INFORMATICS JOURNALS

Research Article

Journal of Natural Remedies
DOI: 10.18311/jnr/2026/51442

eISSN: 2320-3358 | Vol 26(6), 2026 | pp. 1631-1645

From Plant to Target: Multimodal Evaluation of *Boerhavia diffusa*-mediated Antioxidant and Anti-inflammatory Effects against SIRT1 using Molecular Docking Study

Chalini Vijayakumar[1], Ayyalu Jamuna Rani[2] and Saramma Mini Jacob[1*]

[1]Department of Research and Development, Bharath Institute of Higher Education and Research, Sree Balaji Medical College and Hospital, Chennai - 600044, Tamil Nadu, India; saramini@yahoo.com

[2]Department of Biochemistry, Bharath Institute of Higher Education and Research, Sree Balaji Medical College and Hospital, Chennai - 600044, Tamil Nadu, India

Abstract

Background: An imbalance in redox homeostasis, along with sustained low-grade inflammation, is the two biological mechanisms that are gaining prominence as major contributors to the cause of chronic diseases. Current synthetic therapies often have adverse reactions, prompting a shift toward natural products with multi-target therapeutic potential. *Boerhavia diffusa* L. is a traditionally used medicinal plant that possesses antioxidant and anti-inflammatory potential and may have cardioprotective properties. The enzyme Sirtuin1 (SIRT1), which requires NAD^+ for its deacetylase activity, is recognised for its regulatory influence on inflammation, oxidative damage, and cellular ageing, making it a promising therapeutic target. **Aim:** This research analysed the antioxidant and inflammation-modulating potential and plant metabolites of *B. diffusa* by GC-MS and molecular interactions between the phytocompounds and SIRT1 by molecular docking. **Methods:** The ethanolic extract of *B. diffusa* leaves was screened for antioxidant activity via DPPH and ABTS radical scavenging assays, and anti-inflammatory potential using HRBC membrane stabilisation assay. Phytochemical compounds were assessed using GC-MS. *In silico* docking analysis was conducted using the AutoDock tool. **Result:** *B. diffusa* exhibited significant radical scavenging potential with IC50 values of DPPH 486.85 µg/mL (DPPH) and 470.59 µg/mL (ABTS) and strong membrane stabilising (HRBC) action with 82% inhibition. GC-MS showed 21 phytocompounds that included neophytadiene and phytol. The *in silico* study revealed that neophytadiene and phytol exhibited the highest binding potential towards SIRT1 compared to resveratrol, a known SIRT1 activator. All compounds exhibited favourable results in the ADMET profile with good oral bioavailability combined with extensive intestinal absorption, yet non-hepatotoxic with low mutagenicity. **Conclusion:** The ethanolic extract of *Boerhavia diffusa* leaves revealed strong ROS-quenching and inflammation-modulating effects, reducing oxidative damage and slow, long-term inflammation. The phytocompounds of *B. diffusa* could be potential candidates for SIRT1-targeted therapy with multiple therapeutic effects, including cardioprotection.

Major Findings: The phytocompounds of *B. diffusa* leaves are capable of reducing oxidative stress and inflammation. Neophytadiene and phytol exhibited higher binding affinity to SIRT1, indicating their role as natural SIRT1-targeted agents with therapeutic benefits, such as cardioprotection.

Keywords: *Boerhavia diffusa*, *In Silico* Study, Neophytadiene, Phytol, Sirtuin

(Article Chronicle: Article Received on: 10.09.2025; Revised on: 19.05.2026; Accepted on: 26.05.2026)

1. Introduction

An imbalance in redox homeostasis, along with sustained low-grade inflammation, is a two overlapping biological mechanisms that are gaining prominence as major contributors to the global burden of Non-Communicable Diseases (NCDs), such as type 2 diabetes, Cardiovascular Diseases (CVD),

*Author for correspondence

neurodegenerative diseases, chronic kidney diseases, cancer, and ageing[1]. CVDs proved responsible for approximately 18 million fatalities throughout the world during 2019, and accounted for approximately 33% of all deaths. Additionally, predictions show that by 2030, more than 23 million people will lose their lives to CVD[2]. NCDs accounted for 63% of total deaths among the Indian population in 2016, while CVDs contributed to 27% of these NCD-related deaths[3]. Oxidative stress is the excess output of Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS) and an overload of the antioxidant defence mechanisms in the cell, resulting in the buildup of damage to key biomolecules- DNA, proteins, lipids- and alteration of cellular homeostasis[4,5]. ROS are typical byproducts of mitochondrial metabolism and are required for signalling and immunological defence, but an excess causes oxidative damage, resulting in mutation, cellular malfunction, and disease progression like CVDs, carcinogenesis, and neurodegenerative diseases. Therefore, there is a need for holistic, multi-targeted approaches that address both oxidative stress and inflammation. Plant-derived phytochemicals have emerged as attractive candidates for modulating multiple redox and inflammatory pathways via synergistic interactions.

The enzyme Sirtuin1 (SIRT1), which requires NAD^+ for its deacetylase activity, plays an evolutionary part in cellular stress resistance, metabolism, and longevity; thus making new molecular targets in dual-pathway (oxidative stress and inflammation) regulations. Of the seven mammalian sirtuins (SIRT1-SIRT7), SIRT1 stands out as a master regulator of redox and inflammatory homeostasis. SIRT1, found in the nucleus and cytoplasm, deacetylates important transcription factors such Peroxisome proliferator-activated receptor-gamma coactivator (PGC)-1α, Forkhead box O (FOXOs), p53, and Nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB)[6-8]. SIRT1 activation has been found to reduce ROS production, increase antioxidant enzyme expression, and lessen the release of pro-inflammatory cytokines in the regulation of metabolic health. Thus, SIRT1 is a prospective therapeutic target for the oxidative-inflammatory cycle. As a result, natural substances capable of upregulating or activating SIRT1 are being extensively studied for their potential in preventing and treating chronic illnesses[9].

Boerhavia diffusa L. (family: *Nyctaginaceae*), also referred to as *Punarnava* or Red Spiderling, has become a viable contender in the search for natural substances that might target inflammation and oxidative stress via pathways including SIRT1 activation. This perennial herb is abundantly found in tropical and subtropical regions of Africa, the Americas, India, and other Southeast Asian countries. It has been used extensively in traditional medicine, *Ayurveda*, and *Unani*. *B. diffusa* was traditionally utilised in Ayurvedic preparations for its hepatoprotective, diuretic, and anti-inflammatory effects. It is also reported to ameliorate liver, renal, and cardiovascular disorders, conditions often driven by oxidative stress and inflammation[10-12]. Recent studies have confirmed its antioxidant, anti-inflammatory, anticancer, and antifibrinolytic activities, attributed to bioactive constituents including rotenoids, flavonoids, xanthones, and ecdysteroids[13]. These compounds are known to scavenge ROS, enhance antioxidant enzymes, and inhibit NF-κB activation. However, most research has focused on root extracts, while the leaves, rich in polyphenols, remain underexplored.

In this research, we appraised the antioxidant and anti-inflammatory potential of the ethanol fraction of *B. diffusa* leaves. Furthermore, we employed a computational docking study to assess the binding affinity and stability of its major phytoconstituents targeting the SIRT1 protein. By integrating phytochemical analysis with *in silico* target prediction, this study aims to elucidate the mechanistic basis of *B. diffusa's* bioactivity, with a specific focus on its potential to activate SIRT1 and thereby disrupt the oxidative stress-inflammation axis.

2 Experimental Methodology

2.1 Botanical Identification and Preparation of Extract

Boerhavia diffusa plant leaves were collected near Tambaram, Chennai, Tamil Nadu, India, identified and authenticated at Siddha Central Research Institute, Arumbakkam, with a voucher specimen reference no. B23042501D, allotted and preserved for future reference. The *B. diffusa* leaves underwent a thorough wash followed by shade drying and coarsely powdering before performing ethanol cold maceration extraction, and were stored for further analysis.

2.2 Antioxidant Assays

2.2.1 DPPH Radical Scavenging Assay

According to Trease *et al.*,[14] the free radical neutralising effect of the *B. diffusa* ethanol fraction was assessed utilising the DPPH (1, 1-diphenyl-2-picrylhydrazyl). Extracts at concentrations ranging from 200 to 1000 µg/mL were diluted in methanol. For each dilution, 100 µL of the sample was combined with 900 µL of a freshly made DPPH solution (0.1 mM in methanol). The reaction mixture was vortexed and maintained at ambient temperature in the dark to allow maximum interaction (30 min). The decrease of DPPH radical was measured at 517nm with an UV-Vis spectrophotometer. Ascorbic acid was used as the reference standard, and the negative control was a blank with DPPH solution. The percentage of inhibition was estimated using the formula:

$$\text{Scavenging Activity (\%)} = (Ao\text{-}As)/Ao \times 100$$

A_0 and A_s were the control and the sample absorbance, respectively.

2.2.2 ABTS Assay

The Endris *et al.*[15] method was used to evaluate the $ABTS^+$ radical cation scavenging activity. An ABTS stock (7 mM) was combined with potassium persulfate (2.45 mM v/v) and left to incubate at room temperature (12-16 h). The solution was diluted in ethanol, resulting in an absorbance of 0.70 ± 0.02 at 734 nm. In the experiment, 200 µL of extract (200-1000 µg/mL) was combined with 1.8 mL of diluted ABTS solution. The reaction mixture was incubated in the dark (20 min), and the absorbance was measured at 734 nm. The standard used was ascorbic acid, and the results were described in mg TE/g. The % inhibition was determined as follows:

$$\text{Inhibition (\%)} = (Ab\text{-}At)/Ab \times 100$$

Ab and At are the absorbance of the blank and the test sample, respectively.

2.3 HRBC Membrane Stabilisation Assay

The anti-inflammatory effects of an ethanolic extract of *B. diffusa* were assessed using the Human Red Blood Cell (HRBC) membrane stabilisation assay by Karrat *et al.*[16]. Healthy volunteers' blood was blended with an equal volume of sterilised Alsever's solution, centrifuged at 3000 rpm, washed with isotonic saline solution, and resuspended as a 10% v/v suspension. The reaction mixture was composed of phosphate buffer (1 mL), hyposaline (2 mL), HRBC suspension (0.5 mL), and plant extract (0.5 mL) at varying concentrations (50-1000 µg/ml). The standard diclofenac tablet was used as the positive control. The reaction mixtures were left to incubate at 37°C for 30 min and centrifuged at 3000 rpm. The supernatant collected was measured at 560 nm by a spectrophotometer.

2.4 Gas Chromatography-Mass Spectrometric Characterisation

The volatile phytoconstituents in the *B. diffusa* crude extract were examined using GC-MS at the Indian Institute of Technology, Madras (IIT-M). The GC-MS analysis utilised an HP-5MS column with 30 m x 250 µm x 0.25 µm dimensions on an Agilent 5977 instrument for which the first oven temperature reached 75°C and was maintained for 0.5 min. From there, it was raised by 5°C for 3 min to reach 180°C and then by 5°C for 5 min to achieve 350°C. A carrier gas made using highly pure Helium (He) operated through split mode and maintained at a 15:1 split ratio with 18 ml/min split flow rate and 11.367 psi pressure setting. EI 70eV served as the ionisation voltage during the analysis, and used m/z 50-600 amu scan range. The testing sample amount was set at 1µl during a total analysis duration of 53.5 min. The volatile compounds received identification through mass spectral and retention time analysis against the National Institute of Standards and Technology (NIST) - MS library database.

2.5 Computational Docking Study

2.5.1 Ligand Optimisation and Preparation

The ligands were compounds obtained from the ethanol extract of *B. diffusa* leaves by GC-MS analysis. Data like molecular weight, molecular formula, PubChem ID, 3D, and canonical SMILES were procured from the PubChem database. Drug-likeness score and pharmacokinetic and toxicological profile of the ligands were retrieved from the Swiss ADME tool using SMILES.

2.5.2 Protein Preparation

Homo sapiens SIRT1 protein data (PDB ID: 4I5I) was obtained from the RCSB Protein Data Bank in a.PDB file format. Preparation of the SIRT1 protein structure involved removing water molecules and adding hydrogen molecules and more to ensure effective ligand binding.

2.5.3 Molecular Docking and Interactions Visualisation

The computational evaluation of binding interactions between the SIRT1 protein and *B. diffusa* ethanol extract ligands was accomplished with the help of AutoDock software 4.2. Biovia Discovery Studio 3.1 provided visualisation of interactions between ligands and protein that included hydrogen bonds, van der Waals interactions, and hydrophobic forces according to the Dassault Systèmes design principles. This visualisation tool provided 2D and 3D interaction images of ligands and proteins.

2.5.4 ADME Analysis and Drug Likeness Prediction

The ADMET properties of chosen ligands that were extracted from *B. diffusa* ethanol solution underwent analysis. The software platform pkCSM evaluated (Absorption, Distribution, Metabolism, Excretion, and Toxicity) characteristics. pkCSM pharmacokinetics tool.

3. Results and Discussion

Nature provides plants with phytochemical compounds that affect human health in ways that can be either beneficial or harmful[17]. The biological action potential of plants seems to originate from their secondary metabolites. In this study, the ethanol extract of *B. diffusa* leaves showed potential antioxidant and anti-inflammatory potential by a combination of *in vitro* tests, phytochemical screening, and computational molecular docking.

3.1 Radical Neutralisation Assay (*In Vitro*)

3.1.1 Radical Quenching Efficiency by DPPH Assay

The ethanolic leaf extract of *B. diffusa* was evaluated for its antioxidant potential using the DPPH radical neutralisation assay. The extracts exhibited a clear concentration-dependent enhancement in radical scavenging, with inhibition ranging from 30.61% to 69.39% across 200-1000 µg/mL. In comparison, the standard showed inhibition of 42.86 to 87.76% across the same concentration range (Figure 1). The half-maximal inhibitory concentration (IC_{50}) of the plant extract was 486.85 µg/mL, and that of the standard drug was 262.67 µg/mL. These results reveal that *B. diffusa* leaf extract exhibited good radical neutralising potential, indicating its possible application as a natural antioxidant for medicinal and nutraceutical uses. A previous report by Nayak *et al.*,[18] also confirms that *B. diffusa* extracts of the leaves have strong antioxidant activity with the DPPH assay, while the roots showed stronger superoxide radical scavenging.

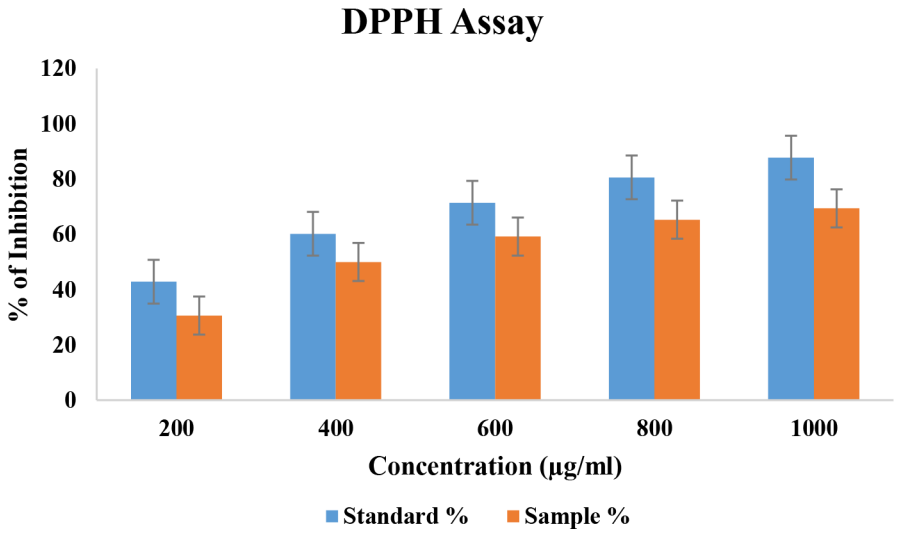


Figure 1. Radical quenching efficiency of *B. diffusa* by DPPH assay.

3.1.2 ABTS Radical Cation Scavenging by B. diffusa Extracts

The ABTS radical cation decolorisation method was employed to further evaluate the radical scavenging potential of the *B. diffusa* leaf ethanol extract. The extracts exhibited a concentration-dependent improvement in radical neutralising, with inhibition ranging between 35.36% to 77.86% at 200 to 1000 µg/mL (Figure 2).

With inhibition percentages of 35.36% to in concentrations ranging from respectively, the extract exhibited a concentration-dependent increase in radical scavenging activity. The ascorbic acid (standard) exhibited greater inhibition values ranging from 48.21% to 83.57% across the same concentration range. The IC_{50} of the extract was 470.59 µg/mL and 248.57 µg/mL for the standard. Kaviya *et al.*[19] earlier reported that the aqueous extract of *B. diffusa* (leaves, roots, and stem) revealed a maximum inhibition against ABTS radical. The results obtained confirmed that the ethanolic extract of *B. diffusa* possessed better ABTS radical neutralisation, supporting its role as a natural antioxidant source.

3.2 HRBC Membrane Stabilisation Assay

Oxidative stress is closely related to inflammation, and maintaining the integrity of the cell membrane is one of the primary predictors of inflammation-modulating potential. The ethanolic leaf extract of *B. diffusa* was examined using the *in vitro* HRBC (human red blood cell) membrane stabilisation model. The extract effectively prevented hypotonicity-induced haemolysis in a concentration-dependent inhibition of 35% to 82% at concentrations of 50-1000 µg/mL, at indicating a strong membrane-stabilising activity (Figure 3). The impact parallels that of the reference medication diclofenac sodium, which exhibited an inhibition of 38-87%. This activity suggested that the extract's anti-inflammatory impact may be achieved by stabilising lysosomal membranes, preventing the release of inflammatory molecules. Previous studies also support that the methanolic extract of BD leaves exhibited strong antioxidant and inflammation-modulating effects, due to its rich polyphenolic composition. By inhibiting the 5-lipoxygenase pathway and scavenging free radicals, its phytochemicals reduce oxidative stress and inflammation[20].

3.3 Bioactive Compounds and their Activity by Gas Chromatography-mass Spectroscopy (GC-MS)

Volatile phytocompounds responsible for therapeutic activities were profiled using the GC-MS technique. In this study, 21 compounds were detected in the *B. diffusa* leaf ethanol extract by analysing with the NIST MS library (Table 1). Sugar analogues such as 3-O-methyl-d-glucose, myo-inositol, and 3-methylmannoside comprised the majority (72.56%) and were linked to metabolic control, osmoprotection, and anti-diabetic properties. Notably, phytol, a diterpene

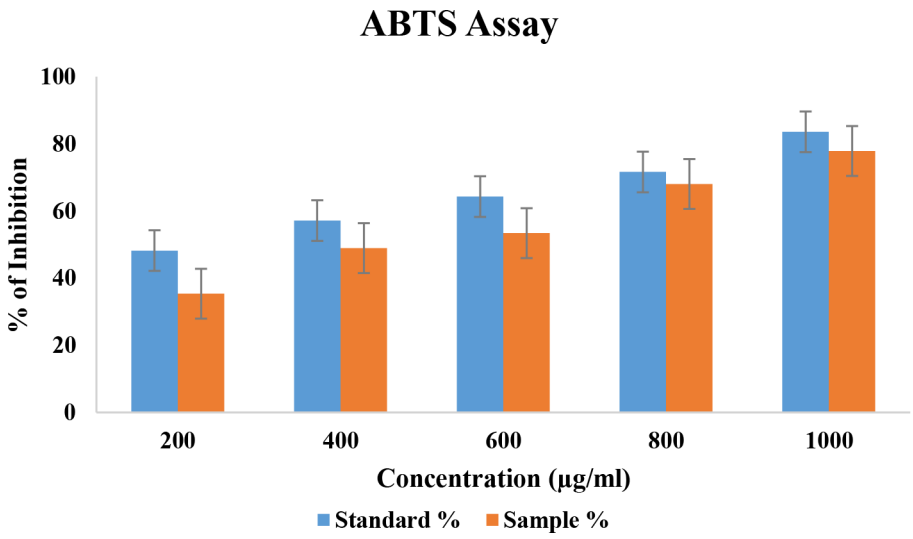


Figure 2. ABTS radical cation scavenging by *B. diffusa* extracts.

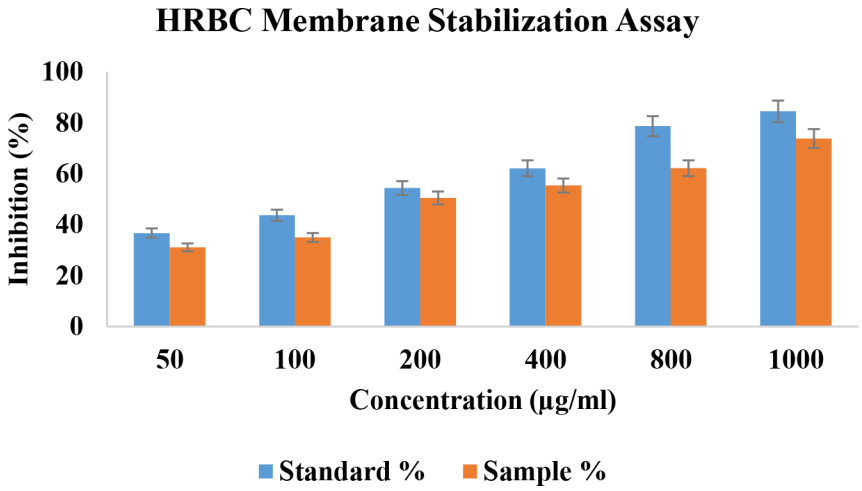


Figure 3. HRBC membrane stabilisation potential of *B. diffusa*.

alcohol (24.01%), was found in abundance and is recognised for its broad pharmacological functions, including antioxidant, anticancer, antidiabetic, and cardioprotective properties. Neophytadiene (3.15%), another prevalent diterpenoid, is renowned for its inflammation-modulating effects, analgesic, ROS-scavenging potential, and antibacterial effects. Other bioactive molecules discovered include benzofuran derivatives (antioxidant and neuroprotective), tricyclic diterpenoids (antidiabetic activity predicted), and aliphatic alcohols such as 3, 7, 11, 15-tetramethyl-2-hexadecen-1-ol and its acetate derivatives (anti-inflammatory, anti-arthritic, and antimicrobial). Several molecules, including the tetraacetyl-d-xylonic nitrile, 10-heptadecen-8-ynoic acid methyl ester, and various cyclic ketones, were found in low levels but had no known biological activity. The GC-MS analysis revealed 21 bioactive constituents, most of which were sugar analogues (72.56 %), diterpene alcohols, including phytol (24.01%) and neophytadiene (3.15%), that have inflammation-modulating effects, ROS-neutralising effects, and antidiabetic properties. The methanolic extract of *B. diffusa* contains Neophytadiene, Myo-Inositol, 4-C-methyl- according to Krishnamoorthy *et al.*,[21]. It has been reported that Phytol, 3, 7, 11, 15-Tetramethyl-2-hexadecen-1-ol, and 2-Hexadecen-1-ol acetate were among the bioactive compounds that were originally found in *B. diffusa*[22]. These compounds showed high antibacterial and antifungal activity[23]. In 2020, Bhardwaj *et al*[22]. reported on the inflammation-modulating and ROS-neutralising potential of the neophytadiene compound as well as on its antimicrobial and analgesic properties[24]. Overall, the chemical fingerprint shows a dominance of sugars and diterpenoid alcohols, which are supplemented by bioactive terpenoids and benzofuran derivatives, indicating that the extract had substantial antioxidant, anti-inflammatory, antidiabetic, and neuroprotective properties.

3.4 *In Silico* Docking Studies

The ethanolic extract of *B. diffusa* revealed the presence of 21 phytocompounds through GC-MS analysis. Six bioactive compounds 3-O-Methyl-d-glucose, 6-Hydroxy-4,4,7a trimethyl-5,6,7,7a tetrahydrobenzofuran-2(4H-one), Neophytadiene, Phytol, 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, and 2-Hexadecen-1-ol acetate were selected for further study based on their respective peak areas and known antioxidant and anti-inflammatory activities. Potential drugs' ability to bind with the human SIRT1 protein was assessed using a computational docking study. The SIRT1 (PDB ID: 4I5I), 3D crystalline structure was obtained from Protein Data Bank (PDB), and 2D chemical structure of the phytocompounds chosen was selected from PubChem database.

3.4.1 Pharmacokinetics and Toxicity Valuation: ADMET Properties Analysis

To compare the drug-likeness and pharmacokinetic properties of *B. diffusa* bioactive compounds. Their ability to Absorb, Distribute, Metabolise, Excrete, and

Table 1. Phytoconstituents profiled in *B. diffusa* leaves ethanol extract by GC-MS with their therapeutic activities

S. No.	Retention time- peak @	Compound name	Peak area%	Chemical nature	Activities
1	3.920	Desulphosinigrin	0.59	Glucosinolate (desulfo form)	Biological effects are mostly from hydrolysis products (*e.g.*, allyl isothiocyanate from sinigrin): antimicrobial, anticancer, anti-inflammatory; desulfo-forms are mainly analytical standards[25,26].
2	3.920	Tetraacetyl-d-xylonic nitrile	0.59	Acylated sugar derivative	Likely an artifact/derivative; no robust pharmacology reports.
3	3.920	10-Heptadecen-8-ynoic acid, methyl ester	0.59	Fatty acid methyl ester	No biological activity
4	13.588	2H-Indeno[1,2-b]furan-2 one	0.29	Furan derivative	Predicted anti-inflammatory (IL-1β inhibitory) activity based on molecular docking studies[27].
5	13.588	1-(3,6,6-Trimethyl 1,6,7,7a tetrahydrocyclopenta[c] p yran-1	0.29	Terpenoid	No biological activity
6	13.588	Cyclohexanone, 2,6-bis(2-methylpropylidene)	0.29	Cyclic ketone	No biological activity
7	19.725	2(4H)-Benzofuranone	0.64	Benzofuran derivative	Antioxidant/neuroprotective effects; enhancing cognitive action and attenuating oxidative stress in an animal model of amnesia[28].
8	19.725	6,6-Dimethyl-10 methylene-1-oxa spiro[4.5]decane	0.64	Spiro compound	Predicted antidiabetic effects: shown strong *in silico* binding to diabetes targets (SGLT2 and α-amylase)[29].
9	19.410	3-O-Methyl-d-glucose	72.56	Non-metabolisable glucose analogue (methylated hexose)	Metabolic regulation, osmoprotection
10	19.410	Myo-Inositol, 4-C-methyl-	72.56	Cyclic polyol	Cell signalling, anti-diabetic[30]
11	19.410	3-Methylmannoside	72.56	Sugar derivative	*In vivo* reports; glycosides can show prebiotic/ osmoprotective roles[31]
12	21.915	6-Hydroxy-4,4,7a trimethyl-5,6,7,7a tetrahydrobenzofuran-2	1.36	Benzofuran derivative	Antioxidant and anti-inflammatory effects[32]
13	21.915	9,10 Dimethyltricyclo[4.2.1.1(2,5)]decane-9,10-diol	1.36	Tricyclic diterpenoid	Predicted antidiabetic effects: demonstrated high binding affinity to α-amylase in docking studies[29]
14	21.915	Ppropiolic acid, 3-(1 hydroxy-2-isopropyl-5 methylcyclohexy	1.36	Carboxylic acid derivative	No biological activity
15	22.013	Neophytadiene	3.15	aliphatic alkene	Anti-inflammatory, analgesic, antioxidant, antipyretic[33]
16	23.680	3,7,11,15-Tetramethyl-2 hexadecen-1-ol	0.53	Alkyne	Anti-inflammatory, analgesic, and antiarthritic effects[34]
17	23.680	9-Eicosyne	0.53	Fatty alcohol	No biological activity
18	23.680	Z,E-2,13-Octadecadien 1-ol	0.53	Diterpene alcohol	No biological activity
19	30.670	Phytol	24.01	Diterpene alcohol	Anti-cancerous, anti-diabetic[35]
20	30.670	2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, acetate,	24.01	Aldehyde derivative	Antioxidant/anti-inflammatory potential: reported to inhibit ROS-forming enzymes and modulate cell signalling pathways[36]
21	30.670	3,7,11,15 Tetramethylhexadec-2 en-1-yl acetate	24.01	Terpenoid ester	Antibacterial and antifungal activity[24]

induce Toxicity (ADMET) is governed. The assessment focused on their therapeutic potential through these tests.

3.4.2 Drug-Likeness analysis based on Lipinski's Rule

Lipinski's rules forecast oral bioavailability of small molecules from the evaluation of six phytocompounds of *B. diffusa* - Neophytadiene, Phytol, 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, and 2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, acetate, [R-[R*, R*-(E)]]- showed log P values > 5, which can be considered as highly lipophilic and may affect solubility[29]. Also, the majority of the compounds had >10 rotatable bonds, which can decrease oral bioavailability (Table 2). The high lipophilicity indicated by log P values of Neophytadiene, Phytol, 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, and 2-Hexadecen-1-ol acetate will interfere with aqueous solubility and absorption. Poor solubility will lead to decreased systemic availability and thus diminish therapeutic effects. Drug delivery techniques that could improve the solubility of poorly soluble medications include chemical modifications, prodrug formulations, and nanoparticles. Equivalently, high rotatable bond numbers (>10) in most of the compounds also signify high molecular flexibility, which can be undesirable for passive diffusion and membrane permeability. Nonetheless, molecular improvement by optimisation of the structure or derivative preparation may improve their molecular properties without losing their bioactivity. Even though these compounds possess such limitations, very lipophilic compounds could favor strong protein binding and membrane integration, which might be advantageous in targeting the lipid-rich systems such as cardiac tissues[37]. Furthermore, *in vitro* and *in vivo* studies could include pharmacokinetic modifications to determine whether such phytocompounds could be optimised for effective drug development[38].

Among the six phytocompounds found in *B. diffusa,* most exhibited good intestinal absorption (90.64% - 93.62%) with 3-O-Methyl-d-glucose (64.75%) and effective Caco-2 permeability that supports their oral delivery. These compounds revealed effective oral bioavailability through their sufficient intestinal absorption that exceeded 90.64%-93.62% thereby demonstrating permeability across epithelial membranes. Surprisingly, none of the ligands were substrates of P-glycoprotein (P-gp), which could limit the possibilities of efflux-based resistance. Their poor skin permeability (log Kp: -2.518 to -3.816) shows that the molecules are not suitable for transdermal products, further establishing their place in systemic and not topical application[39,40]. P-glycoprotein did not transport any of the compounds, thus helping to reduce drug efflux-based resistance and enhance efficacy. The phytocompounds showed inadequate skin permeability, indicating they would work better when administered systemically rather than used topically. Distribution was moderate without peripheral tissue accumulation (VDss: - 0.523 to 0.692). Moderate permeability of these molecules through the blood-brain barrier (BBB) (log BB: -0.97 to 0.983) suggests neuroprotection. Also, the lower CNS permeability (log PS: -1.299 to - 4.087)

Table 2. Drug-likeness parameters of compounds obtained from ethanol extract of *B. diffusa*

S. No	Compound name	Molecular weight (Da)	H-bond donor (HBD ≤ 5)	H-bond acceptor (HBA ≤ 10)	Log P value ≤ 5	Rotatable bonds (≤ 10)	Bioavailability score
1.	3-O-Methyl-d-glucose	194.18	4	6	-2.56	6	0.55
2	6-Hydroxy-4,4,7a trimethyl-5,6,7,7a tetrahydrobenzofuran-2	196.24	1	3	1.49	0	0.55
3	Neophytadiene	278.52	0	0	6.21	13	0.55
4	Phytol	296.53	1	1	5.25	13	0.55
5	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	296.53	1	1	5.25	13	0.55
6	2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, acetate	338.57	0	2	5.47	15	0.55

implied less neurotoxicity risk. Metabolic stability of phytocompounds showed inhibition of CYP1A2 except for 3-O-Methyl-d-glucose and 6-Hydroxy-4, 4,7a trimethyl-5, 6, 7,7a tetrahydrobenzofuran-2(4H-one), which indicates potential for drug-drug interactions. No inhibition was seen for compounds on CYP2C19, CYP2C9, CYP2D6, or CYP3A4. The compounds showed moderate elimination rates (0.967 to 1.764 ml/min/kg) with hepatic metabolism favored over renal excretion due to the absence of renal OCT2 substrate interaction. AMES toxicity testing showed that none of the compounds were mutagenic, which indicated low acute toxicity of LD50 values (1.452 to 1.741mol/kg). None of the compounds showed hepatotoxicity, which further enhances their potential as long-term treatments (Table 3). Experimental research showed these compounds exhibited average tissue absorption and penetrated the blood-brain barrier, implying they could act as neuroprotectives with minimal harmful effects on the nervous system. The slight inhibition of the CYP1A2 enzyme thus created the potential for pharmaceutical interactions but did not affect other dominant drug-metabolising enzymes[41]. It exhibited moderate clearance rates and activated hepatic metabolism, leading to safe long-term therapeutic applications, as it displayed low acute toxicity alongside negative mutagenic and hepatotoxic test results.

3.4.2 Molecular Docking

The target protein SIRT1 was docked with the chosen six bioactive compounds based on their relative peak area, anti-oxidant and inflammation-modulating potential, obtained from the ethanolic extract of *B. diffusa* - 3-O-Methyl-d-glucose, Neophytadiene, Phytol, 6-Hydroxy-4,4,7a trimethyl-5,6,7,7a tetrahydrobenzofuran-2, 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, 2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-acetate, along with resveratrol by Autodock Vina. The binding energy values obtained from target protein SIRT1 with six compounds such as 3-O-Methyl-d-glucose, 6-Hydroxy-4,4,7a trimethyl-5,6,7,7a tetrahydrobenzofuran-2, Neophytadiene, Phytol, 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, and 2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, acetate, and resveratrol were found to be -3.21, -6.74, -7.16, -7.33, -7.06, -6.38, and -6.99 Kcal/mol, respectively. The ligand efficiency values indicate that 6-Hydroxy-4, 4,7a trimethyl-5, 6, 7,7a tetrahydrobenzofuran-2 (-0.48) was most efficient followed by Neophytadiene (-0.36). Phytol (-11.8 kcal/mol) and Neophytadiene (-11.03 kcal/mol) exhibited favorable inter-molecular energy. Van der Waals, hydrogen bonding, and desolvation energy were the same as the intermolecular energy, alongside of electrostatic force. In terms of torsional energy, Phytol and 3, 7, 11, 15-Tetramethyl-2-hexadecen-1-ol and 2-Hexadecen-1-ol, 3, 7, 11, 15-tetramethyl-, acetate, (4.47 kcal/mol). 3-O-Methyl-d-glucose (-2.75 kcal/mol) and 2-Hexadecen-1-ol, 3, 7, 11, 15-tetramethyl-, acetate, (-1.86 kcal/mol) also exhibited relatively lower unbound energy, indicating their high stability of interaction in docking (Table 4). By docking with SIRT1, neophytadiene and phytol (-7.16 and -7.33 Kcal/mol) exhibited a strong binding energy, suggesting that these phytocompounds may regulate the SIRT1 activity and could potentially confer oxidative and inflammatory effects. The docking visualisation of phytocompounds with SIRT1 showed hydrogen and hydrophobic interactions.

SIRT1 is NAD + dependent deacetylase with cardioprotective effects that include pathways related to oxidative stress, inflammation, apoptosis, and lipid metabolism, which are controlled epigenetically. It deacetylates transcription factors containing NF-κB (RelA/p65) and p53 and reduces the expression of pro-inflammatory cytokines and stimulates cardiomyocyte and other cell survival upon stress[42,43]. Resveratrol is a known activator of sirtuin protein and is also known for its cardioprotective effect[44]. Research by Ciccone *et al.*, revealed that SIRT1 regulation is essential for cardiovascular well-being because it regulates endothelial functions as well as oxidative stress and lipid metabolic processes[45]. Neophytadiene showed its therapeutic effect by functioning both as an anti-inflammatory and antioxidant that prevents vascular dysfunction and atherosclerosis, according to Bhardwaj *et al*[22]. Phytol possesses dual roles in cancer and cardiovascular protection through lipid-lowering capabilities and anti-inflammatory properties and performance. Synergistic or secondary interactions enable the four molecules with intermediate binding energies, including 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, 2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-acetate; 6-Hydroxy-4,4,7a trimethyl-5,6,7,7a tetrahydro benzofuran-2, and the 3-O-Methyl-d-glucose may

Table 3. ADMET parameters of plant metabolites from *B. diffusa* ethanol extract

Parameters	Model name/unit	3-O-methyl-d-glucose	6-Hydroxy-4,4,7a trimethyl-5,6,7,7a tetrahydro benzofuran-2	Neophytadiene	Phytol	3,7,11,15-tetramethyl-2-hexadecen-1-ol	2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, acetate
Absorption	Caco2 permeability	-0.328	1.239	1.425	1.399	1.515	1.165
	Intestinal absorption (%)	64.756	95.935	92.85	90.64	90.71	92.783
	P-glycoprotein substrate	No	No	No	No	No	No
	Skin Permeability Numeric (logKp)	-3.093	-3.816	-2.518	-2.631	-2.576	-2.767
Distribution	VDss (log L/kg)	-0.523	0.117	0.692	0.385	0.468	0.305
	BBB permeability (log BB)	-0.97	-0.189	0.983	0.793	0.806	0.758
	CNS permeability (log PS)	-4.087	-3.048	-1.299	-1.527	-1.563	-1.644
Metabolism	CYP1A2 inhibitor	No	No	Yes	Yes	Yes	Yes
	CYP2C19/2C9/2D6/3A4 inhibitor	No	No	No	No	No	No
Excretion	Total Clearance	0.967	1.042	1.764	1.686	1.686	1.684
	Renal OCT2 substrate	No	No	No	No	No	No
Toxicity	AMES toxicity	No	No	No	No	No	No
	Oral Rat Acute Toxicity (LD50) (mol/kg)	1.452	1.94	1.473	1.85	1.607	1.741
	Hepatotoxicity	No	No	No	No	No	No

(Caco2 - human colon adenocarcinoma cell line; VDss - Volume of Distribution at Steady State; BBB- Blood Brain Barrier; CNS - Central Nervous System; CYP1A2 - Cytochrome P450 1A2; Renal OCT2 - Organic Cation Transporter 2)

activate SIRT1 enzymes. It has been reported in earlier studies that moderate SIRT1 activation itself can cause metabolic and vascular benefits, suppressing oxidative stress, hypertension, and atherosclerosis development[46]. The phytol compound found in *B. diffusa* methanolic extract showed hepatoprotection effects by *in silico* docking study[21].

The binding stability emerged from combinations of hydrogen bond and hydrophobic interactions that include Pi-Sigma, Alkyl, and Pi-Alkyl bonds together with specific distances between amino acid pairs that reinforced the ligand-protein binding process (Figure 4). Table 5 represents the amino acid residue, bond types, and distances between all ligand atoms and SIRT1 protein. The residues involved with the hydrogen and hydrophobic bond interactions included Phe273, Phe297, His363, Ile270, Ile316, Val412, and Ile411. In addition, other amino acids such as Arg274, Lys444, Asn465, Glu467, Gln320, Glu315, Pro271, Ala262, Val445, Ile279, and Gln345 were also involved, depending on their proximity and positioning with the binding pockets of SIRT1 (Figure 5). Thus, the present study revealed that SIRT1 showed excellent binding energy for neophytadiene and phytol, which suggested these compounds may be an interesting candidate for anti-inflammatory and oxidative stress mediated cardiovascular drug development.

Table 4. Molecular docking results of bioactive compounds from ethanol extract of *B. diffusa* with maximum binding affinity

S. No	Ligand binding with SIRT1	Δ G binding (Kcal/mol)	Efficiency of ligand	Inter-molecular energy	vdW + Hbond + desolv energy	Electrostatic energy	Torsional energy	Total internal unbound
1	3-O-Methyl-d-glucose	-3.21	-0.25	-6.19	-5.49	-0.7	2.98	-2.75
2	6-Hydroxy-4,4,7a trimethyl-5,6,7,7a tetrahydrobenzofuran	-6.74	-0.48	-7.04	-6.76	-0.28	0.3	0.08
3	Neophytadiene	-7.16	-0.36	-11.03	-11.04	0.0	3.88	-1.1
4	Phytol	-7.33	-0.35	-11.8	-11.77	-0.03	4.47	-0.61
5	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	-7.06	-0.34	-11.02	-11.48	-0.05	4.47	-0.95
6	2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, acetate,	-6.38	-0.27	-10.86	-10.86	0.01	4.47	-1.86
7	Resveratrol	-6.99	-0.41	-8.49	-8.25	-0.23	1.49	-0.57

Table 5. SIRT1 protein interaction with bioactive compounds from ethanol extract of *B. diffusa*

Compound names	Bond type	SIRT1 protein		Ligand atom	Distance (Å)
		Residue	Atom		
3-O-Methyl-d-glucose	Hydrogen	ARG274/ LYS444/ ASN465	N	O	1.94 -3.19
		GLU467	H		
6-Hydroxy-4,4,7a trimethyl-5,6,7,7a tetrahydrobenzofuran	Hydrogen	ARG274	NH2	O	3.22
	Hydrophobic	VAL412/ PHE273/ TYR280/ PHE297/ HIS363/ PHE414	Pi-Sigma / Alkyl	C	1.88-5.49
Neophytadiene	Hydrophobic	PHE273/ PHE297/ HIS363/ ILE270/ ILE316/ ILE347/ ILE411	Pi-Alkyl/ Pi-Sigma	C	3.72-5.45
Phytol	Hydrogen	GLN320/ GLU315	O	O/ H	2.16-2.85
	Hydrophobic	PHE273/ PHE297/ ILE316/ ILE347/ ILE411/ ALA262	Alkyl/ Pi-Alkyl/ Pi-Sigma	C/ O/ H	3.89-5.23
3,7,11,15-Tetramethyl-2-hexadecen-1-ol	Hydrogen	PRO271	O	H	2.00
	Hydrophobic	HIS363/ VAL412/ VAL445/ ILE270/ ILE347/ PHE273/ PHE297/ PHE414	Pi-Orbital/ Alkyl	C	3.67-5.35
2-Hexadecen-1-ol, 3,7,11,15-tetramethyl, acetate,	Hydrogen	PHE414	N	O	3.05
	Hydrophobic	PHE273/ ALA262/ ILE316/ ILE347/ ILE270/ ILE279/ ILE411	Alkyl/ Pi-Alkyl/ Pi-Sigma	C	3.83-5.41
Resveratrol	Hydrogen	ARG274/ HIS363/ TYR280	H-Bond	-	2.13-3.04
	Hydrophobic	PHE414/ PHE273/ PHE297	Stacked / T-shaped	H	4.67-5.11
		GLN345	Alkyl	-	1.96
		ILE347	Pi-Alkyl	C	5.01

The major constraint of this study is the lack of experimental validation for SIRT1 regulation; although the phytocompounds obtained from the *B. diffusa* leaf ethanolic extract by GC-MS analysis have showed good binding affinity towards the SIRT1 target for anti-oxidant and inflammation-modulating potential. Further *in vitro* and *in vivo* experiments, such as enzyme-based activation and

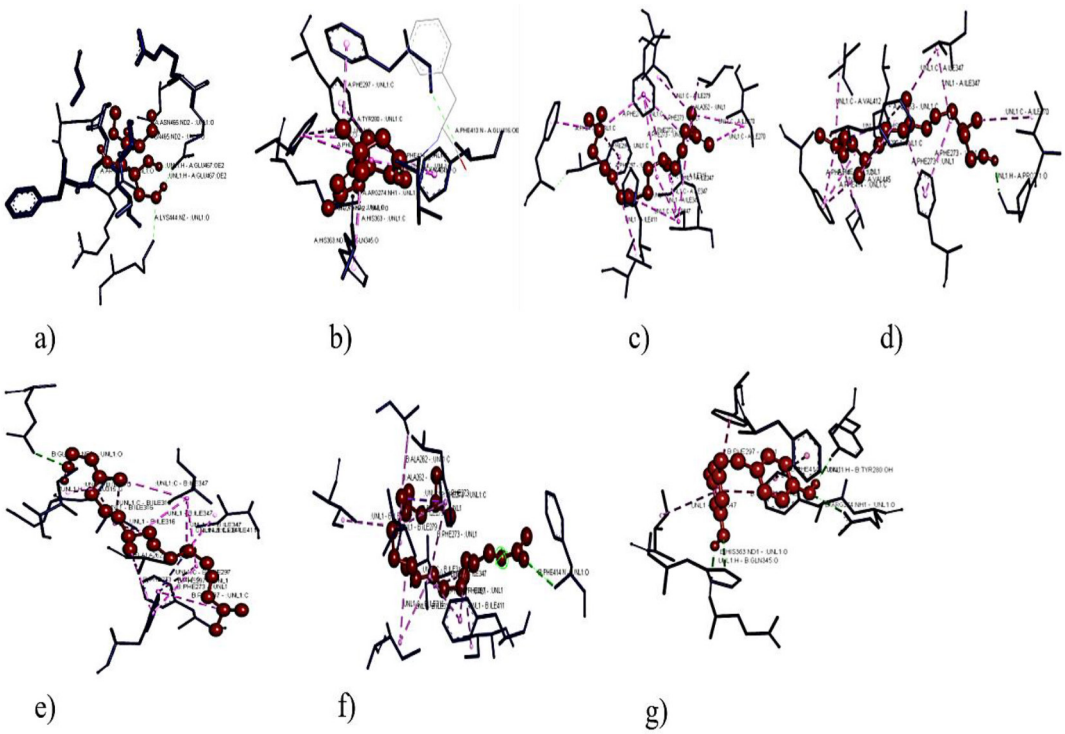


Figure 4. The 3D interactions of phytocompounds from *B. diffusa* with SIRT1. The compounds a-g (3-O-Methyl-d-glucose, 6-Hydroxy-4,4,7a trimethyl-5,6,7,7a tetrahydrobenzofuran-2, Neophytadiene, Phytol, 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, and 2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, acetate, resveratrol) were docked into the SIRT1 active site.

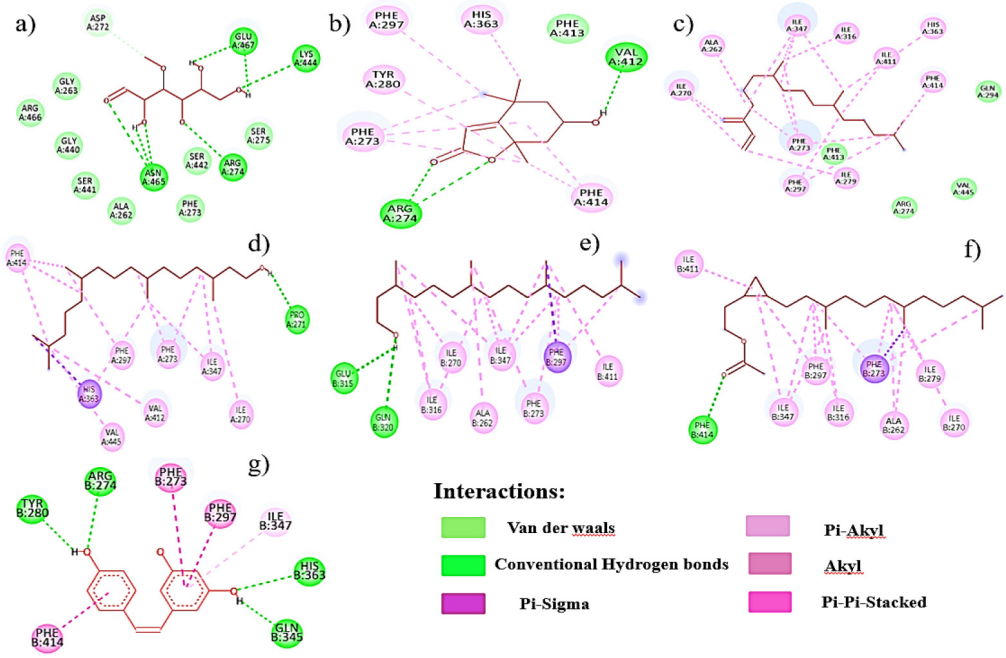


Figure 5. The 2D interactions of phytocompounds from *B. diffusa* with SIRT1. The compounds a-g (3-O-Methyl-d-glucose, 6-Hydroxy-4,4,7a trimethyl-5,6,7,7a tetrahydrobenzofuran-2, Neophytadiene, Phytol, 3,7,11,15-Tetramethyl-2-hexadecen-1-ol, and 2-Hexadecen-1-ol, 3,7,11,15-tetramethyl-, acetate, resveratrol). The green lines represent the hydrogen bond, Van der Waals force, and the pink lines represent hydrophobic interactions.

cell-based models, are essential to substantiate SIRT1 modulation.

4. Conclusion

This research demonstrates the therapeutic possibility of *Boerhavia diffusa*-derived phytocompounds with strong inflammation-modulating potential and ROS quenching ability that are mechanistically linked to the control of SIRT1, a key regulator of inflammation and oxidative stress. The ADMET profile of six major compounds of *B. diffusa* showed excellent intestinal absorption, metabolic stability, and non-toxicity, endorsing their drug-like nature. Lack of hepatotoxicity and mutagenicity enhances their value as safe therapeutic drugs. Molecular docking study revealed that Neophytadiene and Phytol exhibited very strong binding affinities towards SIRT1. The 2D and 3D interaction showed hydrogen bond and hydrophobic interactions, adding strength to their stability within the binding pocket. These results implied that *B. diffusa*-derived metabolites could act as potential modulators of SIRT1, with broad therapeutic roles in ROS neutralisation and mitigating inflammation-driven pathologies such as heart disease, malignancies, and neurodegenerative conditions. The present study is a preliminary analysis to understand the binding interaction between SIRT1 and phytocompounds of *B. diffusa*. Further experiments using enzyme activation assay, cell line study, and molecular dynamic stimulation need to be conducted to validate the modulators of SIRT1.

5. References

1. Nediani C, Ruzzolini J, Dinu M. Oxidative stress and inflammation as targets for novel preventive and therapeutic approaches in non-communicable diseases III. Antioxidants (Basel). 2024; 13(11):1404. https://doi.org/10.3390/antiox13111404 PMid:39594546 PMCid:PMC11591297
2. World Health Organization (WHO). Cardiovascular diseases. [Internet]. Geneva: WHO; [cited 2025 Jan 5]. Available from: https://www.who.int/india/health-topics/cardiovascular-diseases
3. Valenzuela PL, Ruilope LM, Santos-Lozano A, Wilhelm M, Kränkel N, Fiuza-Luces C, *et al*. Exercise benefits in cardiovascular diseases: From mechanisms to clinical implementation. Eur Heart J. 2023; 44(21):1874-1889. https://doi,org/10.1093/eurheartj/ehad170 PMid:37005351
4. Aranda-Rivera AK, Cruz-Gregorio A, Arancibia-Hernández YL, Hernández-Cruz EY, Pedraza-Chaverri J. RONS and oxidative stress: An overview of basic concepts. Oxygen. 2022; 2(4):437-478. https://doi.org/10.3390/oxygen2040030
5. Schieber M, Chandel NS. ROS function in redox signaling and oxidative stress. Curr Biol. 2014; 24(10):R453-R462. https://doi.org/10.1016/j.cub.2014.03.034 PMid:24845678 PMCid:PMC4055301
6. Wu YL, Lin ZJ, Li CC, Lin X, Shan SK, Guo B, *et al*. Epigenetic regulation in metabolic diseases: Mechanisms and advances in clinical study. Signal Transduct Target Ther. 2023; 8:98. https://doi.org/10.1038/s41392-023-01333-7 PMid:36864020 PMCid:PMC9981733
7. Zhu X, Chen Z, Shen W, Huang G, Sedivy JM, Wang H, *et al*. Inflammation, epigenetics, and metabolism converge to cell senescence and ageing: The regulation and intervention. Signal Transduct Target Ther. 2021; 6:245. https://doi.org/10.1038/s41392-021-00646-9 PMid:34176928 PMCid:PMC8236488
8. Liu YP, Wen R, Liu CF, Zhang TN, Yang N. Cellular and molecular biology of sirtuins in cardiovascular disease. Biomed Pharmacother. 2023; 164:114931. https://doi.org/10.1016/j.biopha.2023.114931 PMid:37263163
9. Iside C, Scafuro M, Nebbioso A, Altucci L. SIRT1 activation by natural phytochemicals: An overview. Front Pharmacol. 2020; 11:1225. https://doi.org/10.3389/fphar.2020.01225 PMid:32848804 PMCid:PMC7426493
10. Das S, Singh PK, Ameeruddin S, Kumar Bindhani B, Obaidullah WJ, Obaidullah AJ, *et al*. Ethnomedicinal values of *Boerhaavia diffusa* L. as a panacea against multiple human ailments: A state of art review. Front Chem. 2023; 11:1297300. https://doi.org/10.3389/fchem.2023.1297300 PMid:38033469 PMCid:PMC10682173
11. Belavadi SN. Role of rasayanas as immunomodulator and antioxidant: A conceptual study. AYUSH Int Res J Ayurveda Teachers Assoc. 2023; 2(1):52-57.
12. Gupta V, Virmani T, Singh V. Review on phytochemicals and pharmacological activities of *Boerhaavia diffusa* Linn. Int J Pharm Res. 2021; 13(2):2661-2674. https://doi.org/10.31838/ijpr/2021.13.02.362
13. Gaur PK, Rastogi S, Lata K. Correlation between phytocompounds and pharmacological activities of *Boerhaavia diffusa* Linn with traditional-ethnopharmacological insights. Phytomed Plus. 2022; 2(2):100260. https://doi.org/10.1016/j.phyplu.2022.100260
14. Trease GE, Evans WC. Pharmacognosy. 15th ed. London: Saunders (Elsevier); 2002.
15. Endris YA, Abdu KY, Abate SG. Investigation of bioactive phytochemical compounds of the Ethiopian medicinal plant using GC-MS and FTIR. Heliyon. 2024; 10(15):e34687. https://doi.org/10.1016/j.heliyon.2024.e34687 PMid:39170564 PMCid:PMC11336350

16. Karrat L, Abajy MY, Nayal R. Investigating the anti-inflammatory and analgesic properties of leaves ethanolic extracts of *Cedrus libani* and *Pinus brutia*. Heliyon. 2022; 8(4):e09254. https://doi.org/10.1016/j.heliyon.2022.e09254 PMid:35434396 PMCid:PMC9006851
17. Panse N, Gerk PM. The Caco-2 model: Modifications and enhancements to improve efficiency and predictive performance. Int J Pharm. 2022; 624:122004. https://doi.org/10.1016/j.ijpharm.2022.122004 PMid:35820514
18. Nayak P, Thirunavoukkarasu M. A review of the plant *Boerhaavia diffusa*: Its chemistry, pharmacology and therapeutical potential. J Phytopharmacol. 2016; 5(2):83-92. https://doi.org/10.31254/phyto.2016.5208
19. Kaviya M, Balasubramanian B, Bharathi K, Malaisamy A, Al-Dhabi NA, Mariadhas VA, *et al*. Evaluation of nutritional substances and investigation of antioxidant and antimicrobial potentials of *Boerhaavia diffusa* with *in silico* molecular docking. Molecules. 2022; 27(4):1280. https://doi.org/10.3390/molecules27041280 PMid:35209067 PMCid:PMC8880713
20. Das S, Singh PK, Ameeruddin S, Bindhani BK, Obaidullah WJ, Obaidullah AJ, *et al*. Ethnomedicinal values of *Boerhaavia diffusa* L. as a panacea against multiple human ailments: A state of art review. Front Chem. 2023; 11:1297300. https://doi.org/10.3389/fchem.2023.1297300 PMid:38033469 PMCid:PMC10682173
21. Krishnamoorthy S, Kalaivannan J, Kaliyaperumal SA, Kasinathan S. Phytochemical profiling and *in silico* approach for hepato-protective activity of various extracts of *Boerhavia diffusa* Linn. J Nat Rem. 2025; 25(3):499-506. https://doi.org/10.18311/jnr/2025/34179
22. Bhardwaj R, Sharma RA. *Boerhavia diffusa*-GC-MS analysis of alkaloids and their inhibitory activity against pathogenic microorganisms. J Pharmacogn Phytochem. 2019; 8(2):756-60.
23. Das B, Baidya AT, Mathew AT, Yadav AK, Kumar R. Structural modification aimed for improving solubility of lead compounds in early phase drug discovery. Bioorg Med Chem. 2022; 56:116614. https://doi.org/10.1016/j.bmc.2022.116614 PMid:35033884
24. Bhardwaj M, Sali VK, Mani S, Vasanthi HR. Neophytadiene from *Turbinaria ornata* suppresses LPS-induced inflammatory response in RAW 264.7 macrophages and Sprague Dawley rats. Inflammation. 2020; 43:937-950. https://doi.org/10.1007/s10753-020-01179-z PMid:31981060
25. Tarar A, Peng S, Cheema S, Peng CA. Anticancer activity, mechanism, and delivery of allyl isothiocyanate. Bioeng (Basel). 2022; 9(9):470. https://doi.org/10.3390/bioengineering9090470 PMid:36135016 PMCid:PMC9495963
26. Grosser K, van Dam NM. A straightforward method for glucosinolate extraction and analysis with High-Pressure Liquid Chromatography (HPLC). J Vis Exp. 2017; (121):55425. https://doi.org/10.3791/55425 PMid:28362416 PMCid:PMC5409297
27. Martin DR, Ajmal A, Meyer M, Madiehe AM. *In silico* identification of phytoconstituents from *Capparis sepiaria* as interleukin-1 inhibitors for rheumatoid arthritis: Molecular docking, ADMET profiling, and molecular dynamics simulation. *In silico* Pharmacol. 2025; 13(2):106. https://doi.org/10.1007/s40203-025-00386-6 PMid:40697669 PMCid:PMC12279688
28. Das M, Jaya Balan D, Kasi PD. Mitigation of oxidative stress with dihydroactinidiolide, a natural product, against scopolamine-induced amnesia in Swiss albino mice. Neurotoxicology. 2021; 86:149-161. https://doi.org/10.1016/j.neuro.2021.08.003 PMid:34371027
29. Ibrahim SO, Lukman HY, Ebhohimen IE, Babamale HF, Abdulkadir FR, Hamid AA, *et al*. Chemoinformatic-aided antidiabetic analysis of the therapeutic potential of phytoconstituents in Eremomastax speciosa extracts. Borneo J Pharm. 2024; 7(2):172-186. https://doi.org/10.33084/bjop.v7i2.6820
30. Akter S, Kawsar SMA, Bouzid G, Horchani M, Bulbul MZH, Ghalla H, *et al*. Synthesis, antimicrobial activity, DFT, molecular docking, and dynamic simulations of trityl mannopyranoside derivatives for potential antibacterial agents. Med Chem (Sharjah). 2025; 21(5):403-424. https://doi.org/10.2174/0115734064339243241027024304 PMid:39757636
31. Sharma S, Sharma S, Thakur A, Singla R, Kour J, Sharma P, *et al*. Analysis of polyphenols and antioxidant activity of Punarnava (*Boerhavia diffusa* L.) from Himachal Pradesh, a north-western state of India. J Appl Nat Sci. 2023; 15(4):1760. https://doi.org/10.31018/jans.v15i4.5204
32. Mazumder A, Dwivedi A, du Plessis J. Sinigrin and its therapeutic benefits. Molecules. 2016; 21(4):416. https://doi.org/10.3390/molecules21040416 PMid:27043505 PMCid:PMC6273501
33. Selmy AH, Hegazy MM, El-Hela AA, Saleh AM, El-Hamouly MM. *In vitro* and *in silico* studies of neophytadiene, a diterpene isolated from *Aeschynomene elaphroxylon*, as an apoptotic inducer. Egypt J Chem. 2023; 66(10):149-161. https://doi.org/10.21608/ejchem.2023.178261.7296
34. Carvalho AMS, Heimfarth L, Pereira EWM, Oliveira FS, Menezes IRA, Coutinho HDM, *et al*. Phytol, a chlorophyll component, produces antihyperalgesic, anti-inflammatory, and antiarthritic effects: Possible NFκB pathway involvement and reduced levels of the proinflammatory cytokines TNF-α and IL-6. J Nat Prod. 2020; 83(4):1107-1117. https://doi.org/10.1021/acs.jnatprod.9b01116 PMid:32091204
35. Sujatha J, Asokan S, Rajeshkumar S. Phytochemical analysis and antioxidant activity of chloroform extract of *Cassis alata*. Res J Pharm Technol. 2018; 11(2):439-444. https://doi.org/10.5958/0974-360X.2018.00081.1

36. Al-Marzoqi AH, Hadi MY, Hameed IH. Determination of metabolites products by *Cassia angustifolia* and evaluation of antimicrobial activity. J Pharmacogn Phytother. 2016; 8(2):25-48. https://doi.org/10.5897/JPP2015.0367
37. Climent E, Benaiges D, Pedro-Botet J. Hydrophilic or lipophilic statins? Front Cardiovasc Med. 2021; 8:687585. https://doi.org/10.3389/fcvm.2021.687585 PMid:34095267 PMCid:PMC8172607
38. Ciccone L, Piragine E, Brogi S, Camodeca C, Fucci R, Calderone V, *et al*. Resveratrol-like compounds as SIRT1 activators. Int J Mol Sci. 2022; 23(23):15105. https://doi.org/10.3390/ijms232315105 PMid:36499460 PMCid:PMC9738298
39. Veber DF, Johnson SR, Cheng HY, Smith BR, Ward KW, Kopple KD. Molecular properties that influence the oral bioavailability of drug candidates. J Med Chem. 2002; 45(12):2615-2623. https://doi.org/10.1021/jm020017n PMid:12036371 PMCid:PMC8986010
40. Chen CP, Chen CC, Huang CW, Chang YC. Evaluating molecular properties involved in transport of small molecules in *Stratum corneum*: A quantitative structure-activity relationship for skin permeability. Molecules. 2018; 23(4):911. https://doi.org/10.3390/molecules23040911 PMid:29662033 PMCid:PMC6017021
41. Han S, Mei L, Quach T, Porter C, Trevaskis N. Lipophilic conjugates of drugs: A tool to improve drug pharmacokinetic and therapeutic profiles. Pharm Res. 2021; 38(9):1497-1515. https://doi.org/10.1007/s11095-021-03093-x PMid:34463935
42. Zhao K, Zhang H, Yang D. SIRT1 exerts protective effects by inhibiting endoplasmic reticulum stress and NF-κB signaling pathways. Front Cell Dev Biol. 2024; 12:1405546. https://doi.org/10.3389/fcell.2024.1405546 PMid:38745862 PMCid:PMC11091328
43. Yang Y, Liu Y, Wang Y, Chao Y, Zhang J, Jia Y, *et al*. Regulation of SIRT1 and its roles in inflammation. Front Immunol. 2022; 13:831168. https://doi.org/10.3389/fimmu.2022.831168 PMid:35359990 PMCid:PMC8962665
44. Lee J, Beers JL, Geffert RM, Jackson KD. A review of CYP-mediated drug interactions: Mechanisms and *in vitro* drug-drug interaction assessment. Biomolecules. 2024; 14(1):99. https://doi.org/10.3390/biom14010099 PMid:38254699 PMCid:PMC10813492
45. Carollo C, Sorce A, Cirafici E, Mulè G, Caimi G. Sirtuins and resveratrol in cardiorenal diseases: A narrative review of mechanisms and therapeutic potential. Nutrients. 2025; 17(7):1212. https://doi.org/10.3390/nu17071212 PMid:40218970 PMCid:PMC11990745
46. Olofsson P, Hultqvist M, Hellgren LI, Holmdahl R. Phytol: A chlorophyll component with anti-inflammatory and metabolic properties. In: Recent advances in redox active plant and microbial products: from basic chemistry to widespread applications in medicine and agriculture. Dordrecht: Springer; 2014; p.345-359. https://doi.org/10.1007/978-94-017-8953-0_13 PMid:25242496 PMCid:PMC4185125

Author Contribution

Conceptualisation, C.V.; methodology, C.V. and S.M.J.; formal analysis, S.M.J.; software and data curation, C.V.; draft preparation, C.V. and S.M.J.; review and supervision, A.J.R. and S.M.J. All authors have read and agreed to the published version of the manuscript.