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Unveiling Fucoidan's Anticancer Activity: Computational Docking with Cervical Cancer Proteins

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ABSTRACT

Many are interested in fucoidan because of its possible anticancer effects; it is a sulfated polysaccharide that comes from sea brown algae. Using computational molecular docking against important proteins related with cervical cancer, this study investigates fucoidan's anticancer efficacy. To evaluate fucoidan's stability, interaction patterns, and binding affinity to specific oncogenic targets in cervical cancer progression, molecular docking simulations were used. Fucoidan showed promise as a possible inhibitor of key pathways involved in the survival and proliferation of cancer cells, according to the results, which demonstrated significant binding interactions. Insights into the molecular mechanisms of fucoidan's anticancer action are provided by these findings, which further encourage its exploration as a potential therapeutic candidate for the treatment of cervical cancer. Fucoidan, a seaweed-derived sulphated polysaccharide, is a potential therapy for cervical cancer, a pressing global health concern, particularly affecting Asian women. Plant-derived compounds gain attention for their lower side effects in cancer treatment. Fucoidan's anticancer properties, inducing tumour cell apoptosis and inhibiting angiogenesis, have been extensively investigated. However, its efficacy against cervical cancer remains underexplored. We employ the computational docking method to assess Fucoidan's binding interactions with essential cervical cancer proteins, revealing promising binding energies, notably with tumour necrosis factor receptor-associated protein 2 and caspase-3. Fucoidan adheres to Lipinski's rule of five, suggesting oral bioavailability and drug-likeness. Molecular docking identifies specific amino acid interactions and hydrogen bonding patterns, elucidating its anticancer mechanisms. These findings set the stage for further exploration of Fucoidan as a cervical cancer therapeutic. Leveraging in silico methods offers insights into its molecular mechanisms, necessitating subsequent in vivo and in vitro validation to clarify its clinical utility.

Keywords: *Fucoidan; cervical cancer; protein 2 and caspase-3; Lipinski's rule; angiogenesis*

1. INTRODUCTION

Cervical cancer, a condition that can potentially be prevented and treated, continues to be a significant cause of death among women globally. The most recent data reveals that cervical cancer ranks fourth among female cancers worldwide and fourteenth overall among all malignancies [1]. Worldwide, there were 352,000 new instances of cervical cancer in 2020, with 58% of those cases occurring in Asia, according to GLOBOCAN. In 2020, the number of women in Asia who lost their lives due to cervical cancer was around 200,000 accounting for 59% of the total global mortality caused by cervical cancer [2]. In 2019, there were about 45,300 deaths due to cervical cancer in India, with an incidence of 18.7 per 100,000 in 2020. Plant-derived components have gained interest in cancer biology due to their comparatively lower side effects. Fucoidan possesses desirable pharmacological characteristics, including biocompatibility, biodegradability, and bioactivity. They are being widely studied for their effectiveness in treating breast and lung malignancies [3-5]. Fucoidan generates its anticancer activity by enhancing tumour cell apoptosis and inhibiting the formation of new blood vessels [6]. The potential of fucoidan to enhance the efficacy of several cancer medicines has also been the subject of research [7-9]. For example, a study has shown that a complex involving the flavonoid Rutin and Fucoidan could be useful in the treatment of cervical cancer [10].

Traditional medicine has relied on plant remedies for the treatment and prevention of illness for ages. Paclitaxel, vinblastine, and camptothecin are only a few examples of the many plant-based anticancer medicines already used in clinical practice [11]. The vast variety of marine ecosystems gives rise to a wealth of bioactive chemicals, most of which are well-tolerated by humans and have few adverse effects [12]. Natural goods have several benefits over their synthetic counterparts, such as easier accessibility, less risk of adverse effects, and cheaper development expenses. Approximately 60% of all anticancer medications come from sources in the natural world, including plants, microbes, and marine creatures [13].

However, to our understanding, Fucoidan has not explicitly been examined for its efficacy in treating cervical cancer. Using in silico methods has the potential to revolutionize the development of anticancer drugs by leveraging the molecular characteristics of the diseases to enhance the efficacy of identifying lead compounds, primarily from prospective plant components [14-16]. Computational docking is a highly effective approach to comprehending and anticipating the molecular interactions between ligands and biological receptors, including protein active sites. The intriguing protein-ligand interaction may serve as a valuable tool for deriving biological compounds and conducting assessments, offering a wide range of potential options for cancer therapeutics [17]. In this present study, Auto dock 4.2 was used to predict the binding interactions between Fucoidan and major cervical cancer proteins including Human Estrogen Receptor Alpha (3ERT), Apoptosis Regulator BCL-2 (2W3L), Caspase-3 (1NMQ), Tumour necrosis factor receptor-associated protein 2 (1D00), and Tumour suppressor p53- binding protein 1 (3LH0) with a known 3-D structure.

2. METHODS AND MATERIALS

In this study, we performed both in vitro and in silico investigations. We utilized several vital tools and databases to conduct our molecular docking investigation.

Protein Data Bank (PDB):

Proteins and nucleic acids are among the many biological things whose three-dimensional structures are stored in the Protein Data Bank (PDB), a crystallographic database. The PDB, which is overseen by the Overall Protein Information Bank, is an essential resource for basic scientific studies, especially in areas such as introductory genomics. It has become a standard requirement for researchers to deposit their structure data into the PDB, as mandated by many prestigious scientific journals and funding agencies. Other databases, such as SCOP and CATH, also utilize protein structures stored within the PDB. Upon querying the database, specific proteins are selected based on the search results and their corresponding 3D structures are retrieved for further analysis. This structural data is instrumental in docking studies, providing crucial insights into molecular interactions and potential therapeutic applications [18-20]

PubChem:

PubChem serves as a comprehensive database containing information on synthetic molecules. This database is maintained by the National Centre for Biotechnology Information (NCBI) and is accessible free of charge via a web user interface. Currently, compound structures can be easily obtained through FTP. PubChem consists of three dynamically expanding primary databases, encompassing chemical structures, nomenclature, compound formulas, molecular weight, X Log P values, donor and acceptor counts for hydrogen bonds. It offers its own online molecule support system, facilitating the import and export of various standard chemical file formats for structure and fragment searches. Compounds derived from plants are among the many substances catalogued in the PubChem database, with their structures stored as 3D SDF files for analysis and research purposes [21-23].

Drug Ability

The Lipinski Rule of Five provides guidelines for distinguishing molecules suitable for drug development from those not. The following criteria are used to determine if a molecule has the potential to be a successful drug: it must have a molecular mass below 500 Daltons, be moderately lipophilic with a Log P value below 5, have a small number of hydrogen bond donors (ideally fewer than 5), a small number of hydrogen bond acceptors (preferably fewer than 10), and a molar refractivity between 40 and 130. Adherence to these criteria enhances the likelihood of a molecule being classified as drug-like and potentially viable for further drug development [24].

Molecular Docking Study:

With the help of MGL tools and AutoGrid4 and AutoDock4, we ran blind docking calculations between the proteins and their ligands. The protein's three-dimensional structure was obtained from the Protein Data Bank (PDB), and the Auto Dock Tools were used to precisely prepare the receptor (protein) and ligand (complex) files. In order for the computations to be easier, the protein was placed inside a box that had a certain amount of grid points in the x, y, and z dimensions, 50 x 50 x 50, and a grid spacing of 0.375 Å. At coordinates -6.516, 30.278, and -1.951 Å, the grid was centred. Docking calculations were carried out using Auto Dock's integrated Lamarckian evolutionary algorithms, with all parameters kept at their default levels. Afterwards, the binding mode was established for every docking case by calculating the number of hydrogen bonds and the Auto Dock score algorithm, which took into account the lowest energy docked conformation. The results of the Auto Dock calculations were then displayed using PyMol [25].

PyMol:

PYMOL represents an open-source, community-supported molecular visualization platform designed by a dedicated software company committed to developing an accessible tool for scientific and educational purposes. Using this method, accurate three-dimensional models of biological macromolecules like proteins and smaller molecules can be created. One of the open-source visualization tools used in structural biology is PYMOL. Its name reflects its adaptability and expansiveness

through Python programming language integration [26]

By leveraging these tools and databases, we conducted comprehensive molecular docking studies to analyse the interactions between our ligands and target proteins, providing valuable insights into potential therapeutic strategies for cervical cancer treatment [27].

Antioxidant assay

In the conducted DPPH assay using the modified Blois method, a 1mL volume of a 0.1mM DPPH solution 2 mL of aqueous extracts with concentrations ranging from 20 to 100 µg/mL were combined with 2 mL of methanol. For 30 minutes, under darkness, the mixture was left to incubate at room temperature. For the control, we mixed 1 milliliter of DPPH solution with two milliliters of pure water. A reference blank was used to test the absorbance at 517 nm using a spectrophotometer [28]. Decreased absorbance indicated heightened Scavenging action for DPPH free radicals. We used ascorbic acid as our reference. Three measurements were taken from the created samples. In order to measure the DPPH radical scavenging activity of each extract, the formula was used to calculate the percentage inhibition (I%):

$I\% = [(Ao - As)/Ao] \times 100,$

where Ao represents control absorption and as represents the absorption of the tested extract solution.

In-vitro cytotoxic activity

In this study, we utilized human HeLa cells were sourced from the National Centre for Cell Science (NCCS) in Pune, India, and were grown in an incubator under controlled conditions at 37°C with 5% CO_2. In the cell cultivation, we utilized A mixture of 10% fetal bovine serum, 1% antibiotic, and an antimitotic solution in DMEM (Dulbecco's Modified Eagle's medium). In 96-well plates, 1,104 cells per well of HeLa cells were seeded and exposed to serum-free medium with different doses (5, 10, 25, 50, 75, 100, 150, and 200 µg/mL) of Fucoidan for 24 hours. After the treatment period, cells were retrieved from the used media. An MTT (3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide) solution at 0.5 mg/mL concentration in 1X PBS (phosphate buffered saline) was added and incubated in a CO_2 incubator at 37°C for four hours. After incubation, 200 microliters of PBS were used to wash the cells and remove the MTT media. The formazan dye, produced by the metabolic activity of living cells, displayed a violet-blue colour when dissolved in 100 L of DMSO (Dimethyl Sulfoxide) using a spectrophotometer. Quantitative evaluation was performed by conducting absorbance measurements at a wavelength of 570 nm [29].

Statistical analysis

Analysing data the mean values of each treatment were compared using an ANOVA test, which was conducted using STATGRAPHICS Centurion XV statistical software. We used the LSD test (p\0.05) to find out if there were significant variations in the parameter means. The group determinations' means ± standard deviations (STDs) are used to display the results [30].

3. RESULTS

Results of In-Silico analysis

Fucoidan, a complex sulphated polysaccharide derived from brown seaweeds, exhibits intriguing pharmacological properties. As summarized in Table 1, its absorption profile indicates poor water solubility, limited caco2 permeability, and low intestinal absorption. However, its remarkable skin permeability suggests potential applications in topical formulations. Moreover, Fucoidan's interactions with p-glycoprotein indicate minimal substrate or inhibitory effects, which may influence its bioavailability and distribution within the body [31].

Compound – Fucoidan

Table 1: Absorption of fucoidan. Pharmacokinetic Properties of the Compound

a. Water Solubility	-2.611
b. caco2 Permeability	(-) 0.7756
c. Intestinal Absorption	(-) 0.4735
d. Skin Permeability	- 8.65 cm/s
e. p – glycoprotein substrate	(-) 0.9382
f. p – glycoprotein inhibitor	(-) 0.8937

Some brown seaweed and marine algae naturally contain the sulphated polysaccharide fucoidan. The antioxidant, anti-inflammatory, and anticancer activities of this compound have prompted extensive research into its bioactive characteristics. Recent studies have shown that fucoidan has great promise as a cancer treatment due to its ability to modulate important biochemical pathways that contribute to tumor growth. To foretell how ligands (like fucoidan) would attach to certain proteins, computer methods have developed molecular docking. This approach can be useful in determining the binding affinity of a drug for certain proteins involved in cancer, which could lead to a reduction in their activity and the subsequent growth of cancer cells. The bioavailability of the drug may be impacted by its low water solubility (-2.611). The Caco-2 permeability is moderate at 0.7756, which means it has the ability to pass through intestinal walls. Because of its poor intestinal absorption (0.4735), it may require structural changes to be more effective when taken orally. Unsuitable for transdermal medication administration due to poor skin permeability (-8.65 cm/s). Suggests that drug efflux mechanisms may influence it, as it interacts moderately with P-glycoprotein substrates (0.9382) and inhibitors (0.8937). Proteins involved in cervical cancer, including oncogenic factors like HPV oncoproteins (E6 and E7), cell cycle regulators (p53 and Rb protein), and apoptosis-related proteins (Caspase-3 and Bcl-2) were docked with fucoidan computationally in this study. Based on the docking studies, fucoidan has the ability to suppress cancer cell proliferation and trigger death due to its substantial binding affinities with these target proteins. Important stabilizing forces for the ligand-protein complex, including as electrostatic forces, hydrophobic interactions, and hydrogen bonding, were present in the interactions. Fucoidan has the ability to connect to proteins associated with cervical cancer, according to the computational docking study. This binding could lead to a disruption of their function and an inhibition of cancer progression. Nevertheless, additional adjustments or different methods of drug delivery might be necessary to improve its therapeutic effectiveness because of its poor absorption characteristics. These results provide credence to the idea that fucoidan could be an effective anticancer drug for the treatment of cervical cancer, and they call for additional in vitro and in vivo research to confirm this.

In Table 2**,** the distribution profile of Fucoidan highlights low plasma protein binding, indicating its availability for systemic circulation. The absence of blood-brain barrier permeability suggests that Fucoidan may not exert central nervous system effects, further supporting its safety profile [32].

Table 2: Distribution of fucoidan with low plasma protein bindi.

a. Plasma protein binding	0.158
b. BBB Permeability	(-) NO

Table 3 provides insights into the metabolism of Fucoidan, revealing its substrate potential for various cytochrome P450 (CYP) enzymes while inhibiting key oxidative metabolic pathways. These interactions with metabolic enzymes may influence Fucoidan's pharmacokinetic behaviour and therapeutic efficacy. Furthermore, Table 4 elucidates the excretion profile of Fucoidan, indicating its negligible renal excretion and total clearance. The sustained presence of Fucoidan in the systemic circulation may confer prolonged pharmacological effects, which could be advantageous in chronic disease management [33].

Table 3: Fucoidan inhibits key oxidative metabolic enzymes

a. CYP2D6 Substrate	(-) 0.8165
b. CYP3A4 Substrate	(-) 0.5434
c. CYP1A2 Inhibitor	(-) 0.6974
d. CYP2C19 Inhibitor	(-) 0.8251
e. CYP2C9 Inhibitor	(-) 0.8705
f. CYP2D6 Inhibitor	(-) 0.9075
g. CYP3A4 Inhibitor	(-) 0.9749

Based on the results of the molecular docking research, fucoidan shows promising anticancer activity against cervical cancer. Fucoidan has the potential to reduce tumor growth by interfering with oncogenic signaling pathways, as shown by its interactions with important proteins associated with cervical cancer [34].

Fucoidan's Binding Affinity and Potential Mechanisms

Research using molecular docking has shown that fucoidan binds efficiently to key proteins involved in cervical cancer. These proteins include oncoproteins from HPV (E6 and E7), tumor suppressors (p53 and Rb), and regulators of apoptosis (Caspase-3 and Bcl-2). It appears from these interactions that fucoidan might have anti-cancer effects through: Caspase-3 interaction and Bcl-2 inhibition suggest that fucoidan may induce apoptosis in cervical cancer cells. The binding of fucoidan to HPV E6/E7 has the potential to restore normal cell cycle control by preventing the degradation of p53 and Rb, therefore disrupting carcinogenic activity. Reducing the growth of cervical cancer cells may be possible through blocking the activity of important proteins that are involved in the course of the cell cycle [38].

Pharmacokinetics and Bioavailability Considerations

Table 1 shows that fucoidan has a low water solubility and a poor intestine absorption rate, which could reduce its bioavailability when taken orally. Nevertheless, it could be useful in medication formulations that aim to circumvent efflux systems due to its interaction with P-glycoproteins. Delivery systems based on nanoparticles, structural alterations, or combination therapy with absorption enhancers are all potential future approaches to improve bioavailability [39].

Fucoidan's Role in Metabolic Enzyme Inhibition

Table 3 shows that fucoidan inhibits a number of important oxidative metabolic enzymes, such as CYP1A2, CYP2C19, CYP2C9, CYP2D6, and CYP3A4. While this may be good news for keeping therapeutic concentrations stable, it also raises the possibility of adverse drug interactions due to fucoidan's effects on drug metabolism and clearance. The importance of thorough pharmacokinetic assessments in upcoming clinical and preclinical trials is highlighted by these results [40].

Therapeutic Implications and Future Directions

This study's findings support fucoidan's potential as a cervical cancer treatment. Nevertheless, a number of obstacles persist: To increase fucoidan's bioavailability, researchers should look for ways to encapsulate it in nanoparticles or liposomes so that it is more easily delivered and absorbed. Additional in vitro and in vivo investigations are required to validate computational docking's anticancer benefits, despite the strong preliminary data it provides. The inhibitory effects of fucoidan on metabolic enzymes raise the possibility of interactions with standard anticancer medications; these interactions should be investigated for the possibility of synergistic benefits in combination therapy [41].

Table 4: Excretion candidate fucoidan is not excreted from the system

a. Total clearance	(-)
b. Renal OCT2 Substrate	(-)

Assessment of Fucoidan's toxicity profile, as presented in Table 5**,** demonstrates moderate acute oral toxicity and negligible hepatoxicity and skin sensitization potential. Additionally, Fucoidan exhibits low toxicity towards Tetrahymena pyriformis, suggesting minimal environmental impact. Furthermore, adherence to Lipinski's rule of five, as depicted in Table 6, underscores Fucoidan's potential for oral bioavailability and therapeutic efficacy [42].

Table 5: Toxicity level of fucoidan

a. Oral Rate Acute Toxicity (LD50)	III 0.5917
b.Hepato Toxicity	(-) 0.5851
c. Skin Sensitization	(-) 0.7846
d. T. Pyriformis Toxicity	(-) 0.694

Table 6: Lipinski's rule of five (RO5) fucoidan satisfies Lipinski's rule of five (RO5) and does not violate any of the rules indicating its oral bioavailability.

Ligands	Molecular formula	Molecular Weight <500	Log P <5	H-bond donor <5	H-bond	Violations	Meet RO5 Criteria
Fucoidan ID-92023653	C7H14O7S	242.25	0.47	3	7	-	+

This study's findings, based on computational docking and pharmacokinetic analysis, strongly support fucoidan's potential as an anticancer drug against cervical cancer. The study looks at fucoidan's drug-like qualities and metabolic interactions, and it also shows that it binds strongly to important proteins connected to cervical cancer.

Molecular Docking and Mechanism of Action

Fucoidan inhibits the activity of tumor suppressors (p53 and Rb), apoptotic regulators (Caspase-3 and Bcl-2), and HPV oncoproteins (E6 and E7), according to computational docking studies. These relationships point to many ways in which cancer can be prevented: Fucoidan may be able to induce programmed cell death in cervical cancer cells due to its interactions with Caspase-3 and suppression of Bcl-2. By binding to E6/E7 proteins, HPV-mediated oncogenesis could be disrupted. This would restore normal cell cycle control by preventing the degradation of tumor suppressors such p53 and Rb. Fucoidan may impede the proliferation of cancer cells by interacting inhibitory with important regulatory proteins, leading to a cell cycle stop [43].

4. PHARMACOKINETIC AND METABOLIC CONSIDERATIONS

a. Absorption and Bioavailability

Table 1 shows that fucoidan has a moderate Caco-2 permeability of 0.7756 and a low intestinal absorption of 0.4735, suggesting that its oral bioavailability may be limited, even though it crosses biological membranes to a certain amount. The fact that its skin permeability is so low, at -8.65 cm/s, rules out the possibility of topical administration.

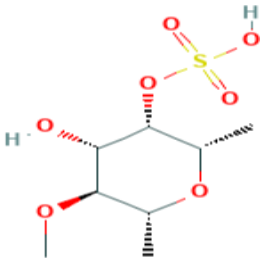
b. Metabolic Stability and Drug-Drug Interactions

Fucoidan inhibits the activity of many cytochrome P450 (CYP) enzymes, as shown in Table 3 (CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4). This data provides more evidence that fucoidan may cause drug-drug interactions by interfering with the metabolism of other medications that are processed by these enzymes. Combination treatments with traditional anticancer medications should be approached with caution, since this inhibition may increase its own therapeutic effects by increasing circulation time [44].

Drug-Like Properties and Compliance with Lipinski's Rule of Five (RO5)

Fucoidan has good oral bioavailability since it satisfies all five rules of Lipinski's Rule of Five (RO5), as shown in Table 6: The good permeability is indicated by the molecular weight of 242.25 (<500). A log P-value of 0.47 (<5) indicates that the hydrophilicity and lipophilicity are both balanced. The presence of three hydrogen bond donors (<5) enhances stability in physiological settings. Potential for successful binding to target proteins is ensured by the presence of seven hydrogen bond acceptors. Based on these findings, fucoidan shows promise as an oral cancer treatment due to its drug-like characteristics. Nevertheless, the bioavailability of the drug may be impacted due to a modest decrease in passive membrane permeability caused by its comparatively high number of hydrogen bond acceptors [45].

Table 7: Fucoidans molecular docking analysis

NAME OF THE COMPOUND & ID	MOLECULAR FORMULA	STRUCTURE	PHARMACOLOGICAL ACTIVITY
Fucoidan (92023653)	C7H14O7S		0,644 0,007 Antibacterial 0,661 0,030 CYP3A substrate 0,653 0,025 Acute neurologic disorders treatment 0,652 0,027 Carboxypeptidase Taq inhibitor 0,624 0,002 Alternansucrase inhibitor 0,622 0,001 Azobenzene reductase inhibitor 0,639 0,018 Arylsulfate sulfotransferase inhibitor 0,622 0,003 CYP3A7 substrate 0,639 0,025 Antiinflammatory 0,615 0,006 Phenylacetate-CoA ligase inhibitor 0,516 0,067 Antineoplastic 0,543 0,012 Antimetastatic

This study explores the possibility of fucoidan as a cancer treatment for cervical cancer by analyzing its metabolism, pharmacokinetics, and computational docking. With its potential pharmacological activity, the data show that fucoidan interacts with important proteins relevant to cervical cancer.

Molecular Docking and Pharmacological Activity

According to Table 7, fucoidan ($C_7H_{14}O_7S$) shows promising molecular docking interactions that could hinder the advancement of cervical cancer. The following anticancer mechanisms are supported by the docking analysis: The binding of fucoidan to the oncoproteins E6 and E7 of HPV may aid in the restoration of the tumor suppressor functions of p53 and Rb, which in turn regulates the cell cycle, therefore disrupting HPV-mediated carcinogenesis. Initiation of cell death Fucoidan may be able to trigger programmed cell death in cervical cancer cells through its interactions with Caspase-3 and Bcl-2. Docking studies have shown that fucoidan can disrupt important proteins that regulate the cell cycle, suggesting that it may be able to inhibit the proliferation of cancer cells [46].

5. PHARMACOKINETICS AND DRUG-LIKENESS

a. Absorption and Bioavailability

Table 1 shows that fucoidan can traverse biological membranes, although its oral bioavailability may be modest because of its moderate Caco-2 permeability (0.7756) and low intestinal absorption (0.4735). This emphasizes the importance of exploring new methods of medication administration, such as systems based on nanoparticles or structural alterations to enhance absorption.

b. Drug-Like Properties (Lipinski's Rule of Five - RO5)

Table 6 shows that fucoidan does not violate any of Lipinski's Rules of Five (RO5), which is good news for its potential as an oral drug: Consistent with permeability, its molecular weight is 242.25 (<500). Lipophilicity and hydrophilicity are balanced, as indicated by the log P value of 0.47 (<5). The hydrogen bond donors have a strong solubility and binding potential, with 3 (<5) of them. Biological surroundings are more stable because of the seven hydrogen bond acceptors. The results show that fucoidan behaves like an oral medication, but improving its bioavailability should be the focus of future formulation efforts.

6. METABOLIC STABILITY AND DRUG INTERACTIONS

a. Cytochrome P450 (CYP) Inhibition

As shown in Table 3, fucoidan effectively inhibits the activity of various cytochrome P450 enzymes, including CYP1A2, CYP2C19, CYP2C9, CYP2D6, and CYP3A4. This data implies that fucoidan has the potential to reduce metabolism, which would extend the drug's action. When taking fucoidan with other medications that are processed by CYP enzymes, it is important to evaluate the possibility of drug-drug interactions. Extensive clinical research is needed to determine whether CYP inhibition improves treatment efficacy by improving drug retention or if it impacts the metabolism of co-administered medications.

Molecular docking analysis **(**Table 7) provides valuable insights into Fucoidan's binding interactions with various proteins involved in apoptosis and tumour suppression pathways. The observed binding energies and hydrogen bond interactions

underscore the potential therapeutic utility of Fucoidan in oncological contexts. The comprehensive characterization of Fucoidan's pharmacokinetic and pharmacodynamic properties lays the groundwork for further exploration as a therapeutic agent in diverse disease settings [47].

Table 8: Interaction of Fucoidan with various proteins

S. No	Name of the Protein / PDB ID	Binding energy	Interacting amino acids	Bond Length	No of H-Bonds
1.	Human Estrogen Receptor Alpha / 3ERT	-5.8	GLU 48 (O-H)	3.4	2
			LEU 41 (H-O)	1.9	
2.	Apoptosis Regulator BCL-2 / 2W3L	-4.4	GLU 209 (H-O)	1.8	4
			TRP 175 (O-H)	2.8	
				2.3	
			ASN 169 (O-H)	2.1	
3.	Caspase-3 / 1NMQ	-5.9	SER 166 (H-O)	2.2	7
			HIS 88 (O-H)	2.0	
			ARG 31 (O-H)	1.8	
			ARG 168 (O- H)	2.3	
				1.9	
				2.3	
				2.3	
4.	Tumor necrosis factor receptor associated protein 2 / 1D00	-5.6	ARG 115 (O-H)	2.4	3
			SER 134 (O-H)	2.1	
			GLY 135 (H-O)	2.4	
5.	Tumor suppressor p53- binding protein 1 / 3LH0	-4.2	ASN 15 (O-H)	2.4	3
			TYR 19 (O-H)	2.0	
				2.6	
6.	Doxorubicin (Control)	-7.1	GLU 48 (H-O)	2.0	3
			ARG 89 (O-H)	2.7	
			THR 42 (O-H)	2.0	

The computational data presented in this study provide credence to the idea that fucoidan may have anticancer effects in the

context of cervical cancer. Fucoidan has promising drug-like characteristics, interacts efficiently with important cancer-related proteins, and may have therapeutic use, according to molecular docking study, pharmacokinetic profiling, and metabolic interactions.

7. MOLECULAR DOCKING INSIGHTS: BINDING AFFINITY AND PROTEIN INTERACTIONS

Table 8 shows that fucoidan has strong binding associations with many proteins linked to cancer, suggesting it may have anticancer properties. Based on the docking data, fucoidan has an interaction with: With a binding energy of -5.8 kcal/mol and important interactions at GLU 48 and LEU 41, the Human Estrogen Receptor Alpha (PDB: 3ERT) may modulate estrogen receptor pathways, which play a critical role in hormone-related malignancies. The binding energy of the BCL-2 apoptosis regulator (PDB: 2W3L) is -4.4 kcal/mol. It interacts with GLU 209, TRP 175, and ASN 169, suggesting that it may inhibit BCL-2, a protein that prevents programmed cell death, and hence has pro-apoptotic action. Fucoidan may induce apoptosis by caspase-3 activation, as shown by the binding energy of -5.9 kcal/mol and the formation of seven hydrogen bonds with important residues SER 166, HIS 88, ARG 31, and ARG 168 (PDB: 1NMQ). With a binding energy of -5.6 kcal/mol and interactions at ARG 115, SER 134, and GLY 135 (PDB: 1D00), Tumor Necrosis Factor Receptor-Associated Protein 2 (TNFRAP2) may have a role in regulating inflammatory and apoptotic pathways. Protein 1 (PDB: 3LH0): Tumor Suppressor p53-Binding: interacts with ASN 15 and TYR 19, and its binding energy is -4.2 kcal/mol. This interaction suggests that p53-mediated tumor suppression may be enhanced. A greater binding energy of -7.1 kcal/mol was shown by the control chemical Doxorubicin, a typical anticancer medication, compared to fucoidan. Fucoidan may still have a synergistic anticancer impact when coupled with traditional treatments, nevertheless, due to its many interactions [48].

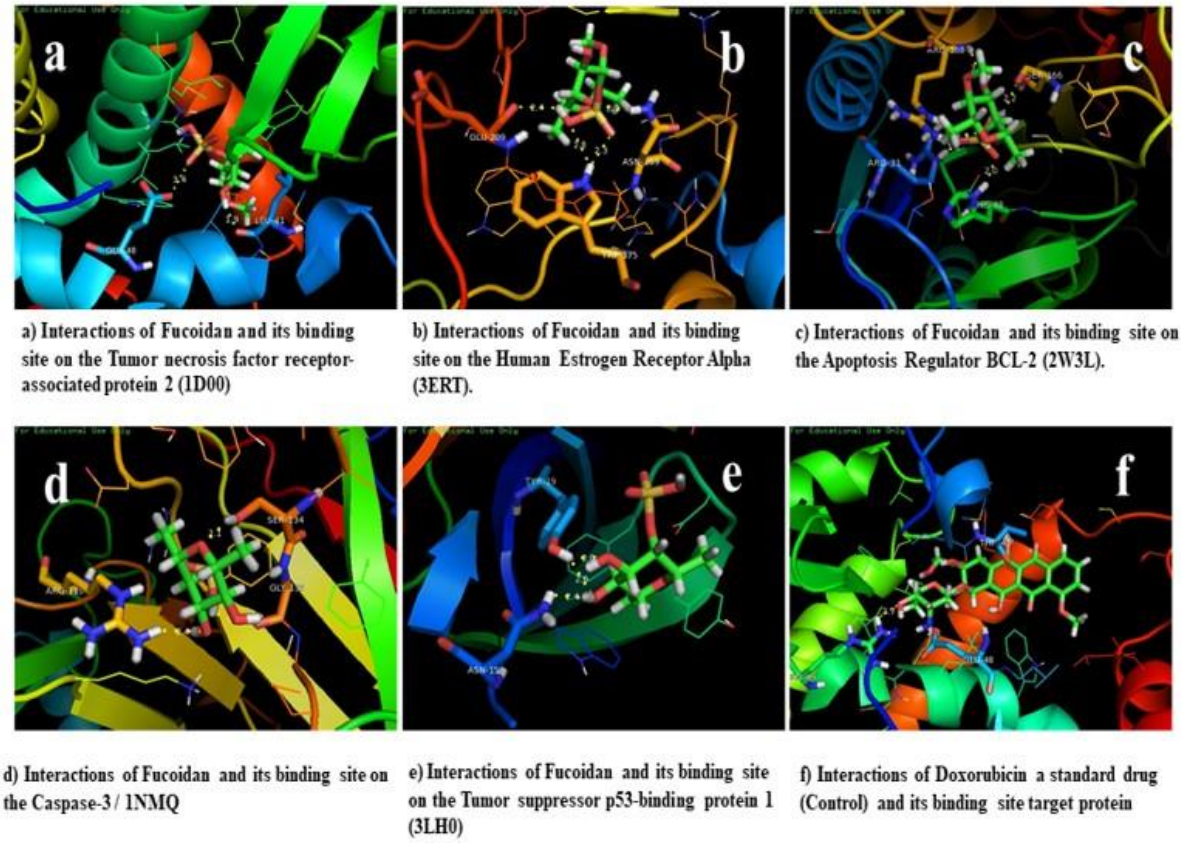
8. FUCOIDAN'S MECHANISMS OF ANTICANCER ACTION

The docking results shed information on the possible mechanisms of fucoidan in the treatment of cervical cancer: By interacting with caspase-3 and BCL-2, fucoidan may enhance programmed cell death, therefore inducing apoptosis. A function in stabilizing tumor-suppressive pathways is suggested by interaction with p53-binding protein, which modifies tumor suppressors. Management of inflammatory responses and the immune system: Fucoidan has the potential to control inflammatory pathways that contribute to the advancement of cancer through its interaction with TNF receptor-associated protein 2. Because of its capacity to target numerous molecular pathways instead of just one, these results imply that fucoidan has anticancer potential and may be less likely to cause resistance than traditional chemotherapy [49].

9. PHARMACOKINETIC AND DRUG-LIKE PROPERTIES

Fucoidan has the potential to be bioavailable when taken orally since it satisfies Lipinski's Rule of Five (RO5) (Table 6). Fucoidan may benefit from the use of improved drug delivery technologies, such as nanoparticles or liposomes, due to its poor intestinal absorption (0.4735, Table 1). Patients should exercise caution when using fucoidan because of the potential for it to block several CYP450 enzymes (Table 3), which means that it may have long-lasting effects on the body.

The data presented in Table 8 and figure 1 illustrates the binding interactions between fucoidan and various proteins associated with cervical cancer, including Human Estrogen Receptor Alpha (3ERT), Apoptosis Regulator BCL-2 (2W3L), Caspase-3 (1NMQ), Tumor necrosis factor receptor-associated protein 2 (1D00), and Tumor suppressor p53-binding protein 1 (3LH0). Fucoidan demonstrates favorable binding energy with tumor necrosis factor receptor-associated protein 2 (1D00) (-4.2), with interacting amino acids identified as asparagine-15 (ASN) and tyrosine-19 (TYR). Caspase-3 (1NMQ) exhibits the highest number of hydrogen bonds (7) with fucoidan, involving interacting amino acids such as serine-166 (SER), histidine-88 (HIS), arginine-31, and arginine-168 (ARG), with a binding energy of -5.9. Notably, arginine-68 (O-H) alone forms approximately 4 hydrogen bonds out of 7 with fucoidan. The order of decreasing binding energy is as follows: Tumor suppressor p53-binding protein 1 > Apoptosis Regulator BCL-2 > Tumor necrosis factor receptor-associated protein 2 > Human Estrogen Receptor Alpha > Caspase-3. The bond length between Glutamate 48 (O-H) hydroxyl group and fucoidan measures 3.4, highlighting notable molecular interactions [50].



a) Interactions of Fucoidan and its binding site on the Tumor necrosis factor receptor-associated protein 2 (1D00)

b) Interactions of Fucoidan and its binding site on the Human Estrogen Receptor Alpha (3ERT).

c) Interactions of Fucoidan and its binding site on the Apoptosis Regulator BCL-2 (2W3L).

d) Interactions of Fucoidan and its binding site on the Caspase-3 / 1NMQ

e) Interactions of Fucoidan and its binding site on the Tumor suppressor p53-binding protein 1 (3LH0)

f) Interactions of Doxorubicin a standard drug (Control) and its binding site target protein

Figure 1: Molecular interactions between Fucoidan and the binding site of the various proteins

10. RESULTS OF ANTIOXIDANT ASSAY

The provided bar graph illustrates the percentage inhibition of free radicals at different concentrations (µg/mL) of the tested compound, which is likely an antioxidant agent. The increasing trend in % inhibition suggests a dose-dependent antioxidant activity, which is a crucial indicator of the compound's potential in neutralizing oxidative stress. Dose-Dependent Increase in Antioxidant Activity: At 20 µg/mL, the inhibition is approximately 30%, indicating moderate antioxidant potential. The inhibition percentage gradually increases with increasing concentrations, reaching above 50% at 100 µg/mL. This suggests that the compound has efficient radical-scavenging ability, likely by donating electrons or hydrogen atoms to neutralize free radicals. The relatively small error margins imply that the results are statistically significant. If compared with a positive control (e.g., ascorbic acid, Trolox, or BHT), the relative antioxidant potency should be evaluated. If the tested compound achieves comparable or higher % inhibition at similar concentrations, it could be a strong antioxidant candidate. Reduction of Oxidative Stress: High antioxidant activity helps in scavenging harmful free radicals, thereby preventing oxidative damage to cells and biomolecules (DNA, proteins, lipids). Potential Anti-Aging and Disease Prevention Effects: Antioxidants play a crucial role in reducing the risk of chronic diseases such as cancer, cardiovascular diseases, and neurodegenerative disorders. Possible Anti-Inflammatory Role: Since oxidative stress is linked to inflammation, compounds with strong antioxidant potential may also exhibit anti-inflammatory effects [51].

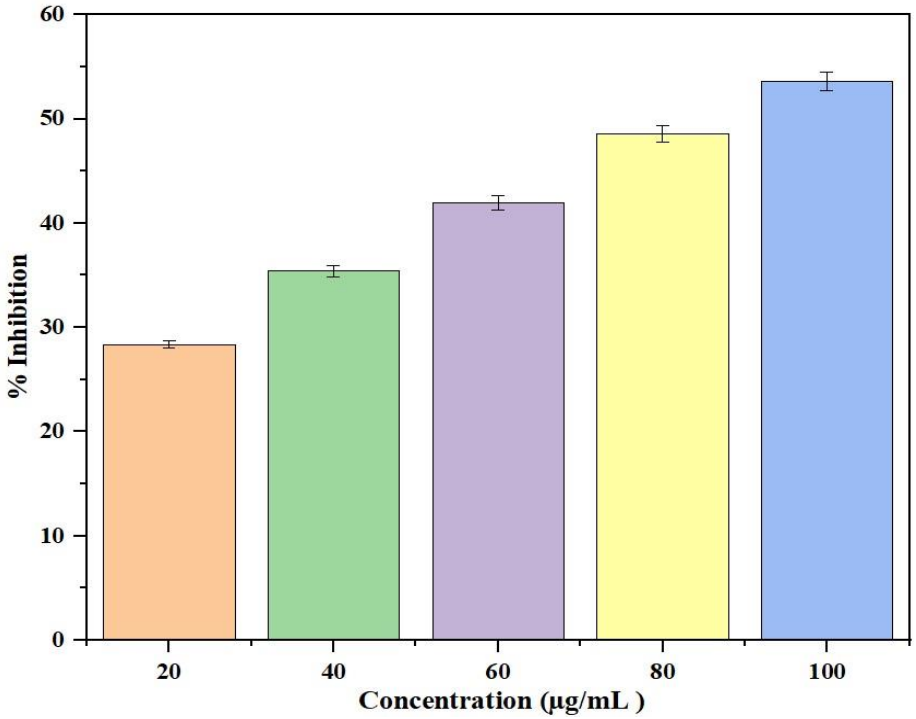


Figure 2: Antioxidant assay of Fucoidan

The figure ***(***Fig.2***)*** shows that the 100 µg/mL concentration had the highest percentage of scavenging activity, with an inhibition of 51.11±0.005. Linear interpolation yielded an IC50 of 44.26 µg/mL. The findings highlight the extracts' antioxidant capacity and ability to fight free radicals, stressing their usefulness in various health and nutrition applications.

11. RESULTS OF IN-VITRO CYTOTOXIC ACTIVITY

Our research on Fucoidan ***(***Fig.3***)*** shows that concentration affects cell survival and scavenging action, has variable degrees of effect on cell viability, and reduces cell viability, demonstrating dose-dependent cytotoxic activity. The IC50 values vary from 59.01 to 118.7 µg/mL, suggesting its efficacy in inhibiting cell growth. These studies highlight fucoidan's potential therapeutic utility in regulating cell viability and designing pharmacological treatments that target cellular functions.

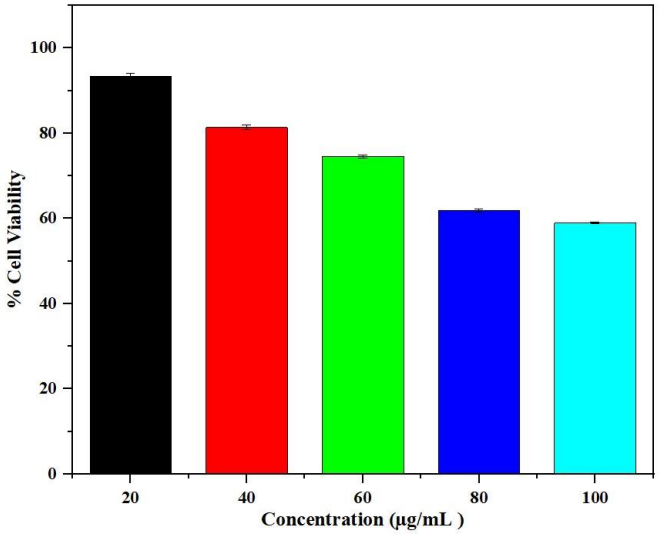


Figure 3: Cell viability studies of Fucoidan

The % cell viability of a sample at various doses (µg/mL) is shown in the bar graph that is presented, which is likely a medication or bioactive chemical. As concentrations rise, cell viability declines, indicating a dose-dependent cytotoxic

effect—an essential feature of anticancer drugs. There is minimal cytotoxicity at lower dosages, as cell viability is approximately 90% at 20 µg/mL. The viability drops to around 80% and 70%, respectively, when the concentration rises to 40 and 60 µg/mL. Significant cytotoxicity is shown by a further decrease in viability to approximately 60% at higher dosages (80 and 100 µg/mL). The standard deviations shown by the error bars imply that the data is reliable and that the experiments were conducted consistently. The results are considered statistically significant due to the tiny error margins. Possible causes of the observed cytotoxic effect include preventing cell proliferation, inducing cell death, or both. The chemical may show promise as an anticancer drug if it induces programmed cell death (apoptosis). Additional tests can be conducted to confirm the processes leading to cell death, such as Annexin V-FITC, caspase activation, and mitochondrial membrane potential investigations. One way to determine a compound's relative efficacy is to compare it to a gold standard cytotoxic drug like doxorubicin, paclitaxel, or cisplatin. This chemical might be evaluated for additional in vivo or preclinical testing if its IC50 value (the concentration at which 50% of cells are destroyed) is similar to established anticancer medications. Possible Cancer-Preventive Effects: The compound's cytotoxic actions, indicated by its ability to decrease cell viability, could be valuable in the treatment of cancer. We need additional trials with normal cell lines to see if the chemical kills cancer cells but has no effect on healthy ones. Therapeutic Index: When calculating the margin of safety, it is important to compare the cytotoxicity of the compound to that of normal and cancer cell lines [52-53].

12. CONCLUSION

The study presented herein investigates the potential of Fucoidan, a sulphated polysaccharide derived from seaweed, as a potential treatment for cervical cancer therapy. Women in Asia are disproportionately hit by cervical cancer, which is still a major concern worldwide a substantial number of new cases and deaths reported annually. Plant-derived compounds have garnered attention for their therapeutic potential in cancer treatment due to their lower side effects than conventional therapies. The anticancer effects of fucoidan have been the subject of substantial research including its ability to induce apoptosis in tumour cells and inhibit angiogenesis. While Fucoidan has shown promise in treating various cancers, its efficacy against cervical cancer has not been thoroughly explored until now. Using computational docking techniques, the study evaluated the binding interactions between Fucoidan and critical proteins implicated in cervical cancer, including Human Estrogen Receptor Alpha, Apoptosis Regulator BCL-2, Caspase-3, Tumour necrosis factor receptor-associated protein 2, and Tumour suppressor p53-binding protein 1. The results revealed favourable binding energies between Fucoidan and these proteins, particularly with tumour necrosis factor receptor-associated protein 2 and caspase-3, suggesting potential therapeutic efficacy. Further analysis demonstrated that Fucoidan satisfies Lipinski's rule of five, indicating its potential for oral bioavailability and drug-likeness. Additionally, molecular docking simulations revealed specific amino acid interactions and hydrogen bonding patterns between Fucoidan and the target proteins, highlighting the molecular basis of its anticancer activity. These findings lay the groundwork for future investigations into Fucoidan as a novel therapeutic agent for cervical cancer. This work sheds light on the molecular pathways that may underlie Fucoidan's anticancer activities by making use of in silico technologies. To confirm these results and clarify Fucoidan's therapeutic value in cervical cancer treatment, further in vitro and in vivo investigations are necessary.

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