ORIENTAL JOURNAL OF CHEMISTRY
An International Open Access, Peer Reviewed Research Journal
www.orientjchem.org

ISSN: 0970-020 X
CODEN: OJCHEG
2025, Vol. 41, No.(1):
Pg. 44-56

Network Pharmacology and Molecular Docking to Identify the Molecular Targets of Novel Indole-quinoline Derivative in Cancer

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http://dx.doi.org/10.13005/ojc/410105

(Received: November 22, 2024; Accepted: February 06, 2025)

ABSTRACT

Cancer is a leading cause of death worldwide. Using network pharmacology and molecular docking techniques, this study aims to investigate the molecular mechanism of novel indole-quinoline derivative (SM7) in cancer by predicting a chain of hallmarks that can be targeted and subsequently inhibited to treat cancer with improved therapeutic effect. Out of total 25005 number of targets, 93 targets of SM7 were identified to be overlapped. David KEGG analysis retrieved 15 signaling pathways. Molecular docking of identified primary targets ie. STAT3, BCL2, ALB, MMP9 through protein-protein interaction analysis and compound-disease target-pathway, was performed. The results showed the significant affinity towards traced hub targets and complies with the data obtained from databases. Functional enrichment analysis also revealed the involvement of various important pathways which are related to cancer. In conclusion, SM7 may exert its anticancer effect by inhibiting the identified targets which are connecting links between various cell signaling pathways involved in cell survival and cancer progression. This study provides the theoretical groundwork for further *in vitro* and *in vivo* investigations of this molecule to develop it as anticancer agent.

Keyword: Molecular docking, Network pharmacology, Anticancer agent.

INTRODUCTION

Cancer is a major concern globally with characteristic features that involve abnormal cellular growth with the capability of spreading to other parts of body.[1,2] According to WHO report, cancer is the leading cause for millions of deaths globally.[3] The statistics showed 9.6 million cases in 2018, and this may be more than 13 million by 2030.[4] It is the second largest cause of deaths after cardiovascular disorders worldwide. The existence of multiple side effects, drug resistance and cancer relapse issues in conventional therapies presented a focus on the search of novel safe and more effective potential anticancer agent. Heterocyclic compounds are potential anticancer agents with various other therapeutic applications.[5] Indole moiety is found in many natural products

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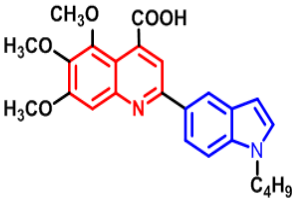
like indolocarbazole, and indenoisoquinoline compounds etc.[6,7] Indole derivatives exhibit a wide range of therapeutic actions, including antituberculosis[8], anti-inflammatory[9,10] anticancer[11,12] anticonvulsant and anticardiovascular effects.[13,14] Many quinoline derivatives have demonstrated anticancer efficacy through a different mechanism of actions.[15] Camptothecin is a natural alkaloid and its semisynthetic analog, topothecan, are two examples of cytotoxic quinolines with exhibits strong antitumor potential by inhibiting the DNA topoisomerasel enzyme.[16,17] Molecular hybridization is a technique for designing novel compounds with objective to increase the effectiveness by combining two or more drug pharmacophores into a single compound.[18] In this present paper, a novel indole-quinoline derivative (SM7) Fig. 1 was designed based on the importance of heterocyclics as therapeutic agents and the existing literature that demonstrated the use of methoxylated flavones as the lead molecules in the design and synthesis of a series of 2-aryl-trimethoxyquinoline analogues as tubulin inhibitors.[19]



2-(1-butyl-1*H*-indole-3yl)-5,6,7 trimethoxyquinoline-4-carboxylic acid (SM7)

Fig. 1. Structure of novel indole-quinoline derivative (SM7)

In today's biomedical environment, network pharmacology is a strong framework that efficiently integrates and manages complex networks including medications, targets, and illnesses. This procedure makes it easier to comprehend intricate pharmacological interactions in their entirety. This method emphasizes high-throughput screening, sophisticated network visualization, and in-depth analysis, which makes it an essential instrument for furthering traditional medical research. A popular computational method in modern drug research, molecular docking is essential for clarifying the mechanism and functionality of drugs. Using target proteins and chemicals under investigation, the program predicts the binding mode and associated binding free energy with high accuracy.[20,21] The aim of the study was to identify the therapeutic targets and putative signaling pathways that are most closely associated with cancer to discover the molecular targets and mechanistic aspects of SM7 in cancer using network pharmacology and molecular docking techniques.

MATERIALS AND METHODS

In silico ADMET and Drug-likeness prediction

The Swiss ADME webtool was used to estimate the drug-likeness and pharmacokinetics qualities of SM7. This tool predicted the following: molecular weight (MW), topological polar surface area, hydrogen bond acceptor count, number of rotatable bonds, H-bond acceptor and donor count, and XLogP3 (octanol-water partition coefficient).[22]

Targets prediction related to drug

The potential therapeutic targets of SM7 were retrieved from Swiss Target Prediction a database which predict target on basis of 2D and 3D structural resemblance of known compound http:/ www.swisstargetprediction.ch/.[23]

Prediction of disease related targets Cancer related genes were retrieved as per the reported literature.[24,25]

Search of common targets of drugs and diseases

Genes common to both designed SM7 and cancer disease were identified by combining data from Swiss Target Prediction, OMIM, and GeneCard databases, and then visualized using a Venn diagram tool available to illustrate the overlap between the two gene sets. *(bioinformatics.psb.ugent.be/webtools/ven)*.

Drug network construction

The 'Drug-Target' network diagram of SM was constructed by using cytoscape 3.7.1 software. Hence these common genes were used to construct the network between the SM7 and the disease target by using cystoscope.[26]

Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis

Target proteins linked pathways were recovered using the Database for Annotation, Visualization and Integrated Discovery (DAVID)[27]. DAVID was used to conduct the KEGG pathway enrichment analysis (https://david.ncifcrf.gov/).

Compound-disease target-pathway (C-D-P) Network construction

A network of disease target pathway was built using data from the KEGG pathway database and then integrated with a pre-existing network of compound-disease targets (C-D network) resulting in a comprehensive Pathway of Compound-Disease Target (C-D-P) network.[28]

Protein-protein (PPI) network construction

PPI network was constructed for identification of connections between disease proteins and therapeutic targets. Using the online tool STRING, interactions were mapped with a confidence score of >0.4, focusing on human proteins (Homo Sapiens). The resulting data was then imported into Cytoscape software and through its CytoHubba plugin key target proteins were identified, known as hub targets, which were ranked and categorized based on their degree of interaction.[29]

Functional Enrichment Analysis

DAVID offers researchers an entire set of useful annotation tools to help them decipher the biological significance of a large gene list. An extensive collection of functional annotations is provided by the software FunRich, which is mostly used for gene functional classification and helps researchers comprehend biological traits.[30,31]

Validation by Molecular Docking

Docking analysis with ligand was used to structural examination of the target's complexes with ligands[32]. The 3D structures of ALB (ID:5YOQ); MMP9 (ID:2OVX)); STAT3(ID:4ZIA); BCL2 (ID:6O0K) were downloaded as PDB. SM7 structure was drawn with chemdraw, energy minimization done with chemdraw pro and converted and saved into PDB format which is compatible to Autodock software. Molecular docking was done by Autodock Vina and analysis via visualization of result with Biovia Discovery software. Before docking between protein and ligand, protein preparation was done by removing the water molecule, inserting hydrogen bond and obtaining the ligand attributes with Biovia Discovery software. After the protein preparation it is imported into Autodock software and Kolleman charges were added and file converted to the PDBQT format. The ligand previously which was converted to the PDB inserted alongwith the protein, gasteiger charges, the root was detected automatic and save to PDBQT format. Docking was done with Autodock vina and scoring of binding affinity in form of scoring kcal/mol received after running over command prompt. The poses received in the output folder are analysed individually after transferring into Biovia Discovery software to visualize the binding of ligand with binding sites of protein.[33]

RESULTS

Drug-likeness, Pharmacokinetics and Toxicity

Lipinski's rule of five was found to be in compliance with SM7's characteristics, indicating that it exhibits good drug similarity properties (Table 1). It can inhibit cytochrome p450 enzymes, has moderate toxicity, and is difficult to diffuse across cell membranes, according to the data.

Table 1: Drug-likeness prediction of SM7

Property	Value	Property	Value
Molecular weight	434.48	LD_{50}	200mg/kg
Polar Surface Area (PSA)	82.81A2	Toxicity class	3
Rotatable bonds	8	GI absorption	HIGH
Hydrogen bonds donors	1	BBB permeant	YES
Hydrogen bonds acceptors	6	Pgp substrate	YES
clogP	4.56	CYP1A2 inhibitor	NO
Molecular refractivity	124.79	CYP2C19 inhibitor	NO
Lipinski violation	0	CYP2D6 inhibitor	YES
Bioavailability	0.56	CYP2C9 inhibitor	NO
Log Kp (cm/s)	-5.71	CYP3A4 inhibitor	NO

BBB, blood–brain barrier; GI, gastrointenstinal; Pgp, P-glycoprotein; Kp, skin permeation coefficient; LD_{50}, Lethal dose at 50%, CYP, cytochrome-p450

Target identification of SM7 and disease for network construction (C-D network)

100 target genes *(H. sapiens)* linked with SM7 were recovered from the Gene Cards databases (Fig. 2). Out of the total 100 SM7 connected targets, and 25005 cancer linked targets, 93 target genes were found to be overlapped. Using cytoscape with 93 targets, a (SM7)–(cancer) target (C-D) network (Fig. 3) was constructed.

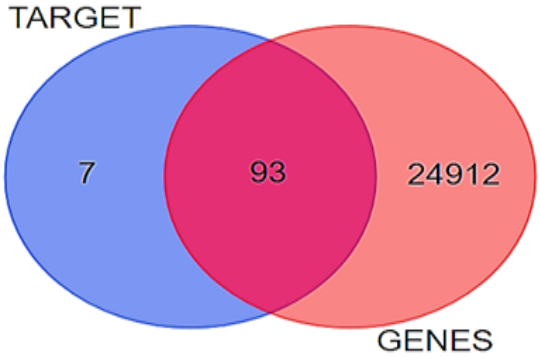


Fig. 2. SM7 and cancer linked targets

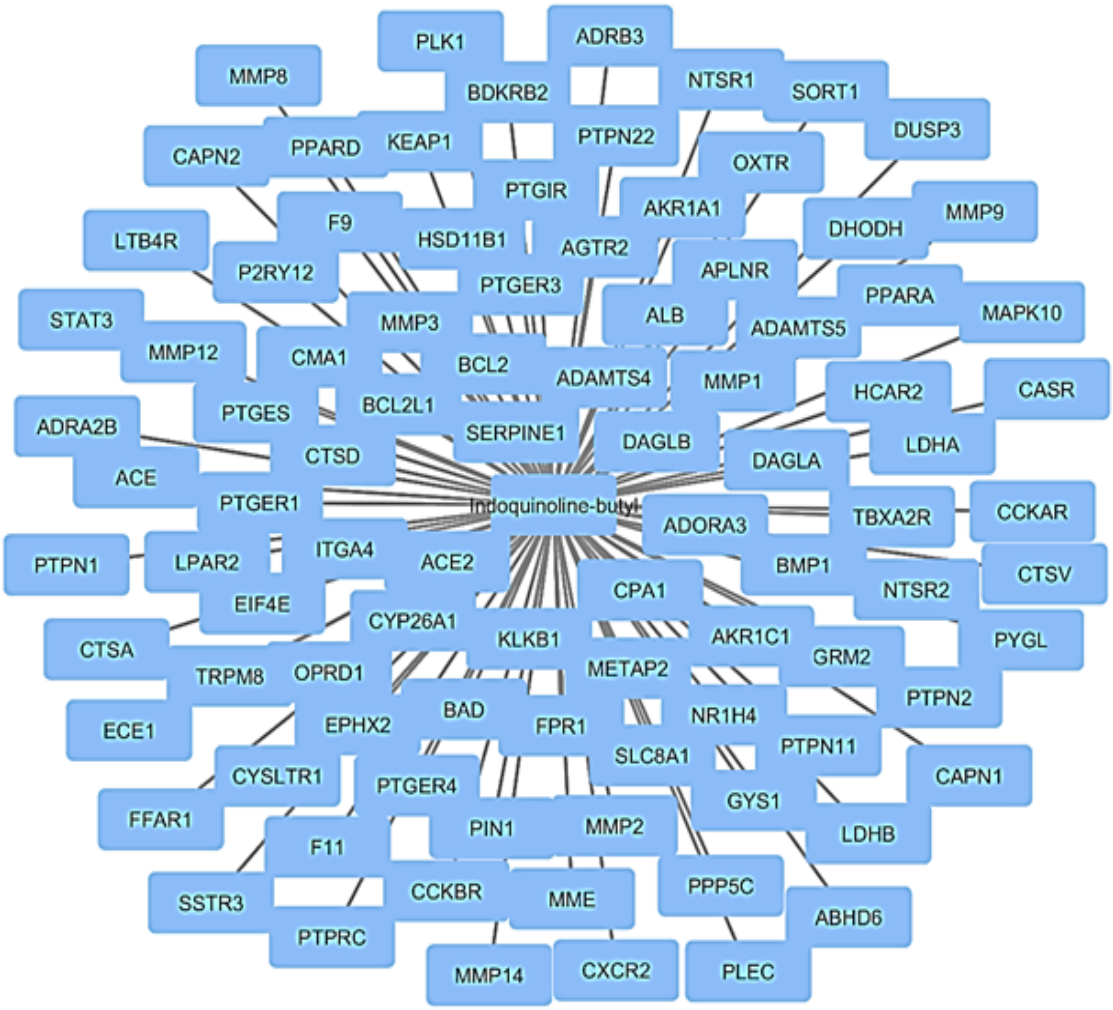


Fig. 3. SM7-Cancer target network constructed with cytoscape

Analysis of KEGG pathway

The 93-cancer linked SM7 targets underwent analysis with DAVID. On the basis of the gene count, top enriched pathways (Table 2) were identified. Reactome diagram with respect to cancer associated with SM7 was retrieved as Fig. 4. (Retrieved from https://davidbioinformatics.nih.gov/)

For pathway analysis, the 93 common target genes were imported into the DAVID. KEGG analysis yielded 15 pathways in total, of which we obtained the top 13 pathways that met criterion $p<0.05$. Among these were the calcium signaling route, cancer pathways, neuroactive ligand-receptor interactions, Apoptosis, Diabetic cardiomyopathy, Lipid and atherosclerosis, Chemical carcinogenesis - reactive oxygen species, Insulin resistance, cGMP-PKG signaling pathway, Renin-angiotensin system, HIF-1 signaling pathway, Insulin signaling pathway, Sphingolipid signaling pathway, EGFR tyrosine kinase inhibitor resistance. The most significant enriched KEGG pathways among them were neuroactive ligand-receptor interaction>Cancer Pathways.> calcium signaling pathway>Apoptosis.

Network of SM7-cancer target-pathway

A disease target-pathway network (D-P) was integrated with the SM7-disease target network (C-D), resulting in a comprehensive network (Fig. 5). In this network, edges signify interactions amonst them and nodes depicted individual targets. Using the Cytoscape plugin CytoHubba, we identified key nodes with the highest degree of connectivity (15), including, MAPK10, BCL2, BAD, STAT3, BDKRB2. These high-degree nodes, or hub genes, are likely to play crucial roles in biological processes.[27]

Cancer linked SM7 targets and their Protein-Protein interaction

To check a protein–protein interaction (PPI) network, the SM7 targets linked to cancer were imported into STRING (Fig. 6). ALB (degree of 32) and MMP9 (degree 29) were the two primary targets that displayed the highest degree.

Table 2: Genes identified in each pathway

Pathway	Count	Annotated genes
hsa04080:Neuroactive ligand-receptor interaction	23	PTGER4, OPRD1, PTGIR, OXTR, PTGER1, PTGER3, FPR1, LPAR2, SSTR3, ADRA2B, LTB4R, GRM2, CYSLTR1, CCKAR, CCKBR, ADRB3, TBXA2R, ADORA3, BDKRB2, APLNR, AGTR2, NTSR1, NTSR2
hsa05200:Pathways in cancer	15	PTGER4, PTGER1, MMP1, BAD, MMP2, PTGER3, STAT3, LPAR2, KEAP1, MMP9, MAPK10, BDKRB2, BCL2, BCL2L1, PPARD
hsa04020:Calcium signaling pathway	11	CYSLTR1, OXTR, CCKAR, CCKBR, ADRB3, TBXA2R, PTGER1, PTGER3, BDKRB2, SLC8A1, NTSR1
hsa04210:Apoptosis	8	MAPK10, BAD, BCL2, CAPN2, CAPN1, CTSV, CTSD, BCL2L1
hsa05415:Diabetic cardiomyopathy	8	MAPK10, GYS1, ACE, CMA1, MMP2, PPARA,CTSD, MMP9
hsa05417:Lipid and atherosclerosis	8	MAPK10, MMP1, BAD, STAT3, MMP3, BCL2, MMP9, BCL2L1
hsa05208: Chemical carcinogenesis-reactive oxygen species	8	MAPK10, PTPN1, BAD, EPHX2, AKR1C1, AKR1A1, KEAP1, PTPN11
hsa04931:Insulin resistance	7	MAPK10, GYS1, PTPN1, STAT3, PTPN11, PYGL, PPARA
hsa04022:cGMP-PKG signaling pathway	7	OPRD1, ADRB3, BAD, ADORA3, BDKRB2, ADRA2B, SLC8A1
hsa04614:Renin-angiotensin system	6	CTSA, ACE2, ACE, MME, CMA1, AGTR2
hsa04066:HIF-1 signaling pathway	6	LDHB, LDHA, STAT3, SERPINE1, BCL2, EIF4E
hsa04071:Sphingolipid signaling pathway	6	MAPK10, OPRD1, ADORA3, BDKRB2, BCL2, CTSD
hsa04910:Insulin signaling pathway	6	MAPK10, GYS1, PTPN1, BAD, PYGL, EIF4E
hsa04217:Necroptosis	6	MAPK10, STAT3, BCL2, CAPN2, CAPN1, PYGL
hsa01521:EGFR tyrosine kinase inhibitor resistance	5	BAD, STAT3, BCL2, EIF4E, BCL2L1

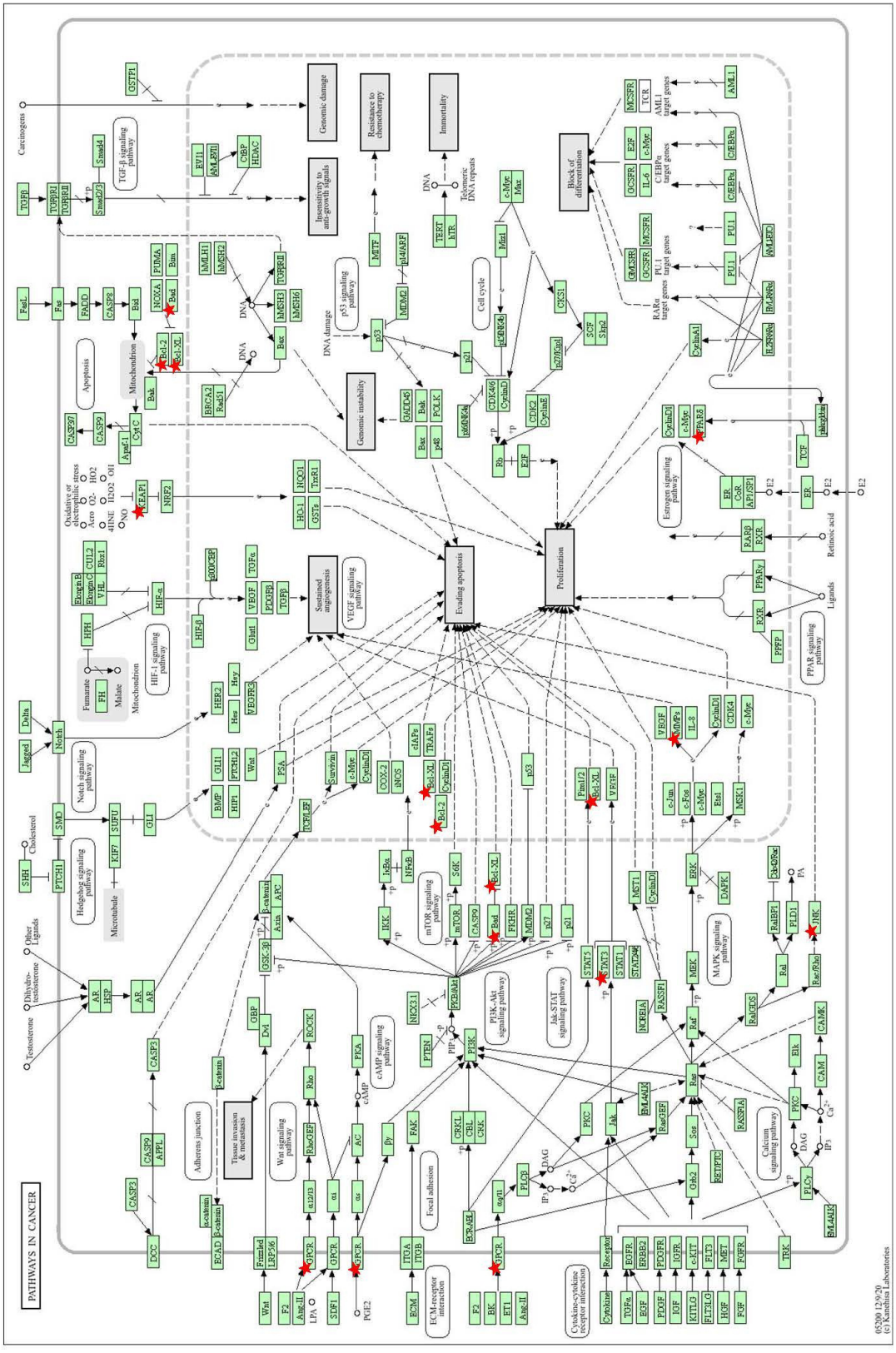


Fig. 4. Pathways in cancer of potential targets of SM7 retrieved from DAVID database

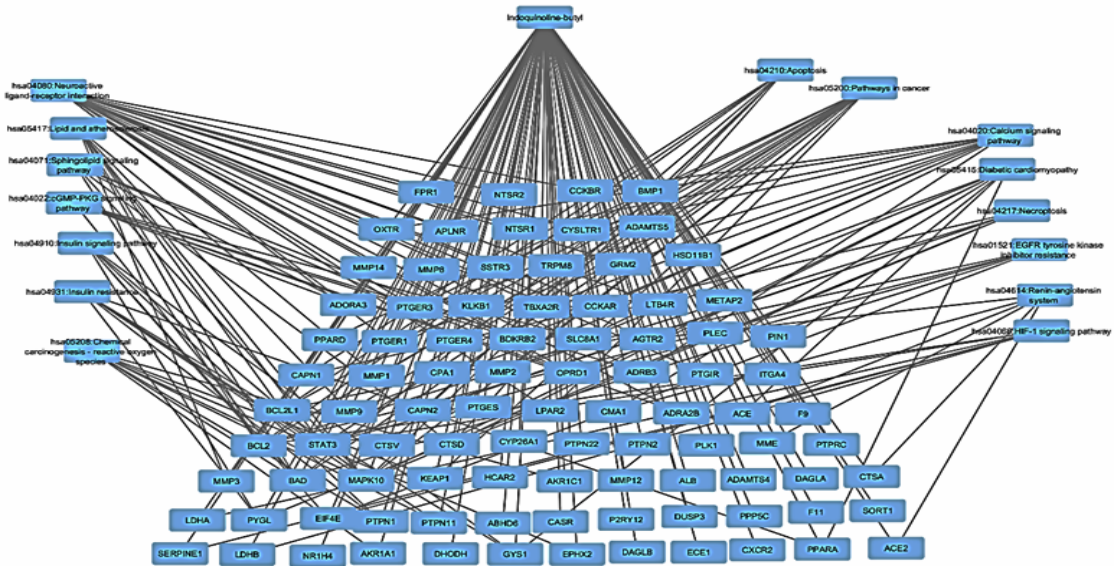


Fig. 5. SM7-cancer target-pathway network through cytoscape

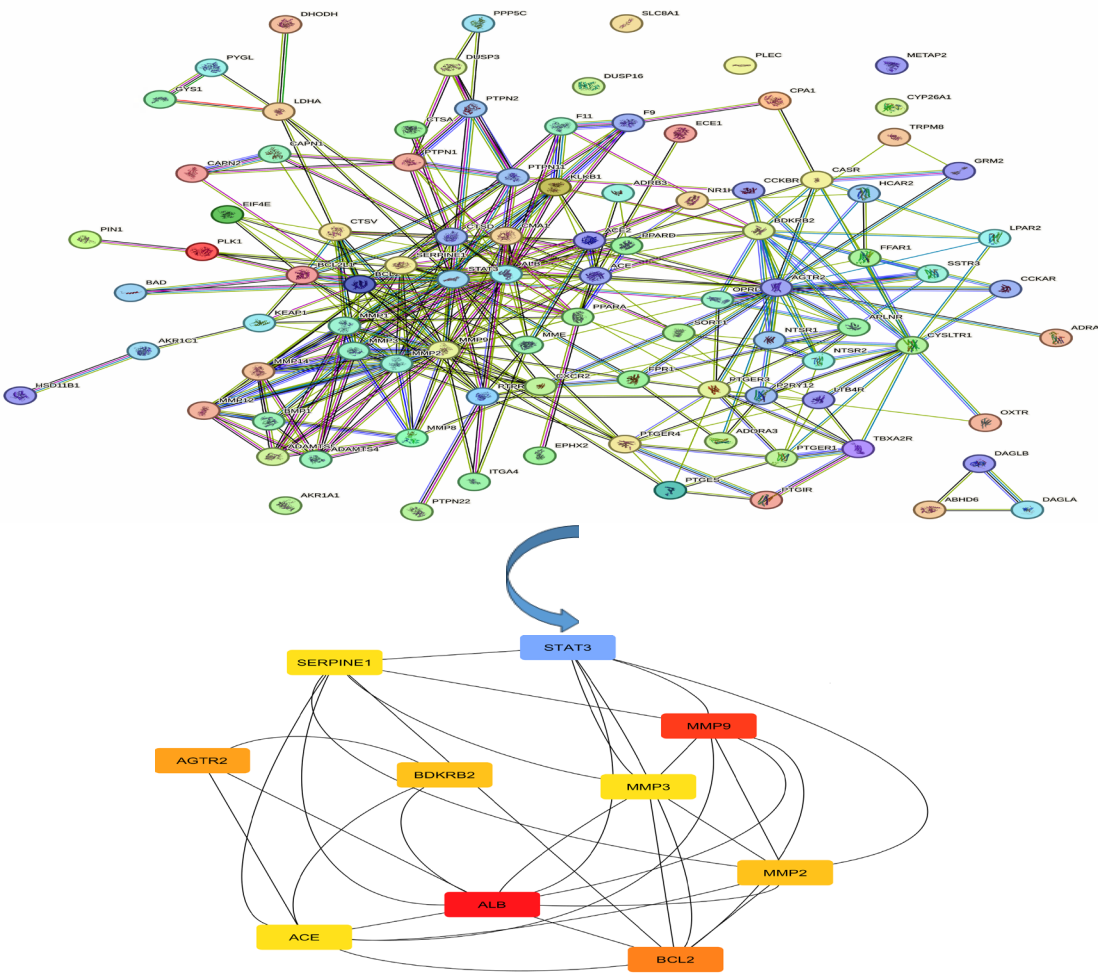


Fig. 6. Interactions of protein to protein in cancer associated SM7 targets generated using STRING any cytoscape

In this protein-to-protein interactions, the core targets are identified as ALB, STAT3, BCL2, MMP9. The said proteins have a main role in the SM7 mediated regulation of cancer disease. Table 3 represents the top 10 genes out of 93 target genes with their ranking and scores which were retrieved using string database.

Table 3: Top 10 in network gene ranked using Degree method from string database

Rank	Name	Score
1	ALB	32
2	MMP9	29
3	STAT3	25
4	BCL2	23
5	AGTR2	22
6	BDKRB2	18
7	MMP2	18
8	ACE	17
9	SERPINE1	17
10	MMP3	17

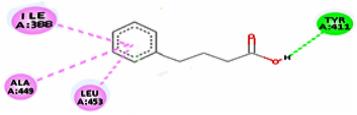
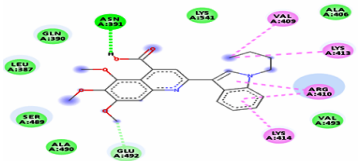
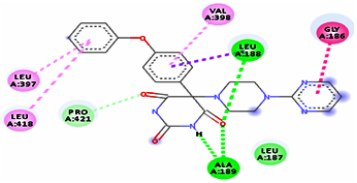
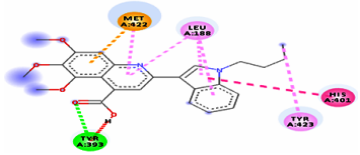
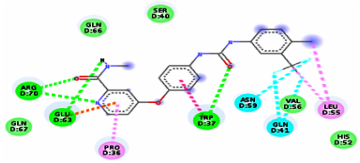
Molecular Docking

ALB, MMP9, STAT3 and BCL2 were traced as four crucial targets for SM7 against cancer from PPI network's analysis. The structural complexes of targets were analyzed using a ligand-target docking technique: ALB (PDB ID:5YOQ); MMP9 (ID: 2OVX); STAT3 (ID: 4ZIA); BCL2 (ID: 6O0k), along-with ligand as SM7 & standards through Auto dock Tools and the results were visualized Biovia Discovery. The binding affinities of SM7 & standard complexes are shown in Table 4.

Pathway Analysis and GO Enrichment for potential SM7's Targets

GO enrichment study concentrated mainly the cellular component, biological function and molecular function[34,35]. The FunRich was used to import the ten probable target genes that were chosen for GO enrichment. These prospective targets' functions were linked to numerous biological processes that may be crucial for signal transduction, cell communication, and protein metabolism, according to the results of GO analysis.

Table 4 Binding affinities of SM7 and standards with key targets and various interactions involved. Complexes were docked with Autodock-Vina and result analysed with Biovia discovery studio software

Complex	PDB ID	Binding affinity Kcal/mol	H-Bonding	Other interactions	Images
ALB:Sodium Phenylbuyrate	5YOQ	-6.5	TYR A:411	ILE A:388, ALA A:449, LEU A:453	
ALB: SM7	5YOQ	-5.8	ASN A:391	VAL A:409, LYS A:413, ARG A:410, LYS A:414, GLU A:492	
MMP9: CID10072851	2OVX	-11.2	LEU A:188, ALA A:189	GLY A:186, VAL A:398, LEU A:397, LEU A:418, PRO A:421,	
MMP9: SM7	2OVX	-7.7	TYR A:393	MET A:422, LEU A:188, HIS A:401, TYR A:423	
STAT3:Sorafenif	4ZIA	-6.4	ARG D:70, GLU D:63, TRP D:37	PRO D:36, ASN D59, GLN D:41, LEU D:55	

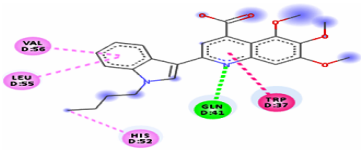
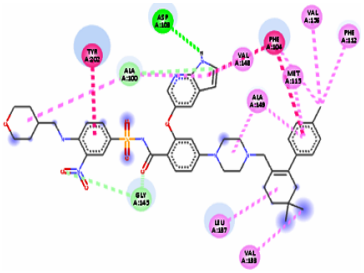
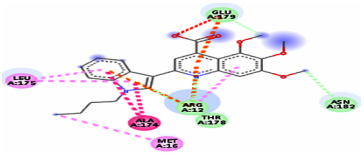
STAT3: SM7	4ZIA	-5.5	GLN D:41	TRP D:37, VAL D:56, LEU D:55, HIS D:52	
BCL2:Venetoclax	6O0k	-11.5	ASP A:108	TYR A:202, ALA A:100, VAL A:148, PHE A:104, ALA A:149, MET A:115, VAL A:156, PHE A:112, LEU A:137, VAL A:133 GLY A:145	
BCL2: SM7	6O0k	-7.0	No Hydrogen	GLU A:179, ASN A:182, ARG A:12, LEU A:175, MET A:16, ALA A:174	

Table 5: Go enrichment analysis of potential targets

Biological pathway	Term	Genes
	Protein metabolism	MMP9; MMP2; ACE; SERPINE1; MMP3
	Transport	ALB
	Cell communication	AGTR2; BDKRB2
	Signal transduction	AGTR2; BDKRB2
	Regulation of nucleobase, nucleoside, nucleotide and nucleic acid metabolism	STAT3
	Apoptosis	BCL2
	Term	Genes
Molecular function	Protease inhibitor activity	SERPINE1
	Transporter activity	ALB
	Hydrolase activity	ACE
	Metallopeptidase activity	MMP9; MMP2; MMP3
	G-protein coupled receptor activity	BDKRB2
	Receptor activity	AGTR2
	Transcription factor activity	STAT3
	Receptor signaling complex scaffold activity	BCL2
	Term	Genes
Cellular Component	Plasma membrane	MMP9; AGTR2; BDKRB2; MMP2; ACE; SERPINE1;
	Integral to plasma membrane	BDKRB2;
	Nucleus	ALB; STAT3; BCL2;
	Nucleolus	STAT3;
	Mitochondrion	STAT3; BCL2;
	Cytosol	BCL2;
	Membrane fraction	ACE;
	Cytoplasm	ALB; STAT3; BCL2; SERPINE1;
	Exosomes	ALB; ACE;
	Lysosome	ALB;
	Endoplasmic reticulum	BCL2;
	Endosome	BDKRB2; ACE;
	Cell surface	STAT3;
	Extracellular	ALB; MMP9; STAT3; MMP2; SERPINE1; MMP3;
	Extracellular region	ALB; SERPINE1;
	Membrane	BCL2;
	Extracellular space	ALB; MMP9; MMP2; ACE; SERPINE1; MMP3;
	Extracellular matrix	STAT3; SERPINE1;
	Cytoskeleton	ALB;
	Platelet alpha granule lumen	ALB;
	Protein complex	ALB;
	Nuclear membrane	BCL2;
	Mitochondrial outer membrane	BCL2;
	Intracellular membrane-bounded organelle	MMP2; MMP3;
	External side of plasma membrane	ACE;
	Mitochondrial membrane	BCL2;

Out of all total 8 molecular functions mainly Metallopeptidase activity found to be highly enriched. Protein metabolism related cellular components were identified, including plasma membrane, cytoplasm, extracellular, extracellular space tabulated as under Table 5.

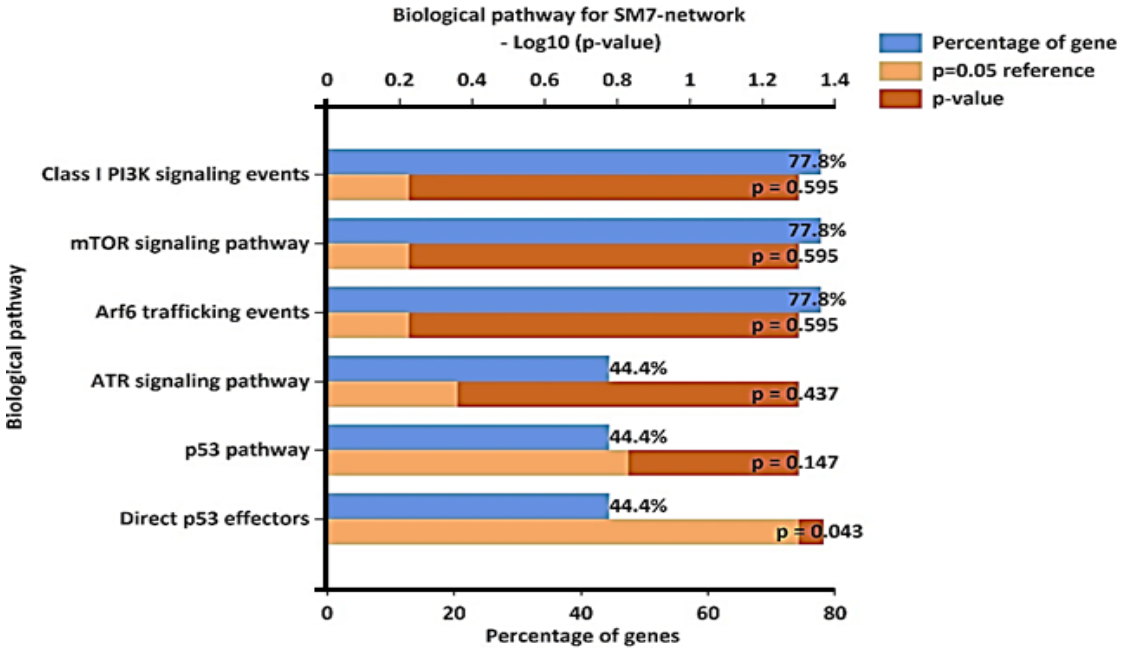


Fig. 7. The biological pathways for SM7 in cancer analysed by Fun Rich software

The biological pathways for SM7 in cancer were analysed by FunRich software and the focussed pathways suggested that SM7 possibly has a contributing role in cancer by participating in the pathways (Figure7).

DISCUSSION

The ADMET properties are crucial for assessing the drug-likeness and potential therapeutic efficacy of novel compounds. ADME profiling results for indole-quinoline derivative (SM7) suggested that SM7 do not violate Lipinski's Rule of Five, indicating good drug-likeness and potential oral bioavailability with molecular weight 434.48, LogP value 4.56 and total polar surface area (TPSA) 82.81. These values suggest moderate lipophilicity and good permeability, which is favourable for oral bioavailability as compounds with very high or very low lipophilicity may face challenges in absorption and distribution. In current study, by focussing on the overlapping targets the possible cancer targets for SM7 were identified which includes ALB, MMP9, STAT3, BCL2, AGTR2, BDKRB2, MMP2, ACE, SERPINE1, and MMP3 etc. It was found that SM7 may affect cancer cells through different targets and signaling pathways, that collectively plays a variety of synergistic roles, when all overlapping targets were examined using the PPI network analysis map. All the identified genes have their own role in various cancers. ALB functions as a tumor suppressor in hepatocellular carcinoma (HCC), and its depletion promotes invasion and metastasis. Its suppression leads towards migration and invasion of HCC cells through increased uPAR, MMP2, MMP9.[36] In cancer, metastasis is major reason of mortality and MMP9 importance was noticed during onset, progression and metastasis in gastric, lung and breast cancer. By decomposing extracellular matrix, metastasis and angiogenesis is promoted.[37] The genes which govern important cellular process like cell growth, survival and immune response are controlled by STATS3. Abnormal high level STAT3often found in various types of cancer. In breast cancer STAT3 is overactive and leads towards tumors by influencing the expression of genes which are responsible for uncontrolled cell division, resistance cell death and angiogenesis.[38] In a study abnormal STAT3 activity was traced leads toward tumor growth, cell proliferation and metastatic and angiogenesis.[39]

Bradykininin receptor B (BDKRB2) linked

to aggressive glioma phenotype, and it promote cancer progression through EMT (Epithelial-to-mesenchymal transition process and can be used as indicator in patient outcome in glioma.[40] MMP2 and MMP are enzymes comes under metalloproteinase enzyme family together known as gelatinous involved in restructuring extracellular matrix by degradation of collagen and gealtin. Both enzymes play dual role in normal physiological process and cancer progression.[41-47] SERPINE1, a key inhibitor of tissue plasminogen and urokinase plays an important role in various cancer. Serpine1 is overexpressed in gastric cancer along with poor survival. Wet studies revealed upregulation of VEGF &IL6 after overexpression of SERPINE1. In immunohistochemistry SERPINE1 overexpression was identified in Gastric cancer. Invivo study with Serpine1 knockdown nude mice reflect that Serpine1 could have important role in cancer progression and might regulate VEGF signalling pathway and JAK/STAT3.[48] The results of the Gene Ontology study indicated that the targets were primarily related to signal transduction, cell communication, and protein metabolism. These biological processes, which were in line with the literature.[41-45], were connected to the Cancer HIF-1 signaling pathway. As a result, SM7's putative targets took part in a variety of biological processes and will be crucial to the development of cancer. Potential targets were mostly implicated in 15 pathways, according to the KEGG pathway analysis. The SM7 targets linked to cancer were primarily associated with pathways such as cancer (chemical carcinogenesis-reactive oxygen species), signalling pathways (HIF-1), EGFR tyrosine kinase inhibitor resistance etc. Hypoxia-Inducible Factor-1 (HIF-1), known as important transcription factor which regulates hypoxic responses. And elevated HIF-1 levels can serve as prognostic markers for metastasis, Chemo/radio resistance development, Poor overall prognosis in cancer patients and this suggests that targeting HIF-1 may offer therapeutic potential for cancer treatment.[49-50] The biological pathways for SM7 in cancer were analysed by FunRich software and the retrieved pathways through this study suggested that SM 7 could play a role in cancer by various mechanism.The phosphoinositide 3-kinase (PI3K) family is known as crucial regulator in cellular and tissue biology which plays as main role in human diseases such as cancer, diabetes, and aging. Through their spatial regulation and multifunctional capabilities, PI3Ks coordinate a broad spectrum of cellular processes, including signalling pathways, membrane trafficking, and metabolic functions, across various cellular membranes. The PI3K family, particularly class I, plays a crucial role in cellular processes. The production of PtdIns P3 and the activation of Akt, which controls cell growth, proliferation, survival, metabolism, and autophagy, are caused by activated RTKs or GPCRs bringing p85-p110 complexes to the plasma membrane. Furthermore, cortical F-actin dynamics are influenced by localized class I PI3K activity, which impacts phagocytosis and chemotaxis.[51] PI3K-AKT pathway deregulation is linked to poor outcomes in various tumors, including brain, breast, prostate, bladder, colon, and lung cancers, and is associated with aggressive tumor behaviour.[52] The mammalian target of rapamycin (mTOR) is involved in several cell signaling networks which involve controls cell division, autophagy, and apoptosis. Numerous research have already revealed that the mTOR signaling pathway have key role for osteoporosis, insulin resistance, cancer, arthritis, and other illnesses. The mTOR signaling system is frequently triggered in malignancies and controls gene transcription and protein synthesis, which impacts immune cell differentiation and cell proliferation. Additionally, it represents the vital function in tumor metabolism.[53] ATR kinase is a crucial regulator of DNA repair, cell-cycle progression, and replication fork stability in response to stress and DNA damage. Inhibiting ATR may offer therapeutic benefits, especially if it can selectively target tumor cells.[54] Thus, the mTOR, ATR, and Class I PI3K signaling events were thought to play important roles in the cancer pathways controlled by SM7 in the current investigation. These results suggested that SM7 can be a potential lead molecule to be screened in cell lines and further in rodents and can be developed as anticancer agents with the involvement of possible targets obtained through network pharmacology approach. Molecular docking studies helps to understand the binding interaction between ligand and target protein which can be quantified by binding affinity score. These scores are very necessary indicators and more negative values shows strong binding between ligand and protein. The binding affinities of indole-quinoline derivative (SM7) with identified proteins were analysed and found to be -5.8, -5.5, -7.0, -7.7 Kcal/mol for the target protein ALB (PDB:5YOQ), STAT3 (PDB:4ZIA), BCL2 (PDB:6O0K), and MMP9 (PDB:2OVX)

respectively with the involvement of hydrogen bonding and other hydrophobic interactions with the different amino acids in the chain that suggested the possibility of stable interaction with the target. These findings highlighted the variability in ligand-protein interactions, which can significantly influence therapeutic efficacy. This underscores the importance of molecular docking as a tool for optimizing drug design and development.

CONCLUSION

The molecular targets and possible mechanisms of SM7's anti-cancer effects were identified and revealed in this work using a unique approach. In order to explore potential cancer targets using KEGG pathway enrichment and GO gene function analyses, the SM7 network diagram was constructed using a variety of software programs and databases. This demonstrated the potential for an anticancer effect by SM7 through the involvement of multiple targets and pathways, which may ultimately change biological processes. SM7 interacts to the proteins ALB, MMP9, STAT3, and BCL2 in a stable manner, according to molecular docking results. Although the study gives predictive insights and a theoretical basis for the development of SM7 as an anticancer drug, its effectiveness has to be further validated through in-vitro, preclinical, and experimental trials.

ACKNOWLEDGEMENT

Authors are thankful to Amity University for the support and infrastructure.

Conflict of interest

The author declare that we have no conflict of interest.

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