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Analyzing *Spathiphyllum wallisii* (Peace Lily) for Anti-Cancer Receptor Targeting: *In vitro* and *In silico* Investigation Across Varying Concentrations

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ABSTRACT:

Objective:

Spathiphyllum wallisii has a rich history in traditional medicine, notably for its anti-inflammatory and anti-cancer properties. Given the pivotal role of growth factors and their receptors in cancer initiation and progression, exploring the potential of Spathiphyllum wallisii phytochemicals as cancer therapeutics targeting these receptors is essential.

Methods:

This study employs an in-silico approach to investigate the cancer therapeutic potential of Spathiphyllum wallisii phytochemicals against growth factor receptors. Molecular docking simulations using PyRx were conducted to predict the binding affinity between the phytochemicals and the receptors.

Results:

Eight phytocompounds sourced from Spathiphyllum wallisii were initially screened based on their binding affinity towards growth factor receptors. Ligands exhibiting strong binding with GFR targets, with a binding score of less than -8.5 kcal/mol, were selected for further investigation. Among these, rotenone displayed notable binding affinity to the receptors, suggesting its potential as a targeted cancer therapy. These findings lay the groundwork for future in-vitro and in-vivo experiments to validate the efficacy of these phytochemicals as cancer treatments.

Conclusion:

The results indicate that Boswellic acid derivatives derived from Boswellia serrata hold promise as potential sources of novel cancer therapies.

Keywords: EGFR, FGFR, ILGFR, PDGFR, VEGFR, cancer, phytocompounds

Introduction

Cancer remains one of the leading causes of mortality worldwide, posing significant challenges to public health systems and necessitating ongoing efforts to develop effective therapeutic interventions [1]. Despite advances in cancer treatment, including targeted therapies and immunotherapies, the complexity and heterogeneity of tumors continue to present obstacles to achieving durable responses and improving patient outcomes [2]. In this context, natural products derived from medicinal plants have emerged as a valuable source of bioactive compounds with the potential to complement existing cancer therapies [3] or serve as leads for the development of novel drugs. *Spathiphyllum wallisii*, commonly known as peace lily, is a plant species belonging to the Araceae family, native to tropical regions of the Americas [4]. In addition to its ornamental value, *Spathiphyllum wallisii* has a rich history of use in traditional medicine, particularly in cultures where herbal remedies are prevalent. Traditionally, extracts from various parts of the plant, including leaves, roots, and flowers, have been utilized for their purported medicinal properties, ranging from anti-inflammatory and analgesic effects to antimicrobial and anti-cancer activities [5]. While empirical evidence supporting the efficacy of *Spathiphyllum wallisii* in cancer treatment is limited, recent scientific investigations have begun to shed light on its potential as a source of bioactive compounds with anti-cancer properties [6]. Central to the pathogenesis of cancer are dysregulated signaling pathways that govern cellular processes such as proliferation, differentiation, survival, and angiogenesis. Among these pathways, the signaling networks involving growth factors and their cognate receptors play pivotal roles in driving tumor initiation, progression, and metastasis. Aberrant activation of growth factor receptors, such as epidermal growth factor receptor (EGFR), fibroblast growth factor receptor (FGFR), insulin-like growth factor receptor (IGFR), platelet-derived growth factor receptor (PDGFR), and vascular endothelial growth factor receptor (VEGFR), has been implicated in various aspects of tumor biology [7], including enhanced cell proliferation, survival, angiogenesis, and metastasis. Consequently, targeted inhibition of growth factor signaling pathways has emerged as a promising therapeutic strategy for cancer treatment [8], with several clinically approved drugs demonstrating efficacy in specific cancer subtypes. Recently, there has been increasing interest in exploring natural products as potential sources of anti-cancer agents that target growth factor receptors [9]. Phytochemicals derived from medicinal plants offer a diverse array of chemical scaffolds with unique pharmacological properties, making them attractive candidates for drug discovery and development [10]. By harnessing the vast chemical diversity present in nature, researchers aim to identify novel compounds capable of modulating growth factor signaling pathways and exerting anti-cancer effects with improved efficacy and safety profiles compared to conventional therapies [11].

The objective of this study is to investigate the potential of phytochemicals derived from *Spathiphyllum wallisii* as anti-cancer agents targeting growth factor receptors. Through a combination of bioinformatics analysis and molecular modeling techniques, we aim to identify candidate compounds from *Spathiphyllum wallisii* that demonstrate favorable binding interactions with key growth factor receptors implicated in cancer [12]. Subsequently, selected phytochemicals will be evaluated in vitro and in vivo to validate their anti-cancer properties and elucidate their mechanisms of action [13]. By elucidating the therapeutic potential of *Spathiphyllum wallisii* phytochemicals, this study aims to contribute to the development of novel cancer therapies with improved efficacy and safety profiles [14].

Methodology

Media Preparation

The experiment design was completely randomized with nine replications. A total of nine test samples were taken for testing under 8/16 hrs, 12/12 hrs and 16/8 hrs of light/dark photoperiodic conditions respectively. In this experiment, The sucrose concentrations were increased by 5 grams for each test from 10g to 50g in MS media salt like 10 g/L, 15 g/L, 20 g/L, 25 g/L, 30 g/L, 35 g/L, 40 g/L, 45 g/L and 50 g/L and named as T1, T2, T3, T4, T5, T6, T7, T8 and T9 respectively (Dewir *et al*. 2006). Prepared media was allowed to stand for 4 day to check any contamination to be observed.

Preparation of Incoculum

Explants were inoculated at a MS media containing various concentration of sucrose and clearly labeled. Incubated at 20±5 ℃,35 μmolem^{-2}s^{-1} of light intensity in a various photo-periods range like 8/16 hrs , 12/12 hrs and 16/8 hrs of light/dark photoperiod respectively. Number of shoot, number of leaves, highest length of shoot, leaf base index, width ansd length of leaves, biomass, total chlorophyll content and carotenoid content were measured.

Relative Growth Rate

Relative growth rate gives the efficiency of the treatment by comparing the biomass weight before and after the incubation period. Relative growth period various with time so that measurement were taken per unit time periods of 30 days.

Chlorophyll Estimation by DMSO Method

To estimate chlorophyll, 100 mg of fresh plants leaves were chopped in fine pieces without mid rip position. In 250 ml conical flash, add 20 ml of 5% DMSO to the chopped plant material and incubate in 65℃ for 5hours. After incubation period, cool the sample to the room temperature. And then optical density (OD) values were taken at 645μm and 669μm. Chlorophyll content can be measured by the formula determined by Aron (1948).

$$\text{Ca} = \text{chlorophyll a } (\mu\text{g ml-1}) = [(12.19 \times a665) - (3.45 \times a649)]$$

$$\text{Cb} = \text{chlorophyll b } (\mu\text{g ml-1}) = [(21.99 \times a649) - (4.68 \times a665)]$$

$$\text{Total chlorophyll a + b } (\mu\text{g ml-1}) = \text{ca + cb}$$

Estimation Of Carotinoids By DMSO Methods

The estimation of carotenoids by DMSO (Dimethyl sulfoxide) methods is similar to the chlorophyll estimation method. By the following formula, by Wellburn (2001) and Iryana *et al*. (2004) carotenoids were measured

$$\text{Total carotinoids} = \frac{1000*a480-(2.14*ca)\ (70.16*cb)}{220}$$

In Silico Analysis

Ligand Acquisition:

The secondary metabolites of *Spathiphyllum wallisii*, a medicinal plant, were obtained from the IMPPAT (Indian Medicinal Plants, Phytochemistry and Therapeutics) database [13]. After removing duplicates, a total of seventy-four metabolites were collected. The canonical SMILES

(Simplified Molecular Input Line Entry System) and 2D SDF (Standard Data Files) formats of these metabolites were retrieved from the PubChem database [14] for further analysis.

Protein Retrieval and Purification:

In this study, Growth Factor Receptors (GFRs), including EGFR, FGFR, ILGFR, PDGFR, and VEGFR, were chosen as molecular targets due to their potential roles in cell signaling and proliferation. The 3D structures of these proteins were downloaded from the RCSB PDB database [15]. The crystal structures of EGFR (PDB ID: 5UGB), FGFR (PDB ID: 6LVM), ILGFR (PDB ID: 3NW5), PDGFR (PDB ID: 5K5X), and VEGFR (PDB ID: 6GQO) were resolved using X-Ray diffraction techniques, with resolutions ranging from 1.87 Å to 2.53 Å. All crystal structures were purified using DS Biovia Discovery Studio Visualizer by removing non-structural water molecules and heteroatoms. To simplify the structures, only the A chains were retained for further analysis. The structures were then optimized by adding polar hydrogen atoms, and the purified structures were utilized for subsequent analyses.

Protein Structure Validation:

Validation of the 3D structures is crucial for molecular docking to understand how ligands interact with proteins. Therefore, the purified GFR structures were validated using web servers such as PDBsum generate [16], ProSA [17], and DS Biovia Discovery Studio.

Molecular Docking:

Computational techniques, such as molecular docking simulations, are employed to evaluate the interaction between small molecules and protein targets. In this study, PyRx virtual screening software was utilized for molecular docking of Spathiphyllum wallisii phytocompounds with GFRs. The purified protein structures were designated as macromolecules, and docking was performed using the AutoDock Vina plugin of PyRx.

The 2D SDF files of the ligands underwent energy minimization by applying the universal force field (UFF) using OpenBabel chemical file converter tools. Prepared protein and ligand files were saved in .pdbqt format, and docking parameters were set using Grid Parameter Files (GPF). The GPF parameters for the GFRs are listed in Table 1. Molecular docking analysis was based on ligand binding affinity with zero RMSD (Root Mean Square Deviation) towards the target GFRs [18]. The best-docked complexes were visualized using DS Biovia Discovery Studio Visualizer to analyze molecular interactions at the binding pocket of the target proteins [19].Table 1: GPF parameters for the GFRs.

Protein	**Grid Dimensions (Angstrom)**
EGFR	X=56.4491, Y=49.7363, Z=-24.8580
FGFR	X=49.7518, Y=59.6079, Z=52.10.9913
ILGFR	X=61.3457, Y=61.3722, Z=51.8915
PDGFR	X=53.8489, Y=53.6268, Z=39.6648
VEGFR	X=56.3868, Y=60.7911, Z=11.2543

Pharmacological studies:

The acceleration and cost-effectiveness of drug discovery and development can be achieved through the identification of pharmacological and ADMET (Absorption, Distribution,

Metabolism, Excretion, and Toxicity) properties of small compounds using computational methods. Employing in-silico investigations allows for the identification of drug candidates with a higher likelihood of success, thereby reducing the risk of drug failure [20]. The physicochemical properties, drug-likeness, and ADMET characteristics of small molecules were assessed utilizing the ADMETlab 2.0 web server [21]. Additionally, the bioactivity of these small molecules against six major drug classes was predicted using the Molinspiration Cheminformatics server [22].

Results:

Ligand Retrieval:

Spathiphyllum wallisii, an Indian tree with a history of use in Ayurvedic medicine for its anti-inflammatory and analgesic properties, contains boswellic acids and terpenoids as its major metabolites, exhibiting various medicinal benefits. Recent research highlights their anti-inflammatory and anti-cancer properties, indicating potential therapeutic applications in conditions such as rheumatoid arthritis and malignancies. Additionally, these bioactive compounds have been found to positively influence the immune system, contributing to overall health and wellness. Ligands from Spathiphyllum wallisii were obtained from the IMPPAT database, and the structures of ligands showing promising binding with GFRs are illustrated in Figure 1.

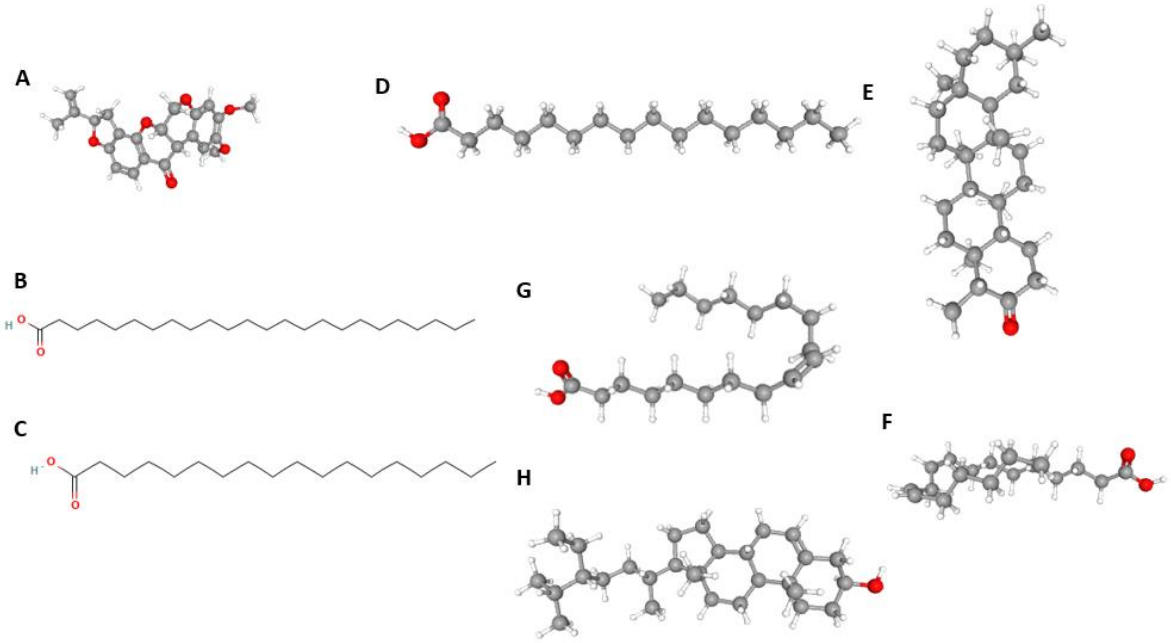

Figure 1. 3D Structures of Phytocompound from *Spathiphyllum wallisii*
A) Rotenone B) Tetracosanoic acid C) Stearic acid *D)* Palmitic acid E) Friedelin F) Oleic acid G) beta-Sitosterol H) Linoleic acid

Protein Structure Validation:

For successful molecular docking, it is crucial to assess the quality of protein structures. Molecular docking predicts how ligands interact with target proteins to identify potential therapeutic candidates. Hence, the purified protein structures underwent thorough validation through the following analyses:

Secondary Structure and Ramachandran Plots:

Analysis of dihedral angle distribution is vital for understanding protein stability and folding. Ramachandran plot analysis offers insights into structural architecture and irregularities. The purified structures of EGFR, FGFR, ILGFR, PDGFR, and VEGFR exhibited favorable distributions in Ramachandran plots, with varying percentages of residues in different regions, as depicted in Figures 2a-6a and 2b-6b, respectively. Predominant secondary structures observed in GFRs include hairpins, beta bulges, sheets, helix-helix interactions, strands, and beta and gamma turns (Figures 2c-6c).

Hydropathy Plots:

Determining hydrophobic and hydrophilic amino acids in targets is crucial for identifying druggable proteins, as drug binding affinity often depends on the hydropathicity of the binding pocket. Hydrophobic drugs tend to bind to hydrophobic regions of proteins, while hydrophilic drugs bind to hydrophilic areas. However, excessively hydrophobic drugs may pose challenges in elimination and potential hazards.

ProSA Model Quality Assessment:

ProSA web server analyzes and validates protein structures based on statistical potentials. The Z-score plot generated by ProSA aids in assessing the quality of protein structures. Negative Z-scores indicate less structured regions, while positive Z-scores suggest highly organized regions compared to predictions. These analyses ensure the reliability and suitability of protein structures for subsequent molecular docking studies, facilitating the identification of potential drug candidates.

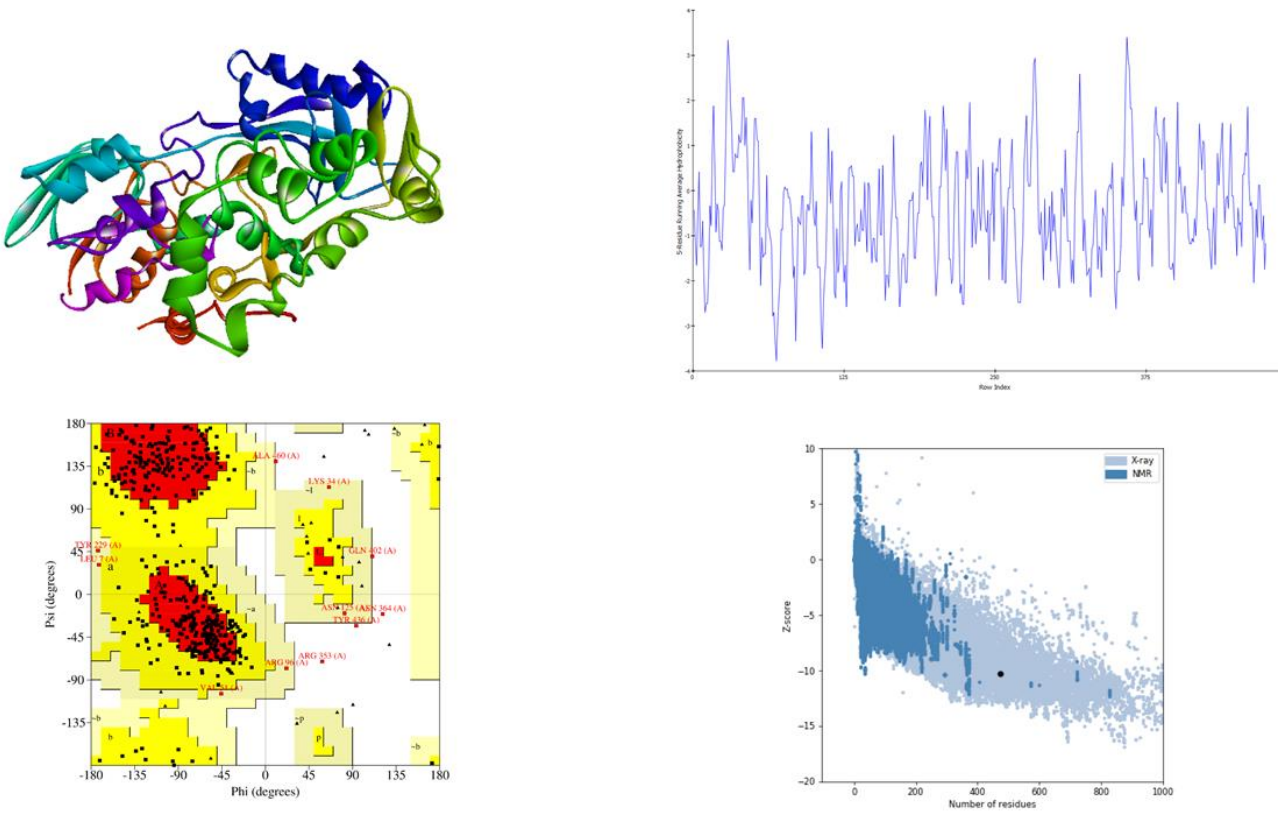

Figure 2: Secondary structure evaluation of EGFR protein

(a) Ramachandran plot (b) Secondary structures EGFR (c) Hydropathy plot for EGFR (d) Z-score analysis

Molecular Docking:

The docking in PyRx assumes ligands and flexible and the macromolecules as rigid. The efficacy of the ligand is determined in terms of binding affinity at zero RMSD. In the present research as the ligands demonstrated better binding with the GFR targets, a binding score less than -7 was considered for further investigation (Table 2). It was found that Alpha-boswellic acid has a better binding with all the target GFRs.

Table 2: Molecular of *Boswellia serrata* phytocompounds with target EGFR

S.NO	LIGAND	EGFR
1	**Rotenone**	-8.8
2	**Tetracosanoic acid**	-8.6
3	**Stearic acid**	-7.7
4	**Palmitic acid**	-7.2
5	**Friedelin**	-6.4
6	**Oleic acid**	-6.6
7	**beta-Sitosterol**	-6.1
8	**Linoleic acid**	-5.6

Visualizations:

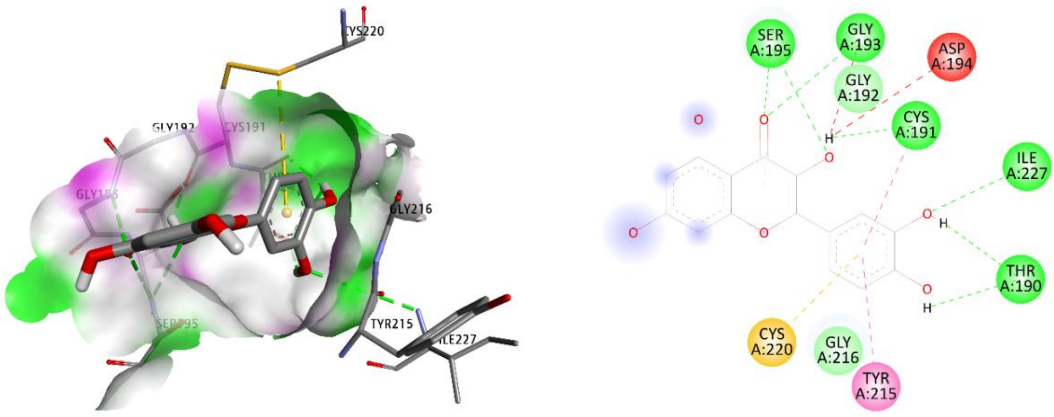

Figure 3. 3D and 2D interaction of amino acids with EGFR and Rotenone complex

Pharmacological studies:

Therapeutic potential of *Boswellia serrata* phytocompounds is studied through ADMT properties as the bioactive compounds should possess favorable drug-likeness properties. The top 8 as appraised through docking were investigated for their physicochemical (Table 3), absorption (Table 4), Distribution (Table 5), medicinal chemistry (Table 6) metabolism and excretion (Table 7), toxicity properties (Table 8) and bioactivity (Table 9). From the phrenological assessment, it is evident all the compounds showed advantageous pharmacological properties.

Table 3: Physicochemical properties of anti-cancer *Boswellia serrata* phytocompounds

No	PubChem CID	MW	Volume	nHD	nHA	n-Rot	n-Ring	Flex	TPSA	Log S
1	**Rotenone**	222.2	257.037	1	1	1	2	0.091	20.23	-3.232
2	**Tetracosanoic acid**	470.34	511.905	2	4	1	5	0.036	74.6	-4.721
3	**Stearic acid**	512.35	552.651	1	5	3	5	0.103	80.67	-5.083
4	**Palmitic acid**	498.37	546.497	1	4	3	5	0.107	63.6	-5.263
5	**Friedelin**	456.36	511.671	2	3	5	4	0.227	57.53	-4.014
6	**Oleic acid**	456.36	505.751	2	3	1	5	0.037	57.53	-4.278
7	**beta-Sitosterol**	426.39	490.807	1	1	0	5	0	20.23	-6.142
8	**Linoleic acid**	456.36	505.751	2	3	1	5	0.037	57.53	-4.62

MW: Molecular weight; **nHA:** Number of hydrogen bond acceptors; **nHD:** Number of hydrogen bond donors; **nRot:** Number of rotatable bonds; **nRing**: Number of rings; **nHet:** Number of heteroatoms; **nRig:** Number of rigid bonds: **Flex:** Flexibility; **TPSA:** Topological polar surface area; **logS:** The logarithm of aqueous solubility value.

Table 4: Absorption properties of anti-cancer *Boswellia serrata* phytocompounds

No	PubChem CID	Caco-2 Permeability	MDCK Permeability	Pgp-inhibitor	Pgp-substrate	HIA	F (20%)
1	**Rotenone**	-4.489	1.45E-05	0.057	0	0.004	0.144
2	**Tetracosanoic acid**	-5.385	1.71E-05	0.079	0.001	0.029	0.003
3	**Stearic acid**	-5.14	1.88E-05	0.227	0	0.012	0.033
4	**Palmitic acid**	-5.063	1.56E-05	0.003	0	0.01	0.005
5	**Friedelin**	-5.248	1.38E-05	0.026	0	0.013	0.123
6	**Oleic acid**	-5.26	1.17E-05	0.001	0	0.023	0.007
7	**beta-Sitosterol**	-5.034	6.76E-06	0.049	0	0.03	0.257
8	**Linoleic acid**	-5.207	1.39E-05	0.002	0	0.013	0.008

Caco-2: Caco-2 Permeability; **MDCK:** Madin−Darby Canine Kidney cells (MDCK) Permeability; **Pgp-inh/ Pgp-sub:** the inhibitor and substrate of P-glycoprotein; **HIA:** Human intestinal absorption; **F(20%):** the human oral bioavailability 20%

Table 5: Distribution properties of anti-cancer *Boswellia serrata* phytocompounds

No	PubChem CID	PPB	VD	BBB Permeation	FU
1	**Rotenone**	94.22%	2.06	0.758	3.24%
2	**Tetracosanoic acid**	97.02%	0.785	0.899	2.71%
3	**Stearic acid**	99.54%	0.628	0.191	2.93%
4	**Palmitic acid**	100.02%	0.722	0.563	1.99%
5	**Friedelin**	96.05%	0.918	0.554	1.88%
6	**Oleic acid**	99.24%	0.869	0.802	3.15%
7	**beta-Sitosterol**	99.78%	1.82	0.749	2.52%
8	**Linoleic acid**	99.38%	0.821	0.777	2.25%

BBB: Blood–brain barrier; **PPB:** Plasma protein binding; **VDss:** Volume Distribution; **Fu:** fraction unbound in plasma; **CL:** Clearance rate; **T1/2:** Half-life of the small molecules.

Table 6: Medicinal chemistry properties of anti-cancer *Boswellia serrata* phytocompounds

No	PubChem CID	QED	SA Score	Fsp3	Lipinski rule	PAINS
1	**Rotenone**	0.663	3.788	0.867	Accepted	0
2	**Tetracosanoic acid**	0.434	5.168	0.867	Accepted	0
3	**Stearic acid**	0.41	4.975	0.844	Rejected	0
4	**Palmitic acid**	0.313	4.907	0.875	Accepted	0
5	**Friedelin**	0.42	4.708	0.833	Accepted	0
6	**Oleic acid**	0.409	4.745	0.9	Accepted	0
7	**beta-Sitosterol**	0.387	4.56	0.933	Accepted	0
8	**Linoleic acid**	0.414	4.869	0.9	Accepted	0

QED: A measure of drug-likeness based on the concept of desirability; **PAINS:** Pan Assay Interference Compounds; **Lipinski Rule of 5:** Molecular weight less than 500 daltons, nHD<5, nHA<10, and lipohilicity<4.15; **Fsp3:** the number of sp3 hybridized carbons/total carbon count; **SAScore:** Synthetic accessibility score were accounted

Table 7: Metabolism & excretion properties of anti-cancer *Boswellia serrata* phytocompounds

No	PubChem CID	CPYP1A2 inhibitor	CYP1A2 substrate	CYP3A4 inhibitor	CYP3A4 substrate	CL	T (1/2)
1	**Rotenone**	0.073	0.554	0.11	0.285	9.095	0.162
2	**Tetracosanoic acid**	0.004	0.7	0.317	0.82	9.864	0.031
3	**Stearic acid**	0.005	0.55	0.203	0.692	1.636	0.04
4	**Palmitic acid**	0.008	0.421	0.136	0.612	2.325	0.021
5	**Friedelin**	0.009	0.464	0.039	0.122	16.249	0.02
6	**Oleic acid**	0.006	0.463	0.109	0.305	4.578	0.024
7	**beta-Sitosterol**	0.021	0.402	0.2	0.522	15.308	0.009
8	**Linoleic acid**	0.008	0.609	0.122	0.601	8.354	0.021

Table 8: Toxicity endpoints of anti-cancer *Boswellia serrata* phytocompounds

No	PubChem CID	hEGR Blockers	DILI	AMES Toxicity	Carcinogenicity	IGC50	LC50 FM
1	**Rotenone**	0.007	0.02	0.004	0.073	3.098	3.276
2	**Tetracosanoic acid**	0.002	0.071	0.043	0.028	4.661	5.436
3	**Stearic acid**	0.001	0.03	0.023	0.043	5.271	6.39
4	**Palmitic acid**	0.001	0.031	0.014	0.063	5.132	6.174
5	**Friedelin**	0.011	0.008	0.01	0.028	4.404	5.413
6	**Oleic acid**	0.002	0.009	0.024	0.061	5.028	5.79
7	**beta-Sitosterol**	0.004	0.008	0.018	0.017	5.442	6.786
8	**Linoleic acid**	0.001	0.014	0.014	0.058	5.049	5.849

hERG: The human ether-a-go-go related gene; **DILI:** Drug-induced liver injury; **AMES:** The Ames test for mutagenicity; **LC50 FM:** 96-hour fathead minnow LC_{50} were examined.

Table 9: Evaluation of the bioactivity of anti-cancer *Boswellia serrata* phytocompounds

NO	PUBCHEM ID	GPCR ligand	Ion channel modulator	Kinase inhibitor	Nuclear receptor ligand	Protease inhibitor	Enzyme inhibitor
1	**Rotenone**	-0.29	0.2	-0.81	0.53	-0.32	0.4
2	**Tetracosanoic acid**	0.23	-0.04	-0.63	0.84	0.36	0.36
3	**Stearic acid**	0.15	-1.1	-0.67	0.74	0.31	0.59
4	**Palmitic acid**	0.16	-0.02	-0.49	0.69	0.28	0.56
5	**Friedelin**	0.18	-0.04	-0.36	0.82	0.09	0.59
6	**Oleic acid**	0.24	-0.01	-0.35	0.67	0.25	0.58
7	**beta-Sitosterol**	0.22	-0.05	-0.31	0.67	0.11	0.56
8	**Linoleic acid**	0.24	0.02	-0.44	0.79	0.33	0.62

Discussion:

Growth factors play a crucial role in the development and proliferation of cancer cells. These molecules bind to specific receptors on cell surfaces, promoting growth, reproduction, and cell viability. In normal cells, the expression of growth factors is tightly regulated by various signaling pathways, including tumor suppressor genes and apoptotic pathways. However, in cancer cells, this regulation is disrupted, leading to uncontrolled cell proliferation [7]. Various cancer subtypes exhibit abnormal activation of growth factor receptors, such as EGFR. This dysregulation can result from receptor overexpression, mutations, or activation of downstream signaling cascades, leading to processes like angiogenesis, metastasis, and evasion of apoptosis. Targeting growth factor signaling has become a potential strategy for chemotherapy, although it comes with challenges. Drug resistance, activation of compensatory pathways, and toxicity are significant concerns associated with these drugs [2-7]. Growth factor inhibitor drugs can have adverse effects such as skin infections, constipation, vertigo, and liver toxicity. They may also exacerbate conditions like hypertension, and thromboembolism, and impair wound healing. Additionally, their high cost and the need for regular administration pose financial burdens on patients and healthcare systems [7]. Furthermore, these drugs may interfere with essential physiological functions like tissue regeneration and repair, potentially harming healthy cells and tissues. Moreover, due to the genetic diversity of cancer cells, some malignancies or patient populations may not respond to growth factor inhibitor medications [2-7].

Plant-based medicines and phytochemicals offer a promising alternative for targeting cancer growth factors. Compounds derived from natural sources, such as EGFR, FGFR, and VEGFR inhibitors, have shown efficacy with lower toxicity and side effects compared to synthetic pharmaceuticals. Additionally, they may be more accessible and cost-effective, as they can be sourced from plants or cultivated crops. Moreover, plant-based medicines often target multiple pathways simultaneously, providing more comprehensive inhibition of cancer cell growth and progression [8]. *Spathiphyllum wallisii*, commonly known as peace lily, is a popular indoor plant prized for its elegant white flowers and lush foliage. Beyond its ornamental value, recent research has revealed potential medicinal properties in certain compounds found within the plant, particularly in the context of cancer treatment. One area of interest is its interaction with epidermal growth factor receptor (EGFR), a protein found on the surface of cells that plays a crucial role in cell growth and division. Abnormal activation of EGFR is associated with various cancers, including lung, breast, and colorectal cancers. Consequently, inhibiting EGFR signaling has become a therapeutic target in cancer treatment. These compounds, often phytochemicals

like flavonoids and alkaloids, have demonstrated the ability to interfere with EGFR activation or downstream signaling cascades involved in cancer cell proliferation and survival.

Based on the outcomes of our study, it is clear that rotenone exhibited notably superior inhibition compared to other compounds. Previous research findings support the notion that rotenone may alleviate cancer-related clinical symptoms due to its anti-inflammatory properties and potential use as an analgesic alongside cancer chemotherapy [20,24]. Moreover, it has been observed that rotenone can modulate various signaling pathways regulated by growth factor receptors (GFRs) and cytokines, induce apoptosis, and inhibit angiogenesis. Consequently, alpha-boswellic acid emerges as a promising candidate for targeting GFR-mediated cancers.

Conclusions:

The involvement of growth factors and their receptors is pivotal in both the onset and progression of cancer, where abnormalities in these pathways can drive uncontrolled cell proliferation. Targeting growth factor receptors (GFRs) has emerged as a promising approach for cancer therapy, with extensive preclinical and clinical investigations showing significant potential for drugs that inhibit GFRs and their downstream signaling pathways.

Spathiphyllum wallisii, an herb utilized in Ayurvedic medicine, underscores the importance of traditional herbal remedies in promoting health and treating diseases. Scientific research has increasingly validated the health benefits attributed to this ancient remedy, sparking growing interest in its integration into modern medical practices. Rotenone emerges as a potential anti-cancer agent, offering the possibility of alleviating cancer-related symptoms and associated disorders. However, a comprehensive understanding of its mechanisms of action and potential clinical applications necessitates further research and investigation.

References:

1. Van Laere, K., França, S.C., Vansteenkiste, H., Van Huylenbroeck, J., Steppe, K. and Van Labeke, M.C., 2011. Influence of ploidy level on morphology, growth and drought susceptibility in Spathiphyllum wallisii. Acta Physiologiae Plantarum, 33, pp.1149-1156.
2. Kakoei, F. and Salehi, H., 2013. Effects of different pot mixtures on spathiphyllum (Spathiphyllum wallisii Regel) growth and development. Journal of Central European Agriculture. 2013, 14(2), p.618-626
3. Kanerva, L., Mäkinen-Kiljunen, S., Kiistala, R. and Granlund, H., 1995. Occupational allergy caused by spathe flower (Spathiphyllum wallisii). Allergy, 50(2), pp.174-178.
4. Eeckhaut, T.G., Werbrouck, S.P., Leus, L.W., Van Bockstaele, E.J. and Debergh, P.C., 2004. Chemically induced polyploidization in Spathiphyllum wallisii Regel through somatic embryogenesis. Plant Cell, Tissue and Organ Culture, 78, pp.241-246.
5. Pavlović, I., Tarkowski, P., Prebeg, T., Lepeduš, H. and Salopek-Sondi, B., 2019. Green spathe of peace lily (Spathiphyllum wallisii): An assimilate source for developing fruit. South African journal of botany, 124, pp.54-62.
6. Parseh, I., Teiri, H., Hajizadeh, Y. and Ebrahimpour, K., 2018. Phytoremediation of benzene vapors from indoor air by Schefflera arboricola and Spathiphyllum wallisii plants. Atmospheric Pollution Research, 9(6), pp.1083-1087.

7. Poojashree, N.R., Suseela, T., Rao, A.V.D.D., Subbaramamma, P. and Sujatha, R.V., 2022. Studies on effect of coloured shade nets on growth of Peace lily (Spathiphyllum wallisii). Pharm Innov J, 11(8), pp.1213-1219.
8. Vanstechelman, I., Vansteenkiste, H., Eeckhaut, T., Van Huylenbroeck, J. and Van Labeke, M.C., 2009, August. Morphological and anatomical characterisation of chemically induced polyploids in Spathiphyllum wallisii. In XXIII International Eucarpia Symposium, Section Ornamentals: Colourful Breeding and Genetics 836 (pp. 79-84).
9. Das, A., Paul, A.K. and Chaudhuri, S., 2000. Micropropagation of Spathiphyllum wallisii-an important ornamental plant. Horticultural Journal, 13(2), pp.71-75.
10. Bercu, R.O.D.I.C.A. and Făgăraş, M., 2010. Anatomical aspects of the ornamental plant Spathiphyllum wallisii Regel. Stud. şi Cerc. Ştiinţ. Biol., Ser. Biol. veg, pp.13-17.
11. Eeckhaut, T., Werbrouck, S., Dendauw, J., Van Bockstaele, E. and Debergh, P., 2001. Induction of homozygous Spathiphyllum wallisii genotypes through gynogenesis. Plant Cell, Tissue and Organ Culture, 67, pp.181-189.
12. Vanstechelman, I., Eeckhaut, T., Van Huylenbroeck, J. and Van Labeke, M.C., 2010. Histogenic analysis of chemically induced mixoploids in Spathiphyllum wallisii. Euphytica, 174, pp.61-72.
13. Safeena, S.A., Shilpa, S.K., Kumar, P.N., Saha, T.N. and Prasad, K.V., 2023. Effect of growth regulators on growth and flower production of a popular indoor plant, peace lily (*Spathiphyllum wallisii*) Environment and Ecology 41 (2A): 979-984.
14. Elbohy, N.F., 2018. Response of Peace Lily (*Spathiphyllum wallisii* Regel) Plants to Foliar Spray with Som. Scientific J. Flowers & Ornamental Plants, 5(4):275-291.