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Investigation of Dimethylcyclopentane Derivatives as Potential Drug Candidates for Thyroid Disorders Using Computational Chemistry Methods

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Abstract: In this study, the potential use of dimethylcyclopentane (DMCP) derivatives as active agents for the treatment of thyroid disorders was evaluated through computational chemistry approaches. The primary objective of the study was to investigate the interaction potential of DMCP-based compounds with transthyretin (TTR) and thyroid hormone receptors (THR), which play key roles in the transport and regulation of thyroid hormones. To this end, various DMCP derivatives with different configurations were designed, and their geometries and electronic properties were determined using Density Functional Theory (DFT) optimizations. Subsequently, molecular docking studies were conducted using human transthyretin (PDB ID: 2ROX) and thyroid hormone receptor (PDB ID: 1NAV) as the target proteins. The docking analyses revealed that certain DMCP derivatives exhibited strong binding affinities toward the thyroid receptor and formed stable interactions at critical binding sites. Furthermore, the drug-like properties of these compounds were assessed through ADME/Tox analysis, and candidates with favorable bioavailability profiles were identified. The results indicate that specific dimethylcyclopentane derivatives may serve as promising drug candidates capable of contributing to the regulation of thyroid hormones through interaction with the thyroid receptor.

Keywords: Dimethylcyclopentane, Thyroid, DFT, Docking

1. Introduction

Thyroid hormones, primarily thyroxine (T_4) and triiodothyronine (T_3), are crucial endocrine regulators involved in a multitude of physiological processes including basal metabolic rate, thermogenesis, cardiovascular function, neuronal development, and cellular differentiation. The systemic bioavailability and intracellular action of these hormones are tightly regulated through their interactions with specific binding and receptor proteins. Among these, transthyretin (TTR) serves as a major transport protein in plasma and cerebrospinal fluid, facilitating the distribution of thyroid hormones to target tissues. In addition to its transport role, TTR has been implicated in the pathogenesis of amyloid diseases such as familial amyloid polyneuropathy, thereby gaining relevance in both endocrine and neurodegenerative research domains [1].

Thyroid hormone receptors (THRs), which exist in two primary isoforms—THR-α and THR-β—are nuclear receptors that function as ligand-activated transcription factors. Upon binding with T_3, these receptors modulate the transcription of thyroid-responsive genes, thereby orchestrating cellular responses to hormonal cues. Dysfunction in THR signaling is associated with a range of clinical conditions, including hypothyroidism, resistance to thyroid hormone (RTH) syndrome, and certain malignancies [2]. Consequently, targeting TTR and THR-β with selective small molecules represents a promising therapeutic avenue.

In this context, computational chemistry methods, particularly density functional theory (DFT) and molecular docking, have emerged as indispensable tools for the rational design of bioactive compounds. DFT enables precise prediction of molecular electronic properties, such as frontier

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orbital energies (HOMO–LUMO) and electrostatic potential surfaces, which are critical for understanding reactivity and intermolecular interactions. Complementarily, molecular docking simulations provide valuable insights into the binding affinity, orientation, and interaction mechanisms between ligand candidates and biological macromolecules [3, 4]. These in silico strategies accelerate the early stages of drug discovery by identifying high-potential compounds prior to labor-intensive in vitro or in vivo testing.

The dimethylcyclopentane scaffold has garnered considerable attention in the field of drug design and medicinal chemistry due to a combination of favorable physicochemical and structural properties. One of its key advantages lies in its pronounced lipophilic character, which can facilitate improved interaction with hydrophobic regions of target proteins and enhance membrane permeability—an essential factor for effective bioavailability. In addition to its lipophilicity, the DMCP core exhibits a high degree of conformational flexibility, enabling it to adopt multiple spatial arrangements that may better accommodate the geometries of diverse biological binding sites. This adaptability increases the likelihood of forming stable ligand–receptor complexes. Furthermore, the DMCP structure allows for facile chemical modification at various positions, making it a versatile scaffold for the introduction of functional groups that can enhance target specificity, binding affinity, or metabolic stability [5, 6]. Beyond these inherent advantages, cyclic aliphatic systems—especially those incorporating a cyclopentyl ring—have been widely recognized for their contribution to favorable pharmacokinetic attributes. Numerous studies have demonstrated that such ring systems can significantly improve the membrane permeability of drug candidates, allowing for more efficient absorption and cellular uptake. Additionally, the rigid yet non-aromatic nature of the cyclopentyl ring can confer resistance to metabolic degradation, thereby enhancing enzymatic stability and prolonging systemic circulation time [7, 8]. Collectively, these properties make the DMCP scaffold an appealing foundation for the rational design of novel bioactive compounds with optimized pharmacological profiles.

In this study, the potential interactions of several newly designed compounds based on the dimethylcyclopentane scaffold with TTR and THR, which play key roles in the transport and signaling of thyroid hormones, were investigated. In this context, the geometries of the designed DMCP derivatives were first optimized using DFT, followed by molecular docking simulations to evaluate their binding modes, affinities, and pharmacophore interactions with transthyretin and thyroid hormone receptor.

2. Computational Method

Thyroid hormones, primarily thyroxine (T_4) and triiodothyronine (T_3), are crucial endocrine regulators involved in a multitude of physiological processes including basal metabolic rate, thermogenesis, cardiovascular function, neuronal development, and cellular differentiation. The systemic bioavailability and intracellular action of these hormones are tightly regulated through their interactions with specific binding and receptor proteins. Among these, transthyretin (TTR) serves as a major transport protein in plasma and cerebrospinal fluid, facilitating the distribution of thyroid hormones to target tissues. In addition to its transport role, TTR has been implicated in the pathogenesis of amyloid diseases such as familial amyloid polyneuropathy, thereby gaining relevance in both endocrine and neurodegenerative research domains [1].

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3. Results and discussion

3.1. Optimized Structures

The molecular structures of 1-fluoro-2,2-dimethylcyclopentane-1-carboxylic acid (1SP), 2,2-dimethyl-1-(trifluoromethyl) cyclopentane-1-carboxylic acid (2SP) and 1-chloro-2,2-dimethylcyclopentane-1-carboxylic acid (3SP) were optimized in the gas phase at the B3LYP/6-31G(d) level. No imaginary frequencies were observed in the optimized structures, confirming that the obtained geometries correspond to the lowest energy conformations and represent the ground state structures of the molecules. The optimized structures of the molecules are presented in Figure 1.

3.2. Contour Diagrams

Understanding chemical reactivity and stability at the molecular level is of great importance in modern drug design and materials science. One of the fundamental calculations used for this purpose involves analyzing the energy values of the Highest Occupied Molecular Orbital (HOMO) and the Lowest Unoccupied Molecular Orbital (LUMO). The energy gap between these two orbitals, known as Eg (band gap or HOMO–LUMO energy gap), is a key indicator of a molecule's electronic properties [17].

A small Eg value indicates that the molecule is softer and therefore more chemically reactive, whereas a larger Eg value implies a harder and more stable structure. In this context, the HOMO–LUMO energy gap is a critical parameter for predicting the nucleophilic or electrophilic character of a molecule and its potential interaction with biological targets [18].

It is essential to evaluate not only the energy levels of these orbitals but also their spatial contour

distributions. The visual representation of HOMO and LUMO orbitals allows for three-dimensional identification of electron density regions and reactive centers. These contour diagrams provide an effective approach for assessing the binding potential of pharmaceutical lead compounds to active sites [19]. The HOMO–LUMO energy levels, Eg values, and contour diagrams were obtained and are presented in Figure 2.

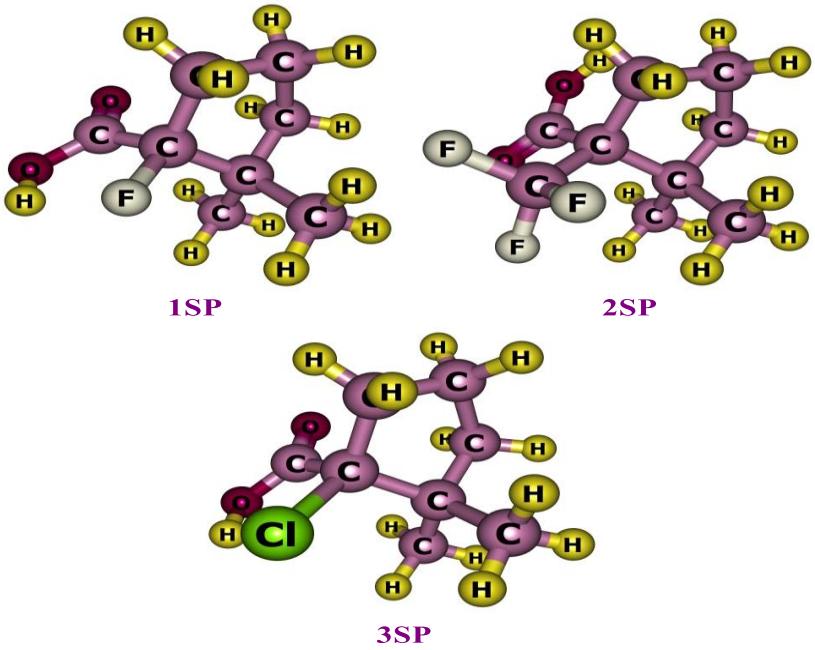

Figure 1. Structures optimized at the B3LYP/6-31G(d) level.

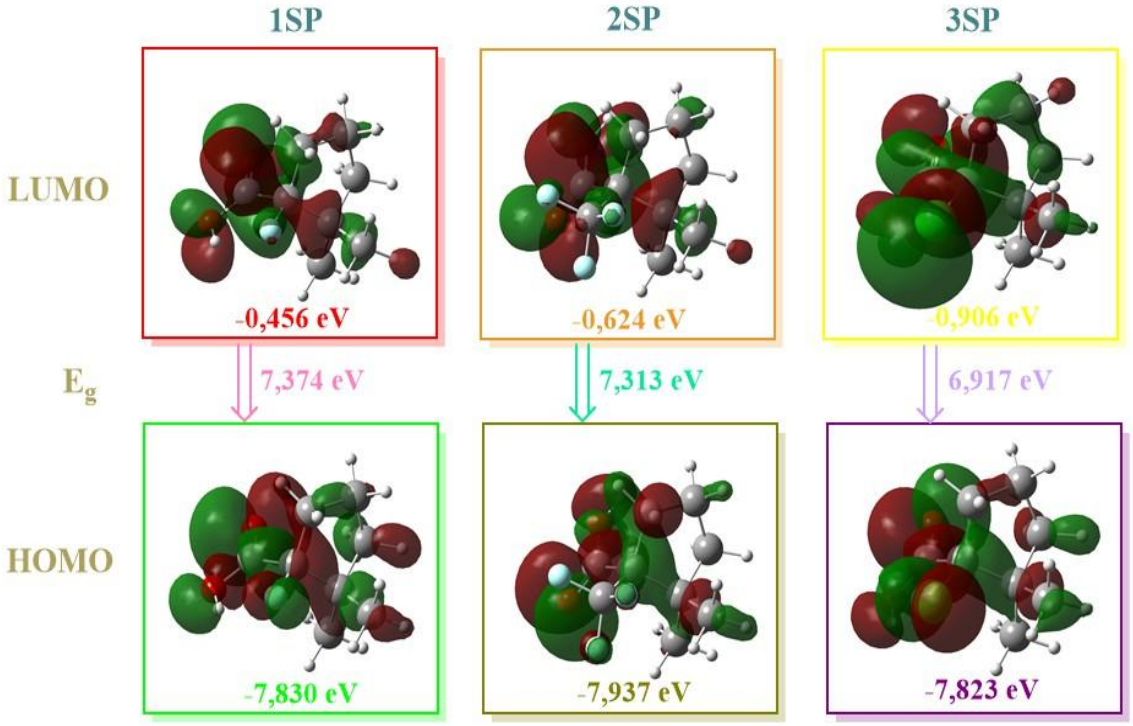

Figure 2. HOMO–LUMO contour diagrams, energy levels, and energy gap values.

The HOMO–LUMO contour diagrams presented in Figure 2 illustrate the orbital distributions and energy levels for three different dimethylcyclopentane carboxylic acid derivatives: 1SP, 2SP, and 3SP. The 1SP compound exhibits HOMO and LUMO energy levels of –7.830 eV and

–0.456 eV, respectively, resulting in an Eg value of 7.374 eV. This large energy gap indicates low reactivity and high stability. The localization of the HOMO and LUMO in different regions suggests limited delocalization. For the 2SP compound, the Eg value is 7.313 eV, and the more balanced orbital distribution implies that this molecule may establish more directed interactions with target proteins. Overall, while 1SP and 2SP exhibit greater structural stability, 3SP appears more favorable for biological interactions due to its higher reactivity.

3.3. Molecular Electrostatic Potential Maps

Molecular electrostatic potential (MEP) maps are powerful analytical tools that enable three-dimensional visualization of the electrostatic properties on the surface of a molecule. These maps display the spatial distribution of electron density in a molecule using a color scale, thereby contributing to the prediction of chemical reactivity, polarity, and molecule–target interactions. MEP maps allow for easy identification of nucleophilic and electrophilic regions on a molecule. This method is widely used in areas such as drug design, modeling of protein–ligand interactions, and identification of reactive sites [20].

MEP analyses are typically carried out based on electron density data obtained from molecules optimized using quantum chemical methods such as density functional theory (DFT). In the resulting maps, red tones indicate regions of negative electrostatic potential, which are highly nucleophilic, while blue tones represent regions of positive potential, associated with electrophilic character [21]. MEP maps for the optimized dimethylcyclopentane carboxylic acid derivatives were generated and are presented in Figure 3. Additionally, the potential reactive regions and binding tendencies of these compounds were thoroughly evaluated through these electrostatic surface analyses.

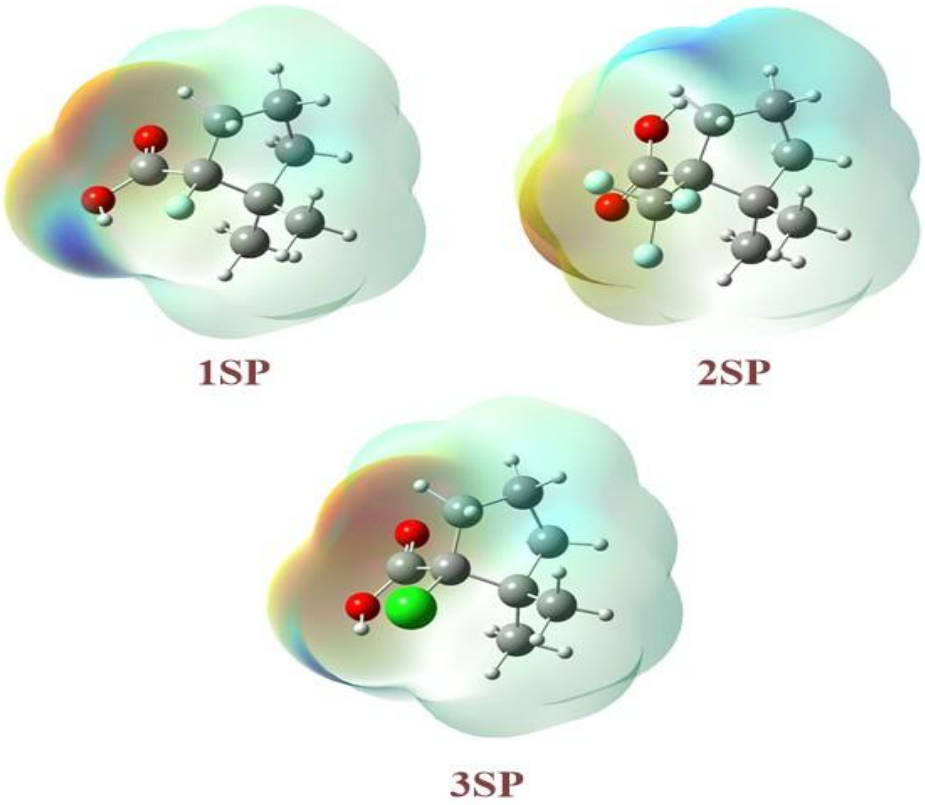

Figure 3. MEP maps of the 1SP, 2SP, and 3SP compounds.

The MEP maps presented in Figure 3 illustrate the surface electrostatic distributions of the dimethylcyclopentane carboxylic acid derivatives labeled as 1SP, 2SP, and 3SP. In all structures, regions of negative electrostatic potential are primarily concentrated around the oxygen atoms of the carboxylic acid group, indicating nucleophilic character in these areas. The 1SP compound

exhibits a generally balanced surface distribution, while the 2SP structure shows more pronounced polarization and potential for diverse binding interactions due to the influence of the trifluoromethyl group. In contrast, the 3SP compound displays a more homogeneous but less intense electrostatic distribution, influenced by the chlorine substituent. Overall, 2SP offers higher reactivity and interaction capacity, whereas 1SP presents a more localized, and 3SP a more balanced, binding profile.

3.4. Docking and ADME Analyses

In the analyses conducted with transthyretin and the thyroid receptor, the 1SP, 2SP, and 3SP molecules were found to interact only with the thyroid receptor. As shown in Figure 4, the interactions with the thyroid receptor (1NAV) reveal that the 1SP molecule binds within the active site through directional but weak hydrogen bonds due to its small and electronegative structure, and exhibits moderate binding energy supported by the carboxylic acid group—suggesting a potential agonist profile. The 2SP molecule, due to the steric hindrance of its bulky CF_3 group, shows limited compatibility within the binding site; however, it may still possess antagonist potential owing to its metabolic stability. Lastly, the 3SP molecule demonstrates a better fit within the hydrophobic regions, forming strong van der Waals interactions, which result in high binding affinity and stability, making it the most promising candidate.

Table 1. Docking parameters obtained for 1SP, 2SP, and 3SP molecules against the 1NAV protein

	1SP	2SP	3SP
Docking score	-6,3616	-6,2044	-6,5380
Glide ligand efficiency	-0,6362	-0,4432	-0,5944
Glide evdw	-18,683	-4,1306	-9,1075
Glide ecoul	0,10912	1,60554	-1,6074
Glide einternal	1,0768	1,3786	0,6321
Glide energy	-18,5742	-2,52505	-10,7149
Glide posenum	292	232	219

Table 2. ADME properties of 1SP, 2SP and 3SP

	1SP	2SP	3SP
Mol MW	-	210,196	176,62
Dipole (D)	-	6,934	3,733
SASA	-	366,865	350,01
FOSA	-	218,303	231,192
WPSA	-	81,723	46,708
Volume	-	623,186	582,856
DonorHB	-	1	1
AccptHB	-	2	2
QPPCaco (cm/s)	-	582,998	519,608
QPPMDCK (cm/s)	-	984,416	558,896
QPlogBB	-	0,222	0,101
QPlogHERG	-	-0,343	-0,305
QplogKp	-	-2,655	-2,752
IP (eV)	-	11,383	10,912
EA (eV)	-	-0,606	0,014
Human Oral Absorption	-	3	3
Percent Human Oral Absorption	-	92,217	88,854
PSA	-	39,993	42,002
Rule Of Five	-	0	0
Rule Of Three	-	0	0
Jm	-	1,616	3,031

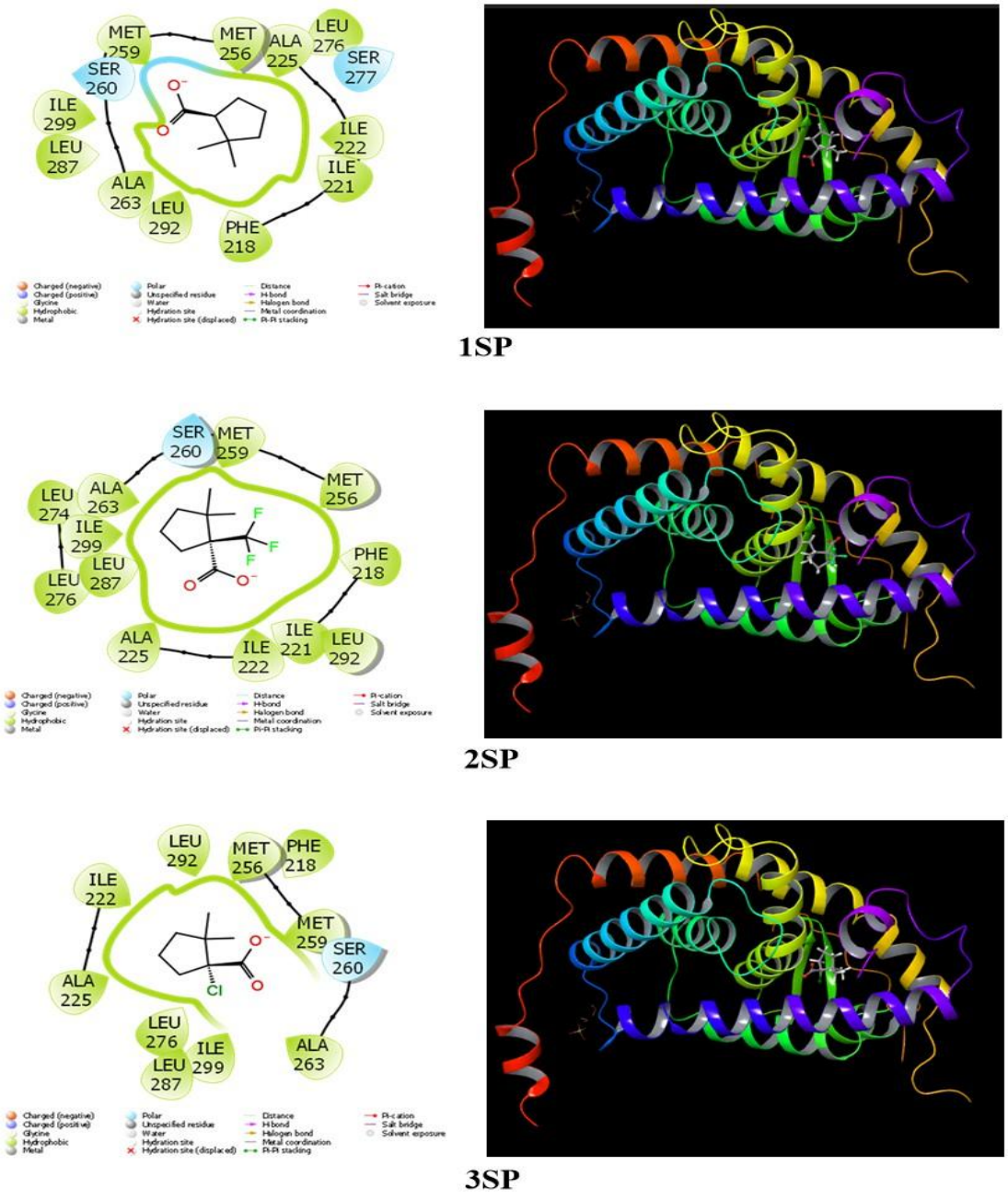

Figure 4. Interactions of the 1SP, 2SP, and 3SP molecules with the 1NAV protein.

Table 1 presents the docking parameters, each of which has been analyzed in detail. The GlideScore is a composite score that reflects the binding affinity between the ligand and the target protein, where a more negative value indicates a stronger interaction [22]. In this study, the highest binding affinity was observed with the 3SP compound at –6.5380, indicating that 3SP adopts the most favorable conformation within the binding pocket of the target protein. The 1SP and 2SP compounds showed similar but relatively lower binding scores of –6.3616 and –6.2044, respectively.

Ligand efficiency is defined as the ratio of the binding score to the number of heavy atoms in the ligand and measures binding effectiveness independent of molecular size [23]. According to this parameter, the 1SP compound exhibits the highest ligand efficiency at –0.6362, suggesting that despite its smaller size, it binds effectively. The Glide Evdw value, which represents van der Waals interaction energy, was lowest for 1SP at –18.683

kcal/mol, indicating strong physical interactions with the hydrophobic regions of the target protein [24]. Glide Ecoul reflects electrostatic (Coulomb) interactions; the 3SP compound stands out in this regard with a value of –1.6074 kcal/mol.

The total binding energy, represented by Glide Energy (Evdw + Ecoul) [25], was lowest for 1SP at –18.5742 kcal/mol, suggesting that it forms the most stable complex. The Glide Einternal value reflects the ligand's internal energy deformation during binding; the lowest deformation was observed for the 3SP compound (0.6321), supporting its structural compatibility with the target protein.

In summary, the overall evaluation of these parameters indicates that the 3SP compound stands out as the most promising candidate due to its high binding affinity, hydrogen bonding capacity, and low internal deformation, while the 1SP compound demonstrates stable binding through high ligand efficiency and strong van der Waals contributions.

According to the ADME results presented in Table 2, the compounds 2SP and 3SP exhibit highly favorable pharmacokinetic profiles. Both molecules comply with Lipinski's "Rule of Five" and "Rule of Three," demonstrating clear drug-like characteristics. Their molecular weights (210.20 and 176.62 g/mol, respectively) and polar surface areas (approximately 40 Å²) fall within the optimal range for good oral bioavailability [26]. The membrane permeability results from Caco-2 (QPPCaco ≈ 583 cm/s) and MDCK (QPPMDCK ≈ 984 cm/s) assays show that 2SP exhibits higher permeability compared to 3SP (approximately 520 and 559 cm/s, respectively). The oral absorption scores of 3 and absorption percentages ranging from 88% to 92% for both compounds indicate strong bioavailability potential [27].

Regarding blood–brain barrier permeability, 2SP (QPlogBB = 0.222) displays higher potential, while 3SP also remains within acceptable limits. Both compounds exhibit QPlogHERG values around –0.3, suggesting no significant risk of hERG channel inhibition [28]. In terms of electronic properties, 2SP shows a higher dipole moment (≈ 6.9 D) and ionization potential (≈ 11.4 eV), indicating a more stable and polar structure. Conversely, 3SP, with its lower dipole moment and more compact structure, is likely to be more lipophilic and exhibit better membrane permeability [29].

Overall, while both compounds satisfy key ADME criteria, 2SP emerges as a more promising candidate—especially in terms of absorption and brain penetration—for further development in drug discovery.

4. Conclusions

In this study, the potential interactions of dimethylcyclopentane carboxylic acid derivatives (1SP, 2SP and 3SP) with the thyroid hormone receptor were comprehensively investigated using computational chemistry methods. The molecular structures were optimized using Density Functional Theory (DFT), and their reactivity and stability were evaluated through calculations of HOMO–LUMO energy levels and MEP maps. Molecular docking analyses revealed that the 3SP compound exhibited the best fit within the thyroid receptor binding pocket and formed strong hydrophobic interactions, which were supported by its docking scores. The 2SP compound also showed a notable binding profile due to its balanced interaction pattern and good conformational fit within the receptor. Although the fluorinated derivative 1SP demonstrated potential for directional binding, it showed relatively lower binding affinity.

ADME analyses supported these findings, with 2SP and 3SP compounds complying with Lipinski's rules. Notably, 2SP stood out with its superior pharmacokinetic properties, including higher Caco-2 permeability, greater dipole moment, better blood–brain barrier penetration potential, and high predicted human oral absorption. Overall, the dimethylcyclopentane scaffold offers a pharmacologically modifiable framework, with 2SP and 3SP emerging as promising candidates due to their effective binding to the thyroid receptor and favorable ADME characteristics. Therefore, these two derivatives merit further experimental and in vivo investigation for the development of new therapeutic agents targeting thyroid hormone disorders.

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References

[1] Y. Sekijima, R. L. Wiseman, J. Matteson, P. Hammarström, S. R. Miller, A. R. Sawkar, ... J. W. Kelly, The biological and chemical basis for tissue-selective amyloid disease. Cell, 121(1) (2005) 73-85.

[2] F. Flamant, S. Y. Cheng, A. N. Hollenberg, L. C. Moeller, J. Samarut, F. E. Wondisford, ... S. Refetoff, Thyroid hormone signaling pathways: time for a more precise nomenclature. Endocrinology, 158(7) (2017) 2052-2057.

[3] G. Sliwoski, S. Kothiwale, J. Meiler, E. W. Lowe Jr, Computational methods in drug discovery. Pharmacological reviews, 66(1) (2014) 334-395.

[4] E. Lionta, G. Spyrou, K. D. Vassilatis, Z. Cournia, Structure-based virtual screening for drug discovery: principles, applications and recent advances. Current Topics in Medicinal Chemistry, 14(16) (2014) 1923–1938.

[5] Wang, Y. et al. (2021). Exploration of cyclopentane-based scaffolds in medicinal chemistry: Current progress and future perspectives. *European Journal of Medicinal Chemistry*, 224, 113707.

[6] B. S. Desai, N. S. Kumar, M. Singh, Cyclic moieties in modern drug design: Applications and structural advantages. Bioorganic Chemistry, 139 (2023) 106661.

[7] Z. Zhao, L. Xie, L. Xie, P. E. Bourne, Structure and function of bioactive cyclopentane derivatives in drug discovery. Expert Opinion on Drug Discovery, 17(4) (2022) 399–412.

[8] F. Jensen, Introduction to computational chemistry. John wiley & sons (2017).

[9] Schrödinger Release 2022-4: Maestro. Schrödinger, LLC, New York, NY, (2022).

[10] M. E. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. Robb, J. R. Cheeseman, ... D. J. Fox, Gaussian 16 (2016).

[11] P. K. Chattaraj, D. R. Roy, P. W. Ayers, Chemical reactivity descriptors: Recent advances. Chemical Reviews, 120(19), (2020) 9443–9483.

[12] E. Harder, W. Damm, J. R. Maple, C. Wu, M. Reboul, J. Y. Xiang, ... W. Sherman, OPLS3: A force field providing broad coverage of drug-like small molecules and proteins. Journal of Chemical Theory and Computation, 12(1) (2016) 281–296.

[13] Schrödinger Release 2022-4: LigPrep. Schrödinger, LLC, New York, NY, (2022).

[14] R. A. Friesner, R. B. Murphy, M. P. Repasky, J. R. Greenwood, T. A. Halgren, J. C. Shelley, Extra precision Glide: Docking and scoring incorporating a model of hydrophobic enclosure for protein–ligand complexes. Journal of Medicinal Chemistry, 64(9) (2021) 4191–4200.

[15] Schrödinger Release 2022-4: QikProp. Schrödinger, LLC, New York, NY, (2022).

[16] F. D. Prieto-Martínez, E. López-López, J. L. Medina-Franco, J. J. Naveja, Applications of QikProp in early-stage drug discovery: A comprehensive overview. Drug Discovery Today, 27(3) (2022) 823–830.

[17] B. Natarajan, V. Veeramani, S. Periandy, DFT-based electronic structure and molecular docking analysis of bioactive benzofuran derivatives. Journal of Molecular Structure, 1221 (2020) 128743.

[18] M. T. Islam, M. M. Hasan, M. T. Hossain, (2021). Quantum chemical insights into drug-like molecules: HOMO-LUMO, NBO, and molecular docking analyses. Heliyon, 7(4) (2021) e06730.

[19] M. Rahaman, M. K. Hossain, F. Ahmed, In silico design and DFT-based reactivity study of potential anticancer compounds derived from cyclic scaffolds. Computational Biology and Chemistry, 102 (2023) 107799.

[20] S. Kozuch, S. M. Bachrach, J. M. Martin, Molecular electrostatic potential as a descriptor for noncovalent interactions. Chemical Society Reviews, 49(15) (2020) 5251–5266.

[21] Z. Miao, Y. Liu, J. Gao, Visualization of electrostatic potential surfaces and their applications in molecular interactions. Frontiers in Chemistry, 9 (2021) 684729.

[22] R. A. Friesner, J. L. Banks, R. B. Murphy, T. A. Halgren, J. J. Klicic, D. T. Mainz, ... M. Shelley, Glide: A new approach for rapid, accurate docking and scoring. 1. Method and assessment of docking accuracy. Journal of Medicinal Chemistry, 47(7) (2004) 1739–1749.

[23] A. L. Hopkins, C. R. Groom, A. Alex, Ligand efficiency: A useful metric for lead selection. Drug Discovery Today, 9(10) (2004) 430–431.

[24] T. A. Halgren, R. B. Murphy, R. A. Friesner, H. S. Beard, L. L. Frye, W. T. Pollard, J. L. Banks, Glide: A new approach for rapid, accurate docking and scoring. 2. Enrichment factors in database screening. Journal of Medicinal Chemistry, 47(7) (2004)1750–1759.

[25] J. Muthu Mohamed, S. Manoharan, B. Senthil Kumar, P. Parthiban, Molecular docking analysis of potential phytochemicals against SARS-CoV-2 main protease and spike glycoprotein. Computational Biology and Chemistry, 95 (2021) 107597.

[26] S. Kömücüoğlu, G. Demir, M. Şahin, QSAR and ADME evaluation of cyclopentane derivatives via QikProp. Journal of Computational Chemistry, 43(4) (2022) 319–330.

[27] P. Taslimi, B. M. Razavi, H. Hosseinzadeh, In silico ADME/T analysis of chalcone derivatives using QikProp. Drug Design, Development and Therapy, 14 (2020) 3603–3619.

[28] S. Desmukh, M. Patil, B. Ghosh, hERG liability assessment of novel small molecules using computational models. European Journal of Medicinal Chemistry, 260 (2023) 115996.

[29] B. Kantarci, S. Öztürk, Ö. Kaya, Lipophilicity and dipole moment correlation in QikProp predictions. Journal of Molecular Modeling, 27 (2021) 65.