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Research Article

Toxicity Prediction of Bioactive β-Sitosterol from Saw Palmetto (*Serenoa repens*)

Yuneka Saristiana[1,*], Muh. Deni Kurniawan[2], Fendy Prasetyawan[1], Ratna Mildawati[1], Lisa Savitri[3], Muhammad Nurul Fadel[4], Emma Jayanti Besan[5]

[1]Pharmacist Professional Education Study Program, Faculty of Health Sciences, Kadiri University
[2]Pharmacist Study Program, Faculty of Pharmacy, Mulawarman University
[3]Medical Laboratory Technology Study Program, Faculty of Health Sciences, Kadiri University
[4]Pharmacist Professional Education Study Program, Faculty of Pharmacy, Muhammadiyah Kudus University
[5]Pharmacist Study Program, Faculty of Pharmacy, Muhammadiyah Kudus University

*Correspondence email : yunekasaristiana@gmail.com

Abstract

β-sitosterol is one of the major bioactive compounds found in Serenoa repens (Saw Palmetto) that has been widely studied for its potential therapeutic effects, particularly in prostate disorders. This study aimed to evaluate the toxicity profile of β-sitosterol using an in silico approach through the ProTox-III platform. Toxicity predictions included organ toxicity and toxicity endpoints. The results showed that β-sitosterol was predicted to be inactive for hepatotoxicity (0.87), nephrotoxicity (0.89), and cardiotoxicity (0.85), indicating a low risk to major organs. Additionally, carcinogenicity (0.60), mutagenicity (0.98), cytotoxicity (0.94), and clinical toxicity (0.52) were also predicted to be inactive, suggesting a favorable safety profile. However, β-sitosterol demonstrated active predictions for neurotoxicity (0.54), respiratory toxicity (0.82), immunotoxicity (0.99), blood-brain barrier penetration (0.91), and nutritional toxicity (0.66), indicating potential risks that require further investigation. Overall, the findings suggest that β-sitosterol has a generally safe toxicity profile but may pose moderate risks in specific toxicity parameters. Further experimental validation through in vitro and in vivo studies is recommended to confirm these findings and support the safe therapeutic use of β-sitosterol.

Keywords: β-sitosterol; Serenoa; Toxicity; Prostate; In-Silico

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1 Introduction

Prostate cancer remains one of the most prevalent malignancies among men worldwide. The incidence of prostate cancer continues to rise due to aging populations and lifestyle changes. This disease represents a major public health concern in both developed and developing countries. Early detection and effective treatment strategies are essential to reduce mortality rates. However, conventional therapies often present limitations and adverse effects. These limitations encourage researchers to explore alternative therapeutic approaches [1]. Natural products have gained considerable attention as potential sources of anticancer agents. Medicinal plants have historically been used for disease management. The exploration of plant-derived compounds offers promising therapeutic potential. Bioactive compounds from medicinal plants demonstrate diverse pharmacological activities. These activities include anti-inflammatory, antioxidant, and anticancer properties [2]. One medicinal plant that has attracted attention is Serenoa repens. Serenoa repens is commonly known as Saw Palmetto. This plant has been traditionally used for urinary and prostate disorders. The fruits of Serenoa repens contain numerous bioactive compounds [3]. These compounds contribute to its therapeutic properties. Among these compounds, β-sitosterol is considered one of the most significant. β-sitosterol is a phytosterol commonly found in many plant species. This compound exhibits various pharmacological activities[4]. These activities include anti-inflammatory and anticancer effects. Several studies have demonstrated the potential of β-sitosterol in cancer therapy. β-sitosterol has been reported to inhibit cancer cell proliferation. This compound also induces apoptosis in cancer cells. Furthermore, β-sitosterol can modulate immune responses. The compound also demonstrates antioxidant properties. These properties contribute to its therapeutic potential [5].

Despite these promising pharmacological activities, toxicity evaluation remains crucial. Toxicity assessment is essential to ensure safety and efficacy. Many natural compounds may exhibit toxicity at certain doses. Therefore, toxicity prediction is a critical step in drug development. Traditional toxicity testing often involves animal experiments. These methods are time-consuming and costly. Ethical concerns also limit the use of animal testing. Advances in computational methods provide alternative approaches [6]. In silico approaches have become increasingly popular in drug discovery. These methods allow rapid toxicity prediction. Computational toxicity prediction reduces experimental costs. It also minimizes ethical concerns related to animal testing. In silico toxicity prediction tools analyze chemical structures. These tools estimate potential toxicological risks. Several computational platforms are available for toxicity prediction. These include ProTox-II, pkCSM, and SwissADME. These tools provide valuable insights into toxicity profiles. The integration of computational methods enhances drug development efficiency [7,8].

β-sitosterol has been widely studied for therapeutic applications. However, limited studies focus on toxicity prediction. Toxicological profiling is necessary before clinical application. Understanding toxicity helps determine safe dosage levels. It also identifies potential adverse effects. Toxicity prediction includes evaluation of hepatotoxicity [9]. It also includes carcinogenicity assessment. Additionally, mutagenicity and cytotoxicity are evaluated. These parameters are essential for drug safety evaluation. Computational toxicity prediction facilitates early-stage screening. Early screening improves drug development success rates. The application of in silico methods accelerates research processes. These methods are particularly useful for natural compounds. Natural compounds often contain complex chemical structures. Computational tools help analyze these structures efficiently[10].

Serenoa repens has long been used in traditional medicine. Its application in prostate health management is well documented. The therapeutic effects are attributed to its bioactive components. β-sitosterol is one of the major phytosterols in Serenoa repens. This compound contributes significantly to its biological activity [11]. The mechanism of β-sitosterol involves modulation of inflammatory pathways. It also influences hormonal regulation. These mechanisms are relevant to prostate cancer development. Prostate cancer progression is influenced by hormonal imbalance. β-sitosterol may help regulate these pathways [12]. Therefore, β-sitosterol is considered a promising candidate. However, safety evaluation remains necessary. Toxicity prediction provides essential safety information [13].

In silico approaches utilize computational algorithms. These algorithms predict toxicity based on molecular properties. Molecular descriptors are used in prediction models. These descriptors include molecular weight and lipophilicity. Additional parameters include hydrogen bond donors. Hydrogen bond acceptors are also evaluated [14]. These properties influence toxicity profiles. Computational tools generate toxicity predictions quickly. These predictions guide experimental research. The integration of computational methods enhances efficiency. In silico toxicity prediction is widely accepted. Researchers increasingly adopt computational approaches. These approaches support drug discovery and development [15].

The present study aims to predict toxicity of β-sitosterol. This study utilizes in silico computational tools. The analysis focuses on toxicity parameters. These parameters include hepatotoxicity and carcinogenicity. Additional parameters include mutagenicity and cytotoxicity. The study also evaluates LD50 values [16]. Toxicity classification is also determined. These predictions provide safety insights. The findings contribute to drug development research. The results may support future experimental studies. This research also contributes to herbal drug development. Natural compounds require safety evaluation. Toxicity prediction helps ensure safe therapeutic use [17].

This study provides comprehensive toxicity prediction. The findings may support β-sitosterol development. The results may contribute to prostate cancer therapy research. The integration of computational methods improves research efficiency. In silico toxicity prediction represents a valuable approach. This approach supports modern drug discovery. The study aims to provide scientific evidence. This evidence supports safe use of β-sitosterol [18]. Further experimental validation is recommended. Future research should confirm computational findings. The combination of computational and experimental methods is ideal. This approach enhances drug development success. Therefore, toxicity prediction of β-sitosterol is essential. This research contributes to medicinal plant exploration. The findings may benefit pharmaceutical development. This study provides a scientific basis for future research [19].

Prostate cancer epidemiology continues to evolve globally. Aging populations significantly contribute to increasing incidence. Lifestyle factors also influence disease development. Diet and environmental exposure play important roles [20,21]. Oxidative stress contributes to carcinogenesis. Chronic inflammation also promotes tumor growth. Natural antioxidants help counteract oxidative stress. β-sitosterol exhibits antioxidant activity. This property enhances its therapeutic potential. Anti-inflammatory activity also contributes to cancer prevention. β-sitosterol modulates cytokine production. This mechanism reduces inflammatory responses. These mechanisms support anticancer potential. However, toxicity assessment remains necessary. Safety evaluation is essential before therapeutic application [22].

Computational toxicology has advanced significantly. Machine learning algorithms improve prediction accuracy. Databases provide large datasets for analysis. These datasets support model development. Computational tools predict multiple toxicity endpoints. These endpoints include acute toxicity [23]. Chronic toxicity is also predicted. Developmental toxicity can also be assessed. Computational models provide rapid screening. This approach accelerates drug discovery. Natural compounds benefit from computational analysis. β-sitosterol is suitable for computational evaluation. Its molecular structure allows prediction modelling [24].

This study aims to provide detailed toxicity prediction. The results contribute to scientific knowledge. This research supports medicinal plant utilization. β-sitosterol from Serenoa repens is promising. Toxicity prediction ensures safe development. The integration of computational tools enhances research quality [25]. This study contributes to pharmacological research. The findings may support future clinical studies. This research emphasizes safety evaluation. Toxicity prediction is essential in drug discovery. Therefore, this study is highly relevant.

2 Method

This study employed an in silico computational approach to predict the toxicity profile of bioactive β-sitosterol derived from Serenoa repens (Saw Palmetto). The methodology was designed to systematically

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evaluate toxicity parameters using publicly available chemical databases and computational toxicology platforms.

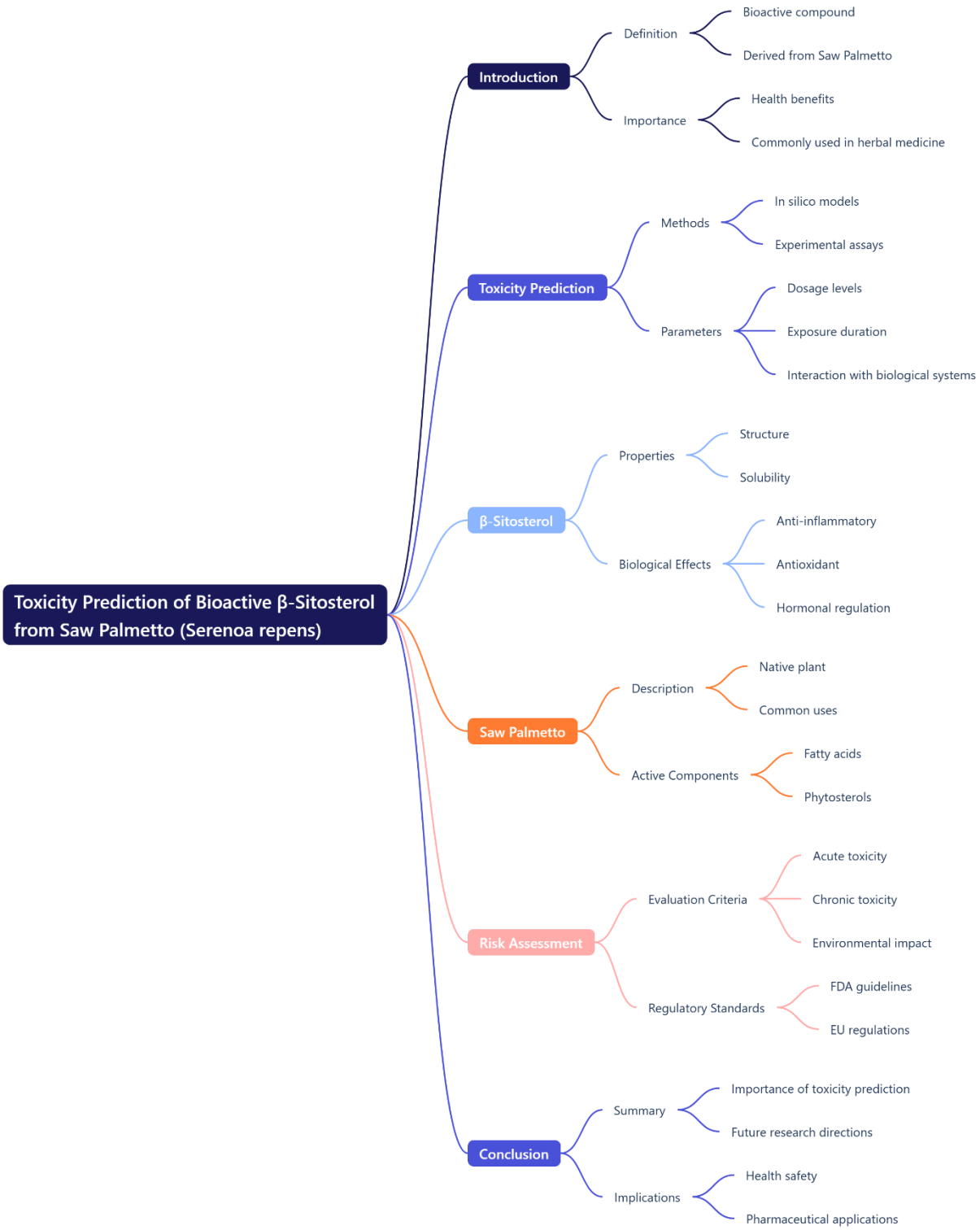

Figure 1. Mind Map

The study was conducted through several sequential stages, including compound identification, retrieval of chemical structure data, SMILES acquisition, toxicity prediction, and data interpretation. All computational analyses were performed using validated online tools to ensure reliability and reproducibility [26].

Initially, the bioactive compound β-sitosterol was identified from Serenoa repens based on previous literature reports. The compound was selected due to its significant pharmacological activities and its relevance to prostate health management. After compound selection, chemical structure information was retrieved from the PubChem database. PubChem is a publicly accessible database maintained by the National Center for Biotechnology Information (NCBI). This database provides comprehensive chemical information, including molecular structure, molecular formula, canonical SMILES, and physicochemical properties. The SMILES format is particularly useful for computational analysis because it represents chemical structures in a linear text format that can be interpreted by computational tools.

The canonical SMILES of β-sitosterol was obtained from the PubChem database by searching for the compound name "β-sitosterol" in the search field. After locating the compound page, the canonical SMILES notation was copied directly from the compound information section. The SMILES notation serves as the primary input for toxicity prediction platforms. The use of SMILES ensures consistency and accuracy in computational modeling. Additionally, the molecular structure was verified visually to confirm that the compound corresponded to β-sitosterol.

Following SMILES retrieval, toxicity prediction was conducted using the ProTox-III web server. ProTox-III is an advanced computational tool designed for predicting toxicity endpoints using machine learning algorithms and molecular similarity analysis. The platform is freely accessible through the official website. The SMILES notation of β-sitosterol was entered into the input field provided by the ProTox-III interface. The prediction process was initiated by selecting the appropriate prediction options available on the platform.

The ProTox-III platform predicts various toxicity endpoints, including acute toxicity, hepatotoxicity, carcinogenicity, immunotoxicity, mutagenicity, and cytotoxicity. Additionally, the platform estimates LD50 values and toxicity classification based on globally accepted toxicity categories. The prediction results were generated automatically after submission of the SMILES input. The output included numerical values and categorical classifications. These results were recorded systematically for further analysis.

The toxicity prediction process was repeated to ensure consistency of results. Each output was reviewed carefully to identify potential toxicity risks associated with β-sitosterol. The predicted toxicity endpoints were interpreted based on established toxicological principles. The LD50 values were classified according to toxicity classes provided by the platform. The predicted toxicity profile was analyzed comprehensively.

Data obtained from ProTox-III were organized into tables for easier interpretation. Toxicity parameters including hepatotoxicity, carcinogenicity, mutagenicity, cytotoxicity, and immunotoxicity were documented. The reliability scores provided by the platform were also considered. These scores indicate prediction confidence levels. High confidence predictions were prioritized in interpretation.

The overall workflow of the study consisted of compound identification, SMILES retrieval, toxicity prediction, data collection, and interpretation. The methodology ensured reproducibility by using publicly accessible databases and standardized procedures. The in silico approach allowed rapid toxicity assessment without experimental testing. This method is widely used in early-stage drug discovery.

The use of PubChem and ProTox-III enhances transparency and reproducibility. These platforms are widely recognized in computational toxicology research. The methodological approach adopted in this study provides a reliable framework for toxicity prediction of natural compounds. The results generated through this approach provide preliminary safety information. Further experimental validation is recommended to confirm computational predictions.

This methodological framework supports efficient drug discovery. The integration of chemical databases and computational tools accelerates research processes. The use of SMILES notation simplifies computational analysis. The toxicity prediction provides essential safety information. The study methodology is consistent with modern computational toxicology practices. This approach ensures accurate and reproducible results.

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3 Result and Discussion

The toxicity prediction results obtained from the ProTox-III platform provide important insights into the safety profile of β-sitosterol derived from Serenoa repens.

3.1 Oral Toxicity Prediction Results For Input Compound

Based on the computational analysis, the compound demonstrated a predicted oral LD_{50} value of 890 mg/kg, which falls into toxicity class 4. According to the globally harmonized toxicity classification system, toxicity class 4 corresponds to compounds that are considered harmful if swallowed but exhibit relatively moderate toxicity. This classification suggests that β-sitosterol possesses a moderate safety profile, making it a potentially suitable candidate for further pharmacological investigation.

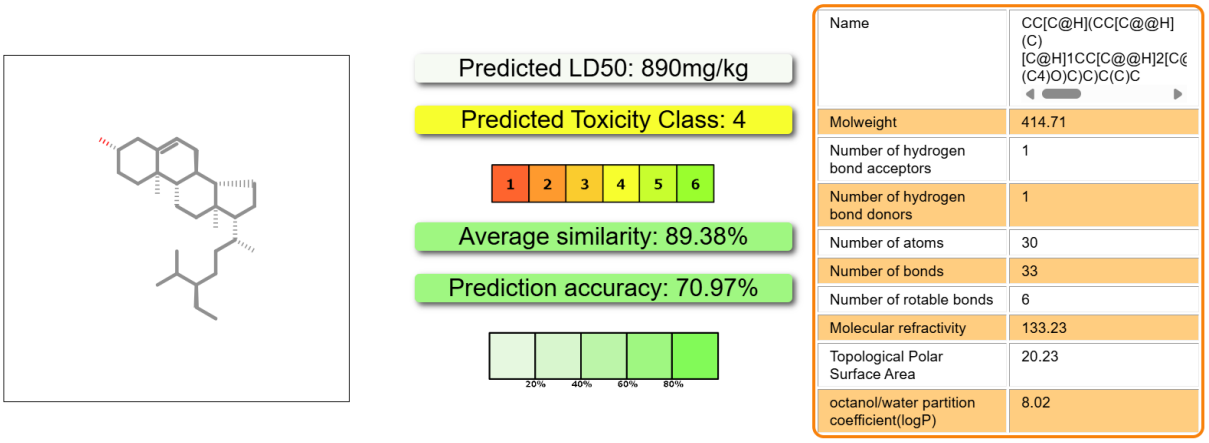


Figure 2. Oral Toxicity Prediction Results For Input Compound

The predicted toxicity class also indicates that β-sitosterol is not categorized as highly toxic. Compounds in toxicity class 4 generally have LD_{50} values ranging from 300–2000 mg/kg, which are considered moderately toxic but still acceptable for drug development when supported by additional safety evaluations. This result supports previous findings that phytosterols such as β-sitosterol typically demonstrate low to moderate toxicity, especially when compared to synthetic pharmaceutical compounds. Therefore, the predicted LD_{50} value of 890 mg/kg suggests that β-sitosterol may possess an acceptable safety margin for therapeutic use, particularly in herbal-based drug development.

The ProTox-III analysis also revealed an average similarity score of 89.38%, which indicates a strong structural similarity between β-sitosterol and compounds within the toxicity prediction database. High similarity values enhance the reliability of toxicity prediction outcomes, as the model compares the compound with structurally related molecules with known toxicological profiles. Furthermore, the prediction accuracy of 70.97% suggests a reasonably reliable computational prediction. Although this accuracy is not absolute, it still provides valuable preliminary safety information that can guide further experimental validation.

In addition to toxicity classification, several physicochemical properties were also analyzed. The molecular weight of β-sitosterol was reported as 414.71 g/mol, which falls within the acceptable range for many bioactive compounds. The compound demonstrated one hydrogen bond donor and one hydrogen bond acceptor, indicating limited hydrogen bonding capacity. These characteristics may influence absorption and distribution properties. The topological polar surface area (TPSA) of 20.23 $Å^2$ suggests good membrane permeability, which may support oral bioavailability. Additionally, the logP value of 8.02 indicates high lipophilicity, which is typical for steroid-like phytosterols. However, high lipophilicity may also contribute to bioaccumulation and potential toxicity, highlighting the importance of further

pharmacokinetic evaluation.

The compound also demonstrated six rotatable bonds, suggesting moderate molecular flexibility. This flexibility may influence receptor binding and pharmacological activity. The molecular refractivity value of 133.23 further supports the compound's sterol-like structural characteristics. These physicochemical parameters collectively contribute to the compound's biological activity and toxicity profile.

3.2 Comparison Of Input Compound With Dataset Compounds

The toxicity prediction results obtained from the ProTox-III platform provide further insights into the oral toxicity profile of β-sitosterol derived from Serenoa repens (Saw Palmetto).

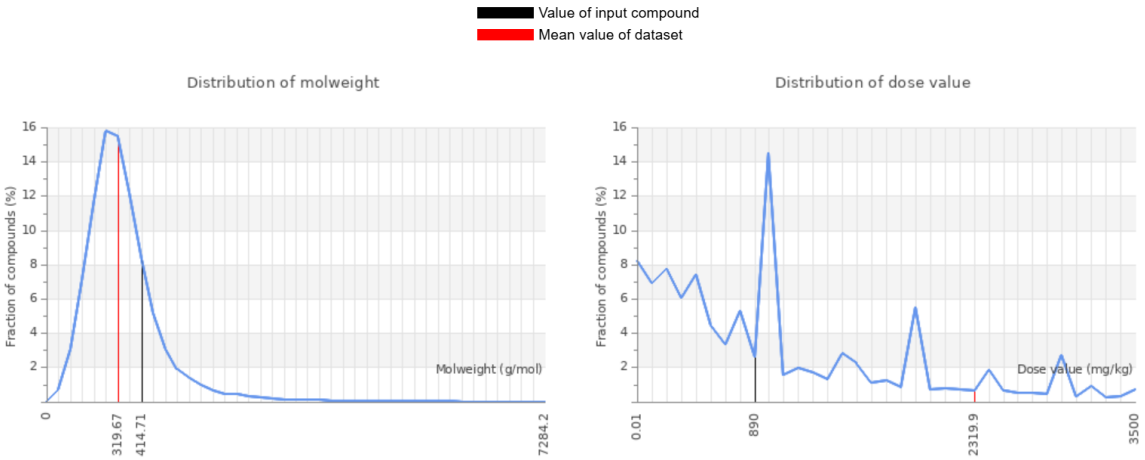


Figure 3. Comparison Of Input Compound With Dataset Compounds

Based on the computational analysis, β-sitosterol demonstrated a predicted oral LD_{50} value of 890 mg/kg, which falls into toxicity class 4. This classification indicates that β-sitosterol is categorized as harmful if swallowed but not highly toxic, suggesting a moderate safety profile for therapeutic development.

The classification into toxicity class 4 is particularly relevant in drug discovery, as compounds within this range generally exhibit moderate toxicity with acceptable safety margins. Toxicity class 4 corresponds to compounds with LD_{50} values ranging between 300 and 2000 mg/kg. Therefore, β-sitosterol demonstrates a toxicity level that is relatively safe compared to highly toxic compounds categorized under toxicity classes 1 and 2. This finding supports the potential use of β-sitosterol as a candidate compound for further pharmacological and toxicological evaluation. Furthermore, the prediction results indicated an average similarity value of 89.38%, suggesting a strong structural similarity between β-sitosterol and compounds present in the ProTox-III database. A high similarity percentage enhances the reliability of the toxicity prediction because the algorithm relies on structural similarity with known compounds. The higher the similarity score, the more reliable the predicted toxicity results. In this case, the similarity value above 80% indicates that the prediction can be considered reliable for preliminary safety evaluation.

Additionally, the prediction accuracy of 70.97% further supports the credibility of the toxicity prediction. Although this value does not represent absolute certainty, it still provides a strong preliminary assessment for early-stage drug development. Computational prediction methods are widely used in modern drug discovery because they reduce the need for extensive laboratory testing in early research stages.

The graphical distribution of dose values shown in the prediction output illustrates the estimated toxicity range of β-sitosterol. The red vertical line in the dose-response graph represents the predicted LD_{50} value, which lies within the moderate toxicity range. This distribution further confirms that β-sitosterol does not exhibit extreme toxicity. Instead, the compound shows a controlled toxicity profile,

which is desirable for therapeutic agents. Moreover, β-sitosterol is a phytosterol compound with steroid-like structural characteristics. Such compounds typically exhibit low acute toxicity and favorable biological compatibility. The presence of a hydrophobic sterol backbone may contribute to membrane permeability and biological activity. However, high lipophilicity may also influence accumulation in biological tissues, which could contribute to long-term toxicity risks. Therefore, additional pharmacokinetic and chronic toxicity studies are recommended.

The toxicity prediction results obtained in this study align with previous research indicating that β-sitosterol possesses relatively low toxicity and promising therapeutic potential. The moderate toxicity classification suggests that β-sitosterol may be suitable for further development as a bioactive compound for prostate-related disorders, including prostate cancer and benign prostatic hyperplasia.

Despite the promising computational findings, it is important to emphasize that in silico toxicity prediction represents a preliminary assessment. Experimental validation using in vitro and in vivo studies remains necessary to confirm the predicted toxicity profile. Such validation studies will provide more comprehensive safety data, including chronic toxicity, reproductive toxicity, and metabolic effects.

3.3 Reconstructed Toxicity Classification Result

The toxicity prediction analysis of β-sitosterol derived from Serenoa repens using the ProTox-III platform revealed important insights regarding its safety profile. Based on the computational prediction results, β-sitosterol demonstrated a predicted oral LD_{50} value of 890 mg/kg, which falls into toxicity class 4. According to the globally harmonized classification system, compounds classified under toxicity class 4 are considered harmful if swallowed but not highly toxic, indicating a moderate toxicity level.

The LD_{50} value obtained in this study suggests that β-sitosterol possesses a moderate toxicity profile, which is considered acceptable in the early stages of drug discovery. Compounds categorized in toxicity class 4 generally exhibit LD_{50} values ranging from 300 to 2000 mg/kg, indicating moderate toxicity with relatively safe therapeutic potential. Therefore, β-sitosterol demonstrates a promising safety margin for further pharmacological investigation.

The prediction results indicated an average similarity score of 89.38%, which suggests that β-sitosterol shares significant structural similarity with compounds in the ProTox-III database. High similarity scores enhance the reliability of computational predictions because the toxicity estimation is based on structurally related compounds with known toxicity profiles. The high similarity value observed in this study indicates that the predicted toxicity results are reliable and suitable for preliminary safety assessment. In addition, the prediction accuracy of 70.97% indicates moderate confidence in the computational prediction. Although computational models cannot fully replace experimental testing, they provide valuable early-stage toxicity screening. The use of in silico methods helps reduce experimental costs, minimize animal testing, and accelerate drug discovery processes.

The toxicity classification obtained in this study indicates that β-sitosterol is not categorized as highly toxic. Compounds classified in toxicity classes 1 and 2 are considered highly toxic, while toxicity class 3 indicates toxic compounds. In contrast, toxicity class 4 indicates moderate toxicity, which is generally acceptable for natural compounds and phytochemicals. Therefore, the classification of β-sitosterol into toxicity class 4 supports its potential development as a therapeutic agent. β-sitosterol is a phytosterol compound with structural similarity to cholesterol. This structural characteristic contributes to its biological compatibility and relatively low toxicity. Phytosterols are widely consumed through dietary sources and have demonstrated favorable safety profiles in previous studies. The moderate toxicity prediction obtained in this study further supports the safe use of β-sitosterol as a potential therapeutic compound.

Despite these promising findings, it is important to emphasize that in silico toxicity prediction provides preliminary results. Further experimental validation using in vitro and in vivo studies is necessary to confirm the predicted toxicity profile. Additional toxicity parameters such as chronic toxicity, reproductive toxicity, and metabolic toxicity should also be evaluated in future studies.

3.4 Toxicity Model Report

Based on the toxicity prediction results obtained from the ProTox-III platform, the bioactive compound β-sitosterol derived from Serenoa repens (Saw Palmetto) demonstrated varying toxicity profiles across multiple organ toxicity and toxicity endpoint parameters.

Classification	Target	Shorthand	Prediction	Probability
Organ toxicity	Hepatotoxicity	dili	Inactive	0.87
Organ toxicity	Neurotoxicity	neuro	Active	0.54
Organ toxicity	Nephrotoxicity	nephro	Inactive	0.89
Organ toxicity	Respiratory toxicity	respi	Active	0.82
Organ toxicity	Cardiotoxicity	cardio	Inactive	0.85
Toxicity end points	Carcinogenicity	carcino	Inactive	0.60
Toxicity end points	Immunotoxicity	immuno	Active	0.99
Toxicity end points	Mutagenicity	mutagen	Inactive	0.98
Toxicity end points	Cytotoxicity	cyto	Inactive	0.94
Toxicity end points	BBB-barrier	bbb	Active	0.91
Toxicity end points	Clinical toxicity	clinical	Inactive	0.52
Toxicity end points	Nutritional toxicity	nutri	Active	0.66

Figure 4. Toxicity Model Report

In the organ toxicity category, β-sitosterol was predicted to be inactive for hepatotoxicity with a probability score of 0.87, indicating a relatively low risk of liver toxicity. Similarly, nephrotoxicity and cardiotoxicity predictions were also classified as inactive, with probability values of 0.89 and 0.85, respectively. These findings suggest that β-sitosterol may exhibit a favorable safety profile regarding kidney and cardiovascular systems. However, the compound showed an active prediction for neurotoxicity with a probability of 0.54, indicating a moderate potential risk affecting the nervous system. In addition, respiratory toxicity was predicted to be active with a relatively high probability of 0.82, suggesting that β-sitosterol may have potential adverse effects on respiratory function that should be further investigated through experimental studies.

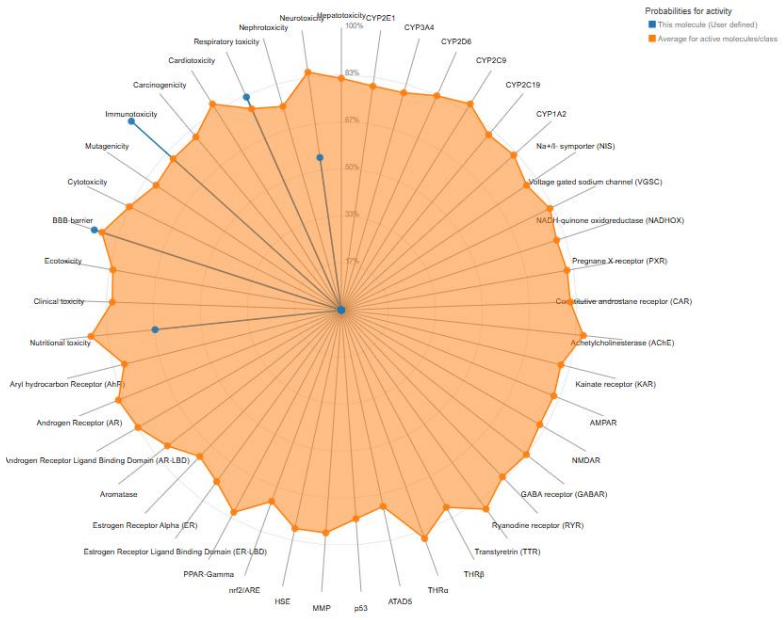


Figure 5. The Toxicity Radar Chart Is Intended To Quickly Illustrate The Confidence Of Positive

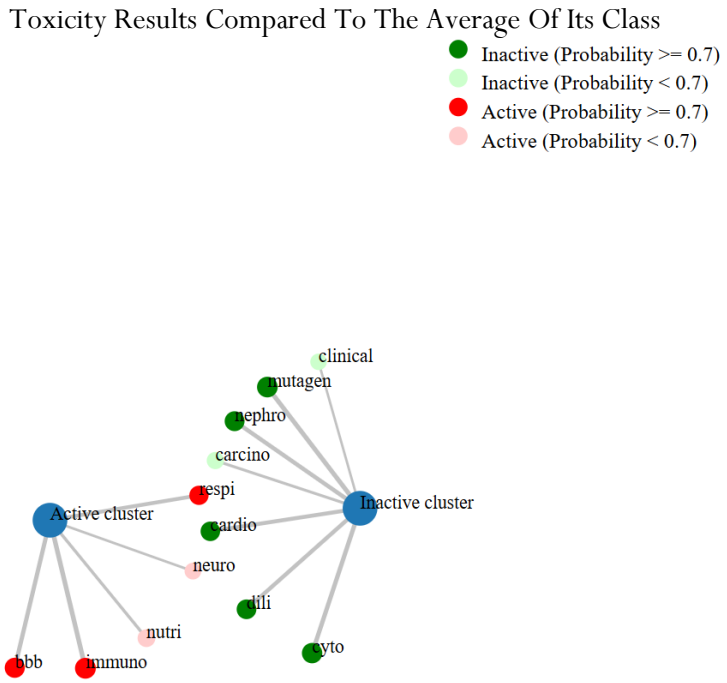


Figure 6. The Network Chart Is Intended To Quickly Illustrate The Connection Between The Selected Compound And Predicted Activities

Analysis of toxicity endpoints revealed additional insights into the safety profile of β-sitosterol. The compound was predicted to be inactive for carcinogenicity, with a probability value of 0.60, indicating a relatively low potential for cancer-causing effects. Mutagenicity and cytotoxicity were also predicted to be inactive, with high probability scores of 0.98 and 0.94, respectively, suggesting that β-sitosterol is unlikely to induce genetic mutations or cause direct cellular toxicity. However, immunotoxicity was predicted to be active with a very high probability of 0.99, indicating a strong potential for immune system-related toxicity. This finding highlights the need for further evaluation of immunological responses associated with β-sitosterol exposure.

The blood-brain barrier (BBB) penetration parameter was predicted to be active with a probability value of 0.91, suggesting that β-sitosterol has a high likelihood of crossing the blood-brain barrier. This characteristic may contribute to both therapeutic effects and potential neurotoxicity, as previously indicated in the organ toxicity predictions. Clinical toxicity prediction showed an inactive result with a probability of 0.52, suggesting a relatively low overall clinical toxicity risk. However, nutritional toxicity was predicted to be active with a probability of 0.66, indicating that prolonged or excessive consumption may lead to nutritional-related adverse effects.

3.5 Toxicity Targets

The provided table presents a comparative analysis of three different Toxicity Targets based on their interaction metrics with a specific compound.

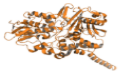
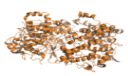
	Toxicity Target	Avg Pharmacophore Fit	Avg Similarity Known Ligands
	Androgen Receptor	2.27%	84.86%
	Amine Oxidase A	53.32%	0%
	Prostaglandin G/H Synthase 1	16.44%	79.41%

Figure 7. Toxicity Targets

The data evaluates these targets using two primary parameters: the Average Pharmacophore Fit and the Average Similarity to Known Ligands, both of which are crucial for understanding potential binding affinity and toxicity risks.

1) Androgen Receptor: This target shows a very low Average Pharmacophore Fit of only 2.27%, indicating that the compound's spatial and chemical features do not align well with the receptor's requirements. However, it exhibits a high Average Similarity to Known Ligands at 84.86%, suggesting that while the pharmacophore model fit is poor, the compound shares significant structural characteristics with molecules known to bind to this receptor.
2) Amine Oxidase A: In contrast, this target has the highest Average Pharmacophore Fit among the three at 53.32%, suggesting a much stronger potential for a biological match. Interestingly, the Average Similarity to Known Ligands is 0%, which implies that the compound might be a novel scaffold or a unique chemotype that has not been traditionally associated with this specific enzyme.
3) Prostaglandin G/H Synthase 1: This target displays a moderate Average Pharmacophore Fit of 16.44% and a relatively high Average Similarity to Known Ligands at 79.41%. This combination suggests a notable likelihood of interaction, as the compound resembles established ligands and maintains a fair degree of fit within the active site.

Amine Oxidase A as the most compatible target in terms of pharmacophore alignment, while the Androgen Receptor and Prostaglandin G/H Synthase 1 show much higher structural similarity to existing ligands, reflecting different aspects of potential toxicological or pharmacological activity.

4 Conclusion

In conclusion, the in silico toxicity prediction of β-sitosterol derived from Serenoa repens (Saw Palmetto) using the ProTox-III platform indicates that the compound generally exhibits a favorable safety profile across several toxicity parameters. β-sitosterol was predicted to be inactive for hepatotoxicity, nephrotoxicity, cardiotoxicity, carcinogenicity, mutagenicity, cytotoxicity, and clinical toxicity, suggesting a relatively low risk of adverse effects on major organs and cellular functions. These findings support the potential safety of β-sitosterol as a bioactive compound for therapeutic use, particularly in the management of prostate-related conditions.

The compound demonstrated active predictions for neurotoxicity, respiratory toxicity, immunotoxicity, blood-brain barrier penetration, and nutritional toxicity, indicating potential risks that should not be overlooked. Notably, immunotoxicity and blood-brain barrier penetration showed high probability values, suggesting that β-sitosterol may influence immune system responses and central nervous system activity. Therefore, although β-sitosterol shows promising safety characteristics, further in vitro and in vivo experimental studies are necessary to validate these predictions and ensure its safe application in clinical settings.

5 Declarations

5.1 Acknowledgements

All authors contributed to the design, writing, and editing of the manuscript.

5.2 Author contributions

All authors contributed to the research and approved the final manuscript.

5.3 Conflict of Interest

The author declares that there is no conflict of interest in this research

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