

Exploring the Inhibitory Potential of Organosulphur Compounds as Potent PKP1 Inhibitor in Ovarian Cancer

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Abstract: The highest number of female reproductive cancer deaths is caused by ovarian cancer. The current treatments for ovarian cancer include debulking surgery and chemotherapy. Chemotherapy can be more disadvantageous than the benefits, such as fatigue, hair loss, appetite changes, weight loss, etc. Our study has mainly focused on a targeted therapeutic approach via exploiting the inhibitory potential of organosulphur compounds against a potent proto-oncogene, PKP1, that has been critically concerned with the progression of ovarian cancer. Organosulfur compounds produced by plants have displayed significant anticancerous potential against several human carcinomas. It has various properties, including antioxidant, anti-inflammatory, and anti-tumorous. We have used *in silico* and *in vitro* techniques to explore the inhibitory potential of selected sixteen organosulphur compounds against the PKP1 protein. The new aspect of this work is figuring out how to suppress PKP-1 in ovarian cancer cells using organosulfur compounds. Allicin has been shown to be the most effective PKP-1 inhibitory organosulphur compound by *in silico* methods. Further, an inverse correlation between allicin and PKP-1 in ovarian cancer has been established via performing MTT and RT-PCR assays in SKOV3 ovarian cancer cells. Altogether, our research findings have strongly validated the ability of allicin as a potent PKP-1 inhibitor in ovarian cancer. However, more detailed research is needed to strengthen the candidature of allicin as a potent anti-ovarian cancer drug candidate.

Keywords: PKP1; organosulphur compounds; molecular docking; anticancer; ovarian cancer.

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1. Introduction

Among all female reproductive tract cancers, ovarian cancer is one of the most fatal conditions. This particular malignancy is detected at a later stage in 70% of cases. Thirty percent of women anticipate surviving in five years. The five-year survival rates for women with ovarian cancer have recently increased for those diagnosed between 1996 and 2002 when

compared to decades like the 1970s and 1980s. Even though the benefits are modest, it is essential to understand the molecular etiology of ovarian cancer in order to identify new therapeutic targets and biomarkers that aid in early detection [1].

PKP1 (plakophilin) is a protein in human genes that is encoded by the PKP1 gene. The arm-repeat (armadillo) and plakophilin gene families are encoded by this gene [2]. Plakophilin protein contains several armadillo repeats that localize to cell desmosomes, and nuclei also participate by linking to cadherins, which means transmembrane proteins that arbitrate cell-to-cell adhesion in animals, to intermediate filaments (the components which are structurally found in vertebrates and few invertebrates) in cytoskeletons [3].

Phytonutrients are extensively confessed for providing human health protection [4]. Organosulphur compounds among the phytonutrients play a key role in preventing several human pathological developments like chronic inflammation, prostaglandin (PG) E₂, interleukin (IL)-1 β , IL-6, tumor necrosis factor (TNF)- α , and IL-17, which all are indicators of inflammation [5-7]. Organosulphur compounds like isopropyl propyl disulfide, dimethyl trisulphide, dipropyl disulfide, cis propenyl propyl trisulphide, 3-mercaptopropionic acid, diallyl disulfide, diallyl sulfide, ajoene, etc, activates NF- κ B (nuclear factor kappa-light-chain-enhancer of activated B cells) consoling the inflammation within the tumor by preventing NF- κ B nuclear transportation by suppressing the activity of NF- κ B protein [8].

The development of resistance to treatment is one of the significant challenges in the reach of epithelial ovarian cancer. TP53 is the transcription factor that generally activates DNA repair and initial apoptosis, and loss of TRAIL-induced it can cause mutation or deletion; thus, cancer cells get drug resistance [9, 10, 11]. NF- κ B and p53 are related oppositely in cancer. The activation of NF- κ B reduces the tumor suppression activity of p53, leading to dominant ontogeny-mediated transformation. They also have antiviral and antibacterial properties [11]. In context to this, elucidating potent organosulphur compounds that can block PKP-1 protein targets in ovarian cells could be a promising and interesting avenue for cancer research. By thoroughly examining these facets, we aimed to provide significant new information regarding the creation of potentially effective new treatments for ovarian cancer, with an emphasis on PKP1 as a possible biomarker inside cancer cells.

2. Materials and Methods

2.1. Ligand (organosulphur compounds) and target protein (macromolecule) preparation.

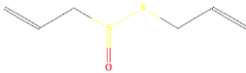
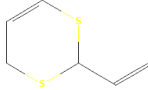
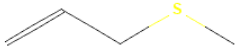



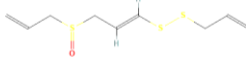






Sixteen potent organosulphur compounds have been selected through literature sources (Table 1), and their 3D structures were obtained from the PubChem (<http://pubchem.ncbi.nlm.nih.gov/>) database [12].

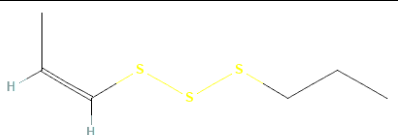
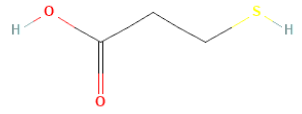
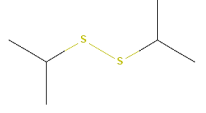
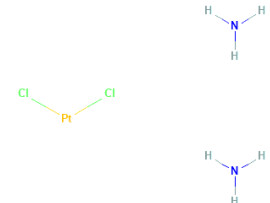


Figure 1. Structure of PKP1(PDB ID: 1XM9).

Their energy minimization was performed before docking, as previously published research reports described. The 3D (crystal) structure of PKP1 (PDB ID: 1XM9) was downloaded from the protein database (PDB) (Figure 1) [13]. Energy minimization and refinement of the 3D structure of PKP1 were downloaded before docking.

Table 1. Selected ligands for docking.

S. No	Pub Chem ID	Compound name	Canonical smile	Chemical structure
1	65036	Allicin	<chem>C=CCSS(=O)CC=C</chem>	
2	133337	2-vinyl-4H-1,3-dithiine	<chem>C=CC1SCC=CS1</chem>	
3	66282	Allyl methyl sulphide	<chem>CSCC=C</chem>	
4	16590	Diallyl disulphide	<chem>C=CCSSCC=C</chem>	
5	11617	Diallyl sulphide	<chem>C=CCSCC=C</chem>	
6	16315	Diallyl trisulphide	<chem>C=CCSSSCC=C</chem>	
7	5386591	Ajoene	<chem>C=CCSSC=CCS(=O)CC=C</chem>	
8	16592	Methyl propyl disulfide	<chem>CCCSSC</chem>	
9	118529	Isopropyl propyl disulfide	<chem>CCCSSC(C)C</chem>	
10	19310	Dimethyl trisulphide	<chem>CSSSC</chem>	
11	12377	Dipropyl disulphide	<chem>CCCSSCCC</chem>	
12	16591	2-propenyl propyl disulfide	<chem>CCCSSCC=C</chem>	
13	12232	Dimethyl disulfide	<chem>CSSC</chem>	

S. No	Pub Chem ID	Compound name	Canonical smile	Chemical structure
14	5352694	Cis-propenyl propyl disulfide	<chem>CCSSSC=CC</chem>	
15	6514	3-mercaptopropionic acid	<chem>C(CS)C(=O)O</chem>	
16	77932	Bis (1-methyl ethyl) disulfide	<chem>CC(C)SSC(C)C</chem>	
17	5702198	Cisplatin	<chem>N.N.Cl[Pt]Cl</chem>	

2.2. Molecular docking using CB-dock software.

CB dock was used to molecularly dock sixteen organosulphur compounds and one standard medication against selected target PKP1 [14,15]. The input is two molecules in PDB format. The server receives molecules that have been downloaded from the Protein Data Bank. The user must input the appropriate chain ID or chains to dock a specific chain or chain. The best 20 answers are shown on a web page created automatically. The user receives a mail with the input provided as the mail ID. The solutions' score, area, and atomic contact energy are displayed in the table. Each line contains a download link for a PDB file that the user can access. The outcomes of 17 solutions were downloaded in this manner. Ajoene demonstrated the highest binding affinity against PKP1 after sixteen organosulphur compounds were examined for their ability to bind to the protein utilizing the CB dock. The results were also compared with the chemotherapeutic drug cisplatin used for the therapeutic intervention for ovarian cancer.

2.3. Lipinski's rule of five.

The drug-likeness of particular organosulphur compounds was determined using the Molinspiration (<http://www.molinspiration.com/cgi-bin/properties>) application [16]. Using Lipinski's rule of five, the drug-likeness of a few chosen organosulphur compounds and a common conventional drug was clarified [17]. The following variables were taken into account for determining drug-likeness: MW, topological polar surface area, LogP, H (hydrogen) bond acceptor sites, number of rotatable bonds, and the number of H (hydrogen) bond donors [18].

2.4. Bioactivity score (BAS) prediction.

BAS (bioactivity score) values indicate if a phytochemical will be a good lead contender in general [19]. A free online program called Molinspiration (<https://www.molinspiration.com/cgi-bin/properties>) was used to compare the drug score of a potential phytochemical to a number of receptors, including ion channels, GPCR, enzymes, <https://nanobioletters.com/>

kinases, and nuclear receptors [20]. Higher bioactivity scores generally show a higher likelihood of an active chemical being present.

2.5. Pharmacokinetic (PK) parameter analysis.

SwissADME (online program) was used to investigate the ADMET properties (of both standard drugs and selected organosulphur compounds) [21]. The blood-brain barrier, CYP2C19, CYP1A2, CYP2D6, CYP2C9, CYP3A4 metabolism, LogKp (skin permeability), and P-gp (P-glycoprotein substrate) are only a few of the important pharmacokinetic features that have been examined [22, 23].

2.6. MTT assay.

The growth inhibitory activity of allicin was assessed via the MTT assay protocol as described previously [24]. Ovarian cancer cell line SKOV3 and normal cell line Hek293 were procured from the National Centre for Cell Science (NCCS, Pune, India). Both the cancer cells were grown in DMEM supplemented with 10% FBS (heat-inactivated) and 1% solution (antibiotic–antimycotic), amphotericin B, and streptomycin (Himedia India, Mumbai, India) in a controlled environment (incubator) with 5% CO₂ at 37°C.

In brief, both of the cell lines were seeded (1×10^4 cells/well) overnight in 96-well (microtiter culture) plates. Stock solution of allicin was prepared by dissolving it in DMSO and thereafter diluted in the same media at several doses (0, 10, 20, 30, 40, and 50 μ M) for treating the cultured cells at different time periods for 24 h. After incubating the cells, absorbance values were observed using MTT dye (5 mg/mL PBS) with the help of an ELISA plate reader (at 490 nm). IC₅₀ values of allicin for the SKOV3 cancer cell line were calculated by using OriginPro software.

2.7. Real-time qPCR analysis.

Gene expression of selected genes was analysed by real-time PCR analysis as described previously [24]. The HiPurATM Total RNA Miniprep Purification Kit (Himedia) was used to extract the RNA from both treated and untreated cells. ThermoScientific's Verso cDNA synthesis kit was used to produce cDNA, and the SYBR Green qPCR kit was used to estimate the target mRNA expression level. The primer sequences employed in this research are:

PKP1: (forward 5'-TTAGTGTTTTATATAGGGGATTTGT-3'; reverse 5'-ACTCCCTACAACACTCCTAACACT-3') GAPDH: (forward 5'-AAGGTCGGAGTCAACGGAT TTGGT-3'; reverse 5'-CATGTGGGCCATGAGGTCCACCAC-3').

2.8. Statistical analysis.

In this study, every test was conducted in triplicate, and the outcomes were shown as the mean \pm standard error of three separate trials. The statistical analysis was performed using Dunnett's multiple comparison test (*p<0.01, **p<0.001 denote significant difference compared to control).

3. Results and Discussion

3.1. Docking analysis of selected organosulphur compounds against PKP1.

CB Dock and PatchDock were utilized for the docking study of selected organosulphur compounds against PKP1. As it is clear from Table 2, all selected organosulphur compounds exhibited significant binding affinity to PKP1-based dissociation constant (Kd) and the best binding energy of ligand-protein interactions. However, allicin displayed the highest binding energy compared to other compounds and standard drugs (Figure 2).

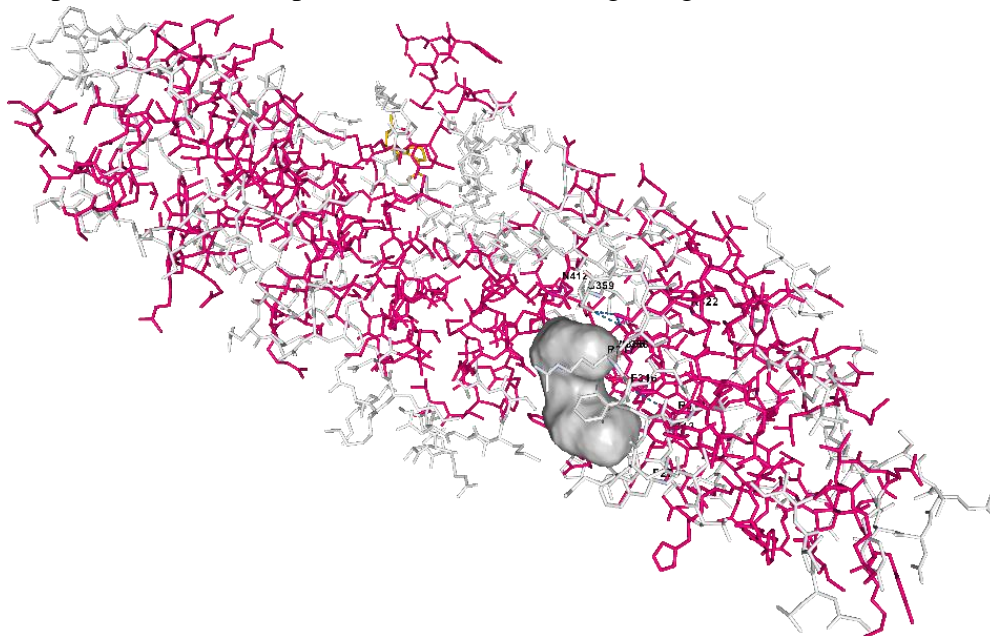


Figure 2. Docked posed structure of PKP1 with allicin.

Table 2. Docking analysis of selected sixteen organosulphur compounds with PKP1 using CB Dock.

S.No.	Ligand	Vina Score	Cavity Size	Residues
1.	Allicin	-4.2	272	PHE274 ARG312 ASN313 PHE316 ARG317 LYS322 TRP355 ASN356 SER359 ASN412
2.	2-vinyl-4H-1,3- dithiine	-3.4	272	MET535 SER538 LYS539 ASP541 LEU544 GLN578 ARG581 LEU582 SER585 GLY586
3.	Allylmethylsulphide	-2.5	200	MET535 LYS539 ASP541 LEU544 GLN578 ARG581 LEU582 SER585 VAL590
4.	Diallyl disulfide	-3.1	272	PHE274 ARG312 ASN313 PHE316 TRP355 ASN356
5.	Diallyl sulfide	-3.1	272	PHE274 GLN275 ASP276 GLU277 LYS280 ARG312 ASN313 PHE316 ARG317 LYS322 TRP355 ASN356 SER359 ASN405 ASN412
6.	Diallyl trisulphide	-3.2	272	PHE274 ARG312 ASN313 PHE316 ARG317 LYS322 GLU345 LYS348 GLN349 TRP355 ASN356 SER359 GLU401 PHE404 ASN405 ASN412
7.	Z-ajoene	-4.2	287	PHE274 ARG312 ASN313 PHE316 ARG317 LYS322 GLY352 TRP355 ASN356 SER359
8.	Methylpropyldisulphide	-2.6	200	GLU452 MET535 GLY536 SER538 LYS539 LYS540 ASP541 ALA542 LEU544 GLN578 ARG581 LEU582 GLN584 SER585 GLY586 ASN587 VAL590
9.	Isopropyl propyldisulfide	-3.2	200	MET535 GLY536 SER538 LYS539 LYS540 ASP541 LEU544 GLN578 ARG581 LEU582 GLN584 SER585 GLY586 VAL590
10.	Dimethyl trisulphide	-2.2	142	TYR463 ARG464 LEU465 ASP466 ALA467 GLN552 ASN553 LEU554 ALA556 SER557 LYS558 SER596 SER599 ASN600 SER639
11.	Dipropyl disulfide	-3.1	272	GLN270 PHE274 GLN275 ASP276 GLU277 LYS280 ARG312 ASN313 PHE316 ARG317 LYS322 TRP355 ASN356 SER359 PHE404 ASN405 ASN412
12.	2-propenyl propyl disulfide	-3.2	272	PHE274 ARG312 ASN313 PHE316 ARG317 LYS322 GLN349 TRP355 ASN356 SER359 ASN412

S.No.	Ligand	Vina Score	Cavity Size	Residues
13.	Dimethyl disulfide	-2	142	TYR463 ARG464 LEU465 ASP466 ALA467 GLN552 ASN553 ALA556 SER557 LYS558 SER596 ASN600 ARG603
14.	Cis-propenyl propyl trisulphide	-3.1	272	PHE274 ARG312 ASN313 PHE316 ARG317 LYS322 GLY352 TRP355 ASN356 SER359 PHE404 ASN405 GLY408 ARG411 ASN412 ASN453
15.	3-mercaptpropionic acid	-3.5	142	TYR463 ARG464 LEU465 ASP466 ALA467 GLU468 GLN552 ASN553 LEU554 THR555 ALA556 SER557 LYS558 SER596 LEU597 SER599 ASN600 ARG603 SER639
16.	Bis (1- methylethyl) disulphide	-3.3	151	ARG411 SER414 SER415 ASP417 ARG420 GLU452 CYS456 HIS459 ASN460 TYR463 ALA542 GLU545 ALA546 GLN552 ASN553 ARG592
17.	Cisplatin	-1.2	272	ILE269 GLN270 HIS271 CYS273 PHE274 LYS280 ALA310 ARG312 ASN313 LEU314 VAL315 PHE316 ARG317 SER318 LYS322 GLN349 GLY352 LEU353 TRP355 ASN356 LEU357 SER359 ASN405

3.2. BAS properties of selected organosulphur compounds.

Our findings strongly reveal that all selected organosulphur compounds are biologically active molecules as per the standard criteria described above (Table 3). Generally, a compound with BAS>0.00 possesses considerable biological potential, whereas compounds with values ranging between 0.50 and 0.00 are considered moderately active. Compounds with BAS<0.50 are considered to be inactive. However, ajoene displayed the best potential to provide physiological actions via numerous mechanisms after interacting with nuclear receptor ligands, GPCR ligands, or acting as enzyme inhibitors [25].

Table 3. Bioactivity score (BAS) of all selected organosulphur compounds.

S. no	Ligand	GPCR ligand	Ion channel modulator	Kinase inhibitor	Nuclearreceptor ligand	Protease inhibitor	Enzyme inhibitor
1.	Methyl propyl Disulphide	-3.50	-3.82	-3.85	-3.71	-3.51	-3.18
2.	Isopropyl propyl Disulphide	-3.10	-3.55	-3.72	-3.54	-3.10	-2.48
3.	Dimethyl Trisulphide	-3.68	-3.78	-3.71	-3.73	-3.67	-3.61
4.	Dipropyl Disulphide	-2.80	-3.27	-3.61	-3.34	-2.92	-2.38
5.	2-propnyl Disulphide	-3.06	-3.55	-3.71	-3.38	-2.96	-2.41
6.	Dimethyl Disulphide	-3.73	-3.85	-3.83	-3.78	-3.71	-3.66
7.	Cis-propenyl propyl trisulphide	-2.20	-2.05	-3.00	-2.43	-2.10	-1.27
8.	3-mercaptpropionic acid	-3.54	-3.69	-3.83	-3.54	-2.34	-2.55
9.	Bis- 1 (methyl allyl) disulphide	-3.34	-3.25	-3.59	-3.48	-3.29	-2.79
10.	S-propyl L-cystein	-0.67	-0.11	-1.57	-1.48	-0.23	-0.09
11.	Diallyl disulphide	-3.12	-3.44	-3.64	-3.28	-3.10	-2.57
12.	Allicin	-2.51	-2.26	-2.95	-2.66	-1.40	-1.52
13.	Diallyl sulfide	-3.71	-3.71	-3.83	-3.66	-3.60	-3.57
14.	Diallyl trisulphide	-2.40	-2.12	-2.65	-2.52	-2.32	-1.65
15.	Z-ajoene	-0.67	-0.99	-1.32	-0.73	-0.63	0.24
16.	2-Vinyl-4H-1,3-Dithiine	-3.56	-3.03	-3.81	-3.56	-3.19	-2.73
17.	Paclitaxel	-2.67	-3.43	-3.51	-3.12	-2.00	-2.87

3.3. ADMET (Absorption, distribution, metabolism, excretion, and toxicity) properties of organosulphur compounds.

The pharmacokinetic viability of all selected sixteen organosulphur compounds (as a prospective lead candidate) was calculated using Swiss ADME software (Table 4). LogP indicates the lipophilic and good absorption nature of organosulphur compounds across the skin. Except for ajoene, 3-mercaptpropionic acid, and the standard drug, all fourteen other

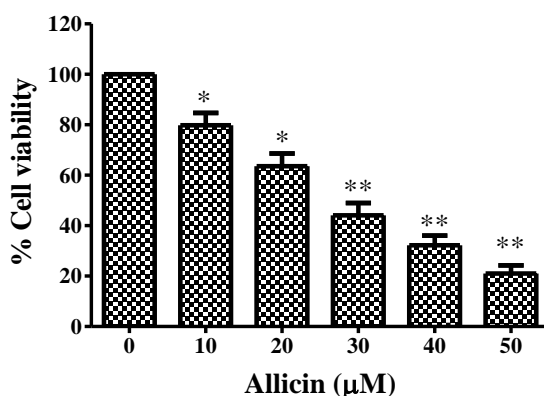
organosulphur compounds have displayed a blood-brain barrier. An ATP-independent bioactivity protein pump called P-gp removes drugs from the biological system. The regular excretion of possible medicine back into the lumen (gut) by P-gp decreases the pharmaceutical medicine (that is identified as P-gp substrate). Cytochrome P450, or CYPs, is a group of metabolic enzymes. Enzymes connected to the biotransformation of xenobiotics [26]. Substances that prevented five classifications increased the cytotoxicity of CYPs (CYP3A4, CYP1A2, CYP2C9, CYP2C19, and CYP2D6), increasing plasma concentrations and enhancing bioavailability. Skin Kp permeability is generally used to describe quantitative chemical penetration through the epidermis or outermost layer of skin.

Table 4. Pharmacokinetic feasibility of all sixteen organosulphur compounds.

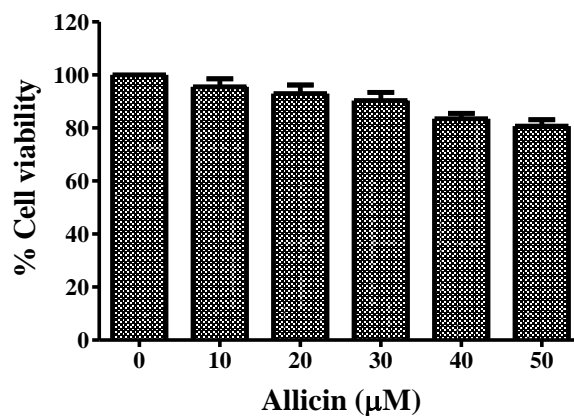
S.No.	Ligand	GI absorption	BBB permeant	CYP1A2 inhibitor	CYP219 inhibitor	LOG Kp
1.	Allicin	High	Yes	No	No	-6.36 cm/s
2.	2-vinyl-4H-1,3- dithiine	High	Yes	No	No	-5.55 cm/s
3.	Allylmethylsulphide	High	Yes	No	No	-5.76 cm/s
4.	DADS	High	Yes	No	No	-5.63 cm/s
5.	DAS	High	Yes	No	No	-5.46 cm/s
6.	diallyl trisulphide	High	Yes	No	No	-5.51 cm/s
7.	Z-ajoene	High	No	No	No	-6.52 cm/s
8.	Methylpropyl disulfide	High	Yes	No	No	-5.77 cm/s
9.	Isopropyl propyl disulfide	High	Yes	No	No	-5.37 cm/s
10.	Dimethyl trisulphide	High	Yes	No	No	-6.11 cm/s
11.	Dipropyl disulfide	High	Yes	No	No	-5.30 cm/s
12.	2-propenyl propyl disulfide	High	Yes	No	No	-5.47 cm/s
13.	Dimethyl disulfide	High	Yes	No	No	-5.62 cm/s
14.	Cis-propenyl propyltrisulphide	High	Yes	No	No	-5.30 cm/s
15.	3-mercaptpropionicacid	High	No	No	No	-6.64 cm/s
16.	Bis(1- methylethyl)disulfidede	High	Yes	No	No	-5.43 cm/s
17.	Paclitaxel	Low	No	No	No	-8.91 cm/s

3.4. Allicin reduced cell viability of ovarian cancer SKOV-3 cells.

In this study, ovarian cancer SKOV3 cells were treated with various concentrations of allicin for 24 h. The results showed a clear cell viability inhibition of ovarian cancer cells in a dose-dependent manner (figure 3A). The IC₅₀ value of allicin on SKOV3 ovarian cancer cells was reported to be 26.43 μM at 24 h. Thus, these findings strongly suggested that allicin treatment exhibited decreased cancer cell growth in dose-dependent order, while mild cytotoxicity was reported only at higher doses of allicin on normal cell lines (Figure 3B).



(a)



(b)

Figure 3. Cell viability results of (a) allicin-treated SKOV3 ovarian cancer cells; (b) normal Hek-293 cells after 24 h and 48 h of treatment. The mean and standard error mean of three independent tests completed in triplicate presented here (* $p < 0.01$, ** $p < 0.001$ indicate a significant difference from the control).

3.5. Allicin-mediated downregulation of PKP-1 level in SKOV3 cells.

We have employed RT-PCR techniques to elucidate the efficacy of allicin against PKP-1 targets involved in ovarian carcinogenesis. These results displayed a significant reduction in PKP-1 at mRNA expression levels in allicin-treated SKOV3 ovarian cancer cells (Figure 4).

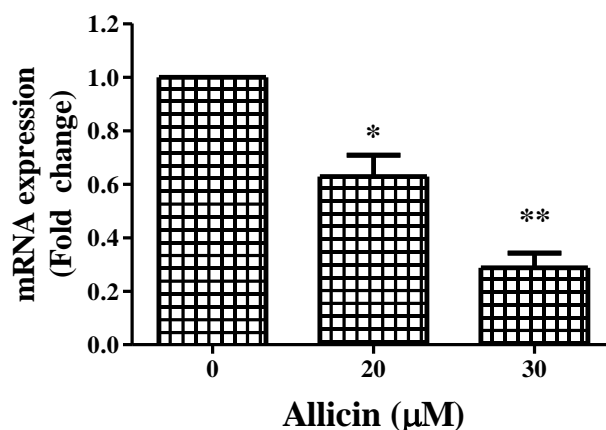


Figure 4. Allicin mediated decreased expression of PKP-1 in ovarian cancer SKOV3 cell line. The mean and standard error mean of three independent tests completed in triplicate presented here (* $p < 0.01$, ** $p < 0.001$ indicate a significant difference from the control).

PKP1 overexpression has been extensively studied and reported to be crucially associated with progression (metastasis) in ovarian cancer, either by positively regulating cancer cell growth or via inactivating numerous tumor suppressors. In this research, we have utilized in-silico studies to elucidate potential organosulphur compounds against PKP1 to explore potent drug candidates for the management of this crucial malignancy. Organosulphur compounds have revealed potent anti-inflammatory and anticancerous efficacies via inducing apoptosis in numerous carcinomas [27]. CB-dock was utilized for the docking study of selected organosulphur compounds against PKP1. Organosulphur compounds have gained wider attention by displaying significant apoptosis-inducing efficacy in several cancer cell lines, such as ID8-P1. Therefore, this research study is mainly targeted to elucidate the inhibitory efficacy of selected organosulphur compounds against PKP1 in ID8-P1 [28]. Developing potent anticancerous lead or drug candidates is a very time-consuming task; thus, a systematic (and planned) protocol is mandatory for rational drug design to overcome the associated

disadvantages (limitations) of chemotherapeutic approaches. Minimal studies have been reported in favor of the PKP1 inhibitory potential of these selected organosulphur compounds in ovarian cancer. This has motivated us to target this oncogene with potent organosulfur compounds to identify a better therapeutic approach to managing ovarian cancer. Thus, in this study, we have selected sixteen organosulphur compounds to establish their PKP1 inhibitory potential in ovarian cancer using various *in silico* and *in vitro* techniques.

In silico research conducted in our studies has strongly displayed the inhibitory potential of most of the organosulphur compounds against PKP-1. However, allicin emerged as the best PKP-1 inhibitor amongst all potent sixteen compounds via exhibiting maximum *vina* score in comparison to standard drugs. Hence, we have selected allicin for *in vitro* studies to further validate its inhibitory potential against PKP-1 in ovarian cancer cells. We have performed *in vitro* assays, including MTT and RT-PCR techniques, to validate the growth-inhibiting potential of allicin against ovarian cancer via targeting PKP-1, which has not yet been elucidated [28]. Numerous studies have reported the aberrant expression of PKP-1 oncogene in various human cancers [29-31]. Recent studies also reported the anti-ovarian cancer role of various natural compounds by targeting specific genes in a similar way [32-34]. This demands an urgent need to elucidate potential PKP-1 inhibitors or activators. Thus, we have investigated the alterations in the mRNA level of PKP-1 mRNA expression levels in allicin-treated SKOV3 ovarian cancer cells. Our findings clearly demonstrated that allicin treatment significantly down-regulated the PKP-1 expression levels in SKOV3 ovarian cancer cells. Hence, it can be concluded that allicin could be a strong lead candidate for elucidating a potent drug for the efficient management of ovarian cancer.

4. Conclusion

After examining the *in vitro* and *in silico* data, we concluded that out of all the other chosen organosulfur compounds, allicin is an effective compound that is lead-like, druggable, has good bioavailability, and has medicinal chemistry. Additionally, it demonstrated a consistent and strong binding affinity, as well as an energy landscape with target PKP1, with few energy frustrations and clashes. Despite the encouraging results, additional clinical and pre-clinical investigations are required to fully understand the mechanism linked to the potential of allicin to suppress PKP1 in ovarian cancer. The necessity for the ongoing investigation of natural products for oncology uses is highlighted by the fact that organosulfur compounds provide an additional pathway to current treatments, improving patient health while reducing treatment-related adverse effects.

Author Contributions

Conceptualization, F.K., M.V., and V.J.U.; methodology, A.S.; software, M.V.; validation, V.J.U, G.J., and P.P.; formal analysis, F.K.; investigation, M.V.; resources, A.S.; data curation, V.J.U.; writing—original draft preparation, F.K., M.V., and V.J.U.; writing—review and editing, A.S., G.J., and P.P.; visualization, G.J. and P.P.; supervision, V.J.U.; project administration, F.K. All authors have read and agreed to the published version of the manuscript.

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Data Availability Statement

Data supporting the findings of this study are available upon reasonable request from the corresponding author.

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Conflicts of Interest

The authors declare no conflict of interest.

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