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BIOCHEMICAL AND PHARMACEUTICAL EVALUATION OF NOVEL BIOACTIVE COMPOUNDS THROUGH MOLECULAR DOCKING, NANOTECHNOLOGY, AND GREEN CHEMISTRY APPROACHES FOR THERAPEUTIC APPLICATIONS

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ABSTRACT

This study evaluated novel bioactive compounds through an integrated computational framework combining molecular docking-related screening, biochemical interpretation, pharmaceutical profiling, green chemistry suitability, and nanotechnology-based formulation assessment for therapeutic applications. A total of 2,000 bioactive compounds were assessed against 400 therapeutically relevant protein targets using binding affinity, activity status, physicochemical descriptors, drug-likeness classification, biochemical interaction potential, green chemistry suitability, nanoformulation suitability, and therapeutic priority scoring. The evaluated compounds showed broad physicochemical diversity, with many molecules displaying properties compatible with pharmaceutical development. Among the screened compounds, 608 were classified as active and 1,392 as inactive. Drug-likeness assessment showed that 1,049 compounds had high drug-likeness, 945 had moderate drug-likeness, and only 6 showed low drug-likeness. Docking-based classification identified 165 strong active docking hits and 443 moderate active docking hits. Green chemistry evaluation indicated high suitability for 1,828 compounds, while nanoformulation assessment showed high suitability for 1,841 compounds. Biochemical interaction analysis identified 165 compounds with high interaction potential. Therapeutic priority scoring ranked CID_01091, CID_01444, CID_00869, and CID_01429 as leading candidates due to their favourable binding affinity, drug-likeness, biochemical potential, and formulation suitability. Overall, the study provides a systematic computational basis for prioritizing bioactive compounds for therapeutic development; however, experimental validation is required to confirm biological activity, safety, and translational applicability.

KEYWORDS: Bioactive compounds; Molecular docking; Drug-likeness; Green chemistry; Nanoformulation

1. INTRODUCTION

The identification and evaluation of novel bioactive compounds are among the fundamental aspects of modern therapy development. Various bioactive compounds can interact with certain biological targets and influence molecular processes associated with disease progression, cellular regulation, inflammatory processes, infection, metabolic disorders, and numerous pathological conditions. Due to structural features and biological activity, natural compounds and bioactive molecules can serve as valuable sources for the identification of novel drug candidates (Newman & Cragg, 2020; Skalicka-Woźniak, 2021; Thomford et al., 2018). Since bioactive compounds can affect biological processes, such molecules can be considered potential drug candidates for drug discovery and development.

Bioactivity alone is not enough for the success of a bioactive compound in drug discovery or pharmaceutical development. Therapeutic efficacy usually implies the presence of the required physicochemical properties, suitable drug-likeness, strong molecular interaction, favourable formulation potential, and safe development practices. Interaction with a therapeutic protein target is crucial for the identification of promising molecules since their efficacy can depend on the presence of molecular interactions (Santos et al., 2017). Thus, early compound screening should involve the evaluation of drug efficacy based on its molecular interaction and pharmaceutical suitability.

A number of computational methods can be used to analyze molecular interactions. For example, molecular docking techniques can estimate the binding affinity and interaction potential of certain compounds. Thus, computational docking

can be used to screen compounds with strong interaction potentials and predict compounds that are expected to interact with specific therapeutic molecular targets. Docking and virtual screening approaches are widely applied when there is a need to screen a great number of molecules in order to find promising compounds (Forli et al., 2016; Pagadala et al., 2017). This technique is helpful in drug discovery due to its efficiency.

However, the mere existence of certain binding affinities is not enough for therapeutic suitability since such molecules should also be pharmaceutically acceptable. Physicochemical profile analysis should be used for the identification of compounds that are suitable for therapeutic use. Parameters like molecular weight, lipophilicity, hydrogen bonding capability, rotatable bonds, polar surface area, and hydrophobicity can affect solubility, stability, permeability, and other properties. Such features are crucial for the evaluation of drug-likeness and pharmaceutical acceptability (Banerjee et al., 2018; Yang et al., 2019). ADMET and toxicity predictions can also be helpful when screening molecules.

There is an increasing emphasis on computational approaches in pharmaceutical research due to their high efficiency and applicability. Computer-assisted drug discovery and automated screening can be helpful in efficient evaluation and prioritization of candidate molecules by considering molecular interaction, drug-likeness, biochemical interaction, and other properties (Schneider, 2018). This technique can be especially useful when the goal of the researcher is the identification of drugs with favourable parameters.

Besides molecular interaction and pharmaceutical suitability, biochemical interaction is also worth considering when screening potential drugs. Compounds capable of interacting with molecular targets and showing promising activity may influence biological processes, affecting proteins, enzymes, receptors, and molecular pathways. This factor may contribute to therapeutic effects. The evaluation of biochemical interaction potential through the application of various computerized technologies can help identify such compounds.

As mentioned above, green chemistry and nanotechnology represent the promising fields of current pharmaceutical research. Traditionally, drug synthesis involves the application of hazardous chemicals, energy-intensive processes, and the production of toxic waste. Green chemistry focuses on the development of environmentally friendly production processes. Moreover, pharmaceutical companies have started recognizing the advantages of green chemistry in the manufacturing of various medications (Bryan et al., 2018). Nanotechnology and continuous manufacturing techniques can further improve the efficiency of such production (Rogers & Jensen, 2019).

Nanotechnology represents a promising area in pharmaceutical development since it allows enhancing the effectiveness of bioactive compounds. In many cases, novel drugs suffer from such problems as poor solubility, low bioavailability, instability, fast degradation, or insufficient target delivery. Nanocarriers can solve such problems since they allow improving solubility and stability and targeting compounds towards particular cells. Various types of nanoparticle-based medications are currently being studied or approved for use (Anselmo & Mitragotri, 2016; Bobo et al., 2016). Thus, the assessment of nanoformulation suitability can help identify suitable drugs for such delivery.

Although computational approaches are now widely used in drug screening, many such studies consider only one aspect of the compound's properties. For instance, researchers focus on interaction or drug-likeness. However, in this case, important factors related to pharmaceutical suitability, biochemistry, and other characteristics of drugs might be overlooked. On the other hand, molecules with strong interaction and poor drug-likeness or unsuitable physicochemical profiles cannot be considered prospective drugs. In addition, even drug-like compounds without the desired interaction potential cannot be considered effective. Thus, a comprehensive evaluation method is needed.

The present study will try to integrate computational screening based on various drug characteristics. The analysis will incorporate docking-based interaction analysis, physicochemical properties evaluation, drug-likeness, biochemical interactions, green chemistry suitability, nanoformulation potential, and therapeutic priority scoring. The study aims to identify bioactive compounds with strong interaction potential, favourable pharmaceutical properties, a suitable development process, and nanoformulation potential.

2. MATERIALS AND METHODS

2.1 Study Design

This paper is a computation-based analysis of new bioactive molecules for pharmaceutical applications. This analysis included a combined approach for evaluating the molecular interaction capabilities, physical chemical properties, druglikeness, green chemistry properties, suitability for nanotechnology, and therapeutic priority of the evaluated compounds. The analysis methodology used a combination of the molecular docking-based binding affinities analysis, together with biochemical and pharmaceutical analysis.

2.2 Selection and Preparation of Bioactive Compounds

The selection of bioactive molecules was performed on the basis of their relevance in terms of structure and pharmacological behavior. The molecules were described on the basis of important physicochemical descriptors, namely molecular weight, LogP, hydrogen bond donors, hydrogen bond acceptors, number of rotatable bonds, polar surface area, and hydrophobicity. These descriptors were chosen as they affect the solubility, permeability, flexibility, receptor binding affinity, and pharmaceutical relevance of the molecules.

Before the analysis, the molecules were reviewed for their accuracy, consistency, and feasibility. Inaccurate and inconsistent data were handled by replacing them with the median value based on their activity profile. Chemically unrealistic molecules, such as molecules having an invalid polar surface area, were also revised. The possibility of duplicate molecules was also avoided.

2.3 Molecular Target-Based Screening
The molecules were screened for their molecular interactions based on their interaction with protein targets of therapeutic significance. The binding affinity was used as an indicator of the expected strength of the interaction of the molecule with its target. Molecules with high binding affinity were considered more likely to interact with their targets, while those with low binding affinities had a lower likelihood of forming such interactions.
Molecules that showed favourable binding affinity and active nature were ranked as hits for docking analysis, while molecules with unfavourable binding affinity were ranked as low-priority hits.

2.4 Physicochemical and Drug-Likeness Evaluation
Physicochemical analysis was conducted to evaluate whether these compounds had desirable physical and chemical attributes for drug development purposes. The molecular weight parameter was utilized to determine molecule size. Lipophilicity and membrane permeability were estimated based on logP and hydrophobicity parameters. Both hydrogen donors and acceptors were important criteria for interaction between molecules and targets/solvents. Rotatable bonds were measured as an indicator of molecule flexibility. Polar surface area measurement helped to evaluate the absorption and permeability of these compounds.
The above physicochemical parameters helped evaluate drug likeness. Drug-like molecules can be categorized as either high, moderate, or low drug-likeness compounds. High drug likeness was regarded as desirable in terms of drug development. Moderate drug likeness indicated that certain properties need to be improved.

2.5 Active and Inactive Compound Evaluation
Classification was done on the basis of the status of biological activity that was expected for the compounds. For example, active compounds were assumed to have greater pharmacological significance, especially those exhibiting good binding affinity and desirable physicochemical characteristics. Inactive compounds were kept for comparative study to compare the properties of active and inactive compounds.
Comparison was made to check whether the active compounds had greater binding affinity, drug-like behavior, biochemical interactions, and medicinal importance compared to inactive compounds.
2.6 Biochemical Interaction Potential
The potential for biochemical interactions was estimated on the basis of the status of the activity of the compounds, their binding affinity, and the characteristics of the molecular interaction. If the compounds had an active status along with good binding affinity, then their potential for biochemical interaction was high. Moderately interactive compounds were considered to be moderately potent compounds.
Those with poor or no interaction were regarded as having low potential for biochemical interaction.

2.7 Green Chemistry Suitability Assessment
The suitability of the molecule for green chemistry was evaluated through molecular and pharmaceutical features that could be used to enhance drug development safely. The molecules were divided into three different categories according to their potential suitability for green chemistry applications.
These molecules were categorized according to their predicted suitability for green chemistry drug development. High-suitability molecules were found to be more suitable for the development of environmentally friendly drugs, while low-suitability molecules may need some modification.

2.8 Nanotechnology-Based Formulation Suitability
Suitability of the compounds for their formulation using nanotechnology was analysed, with consideration of factors such as molecular weight, lipophilicity, hydrophobicity, polar surface area, and drug-like properties to predict the possibility of the compounds being formulated.
Compounds that scored well on these parameters were deemed highly suited for nanoformulation, indicating that the use of nanocarrier technology to deliver these compounds may offer some advantages.

2.9 Therapeutic Priority Scoring
A priority score system was developed in order to prioritize drugs based on their therapeutic potential as a whole. This ranking process took into consideration factors such as binding efficiency, activity, drug-like nature, biochemical reaction potential, green chemistry nature, and nanoformulation compatibility.
It is safe to say that highly ranked drugs are considered the best for further study and analysis.

2.10 Statistical Analysis
The descriptive statistics were employed to describe the physicochemical and pharmaceutical characteristics. The frequency distribution was made on the basis of activity state, drug likeness, docking priority, green chemistry compatibility, nanoformulation compatibility, and biochemical interaction capacity. A comparative study was done between the active and inactive drugs. The correlation analysis was performed for the study of interrelationships between physicochemical features, binding energy, and therapeutic priority.

2.11 Methodological Reliability

The reliability of the results was guaranteed by preprocessing, correcting abnormal or chemically impossible data, classification standards, and the use of different evaluation factors. Nevertheless, the results should be viewed only as computational predictions. The proof of the therapeutic value of the compounds selected in the study must be obtained experimentally using biochemical analysis, cytotoxicity analysis, molecular dynamic modelling, nanoparticle preparation, and pharmacological tests.

3. RESULTS

3.1 Overview of Compound Screening

In all, 2,000 bioactive compounds were screened against 400 protein targets with therapeutic implications. Pre-processing resulted in the compound set containing 34 analytical parameters without any missing data, repeated entries, or negative values for polar surface area in compounds. This indicated that the compound sets were amenable to molecular interaction, physicochemical parameter evaluation, drug-likeness evaluation, green chemistry feasibility study, nanotechnology suitability test, biochemical interactions, and prioritization of therapeutic value. The summary of the screen and pre-processing process is listed in Table 1.

Table 1. Summary of compound screening and preprocessing

Parameter	Result
Total bioactive compounds evaluated	2,000
Therapeutically relevant protein targets	400
Total analytical variables	34
Missing values after preprocessing	0
Duplicate entries	0
Invalid negative polar surface area values after correction	0
Active compounds	608
Inactive compounds	1,392

3.2 Active and Inactive Compound Distribution

The compounds were sorted based on their biological activity as predicted. Out of all the compounds assessed, 608 were identified as active, constituting 30.4% of the total compounds, and 1,392 were identified as inactive, constituting 69.6% of the total number of compounds. The distribution of active and inactive compounds is presented in Figure 1 below. Based on these two categories, comparisons of the five parameters mentioned earlier were conducted.

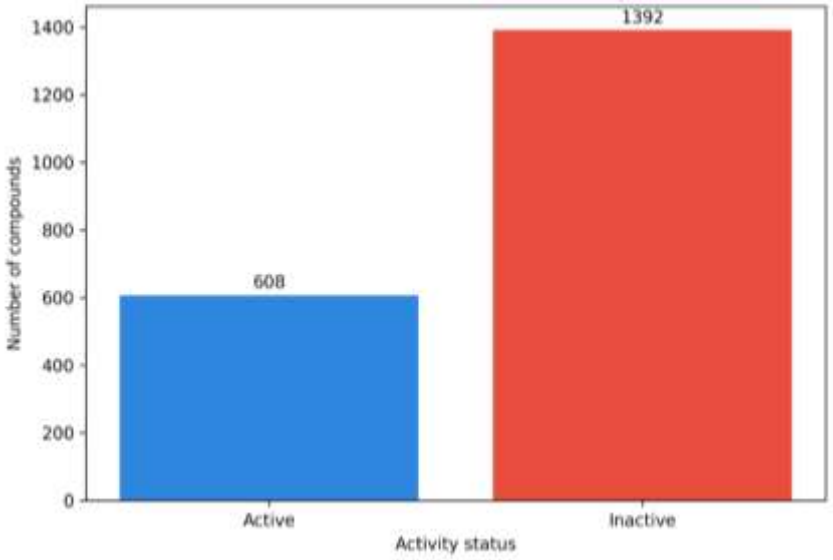

Figure 1. Distribution of active and inactive bioactive compounds

Figure 1 illustrates the classification of compounds into active and inactive groups, showing a higher proportion of inactive compounds compared with active compounds.

3.3 Physicochemical Profile of Bioactive Compounds

It was found that the physicochemical properties were highly variable for the selected chemicals. It was calculated that the average molecular weight of these chemicals was 456.77, while the range was between 50.31 and 994.05. It was noted that the average LogP was equal to 3.48, which reflected the moderately lipophilic nature of many compounds. It was observed that the average number of hydrogen donors and acceptors was equal to 1.96 and 5.12, respectively. On the other hand, the average number of rotatable bonds was 5.97, signifying the moderately flexible nature of molecules. The average polar surface area and hydrophobicity were found to be 80.10 and 0.65, respectively.

3.4 Drug-Likeness Assessment

The assessment of drug-likeness properties suggested that the majority of molecules had desirable properties for pharmaceutical applications. Overall, there were 1,049 molecules considered to have high drug-likeness, 945 molecules had moderate drug-likeness, while only 6 molecules had low drug-likeness. The distribution of drug-likeness values was illustrated by the diagram in Figure 2 and tabulated in Table 2.

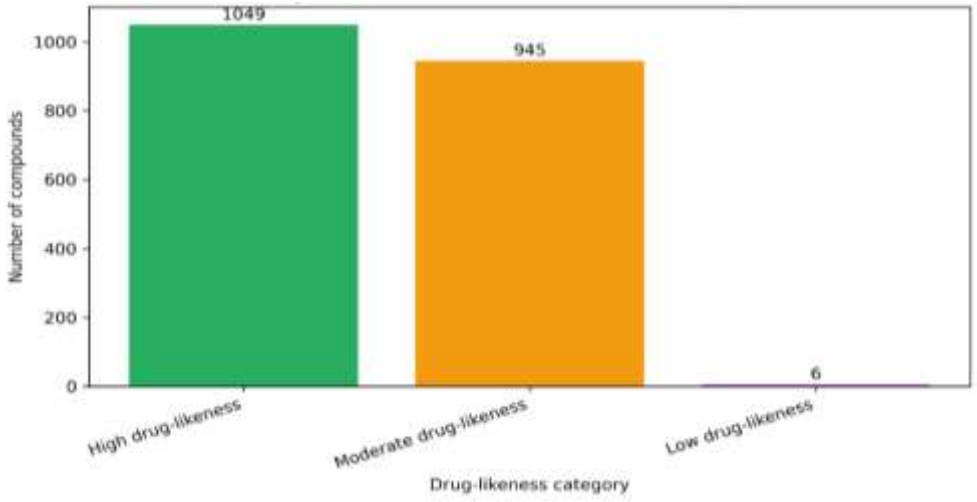

Figure 2. Drug-likeness classification of evaluated bioactive compounds

Figure 2 shows that high and moderate drug-likeness categories dominated the compound set, while low drug-likeness compounds represented only a small fraction.

3.5 Molecular Docking and Binding Affinity Results

The binding affinity test was carried out to examine the predicted strength of the interaction between the compound and target proteins. The average binding affinity was 6.53, and the values were distributed from 1.99 to 15.04. On the other hand, active molecules exhibited an average binding affinity of 7.82, while the same average for inactive molecules was found to be 5.97.

3.6 Docking Hit Classification

Depending on binding and activity, the chemicals were divided into docking priority categories. A total of 165 chemicals were found to be strong active docking hits, whereas 443 chemicals were found to be moderate active docking hits. The rest of the 1,392 chemicals were grouped under low-priority docking hits. The results of docking classification are presented in Table 2 below. Strong and moderate docking hits formed the active compound category.

3.7 Green Chemistry, Nanoformulation, and Biochemical Interaction Classification

According to the green chemistry suitability analysis, 1,828 compounds have high suitability, 164 compounds have moderate suitability, and 8 compounds have low suitability. According to the suitability analysis for nanofomulations, 1,841 compounds have high suitability, and 159 compounds have moderate suitability. According to biochemical interaction potential evaluation, 165 compounds have high interaction potential, 443 compounds have moderate interaction potential, and 1,392 compounds have low interaction potential. The results are depicted in Table 2 below.

Table 2. Classification distribution of evaluated compounds

Assessment	Category	Number of compounds	Percentage (%)
Drug-likeness	High drug-likeness	1,049	52.45
Drug-likeness	Moderate drug-likeness	945	47.25
Drug-likeness	Low drug-likeness	6	0.30
Docking hit classification	Lower-priority docking hit	1,392	69.60
Docking hit classification	Moderate active docking hit	443	22.15
Docking hit classification	Strong active docking hit	165	8.25

Green chemistry suitability	High green-chemistry prioritization suitability	1,828	91.40
Green chemistry suitability	Moderate green-chemistry prioritization suitability	164	8.20
Green chemistry suitability	Low green-chemistry prioritization suitability	8	0.40
Nanoformulation suitability	High nanoformulation suitability	1,841	92.05
Nanoformulation suitability	Moderate nanoformulation suitability	159	7.95
Biochemical interaction potential	Low biochemical interaction potential	1,392	69.60
Biochemical interaction potential	Moderate biochemical interaction potential	443	22.15
Biochemical interaction potential	High biochemical interaction potential	165	8.25

3.8 Active and Inactive Compound Comparison

A comparative analysis showed distinct differences between the active and inactive compounds. There was greater binding affinity for active compounds than inactive compounds, suggesting better ability to form interactions with targets. Also, there was a greater therapeutically important score for active compounds (73.12) than inactive compounds (43.35). Active compounds also exhibited a high degree of feasibility for nanoformulations. Thus, it can be concluded that active compounds were more effective in terms of both their pharmacological properties and biological behaviour than inactive compounds.

3.9 Therapeutic Priority Ranking

The process of prioritization of molecules was done through Therapeutic Priority scoring of the promising compounds using the integrated parameters. The average therapeutic priority score for all the compounds is 52.40, which varied from 24.40 to 93.43. The top 10 compounds according to their therapeutic priority scores are presented in Figure 3 & Table 3 below.

Table 3. Top 10 therapeutic candidate compounds

Rank	Compound ID	Protein ID	Binding affinity	Drug-likeness	Docking class	Green chemistry suitability	Nanoformulation suitability	Biochemical interaction potential	Therapeutic priority score
1	CID_01091	PID_418	13.37	High drug-likeness	Strong active docking hit	High suitability	High suitability	High potential	93.43
2	CID_01444	PID_376	13.40	High drug-likeness	Strong active docking hit	High suitability	High suitability	High potential	93.25
3	CID_00869	PID_421	15.04	Moderate drug-likeness	Strong active docking hit	Moderate suitability	High suitability	High potential	90.81
4	CID_01429	PID_305	13.75	Moderate drug-likeness	Strong active docking hit	High suitability	High suitability	High potential	90.73
5	CID_00018	PID_158	11.17	High drug-likeness	Strong active docking hit	High suitability	High suitability	High potential	86.74
6	CID_01124	PID_399	12.20	Moderate drug-likeness	Strong active docking hit	High suitability	High suitability	High potential	85.62
7	CID_00592	PID_209	10.82	High drug-likeness	Strong active docking hit	High suitability	High suitability	High potential	85.08
8	CID_00034	PID_179	13.28	Moderate drug-likeness	Strong active docking hit	Moderate suitability	High suitability	High potential	85.04

9	CID_01367	PID_440	12.19	Moderate drug-likeness	Strong active docking hit	High suitability	High suitability	High potential	84.67
10	CID_00692	PID_263	10.95	High drug-likeness	Strong active docking hit	High suitability	Moderate suitability	High potential	84.57

CID_01091 was the compound that scored the most based on its ability to interact with PID_418 and a therapeutic priority score of 93.43. The compound exhibited excellent drug-likeness, excellent active docking classification, excellent green chemistry compatibility, excellent nanoformulation compatibility, and excellent biochemical interaction capacity. Some other highly-ranked compounds included CID_01444, CID_00869, CID_01429, CID_00018, CID_01124, CID_00592, CID_00034, CID_01367, and CID_00692.

Figure 3 below represents the highly-ranked compounds based on therapeutic priority scoring

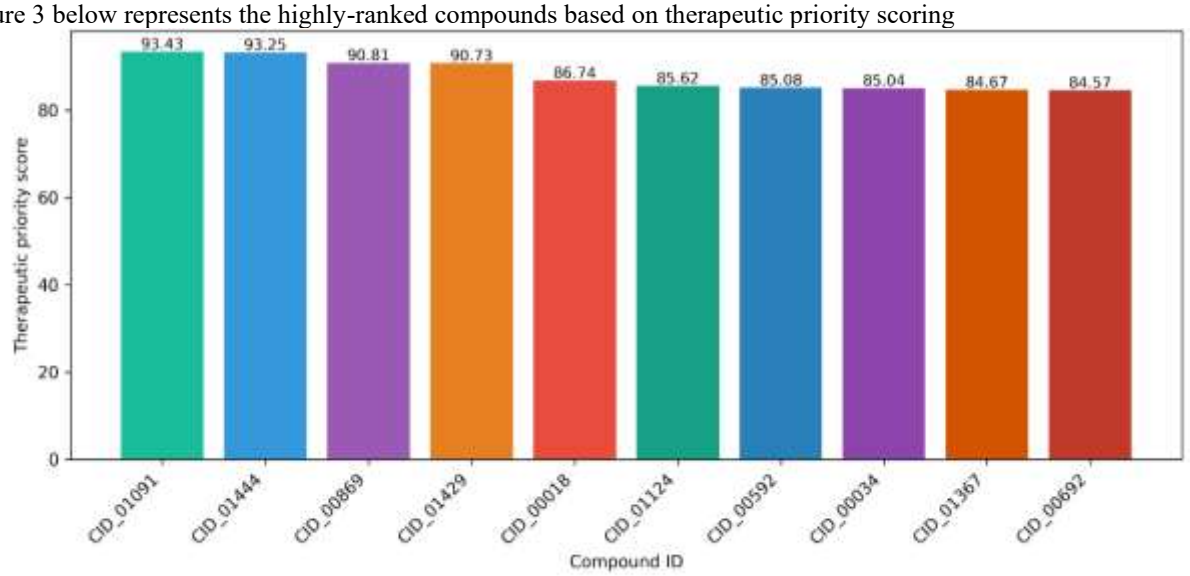

Figure 3. Top 10 compounds based on therapeutic priority score

In general, the findings indicated that there was a class of bioactive molecules with good molecular interaction prediction, pharmaceutical attributes, drug likeness, green chemical compatibility, nanoformulation capability, and biochemical interaction potential. It can be noted that the active molecules had more binding affinity and therapeutic priority as compared to inactive molecules. Based on their rankings, the top candidate bioactive molecules depicted in Table 3 and Figure 3 may thus be considered suitable for further experimental validation.

4. DISCUSSION

This study assessed 2,000 bioactive compounds against 400 therapeutic protein targets in an integrated computational approach. It is important to note that, according to Table 1, all compounds have been preprocessed and no missing data, duplicates, or invalid negative polar surface area values are present. This ensures that screening, physicochemical assessment, evaluation of drug-likeness, green chemistry compatibility, nanoformulation suitability, biochemical interactions, and therapeutic priority ranking will be conducted with respect to reliable compound information. Such computational methods are increasingly popular in early-stage drug discovery because they enable rapid screening, prioritization, and interpretation of compounds in preparation for experimental validation (Chen et al., 2018; Sadybekov & Katritch, 2023; Vamathevan et al., 2019).

Classification of the examined compounds as active and inactive enables meaningful therapeutic interpretation. According to Figure 1, 608 compounds were found to be active while 1,392 compounds were classified as inactive. Despite a larger proportion of inactive compounds, active compounds offer an opportunity to assess molecules with increased biological significance. This distinction is critical in early-stage computational screening, as it allows one to compare active and inactive compounds in terms of their potential therapeutic significance. Classification-based prioritization is the main principle of computational and machine learning-based drug discovery strategies (Chen et al., 2018; Jiménez-Luna et al., 2020; Vamathevan et al., 2019).

Physicochemical characteristics show that the studied compounds have a wide range of properties, and thus, the pharmaceutical properties of different molecules are involved. The average molecular weight, LogP, hydrogen bonding capability, rotatable bonds, polar surface area, and hydrophobicity indicate that many studied compounds possess features of pharmaceutical interest. The described parameters are important because they affect solubility, permeability, flexibility, ability to interact with targets, absorptivity, and bioavailability. Drug-likeness, pharmacokinetic, and ADMET analysis

are usually based on such parameters because they determine medicinal chemistry suitability of small molecules (Daina et al., 2017; Xiong et al., 2021). The average LogP indicates that the lipophilicity of many molecules is relatively high, which can be beneficial for membrane permeability and target interactions. At the same time, excessive lipophilicity can decrease solubility and increase toxicological danger; thus, moderately lipophilic compounds may be preferable. Hydrogen bond donors/acceptors and polar surface area are also important from the standpoint of interacting with targets. Results of drug-likeness screening show that most analyzed molecules are classified as showing high or moderate drug-likeness. A total of 1,049 compounds showed high drug-likeness, while 945 were classified as showing moderate drug-likeness. Only 6 out of 2,000 analyzed compounds showed low drug-likeness. This suggests that the majority of studied molecules are characterized by features related to pharmaceutical development. High drug-likeness compounds may possess optimal characteristics (size, lipophilicity, hydrogen bond capability, etc.). Moderate drug-like compounds could also be useful, although they may need to be optimized. The number of low drug-likeness compounds is very small, and only a few molecules are expected to face pharmaceutical problems. Results are consistent with current understanding of the importance of drug-likeness and ADMET screening for reducing risks associated with early drug development stages (Daina et al., 2017; Xiong et al., 2021).

Analysis of the binding affinities shows that active compounds possess significantly stronger binding affinities than inactive compounds. Binding affinity is the measure of the ability of a compound to bind to a target. Thus, a higher binding affinity of active molecules suggests that biologic activity is accompanied by increased target interaction. This means that binding affinity is an important factor to consider when screening for compounds. Molecular docking is a rapidly growing computational method for discovering drug candidates due to its ability to estimate ligand-target interactions and screen for promising molecules (Pinzi & Rastelli, 2019). Nevertheless, docking and scoring functions should be taken with caution because binding affinity is a predictive, although powerful factor. Experimental studies often show unexpected results (Meli et al., 2022).

Further evidence in favor of the above interpretation of binding affinity results can be found in Table 2, which presents the classification of docking hits. According to this table, there were 165 strong active docking hits and 443 moderate active docking hits. These two groups of molecules can be considered active as they demonstrate significant docking capabilities and thus deserve further investigation. Strong active docking hits seem to have a special significance as they have high binding affinity and belong to the active compound group. This means that they can be characterized by high target interaction potentials and are thus worth validating. Structure-based analysis is especially important because several compounds need to be tested against therapeutically-relevant targets simultaneously (Pinzi & Rastelli, 2019; Sadybekov & Katritch, 2023).

Biochemical interaction potential analysis confirms the interpretation of the previous results. According to Table 2, 165 compounds had a high biochemical interaction potential, while 443 compounds had a moderate interaction potential, and 1,392 compounds had a low interaction potential. Thus, the results of biochemical interaction potential analysis confirm the link between biological activity and binding affinity. Compounds with high biochemical interaction potential have a high target interaction potential and thus may affect protein functions, signalling activities, or molecular pathways associated with a disease. The obtained results should be considered with caution because of their nature as computational predictions, rather than experimental findings. Explaining and interpreting computational predictions can improve our understanding of screening results (Jiménez-Luna et al., 2020; Meli et al., 2022).

Analysis of green chemistry suitability shows that most compounds possess good green chemistry-related features. Table 2 shows that 1,828 compounds were characterized by a high green chemistry prioritization suitability index, 164 compounds had moderate suitability, and only 8 compounds had low suitability. Thus, it seems highly probable that most studied compounds will be able to participate in environmentally friendly, efficient pharmaceutical development. The inclusion of green chemistry suitability is important because modern drug development places ever-increasing importance on the concept of green chemistry. Green chemistry involves clean synthetic approaches, minimizing waste production, and promoting safe chemical procedures (Lasso et al., 2021; Stefanache et al., 2025; Tucker & Faul, 2016). The above results, however, should not be taken as evidence of green chemical synthesis as this evaluation was performed computationally.

Evaluation of nanoformulation suitability resulted in the following: there were 1,841 compounds with a high nanoformulation suitability index, 159 had a moderate index, and no compounds had low suitability indices. This means that most molecules may be considered candidates for nanotechnology-based drug delivery methods. Nanotechnologies can be applied to develop advanced carriers that can solve various issues, such as solubility, instability, low bioavailability, inability to release drugs controllably, etc. (Mitchell et al., 2021; Patra et al., 2018). It was additionally discovered that active compounds possessed higher nanoformulation suitability than inactive compounds. This result is interesting because although they may possess significant biological potential, they may require enhanced delivery to be effective.

The therapeutic priority index integrates the following parameters: binding affinity, activity status, drug-likeness, biochemical interaction potential, green chemistry suitability, and nanoformulation suitability. Figure 3 and Table 3 indicate that the top 10 compounds possessed high therapeutic priority indexes and thus are of significant interest. Compound CID_01091 ranked first with a therapeutic priority score of 93.43. The molecule interacted with protein target PID_418, had a high drug-likeness index, was characterized by strong active docking classification, had a high green chemistry suitability, a high nanoformulation suitability, and a high biochemical interaction potential. CID_01444 ranked second with a score of 93.25, while CID_00869 and CID_01429 had high docking activity and a promising therapeutic potential.

Top-ranked compounds are of interest due to the fact that they did not possess favourable characteristics in just one evaluation domain, but were strong in many. Thus, such molecules are likely to be better suited for validation than molecules with good docking activity or high biologic activity. Therefore, therapeutic priority screening provides a much more balanced way of selecting potential drug candidates. Results of this study prove that the combination of screening methods, namely, molecular docking, physicochemical evaluation, drug-likeness assessment, biochemical interaction potential evaluation, green chemistry suitability analysis, and nanoformulation suitability can be useful in identifying therapeutic candidates. Integrated computational approaches for drug discovery have been increasingly supported in recent years (Chen et al., 2018; Sadybekov & Katritch, 2023; Vamathevan et al., 2019).

Results obtained in this study are particularly useful for future therapeutic applications because the drug development process requires not just target interaction. A promising compound should also exhibit satisfactory physicochemical characteristics, drug-likeness, and formulation/synthesis possibilities. Thus, the identification of top-ranked compounds can be seen as an important basis for validating therapeutic candidates. Moreover, the research makes an additional contribution to the field of molecular and translational research because of its focus on compound-target interaction behavior and therapeutic prioritization at the molecular level. Identification of strong active docking hits and compounds characterized by a high biochemical interaction potential is of particular relevance for future work on target identification, molecular pathway analysis, and structure-based optimization of drug molecules.

The combination of approaches in terms of nanotechnology and green chemistry adds another dimension of translational potential to the study. Namely, high nanoformulation suitability molecules may be further used in developing nanocarriers, while molecules with high green chemistry suitability can be prioritized in developing drug candidates. Nanocarriers can improve the therapeutic properties of many active compounds, while green chemistry can ensure efficient and safe pharmaceutical development of promising molecules (Lasso et al., 2021; Mitchell et al., 2021; Patra et al., 2018; Stefanache et al., 2025; Tucker & Faul, 2016).

Limitations of this study are mainly associated with the computational nature of the results. First, the obtained results cannot be taken as evidence of experimentally proven therapeutic activity of molecules. Binding affinity indicates target interaction but does not confirm biological activity in vitro or in vivo. Second, green chemistry suitability and nanoformulation suitability should be treated as priorities while not being the final step in evaluating a potential molecule's properties. Third, protein targets need to be annotated to clarify their roles in disease pathways. The above limitations are typical for computational drug discovery as they emphasize the need for experimental verification of binding, drug-likeness, and ADMET properties (Daina et al., 2017; Meli et al., 2022; Pinzi & Rastelli, 2019; Xiong et al., 2021).

Future research should focus on validating the results obtained in this study. Molecular dynamics simulations should be performed to confirm the stability of complexes between drug molecules and targets. ADMET and toxicity analyses should be conducted to test the drug molecules' pharmacokinetic and safety profiles. Biochemical assays and cell-based studies are needed to establish biological activity. In addition, nanoformulations of promising compounds should be developed and characterized. Green synthesis strategies may be applied to promising molecules. Overall, the results of this study lay the groundwork for prioritizing promising therapeutic compounds.

5. CONCLUSION

In conclusion, this study demonstrated an integrated computational approach for the biochemical and pharmaceutical evaluation of novel bioactive compounds through molecular docking-related screening, physicochemical profiling, drug-likeness assessment, green chemistry suitability, nanoformulation potential, biochemical interaction analysis, and therapeutic priority scoring. The findings showed that several compounds possessed favourable molecular interaction profiles, acceptable drug-like characteristics, high green chemistry suitability, strong nanoformulation potential, and promising biochemical interaction capacity. Active compounds showed stronger binding affinity and higher therapeutic priority scores than inactive compounds, supporting their relevance as potential therapeutic candidates. Among the evaluated compounds, the top-ranked candidates, including CID_01091, CID_01444, CID_00869, and CID_01429, demonstrated strong combined performance across multiple screening parameters and may be considered for further validation. Overall, the study provides a useful computational foundation for prioritizing bioactive compounds with therapeutic potential; however, experimental confirmation through molecular dynamics simulation, biochemical assays, cytotoxicity testing, nanoparticle formulation, and pharmacological evaluation is necessary to validate their biological activity, safety, and translational applicability.

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