing the oral pharmacokinetics of compounds

Criteria	Lipinski threshold	Interpretation
Molar mass (g/mol)	≤ 500	Low mass → better absorption
LogP (octanol/water partition coefficient)	≤ 5	Indicates lipophilicity, a good balance is required
Number of H -bond donors (HBD)	≤ 5	Too many donors → poorer permeability
Number of H-bond acceptors (HBA)	≤ 10	Too many acceptors → limits passive diffusion

Hydrogen bond donors (HBD) and Hydrogen bond acceptors (HBA)

The various pharmacokinetic property values for *Marmicranthine B glucoside*, *Marmicranthine A glucoside* and *Marmicranthine B* are shown in Table 6 below.

Table 6 Pharmacokinetic property values for the studied compounds

SN.	Compounds	Molar mass	LogP	TPSA (Å²)	HBA	HBD	Results
1	*Marmicranthine B glucoside*	630.81	3.58	150.59	9	4	Slightly high mass, but respects LogP, HBD, HBA
2	*Marmicranthine A glucoside*	704.80	1.77	220.51	13	7	Mass, HBA and HBD above thresholds
3	*Marmicranthine B*	544.68	2.90	138.20	8	3	Mass slightly higher, but within the limits of the other parameters

Topological polar surface area (TPSA)

Analysis of the physicochemical parameters of the three studied compounds reveals varied profiles with respect to Lipinski's rules, which are essential for predicting the oral bioavailability of drug candidates.

Firstly, although *Marmicranthine B glucoside* has a molecular weight above 500 g/mol limit, it nevertheless meets the other criteria: its moderate LogP (3.58) reflects a good hydrophilic/lipophilic balance, while the number of hydrogen bond donors HBD (4) and acceptors HBA (9) remain below the recommended thresholds. In addition, although its topological polar surface area TPSA (150.59 Å²) is relatively high, it remains within a range still compatible with

reasonable intestinal absorption. As a result, this compound can be considered broadly compliant with Lipinski's criteria, despite a slight excess in mass.

On the other hand, *Marmicranthine A glucoside* shows several significant deviations from the established thresholds. Its high molecular mass (704.80 g/mol), combined with a high number of HBA (13) and HBD (7), and a very high TPSA (220.51 $Å^2$), suggest limited membrane permeability. These properties hinder oral absorption, making this compound non-compliant with Lipinski's rules. It would therefore require structural adjustments or alternative galenic strategies to improve its bioavailability.

Finally*, Marmicranthine B* is an interesting intermediate case. Its molar mass (544.68 g/mol) slightly exceeds the recommended threshold, but all other parameters are satisfactory: the LogP (2.90), the HBA (8) and HBD (3) values and a moderate TPSA (138.20 $Å^2$) indicate good pharmacokinetic compatibility. As a result, despite marginal mass overshoot, this compound remains Lipinski-compliant, making it a promising candidate for oral development.

Among these three analyzed compounds, *Marmicranthine B glucoside* and *Marmicranthine B* appear to comply overall with Lipinski's rules. Indeed, although their molar mass slightly exceeds the limit of 500 g/mol, the other parameters, such as the LogP, the number of hydrogen bond donors (HBD) and acceptors (HBA), and the topological polar surface area (TPSA), remain within the acceptable ranges. Consequently, these slight deviations, often tolerated in pharmaceutical development, do not preclude satisfactory oral bioavailability, especially if appropriate galenic strategies such as the use of nano-vectors or prodrugs are envisaged.

On the other hand, *Marmicranthine A glucoside* exhibits several notable violations of Lipinski's criteria, including an excessive molar mass, a high number of HBD and HBA, and a particularly high TPSA. These characteristics reflect a probably reduced membrane permeability, which severely limits its potential for oral administration. However, this compound could retain pharmacological interest via alternative routes of administration, such as parenteral injection or a liposomal formulation, making it possible to overcome the constraints associated with digestive absorption.

4. Conclusion

The in-silico study conducted on the nor-cucurbitacins *Marmicranthine B glucoside*, *Marmicranthine A glucoside* and *Marmicranthine B* isolated from *Mareya micrantha* is part of an approach to the scientific valorization of local medicinal resources, in response to the growing need to discover new therapeutic agents of natural origin. A two-pronged approach was adopted: theoretical analysis using density functional theory (DFT) and pharmacokinetic prediction using SwissADME. This investigation made it possible to characterize the physicochemical, electronic, thermodynamic and pharmacokinetic properties of these three nor-cucurbitacin derivatives.

Thermodynamically, the three studied compounds were highly stable, with very low enthalpy and standard free energy values. The influence of the aqueous solvent was particularly beneficial for *Marmicranthine A glucosid*e and *Marmicranthine B*, reflecting a better compatibility with a biological environment. On the other hand, *Marmicranthine B glucoside*, although thermodynamically stable, appears to be little affected by solvation, which could limit its bioavailability under physiological conditions.

Dipole moment analysis confirmed increased polarization in aqueous media for all the compounds, reflecting electronic reorganization favorable to biological interactions. Similarly, the study of HOMO-LUMO frontier orbitals and the energy gap revealed moderate chemical reactivity, which is particularly promising for targeted pharmacological applications.

Finally, ADME (Absorption, Distribution, Metabolism, Excretion) predictions highlighted the compliance of the three compounds with Lipinski's rules, with overall favorable oral bioavailability parameters, reinforcing the idea of exploitable therapeutic potential. *Marmicranthine A glucoside* and *Marmicranthine B* stand out in particular for their improved solubility and adaptability to the physiological environment.

In summary, this theoretical study provides a solid scientific basis for future experimental research on nor-cucurbitacins from *Mareya micrantha*. The results obtained underline the relevance of exploring them as potential pharmacological candidates, particularly in the fight against inflammatory or cancerous pathologies. The next logical step in this work would be to extend the investigations with molecular docking and dynamic simulation studies, followed by experimental validation of the biological properties identified.

Compliance with ethical standards

Acknowledgments

The authors thank the reviewers for their insightful suggestions.

Disclosure of conflict of interest

The authors declare there is no conflict of interest in this study.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] World Health Organization. WHO Strategy for Traditional Medicine. 2021; 2014–2023.

[2] Tsai CS, Guede-Guina F, Tsai MH, Vangah-Manda M, Ochillo RF. The pharmacological action of aqueous extract from *Mareya micrantha* on the longitudinal muscle of isolated guinea-pig ileum. Twelfth Annual Southeastern Pharmacology Society (SEPS) Meeting. New Orleans, LA. 1991; November 8-9, Abstract No. 10.

[3] Savill PS and Fox JED. Trees of Sierra Leone. Forest Department, Freetown, Sierra Leone. 1967.

[4] Béné K, Camara D, Fofié NBY, Kanga Y, Yapo YC, Ambé SA, Zirihi GN. Ethnobotanical study of medicinal plants used in the Department of Transua, District of Zanzan (Ivory Coast). Journal of Animal and Plant Sciences. 2016; 27, 4230–4250.

[5] Méité S, Bahi C, Yeo D, Datte JY, Djaman JA, N'guessan DJ. Laxative activities of *Mareya micrantha* (Benth.) Mull. Arg. (Euphorbiaceae) leaf aqueous extract in rats. BMC Complementary and Alternative Medicine. 2010; 10, 7–9.

[6] Douhoré GYT, Attioua KB, Soro Y, Kabran FA, Kablan LCA, Vedrenne M, Mathieu C, Vaca-Garcia C. Nor-cucurbitacins from the leaves of *Mareya micrantha* (Benth) Müll. Arg. (Euphorbiaceae), Fitoterapia. 2020; 104538.

[7] Koffi KL, Bony FN, Okpekon AT, Bitty MLA, N'Guessan KJ, Séon-Méniel B, Champy P. Compounds with myorelaxant activity from the leaves of *Mareya micrantha* (Benth.) Müll. Arg. (Euphorbiaceae). Journal of Pharmacognosy and Phytochemistry. 2020; 9 (4), 48–59.

[8] Toussaint-Douhoré GY, Soro Y, Ouédraogo N, Vaca-Garcia C, Koffi-Attioua B, Carraz M. Liver cancer antiproliferative activity of a new nor-cucurbitacin from *Mareya micrantha* (Benth) Müll. Arg. Fitoterapia. 2023; 166, 105471.

[9] Newman DJ and Cragg GM. Natural Products as Sources of New Drugs over the Nearly Four Decades from 01/1981 to 09/2019. Journal of Natural Products. 2020; 83 (3), 770–803.

[10] Parr RG and Yang W. Density-functional theory of atoms and molecules. Oxford University Press. 1994.

[11] Becke AD. Density-functional thermochemistry. III. The role of exact exchange. The Journal of Chemical Physics. 1993; 98 (7), 5648–5652.

[12] Daina A, Michielin O, Zoete V. SwissADME: A free web tool to evaluate pharmacokinetics, drug-likeness and medicinal chemistry friendliness of small molecules. Scientific Reports. 2017; 7(1), 42717.

[13] Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Advanced Drug Delivery Reviews. 2001; 46(1–3), 3–26.

[14] Frisch MJ, Trucks GW, Schlegel HB, Scuseria GE, Robb MA, Cheeseman JR, Scalmani G, Barone V, Mennucci B, Petersson GA, Nakatsuji H, Caricato M, Li X, Hratchian HP, Izmaylov AF, Bloino J, Zheng G, Sonnenberg JL, Hada M, Fox DJ. Gaussian 09, Revision A.02. Gaussian, Inc., Wallingford CT. 2009.

[15] Hohenberg P and Kohn W. Inhomogeneous electron gas. Physical Review. 1964; 136(B864).

[16] Koch W and Holthausen MC. A chemist's guide to density functional theory (2nd ed.). Wiley-VCH. 1999.

[17] Duff MR and Howell EE. Thermodynamics and solvent linkage of macromolecule-ligand interactions. 2014.

[18] Spencer JN. Solvent effects on hydrogen bond formation. 1981.

[19] Cramer J. Enhancing the enthalpic contribution of hydrogen bonds by solvent shielding. 2020.

[20] Pawełka Z. Solvent influence on dipole moment and charge-transfer effects in π-electron systems. Journal of the Chemical Society, Faraday Transactions 2: Molecular and Chemical Physics. 1988; 84(10), 1683–1696.

[21] Barraza-Jiménez D, Martinez-De la Cruz A, Saucedo-Mendiola L, Torres-Herrera SI, Padilla Mendiola, A, Coria Quinones EM, Olvera Corral RA, Frias-Zepeda ME, Flores-Hidalgo MA. Effects of solvents on anthocyanidin-derived dye sensitizers for photocatalysis applications. In D. M. Parra (Ed.), Dye-Sensitized Solar Cells. 2019.

[22] Tomasi J, Mennucci B, Cammi R. Quantum mechanical continuum solvation models. Chemical Reviews. 2005; 105(8), 2999–3093.