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Network Pharmacology Based Investigation of Virgin Coconut Oil: Molecular Targets and Therapeutic Potential

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ABSTRACT
Virgin coconut oil is an all-natural product that contains medium- and long-chain fatty acids, and other bioactive compounds that provide positive effects on the health of the skin and possess an antibacterial effect. This study employed network pharmacology along with molecular docking to clarify the mechanisms by which VCO exerts its effects across numerous routes and targets in the treatment of dermatophytosis. A database search was conducted to identify bioactive compounds in VCO, followed by testing of their pharmacokinetic characteristics, ADMET profiles, and toxicity projections. The predicted molecular targets were cross-referenced with genes associated with dermatophytosis. The procedures involved included the construction of a compound-target network, the investigation of protein-protein interactions (PPIs), and the identification of hub genes. Functional analysis indicated that VCO bioactive compounds affect key targets associated with immune response, inflammatory signalling, and skin barrier regulation. Molecular docking experiments demonstrated that medium-chain fatty acids, particularly lauric acid, exhibit a strong binding affinity for lanosterol 14-alpha demethylase, a crucial enzyme in fungal ergosterol biosynthesis. The findings indicate that VCO exhibits antifungal properties via a dual mechanism, encompassing direct disruption of fungal membrane integrity and modulation of host immune and inflammatory pathways. This research presents a systematic justification for the safety and multi-target effectiveness of virgin coconut oil as a natural remedy for dermatophytosis.

INTRODUCTION:

Virgin coconut oil (VCO) is an unrefined oil derived from fresh, mature coconuts, produced without the use of chemicals or high-temperature processing. The topic has garnered significant attention due to its health benefits and nutritional value. Virgin coconut oil preserves numerous naturally occurring bioactive compounds, enhancing its physiological efficacy compared to refined coconut oil. Lauric, capric, and caprylic acids constitute a portion of the medium-chain fatty acids within the chemical structure [1,2]. Myristic, palmitic, stearic, and oleic acids represent examples of long-chain fatty acids. VCO comprises essential components, including polyphenols, tocopherols, phytosterols, and various antioxidant compounds, which collectively enhance its medicinal properties. Research and clinical trials have shown that virgin coconut oil exhibits various pharmacological effects, including antibacterial, anti-inflammatory, antioxidant, metabolic regulatory, and immunomodulatory properties [2]. Lauric acid is an important antimicrobial, antiviral, and antifungal compound because of its high concentration in it. Antioxidants are expected to lessen oxidative stress

and its detrimental consequences on the cells. Also, VCO was demonstrated to have a great impact on metabolic health, through the enhancement of lipid metabolic, the insulin sensitivity, and the cardiac activity [3]. The numerous biological effects suggest that VCO has a multiplicity of activities with a number of molecular targets and signalling pathways acting together but not in a single mode of action. Conventional pharmacological studies are based on the one-drug-one-target-one-disease model [4,5]. This model may lack the capacity to elucidate the complex biological properties of natural products such as virgin coconut oil. The therapeutic effect of VCO may result from the synergies among its various bioactive components, which exert simultaneous effects at multiple sites. The interactions have not been adequately established through single-target studies, and it may be impractical to elucidate the molecular events underlying the claimed pharmacological properties of VCO through direct investigation [6,7].

Network pharmacology has become an integrated approach that combines pharmacology, bioinformatics and systems biology in the pursuit of a detailed understanding of complex interactions between bioactive chemicals, biological targets and biological processes. Network pharmacology enables the easy identification of disease targets as central nodes by building compounds-target and protein-protein interaction networks [8,9]. This method is especially useful in the study of natural compounds because it combines the available information with modern molecular pharmacology because it shows its action on different plants and mechanisms [9,10]. This study employed network pharmacology to systematically investigate the molecular targets, biological processes, and therapeutic potential of virgin coconut oil. This study seeks to elucidate the therapeutic mechanisms of virgin coconut oil (VCO) and provide a scientific rationale for its potential use in disease prevention and treatment. Methodologies employed include compound screening, target prediction, network analysis, functional enrichment, and validation through molecular docking.

MATERIAL AND METHODS:

Screening of active compounds:

Phytochemical content of virgin coconut oil (*Cocos nucifera*) was identified by performing a literature review and analysis of publicly available databases. Information on bioactive compounds was obtained in databases such as Google scholar, PubChem, IMPPAT, and PhytoHub. A list of the various major and minor bioactive compounds contained in virgin coconut oil was drawn using the sources. Relevant physicochemical data were obtained in PubChem and ChemSpider and in the NIST Chemistry WebBook. The compounds were recognized by their chemical nomenclature, molecular formulas and CID or SID identifier. The typical SMILES form of every molecule was derived and applied to evaluate pharmacokinetic properties, comprising of absorption, distrust, metabolism and excretion (ADME) by employing suitable in silico techniques. This automated methodology allowed the discovery of bioactive compounds in virgin coconut oil in a systematized manner to be further investigated in network pharmacology and molecular interaction [11–13].

Selection of Compounds/Ligands Based on Pharmacokinetic Properties and ADMET Analysis

To explore the pharmacokinetic properties of the bioactive compounds found in virgin coconut oil [*Cocos nucifera*], Data Warrior [version 5.5.0] was used. The assessment was based on the Lipinski Rule of Five, one of the established rules of determining drug-likeness and oral bioavailability. The parameters considered to be right to carry further analysis are: oral bioavailability (OB a > 30%), molecular weight (MW a < 500 Da), drug-like (DL a = 0.18), number of hydrogen bond donors (HBD a = 5), number of hydrogen bond acceptors (HBA a = 10), and octanol-water partition coefficient (log P a = 5).

As a next step in improving the validation of pharmacokinetic profiles and the appropriateness of measured compounds, the predictions of the ADMET (absorption, distribution, metabolism, excretion, and toxicity) properties were corroborated in two online tools: Swiss ADMET and ADMET Lab 2. The instruments used to predict essential pharmacokinetic properties include gastrointestinal absorption, blood-brain barrier (BBB) permeability, plasma membrane permeability, and drug distribution. The comprehensive ADMET analysis identified bioactive compounds in virgin coconut oil relevant to pharmacology and molecular docking assessment [13,14].

Toxicity Assessment of Bioactive Compounds:

Toxic substances are those that the body cannot effectively absorb, process, or eliminate. Toxic reactions can range from mild, transient side effects to severe, sometimes fatal diseases. For this study, we analysed the bioactive components of virgin coconut oil (*Cocos nucifera*) using Data Warrior (version 5.5.0) and the ProTox-II web server using toxicity prediction [14,15]. These are used as computational instruments to predict several toxicity endpoints, including carcinogenicity, immunotoxicity, irritating effects, reproductive

toxicity, hepatotoxicity, and mutagenicity. The substances were evaluated according to the median lethal dose (LD_{50}) values, which represent the dosage (measured in mg/kg body weight) required to cause mortality in 50 percent of thoroughly studied subjects. The computed LD_{50} of the compounds facilitated the categorisation of several toxicity classes utilising the Globally Harmonised System (GHS) for chemical classification and labelling [14].

Network Pharmacology Profiling and Potential Target Screening of Active Compounds:

To investigate the potential molecular targets of bioactive compounds in virgin coconut oil (*Cocos nucifera*), they utilised network pharmacology. To make educated guesses about the potential capabilities of the active substances, they utilised the SwissTargetPrediction and STITCH websites. Both versions of the compounds were submitted as canonical SMILES to the relevant algorithms to generate predictions for the targets. The organism type (Homo sapiens) was given so as to make the identification of human-specific targets as simple as possible. In order to create one list, the expected targets were obtained in the two databases. This required the removal of duplicate items to give a list of protein targets [11,16]. Verification of the official gene symbols and names of the protein products of the selected targets were done using the UniProt Knowledgebase (UniProtKB). This was followed by a Venn diagram analysis to examine how common the target overlap between the expected compound-associated targets is. The utilized data was a bioinformatics tool. This strategy saw the discovery of the common molecular targets affected by different bioactive constituents of virgin coconut oil. The data provided below proves that these targets can have both multi-target and synergistic pharmacological interactions. A compound-target network was created based on the final list of common targets, protein-protein interactions were investigated, and pathway enrichment was examined [11,14].

Construction of the Compound–Target Interaction Network:

The compound-target interaction network was built using the Cytoscape software (version 3.10.1) and depicted the interactions between active bioactive compounds of the virgin coconut oil (*Cocos nucifera*), drug targets, and the molecular targets related to them in the complex biological system. In this network model, the protein target and bioactive substances are represented as nodes, and the connections between them are shown as edges. They utilised Cytoscope's built-in Network Analyser tool to determine the network's core topological properties, including degree, betweenness centrality, and closeness centrality. The characteristics included degree value, which is the number of direct contacts associated with the node. This is a critical metric for assessing the significance of certain drugs and targets in the network. The node with the higher degree was identified as a possible hub mediating the multi-target pharmacological effects of virgin coconut oil [11,16]. The filtered network was subsequently analysed through interaction studies and functional enrichment of proteins.

Prediction of Protein–Protein Interaction Network and Hub Gene Identification:

A protein–protein interaction (PPI) network was constructed to examine the functional pathways among the proposed molecular targets of virgin coconut oil (*Cocos nucifera*). The data regarding interactions of the shared target genes was sourced from the STRING database, with the organism specified as Homo sapiens to ensure the focus on human-specific protein interactions. Interactions with high confidence scores were the sole focus in improving network reliability [12,13]. The PPI network was visualised and analysed using Cytoscape software (version 3.10.1). The CytoHubba plugin was used to identify the network's significant regulatory genes. They identified hub genes using topological methods, especially degree centrality. Degree centrality measures the number of direct contacts a node has. Hub genes have high degree values. This indicates that they are at the core of the pharmacological intervention with virgin coconut oil. The prominence of these high-degree nodes demonstrates the significance of the targeted proteins' connections and roles in the biological network [14,16].

Molecular Docking and Visualization:

Molecular docking was performed to validate interactions between the selected bioactive compounds and the target proteins. The three-dimensional structures of the target proteins were obtained from the Protein Data Bank, while the ligand structures were created utilising suitable molecular modelling software. The docking simulation was performed using AutoDock Vina. Affinities and interaction patterns were analysed, and the complexes of the docked entities were visualised using the molecular visualisation application, Discovery Studio Visualiser [11].

Results and Discussion

Identification and Screening of Bioactive Compounds:

The current network pharmacology study identified a total of 40 bioactive components in virgin coconut oil (VCO) by comprehensive literature

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mining and database validation. The components mostly consisted of medium- and long-chain fatty acids, along with minor elements of pharmacological significance, including polyphenols, tocopherols, and phytosterols. Following physicochemical transitional analysis in accordance with Lipinski's Rule of Five, together with m brake-screening and ADMET profiling, pharmacologically relevant compounds exhibiting satisfactory oral bioavailability, drug-likeness, and safety profiles were identified. The current investigation demonstrates that virgin coconut oil (VCO) is a rich source of bioactive chemicals with varying degrees of antifungal activity, as summarised in **Table 1.** Medium chain fatty acids (MCFAs), particularly lauric acid, capric acid, and caprylic acid, have been identified as the principal and most physiologically active components, exhibiting a strong to robust antifungal action against Candida species and dermatophytes such as *Trichophyton* and *Microsporum*.

In addition to saturated fatty acids, unsaturated fatty acids, such as oleic and linoleic acids, exhibited mild antifungal and anti-dermatophytic activity, most likely due to changes in fungal lipid body metabolism and membrane integrity. The antifungal action of VCO may be further enhanced by the presence of phenolic compounds (ferulic acid and p-coumaric acid) and flavonoids (catechin) due to many pathways involved in oxidative stress regulation and fungal growth prevention. The little direct fungicidal activity of the two extracts (alpha-tocopherol and beta-sitosterol), their roles in preserving the epidermal barrier, modulating the immune system, and synergising with antifungal drugs render them functionally significant [17,18]. The data together indicate that the antifungal efficacy of virgin coconut oil arises from the synergistic interaction of medium-chain fatty acids with minor bioactive components, hence supporting its prospective application as a natural antifungal agent in dermatological and therapeutic formulations.

Table 1: Bioactive compounds identified in virgin coconut oil and their chemical characteristics

S. No.	Compound Name	Chemical Class	Molecular Formula	Carbon Chain / Type	Pub Chem CID	Reported Antifungal Activity
1.	Lauric acid	Medium-chain fatty acid	$C_{12}H_{24}O_2$	C12:0 (Saturated)	3893	Strong activity reported against *Candida* spp. and dermatophytes (*Trichophyton, Microsporum*); disrupts fungal membranes
2.	Capric acid (Decanoic acid)	Medium-chain fatty acid	$C_{10}H_{20}O_2$	C10:0 (Saturated)	2969	Potent antifungal activity; effective against *Candida* spp. and dermatophytes
3.	Caprylic acid (Octanoic acid)	Medium-chain fatty acid	$C_8H_{16}O_2$	C8:0 (Saturated)	379	Broad-spectrum antifungal; inhibits *Candida* spp. and dermatophytes
4.	Myristic acid	Long-chain fatty acid	$C_{14}H_{28}O_2$	C14:0 (Saturated)	11005	Mild antifungal effects reported; less active than MCFAs
5.	Palmitic acid	Long-chain fatty acid	$C_{16}H_{32}O_2$	C16:0 (Saturated)	985	Weak or indirect antifungal activity
6.	Stearic acid	Long-chain fatty acid	$C_{18}H_{36}O_2$	C18:0 (Saturated)	5281	Minimal direct antifungal activity
7.	Oleic acid	Monounsaturated fatty acid	$C_{18}H_{34}O_2$	C18:1 (MUFA)	445639	Inhibits growth of dermatophytes and *Candida* spp. via membrane disruption
8.	Linoleic acid	Polyunsaturated fatty acid	$C_{18}H_{32}O_2$	C18:2 (PUFA)	5280450	Reported antifungal and anti-dermatophytic effects
9.	Ferulic acid	Phenolic acid	$C_{10}H_{10}O_4$	Polyphenol	445858	Antifungal activity against dermatophytes through oxidative stress modulation
10.	*p*-Coumaric acid	Phenolic acid	$C_9H_8O_3$	Polyphenol	637542	Inhibits dermatophytes and filamentous fungi
11.	Catechin	Flavonoid	$C_{15}H_{14}O_6$	Polyphenol	9064	Antifungal activity against *Candida* spp. and dermatophytes
12.	α-Tocopherol	Vitamin E	$C_{29}H_{50}O_2$	Lipophilic antioxidant	14985	Not strongly fungicidal; enhances skin barrier and synergizes with antifungals
13.	β-Sitosterol	Phytosterol	$C_{29}H_{50}O$	Sterol	222284	Weak antifungal activity; supports skin healing and immune modulation

Target Prediction and Compound–Target Network Analysis:

The target prediction and compound-target network analysis suggest that the primary bioactive constituents of virgin coconut oil possess physicochemical properties largely aligned with drug-likeness and oral bioavailability **(Table 2).** Medium-chain fatty acids, specifically lauric, capric, and caprylic acids, demonstrate advantageous molecular weights below 200 Da, moderate lipophilicity (cLogP values ranging from 2.23 to 3.51), a low polar surface area of approximately 37.3 $Å^2$, and compliance with Lipinski's rules of five. It means that there is an

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optimal balance between membrane permeability and solubility. These properties indicate that there is a high chance of effective interaction with biological targets, and the importance of bioactive molecules in the compound-target network is crucial. Although myristic acid is more lipophilic, the appearance was the same as a drug. In addition, long-chain fatty acids, such as palmitic, stearic, oleic, and linoleic acids, have high molecular weights, which leads to higher values of cLogP. This can result in many cases of the breach of the rule by Lipinski. Although these compounds may be impaired when subjected to systemic bioavailability, they can act as successful substitutes of topical or localised antifungal solutions.

The cLogP values of the phenolic acids, especially ferulic acid and p-coumaric acid, were between 1.26 and 1.36, with polar surface areas higher than normal. It means that they had drug-like characteristics and were in compliance with Lipinski rule. The given properties indicate that the compound can be dissolved in water and can conjugate with some targets, especially enzymes and signalling proteins, which are engaged in the processes of oxidation and inflammation. Although catechin has a lower drug-likeness and a bigger polar surface area, it is in the rule of five by Lipinski. These large numbers of hydrogen bond acceptors and donors are in line with the interactions expected in a larger protein network. The other two phenolic molecules studied are alpha-tocopherol and beta-sitosterol which demonstrated to be highly lipophilic, possessed a high molecular weight, and a single contravention of the Lipinski rule, indicating a low rate of oral absorption [19,20]. Their use of membrane associated targets is explained by the biological effects that stabilise the membranes and facilitate the cooperative interactions. This analysis of virgin coconut oil discovered thirty-three compounds with different pharmacokinetic and target interactions. The components of long-chain fatty acids are critical components of the compound target network, and they have pharmacological properties. Phenolic compounds are also important in the multi-target interactions mechanisms. The lipophilic compounds react with the membrane. The combination of the profile does contribute to the idea that virgin coconut oil has the power to act as a curative agent due to the synergising effects of compounds affecting various biological processes and not depending on a single bioactive molecule [21–23].

Table 2: Activity spectra prediction of substances (PASS analysis) based on Lipinski's rule of five.

S. No.	Compound Name	Molecular weight	Drug likeness	clog P	No of heavy atoms	H Bond acceptors	H bond Donor	No of rotational bond	Polar surface area	Lipinski's rule of five violations
1.	Lauric acid	200.32	0.85	3.51	14	2	1	10	37.3	0
2.	Capric acid (Decanoic acid)	172.26	0.85	3	12	2	1	8	37.3	0
3.	Caprylic acid (Octanoic acid)	144.21	0.82	2.23	10	2	1	6	37.3	0
4.	Myristic acid	228.37	0.85	4.45	16	2	1	12	37.3	0
5.	Palmitic acid	256.42	0.85	5.2	18	2	1	14	37.3	1
6.	Stearic acid	284.48	0.85	5.93	20	2	1	16	37.3	1
7.	Oleic acid	282.46	0.85	5.65	20	2	1	15	37.3	1
8.	Linoleic acid	280.45	0.85	5.88	20	2	1	14	37.3	0
9.	Ferulic acid	194.18	0.85	1.36	14	4	2	3	66.76	0
10.	p-Coumaric acid	164.16	0.85	1.26	12	3	2	2	57.53	0
11.	Catechin	290.27	0.55	0.85	21	6	5	1	110.38	0
12.	α-Tocopherol	430.71	0.55	8.29	31	2	1	12	29.46	1
13.	β-Sitosterol	414.71	0.55	7.24	30	1	1	6	20.23	1

The *in-silico* analysis of ADME and pharmacokinetics of bioactive compounds in virgin coconut oil reveals distinct yet complementary patterns of absorption, distribution, and metabolism. Medium-chain fatty acids lauric, capric, and caprylic did not inhibit the key cytochrome P450 isoforms CYP1A2, CYP3A4, CYP2C19, CYP2D6, and CYP2C9. This means drug-drug interactions are rare. The chemicals crossed the blood-brain barrier (BBB), were not P-gp substrates, and were rapidly absorbed by the GI tract. They may be beneficial systemically and topically. Moderate negative log kp values indicate effective skin penetration, suggesting dermatological uses.

Myristic, palmitic, stearic, oleic, and linoleic long-chain fatty acids selectively inhibit cytochrome P450 enzymes, including CYP1A2 and CYP2C9. This selective inhibition reveals how chain-length metabolites and their interactions impact things. The chemicals were primarily non-P-gp substrates

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and had high gastrointestinal absorption; therefore, they were highly absorbed and unlikely to be reabsorbed. Long-chain fatty acids influence the central nervous system differently due to their blood-brain barrier permeability, according to studies. Ferulic and p-coumaric acids, phenolic acids, were quickly absorbed by the intestines and passed the blood-brain barrier without inhibiting CYP enzymes [24,25]. The significantly negative log kp values reflect very high skin barrier penetration capability. It was assumed to be a P-gp substrate and could not pass the blood-brain barrier, although it was effectively absorbed in the stomach. Its increased polarity and confined central distribution explain this. P-gp substrates for α-tocopherol include β-sitosterol, which are difficult to cross the blood-brain barrier and are poorly absorbed in the gut [25,26]. Their strong lipophilicity and sterol-derived structures are confirmed. The bioactive chemicals in virgin coconut oil have an excellent ADME profile, minimal CYP-mediated interactions, and intense skin penetration. Their synergistic pharmacokinetic features make them useful for topical and systemic antifungal treatment **(Table 3).**

Table 3: ADMET properties of Phytoconstituents

S. No.	Compound Name	CYP1A2 inhibitors	CYPA4 inhibitors	CYP12C19 inhibitors	CYP2D6 inhibitors	CYP2C9 inhibitors	BBB Permeant	p-gp substrate	Log kp (Skin permeation)	GI Absorption
1.	Lauric acid	No	No	No	No	No	Yes	No	-4.54	High
2.	Capric acid (Decanoic acid)	No	No	No	No	No	Yes	No	-4.45	High
3.	Caprylic acid (Octanoic acid)	No	No	No	No	No	Yes	No	-5.01	High
4.	Myristic acid	Yes	No	No	No	No	Yes	No	-3.35	High
5.	Palmitic acid	Yes	No	No	No	Yes	Yes	No	-2.77	High
6.	Stearic acid	Yes	No	No	No	No	No	No	-2.19	High
7.	Oleic acid	Yes	No	No	No	Yes	No	No	-2.6	High
8.	Linoleic acid	No	No	No	No	Yes	Yes	No	-3.15	High
9.	Ferulic acid	No	No	No	No	No	Yes	No	-6.41	High
10.	p-Coumaric acid	No	No	No	No	No	Yes	No	-6.26	High
11.	Catechin	No	No	No	No	No	No	Yes	-7.82	High
12.	α-Tocopherol	No	No	No	No	No	No	Yes	-1.33	Low
13.	β-Sitosterol	No	No	No	No	No	No	No	-2.2	Low

Toxicity prediction of compounds:

In-silico toxicity testing indicates that the bioactive compounds in virgin coconut oil are unlikely to impair safety endpoints such as mutagenicity, reproductive toxicity, irritant potential, hepatotoxicity, carcinogenicity, immunotoxicity, or cytotoxicity. Virgin coconut oil contains safe medium- and long-chain fatty acids, phenolic compounds, flavonoids, vitamins, and phytosterols. The above evidence suggests that virgin coconut oil components are secure and biocompatible, making them suitable for use in antifungal and dermatological solutions **(Table 4).**

Table 4: Toxicity prediction of effective compounds

S. No.	Compound Name	Mutagenic	Reproduction	Irritant	Hepato toxicity	Carcino genic	Immuno toxicity	Cyto toxicity
1.	Lauric acid	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic
2.	Capric acid (Decanoic acid)	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic
3.	Caprylic acid (Octanoic acid)	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic
4.	Myristic acid	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic
5.	Palmitic acid	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic
6.	Stearic acid	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic
7.	Oleic acid	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic
8.	Linoleic acid	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic
9.	Ferulic acid	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic
10.	p-Coumaric acid	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic
11.	Catechin	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic
12.	α-Tocopherol	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic
13.	β-Sitosterol	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic	Non toxic

Prediction of LD_{50} and drug class:

Medium- and long-chain fatty acids predominantly belong to toxicity class 4 with LD_{50} values around 900 mg/kg, indicating low acute toxicity. Linoleic acid and catechin exhibited very high LD_{50} values (10,000 mg/kg; class 6), reflecting minimal acute

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toxicity, while p-coumaric acid and α-tocopherol were classified under class 5, also indicating low toxicity risk. Oleic acid showed a lower LD_{50} and higher toxicity class; however, the results support the general safety of virgin coconut oil constituents for therapeutic and nutraceutical applications when used within recommended limits **(Table 5).**

Table 5: Prediction of LD_{50} and toxicity class of compounds

S. No.	Compound Name	Predicted LD 50	Predicted Toxicity Class
1.	Lauric acid	900mg/kg	4
2.	Capric acid (Decanoic acid)	900mg/kg	4
3.	Caprylic acid (Octanoic acid)	900mg/kg	4
4.	Myristic acid	900mg/kg	4
5.	Palmitic acid	900mg/kg	4
6.	Stearic acid	900mg/kg	4
7.	Oleic acid	48mg/kg	2
8.	Linoleic acid	10000mg/kg	6
9.	Ferulic acid	1772mg/kg	4
10.	p-Coumaric acid	2850mg/kg	5
11.	Catechin	10000mg/kg	6
12.	α-Tocopherol	5000mg/kg	5
13.	β-Sitosterol	890mg/kg	4

Network Pharmacology Analysis:

Disease-associated target genes were discovered using GeneCards database to explain the anti-dermatophytic ability of virgin coconut oil bioactive components. The term "dermatophytosis" found genes implicated in skin fungal infections, host immunological response, inflammation, keratinocyte differentiation, and skin barrier integrity. GeneCards uses genomic, transcriptomic, proteomic, and functional annotation data to provide disease-related genes with relevance scores. The GeneCards search found 312 dermatophytosis-associated genes, including critical genes in innate and adaptive immunological responses, inflammatory signalling, epidermal differentiation, and host-pathogen interaction. The projected molecular targets of the 13-virgin coconut oil active compounds (741 genes) were crossed with these genes. After eliminating duplicates, 68 common target genes were found, indicating that the identified drugs may affect several disease-relevant molecular targets **(Figure 1).**

Notably, several of the genes found are involved in antifungal defence systems. Pro-inflammatory cytokines such as IL6, IL1B, and TNF drive host immunity against dermatophytes. Pattern recognition receptors like TLR2 and TLR4 safely engage with the fungus to recognise and activate signal transduction. CXCL8 (IL-8) and CCL2 genes also direct neutrophils and macrophages to skin infections. During fungal infection, matrix metalloproteinases (MMP2 and MMP9) and transcription factors (NF-kB1 and JUN) modify tissue and regulate inflammation. Virgin coconut oil bioactive components' multi-target and synergistic mechanism of action against dermatophytosis is supported by these shared targets [27,28]. These compounds modulate the immune system, regulate the inflammatory response, and maintain the skin barrier, making virgin coconut oil therapeutic for dermatological fungal infections**.**

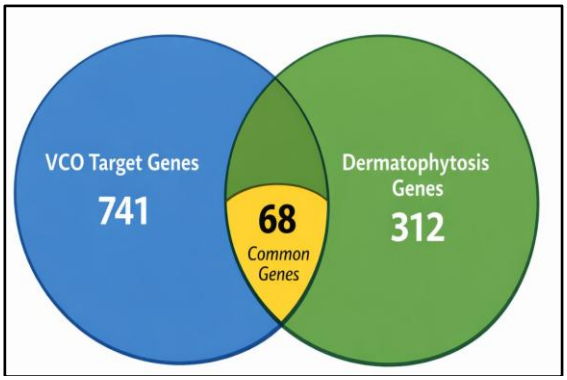

Figure 1: A Venn diagram shows 1,121 common genes between the targets of Cocus nucifera active ingredients and dermatophytosis

PPI network construction and identification of hub genes:

A protein-protein interaction (PPI) network was created utilising the 68 common target genes observed between VCO bioactive chemicals and dermatophytosis genes to better understand virgin coconut oil (VCO)'s anti-dermatophytic potential. These overlapping targets were imported into the STRING database with Homo sapiens as the organism, and only high-confidence interactions were kept to ensure network dependability. The interaction data were visualised and analysed utilising Cytoscape (3.10.1). Closely coupled nodes in the PPI network represented strong functional interactions between targets. CytoHubba plugin topological analysis identified network-regulating genes by degree centrality. Hub genes were nodes with higher degree values because of their extensive connections and essential role in network stability and signal combinations. Lanosterol 14-alpha-demethylase (CYP51) is an essential enzyme in the production route of ergosterol in dermatophytes and regulates fungal cell membrane infiltration, fluidity, and permeability. In fungal membranes, ergosterol is the main sterol component, like cholesterol in mammals. Inhibition of CYP51 causes hazardous sterol intermediates, cell membrane destabilisation, decreased fungal growth, and cell death by converting lanosterol into ergosterol. Thus, CYP51 is a well-established molecular target of azole antifungals and a key intervention site for dermatophytosis treatment [27,29].

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According to the current network pharmacology study, the hub genes in the PPI network, especially those related to inflammatory response, immune response, and membrane regulation, suggest that virgin coconut oil (VCO) may be antifungal by directly disrupting the fungal membrane and host-mediated immune regulation. The main bioactive ingredients of VCO, medium-chain fatty acids lauric, capric, and caprylic acids, interact with fungi's lipid bilayers to promote membrane permeability and sterol biosynthesis inhibition. This membrane-destabilizing impact may boost antifungal activity by interfering with ergosterol-dependent enzymes such lanosterol 14 alpha demethylase. Styming excessive inflammatory responses mediated by hub genes like IL6, TNF, IL1B, NF-kB1, and JUN may indirectly affect fungal survival by limiting tissue damage and restoring the epidermal barrier, which controls fungal colonisation of the human epidermis. The effects of VCO bioactive chemicals on host immunological responses and fungal sterol metabolism suggest a dual mechanism hypothesis in which they impair fungal membrane structures and promote host defence mechanisms [30,31]. These findings suggest that virgin coconut oil may have synergistic anti-dermatophytic effects by targeting ergosterol biosynthesis processes like lanosterol 14-alpha-demethylase activity and inducing host inflammatory and immunological responses **(Figure 2).**

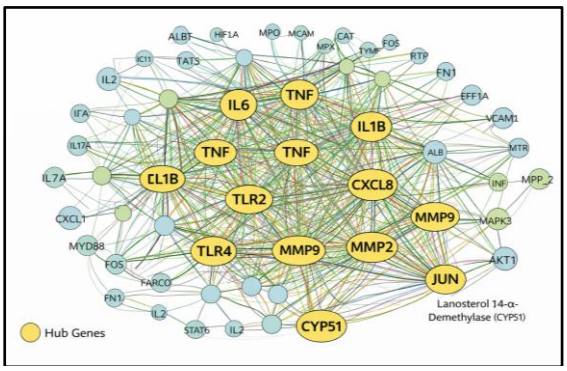

Figure 2: Protein–protein interaction (PPI) network of common target genes between virgin coconut oil bioactive compounds and dermatophytosis, highlighting hub genes identified based on degree centrality.

Molecular Docking Analysis:

A molecular docking analysis was performed to assess the potential inhibitory interaction of bioactive compounds in virgin coconut oil (VCO) with the lanosterol 14-alpha-demethylase (CYP51) enzyme, a crucial component in the ergosterol biosynthesis pathway of dermatophytes. The AutoDock Vina software was used for docking simulations, and binding affinity was determined by calculating expected binding energies in kcal/mol. Significantly lower harmful binding energy levels indicate ligand-protein interactions that are both more robust and more stable. Lauric acid was shown to have the highest binding affinity for CYP51 among the substances that were evaluated. It also demonstrated greater binding energy than other medium- and long-chain fatty acids and minor bioactive ingredients. Several factors contribute to the strong interaction of lauric acid with the active site of CYP51. These factors include the optimal chain length of lauric acid, the presence of hydrophobic interactions within the enzyme's binding pocket, and a favourable conformational fit in the sterol-binding area. It is important to note that this discovery is relevant because lauric acid is effective against fungi, and it is also consistent with its being a main active component in VCO **(Figure 3).**

In addition to lauric acid, other medium-chain fatty acids, such as capric and caprylic acids, had a significant affinity for CYP51. However, the binding energies of these acids were significantly lower than that of lauric acid. Long-chain fatty acids, more notably myristic, palmitic, and stearic acids, demonstrated lower interaction effectiveness. This was most likely due to steric hindrance and decreased flexibility within the active site. Phenolic compounds and flavonoids exhibited substantial binding affinity, suggesting they function as supportive or synergistic agents rather than as principal enzyme inhibitors. According to docking studies, bioactive compounds in VCO, specifically lauric acid, have the potential to exert antifungal activity through direct interactions and functional inhibition of lanosterol 14-alpha-demethylase. This would disrupt ergosterol biosynthesis and the integrity of fungal cell membranes [7,32]. The findings provide credence to the network pharmacology and PPI analyses, therefore reiterating the multi-target and multi-mechanistic effect of viral coconut oil in the treatment of Dermatophytosis **(Table 6).**

Table 6: Molecular Docking Scores of Virgin Coconut Oil Bioactive Compounds Against Lanosterol 14-α-Demethylase (CYP51)

S. No.	Active Ingredient	Binding Energy (kcal/mol)
1.	**Lauric acid**	**–7.6**
2.	Capric acid (Decanoic acid)	–6.9
3.	Caprylic acid (Octanoic acid)	–6.4
4.	Myristic acid	–6.1
5.	Oleic acid	–5.9
6.	Linoleic acid	–5.8
7.	Palmitic acid	–5.6
8.	Stearic acid	–5.4
9.	Ferulic acid	–5.7
10.	p-Coumaric acid	–5.5
11.	Catechin	–6.0
12.	α-Tocopherol	–5.2
13.	β-Sitosterol	–5.0

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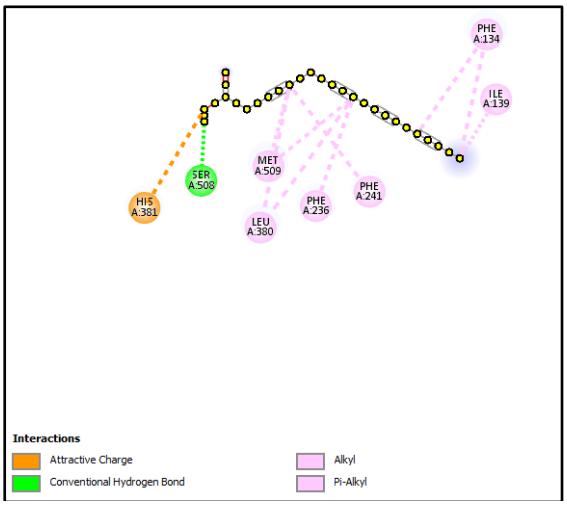

Figure 3: Molecular docking interactions of lauric acid with CYP51

CONCLUSION:

This research utilises network pharmacology to provide a comprehensive systems-level examination of the anti-dermatophytic properties of virgin coconut oil (VCO). The study demonstrates that VCO exerts its therapeutic benefits via a multi-component, multi-target, multi-pathway mechanism. Medium-chain fatty acids, especially lauric acid, are essential bioactive compounds with good pharmacokinetic properties and are generally safe. They have the highest binding affinity for lanosterol 14α-demethylase (CYP51), a key enzyme in fungal ergosterol biosynthesis. Network analysis and characterisation of the disturbance in protein-protein interactions (PPI) revealed that the bioactive components of VCO affect essential hub genes involved in the regulation of inflammation, immunological responses, and epidermal barrier integrity. This indicates a multifaceted mechanism of direct antifungal activity, combined with host-immune-mediated regulation. The molecular docking experiments demonstrated that both portions of VCO, specifically lauric acid, might disrupt fungal membranes and affect sterol breakdown. This justifies the mechanistic significance of network pharmacology. To test these *in silico* predictions both in the laboratory and in real organisms' antifungal assays against dermatophyte species ought to be employed. The quantitative measurements are required to ensure that the components of the VCO block CYP51 decrease the level of ergosterol and disrupt the membranes. Further research on optimal technology of topical delivery, combinations of certain compounds with traditional antifungals, and dose optimisation is likely to enhance treatment. To use in dermatological clinical practice, the safety, efficacy, and long-term effects of VCO-based antifungal formulations are of critical importance. They have strong scientific evidence to recommend virgin coconut oil as a safe, natural, multi-target therapy for dermatophytosis.

DATA AVAILABILITY STATEMENT:

The data that support the findings of this research are available from the corresponding author upon reasonable request.

COMPETING INTERESTS:

The authors declare no competing interests.

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