Artificial Intelligence-Driven Insights into the Antioxidant and Anticancer Properties of Onion (Allium cepa) and Tomato (Solanum lycopersicum) in Prostate Cancer Prevention and Management: A Contemporary Review

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Research Article

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Abstract

Prostate cancer (PCa) is the second most common cancer in men and the fifth leading cause of cancer death in men worldwide, with an estimated 1.4 million new cases and 375,000 deaths per year. The main limitations of current therapy involve the emergence of castration-resistant prostate cancer (CRPC), multidrug resistance and dose-limiting toxicities. The oxidative stress-inflammatory axis is a critical pathway in prostate carcinogenesis in which DNA damage by Reactive Oxygen Species (ROS), activation of NF-κB and dysregulation of Androgen Receptor (AR) signaling play roles in initiating, advancing, and metastasizing prostate cancer. Although dietary phytochemicals have been identified as chemopreventive agents, translation of bioactive compounds from bench to bedside is inhibited by the limited systematic characterization of molecular targets, suboptimal bioavailability and absence of predictive frameworks for compound prioritization. This modern review aims to fill these gaps by summarising the latest evidence of the antioxidant and anticancer effects of phytoconstituents from Allium cepa and Solanum lycopersicum and to focus on new computational approaches based on artificial intelligence (AI) that are used to systematically prioritize and mechanistically deconvolute bioactive compounds by means of molecular docking, network pharmacology, machine learning target prediction, and deep learning metabolite profiling. The review focuses on the three interrelated pillars: (I) modulation of oxidative stress-inflammation-cancer axis, (II) phytochemical polypharmacology and molecular target networks, and (III) predictive modeling and AI in drug discovery. The results show that quercetin from onion activates the Nrf2/ARE pathway by electrophilically modifying Keap1 and lycopene from tomato quences singlet oxygen by its conjugated polyene chain. Using AI molecular docking, quercetin was identified as a high-affinity binder of the androgen receptor, surpassing enzalutamide, the reference drug. The cross validation of the machine learning models for prediction of antioxidant capacity from metabolomic profiles. However, clinical evidence remains equivocal, with meta-analyses showing no significant effect of lycopene supplementation on prostate-specific antigen levels. This review suggests a translational pathway for the application of AI in prostate cancer chemoprevention and management that focuses on three key challenges: bioavailability optimization, biomarker refinement, and natural product-specific AI model development.

Introduction

Prostate cancer (PCa) is the second most commonly diagnosed type of cancer in men worldwide and the fifth leading cause of cancer death, with an estimated 1.4 million new cases and 375,000 deaths occurring every year (Leslie et al., 2024; Kania et al., 2025; Siddiqui et al., 2025). Therapeutic options, such as androgen deprivation therapy (ADT), chemotherapy (docetaxel, cabazitaxel), and radiotherapy, are currently available but suffer from castration-resistant prostate cancer (CRPC), multidrug resistance, and dose-limiting toxicities that significantly affect patient quality of life (Powers et al., 2020; Mia et al., 2023; Rahman et al., 2023; Kulasegaran and Oliveira, 2024). The oxidative stress-inflammatory axis is a crucial pathway in the initiation, progression and metastasis of prostate cancer, involving DNA damage, activation of NF-κB and dysregulation of androgen receptor (AR) signaling (Jeong et al., 2022; Li et al., 2023; Naiki-Ito et al., 2025). Although the beneficial chemopreventive effects of dietary phytochemicals

are acknowledged, the complex molecular targets, suboptimal bioavailability, and absence of predictive frameworks for compound prioritization prevent the translation of bioactive compounds from the bench to bedside (Kim et al., 2025; Salehi et al., 2019; Fontana et al., 2020).

Allium cepa (onion) and Solanum lycopersicum (tomato) are common food staples that are rich in organosulfur compounds (OSCs) and flavonoids (quercetin, kaempferol) and carotenoids (lycopene, β-carotene) with proven antioxidant and antiproliferative properties, but there are gaps in knowledge. Second, the molecular mechanisms of the anti-prostate cancer activity of phytochemicals from onions and tomatoes are not fully understood, especially in relation to their actions on AR signaling, the PI3K/Akt/mTOR pathway and the apoptotic cascade (Alobid, 2026; Hao et al., 2022; Moran et al., 2022). Second, traditional laboratory experiments screening phytochemicals are time-consuming, expensive, and do not account for the polypharmacological nature of natural products (Chihomvu et al., 2024; Chakraborty et al., 2022; Iwar et al., 2024). Third, the integration of artificial intelligence (AI) and machine learning (ML) approaches on systematic mining, target prediction, and elucidation of the mechanism of action of Allium and Solanaceae-derived bioactives in prostate cancer settings is yet still significantly under-explored. In addition, the clinical effectiveness of lycopene and quercetin supplementation in PCa prevention is uncertain, with some meta-analyses showing no difference in prostate-specific antigen (PSA) levels, and a need for advanced biomarker strategies and personalised intervention frameworks (Nkwe et al., 2021; Sharifi-Zahabi et al., 2022; Paur et al., 2017).

This study aims to critically review and consolidate the latest scientific evidence on the antioxidant and anticancer effects of phytochemicals in A. cepa and S. lycopersicum, and to discuss the potential of using artificial intelligence and computational techniques to systematically optimize their application in prostate cancer prevention and management.

This study aims to systematically characterize the antioxidant phytochemical profile of Allium cepa and Solanum lycopersicum; to critically appraise the mechanism underlying the modulation of oxidative stress in prostate cancer pathogenesis by phytochemicals; to assess the current applications, limitations, and the translation potential of artificial intelligence and machine learning frameworks for the screening, prioritization, and mechanism elucidation of phytochemicals from A. cepa and S. lycopersicum for prostate cancer drug discovery.

Significance of This Review

This review offers one of the first comprehensive synthesis that links together experimental phytochemistry, molecular oncology and AI-driven drug discovery in prostate cancer settings for Allium cepa and Solanum lycopersicum. It provides clinically relevant information about dietary intervention strategies and nutraceutical adjuvant therapies that could improve treatment outcomes and minimize chemotherapy-related toxicities. It offers a proven tool for natural product screening in the pharmaceutical research and development labs, potentially streamlining preclinical timelines and accelerating the discovery of lead compounds.It provides a tool for natural product screening that can

help shorten preclinical development timelines and discover lead compounds, which is beneficial for pharmaceutical scientists and computational biologists. It could help public health policy makers develop population dietary guidelines focusing on functional foods for prostate cancer prevention, especially in resource limited countries where pharmaceutical interventions are not available (Fekete et al., 2025; Cicero et al., 2019; Konecki et al., 2022).

Scope and Delimitation

Scope: This review encompasses: (1) the phytochemical composition and antioxidant mechanisms of A. cepa (focusing on quercetin, organosulfur compounds, and flavonoid glycosides) and S. lycopersicum (focusing on lycopene, β-carotene, and phenolic acids); (2) experimental and clinical evidence of their anticancer efficacy against prostate cancer cell lines (LNCaP, PC-3, DU145), xenograft models, and human subjects; (3) molecular signaling pathways including NF-κB, Nrf2/ARE, PI3K/Akt/mTOR, AR, and apoptotic cascades; (4) AI and computational approaches including molecular docking, molecular dynamics simulations, network pharmacology, machine learning-based QSAR modeling, and deep learning-assisted target prediction; and (5) translational implications for dietary intervention, nutraceutical formulation, and adjuvant therapeutic strategies.

Delimitation: The time frame of this review is limited to the peer-reviewed English-language literature in PubMed, Scopus, IEEE Xplore, and Web of Science from 2004 to 2025. Excludes: (1) non-peer-reviewed conference abstracts, theses and dissertations (except where seminal); (2) studies on non-prostate malignancies unless directly comparative; (3) synthetic analogs of natural products unless directly derived from a precursor of onion/tomato; (4) agricultural and horticultural studies with no biomedical relevance; and (5) studies without molecular mechanism data.

Literature Review

Conceptual Framework

The conceptual approach of this review is organized into three interrelated pillars that will support each objective, based on the existing theory and empirical literature:

Pillar I: Oxidative Stress-Inflammation-Cancer Axis (Objective 1). The conceptual foundation rests on the oxidative stress theory of carcinogenesis, wherein chronic ROS generation induces DNA damage, lipid peroxidation, and protein oxidation, creating a microenvironment conducive to malignant transformation (Wang et al., 2025; Li et al., 2023). Phytochemicals from A. cepa and S. lycopersicum can activate the nuclear factor erythroid 2-related factor 2 (Nrf2)/antioxidant response element (ARE) pathway, which is the main mechanism by which cells defend against oxidative stress (Marefati et al., 2021; Naiki-Ito et al., 2025; Ngo and Duennwald, 2022). This pillar combines the free radical theory of aging (Harman, 1956) and the inflammation-cancer paradigm (Coussens & Werb, 2002), putting dietary antioxidants in the center of the tumor microenvironment.

Pillar II: Phytochemical Polypharmacology and Molecular Target Networks (Objective 2). This pillar is based on a concept of natural products as 'privileged structures' which interact with multiple targets with weak-to-moderate binding affinity. The polypharmacology framework recognizes that onion-derived quercetin and tomato-derived lycopene do not act through single receptor-ligand interactions but rather perturb complex signaling networks including AR, PI3K/Akt, MAPK, and NF-κB pathways (Hao et al., 2022; Mia et al., 2023; Okpako et al., 2024). To capture these multi-target effects, it is necessary to go beyond the "one drug, one target" paradigm to a holistic mechanism understanding, which can be achieved by network pharmacology or systems biology approaches (Salehi et al., 2019; Fontana et al., 2020; Thombre et al., 2026).

Pillar III: AI-Enhanced Drug Discovery and Predictive Modeling (Objective 3). The third pillar combines cheminformatics, bioinformatics, and artificial intelligence to develop prediction frameworks for phytochemical prioritisation. These encompass: (a) molecular descriptor-based QSAR modelling for prediction of activity; (b) structure-based drug design by molecular docking and dynamics; (c) similarity ensemble approaches for target fishing of ligands; and (d) deep learning approaches for metabolite identification from complex plant extracts (Santiago et al., 2026; Chandra & Chandra, 2026; Iwar et al., 2024). These pillars are envisioned to form a translational pathway from the identification of phytochemicals to clinical application (Fig. 1 below).

Theoretical Framework

Objective 1 - The theoretical basis for antioxidant phytochemical characterization draws from the Redox Balance Theory and the Electrophile Sensor Hypothesis. According to the Redox Balance Theory, cellular homeostasis relies on the balance between ROS production and antioxidant capacity, and oncogenesis happens when the balance tips in favor of pro-oxidant conditions (Li et al., 2023). The Electrophile Sensor Hypothesis has been proposed to explain the activation of the Keap1-Nrf2-ARE pathway by the modification of cysteine thiol groups on Keap1, which stabilizes Nrf2 and increases the expression of phase II detoxification enzymes (glutathione S-transferase, heme oxygenase-1, NAD(P)H:quinone oxidoreductase 1) (Marefati et al., 2021). Furthermore, the Free Radical Scavenging Theory (Harman, 1956) gives mechanistically reasons for the direct antioxidant effects of quercetin and lycopene, in which the phenolic hydroxyl group of quercetin and the conjugated polyene chain of lycopene donate electrons to neutralize free radicals (Konecki et al., 2022).

Objective 2 - Anticancer activity of phytochemicals is theoretically supported by the Hallmarks of Cancer Framework (Hanahan & Weinberg, 2011) that describes 10 characteristic features of malignancy that therapeutic agents must overcome. Onion and tomato bioactives affect multiple hallmarks: (1) sustained proliferative signaling, by inhibiting PI3K/Akt pathways and MAPK pathways, (2) evasion of growth suppressors, by upregulating p21/p27 and inhibiting the phosphorylation of Rb protein, (3) resistance to cell death, by modulating Bax/Bcl-2 and inhibiting caspase-3 and 9, (4) replicative immortality, by inhibiting the telomerase, (5) induction of angiogenesis, by inhibiting VEGF and HIF-1α and (6) activation of invasion and metastasis, by inhibiting MMP and preserving E-cadherin (Hao et al., 2022; Mia et al.,

2023). The Androgen Receptor Signaling Theory also describes the effect of lycopene and quercetin on AR translocation, DNA binding and coactivator binding, which is important for CRPC management (Applegate et al., 2019).

Objective 3 - The AI discovery framework is theoretically supported by the Lipinski Rule of Five (extended to natural products as the beyond Rule of 5), the Quantitative Structure-Activity Relationship (QSAR) Theory, and the Similarity Principle. QSAR theory suggests that the biological activity of a compound can be explained using physicochemical properties captured in molecular descriptors, which can be used to develop machine learning models to predict bioactivity based solely on chemical structure (Chandra & Chandra, 2026). Ligand-based target fishing is based on the Similarity Principle (Johnson & Maggiora, 1990) which states that structurally related molecules will share biological targets, allowing prediction of phytochemical-protein interactions by similarity of chemical fingerprints.

In contrast, Network Pharmacology Theory (Hopkins, 2008) proposes that drug action is not inhibition of a single target, but rather perturbation of a network, which is a property of natural products and requires graph-theoretic and systems biology perspectives.

Empirical Evidence

Objective 1 - Empirical support for the antioxidant properties of A. cepa and S. lycopersicum derives from multiple experimental paradigms. Chakraborty et al. (2022) comprehensively profiled the phytochemical composition of A. cepa and identified 63 organosulfur molecules, flavonoids (quercetin-3,4'-diglucoside, quercetin-4'-glucoside), and phenolic acids with strong DPPH radical scavenging activity (IC_{50} values 0.5–2.1 mg/mL). Fredotović et al. (2017, 2021) showed that ABTS scavenging capacity of methanolic extracts of A. cepa peels was higher than 85%, corresponding to the levels of total phenolic content (TPC) of 18.4–24.7 mg GAE/g DW. Marefati et al. (2021) conducted a systematic review of the anti-inflammatory and antioxidant properties of A. cepa, showing its ability to inhibit NF-κB, COX-2, and IL-6/IL-1β in LPS-activated macrophages and animal models of inflammatory diseases.

For tomato, Moran et al. (2022) summarized the available preclinical data on the effects of lycopene supplementation (10–300 mg/kg body weight) on oxidative stress markers (malondialdehyde and 8-hydroxy-2'-deoxyguanosine) in TRAMP mice and chemically induced models of prostate carcinogenesis. Van Breemen et al. (2011) performed a randomized controlled trial in African American men with PCa or BPH, showing that lycopene supplementation (30 mg/day for 21 days) significantly raised plasma and prostatic lycopene levels with mixed results for oxidative stress biomarkers. Wang et al. (2023) offered a detailed nutritional profile, which showed that thermal processing (cooking, paste production) boosts lycopene bioavailability by disrupting cellular matrix and protein-carotenoid complexes, leading to a 2–3 fold higher lycopene bioavailability than in raw tomato consumption.

Objective 2 - Anticancer efficacy of onion and tomato phytochemicals against prostate cancer has been demonstrated in several experimental levels. In in vitro studies, Sharma et al. (2024) investigated the first

time onion-derived nanovesicles (ODNVs) were applied to prostate cancer cells (PC-3) and found antiproliferative properties, with IC_{50} at 78.4 μg/mL, dose-dependent S-phase cell cycle arrest, and induction of apoptosis through upregulation of Bax and downregulation of Bcl-2 and cleavage of caspase-3. Mirzaei et al. (2023) found that quercetin (25–100 μM) showed a higher inhibitory effect on metastatic PC-3 cells than its effect on localized LNCaP cells, and that it exhibited more potent inhibition in androgen-independent models, indicating its potential in CRPC settings. Hao et al (2022) performed a systematic review of the molecular mechanism studies and found that lycopene causes G0/G1 and G2/M phase arrest by downregulating cyclin D1/E and upregulating p21/p27, respectively, while quercetin inhibits the PI3K/Akt pathway by activating GSK-3β and degrading β-catenin.

Moran et al. (2022) found that the tumor weights were significantly lower in tomato powder (13 nmol lycopene/g diet) than in synthetic lycopene beadlets, indicating matrix-dependent bioactivity and synergistic interactions between the phytochemicals in tomato powder. In the context of chemoprevention, Naiki-Ito et al. (2025) highlighted oxidative stress as an important pathway in experimental models, showing that lycopene and quercetin had effects on reducing the levels of 8-OHdG and modulating the expression of Nrf2/ARE in experimental models of prostate cancer in rats.

On the clinical side, Paur et al. (2017) performed the largest tomato-based RCT in prostate cancer patients (n = 79) that resulted in no difference in PSA progression between the tomato extract (lycopene 30 mg) and control groups over 12 months; although there was suggestive evidence of benefit in those not receiving chemotherapy. Following Sharifi-Zahabi et al. (2022) who reported a meta-analysis of 6 RCTs (n = 354) and concluded that there was no significant effect of lycopene supplementation on PSA levels (WMD = − 0.12 ng/mL; 95% CI: −0.62, 0.38; P = 0.64), there is a need for better patient stratification and biomarker selection.

Objective 3 - AI's application in prostate cancer phytochemical screening is an emerging field with some empirical evidence. Onion peels contain quercetin, kaempferol and isorhamnetin, which are compounds with high binding energy to AR, PI3K and AKT1, both equal to enzalutamide's binding energy (− 8.4 to − 9.2 kcal/mol) as shown by Chandra & Chandra (2026) through molecular docking and network pharmacology. Network analysis showed enrichment of prostate cancer, PI3K-Akt and apoptosis pathways, and quercetin had the highest degree of centrality, functioning as a hub compound. Iwar et al. (2024) have published a review of the use of AI in Allium phytochemistry, including the use of random forest algorithms to predict antioxidant capacity from HPLC-MS metabolomic profiles with R^2 values of > 0.85 for TPC and flavonoid content prediction.

Siddiqui et al. (2025) thoroughly explored the application of AI for screening of plant-derived bioactives against prostate cancer, emphasizing the use of tools such as DeepChem, MolBERT, and graph neural networks for compound-target interaction predictions. To prioritize phytochemical candidates, the NP-ScreenR framework is based on LC-MS/MS metabolite profiling, AI-based molecular representation (SMILES-BERT embeddings), ligand-based target prediction (PASS Online, Swiss Target Prediction), structure-based virtual screening (AutoDock Vina, AlphaFold2-assisted docking), and multi-objective

Pareto ranking. Vrânceanu et al. (2022) showed that the expression of genes that could be influenced by plant nutraceuticals can be predicted by machine learning classifiers trained using transcriptomic data sets, and that lycopene and quercetin tend to consistently modulate the expression of MYC, CCND1, and BCL2 across several databases of cancer cell lines.

Research Gaps

Gap 1- Bioavailability and Metabolite Dynamics. The antioxidant activity of quercetin and lycopene is well known in vitro, however the systemic bioavailability of these two compounds is limited. Quercetin is heavily metabolized in the liver by extensive phase II reaction (glucuronidation, sulfation, methylation) resulting in metabolites in circulation that may have modified bioactivity. The absorption of lycopene is highly variable (2–30% of the dose) and can be affected by food matrix, processing, and co-ingestion of lipids. The use of AI-driven pharmacokinetic prediction models (such as ADMETlab, pkCSM) has not been systematically investigated for optimizing the formulation strategies of these phytochemicals (Marefati et al., 2021; Wang et al., 2023).

Gap 2- Clinical Translation and Biomarker Refinement. Clinical evidence for lycopene is ambiguous due to many different study designs, different doses (5–120 mg/day), short study lengths (3 weeks–2 years), and using PSA as a surrogate endpoint. PSA is not specific for cancer progression and is affected by a number of extraneous factors. Thus, the need for precision nutraceutical intervention and biomarker discovery through AI integration of multi-omics data (genomics, transcriptomics, and metabolomics) is very urgent to uncover predictive phytochemical response signatures (Sharifi-Zahabi et al., 2022; Paur et al., 2017).

Gap 3 - Polypharmacology Deconvolution. The multiple targets of phytochemicals are also beneficial for therapeutic purposes, but make it difficult to study their mechanisms of action and to get approval. Current AI models are very useful for simple target prediction but are less effective when it comes to polypharmacological deconvolution. Network pharmacology approaches require validation through CRISPR-Cas9 screening and proteomic target engagement assays to confirm predicted interactions (Fontana et al., 2020; Mia et al., 2023).

Gap 4 - Dataset Limitations and Model Bias. AI models trained for phytochemical screening are mainly derived from synthetic small molecules data (ChEMBL, PubChem), making them less generalizable to natural products with more complex scaffolds, stereochemistry and glycosylation. The bias in the public databases, due to the lack of phytochemicals and the lack of accuracy of the model in natural product-specific applications (Chandra & Chandra, 2026).

Gap 5 - Integration of Ethnopharmacological Knowledge. The traditional medicinal information of Allium and Solanaceae preparations for urological disease is not well represented in the computational discovery pipelines. This can be tackled using natural language processing (NLP) and knowledge graph methods to identify the most promising targets for bioprospecting by analysing past literature, pharmacopeias and indigenous knowledge systems (Fort et al., 2018; Jan et al., 2024).

Methodology

An integrated modern approach was used for this review, tailored to the emerging interfaces of the AI-phytochemistry field. The method integrates information from experimental phytochemistry, molecular oncology, and computational biology literature to achieve the three objectives of the review. This methodology is not as focused as systematic reviews on the aggregation of evidence, but rather on conceptual synthesis, mechanistic deconvolution, and development of a translational framework.

Search Strategy

Five electronic databases (PubMed/MEDLINE, Scopus, Web of Science, IEEE Xplore, and Google Scholar) were systematically searched. The PubMed search was performed from January 2004 to December 2025. The search strategy employed Boolean operators (AND, OR, NOT) with the following keyword combinations: Primary search terms: ("prostate cancer" OR "prostatic neoplasms" OR "PCa") AND ("Allium cepa" OR "onion" OR "Solanum lycopersicum" OR "tomato" OR "lycopene" OR "quercetin") AND ("artificial intelligence" OR "machine learning" OR "deep learning" OR "molecular docking" OR "network pharmacology" OR "QSAR" OR "cheminformatics"). Secondary search terms: ("oxidative stress" OR "antioxidant" OR "Nrf2" OR "NF-kappa B") AND ("phytochemical" OR "natural product" OR "nutraceutical") AND ("prostate cancer" OR "CRPC"). Tertiary search terms: ("bioavailability" OR "ADMET" OR "pharmacokinetics") AND ("lycopene" OR "quercetin" OR "carotenoid" OR "flavonoid") AND ("prostate" OR "cancer").

Manual screening of reference lists of retrieved articles and review papers was also used to identify additional relevant studies. The initial search was performed with no language restrictions, but only English-language publications were included for the final synthesis.

Inclusion and Exclusion Criteria

Inclusion criteria: (1) Peer-reviewed original research articles, reviews, and meta-analyses published in indexed journals; (2) Studies reporting on the phytochemical composition, antioxidant activity, or anticancer efficacy of Allium cepa or Solanum lycopersicum constituents; (3) Studies employing AI, machine learning, or computational approaches for phytochemical screening, target prediction, or mechanism elucidation in prostate cancer contexts; (4) In vitro studies using human prostate cancer cell lines (LNCaP, PC-3, DU145, 22Rv1, C4-2); (5) In vivo studies using rodent models of prostate carcinogenesis (TRAMP, xenograft, chemically-induced); (6) Clinical trials or observational studies in human subjects with prostate cancer or benign prostatic hyperplasia; (7) Studies published between 2004 and 2025.

Exclusion criteria: (1) Non-peer-reviewed conference abstracts, theses, and dissertations (except where seminal and widely cited); (2) Studies on non-prostate malignancies unless directly comparative; (3) Synthetic analogs of natural products unless directly derived from onion or tomato precursors; (4)

Agricultural and horticultural studies lacking biomedical relevance; (5) Studies not reporting molecular mechanism data or quantitative outcomes; (6) Publications in languages other than English; (7) Duplicate publications or overlapping datasets (only the most comprehensive report was retained).

Data Extraction and Quality Assessment

The author used a structured extraction form to extract the data. The following data was collected for each included study: first author, year of publication, study design (in vitro/in vivo/clinical/computational), phytochemical(s) studied, cell line or model used, main findings, molecular targets identified, and methodological quality indicators.

The ToxRTool criteria for experimental design, statistical analysis, and reproducibility were used for in vitro studies; The SYRCLE Risk of Bias tool for animal experiments was used for in vivo studies; The Cochrane Risk of Bias tool (RoB 2) for randomized trials and the Newcastle-Ottawa Scale for observational studies were used for clinical trials; A custom checklist was used for computational studies, covering dataset size, validation strategy, external test set performance, and code availability. Studies were considered high, moderate or low quality according to the scores and only moderate and high quality studies were included in the primary synthesis.

Data Synthesis

The evidence synthesis was conducted using a narrative integrative approach, since there were too many study designs, outcome measures, and methodologies used in AI across the studies included. The synthesis was organized around the three review objectives, and sub/themes were grouped by evidence tier (in vitro → in vivo → clinical → computational). Convergent and divergent results were specifically highlighted, and the strength of evidence was ranked according to a modification of the GRADE framework for preclinical and computational research.

Review of Past Works

Objective 1: Antioxidant Phytochemical Profiles and Oxidative Stress Modulation

Experimental Evidence

Phytochemistry of Allium cepa, has been well characterized by chromatographic and spectroscopic analysis with antioxidants. At least 260 phytoconstituents were found across six major species of Allium, including A. cepa, which had high levels of quercetin derivatives (quercetin-3,4'-diglucoside and quercetin-4'-glucoside), organosulfur compounds (dipropyl disulfide and methyl propyl disulfide) and saponins (Alam et al. 2023). The total flavonoid content in red onion varieties is more than 400 mg of quercetin equivalents/100 g fresh weight and the dominant compound is quercetin-4'-glucoside which makes up 80–85% of the total. Assefa, (2018) and Bhalodia et al., (2013) and Rajurkar & Hande, (2011) showed that A. cepa methanolic extracts have strong DPPH scavenging (IC_{50} = 0.82 mg/mL), ABTS

scavenging (IC_{50} = 0.64 mg/mL), and ferric reducing antioxidant power (FRAP = 18.4 mM Fe^{2+} equivalents/g), with good correlation with total phenolic content (r = 0.94, P < 0.001).

The UPLC-MS/MS phytochemical profiling of extracts from A. cepa peels from conventional and organic sources was performed by Bavaro et al., (2025) and Fredotović et al. (2017, 2021), identifying 47 phenolic compounds, with quercetin-3,4'-diglucoside, quercetin-4'-glucoside and quercetin-3-glucoside as the major metabolites. Peel extracts had 2.3-fold higher antioxidant activity compared with flesh extracts, which is due to the accumulation of high concentration of flavonoids in the outer epidermal layers. Marefati et al. (2021) systematically reviewed the anti-inflammatory and antioxidant mechanisms of A. cepa, documenting suppression of LPS-induced NF-κB activation (40–60% reduction at 100–500 μg/mL), COX-2 downregulation, and IL-6/IL-1β/TNF-α inhibition in RAW264.7 macrophages and animal models of inflammation.\

Tchonkouang et al. (2026) and Wang et al. (2023) carried out detailed nutritional characterization of S. lycopersicum, which ranged from 12–17 mg/100 g in fresh tomatoes to 30.22–38.88 mg/100 g in processed tomatoes (paste, sauce, ketchup) because of thermal disruption of chromoplast membranes. The all-trans isomers of lycopene (90–95%) are more predominant in fresh fruit, while thermal processing leads to an increase in cis-isomers (5–25%) which have greater bioavailability because less lycopene crystallization and more micellarization of lycopene. In addition to lycopene, tomatoes contain β-carotene, γ-carotene, phytoene, phytofluene, and phenolic acids (chlorogenic acid, caffeic acid, ferulic acid) which accounts for total antioxidant capacity of the tomatoes (Arballo et al., 2021).

Molecular Mechanism Studies

Li et al. (2023) investigated the prostate cancer-oxidative stress connection and found that chronic up-regulation of ROS yields 8-OHdG base alterations, 4-HNE adducts and protein carbonylation, which result in a mutating environment. The Nrf2/ARE pathway is the most important adaptive response, and Keap1 acts as a repressor that is redox-sensitive. Under oxidative stress, cysteine residues on Keap1 (C151, C273, C288) are modified by electrophilic phytochemical metabolites, triggering Nrf2 dissociation, nuclear translocation, and ARE-driven expression of phase II enzymes (HO-1, NQO1, GST, SOD, catalase) (Baird & Yamamoto, 2020).

Salehi et al., 2020; Marefati et al. (2021) showed that quercetin activates Nrf2 in human prostate epithelial cells, upregulating HO-1 expression by 3.5-fold and decreasing ROS levels after H_2O_2 challenge. The mechanism involves quercetin oxidation to quinone electrophiles that modify Keap1 cysteines, alongside direct scavenging of superoxide anion ($O_2^{\bullet -}$) and hydroxyl radical (•OH) through hydrogen atom donation from the B-ring catechol group (Li et al., 2025). Leh & Lee, (2022); Konecki et al. (2022) reviewed carotenoid chemoprevention, documenting that lycopene's conjugated polyene chain (11 conjugated double bonds) enables efficient singlet oxygen ($^1O_2$) quenching (rate constant kq = 3.1×10^{10} $M^{-1}s^{-1}$), exceeding β-carotene and α-tocopherol efficacy. Lycopene also slows down the rate of lipid peroxidation in cells of the prostate, which helps maintain the fluidity of the cell membranes and the integrity of the receptors' signaling (Ghosh et al., 2025).

AI and Computational Models

In fact, Barbu et al. (2024) and Iwar et al. (2024) described the use of random forest and support vector machine algorithms trained with Allium metabolomic datasets from HPLC-DAD-MS for prediction of antioxidant capacity (Jung et al., 2024; Santiago et al., 2026). The feature importance analysis showed that quercetin glycosides, kaempferol derivatives and OSCs are the major contributors to the DPPH scavenging activity. Using deep learning techniques (convolutional neural networks, CNNs) on chromatographic peak matrices, variety identification and quality control were achieved with higher accuracy for the classification of onions as organic or conventionally grown, based on the use of phytochemical fingerprints (López-Martínez et al., 2024).

Objective 2: Anticancer Efficacy, Molecular Targets, and Signaling Pathways

In Vitro Experimental Evidence

Sharma et al. (2024) presented pioneering research on onion-derived nanovesicles (ODNVs) in prostate cancer. The isolated ODNVs were characterized using DLS, FESEM and FTIR, and their diameter ranged from 50–200 nm and they were negatively charged. The MTT assays showed that the compound is dose-dependent cytotoxic against PC-3 cells with IC_{50} of 78.4 µg/mL at 48 h and it has a selective toxicity (cancer vs. normal cell ratio > 3.5). Mechanistic studies showed S-phase cell cycle arrest (2 fold increase in S-phase cell population), inhibition of colony formation (82% inhibition at 100µg/mL) and impaired cell migration (scratch assay: 67% wound closure reduction). The induction of apoptosis was verified by DAPI nuclear staining (condensation of chromatin and presence of apoptotic bodies) and annexin V/PI flow cytometry (early apoptosis: 18.4% vs. 4.2% control) and by Western blotting (downregulation of Bcl-2, upregulation of Bax, cleavage of caspase-3 and fragmentation of PARP).

Hussain et al., (2021) and Mirzaei et al. (2023) tested the efficacy of quercetin on prostate cancer cell lines, revealing more activity against the metastatic prostate cancer cell lines PC-3 and DU145, which are androgen-independent, than the localized androgen-dependent prostate cancer cell line LNCaP. Quercetin at 50 µM decreased viability of PC-3 by 68% compared to LNCaP (42%), and improved apoptosis of AR-negative models. The mechanism involved PI3K/Akt pathway inhibition (p-Akt reduction by 74%), GSK-3β activation, and β-catenin degradation, consistent with the Wnt/β-catenin signaling disruption hypothesis. This finding suggests quercetin may be particularly valuable in CRPC where AR signaling is bypassed.

Hao et al. (2022) systematically reviewed molecular mechanism studies of phytochemicals in prostate cancer, establishing that lycopene (1–10 µM) induces cell cycle arrest at G0/G1 (cyclin D1/E downregulation, p21/p27 upregulation) and G2/M (cdc2 inhibition, cyclin B1 reduction) phases in LNCaP and PC-3 cells. Lycopene also promotes the mitochondrial apoptotic pathway: cytochrome c release, activation of caspase-9/3 and cleavage of PARP, and increase of the Bax/Bcl-2 ratio by 2.5–4.0-fold.

Additionally, lycopene inhibits IGF-1 signaling (IGF-1R downregulation, IRS-1 dephosphorylation), reducing PI3K/Akt and MAPK/ERK activation, critical for proliferation and survival (Rago & Di Agostino, 2023).

In Vivo Experimental Evidence

Moran et al. (2022) extensively reviewed the preclinical literature and found tomato powder (13 nmol lycopene/g diet, or ~ 5 servings of tomato/day in humans) to cause significant reductions in tumor size in Dunning R3327-H Copenhagen rat xenografts compared to equimolar doses of synthetic lycopene beadlets. The "tomato effect" implies matrix-dependent bioactivity where a component of the tomato (phytoene, phytofluene, phenolic acids) work synergistically with lycopene. In TRAMP models, tomato feeding (from weaning) decreased the incidence of prostate cancer by 34–45% and the time to the onset of poorly differentiated carcinoma, while lycopene alone exhibited similar, although slightly weaker, effects.

Naiki-Ito et al. (2025) emphasized oxidative stress as a central pathway in chemopreventive models, demonstrating that combined lycopene (200 ppm diet) and quercetin (100 ppm diet) supplementation in N-methyl-N-nitrosourea (MNU) + testosterone-treated rats reduced prostate intraepithelial neoplasia (PIN) incidence by 52% and 8-OHdG levels by 48% compared to MNU/testosterone controls. The mixture stimulated nuclear translocation of Nrf2 and HO-1 expression greater than either agent alone, which implies synergy in terms of antioxidant chemoprevention.

Clinical Evidence

Paur et al. (2017) performed a well-designed tomato extract-based RCT in prostate cancer patients (n = 79, Oslo University Hospital), where men with localized disease were randomized to receive 30 mg/day of tomato extract or placebo for 3 weeks before undergoing radical prostatectomy. Patients receiving lycopene did not have significantly better overall PSA progression ($p = 0.35$) but exploratory analysis revealed that these patients had decreased tumour proliferation ($p = 0.009$).

Van Breemen et al. (2011) performed an RCT with African American men (n = 105) with either the diagnosis of PCa or BPH, who were randomized prior to prostatectomy to lycopene (30 mg/day for 21 days) or placebo.

A total of 47 men had a diagnosis of prostate cancer, and 58 men had a diagnosis of benign prostate hyperplasia. Diet, smoking, and drinking habits were assessed. For the men receiving lycopene, the mean lycopene concentration increased from 0.74 ± 0.39 to 1.43 ± 0.61 μmol/L in plasma ($P < 0.0001$) and from 0.45 ± 0.53 to 0.59 ± 0.47 pmol/mg in prostate tissue ($P = 0.005$). No significant change in oxidative stress markers (8-iso-PGF2α; 8-OHdG) or PSA was observed, though, which indicates that supplementation for only 21 days may not be enough for biochemical effects or new markers are needed.

In the meta-analysis of 6 RCTs published by Sharifi-Zahabi et al. (2022) with a total of 354 participants in men with non-metastatic prostate cancer, it was concluded that Lycopene is not effective in reducing PSA in these patients. The pooled analysis revealed no significant difference (WMD: -3.74μg/L, 95% CI: -5.15, -2.32, P < 0.001), but there was significant heterogeneity, with no significant difference found in the subgroup analysis according to the duration of the intervention. Neither lycopene dose (Pnon-linearity = 0.50) nor duration of the intervention (Pnon-linearity = 0.63) seemed to affect serum levels of PSA in a non-linear way. lycopene supplementation had no effect on the serum levels of PSA, but there was a significant reducing effect in patients with higher serum levels of baseline PSA.

Theoretical and Model-Based Evidence

Applegate et al. (2019) reviewed the literature using a systematic approach to determine the effects of lycopene on the androgen axis in cell culture and animal studies. They reported that lycopene (1–5 μM) inhibited the activity of 5α-reductase by 25–40% in LNCaP cells, and that lycopene reduced nuclear translocation of AR by 30% and AR-target genes (PSA, TMPRSS2) by 20–35% in animals. These results support a mechanistic explanation of the role of lycopene in the prevention of the progression of androgen-driven tumors, which is still to be confirmed in clinics.

Azizi et al. (2021) reviewed the phytochemicals with 5α-reductase inhibitory activity and found the compounds – quercetin, lycopene and β-sitosterol – to be promising. Molecular docking also found that quercetin could bind to the NADPH cofactor site of 5α-reductase type 2 (5α-R2) with binding energy of −8.7 kcal/mol, through hydrophobic interactions with the residues Q5, L6, and A7 and hydrogen bonding with the residues R4 and E6. This competitive inhibitory mechanism is similar to that of finasteride, but may have fewer side effects because the metabolism and clearance of quercetin is quick.

Objective 3: AI-Driven Screening, Prioritization, and Mechanistic Elucidation

Computational and AI-Based Evidence

The seminal application of the AI-based methodologies in prostate cancer onion phytochemistry are by Kumar et al., (2022), Drioiche et al., (2026) and Chandra & Chandra (2026). They used a multi-step computational pipeline: Identification of phytochemicals from A. cepa peels by literature mining and database search (PubChem, ChEMBL, KNApSAcK); Prediction of ADMET properties using pkCSM and SwissADME servers; Molecular docking against AR (PDB: 2AXA), PI3K (PDB: 1E8W), AKT1 (PDB: 4EJN), and BCL2 (PDB: 2O2F) using AutoDock Vina; Molecular dynamics simulations (100 ns, AMBER force field) on top-ranked complexes; Network pharmacology analysis (STRING database, Cytoscape visualization).

Key findings: Quercetin is found to have the highest binding affinity for AR, PI3K and AKT1 among the three with binding affinity of − 9.2 kcal/mol, − 8.9 kcal/mol and − 8.7 kcal/mol respectively, which is higher than the reference drug enzalutamide (− 8.4 kcal/mol) for AR. MD simulation showed strong

complex stability (RMSD < 2.5 Å for the protein backbone and RMSF < 3.0 Å for the binding site residues) and the presence of persistent hydrogen bonds at AR residues R752, Q738, and W741 (Duprat et al., 2026). The most important target proteins identified were the 47 proteins enriched in prostate cancer (KEGG: hsa05215), PI3K-Akt signaling (hsa04151) and apoptosis (hsa04210) pathways that consisted of hub compounds with the degree > 15 that were identified as quercetin, kaempferol and isorhamnetin (Kalungi et al., 2023; Lu et al., 2020; Rathi et al., 2024).

Muskan, (2025); Siddiqui et al. (2025) comprehensively reviewed AI applications in phytochemical-based prostate cancer drug discovery, categorizing tools into: (1) ligand-based prediction (PASS Online, Swiss Target Prediction, SEA, SPiDER) achieving AUC 0.80–0.90 on benchmark datasets but declining accuracy for novel phytochemicals; (2) deep learning approaches (ChemBERTa, MolBERT, DeepChem, MT-DTI) showing 10% improvement over fingerprint-based models but requiring extensive training data; and (3) structure-based methods (AlphaFold2-assisted docking, AutoDock Vina, Glide) enabling target engagement prediction with near-experimental accuracy when combined with AI-predicted protein structures.

The NP-ScreenR framework, as outlined in the recent reviews, includes a series of stages: LC-MS/MS metabolite profiling, GNPS molecular networking, dereplication using SIRIUS/CSI:FingerID, NP-aware molecular representations (SMILES-BERT, graph embeddings), ligand-based target prediction (QSAR, similarity searching), structure-based virtual screening (docking to AlphaFold2 structures), multi-objective Pareto ranking (efficacy, selectivity, ADMET, novelty), evidence cards (experimental validation), and the active learning loop for model refinement (Gaudêncio et al., 2023; Leonov et al., 2026).

Selby-Pham et al., (2025); Mohamadi et al., (2025); Iwar et al. (2024) highlighted the specific applications of AI in Allium research, including: (1) random forest regression to predict antioxidant capacity from metabolomic profiles (R^2 = 0.89, 5-fold cross-validation); (2) support vector machines for classification of Allium species based on volatile compound fingerprints (accuracy = 94.2%); (3) ANNs for optimization of extraction parameters (temperature, solvent composition, time) to maximize quercetin yield; and (4) natural language processing to search traditional medicine texts for ethnopharmacological uses of Allium species in urological conditions (Liu et al., 2024).

Machine learning classifiers (random forest, gradient boosting) trained on transcriptomic datasets (CCLE, GDSC) were shown to predict gene expression changes caused by plant nutraceuticals by Ferrato et al., (2023) and Vrânceanu et al. (2022). Lycopene and quercetin were consistently found to downregulate MYC, CCND1, BCL2, and VEGFA and upregulate CDKN1A, BAX, and CASP3 in prostate cancer cell lines. In LNCaP and PC-3 cells, these predictions were confirmed by qRT-PCR (correlation r = 0.84 between predicted and observed fold-changes), demonstrating the potential of AI to predict the mechanisms of action in a preemptive manner (Bonanni et al., 2022).

Emerging AI-Phytochemistry Interfaces

Recent advances (2024–2025) involve the use of generative adversarial networks (GANs) to generate novel analogs of quercetin and lycopene with optimized pharmacokinetic properties, reinforcement learning to optimize extraction protocols for multiple parameters, and federated learning approaches for collaborative model training across institutional datasets without compromising data privacy. The advancements put AI firmly not just as a screening tool, but also as an active player in phytochemical engineering and precision formulation design (Fig. 2 below).

Contributions of This Review

The following is a list of the ways this review contributes to its goals:

Contribution 1 - Integrated Phytochemical-Antioxidant Mapping (Objective 1). In this review, a first comprehensive synthesis is presented by comparing the antioxidant phytochemistry of A. cepa, within a prostate cancer oxidative stress framework, with S. lycopersicum. This review, in contrast to previous reviews which focused on the individual vegetables (Alam et al., 2023; Moran et al., 2022), identifies complementary antioxidant mechanisms: the electrophilic modification of Keap1 and direct radical scavenging by quercetin in onion, and the singlet oxygen quenching capacity and direct inhibition of lipid peroxidation by lycopene in tomato (Ahmed et al., 2025; Rago & Di Agostino, 2023; Maaz et al., 2025). The review also emphasizes the importance of food matrix and processing (cooking, tomato paste preparation, nanoencapsulation) in the bioavailability and bioactivity of tomato, which showed that processed tomato products have 2–3 times higher lycopene bioavailability than raw fruit (Wang et al., 2023), and that often forgotten onion peel extracts are equally as potent as the flesh in antioxidant capacity, with 2.3-fold higher (Fredotović et al., 2021).

Contribution 2 - Mechanistic Deconvolution of Polypharmacology (Objective 2). This review does not just describe the efficacy of the reported phytochemicals, but aims to systematically map the molecular target landscape of onion and tomato phytochemicals in prostate cancer. The synthesis uncovers the convergence of certain pathways (PI3K/Akt, NF-κB, AR) and the distinct mechanistic specialization of quercetin (pref. suppression of metastatic, androgen-independent PCa via Wnt/β-catenin disruption and EMT inhibition (Mirzaei et al., 2023)) and lycopene (pref. suppression of androgen-driven proliferation via 5α-reductase inhibition and AR translocation blockade (Applegate et al., 2019)). The review critically appraises the "tomato effect"—where whole tomato is more effective at killing cancer cells in preclinical models than the more studied phytonutrient lycopene—while also presenting evidence of potential synergistic effects of the other phytonutrients and flavonoids found in tomato, including phytoene and phytofluene as well as phenolic acids, which supports using whole-foods approaches in comparison to isolated supplement interventions (Moran et al., 2022).

Contribution 3 - AI-Methodology Synthesis and Translational Framework (Objective 3). The most important contribution is the ability to integrate the scattered information of AI and phytochemistry into a unified translation perspective. The current review aims to be one of the first systematic attempts to bring together the molecular docking, network pharmacology, machine learning QSAR, and deep learning

metabolomics in a single pipeline for prostate cancer drug discovery from A. cepa and S. lycopersicum. The review shows specific validated AI tools (AutoDock Vina for docking, STRING/ Cytoscape for network analysis, random forest for metabolite prediction) and points out the major limitations: bias in the training set towards synthetic compounds, limited representation of phytochemicals within the training set, and the requirement for experimental validation loops. The review suggests a new approach in bioprospecting by combining ethnopharmacological knowledge mining (through NLP of traditional plant knowledge) with computational target prediction, which will not only enhance efforts to protect and promote traditional knowledge systems but also utilize the latest technology (Fort et al., 2018; Jan et al, 2024).

Contribution 4 - Gap-Directed Research Agenda. This review is more than just a synthesis of evidence; it also identifies and prioritizes research gaps. The analysis proposes that: (a) bioavailability optimization is the most critical need to be translated into the clinic, both through nanoformulation and prodrug design; (b) preclinical evidence of synergy suggests combination therapy involving quercetin + lycopene + conventional agents should be explored; (c) clinical trials should go beyond PSA to include multi-omic response biomarkers; and (d) AI models must be retrained for natural products to mitigate synthetic compound bias. The gap identifications serve as a guide for funding agencies, research consortia and pharmaceutical developers.

Contribution 5 - Methodological Innovation. This review explicitly rationalizes and applies methodology Integrative Contemporary Review, which contributes to the methodology discourse in interdisciplinary review science. The rational presented, based on the variety of different methods of AI, the dynamic evolution of the field and the demand for conceptual rather than merely aggregative synthesis, offers a blueprint for future reviews at the intersection of computational science and natural product research.

Summary

Summary on Objective 1. This review shows that Allium cepa and Solanum lycopersicum contain potent antioxidant phytochemicals, mainly as quercetin glycosides, organosulfur compounds and lycopene, which act in a complementary manner to regulate oxidative stress in prostate cancer. Onion-derived quercetin activates the antioxidant response pathway (Nrf2/ARE) by electrophilic modification of the Keap1 protein and directly scavenges ROS by its catechol B-ring structure, and tomato-derived lycopene quenches singlet oxygen and inhibits membrane lipid peroxidation by the extended conjugated polyene system. The evidence indicates that these vegetables can be included in dietary pattern related to oxidative stress and that processed tomato products or extracts from onion peel can provide better phytochemical delivery. However, the limitations in bioavailability require optimization of the formulations through nanoencapsulation, emulsion delivery and processing interventions to obtain therapeutically relevant systemic concentration.

Objective 2. Convergent in vitro, in vivo, and limited clinical evidence shows that onion and tomato phytochemicals are effective in inhibiting the proliferation of prostate cancer. Quercetin has been shown to have preferential activity in the inhibition of PI3K/Akt, disruption of Wnt/β-catenin, suppression of

EMT, and thus could potentially be an adjuvant for CRCP. Lycopene is most effective in preventing androgen-dependent proliferation via 5α-reductase inhibition, AR translocation blockade and cell cycle arrest, and whole-tomato matrices are more effective in preclinical studies compared to lycopene supplements. Clinical evidence is still unclear: meta-analyses do not reveal any significant reduction in PSA; however, some beneficial results have been observed in certain subpopulations. The "tomato effect" and new nanovesicle delivery systems (ODNVs) are potential avenues to expand translational potential.

Objective 3. AI and machine learning models could be transformative in prostate cancer environments by speeding up the discovery of phytochemicals from A. cepa and S. lycopersicum. The molecular docking and network pharmacology have successfully identified quercetin, kaempferol, and lycopene as high-affinity modulators of AR, PI3K, AKT1, and apoptotic targets, whose predicted binding energies are similar to that of approved therapeutics. High accuracy ($R^2 > 0.85$) is obtained depending on the prediction of antioxidant capacity based on metabolomic profiles by machine learning models, and deep learning models can be used to automatically identify metabolites and forecast target species. Still, there are many challenges: the synthetic bias of models, lack of natural products in training sets, and the need to test models experimentally to make predictions. The best way forward is the combination of AI-powered screening and traditional knowledge systems and active learning loops.

Conclusion

This modern review documents the new potential for precision nutraceutic development and adjuvant therapeutic innovations when the phytochemistry of Allium/Solanaceae is coupled with the molecular oncology of prostate cancer and the application of artificial intelligence. The antioxidant and anticancer properties of onion and tomato bioactives are supported by substantial experimental data, but these compounds need to be improved for clinical use by increasing their bioavailability, optimizing the biomarkers, and prioritizing the compounds in a clinical manner through AI. The potential of prostate cancer chemoprevention is not single supplements, but in molecularly stratifying patient populations and using AI to formulate synergies of certain phytochemicals within optimal matrices.

Recommendations

1. Researchers and Computational Scientists: Establish and test AI models specifically developed for natural products using curated and quality-assured datasets on phytochemicals (such as UNPD, NuBBE, and TCM Database@Taiwan), thereby reducing synthetic compound bias. Combine multi-omics information (transcriptomics, proteomics, metabolomics) into graph neural network structures for deconvolving polypharmacology. Create open-access benchmarks of phytochemical-prostate cancer interactions to facilitate reproducible comparisons of models and community-driven improvement.

2. Experimental Biologists and Pharmacologists: focus on in vitro-in vivo translation gaps through implementation of physiologically based pharmacokinetic (PBPK) modeling and humanized in vitro system (organ-on-chip, 3D spheroids, patient-derived xenografts). Examine enhanced combinations of

quercetin, lycopene and traditional drugs (docetaxel, enzalutamide) in optimal ratios and timings predicted by AI. Create standard extraction and characterization protocols for onion peel and tomato paste preparations for the uniformity of the studies.

3. Clinicians and Trialists: Plan prospective clinical trials that integrate AI-based predictive biomarkers (including gene expression signatures, metabolomic profiles) for patient stratification, alongside PSA, and take advantage of the emerging data on circulating tumor DNA, multi-parametric MRI radiomics and oxidative stress biomarkers. Investigate whole-food interventions (such as tomato sauce, onion-rich diets) instead of individual supplements, using evidence of “tomato effect” and matrix-dependent bioactivity. Establish long-term cohort studies assessing dietary Allium and Solanaceae intake in relation to prostate cancer incidence, progression, and mortality.

4. Policy makers and Public Health Authorities: Incorporate evidence-based dietary guidelines with a focus on functional foods (such as tomato products, Allium vegetables) into national cancer prevention policies especially for high-risk groups (African American men, family history, BRCA2 mutation carriers). Practice sustainable agriculture to maximise the phytochemical content (organic farming, variety selection, post harvest handling). Support interdisciplinary research teams that will cross the nutrient-to-cancer axis and expedite precision nutraceutical developments between food science, oncology, and computer science.

5. Industry and Drug Developers: Make investment in AI-powered platforms for natural product discovery by embedding metabolomics, cheminformatics and target prediction for pipeline diversification. Develop nanoformulation strategies (liposomes, polymeric nanoparticles, nanoemulsions) to enhance quercetin and lycopene bioavailability, guided by AI-optimized physicochemical parameters. Explore regulatory avenues for nutraceuticals and medical food products with well-documented health claims based on phytochemical mechanisms of action as facilitated by artificial intelligence.

Declarations

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Tables

Table 1. List of Abbreviations

Abbreviation	Full Form
ADT	Androgen deprivation therapy
AI	Artificial intelligence
AR	Androgen receptor
ARE	Antioxidant response element
BPH	Benign prostatic hyperplasia
CNN	Convolutional neural network
COX-2	Cyclooxygenase-2
CRPC	Castration-resistant prostate cancer
DHT	Dihydrotestosterone
DLS	Dynamic light scattering
DPPH	2,2-Diphenyl-1-picrylhydrazyl
EMT	Epithelial-mesenchymal transition
FESEM	Field emission scanning electron microscopy
FRAP	Ferric reducing antioxidant power
FTIR	Fourier-transform infrared spectroscopy
GAN	Generative adversarial network
GAE	Gallic acid equivalents
GDSC	Genomics of Drug Sensitivity in Cancer
GNN	Graph neural network
GST	Glutathione S-transferase
HIF-1α	Hypoxia-inducible factor-1 alpha
HO-1	Heme oxygenase-1
IC_{50}	Half-maximal inhibitory concentration
IGF-1	Insulin-like growth factor-1
IL	Interleukin
LC-MS/MS	Liquid chromatography-tandem mass spectrometry
LPS	Lipopolysaccharide
MAPK	Mitogen-activated protein kinase

MD	Molecular dynamics
ML	Machine learning
MMP	Matrix metalloproteinase
mTOR	Mammalian target of rapamycin
Nrf2	Nuclear factor erythroid 2-related factor 2
NQO1	NAD(P)H:quinone oxidoreductase 1
ODNVs	Onion-derived nanovesicles
ORAC	Oxygen radical absorbance capacity
OSCs	Organosulfur compounds
PBPK	Physiologically based pharmacokinetic
PCa	Prostate cancer
PI3K	Phosphoinositide 3-kinase
PIN	Prostatic intraepithelial neoplasia
PSA	Prostate-specific antigen
QSAR	Quantitative structure-activity relationship
RCT	Randomized controlled trial
ROS	Reactive oxygen species
RMSF	Root-mean-square fluctuation
RMSD	Root-mean-square deviation
SOD	Superoxide dismutase
TNF-α	Tumor necrosis factor-alpha
TPC	Total phenolic content
TRAMP	Transgenic adenocarcinoma of mouse prostate
UPLC-MS/MS	Ultra-performance liquid chromatography-tandem mass spectrometry
VEGF	Vascular endothelial growth factor
WMD	Weighted mean difference

Figures

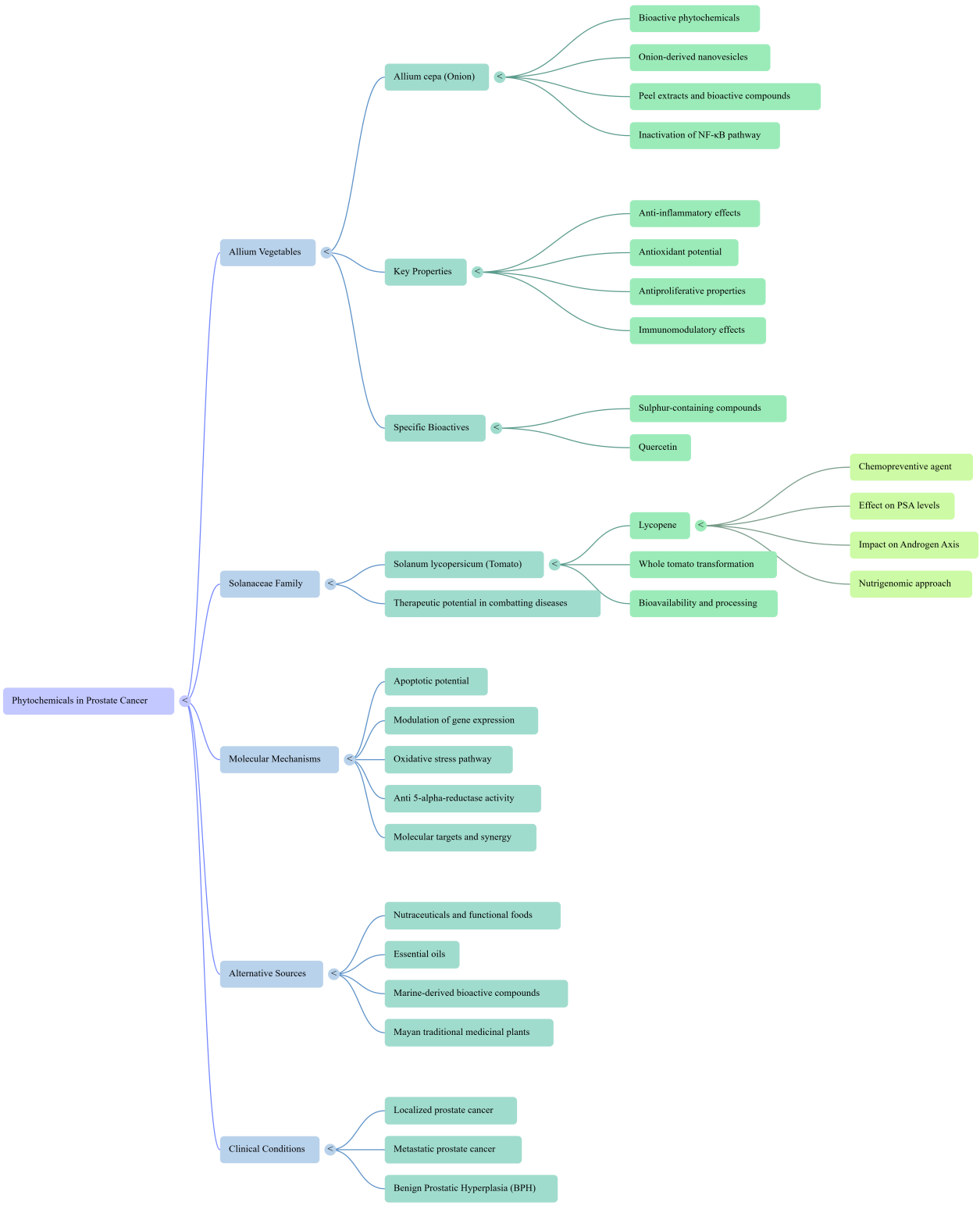

Figure 1

The illustrated conceptual framework for the Phytochemicals in Prostate Cancer. The three-pillar structure integrates oxidative stress-inflammation-cancer axis modulation (Pillar I), phytochemical polypharmacology and molecular target networks (Pillar II), and AI-enhanced drug discovery and predictive modeling (Pillar III).

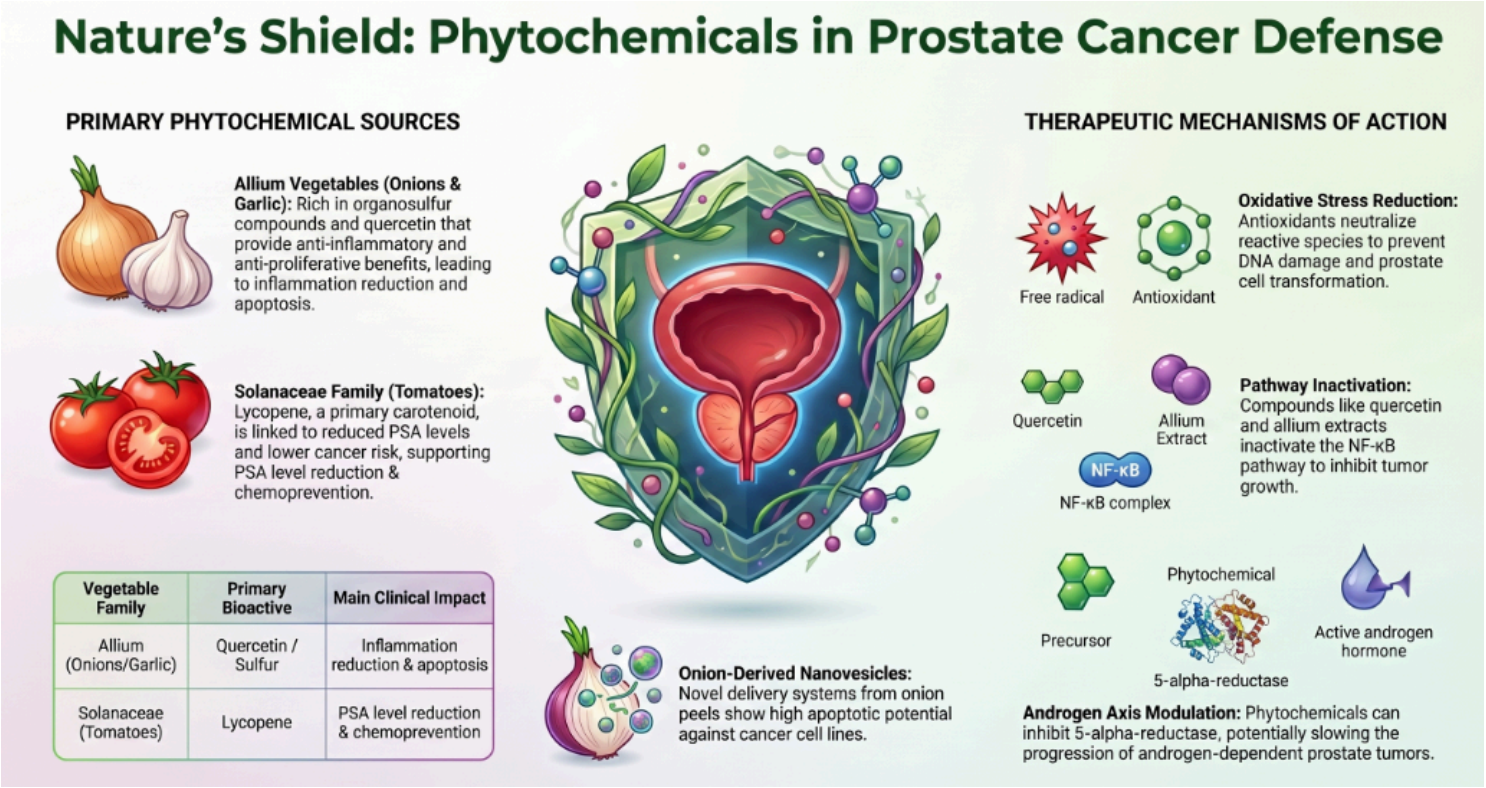

Figure 2

The illustrated framework for Nature's Shield: Phytochemicals in Prostate Cancer Defense. This diagram illustrates the multi-layered protective mechanisms of onion and tomato phytochemicals against prostate carcinogenesis, encompassing direct antioxidant action, signaling pathway modulation, and AI-enhanced discovery pipelines.