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An N-Glycan-Specific Lectin from *Xanthosoma violaceum* Restrains Growth and Migration of Androgen-Independent Prostate Cancer

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ABSTRACT

Prostate cancer is a major global health concern, particularly in its androgen-independent and treatment-resistant forms. Aberrant glycosylation of cell-surface receptors is a hallmark of prostate cancer progression, making glycan-targeting biomolecules attractive candidates for modulating cancer-associated molecular risks. Plant lectins, owing to their carbohydrate-binding specificity, have emerged as promising bioactive agents with selective anticancer potential. The present study evaluated the in vitro antiproliferative and anti-migratory effects of a complex N-glycan-specific lectin isolated from the tuber of *Xanthosoma violaceum* (XVL) on androgen-independent human prostate cancer cell lines PC-3 and DU-145, and investigated its influence on EGFR-associated signaling pathways. Cytotoxicity and antiproliferative activity were assessed using the MTT assay, while long-term survival and migratory behavior were examined using clonogenic and wound-healing assays, respectively. Western blot analysis was performed to evaluate the modulation of EGFR and downstream AKT signaling proteins, and cytotoxic selectivity was assessed using normal fibroblast cells. XVL treatment resulted in a significant, dose-dependent reduction in viability of PC-3 and DU-145 cells while exhibiting minimal cytotoxicity toward normal fibroblasts. XVL also markedly suppressed clonogenic survival and inhibited cell migration, accompanied by reduced EGFR expression, EGFR phosphorylation, and downstream AKT activation. These findings demonstrate that XVL selectively suppresses proliferation and migration of androgen-independent prostate cancer cells through inhibition of EGFR/AKT signaling pathways, highlighting its relevance as a glycan-targeting biomolecule for modulating cancer-associated molecular risks.

Keywords: *Xanthosoma violaceum*; plant lectin; prostate cancer; glycosylation; EGFR signaling

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INTRODUCTION

Prostate cancer is one of the most frequently diagnosed malignancies among men worldwide and remains a leading cause of cancer-related morbidity and mortality[1]. Although early-stage prostate cancer can often be managed effectively, progression to androgen-independent and treatment-resistant disease presents a major clinical challenge[1]. Current therapeutic strategies, including chemotherapy and targeted therapies, are frequently associated with systemic toxicity, resistance development, and limited long-term efficacy, highlighting the need for alternative bioactive agents with improved selectivity and safety profiles[2].

Aberrant glycosylation is a recognized hallmark of cancer and plays a critical role in tumour initiation, progression, metastasis, and therapeutic resistance[3]. Cancer cells often exhibit altered expression of cell-surface glycoproteins and glycolipids, leading to changes in receptor stability, ligand binding, and intracellular signaling[4]. Among these receptors, epidermal growth factor receptor (EGFR) is heavily glycosylated and is frequently overexpressed or dysregulated in advanced prostate cancer, where it contributes to enhanced proliferation, survival, migration, and resistance to therapy through activation of downstream signaling pathways such as PI3K/AKT[5],[6].

Plant lectins are carbohydrate-binding proteins of non-immune origin that recognize specific glycan structures without altering their covalent configuration[7]. Due to their high affinity for distinct carbohydrate moieties, lectins have gained attention as biologically active molecules capable of selectively targeting aberrant glycosylation patterns on cancer cells[8]. Numerous studies have demonstrated that lectins can exert antiproliferative, pro-apoptotic, and anti-migratory effects in cancer cells by interacting with surface glycoproteins and modulating key signaling pathways[9],[10]. Importantly, lectin-based mechanisms differ from classical kinase inhibition, offering potential advantages in overcoming drug resistance associated with conventional targeted therapies.

Lectins derived from underground storage organs such as bulbs and tubers are of particular interest due to their abundance, structural stability, and unique carbohydrate specificity[11]. *Xanthosoma violaceum* (family Araceae) is a tuberous plant traditionally cultivated in India for culinary and medicinal purposes. A complex N-glycan-specific lectin isolated from *X. violaceum* tubers (XVL) has previously been reported to exhibit selective anticancer activity in different cancer cell models, while sparing normal cells[12]–[14]. However, the effects of XVL on androgen-independent prostate cancer cells and its potential influence on EGFR-associated signaling pathways remain insufficiently explored.

Given the growing interest in glycan-targeting biomolecules as modulators of cancer-associated molecular risks, the present study investigates the in vitro antiproliferative, anti-migratory, and molecular effects of XVL in androgen-independent human prostate cancer cell lines PC-3 and DU-

145. By examining cell viability, migration, clonogenic survival, and EGFR-mediated signaling, this study aims to provide insights into the potential relevance of XVL as a bioactive lectin with implications for prostate cancer management.

MATERIALS AND METHODS

Source of Lectin (XVL)

Xanthosoma violaceum lectin (XVL), isolated from the tubers of *Xanthosoma violaceum*, was previously purified and characterized using conventional analytical techniques and subsequently evaluated for its potential cell growth–inhibitory and apoptosis-inducing activities[12].

Cell Culture and Maintenance

Human androgen-independent prostate cancer cell lines PC-3 and DU-145 were obtained from the National Centre for Cell Science (NCCS), Pune, India. Cells were maintained in RPMI-1640 medium (HiMedia, India) supplemented with 10% fetal bovine serum (FBS), penicillin (100 U/mL), and streptomycin (100 µg/mL) at 37 °C in a humidified atmosphere containing 5% CO_2. Cells were routinely monitored for morphology and confluency, subcultured using standard aseptic techniques, and only cells in the exponential growth phase were used for experiments.

MTT Assay for Cell Viability

The cytotoxic and antiproliferative effects of XVL were evaluated using the MTT assay[14]. PC-3 and DU-145 prostate cancer cells and NIH 3T3 normal fibroblast cells were seeded into 96-well plates at a density of 1 × 10^4 cells/well and allowed to adhere overnight at 37 °C in a humidified atmosphere containing 5% CO_2. After attachment, PC-3 and DU-145 cells were treated with XVL at concentrations of 0.5–5.0 µg/mL, while NIH 3T3 cells were treated with 0.5–10 µg/mL. Untreated cells served as controls. All treatments were carried out for 48 h. Following treatment, the medium was replaced with fresh medium containing MTT reagent (0.5 mg/mL) and incubated for 4 h. The resulting formazan crystals were dissolved in dimethyl sulfoxide (DMSO), and absorbance was measured at 570 nm. Cell viability was calculated using the following formula:

Cell viability (%) = (Atreated / Acontrol) × 100

where Atreated and Acontrol represent the absorbance values of treated and untreated control cells, respectively. The IC_{50} value was determined from the dose–response curve. Experiments were performed in triplicate, and results were expressed as mean ± SD.

Wound-Healing Assay for Cell Migration

The effect of XVL on cell migration was assessed using an in vitro wound-healing assay[15]. PC-3 cells were seeded into 6-well plates at a density of 5 × 10^5 cells/well and grown to near confluence. A uniform scratch was created using a sterile pipette tip, and detached cells were removed by washing with phosphate-buffered saline (PBS).

Cells were then treated with XVL, while control wells received culture medium alone. Images of the wound area were captured at 0, 12, and 24 h using an inverted phase-contrast microscope. Wound closure was quantified using ImageJ software and calculated using the following formula:

Wound closure (%) = [(W0 − Wt.) / W0] × 100

where W0 represents the wound width at 0 h and Wt represents the wound width at the indicated time point.

Clonogenic Assay for Long-Term Cell Survival

The long-term reproductive survival of prostate cancer cells following XVL treatment was evaluated using a clonogenic assay[16]. PC-3 cells were seeded at a low density of 500 cells/well in 6-well plates and allowed to adhere overnight. Cells were then treated with XVL for a defined exposure period, after which the treatment medium was replaced with fresh drug-free medium. Cells were incubated for 10–14 days to allow colony formation. Colonies were fixed, stained, and counted manually. Colonies containing ≥50 cells were considered viable. Clonogenic survival was calculated using the following formula:

Clonogenic survival (%) = ($N_{treated}$ / $N_{control}$) × 100

Where $N_{treated}$ and $N_{control}$ represent the number of colonies formed in treated and control cells, respectively. All experiments were performed in triplicate.

Western Blot Analysis

Western blotting was performed to evaluate the effect of XVL on EGFR-associated signaling pathways[17]. Androgen-independent prostate cancer cell lines PC-3 and DU-145 were seeded in 6-well plates at a density of 2 × 10^5 cells/well and allowed to adhere overnight. Cells were treated with XVL at concentrations of 2.5 and 5.0 µg/mL for 48 h, while untreated cells served as controls.

Following treatment, cells were washed with ice-cold phosphate-buffered saline (PBS) and lysed using RIPA buffer supplemented with protease and phosphatase inhibitor cocktails. Total protein concentration was determined using the bicinchoninic acid (BCA) assay. Equal amounts of protein (25–40 µg) were resolved on 10% SDS–polyacrylamide gels and transferred onto polyvinylidene difluoride (PVDF)

membranes.

Membranes were blocked with 5% bovine serum albumin (BSA) in Tris-buffered saline containing 0.1% Tween-20 (TBST) and incubated overnight at 4 °C with primary antibodies against EGFR, phosphorylated EGFR (pEGFR), phosphorylated AKT (pAKT), and GAPDH (1:1000) (Cell Signaling Technology, USA). After washing, membranes were incubated with appropriate horseradish peroxidase (HRP)-conjugated secondary antibodies (1:3000).

Immunoreactive bands were visualized using an enhanced chemiluminescence (ECL) detection system and imaged using a gel documentation system. Band intensities were quantified using ImageJ software. Phosphorylated protein levels were normalized to their corresponding total protein levels, and all protein expression data were subsequently normalized to GAPDH.

RESULTS

Antiproliferative Effect of XVL Assessed by MTT Assay

The cytotoxic and antiproliferative effects of the *Xanthosoma violaceum* lectin (XVL) were evaluated in androgen-independent prostate cancer cell lines (PC-3 and DU-145) and compared with normal NIH 3T3 fibroblast cells using the MTT assay.

As shown in Figure 1a, treatment of NIH 3T3 cells with XVL at concentrations ranging from 0.5 to 10 µg/mL for 48 h did not result in any significant reduction in cell viability. More than 90% cell viability was retained even at the highest concentration tested, indicating that XVL is largely non-toxic to normal cells under the experimental conditions.

In contrast, XVL treatment caused a marked and concentration-dependent reduction in cell viability in both prostate cancer cell lines. In PC-3 cells (Figure 1b), XVL significantly inhibited cell proliferation beginning at 0.5 µg/mL, with a progressive decrease in viability observed at higher concentrations. Approximately 50% inhibition of cell viability was observed at ~2.5 µg/mL, indicating the IC_{50} value for PC-3 cells. At 5.0 µg/mL, cell viability was reduced to nearly 25%, demonstrating strong antiproliferative activity.

Similarly, DU-145 cells (Figure 1c) exhibited significant sensitivity to XVL treatment in a dose-dependent manner. A clear reduction in cell viability was evident from 0.5 µg/mL onward, with an IC_{50} value of approximately 2.5 µg/mL. At the highest concentration tested (5.0 µg/mL), cell viability decreased to ~20–25%, comparable to the response observed in PC-3 cells.

Overall, the MTT assay results demonstrate that XVL selectively inhibits the proliferation of androgen-independent prostate cancer cells while sparing normal fibroblast cells, highlighting its selective anticancer potential.

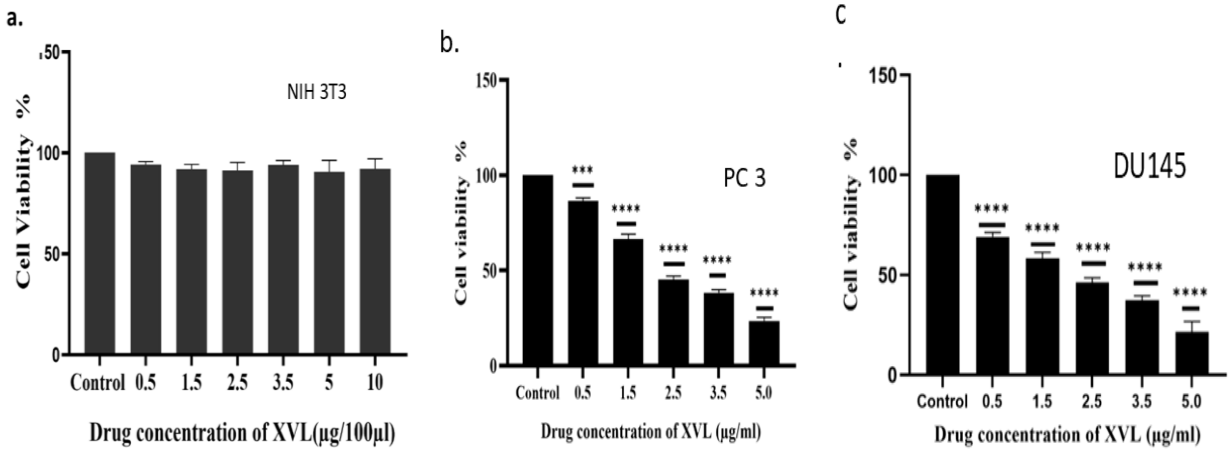

Figure 1. Effect of *Xanthosoma violaceum* lectin (XVL) on cell viability assessed by MTT assay. (a) Effect of XVL on normal NIH 3T3 fibroblast cells treated with increasing concentrations of XVL (0.5–10 µg/mL) for 48 h. (b) Dose-dependent inhibition of cell viability in PC-3 prostate cancer cells following XVL treatment (0.5–5.0 µg/mL) for 48 h. (c) Dose-dependent inhibition of cell viability in DU-145 prostate cancer cells following XVL treatment (0.5–5.0 µg/mL) for 48 h. Cell viability is expressed as a percentage relative to untreated control cells (100%). Data represent mean ± SD of three independent experiments performed in triplicate.

Effect of XVL on Cell Migration Assessed by Scratch Assay

The anti-migratory effect of *Xanthosoma violaceum* lectin (XVL) on androgen-independent prostate cancer cells was evaluated using an *in vitro* scratch (wound-healing) assay in PC-3 cells. As shown in Figure 2, untreated control cells exhibited rapid migration into the wound area, resulting in substantial wound closure within 24 h. In contrast, XVL-treated (IC_{50} 2.5 µg/mL) cells displayed a marked delay in wound closure, indicating significant inhibition of cell migration.

At 0 h, no significant difference in wound width was observed between control and XVL-treated groups, confirming uniform scratch generation. After 12 h of incubation, control cells showed pronounced migration, whereas XVL-treated cells exhibited significantly reduced wound closure ($p < 0.001$). At 24 h, control cells achieved near-complete wound closure, while XVL-treated cells retained a substantial open wound area, demonstrating strong suppression of migratory capacity ($p < 0.0001$).

Quantitative analysis further confirmed that XVL significantly inhibited wound closure in a time-dependent manner compared with untreated controls. These results indicate that XVL effectively suppresses the migratory behavior of PC-3 prostate cancer cells, suggesting its potential role in limiting cancer cell motility and metastatic progression.

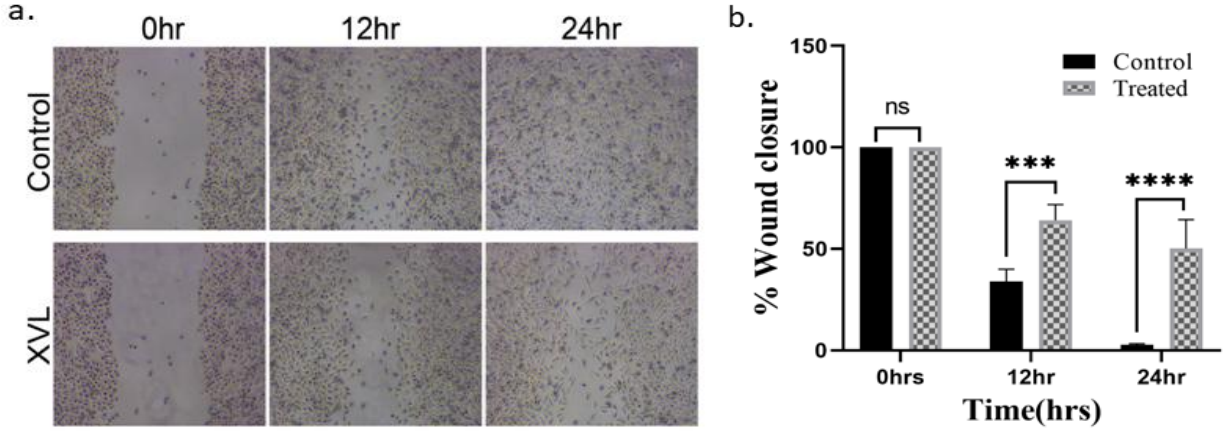

Figure 2. Effect of *Xanthosoma violaceum* lectin (XVL) on migration of PC-3 prostate cancer cells assessed by scratch assay.

(a) Representative phase-contrast micrographs showing wound closure in control and XVL-treated PC-3 cells at 0, 12, and 24 h following scratch generation. (b) Quantitative analysis of percentage wound closure at indicated time points. Data are expressed as mean ± SD of three independent experiments performed in triplicate. Statistical significance compared with control is indicated as ns (not significant), ***$p < 0.001$, and ****$p < 0.0001$.

Effect of XVL on clonogenic survival of PC-3 cells

To evaluate the effect of XVL on the long-term reproductive viability of prostate cancer cells, a clonogenic assay was performed using PC-3 cells. As shown in Figure 3, untreated control cells formed a large number of well-defined colonies, indicating high clonogenic potential. In contrast, XVL treatment resulted in a marked, dose-dependent suppression of colony formation.

Treatment with XVL at 2.5 µg/mL (IC_{50}) significantly reduced the number of colonies formed compared with control cells, indicating impaired clonogenic survival. A more pronounced reduction was observed at 5.0 µg/mL, where only a minimal number of colonies were detected. Quantitative analysis revealed a significant decrease in the percentage of colony numbers at both concentrations, with near-complete suppression of colony formation at the higher dose.

These results demonstrate that XVL effectively inhibits the long-term proliferative and self-renewal capacity of androgen-independent PC-3 prostate cancer cells, supporting its potent antiproliferative activity observed in short-term viability assays.

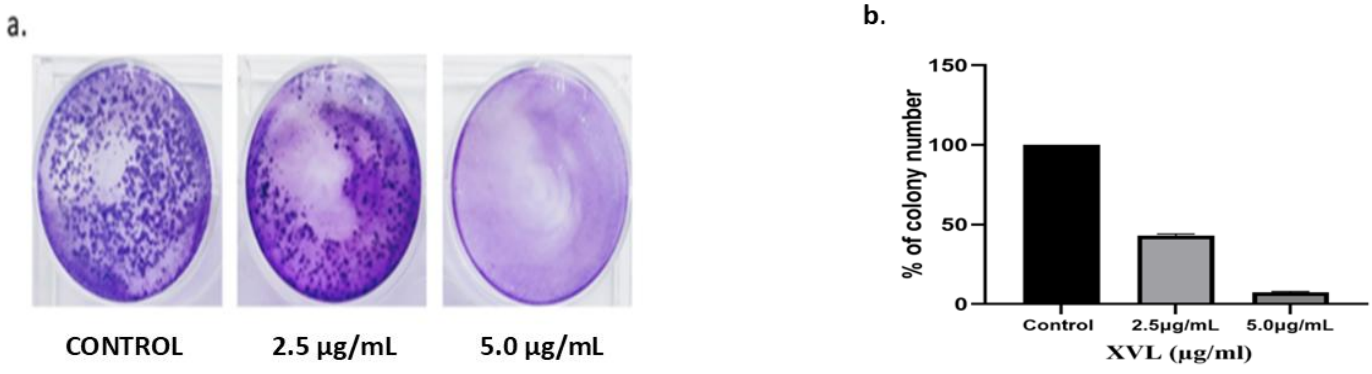

Figure 3. Effect of XVL on clonogenic survival of PC-3 prostate cancer cells.
(a) Representative images showing colony formation in PC-3 cells treated with XVL (2.5 and 5.0 µg/mL) compared with untreated control cells. (b) Quantitative analysis of clonogenic survival expressed as percentage of colony number relative to control (100%). XVL treatment resulted in a significant, dose-dependent reduction in colony formation. Data are presented as mean ± SD of three independent experiments.

Effect of XVL on EGFR and AKT Signaling Pathways

Western blot analysis was performed to evaluate the effect of XVL on EGFR expression and downstream signaling in androgen-independent prostate cancer cells. Treatment of PC-3 cells with XVL at 2.5 and 5.0 µg/mL for 48 h resulted in a dose-dependent reduction in total EGFR protein levels compared to untreated controls. A corresponding decrease in EGFR phosphorylation (pEGFR) was observed, indicating suppression of receptor activation.

In DU-145 cells, XVL treatment led to a marked reduction in pEGFR levels, suggesting effective inhibition of EGFR signaling in this cell line as well. Consistent GAPDH expression across all samples confirmed equal protein loading.

In addition to EGFR modulation, XVL treatment significantly reduced AKT phosphorylation (pAKT) in PC-3 cells, indicating attenuation of the downstream PI3K/AKT survival signaling pathway. The reduction in pAKT levels closely paralleled the decrease in pEGFR, supporting the involvement of EGFR-mediated signaling in XVL-induced effects.

Overall, these findings demonstrate that XVL suppresses EGFR activation and downstream AKT signaling in androgen-independent prostate cancer cells, supporting its role as a glycan-targeting lectin capable of modulating key molecular pathways associated with prostate cancer progression.

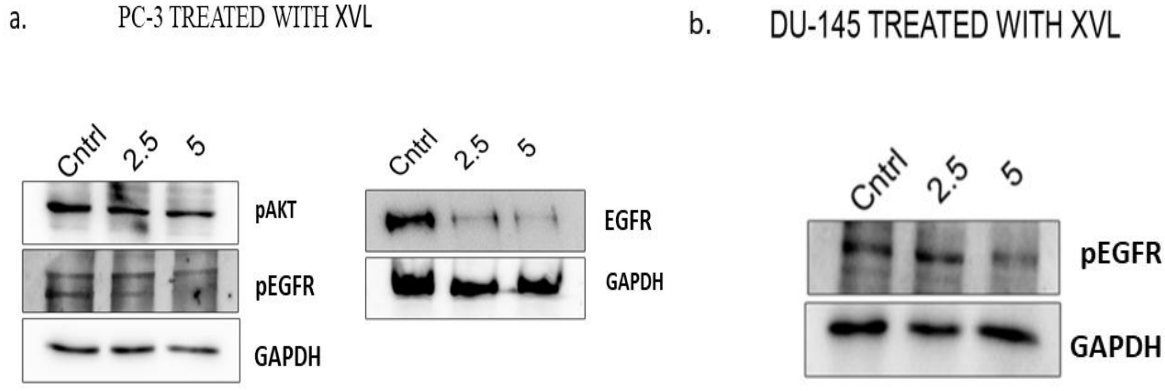

Figure 4. Effect of *Xanthosoma violaceum* lectin (XVL) on EGFR-associated signaling pathways in androgen-independent prostate cancer cells.
(a) Representative Western blot images showing the effect of XVL treatment on phosphorylated AKT (pAKT), phosphorylated EGFR (pEGFR), and total EGFR expression in PC-3 cells treated with XVL at 2.5 and 5.0 µg/mL for 48 h.(b) Representative Western blot images showing the effect of XVL on EGFR phosphorylation (pEGFR) in DU-145 cells treated with XVL at 2.5 and 5.0 µg/mL for 48 h. GAPDH was used as a loading control in all experiments. XVL treatment resulted in a dose-dependent reduction in EGFR expression and phosphorylation, accompanied by decreased AKT phosphorylation, indicating suppression of EGFR/AKT signaling. Blots shown are representative of three independent experiments.

DISCUSSION

The present study demonstrates that the complex N-glycan-specific lectin isolated from *Xanthosoma violaceum* (XVL) exerts selective antiproliferative and anti-migratory effects in androgen-independent prostate cancer cell lines PC-3 and DU-145, while exhibiting minimal cytotoxicity toward normal fibroblast cells. These findings support the growing concept that aberrant glycosylation represents a critical molecular vulnerability in advanced prostate cancer and can be selectively targeted using glycan-binding biomolecules.

Aberrant glycosylation is a well-recognized hallmark of cancer and plays a pivotal role in tumor initiation, progression, metastasis, and therapeutic resistance by modulating receptor stability, ligand binding, and intracellular signaling pathways[3,4,18,19]. In prostate cancer, alterations in N-glycan branching and increased expression of complex and high-mannose glycans have been associated with aggressive phenotypes and androgen-independent growth[18,19]. These cancer-associated glycan signatures provide a biochemical basis for the selective recognition of malignant cells by lectins.

In the present study, XVL induced a significant, dose-dependent reduction in cell viability in both PC-3 and DU-145 cells, with IC_{50} values of approximately 2.5 µg/mL, while maintaining high viability in NIH 3T3 normal fibroblast cells. This selective cytotoxicity is consistent with previous reports demonstrating that plant lectins preferentially bind aberrantly glycosylated receptors overexpressed on cancer cells while sparing normal cells with comparatively lower glycan density or distinct glycan architecture[9,12,20]. Such selectivity is particularly relevant in prostate cancer therapy, where

systemic toxicity and resistance limit the long-term efficacy of conventional chemotherapeutic and targeted agents[2].

Beyond short-term cytotoxic effects, XVL markedly suppressed clonogenic survival of PC-3 cells, indicating impairment of long-term proliferative capacity and self-renewal potential. The clonogenic assay is widely regarded as a stringent indicator of tumorigenic potential and therapeutic response, as it reflects the ability of a single cell to undergo sustained proliferation and form a colony[16]. The pronounced reduction in colony formation observed following XVL treatment suggests that the lectin interferes with signaling pathways essential for reproductive cell survival rather than merely inducing transient growth inhibition.

Cell migration is a key determinant of invasion and metastatic dissemination, particularly in advanced and androgen-independent prostate cancer[1]. In the wound-healing assay, XVL significantly inhibited PC-3 cell migration in a time-dependent manner. Importantly, the concentrations used in migration assays were below the IC_{50} values obtained from the MTT assay, indicating that the observed anti-migratory effect was not a secondary consequence of cytotoxicity. Similar inhibition of cancer cell motility by plant lectins has been reported previously and has been attributed to altered signaling through glycosylated receptors involved in cytoskeletal remodeling and cell–matrix interactions[12].

Mechanistically, the present study provides evidence that XVL modulates EGFR-associated signaling pathways. EGFR is a heavily glycosylated receptor tyrosine kinase that is frequently overexpressed or dysregulated in androgen-independent prostate cancer and is associated with enhanced proliferation, migration, and resistance to therapy[5]. Western blot analysis revealed that XVL treatment reduced both total EGFR expression and EGFR phosphorylation, accompanied by a concomitant decrease in AKT phosphorylation. The PI3K/AKT pathway is a major downstream effector of EGFR signaling and plays a central role in prostate cancer cell survival and metastatic progression[6],[22].

Unlike classical EGFR inhibitors that target the intracellular kinase domain, lectins interact with extracellular glycan moieties on the receptor, potentially affecting receptor conformation, clustering, dimerization, and ligand binding[7],[10],[13]. This glycan-dependent mechanism of action may offer advantages in overcoming resistance associated with kinase-domain mutations or compensatory activation of parallel signaling pathways that frequently limit the efficacy of conventional targeted therapies[21]. The observed suppression of EGFR/AKT signaling by XVL therefore supports the concept that targeting receptor glycosylation represents a complementary and mechanistically distinct strategy for modulating oncogenic signaling.

From a broader perspective, these findings extend beyond cancer biology and have implications for chemical and molecular health risk research. Naturally derived lectins such as XVL represent bioactive agents capable of modulating disease-associated molecular pathways through non-genotoxic mechanisms, potentially offering improved selectivity and safety profiles[10]. The ability of XVL to selectively target aberrant glycosylation highlights its relevance as a molecular risk-modifying biomolecule in prostate cancer.

CONCLUSION

In conclusion, the present study demonstrates that the complex N-glycan-specific lectin isolated from *Xanthosoma violaceum* selectively inhibits proliferation, clonogenic survival, and migration of androgen-independent prostate cancer cells PC-3 and DU-145, while sparing normal fibroblast cells. The anticancer effects of XVL are associated with suppression of EGFR expression and phosphorylation, accompanied by inhibition of downstream AKT signaling.

These findings underscore the pharmaceutical relevance of targeting aberrant glycosylation as a strategy for modulating cancer-associated molecular risks and highlight plant lectins as promising bioactive agents with mechanisms of action distinct from conventional kinase inhibitors. The glycan-specific activity of XVL may offer advantages in selectivity and reduced toxicity, particularly in treatment-resistant forms of prostate cancer.

While the present study provides strong in vitro evidence supporting the anticancer potential of XVL, further investigations are warranted to elucidate its precise glycan-binding interactions, evaluate its effects on additional signaling pathways, and assess its efficacy and safety in in vivo prostate cancer models. Overall, this work supports the continued exploration of lectin-based biomolecules in prostate cancer research and their potential relevance in chemical and molecular health risk assessment.

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ETHICAL APPROVAL

This study did not involve human participants or animals. All experiments were performed using established human cancer cell lines obtained from authorized repositories.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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