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Exploring the Antioxidant Activity of Phytol from the *Scoparia dulcis* Through *In-silico* Analysis

A. Clara Mary Arulandhu[1], M. Viji[2], S. Aishwariya[2], Vijayalakshmi P.[1], Rajagopal P.[3], M. Rajalakshmi[1,2,4*]

[1]PG & Research Department of Biotechnology& Bioinformatics, DBT-BIF Centre, Holy Cross College (Autonomous), Affiliated to Bharathidasan University, Tiruchirappalli, Tamil Nadu, India

[2]DBT-BIF Centre, Holy Cross College (Autonomous), Tiruchirappalli

[3]Central Research Laboratory, Meenakshi Ammal Dental College and Hospital, Meenakshi Academy of Higher Education and Research (Deemed to be University), Chennai, 600095, India

[4]PG & Research Department of Zoology, Holy Cross College (Autonomous), Tiruchirappalli

Abstract

Diabetes is a long-term physiological disorder that affects people of all ages and has a major negative impact on people's ability to live normal, harmonious lives across the globe. The discovery of innovative antidiabetic medications is necessary due to the emergence of resistance and adverse effects of existing oral antidiabetic drugs, even with the availability of insulin preparations and various synthetic alternatives. Due to the side effects, Scientists are focusing on Phytotherapy. This computational study aimed to elucidate the antioxidant activity of Phytol by utilizing molecular docking. The objective of the current research is to predict the Lipinski rule of 5 for Phytol. To examine the ADMET properties of Phytol. To analyse the protein-ligand interaction of Phytol with ROS proteins like Superoxide dismutase (PDB ID:1SPD_A), Catalase (PDB ID:1QQW_A), Glutathione peroxidase (PDB ID:2HE3_A), Peroxiredoxin (PDB ID:1OC3_A). The results of the in-silico studies infer that Phytol follows the Lipinski rule of 5, having a higher binding affinity with catalase protein and better hydrogen bond interactions with Superoxide dismutase and Glutathione peroxidase. The current study provides evidence that Phytol reduces oxidative stress. However, additional in-vitro and in-vivo research are needed to understand the prediction process.

Keywords: *Diabetes Mellitus, Docking, ROS (Reactive Oxygen Species), Phytol.*

Introduction

Worldwide, an estimated 537 million people have been diagnosed with diabetes, of which 90–95% have type 2 diabetes (T2D). The International Diabetes Federation estimates that by 2050, there will be 784 million of them, along with significant and rising socioeconomic costs [1]. Because it inhibits apoptotic signaling and has cytotoxic effects on oral cancer cells, β-sitosterol shows promise as a therapy for oral cancer [2]. Diabetes mellitus is a chronic metabolic disorder characterized by insufficient insulin activity and secretion, leading to abnormalities in proteins, carbohydrates, and lipids metabolism. The disease affects a significant portion of the global population and can have severe consequences if left untreated, such as ketoacidosis or hyperosmolar disorders. Classification of diabetes into types like type 1, type 2, and gestational diabetes is crucial for treatment strategies, although some individuals

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****Corresponding Author: rajalakshmi@hcctrichy.ac.in.***

may not neatly fit into a single category, requiring revaluation [3]. Therefore, in both forms of diabetes, chronic oxidative stress brought on by hyperglycemia may be a major factor in the development of β-cell dysfunction. Research has indicated that antioxidants can prevent this [4].

There is a strong correlation between the severity of dental caries and the presence of *H. pylori* in deep carious lesions, indicating that the bacteria may exacerbate dental caries [5]. Antioxidants are a class of chemicals that considerably slow down or prevent oxidation processes when present in small amounts relative to oxidizable compounds. The two damaged electrons in the O2 molecule have the same spin quantum number, making it a free radical. Because of this spin constraint, O2 prefers to take its electrons one at a time, which can cause damage to cells by generating what are known as ROS (Reactive Oxygen Species). Additionally, ROS are continuously created as byproducts of various metabolic pathways found in several cellular compartments, including peroxisomes, mitochondria, and chloroplasts [6].

Numerous human illnesses, including ageing, arthritis, cancer, AIDS, diabetes, and others, are frequently associated with oxidative stress. Enzymatic antioxidant systems, which comprise a range of enzymatic scavengers like superoxide dismutase (SOD), glutathione peroxidase (GPX), and catalase (CAT), prevent the buildup of ROS brought on by stress. Superoxide dismutase catalyzes the dismutation of superoxide into oxygen and hydrogen peroxide. This hydrogen peroxide will be destroyed as water and oxygen molecules, in the presence of catalase and glutathione peroxidase. The deficiency of natural antioxidant enzymes, specifically catalase (CAT), glutathione peroxidase (GPx), and superoxide dismutase (SOD), results in an oxidative environment within cells. Diabetes mellitus is known to cause non-enzymatic glycosylation and oxidation, which inhibits these enzymes. Antioxidant molecules in food play a significant role as a health-protecting element. Antioxidants may lower the risk of chronic illnesses including cancer and heart disease, according to scientific research. The main natural sources of antioxidants are fruits, vegetables, and whole grains [7]. Calotropin inhibits cell proliferation, induces apoptosis, and suppresses migration in HSC-3 oral cancer cells, highlighting its potential as a therapeutic agent for oral cancer [8].

Various antidiabetic drugs are available to manage hyperglycemia by improving insulin sensitivity, enhancing insulin secretion, and promoting glucose uptake. However, drugs like metformin and sulfonylureas can have unwanted side effects such as diarrhoea, lactic acidosis, hepatic failure, weight gain, tachycardia, and hypothyroidism. Plant-based sources are being explored for their potential antidiabetic properties, as they have shown promising efficacy in recent studies and are considered reliable alternatives to synthetic drugs [9].

Plant-based sources of antidiabetic agents have been utilized since ancient times due to their perceived safety, affordability, and presence in traditional medicines like those from Indian, Korean, and Chinese cultures. These natural remedies are believed to improve diabetic conditions through various mechanisms, including enhancing insulin secretion and sensitivity, promoting glucose uptake by cells, inhibiting glucose absorption, and displaying anti-inflammatory properties. As a result, the popularity of functional foods and phytotherapies for managing diabetes is increasing globally [10]. Various genetic alterations in oral squamous cell carcinoma grades, offering information for better customized medication and treatment approaches [11].

The medicinal botanical herb *Scoparia dulcis* L., also known as *S. dulcis*, has been utilised for many years in southern China, India, Brazil, Paraguay, and Nigeria. *S. dulcis*

is thought to have stomachic, diuretic, antitussive, heat-clearing, and toxin-absorbing properties in traditional Chinese medicine. From ancient times, it has been used in traditional Chinese herbal medicine to treat a variety of conditions including fever, eczema, miliaria, abnormal urine, sore throats, coughs with lung heat, and colds. In southern China, *S. dulcis* is also frequently added to herbal teas for health purposes. *S. dulcis* is also utilised in various ethnomedical groups to treat respiratory, hepatic, and stomach disorders as well as oedema. *S. dulcis* has pharmacological activities like anti-inflammatory, anti-atherosclerotic, anti-arthritic, hepatoprotective, anti-oxidative, anti-hyperlipidemia, anti-inflammatory, and anti-urolithiasis properties [12].

Phytol (3,7,11,15-tetramethylhexadec-2-en-1-ol) is a type of fatty alcohol found in the chlorophyll pigment, primarily released in the digestive system of ruminant animals possibly by gut bacteria. Due to this process, phytol is present in relatively high amounts in the adipose tissues and dairy products of these animals [13]. Anxiolytic, metabolism-modulating, cytotoxic, antioxidant, autophagy- and apoptosis-inducing, antinociceptive, anti-inflammatory, immune-modulating, and antibacterial properties have all been shown in recent Phytol investigations [14]. Salivary MMP-9 levels were considerably greater in OSCC patients than in those with normal mucosa and oral leukoplakia, indicating that it may be a symptom of malignant transformation [15].

The objective of the study is to predict the Lipinski's rule of 5 and ADMET properties (Absorption, Distribution, Metabolism, Excretion, Toxicity) for the bioactive compound Phytol. To analyse the protein-ligand interaction of Phytol with ROS targets like Superoxide dismutase, Catalase, Glutathione peroxidase, Peroxiredoxin. The present study aimed to analyze the molecular interaction of phytol with ROS (Reactive Oxygen Species) proteins like Superoxide dismutase, Catalase, Glutathione and Peroxiredoxin through docking.

Materials and Methods

Ligand Preparation

The National Institutes of Health (NIH) in the United States created and maintains the public chemical information collection known as PubChem. PubChem gathers biological activity descriptions of chemical substances from hundreds of data sources and makes them freely available to the public. The canonical SMILES of phytol were taken from PubChem. The 2D structure of ligand phytol was drawn using ACD/ChemSketch.

Drug-Likeliness Properties

The pharmacokinetic properties like the LIPINSKI rule of 5 and ADMET properties were analyzed using the SwissADME tool.

Target Preparation

The 3D structure of ROS (Reactive Oxygen Species) proteins like Superoxide dismutase (PDB ID:1SPD_A), Catalase (PDB ID:1QQW_A), Glutathione peroxidase (PDB ID:2HE3_A), Peroxiredoxin (PDB ID:1OC3_A), were obtained from Protein Data Bank (PDB). The receptors were prepared via the BIOVIA Discovery Studio Visualizer 2021 Client software.

Molecular Docking

The docking studies were performed utilizing PyRx version 0.8. PyRx was used to convert all PDB files for proteins and ligands into PDBQT format. An open babel was used to import the ligand. The optimisation method employed conjugate gradient descent, and the energy reduction parameter was the Universal Force Field (UFF). The findings were downloaded in 2 different formats, PDB and CSV file formats. The binding affinity of the ligand was downloaded in CSV format. The

target-ligand interactions were downloaded in PDB format.

Visualization of Target-Ligand Interaction

By importing the result into the BIOVIA Discovery Studio Visualizer 2021 Client software which displayed the 2D and 3D interactions of the docking result with the bond length, we were able to discover a significant interaction between the ligands and the receptor binding site.

Results and Discussion

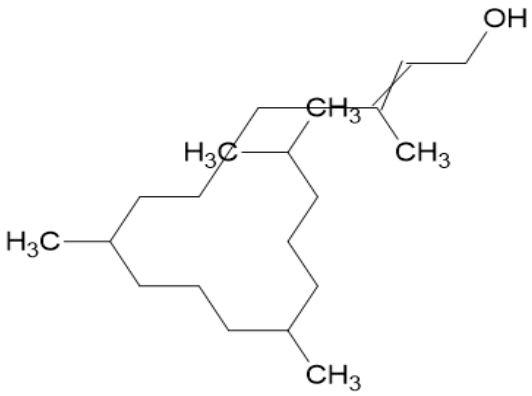

Figure 1. 2D Structure of Phytol

Table 1. LIPINSKI Rule of 5 Phytol was Obtained through SwissADME.

Ligand	Mol. Weight g/mol	LogP	Rotatble bonds	Acceptors	Donors	Surface area Å^2
Phytol	296.53	6.36	13	1	1	20.23

Table 2. ADMET Properties of Phytol were Obtained through SwissADME.

ADMET PROPERTIES	PREDICTED VALUES
Gastrointestinal absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	No
Bioavailability Score	0.55

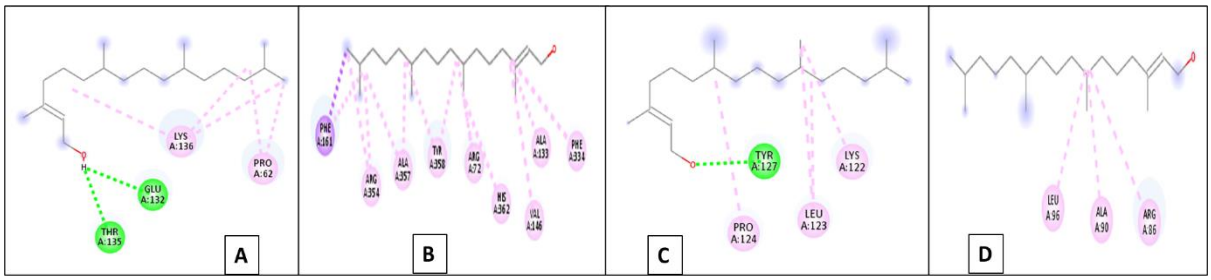

Figure 2. Molecular Interaction between Phytol and ROS Proteins

Table 3. Depicting the Binding Affinity and H bond Interaction

Target Type	**Target**	**Binding Affinity**	**Hydrogen bond Interactions**	**Other Interactions**
		LIGAND		
		Phytol		
ROS proteins	**Superoxide dismutase**	-4.5	GLU A:132 (2.66 Å)	**Alkyl interactions**: PRO A:62 (4.62Å,4.90Å)
				LYS A:136 (4.09Å,4.74 Å,5.04 Å)
			THR A:135 (2.61 Å)	
	Catalase	-8.1	-	**Alkyl interactions**: ARG A:354 (4.07Å, 4.29Å)
				ALA A:357 (3.90Å, 4.04Å)
				TYR A:358 (3.88Å, 4.91Å)
				ARG A:72 (3.89Å, 4.56Å)
				Pi-Alkyl interactions: HIS A:362 (4.44Å)
				VAL A:146 (5.11Å)
				ALA A:133 (4.81Å)
				PHE A:334 (5.24Å)
				Pi-Sigma interaction: PHE A:161(3.94Å)
	Glutathione peroxidase	-4.4	TYR A:127 (2.42 Å)	**Alkyl interactions**: PRO A:124 (5.42Å)
				LEU A:123 (5.18 Å,5.46Å)
				LYS A:122(4.26Å)

	Peroxiredoxin	-4.7	-	**Alkyl interactions**: LEU A:96 (4.62Å)
				ALA A:90 (4.71Å)
				ARG A:86(5.33Å)

The finding of active compounds from natural materials has gained significant importance in the realm of drug discovery. Natural antioxidants are becoming more and more necessary as concerns over the safety of synthetic antioxidants develop [16,17,19]. miRNAs' promise as therapeutic targets and biomarkers for oral premalignant illnesses, highlighting their importance in early detection and individualized treatment plans [18].

The search for novel plant-based medications employs a multidisciplinary approach that combines botanical, ethnobotanical, phytochemical, and biological techniques. The typical early steps in the drug development process involve identifying structural patterns shared by active compounds or examining binding sites in target proteins. *In-silico* molecular docking is crucial for structure-based drug design because it is one of the best techniques for discovering novel ligands for receptors with known structures [20-25].

Molecular docking, which scores and aligns tiny compounds in a protein's binding site, is still a promising approach in the discipline of computer-based drug creation. Using the scoring functions, the docking procedure predicts the orientation and confirmation of the ligands within the intended binding site, and their interaction energies are computed. A lack of balance between antioxidants and oxidants is known as oxidative stress, and it is the root cause of numerous diseases, including diabetes, atherosclerosis, cardiovascular issues, and others. It also causes biochemical alterations [26-28]. Exosomal miRNAs miRNA 21, 145, and 184 that circulate in plasma may be used as potential biomarkers to detect OSMF and leukoplakia patients who are at high risk of developing malignant transformation.

2D structure of Phytol was obtained through ACD/ChemSketch software (Fig:1). Lipinski's rule of 5 is widely used as a filter and measurement of the drug likeliness of a series of compounds which was obtained through SwissADME for Phytol (Table 1). The Lipinski rule is another important component in computer-based medication development. The "rule of five" is used to predict how much or how permeable substances will be when they come into contact with the lipid bilayers in the body. When assessing these features, Lipinski's "rule of five" states that a chemical satisfies the drug-like criteria if it satisfies all five of the following criteria. The molecular weight is less than 500 g/mol. The calculated octanol/water partition coefficient (log P 5) is less than 5. There are less than five donors of hydrogen bonds. Ten hydrogen bond acceptors maximum, primarily N and O atoms. The molecular weight of Phytol was 296.53Da, LogP was 6.36, Hydrogen bond acceptors were 1 and Hydrogen bond donors were 1. It has 13 rotatable bonds and the surface area was 20.23Å^2. The results show that Phytol follows the Lipinski rule of 5. Vitamin D supplementation may lengthen treatment time with less tissue effects, as evidenced by the negative link observed between salivary 1-25dihydroxycholecalciferol and IL-17A levels after orthodontic treatment.

ADMET (Absorption, Distribution, Metabolism, Excretion, Toxicity) properties were obtained through SwissADME for Phytol (Table 2). ADMET properties play a key role in the drug-designing process. Phytol was discovered to have a low level of gastrointestinal absorption in humans and no

blood-brain barrier permeability, suggesting that the molecule can be readily absorbed from the stomach and has no negative effects on the brain because it cannot cross the BBB. Compounds that are either substrates or non-substrates of the permeability glycoprotein can be used to understand how the protein actively moves across biological membranes, such as the gastrointestinal wall, to reach the lumen or the brain. Phytol, a substrate for P-gp, may be effluxed out of the brain or gastrointestinal tract. Phytol is an inhibitor of CYP2C9, and it is not an inhibitor of CYP1A2, CYP2C19, CYP2D6 and CYP3A4. The bioavailability score is 0.55.

Phytol interacts with 4 ROS (Reactive Oxygen Species) proteins like Superoxide dismutase (PDB ID:1SPD_A), Catalase (PDB ID:1QQW_A), Glutathione peroxidase (PDB ID:2HE3_A), Peroxiredoxin (PDB ID:1OC3_A). The lower binding energy score indicates a greater binding capacity. The binding affinity of phytol with Superoxide dismutase is -4.4, Catalase is -8.1, Glutathione peroxidase is -4.4 and Peroxiredoxin is -4.7. Among them, catalase shows higher binding affinity. For Superoxide dismutase the compound shows two hydrogen bond interactions GLU A:132 (2.66 Å) and THR A:135 (2.61 Å). Glutathione peroxidase shows one hydrogen bond interaction TYR A:127 (2.42 Å). Catalase and Peroxiredoxin have no hydrogen bond interactions (Fig:2), (Table 3).

Conclusion

In conclusion, the *In-silico* study revealed that Phytol follows Lipinski's rule of 5 and ADMET properties. Phytol has a better H bond interaction with Superoxide dismutase and Glutathione peroxidase. The phytol has a better binding affinity with catalase. From this docking study, we conclude that phytol may reduce oxidative stress. Thus, the compound can be used as an effective herbal therapeutic molecule with further explorations.

Conflict of Interest

The authors hereby declare that there is no conflict of interest.

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References

[1]. GBD, 2021, Diabetes Collaborators, 2023, Global, regional, and national burden of diabetes from 1990 to 2021, with projections of prevalence to 2050: a systematic analysis for the Global Burden of Disease Study 2021. *Lancet* (London, England), *402*(10397), 203–234. https://doi.org/10.1016/S0140-6736(23)01301-6.

[2]. Jayaraman, S., Natarajan, S. R., Ponnusamy, B., Veeraraghavan, V. P., & Jasmine, S., 2023, Unlocking the potential of beta sitosterol: Augmenting the suppression of oral cancer cells through extrinsic and intrinsic signalling mechanisms. *The Saudi Dental Journal*, *35*(8), 1007-1013.

[3]. Kharroubi, A. T., & Darwish, H. M., 2015, Diabetes mellitus: The epidemic of the century. *World Journal of Diabetes*,*6*(6),850–867. https://doi.org/10.4239/wjd.v6.i6.850.

[4]. Baynes, J. W., & Thorpe, S. R., 1999, Role of oxidative stress in diabetic complications: A new perspective on an old paradigm. *Diabetes*, *48*(1), 1–9. https://doi.org/10.2337/diabetes.48.1.1

[5]. Sruthi, M. A., Mani, G., Ramakrishnan, M., & Selvaraj, J., 2023, Dental caries as a source of Helicobacter pylori infection in children: An RT-PCR study. *International Journal of Paediatric Dentistry*, *33*(1), 82-88.

[6]. Navrot, N., Rouhier, N., Gelhaye, E., & Jacquot, J. P., 2007, Reactive oxygen species generation and antioxidant systems in plant mitochondria. *Physiologia Plantarum*, *129*(1), 185-195.

[7]. Mittler, R., Vanderauwera, S., Gollery, M., & Van Breusegem, F., 2004, Reactive oxygen gene

network of plants. *Trends in Plant Science*, *9*(10), 490–498. https://doi.org/10.1016/j.tplants.2004.08.009.

[8]. Jayaraman, S., Natarajan, S. R., Veeraraghavan, V. P., & Jasmine, S., 2023, Unveiling the anti-cancer mechanisms of calotropin: Insights into cell growth inhibition, cell cycle arrest, and metabolic regulation in human oral squamous carcinoma cells (HSC-3). *Journal of Oral Biology and Craniofacial Research*, *13*(6), 704-713.

[9]. Li, G. Q., Kam, A., Wong, K. H., Zhou, X., Omar, E. A., Alqahtani, A., Li, K. M., Razmovski-Naumovski, V., & Chan, K., 2012, Herbal medicines for the management of diabetes. *Advances in Experimental Medicine and Biology*, *771*, 396–413. https://doi.org/10.1007/978-1-4614-5441-0_28.

[10]. Kazeem, M. I., & Davies, T. C., 2016, Anti-diabetic functional foods as sources of insulin secreting, insulin sensitizing and insulin mimetic agents. *Journal of Functional Foods*, *20*, 122-138.

[11]. Krishnan, R. P., Pandiar, D., Ramani, P., & Jayaraman, S., 2025, Molecular profiling of oral epithelial dysplasia and oral squamous cell carcinoma using next generation sequencing. *Journal of Stomatology, Oral and Maxillofacial Surgery*, *126*(4), 102120.

[12]. Reshma Rajan, R. R., Mahima Vedi, M. V., Badrinathan Sridharan, B. S., Himaja, M., Sabina, E. P., & Raj, N. A. N., 2014, In vitro and in vivo study on the effect of Scoparia dulcis in inhibiting the growth of urinary crystals. *Internatinal Journal of Phytomedicine* 6, 617-624.

[13]. Pazhani, J., Chanthu, K., Jayaraman, S., & Varun, B. R., 2023, Evaluation of salivary MMP-9 in oral squamous cell carcinoma and oral leukoplakia using ELISA. *Journal of Oral and Maxillofacial Pathology*, *27*(4), 649-654.

[14]. Brown, P. J., Mei, G., Gibberd, F. B., Burston, D., Mayne, P. D., McClinchy, J. E., & Sidey, M., 1993, Diet and Refsum's disease. The determination of phytanic acid and phytol in certain foods and the application of this knowledge to the choice of suitable convenience foods for patients with Refsum's disease. *Journal of Human Nutrition and Dietetics*, 6(4), 295-305.

[15]. Islam, M. T., Ali, E. S., Uddin, S. J., Shaw, S., Islam, M. A., Ahmed, M. I., Chandra Shill, M., Karmakar, U. K., Yarla, N. S., Khan, I. N., Billah, M. M., Pieczynska, M. D., Zengin, G., Malainer, C., Nicoletti, F., Gulei, D., Berindan-Neagoe, I., Apostolov, A., Banach, M., Yeung, A. W. K.,Atanasov, A. G., 2018, Phytol: A review of biomedical activities. Food and chemical toxicology: *An International Journal Published for the British Industrial Biological Research Association*, 121, 82–94. https://doi.org/10.1016/j.fct.2018.08.032.

[16]. Fathima, J. S., Jayaraman, S., Sekar, R., & Syed, N. H., 2024, The role of MicroRNAs in the diagnosis and treatment of oral premalignant disorders. *Odontology*, 1-10.

[17]. Eliza, J., Daisy, P., & Ignacimuthu, S., 2010, Antioxidant activity of costunolide and eremanthin isolated from *Costus speciosus* (Koen ex. Retz) Sm. *Chemico-Biological Interactions*, 188(3), 467–472. https://doi.org/10.1016/j.cbi.2010.08.002.

[18]. Brooijmans, N., & Kuntz, I. D., 2003, Molecular recognition and docking algorithms. *Annual Review of Biophysics and Biomolecular Structure*, 32, 335–373. https://doi.org/10.1146/annurev.biophys.32.110601.142532.

[19]. Kitchen, D. B., Decornez, H., Furr, J. R., & Bajorath, J., 2004, Docking and scoring in virtual screening for drug discovery: methods and applications. Nature reviews. *Drug Discovery*, 3(11), 935–949. https://doi.org/10.1038/nrd1549.

[20]. Pari, L., & Latha, M., 2004, Protective role of Scoparia dulcis plant extract on brain antioxidant status and lipidperoxidation in STZ diabetic male Wistar rats. *BMC Complementary and Alternative Medicine*, 4, 16. https://doi.org/10.1186/1472-6882-4-16.

[21]. Lin, H. D., Lee, Y. C., Chiang, C. Y., Lin, Y. J., Shih, C. Y., Tsai, R. K., Lin, P. Y., Lin, S. Z., Ho, T. J., & Huang, C. Y., 2023, Protective effects of Scoparia dulcis L. extract on high glucose-induced injury in human retinal pigment epithelial cells. *Frontiers in Nutrition*, 10, 1085248. https://doi.org/10.3389/fnut.2023.1085248.

[22]. Sivasankarapillai, V. S., Krishnamoorthy, N., Eldesoky, G. E., Wabaidur, S. M., Islam, M. A., Dhanusuraman, R., & Ponnusamy, V. K., 2022, One-pot green synthesis of ZnO nanoparticles using Scoparia dulcis plant extract for antimicrobial and antioxidant activities. *Applied Nanoscience*, 1–11.Advance online publication. https://doi.org/10.1007/s13204-022-02610-7.

[23]. Mishra, M. R., Mishra, A., Pradhan, D. K., Panda, A. K., Behera, R. K., & Jha, S., 2013, Antidiabetic and Antioxidant Activity of *Scoparia dulcis* Linn. *Indian Journal of Pharmaceutical Sciences*, *75*(5), 610–614.

[24]. Moniruzzaman, M., Atikur Rahman, M., & Ferdous, A., 2015, Evaluation of Sedative and Hypnotic Activity of Ethanolic Extract of *Scoparia dulcis* Linn. Evidence-based complementary and alternative medicine: *eCAM*, 2015, 873954. https://doi.org/10.1155/2015/873954.

[25]. Benarfa, A., Gourine, N., Mahfoudi, R., Harrat, M., & Yousfi, M., 2019, Effect of Seasonal and Regional Variations on Phenolic Compounds of *Deverra scoparia* (Flowers/Seeds) Methanolic Extract and the Evaluation of Its in Vitro Antioxidant Activity. *Chemistry & Biodiversity*, 16(11), e1900420. https://doi.org/10.1002/cbdv.201900420.

[26]. Coulibaly, A. Y., Kiendrebeogo, M., Kehoe, P. G., Sombie, P. A., Lamien, C. E., Millogo, J. F., & Nacoulma, O. G., 2011, Antioxidant and anti-inflammatory effects of *Scoparia dulcis* L. *Journal of Medicinal Food*, *14*(12), 1576–1582. https://doi.org/10.1089/jmf.2010.0191.

[27]. Yasothkumar, D., Ramani, P., Jayaraman, S., Ramalingam, K., & Tilakaratne, W. M., 2024, Expression Profile of Circulating Exosomal microRNAs in Leukoplakia, Oral Submucous Fibrosis, and Combined Lesions of Leukoplakia and Oral Submucous Fibrosis. *Head and Neck Pathology*, *18*(1), 28.

[28]. Sagar, S., Ramani, P., Moses, S., Gheena, S., & Selvaraj, J., 2024, Correlation of salivary cytokine IL-17A and 1, 25 dihydroxycholecalciferol in patients undergoing orthodontic treatment. *Odontology*, 1-10.