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Research Article

Molecular docking and ADMET profiling of bioactive compounds from *Thalictrum dalzellii*: A multitarget approach against Oxidative Stress, Inflammation, and Diabetes

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Article Info

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Abstract

Using a thorough *in silico* methodology, the current work examines the bioactive chemicals from *Thalictrum dalzellii* for their potential as antioxidants, anti-inflammatory agents, and antidiabetic agents. GC-MS-identified phytochemicals were molecularly docked against important protein targets, such as PPARγ complexes (1FM6, 2HWQ), superoxide dismutase (1CB4), glutathione peroxidase (2P31), myeloperoxidase (1DNU), COX-2 (3CTT), α-glucosidase (3W37), and TNF-α (1DPU). iGEMDOCK v2.1 was used for docking, and AdmetSAR and Molsoft tools were used to evaluate drug-likeness and pharmacokinetic profile. With a binding energy of -80.47 kcal/mol against 1CB4, isoschizogamine was the compound with the highest antioxidant potential. On the other hand, 3-ethenylphenol and phenol 2,6-dimethoxy-exhibited notable anti-inflammatory (-71.09 kcal/mol against 3CTT) and antidiabetic (-71.25 kcal/mol against 1FM6) properties, respectively. According to ADMET profiling, more than 80% of the phytochemicals that were tested met Lipinski's rule of five, were non-mutagenic, non-carcinogenic, and exhibited favourable permeability across the blood-brain barrier. Interestingly, a number of phytochemicals showed greater binding affinities than common medications including metformin, ampicillin, and ascorbic acid. These findings suggest that *T. dalzellii* harbours multitarget therapeutic compounds with promising pharmacokinetic profiles, supporting its traditional medicinal use and providing a basis for further in vitro and in vivo validation in drug discovery research.

Keywords: *Thalictrum dalzellii*, molecular docking, ADMET, Molsoft, iGEMDOCK and Biovia discovery studio visualizer.

1. Introduction

Chronic non-communicable diseases (NCDs) such diabetes mellitus, oxidative stress-induced illnesses, and inflammation are significant worldwide health issues. The World Health Organization (2021) estimates that noncommunicable diseases (NCDs) cause more than 70% of all fatalities globally, with diabetes alone accounting for almost 1.5 million deaths annually. Oxidative stress, which is characterized by an excess of reactive oxygen species (ROS), is a key mediator that sets off inflammatory cascades, interferes with insulin signalling, and encourages metabolic and cellular dysfunction. These diseases frequently share interrelated biochemical pathways [1,2,3]. These illnesses are particularly harmful to older people and those who also have autoimmune, metabolic, or cardiovascular diseases.

The oxidation of biomolecules and the pathophysiology of chronic diseases including type 2 diabetes, atherosclerosis, and neurodegeneration are caused by oxidative stress, which occurs when the production of ROS surpasses the body's natural antioxidant defences [3]. At the same time, inflammation, which is characterized by the overexpression of cytokines like interleukin-1β (IL-1β) and tumour necrosis factor-α (TNF-α) as well as enzymes like cyclooxygenase-2 (COX-2), makes cellular damage even worse. Persistent hyperglycaemia in diabetes, especially type 2, is caused by insulin resistance and β-cell dysfunction, both of which are made worse by oxidative and inflammatory imbalances [4].

Despite their widespread use, synthetic medications like NSAIDs (anti-inflammatory drugs), metformin and gliptins (antidiabetic), and synthetic antioxidants are frequently linked to drawbacks like adverse effects, excessive prices, drug resistance, and low compliance, particularly in developing nations [5]. This has led to a rise in interest in natural chemicals derived from plants that have the ability to function on a variety of therapeutic targets with no harm. Flavonoids, alkaloids, terpenoids, and phenolic acids are examples of phytochemicals that have shown encouraging effects against diabetes, inflammation, and oxidative stress [6,7,8].

Many traditional medical systems use the genus *Thalictrum* (family Ranunculaceae) to treat inflammatory diseases, wounds, fever, and infections. One of its members, *Thalictrum dalzellii,* is an endemic and rare species that is indigenous to India's Western Ghats and has a long history of use in traditional medicine. It is still not well understood scientifically, nevertheless, with limited knowledge of its molecular methods of action or phytochemical makeup. Using contemporary methods to unlock its bioactive potential may provide new drug discovery leads.

By making it possible to quickly and affordably analyse how natural products interact with disease-related protein targets, advances in computational biology and *in silico* drug discovery have completely changed the screening process. Important early insights into the pharmacological potential of plant compounds are provided by tools including drug-likeness evaluation, ADMET (Absorption, Distribution, Metabolism, Excretion, and Toxicity) prediction, and molecular docking [9,10]. These methods are especially useful for finding multitarget agents that interact with enzymes like aldose reductase, α-glucosidase, and α-amylase (antidiabetic pathway), COX-2 and TNF-α (inflammatory pathway), superoxide dismutase (SOD) and the Nrf2/Keap1 complex (antioxidant pathway), and others [11,12,13].

Through *in silico* molecular docking with iGEMDOCK, the current study seeks to assess the phytochemicals from *T. dalzellii*'s multitarget medicinal potential. Twelve protein targets linked to diabetes, inflammation, and oxidative stress were docked with bioactive chemicals found by GC-MS analysis. In order to evaluate their safety and appropriateness as treatment phytochemicals, their pharmacokinetic profiles were also inspected using ADMET and drug-likeness filters. The

logical discovery of plant-derived, multitarget therapeutic leads for the treatment of complicated metabolic illnesses is supported by this integrated computational technique.

2. Materials and Methods

2.1 Choosing bioactive substances for *in-silico* examination

To determine the phytochemical components of *T. dalzellii*, GC-MS analysis was performed on the methanol extract. After identifying the compounds, a thorough review of the literature was done to narrow down the list of phytochemicals that were thought to have anti-diabetic, anti-inflammatory, and antioxidant properties. Their structural traits, biological significance, and previously documented, capacity to interact with particular protein targets linked to oxidative stress, inflammation, and diabetes are considered as the basis for the selection. Based on their matching target proteins. Based on the literature, selected 03 oxidant proteins (1CB4, 3P31, 1DNU), inflammatory proteins (3CTT, 3W37, 1DPU) and diabetic proteins/ enzymes (1FM6, 2HWQ, 1CB4) for the present study. The methanol extract of *T. dalzellii* yielded 29 phytochemicals. The study was not used all the phytochemicals against all the oxidant, inflammatory and diabetic proteins/ enzymes. Nine phytochemicals for 1CB4, 10 phytochemicals for 2P31, 9 phytochemicals for 1DNU, 10 phytochemicals for 3W37 and 3CTT, 8 phytochemicals for 1DNU, 9 phytochemicals for 1FM6 and 2HWQ.

Three common reference drugs were used in the investigation to compare the docking performance of the chosen phytocompounds: metformin (antidiabetic), ampicillin (anti-inflammatory), and ascorbic acid (antioxidant). These medications were used as positive controls to assess the plant-derived compounds binding effectiveness and interaction patterns.

2.2 ADMET and Drug-Likeness Analysis

All selected plant secondary metabolites were screened using online tools such as admetSAR (http://lmmd.ecust.edu.cn/admetsar1/) and Molsoft (https://www.mn-am.com/online_demos/corina_demo) to evaluate their Absorption, Distribution, Metabolism, Excretion, and Toxicity (ADMET) profiles, along with drug-likeness properties [14]. From this analysis, compounds can be identified as non-toxic, non-carcinogenic, and exhibiting favourable drug-like characteristics.

2.3 Preparation of ligand structures

By copying the canonical SMILES of each compound from the PubChem database, the Novoprolabs an online 3D structure building tool (https://www.novoprolabs.com/tools/smiles2pdb) was used to create the 3D structures of the chosen phytochemicals. Subsequent molecular docking investigations were conducted using the derived PDB data.

2.4 Selection, Preparation, and Retrieval of Proteins

A total of 9 human protein targets associated with oxidative stress, inflammation, and diabetes were selected for molecular docking studies based on an extensive literature review. These proteins represent critical molecular targets involved in reactive oxygen species regulation, inflammatory signalling, and glucose metabolism, making them highly relevant for antioxidant, anti-inflammatory, and antidiabetic therapeutic screening.

2.5 Protein Structure Retrieval and Pre-processing for *In-Silico* Studies

The corresponding 3D crystal structures were retrieved in PDB format from the RCSB Protein Data Bank (https://www.rcsb.org). Each protein structure was pre-processed by removing water molecules within 3 Å of heteroatoms and any co-crystallized ligands or ions using molecular visualization tools. This step ensured the accurate simulation of binding interactions during docking analysis. The list of selected proteins along with their PDB IDs and biological roles is presented (Table 1).

Table 1. Protein Structure Retrieval and Pre-processing for *In-Silico* Studies

PDB ID	Protein Name	Biological Function/Role
Antioxidant proteins		
1CB4	Copper–zinc superoxide dismutase (bovine Cu/Zn SOD)	Catalyzes conversion of superoxide radicals (O_2^-) into O_2 and H_2O_2, protecting cells from oxidative stress
2P31	Human glutathione peroxidase 7 (GPx7)	Reduces H_2O_2 and organic hydroperoxides, helping maintain redox balance
1DNU	Human myeloperoxidase (MPO) complex with cyanide	Generates reactive species (e.g., hypochlorous acid) during immune response; can contribute to oxidative damage in inflammation
Anti-inflammatory proteins		
3CTT	N-terminal domain of human maltase–glucoamylase complexed with casuarine	Involved in starch digestion; target for anti-inflammatory design via inhibiting related glycosidases
3W37	Sugar beet α-glucosidase bound to acarbose	Mimics human α-glucosidase – digests carbohydrates; inhibition reduces glucose absorption (antidiabetic strategy)
1DPU	Assumed structure for TNF-α protein – user platelet	Tumor necrosis factor-α, a cytokine central to inflammation and immune signalling
Anti-diabetic proteins		
1FM6	Human PPARγ–RXRα ligand-binding domains heterodimer with rosiglitazone (TZD)	Nuclear receptor regulating glucose/lipid metabolism; TZDs are antidiabetic agents
2HWQ	Human PPARγ ligand-binding domain complexed with indole-based agonist	Shows structural basis for PPARγ activation – relevant for antidiabetic drug development
1CB4	Copper–zinc superoxide dismutase (bovine Cu/Zn SOD)	Catalyses conversion of superoxide radicals (O_2^-) into O_2 and H_2O_2, protecting cells from oxidative stress

2.6 Molecular Docking Studies

Docking studies were conducted using iGEMDOCK v2.1 software. Parameters were set with a population size of 200, 70 generations, and two final solutions per docking run. Each of the 10 plant-derived compounds were individually docked against the 3 selected antioxidant, anti-inflammatory and anti-diabetic target proteins. Additionally, standard drugs (metformin (antidiabetic), ampicillin (anti-inflammatory), and ascorbic acid (antioxidant)) were included for comparative docking.

Interaction Studies and Identification of Binding Residues Post-docking analyses were performed using iGEMDOCK v2.1 to study ligand-protein interactions, identify interacting amino acids, and assess binding energy components including van der Waals forces and hydrogen bonding. To improve accuracy, docking was repeated in four independent rounds. The results were validated and visualized using Biovia discovery studio visualizer software to confirm amino acid interactions at the active sites [15].

3. Results

3.1. GC-MS Analysis and Phytochemical Selection

The methanolic extract of *T. dalzellii* was analysed using GC-MS, which led to the identification of bioactive compounds. These compounds include a variety of phenolics, flavonoids, terpenoids, alkaloids, and fatty acid derivatives, many of which have been previously reported for their pharmacological relevance. Based on their chemical nature, structural diversity, and available literature, these compounds were shortlisted for further evaluation of their therapeutic potential against oxidative stress, inflammation, and diabetes. Canonical SMILES of all compounds were retrieved from the PubChem database and converted into 3D PDB format using Novoprolabs (https://www.novoprolabs.com/tools/smiles2pdb) for molecular docking (Table 2).

Table 2. The major phytocompounds detected in the methanol extract of *Thalictrum dalzellii* by GC-MS analysis

Identified compounds	Retention time
Phenol, 2-methoxy-	7.670
Undecane	7.840
Catechol	9.249
Dodecane	9.345
Undecane, 2,6-dimethyl-	9.530
3-Ethenylphenol	9.597
Propanoic acid, 2-[(trimethylsilyl)oxy]-, ethyl ester	9.880
Hydroquinone	10.361
Dodecane, 2,6,11-trimethyl-	10.780
7-Hydroxycoumarin	10.948
Phenol, 2,6-dimethoxy-	11.433
3-Deoxy-d-mannoic lactone	14.525
Dodecanoic acid, 3-hydroxy-	14.828
n-Decanoic acid	15.396
Neophytadiene	17.461
Neophytadiene	18.111
Hexadecanoic acid, methyl ester	18.811
n-Hexadecanoic acid	19.351
3,7,11,15-Tetramethyl-2-hexadecen-1-ol	21.887
Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	28.388
Octadecanoic acid, 2,3-dihydroxypropyl ester	31.502
24-Noroleana-3,12-diene	35.757
Isoschizogamine	38.270
(3S,8S,9S,10R,13R,14S,17R)-17-((2R,5R)-5-Ethyl-6-methy	39.436

3.2. ADMET and Drug-Likeness Profiling

To ensure drug-likeness and safety, the selected phytochemicals were evaluated using admetSAR and Molsoft platforms. Key pharmacokinetic and toxicological parameters were assessed, absorption: most compounds exhibited high gastrointestinal (GI) absorption, distribution: several compounds showed favourable blood-brain barrier permeability, metabolism: many compounds were non-inhibitors of major CYP450 enzymes, reducing drug–drug interaction risk and excretion and toxicity: The majority were non-carcinogenic, non-mutagenic, and non-hepatotoxic.

Drug-likeness was assessed using Lipinski's Rule of Five, with over 80% of the compounds meeting acceptable criteria in terms of molecular weight, hydrogen bond acceptors/donors, and logP values. These results indicated that the compounds were suitable for further computational screening (Table 2, Table 3, Fig 1 and SF 1)

Table 3. Predicted molecular and drug-relevant properties of bioactives

Sl. No.	Compound Name	Molecular Formula	Mol. Wt	logP	logS	HBD	HBA	TPSA	Rot. Bonds	pKa	Stereo Centers
1	Ascorbic acid	$C_6H_8O_6$	175.12	-2.06	-1.13	4	6	110.05	2	4.17	4
2	AMP	$C_{10}H_{14}N_5O_7P$	347.22	-2.51	-2.98	6	10	192.92	6	1.00	3
3	Ampicillin	$C_{16}H_{19}N_3O_4S$	349.41	-1.39	-3.50	4	7	134.80	5	2.55	3
4	Metformin	$C_4H_{11}N_5$	129.16	-1.43	-1.10	3	5	91.49	3	12.40	0
5	Isoschizogamine	$C_{27}H_{39}NO_4$	441.57	4.71	-5.20	0	4	47.56	2	7.82	2
6	3-Ethylene phenol	$C_8H_{10}O$	122.17	1.69	-2.16	1	1	20.23	2	10.00	0
7	Phytol	$C_{20}H_{40}O$	296.53	8.18	-6.30	1	1	20.23	16	15.00	1

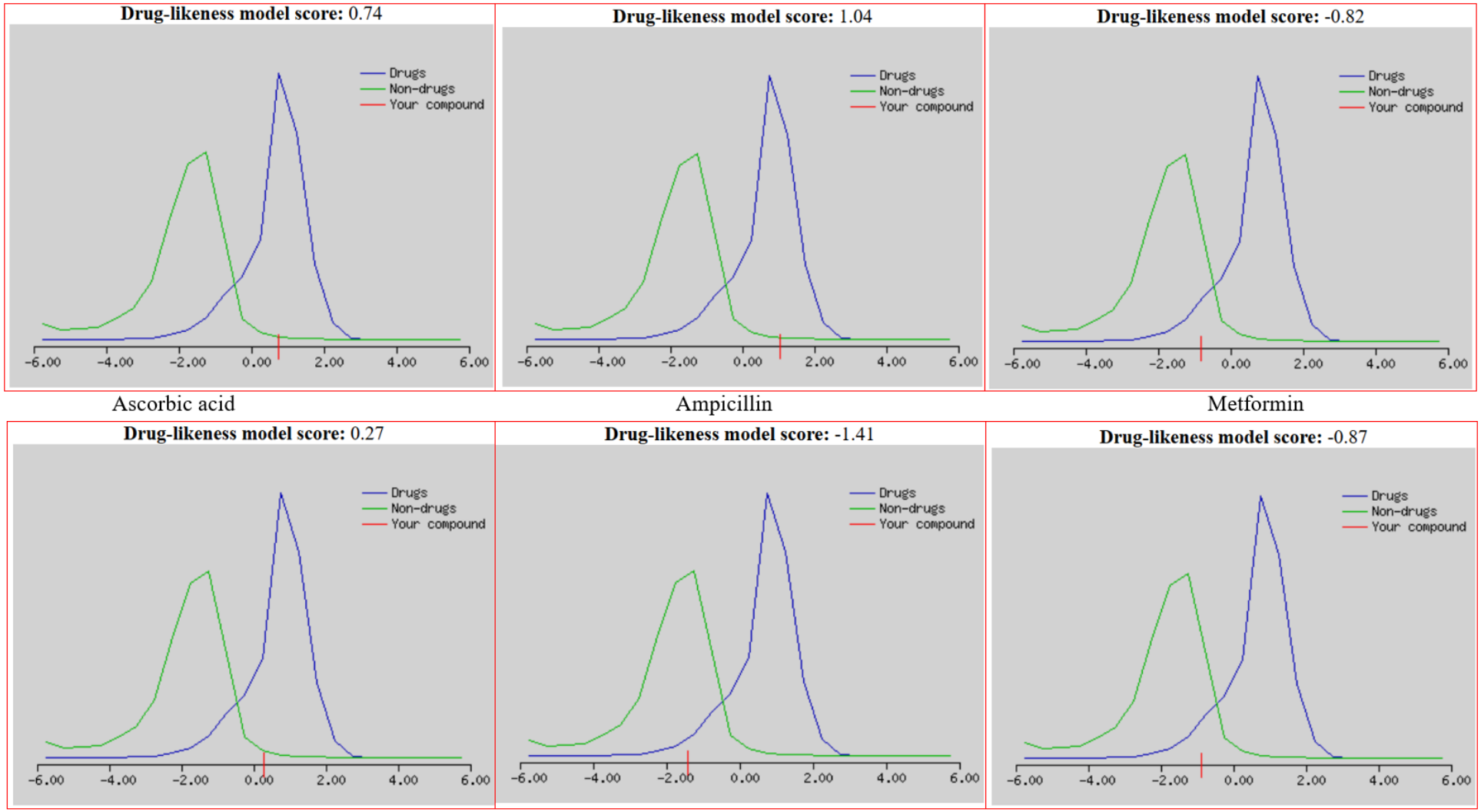

Fig 1. Drug-likeness model scores of selected standard and phytochemical compounds.

Table 4. ADMET-SAR Predicted Properties of Selected Phytochemical Compounds from *T. dalzellii*

Property	3-ethylene phenol	Phenol, 2-methoxy-	Catechol	Dodecane	Undecane, 2,6-dimethyl-	Propanoic acid	Hydroquinone	7-Hydroxycoumarin	Phenol, 2,6-dimethoxy
ABSORPTION									
Blood-Brain Barrier	BBB+	BBB+	BBB+	BBB+	BBB+	BBB+	BBB+	BBB+	BBB+
Human Intestinal Absorption	HIA+	HIA+	HIA+	HIA+	HIA+	HIA+	HIA+	HIA+	HIA+
Caco-2 Permeability	$CaCo^{2+}$	$CaCo^{2+}$	$CaCo^{2+}$	$CaCo^{2+}$	$CaCo^{2+}$	$CaCo^{2+}$	$CaCo^{2+}$	$CaCo^{2+}$	$CaCo^{2+}$
P-glycoprotein Substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate
P-glycoprotein Inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
Renal Organic Cation Transporter	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
DISTRIBUTION									
Sub cellular localisation	Lysosome	Mitochondria	Mitochondria	Lysosome	Lysosome	Mitochondria	Mitochondria	Mitochondria	Mitochondria
METABOLISM									
CYP450 2C9 Substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate
CYP450 2D6 Substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate
CYP450 3A4 Substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate
CYP450 1A2 Inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Inhibitor	Non-inhibitor
CYP450 2C9 Inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
CYP450 2D6 Inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
CYP450 2C19 Inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
CYP450 3A4 Inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor

CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity
EXCRETION AND TOXICITY									
Human Ether-a-go-go-Related Gene Inhibition	Weak inhibitor	Weak inhibitor	Weak inhibitor	Weak inhibitor	Weak inhibitor	Weak inhibitor	Weak inhibitor	Weak inhibitor	Weak inhibitor
Inhibition	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
AMES Toxicity	Non AMES toxic	Non AMES toxic	Non AMES toxic	Non AMES toxic	Non AMES toxic	Non AMES toxic	Non AMES toxic	Non AMES toxic	Non AMES toxic
Carcinogens	Non-carcinogens	Non-carcinogens	Non-carcinogens	Carcinogens	Carcinogens	Carcinogens	Non-carcinogens	Non-carcinogens	Non-carcinogens
Fish Toxicity	Low FHMT	Low FHMT	High FHMT	High FHMT	High FHMT	Low FHMT	Low FHMT	High FHMT	High FHMT
Tetrahymena Pyriformis Toxicity	Low TPT	High TPT	High TPT	High TPT	High TPT	Low TPT	High TPT	High TPT	High TPT
Honey Bee Toxicity	Low HBT	High HBT	High HBT	High HBT	High HBT	High HBT	High HBT	High HBT	High HBT
Biodegradation	Not Ready biodegradable	Ready biodegradable	Ready biodegradable	Ready biodegradable	Ready biodegradable	Ready biodegradable	Ready biodegradable	Not ready biodegradable	Ready biodegradable
Acute Oral Toxicity	III	III	II	III	IV	III	II	III	III
Carcinogenicity (Three-class)	Non-required	Warning	Warning	Non-required	Non-required	Non-required	Non-required	Non-required	Non-required
ADMET PREDICTED PROFILE REGRESSION									
Aqueous solubility	1.5176	-1.4088	-0.0276	-5.1776	-5.7639	0.6067	-0.2325	-2.7456	-1.8467
Caco-2 Permeability	1.2751	1.5094	1.1463	1.3807	1.3295	1.1352	1.5782	1.3028	1.3655
Rat Acute Toxicity	1.0771	2.3338	2.5957	1.3444	1.1867	1.4864	2.0465	2.2141	2.4169
Fish Toxicity	3.2563	1.6594	1.0318	-0.7109	-0.5110	3.5551	1.8853	0.9978	1.6634
Tetrahymena Pyriformis Toxicity	-1.1131	-0.3850	0.6327	0.3450	0.9346	-0.6348	0.3447	0.3612	-0.2323

Property	Hexadecanoic acid, methyl ester	n-Hexadecanoic aciD	3,7,11,15-Tetramethyl-2-hexadecen-1-ol	24-Noroleana-3,12-diene	3-deoxy-D manioc lactone	Neophytadiene	Isoscoleptin	Octadecanoic acid
ABSORPTION								
Blood-Brain Barrier	BBB+	BBB+	BBB+	BBB+	BBB+	BBB+	BBB+	BBB+
Human Intestinal Absorption	HIA+	HIA+	HIA+	HIA+	HIA+	HIA+	HIA+	HIA+
Caco-2 Permeability	Caco2+	Caco2+	Caco2+	Caco2+	Caco2-	Caco2+	Caco2+	Caco2+
P-glycoprotein Substrate	Non-substrate	Non-substrate	Non-substrate	Substrate	Non-substrate	Non-substrate	Substrate	Non-substrate
P-glycoprotein Inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
Renal Organic Cation Transporter	Non-inhibitor	Non-inhibitor	Non-inhibitor	Inhibitor	Non-inhibitor	Inhibitor	Non-inhibitor	Non-inhibitor
DISTRIBUTION								
Sub cellular localisation	Mitochondria	Mitochondria	Lysosome	Lysosome	Mitochondria	Nucleus	Mitochondria	Mitochondria
METABOLISM								
CYP450 2C9 Substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate
CYP450 2D6 Substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate
CYP450 3A4 Substrate	Non-substrate	Non-substrate	Non-substrate	Substrate	Non-substrate	Non-substrate	Non-substrate	Non-substrate
CYP450 1A2 Inhibitor	Non-inhibitor	Inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Inhibitor	Inhibitor
CYP450 2C9 Inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
CYP450 2D6 Inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
CYP450 2C19 Inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
CYP450 3A4 Inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity	Low CYP Inhibitory Promiscuity
EXCRETION AND TOXICITY								
Human Ether-a-go-go-Related Gene Inhibition	Weak inhibitor	Weak inhibitor	Weak inhibitor	Weak inhibitor	Weak inhibitor	Weak inhibitor	Weak inhibitor	Weak inhibitor
Inhibition	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor	Non-inhibitor
AMES Toxicity	Non AMES toxic	Non AMES	Non AMES toxic	Non AMES	Non AMES	Non AMES	Non AMES	Non AMES toxic

		toxic		toxic	toxic	toxic	toxic	
Carcinogens	Carcinogens	Non-carcinogens	Non-carcinogens	Non-carcinogens	Non-carcinogens	Carcinogens	Non-carcinogens	Non-carcinogens
Fish Toxicity	High FHMT	High FHMT	High FHMT	High FHMT	High FHMT	High FHMT	High FHMT	High FHMT
Tetrahymena Pyriformis Toxicity	High TPT	High TPT	High TPT	High TPT	High TPT	High TPT	High TPT	High TPT
Honey Bee Toxicity	High HBT	High HBT	High HBT	High HBT	High HBT	High HBT	High HBT	High HBT
Biodegradation	Ready biodegradable	Ready biodegradable	Ready biodegradable	Not ready biodegradable	Ready biodegradable	Ready biodegradable	Not ready biodegradable	Ready biodegradable
Acute Oral Toxicity	III	IV	III	III	III	III	III	IV
Carcinogenicity (Three-class)	Non-required	Non-required	Non-required	Non-required	Non-required	Warning	Non-required	Non-required
ADMET PREDICTED PROFILE REGRESSION								
Aqueous solubility	-3.3987	-3.5022	-2.4720	-5.2150	0.2218	-5.2549	-3.3060	-3.5022
Caco-2 Permeability	1.2386	1.3950	1.2481	1.7921	0.1507	1.3417	0.9465	1.3950
Rat Acute Toxicity	1.4915	1.3275	1.6146	1.4459	1.4924	1.4720	2.6022	1.3275
Fish Toxicity	0.8236	1.8920	0.6732	-0.8936	2.8207	-0.8334	0.2623	1.8920
Tetrahymena Pyriformis Toxicity	0.6648	0.3852	1.0249	1.3037	-1.1537	0.9633	0.6538	0.3852

3.3. Molecular Docking with Disease-Related Targets

Molecular docking studies were performed using iGEMDOCK v2.1, where the 12 selected phytochemicals were docked against 9 protein targets implicated in antioxidant, anti-inflammatory, and antidiabetic pathways. Three standard drugs ascorbic acid, ampicillin, and metformin were included as reference compounds and also for comparison.

3.3.1. Antioxidant Target Binding

Molecular docking analysis of selected antioxidant compounds revealed several promising interactions with the target proteins 1CB4, 2P31, and 1DNU.

For 1CB4 (superoxide dismutase), Isoschizogamine showed the strongest binding energy of -80.47 kcal/mol, forming hydrogen bonds with Asp-A:25, Thr-A:26, and Ala-A:22. Phenol, 2-methoxy- also exhibited good binding energies of -61.66 kcal/mol respectively, interacting with residues such as Val-A:5, and Val-A:7 (Table 5, Fig 2, SF 2)

For 2P31 (peroxiredoxin-5), Phenol, 2-methoxy- was the top binder with –75.12 kcal/mol and formed hydrogen bonds with Lys-A:98, Glu-A:99, Ser-102, Glu-B:99, and Phe-B:103. 24-Noroleana-3,12-diene and Catechol also showed notable affinities (-67.13 and -55.16 kcal/mol), interacting with His-B:63 and Gln-B:62 (Table 6, SF 3,4 and 5)

In the case of 1DNU (thioredoxin reductase/myeloperoxidase), Isoscopoletin showed the best binding energy of -66.99 kcal/mol, with hydrogen bond interactions involving Pro-A:57, Lys-C:129, Leu-A:60 and Ala-A:63. Phenol, 2-methoxy- followed closely (-52.64 kcal/mol), interacting with Val-A:58, GLN-C:467, Ala-:59, Leu-A:60 and Pro-A:57 (Table 7, and SF 6 and 7).

These interactions suggest that the antioxidant mechanism of these compounds may involve direct binding and modulation of key redox-related enzyme

Table 5. Docking Scores and Binding Interactions of Ligands with Target Protein-1CB4

1CB4	Energy	VDW	H bond	Elec	Interacting amino acids
Hydroquinone	-43.42	-43.42	0	0	Ala-A:1, Leu-A:104, Ala-A:22
Catechol	-40.75	-40.75	0	0	Ala-A:22, Leu-A:104, Asp-A:25
7-Hydroxycoumarin	-61.06	-61.06	0	0	Asp-A:83, Asp-A:126, Arg-A:143, Lys-A:136
Isoschizogamine	-80.47	-75.54	-4.93	0	Asp-A:25, Thr-A:26, Ala-A:22
3-Ethenylphenol	-50.79	-50.79	0	0	Val-A:5,Val-A:7
Phenol, 2-methoxy-	-61.66	-56.45	-5.21	0	Val-A:7, Val-A:5
3-Deoxy-D-mannoic lactone	-52.31	-47.81	-4.5	0	Val-A:146, Val-A:7
(3S,8S,9S,10R,13R,14S,17R)-Steroid-like compound	-69.97	-69.97	0	0	Val-A:7, Val-A:146, Val-A:9
Phenol, 2,6-dimethoxy-	-53.18	-44.76	-8.42	0	Interaction not shown
Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	-58.91	-58.91	0	0	Val-A:7, Val-A:9, Val-A:146

Table 6. Docking Scores and Binding Interactions of Ligands with Target Protein-2P31

2P31	Energy	VDW	Hbond	Elec	Interacting amino acids
n-hexadecanoic acid	-58.33	-58.33	0	0	Lys-B:29, Pro-B:127, His-B:126, ILE-B:118, Ala-B:30, Val-B:31
Hexadecenoic acid	-56.044	-53.54	-2.5	0	Lys-B:117, Ser-B:116, Val-B:31, His-B:126, Ile-B:118, Ala-B:119
Octadecanoic acid, 2,3-dihydroxypropyl ester	-63.801	-63.16	-0.637	0	Arg-B:177, His-B:73, Pro-B:151, Ala-B:150
3,7,11,15-Tetramethyl-2-hexadecen-1-ol	-57.71	-57.71	0	0	Interaction not shown
Catechol	-55.16	-55.16	0	0	Ser-B:102, Ser-A:102, Thr-B:102
Phenol, 2-methoxy- (Guaiacol)	-75.12	-66.62	-8.5	0	Lys-A:98, Glu-A:99, Ser-A:102, Glu-B:99, Phe-B:103
Hexadecanoic acid, 2-hydroxy-1-(hydroxymethyl)ethyl ester	-56.08	-53.28	-2.5	0	Val-A:7, Val-A:9, Val-A:146
24-Noroleana-3,12-diene	-67.13	-67.13	0	0	His-B:63, Gln-B:62
Undecane, 2,6-dimethyl-	-50.1	-50.1	0	0	His-A:63, Val-A:165, Ala-A:66, Arg-A:65
n-hexadecanoic acid	-58.33	-58.33	0	0	Lys-B:29, Pro-B:127, His-B:126, ILE-B:118, Ala-B:30, Val-B:31

Table 7. Docking Scores and Binding Interactions of Ligands with Target Protein-1DNU

1DNU	Energy	VDW	Hbond	Elec	Interacting amino acids
catechol	-36.91	-36.91	0	0	Pro-A:57
Hexadecanoic acid	-42.64	-39.22	-3.42	0	Pro-A:57, Leu-A:60, Val-A:58, Ala-A:59, Val-A:64
Phenol, 2-methoxy-	-52.64	-40.41	-12.23	23.81	Val-A:58, GLN-C:467, Ala-A:59, Pro-A:57, Leu-A:60
n-Hexadecanoic acid (Palmitic acid)	-49.1	-49.1	0	0	Pro-A:57, Val-A:58, Leu-A:60, GLN-C:467
3,7,11,15-Tetramethyl-2-hexadecen-1-ol (Phytol)	-53.1	-53.1	0	0	CLN-C:467, Pro-A:57, Leu-A:60, Ala-A:63, Val-A:58
Octadecanoic acid, 2,3-dihydroxypropyl ester (Glyceryl stearate)	-57.65	-57.65	0	0	Val-A:58, Ala-A:59, Val-A:64. Tyr-C:468, Ala-A:61, Lys-C:129, Leu-A:60
24-Noroleana-3,12-diene	-66.41	-66.41	0	0	Pro-A:57, Lys-C:129, Leu-A:60
Dodecanoic acid (Lauric acid)	-47.57	-47.57	0	0	Pro-A:57, Val-A:58, Leu-A:60
Isoscopoletin	-66.99	-63.45	-3.5	0	Pro-A:57, Lys-C:129, Ala-A:63, Leu-A:60
catechol	-36.91	-36.91	0	0	Pro-A:57

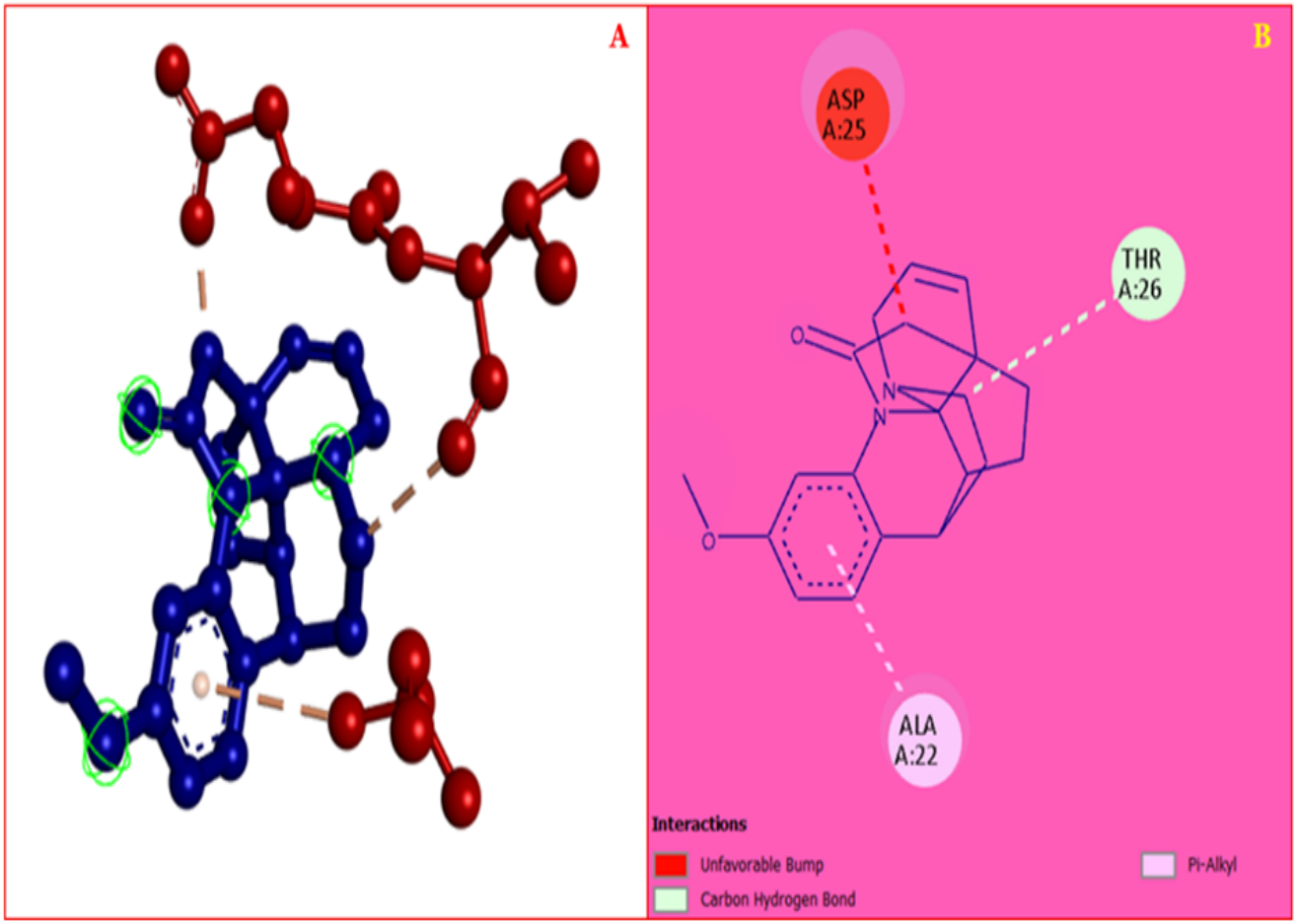

Figure 2. Molecular interaction of Isoschizogamine with 1CB4 protein A:3D binding pose B: 2D interaction diagram

3.3.2. Anti-inflammatory Target Binding

Molecular docking against three anti-inflammatory targets COX-2 (PDB IDs: 3CTT, 3W37) and TNF-α (1DPU) identified several ligands with strong binding potential. In the case of 3CTT, 3-Ethenylphenol exhibited the best binding affinity with a total energy of -71.09 kcal/mol and hydrogen bonding energy of -8.83 kcal/mol, interacting primarily with Arg-A:308. Similarly, Phenol, 2-methoxy showed good binding (-52.67 kcal/mol, H-bond: -12.31 kcal/mol) interactions with Asp-A:305, Arg-A:308, and Glu-A:363. 7-Hydroxycoumarin (-51.31 kcal/mol) also displayed favourable interaction with Arg-A:308 (Table 8, Fig 3, SF 8 and 9)

For 3W37, Phenol, 2-methoxy emerged as the top compound with a total energy of -64.16 kcal/mol and -6.17 kcal/mol hydrogen bonding, forming interactions with Tyr-A:427, Leu-A:429, and Pro-A:435. Neophytadiene followed with -51.05 kcal/mol, binding at pro-A:426, tyr-A:427, leu-A:429, Pro-A:435, Gly-A:429. These interactions were mainly stabilized by vander Waals and hydrophobic contacts (Table 9, SF 10 and 11).

Against 1DPU (TNF-α), Neophytadiene showed highest docking score of -63.76 kcal/mol, forming stable interactions with residues including Val-A:246, Phe-A:227, Lys-A:231, IleA:242, Ile-A:216, Ile-A:230, Val-A:212, Leu-A:234 and Met-A:237. Phenol, 2,6-dimethoxy also showed strong affinity (–59.32 kcal/mol, H-bond:-12.43 kcal/mol), though specific residues were not detailed. Additionally, n-Hexadecanoic acid presented significant binding (-59.03 kcal/mol), interacting with Met-A:237, Ile-A:242, and Val-A:2469 (Table 10, SF 12,13 and 14)

These results highlight the potential of *T. dalzellii* compounds in modulating inflammatory cytokine actives.

Table 8. Docking Scores and Binding Interactions of Ligands with Target Protein-3CTT

3CTT	Energy	VDW	Hbond	Elec	Interacting amino acids
3,7,11,15-Tetramethyl-2-hexadecen-1-ol	**Docking not shown**				Arg-A:306, Leu-A:304
7-Hydroxycoumarin	-51.31	-51.31	0	0	Arg-A:308, Leu-A:304
Phenol, 2,6-dimethoxy-	-52.69	-40.45	-12.23	0	Asp-A:305, Glu-A:353
Neophytadiene	-39.35	-39.35	0	0	Leu-A:304, Arg-A:308
Hexadecanoic acid, methyl ester	Docking not shown				Glu-A:353, Leu-A:304, Phe-A:350, Arg-A:308
n-Hexadecanoic acid	-49.09	-49.09	0	0	Leu-A:304, Arg-A:308
Catechol	-36.9	-36.9	0	0	Arg-A:308, Glu-A:353
Hydroquinone	-39.91	-39.91	0	0	Arg-A:308
3-Ethenylphenol	-71.09	-62.27	-8.83	0	Arg-A:308
Phenol, 2-methoxy-	-52.67	-40.36	-12.31	0	Asp-A:305, Arg-A:308, Phe-A:360, Glu-A:363

Table 9. Docking Scores and Binding Interactions of Ligands with Target Protein-3W37

3W37	Energy	VDW	Hbond	Elec	Interacting amino acids
Phytol (3,7,11,15-Tetramethyl-2-hexadecen-1-ol)	Docking not shown				Pro-A:435, Leu-A:428
7-Hydroxycoumarin	-45.97	-45.97	0	0	Leu-A:428
Phenol, 2,6-dimethoxy-	-46.15	-30.01	-16.14	0	Pro-A:435, Leu-A:428
Neophytadiene	-51.05	-51.05	0	0	Leu-A:429, Ile-A:477, Tyr-A:437
Hexadecanoic acid, methyl ester	-44.85	-26.94	-17.92	0	Leu-A:428, Tyr-A:427
n-Hexadecanoic acid (Palmitic acid)	-48.82	-48.82	0	0	Leu-A:428, Ter-A:430
Catechol	-34.3	-34.3	0	0	Leu-A:428
Hydroquinone	-34.25	-34.25	0	0	Leu-A:428
3-Ethenylphenol	-37.44	-34.44	0	0	Leu-A:428
Phenol, 2-methoxy- (Guaiacol)	-64.16	-57.45	-6.17	0	Pro-A:426, Tyr-A:427, Leu-A:429, Pro-A:435, Gly-A:429

Table 10. Docking Scores and Binding Interactions of Ligands with Target Protein-1DPU

1DPU	Energy	VDW	Hbond	Elec	Interacting amino acids
3,7,11,15-Tetramethyl-2-hexadecen-1-ol	-69.12	-69.12	0	0	Gln-C:467, Pro-A:57, Leu-A:60, Val-A:58
7-Hydroxycoumarin	-51.32	-51.32	0	0	Val-A:58, Leu-A:60, Pro-A:57
Propanoic acid, 2-[(trimethylsilyl)oxy]-, ethyl ester	-30.68	-30.68	0	0	Pro-A:57, Leu-A:60
Neophytadiene	-39.37	-39.37	0	0	Ala-A:63, Val-A:58, Leu-A:60, Pro-A:57
n-Hexadecanoic acid	-49.12	-49.12	0	0	Ala-A:57, Val-A:58, Leu-A:60, Pro-A:57
3-Deoxy-D-mannoic lactone	-51.7	-46.08	-5.61	0	Val-A:58
Phenol, 2-methoxy-	-51.59	-43.94	-7.65	0	Ala-A:59, Pro-A:57, Val-A:58, Gln-C:467, Leu-A:60
24-Noroleana-3,12-diene	-66.42	-66.42	0	0	Lya-C:129, Leu-A:60, Pro-A:57
3,7,11,15-Tetramethyl-2-hexadecen-1-ol	-69.12	-69.12	0	0	Gln-C:467, Pro-A:57, Leu-A:60, Val-A:58
7-Hydroxycoumarin	-51.32	-51.32	0	0	Val-A:58, Leu-A:60, Pro-A:57

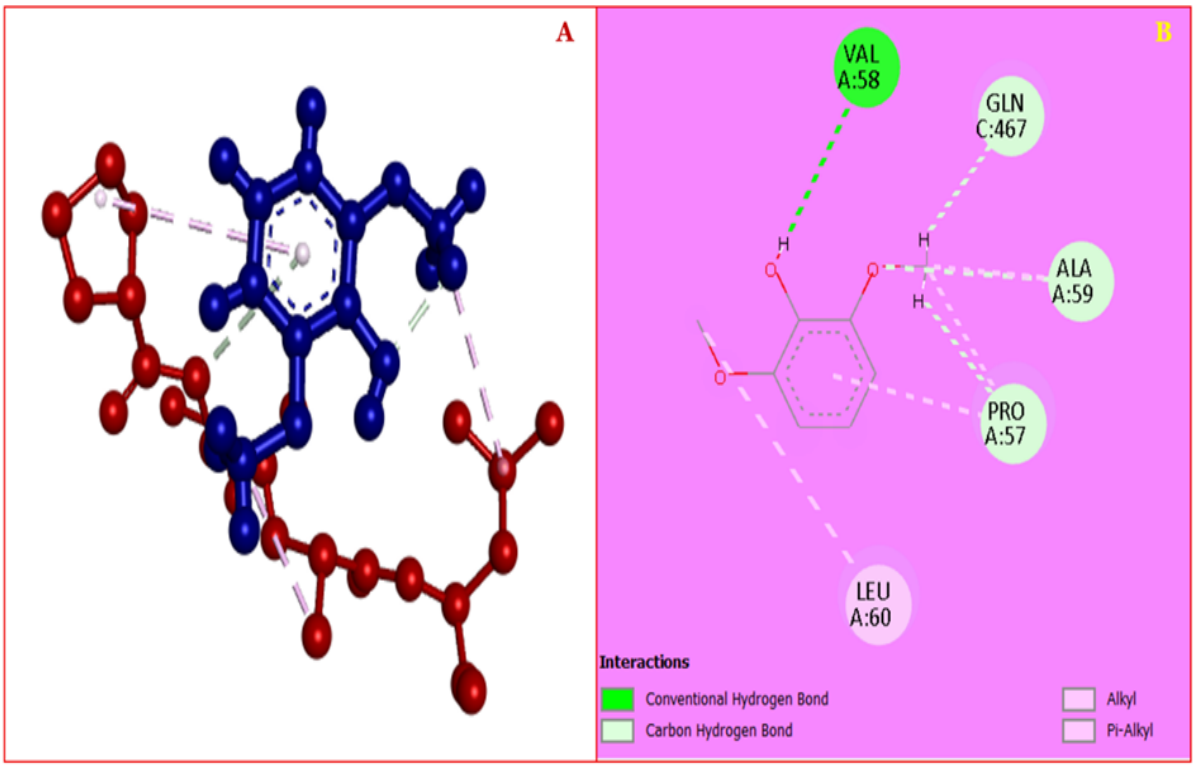

Figure 3. Molecular interaction of 3-Ethenylphenol with 3CTT protein A:3D binding poses B: 2D interaction diagram

3.3.3. Antidiabetic Target Binding

Molecular docking studies were performed on selected phytochemicals against three key protein targets: aldose reductase (1DNU), cyclooxygenase-2 (1FM6), and 2HWQ. The results were analyzed based on binding energy, hydrogen bonding potential, and interaction with active site amino acid residues.

For 1DNU, the compound 3,7,11,15-tetramethyl-2-hexadecen-1-ol showed the most favourable binding affinity, with a binding energy of -69.12 kcal/mol, interacting predominantly with Gln-C:467, Pro-A:57, Leu-A:60, and Val-A:58. This suggests a strong and stable interaction within the active site. Although phenol, 2-methoxy exhibited a less negative energy value (-51.59 kcal/mol), it demonstrated significant hydrogen bonding (H-bond energy: -7.65 kcal/mol) with Ala-A:59, Pro-A:57, Val-A:58, Gln-C:467, and Leu-A:60, indicating enhanced binding specificity. Similarly, 3-deoxy-D-mannoic-lactone showed moderate binding (-51.70 kcal/mol) with H-bond formation involving Val-A:58 (Table 11, Fig 4 and SF 15 and 16).

In the case of 1FM6, phenol, 2,6-dimethoxy- emerged as the top binder, with a binding energy of -71.25 kcal/mol and a notable hydrogen bond energy of -10.42 kcal/mol, interacting with Ala-A:387, Pro-A:378, and Glu-A:390. This strong H-bonding underscores its potential as an effective COX-2 inhibitor. 7-hydroxycoumarin closely followed with a similar energy value (-71.08 kcal/mol) but lacked hydrogen bonding. Other compounds like neophytadiene and n-hexadecanoic acid also displayed reasonable binding, though without hydrogen bonds, suggesting a less stable interaction (Table 12, and SF 17,18,19 and 20).

For 2HWQ, the compound Neophytadiene stood out with both reasonable binding energy (-50.96 kcal/mol) and with multiple residues, including Ala-A:331, Lys-230, Leu-379, Phe-374, Val-372. 3-deoxy-D-mannoic-lactone also showed hydrogen bonding with ser-332, Asn-375, Lys-230 further validating its potential (Table 13, SF 21 and 22).

Table 11. Docking Scores and Binding Interactions of Ligands with Target Protein-1DNU

Compopunds (1DNU)	Energy	VDW	Hbond	Elec	Interacting amino acids
3,7,11,15-Tetramethyl-2-hexadecen-1-ol	-69.12	-69.12	0	0	Gln-C:467, Pro-A:57, Leu-A:60, Val-A:58
7-Hydroxycoumarin	-51.32	-51.32	0	0	Val-A:58, Leu-A:60, Pro-A:57
Propanoic acid, 2-[(trimethylsilyl)oxy]-, ethyl ester	-30.68	-30.68	0	0	Pro-A:57, Leu-A:60
Neophytadiene	-39.37	-39.37	0	0	Ala-A:63, Val-A:58, Leu-A:60, Pro-A:57
n-Hexadecanoic acid	-49.12	-49.12	0	0	Ala-A:57,Val-A:58, Leu-A:60, Pro-A:57
3-Deoxy-D-mannoic lactone	-51.7	-46.08	-5.61	0	Val-A:58
Phenol, 2-methoxy-	-51.59	-43.94	-7.65	0	Ala-A:59, Pro-A:57, Val-A:58, Gln-C:467, Leu-A:60
24-Noroleana-3,12-diene	-66.42	-66.42	0	0	Lys-C:129, Leu-A:60, Pro-A:57

Table 12. Docking Scores and Binding Interactions of Ligands with Target Protein-1FM6

1FM6	Energy	VDW	Hbond	Elec	Interacting amino acids
Catechol	-52.79	-52.79	0	0	Pro-A:386, Pro-A:378
Hydroquinone	-52.61	-52.61	0	0	Pro-A:378, Glu-A:390
7-Hydroxycoumarin	-71.08	-71.08	0	0	Pro-A:386, Pro-A:378, Glu-A:390
Phenol, 2,6-dimethoxy-	-71.25	-60.83	-10.42	0	Ala-A:387, Pro-A:378, Glu-A:390
Hexadecanoic acid, methyl ester	Docking not shown				Pro-A:378, Ala-A:387, Pro-A:386
Neophytadiene	-68.13	-68.13	0	0	Ala-A:391, Pro-A:378, Pro-A:386, Ala-A:387
3-Ethenylphenol	-59.89	-59.89			Pro-A:385, Ala-A:387

Table 13. Docking Scores and Binding Interactions of Ligands with Target Protein-2HWQ

2HWQ	Energy	VDW	Hbond	Elec	Interacting amino acids
Catechol	-34.31	-34.31	0	0	Leu-B:379
Phenol, 2,6-dimethoxy-	-44.94	-27.48	-17.46	0	Lys-B:230, Arg-B:234, Ala-B:376
Hexadecanoic acid, methyl ester	Docking not shown				Leu-B:379, Phe-B:374, Leu-B:384 Lys-B:230, Ala-B:331
7-Hydroxycoumarin	-45.95	-45.95	0	0	Arg-B:234
n-Hexadecanoic acid	-48.77	-48.77	0	0	Ala-B:331, Leu-B:384, Lys-B:230, Phe-B:374
Neophytadiene	-50.96	-50.96	0	0	Phe-B:374, Leu-B:379, Lys-B:230, Ala-B:331, Val-B:372
Hydroquinone	-32.45	-32.45	0	0	Asn-B:375, Lys-B:230, Arg-B:234
Dodecanoic acid, 3-hydroxy-	-46.98	-46.98	0	0	Arg-B:234, Lys-B:230, Phe-B:374, Ala-B:331
3-Deoxy-d-mannoic lactone	-40.8	-35.5	-5.3	0	Ser-B:332, Lys-B:230, Asn-B:379
Catechol	-34.31	-34.31	0	0	Leu-B:379

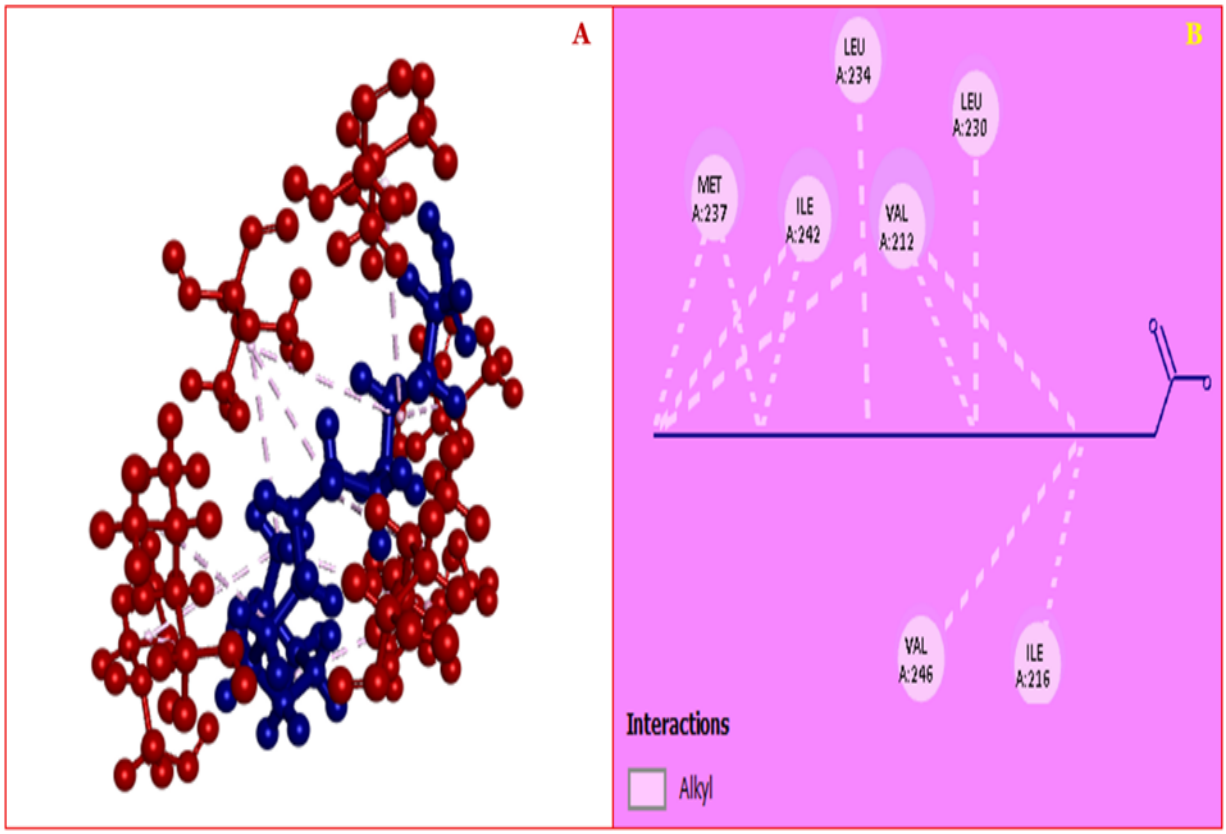

Figure 4. Molecular interaction of 3,7,11,15-Tetramethyl-2-hexadecen-1-ol with 1DNU protein A:3D binding pose B: 2D interaction diagram

3.4. Comparative Docking Performance

This comparison shows that several *T. dalzellii*- derived compounds bind more efficiently to their targets than clinically used drugs, suggesting promising therapeutic efficacy (Table 14).

Table 14 Comparative Docking Performance

Target Class	Standard Drug	Binding Energy (kcal/mol)	Best Compound from *T. dalzellii*	Binding Energy (kcal/mol)
Antioxidant (1CB4)	Ascorbic acid	−43.12	Isoschizogamine	−80.47
Anti-inflammatory (3CTT)	Ampicillin	−49.10	3-Ethenylphenol	−71.09
Anti-Diabetic (2HWQ)	Metformin	−40.22	Phytol	−69.12

3.5. Protein–Ligand Interaction Analysis

Visualization and post-docking analyses confirmed that most high-affinity ligands engaged in, hydrogen bonding with active site residues (e.g., Asp83, Ser210, Tyr48), Van der Waals interactions with hydrophobic pockets, and in some cases, π–π stacking and electrostatic interactions.

These diverse binding modes contribute to the enhanced docking performance and biological potential of the compounds.

4. Discussion

The present study employed a robust *in silico* approach combining multi-target molecular docking, GC–MS-guided phytochemical profiling, and ADMET/drug-likeness evaluations to examine the therapeutic potential of *Thalictrum dalzellii*. This methodology enhanced screening efficiency and provided mechanistic insights into bioactive interactions with proteins implicated in oxidative stress, inflammation, and diabetes.

Among the compounds, isoschizogamine showed the highest antioxidant potential (−80.47 kcal/mol) against Cu/Zn superoxide dismutase (PDB: 1CB4), engaging residues Asp-A:25 and Thr-A:26. While docking studies on isoschizogamine itself are rare, nitrogen-rich indole alkaloids from *Tinospora cordifolia* have shown strong SOD binding via hydrogen bonds and π–π stacking, supporting the efficacy of such scaffolds in antioxidant defense [16].

Phenol, 2-methoxy- demonstrated notable multi-target binding, engaging both anti-inflammatory (COX-2: 3CTT, 3W37) and antidiabetic (PPARγ: 1FM6, aldose reductase: 1DNU) targets. Methoxy-substituted phenols from *Curcuma longa* displayed similar docking profiles across these classes, reinforcing their polypharmacological potential [17].

For inflammation, 3-ethenylphenol bound COX-2 (−71.09 kcal/mol) and interacted with Arg-A:308—a residue essential for enzymatic activity. This mirrors findings in *Camellia sinensis* styrene derivatives that engage Arg-308 in COX-2, highlighting this residue as key for ligand stabilization in anti-inflammatory roles [18].

Neophytadiene showed favorable interactions with α-glucosidase and TNF-α, aligning with studies where neophytadiene and phytol were their recognized α-glucosidase inhibitors, demonstrating dual anti-inflammatory and antidiabetic effects [19].

Phytol (−69.12 kcal/mol against PPARγ) and phenol, 2,6-dimethoxy- (−71.25 kcal/mol against aldose reductase) exhibited high-binding affinities. Similar long-chain alcohols and oxygenated phenolics, including phytol metabolites and phenolic esters from *Ocimum* and *Gymnema sylvestre*, have been shown to effectively inhibit these targets, reinforcing their roles in glucose metabolism modulation [20,21,22].

Repeated docking cycles improved prediction reliability, as noted by Ayodele *et al.* (2023), and visual validation in BIOVIA Discovery Studio confirmed consistent ligand-active-site interactions—paralleling similar methods applied in plant phytochemical screenings [23].

In ADMET profiling, over 80% of the compounds adhered to Lipinski's Rule of Five, with predicted non-mutagenicity, absence of carcinogenicity, and BBB permeability. A comparable pharmacokinetic profile was observed in phytochemicals from *Berberis aristata*, further endorsing the drug-likeness of plant-derived molecules [24].

The docking profiles and ADMET properties of *T. dalzellii* phytocompounds are consistent—to those found in other medicinal plants. Their multi-target activities against complex diseases like diabetes and inflammation are in line with earlier work on *Thalictrum minus* and *T. foliolosum*, whose alkaloids demonstrated antioxidant and anti-inflammatory effects both *in vitro* and *in silico* [25].

Conclusion

The overall results of the present study clearly indicate the role of phytochemicals in antioxidant, anti-inflammatory and antidiabetic activity. The different phytochemicals shown activity on different proteins, the isoschizogamine showed potent antioxidant activity, the 3-ethylphenol exhibited strong anti-inflammatory activity whereas phytol was significant anti-diabetic activity. The results were compared with standard drug and the phytochemicals activity were more significant than standard drug. The *T. dalzellii* phytochemicals exhibited strong antioxidant, anti-inflammatory and antidiabetic activity from *in silico* studies. The phytochemicals after binding with proteins/ enzymes changes their structure and functions with highest biding energy. The same compounds also proven as significant antioxidant, anti-inflammatory and antidiabetic activity in *in vitro* studies. The *T. dalzellii* phytochemicals can be used as drug to treat above diseases after in vivo studies.

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References

1. Lobo V, Patil A, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: Impact on human health. Pharmacognosy Reviews 2010; 4(8):118–126.
2. Brownlee M. Biochemistry and molecular cell biology of diabetic complications. Nature 2001; 414(6865):813–820.
3. Reuter S, Gupta SC, Chaturvedi MM, Aggarwal BB. Oxidative stress, inflammation, and cancer: How are they linked? Free Radical Biology and Medicine 2010; 49(11):1603–1616.
4. Donath MY, Shoelson SE. Type 2 diabetes as an inflammatory disease. Nature Reviews Immunology 2011; 11(2):98–107.
5. Ahmed F, Urooj A, Karim AA. Antidiabetic potential of various extracts of Cinnamon zeylanicum bark on alloxan-induced diabetic rats. Pakistan Journal of Nutrition 2013; 12(11):902–908.
6. Nathan DM. Initial management of glycemia in type 2 diabetes mellitus. The New England Journal of Medicine 2002; 347(17):1342–1349
7. Kumar S, Kumar D, Deshmukh RR, Lokhande PD, More SM. Antidiabetic and antihyperlipidemic activities of *Thespesia populnea* Linn. root in alloxan-induced diabetic rats. Asian Journal of Pharmaceutical and Clinical Research 2011; 4(3):128–132
8. Pan MH, Lai CS, Ho CT. Anti-inflammatory activity of natural dietary flavonoids. Food & Function 2013; 4(6):819–828.
9. Mani JS, Johnson JB, Steel JC, Broszczak DA, Neilsen PM, Walsh KB, Naiker M. Natural product-derived phytochemicals as potential agents against coronaviruses: A review. Virus Research 2020; 284:197989
10. Gurung AB, Ali MA, Lee J, Farah MA, Al-Anazi KM. Unravelling lead anticancer compound targeting cyclin-dependent kinase 2 using pharmacophore modeling, molecular docking and molecular dynamics simulation studies. Saudi Journal of Biological Sciences 2020; 27(10):2660–2669.
11. Patel H, Mistry BM, Jha BH, Rajan MGR, Parmar P. In silico investigation of phytochemicals as effective antiviral agents against COVID-19 using molecular docking and ADMET profiling. Journal of Biomolecular Structure and Dynamics 2020.
12. Srivastava SK, Ramana KV, Bhatnagar A. Role of aldose reductase and oxidative damage in diabetes and the consequent potential for therapeutic intervention. Current Medicinal Chemistry 2005; 12(22):2755–2767.
13. Tundis R, Loizzo MR, Menichini F. Natural products as α-amylase and α-glucosidase inhibitors and their hypoglycemic potential in the treatment of diabetes: An update. Mini Reviews in Medicinal Chemistry 2010; 10(4):315–331.
14. Govindappa M, Thanuja V, Tejashree S, Soukhya CA, Suresh B, Arthikala M, Rai VR. In vitro and in silico antioxidant, anti-diabetic, anti-HIV and anti-Alzheimer activity of endophytic fungi

Cladosporium uredinicola phytochemicals. J Drug Delivery Ther. 2019;9(3-s):510–26.
15. Ayodele PF, Bamigbade A, Bamigbade OO, Muritala OT, Oyinloye BE, Adefegha SA. Illustrated procedure to perform molecular docking using PyRx and BIOVIA Discovery Studio Visualizer: a case study of 10KT with atropine. Prog Drug Discov Biomed Sci. 2023;6(1): a0000424.
16. Bhosale SS, et al. Molecular docking and in vitro evaluation of *Tinospora cordifolia* phytocompounds: α-amylase, α-glucosidase and aldose reductase inhibition. Future J Pharm Sci. 2024; 10:107.
17. Kumar S, Kushwaha PP, Singh AK, Prajapati KS, Bajpai R, Yadav A. Identification of compounds from *Curcuma longa* with in silico binding potential against SARS-CoV-2 and human host proteins involved in virus entry and pathogenesis. Indian J Pharm Sci. 2021;83(6):1108–17.
18. Wang Z, Chen B, Zhao X, Li S, Fang Z, Liu Y, Zeng Z, Li C, Chen H. Probing the binding mechanism of tea polyphenols from different processing methods to anti-obesity and TMAO production-related enzymes through in silico molecular docking. Food Chem X. 2024;21: 101053.
19. Singh KP, Singh S, Tripathi S, Singh MP. Phytol/phytanic acid docking to PPARγ and RXRα/PPARγ heterodimer: mechanisms for insulin resistance elevation. J Mol Model. 2012;18(10):465–79.
20. Ononamadu CJ, Ibrahim A. Molecular docking and prediction of ADME/drug-likeness properties of potentially active antidiabetic compounds isolated from aqueous-methanol extracts of *Gymnema sylvestre* and *Combretum micranthum*. *BioTechnologia (Pozn)*. 2021;102(1):85–99.
21. Saeed A, Tehseen Y, Rafique H, Furtmann N, Bajorath J, Flörke U, Iqbal J. Benzothiazolyl substituted iminothiazolidinones and benzamido-oxothiazolidines as potent and partly selective aldose reductase inhibitors. Med Chem Commun. 2014;5(9):1371–80.
22. Oso BJ, Olaoye TO. GC–MS and molecular docking analysis of phytol, neophytadiene and β-caryophyllene against α-glucosidase. J Food Biochem. 2020;44(2): e13102.
23. Sharma A, Sharma S, Gupta M, Fatima S, Saini R, Agarwal SM. Pharmacokinetic profiling of anticancer phytocompounds using computational approach. Phytochem Anal. 2018;29(6):559–68.
24. Wang Y, Hamburger M, Yang L, Yuan H, Zhang X, Qin G. Bioactive alkaloids from *Thalictrum* species: a phytochemical review. Phytochem Rev.2017;16(3):461–77.