



## Review Article

## Phytochemicals and Medicinal Plants as Therapeutic Agents in Prostate Cancer: A Narrative Review

Nida Saleem<sup>1</sup>, Gu Lin<sup>\*2</sup><sup>1</sup>Shifa College of Pharmaceutical Sciences, Shifa Tameer-e-Millat University, Islamabad, Pakistan.<sup>2</sup>Yangtze Pharmaceutical Group, Nanjing Hailing Pharmaceutical Co., Ltd, Nanjing 210049, China.\*Correspondence: [gulin@yangzijiang.com](mailto:gulin@yangzijiang.com)

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## Abstract

Prostate cancer is the second most common malignancy in men worldwide, with androgen deprivation therapy eventually failing due to castration resistance. Phytochemicals offer promising chemopreventive and therapeutic options through multi-targeted mechanisms and favorable safety profiles. This review examines key anti-prostate cancer plant-derived compounds, including those extracted from *Tamarix articulata*, *Castanea sativa*, *Paris forrestii*, *Crateva adansonii*, *Biarum bovei*, *Curcuma Longa*, *Ipomoea batatas*, *Moringa oleifera*, *Dracocephalum palmatum*, *Salvia miltiorrhiza*, *Euodia ruticarpa*, and *Erythrina excelsa*. These agents inhibit androgen receptor signaling, downregulate prostate-specific antigen expression, induce apoptosis via PI3K/Akt/mTOR and NF- $\kappa$ B pathway suppression, trigger cell cycle arrest, inhibit metastasis through epithelial-to-mesenchymal transition reversal and matrix metalloproteinase inhibition, and sensitize cells to enzalutamide/docetaxel. Studies demonstrate that these phytochemicals delay prostate-specific antigen progression and improve quality of life. Enhanced bioavailability via nanoparticle delivery further strengthens translational potential. Phytochemicals represent valuable adjuvant strategies for both hormone-sensitive and castration-resistant prostate cancer management.

**Keywords:** Prostate cancer, medicinal plants, phytochemicals, phytopharmacology, preclinical evidence

## 1. Introduction

Prostate cancer (PCa) is the second most prevalent solid tumor/cancer and the fifth leading cause of mortality among men globally. At the early stages, PCa may be asymptomatic, which is why it requires active medical surveillance (Rawla 2019). According to (Gandaglia et al. 2021), family history, race, and hereditary syndromes are well-established risk factors for PCa. Unfortunately, there is little evidence for any clear indication for prevention other than early diagnosis to reduce PCa-associated mortality. Moreover, PCa incidence varies considerably across different continents. Asia is traditionally considered a low-incidence area, but the incidence and mortality of PCa have rapidly increased across the continent (Zhu et al. 2021). There are many factors

contributing to the heterogeneous nature of this cancer. For instance, a study found that genomic alterations in patients of Chinese descent were distinct from those of Western cohorts. Notably, 41% of tumors contained *FOXA1* mutations, and 18% each had deletions in *ZNF292* and *CHD1*. In addition to genome variations, epigenomic alterations were correlated and found to be predictive of disease phenotype and progression (Li et al. 2020). Furthermore, socio-economic factors also determine PCa incidence and mortality. Social determinants such as access to healthcare, socioeconomic status, education, social support, immigration status, and quality of social relations play a pivotal role in PCa stage at diagnosis and survival (Coughlin 2020). Additional elements contributing to PCa

development are individual body mass index and nutritional status. Obesity was also associated with a higher risk of PCa-related mortality (Tzenios, Tazani, and Chahine 2022), whereas dietary interventions are reported to be beneficial for PCa prevention (Matsushita, Fujita, and Nonomura 2020). Moreover, an individual patient may carry genomically and phenotypically distinct primary PCa. Notably, a single clone in the primary tumour may produce lethal metastatic PCa; however, it can also exhibit subclonal heterogeneity at the genomic, epigenetic, and phenotypic levels. This complex web of molecular alterations poses obstacles for the diagnosis and treatment of PCa (Haffner et al. 2021). Even though encouraging trends have been observed in recent PCa epidemiological reports, with decreasing incidence and mortality rate (Wang et al. 2022), a holistic approach encompassing personal, socioeconomic, ethnic, and regional factors is needed to overcome the second most prevalent form of cancer (Siegel et al. 2020, Culp et al. 2020).

## 2. Prostate Cancer Pathophysiology

The prostate is a glandular tissue that produces fluid that constitutes about 25% to 30% of the semen. This prostatic portion of the semen nourishes the sperm, as well as provides alkalinity. Maintain a higher pH. Whereas the seminal vesicles produce the rest of the seminal fluid (Toivanen and Shen 2017). The prostate gland requires androgen (testosterone) to function optimally. This is responsible for the hormonal therapy, i.e., testosterone deprivation therapy efficacy. Notably, castrate-resistant tumors are thought to generate intracellular androgens (Alukal and Lepor 2016).

Cancer originates with a mutation in normal prostate glandular cells, usually starting with the peripheral basal cells (Lee and Shen 2015). PCa, primarily in the peripheral zone, is classified as an adenocarcinoma with glandular patterns. Cancer cells form a localized tumor within the prostate, potentially extending beyond the extension. It

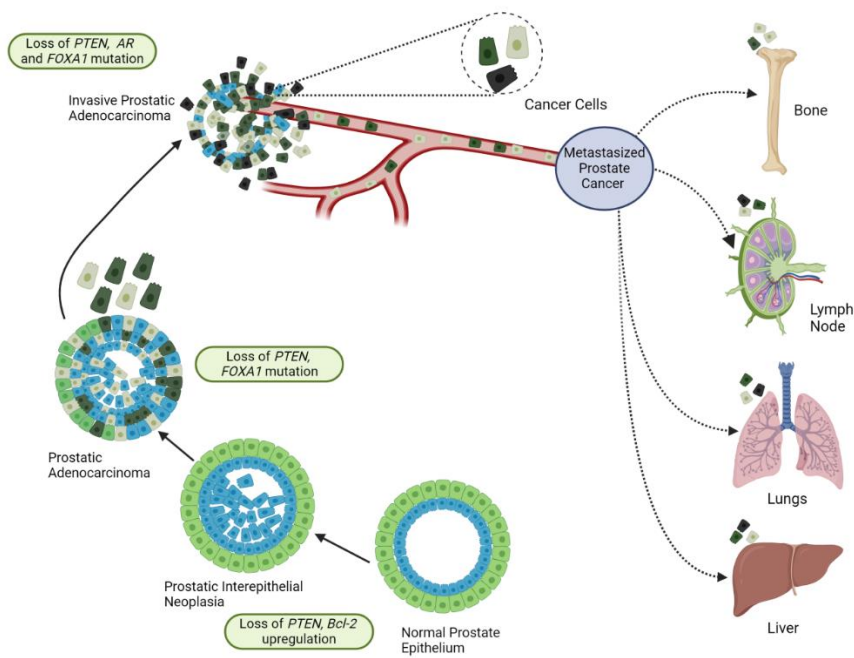
frequently metastasizes to bones and lymph nodes, facilitated by drainage through the prostatic venous plexus into vertebral veins (Skelton 2023). PCa progression involves the transformation of benign epithelial cells into malignant forms, often starting with prostatic intraepithelial neoplasia. High-grade prostatic intraepithelial neoplasia is a significant predictor of PCa occurrence (Brawer 2005). Androgen receptor (AR) activation, driven by testosterone and dihydrotestosterone, is initially crucial for PCa growth. However, elevated serum androgen levels are not directly linked to PCa risk, and low-androgen environments may promote androgen-independent survival of cells (Culig et al. 2002).

In the progression to castration-resistant prostate cancer (CRPC), AR mutations become prevalent, contributing to androgen-independent pathways (Taplin et al. 1995, Tan et al. 2015). Peptide growth factors, such as TGF- $\beta$  and EGF, facilitate AR-regulated proliferation through 'cross-talk' (Zhu and Kyprianou 2008). Reduction in AR activation hypersensitizes alternative pathways like the PI3K-AKT-mTOR pathway (Shorning, Dass, and Smalley 2020). Mutations in the tumor suppressor gene *PTEN* are observed in CRPC, impacting the regulation of the PI3K-AKT-mTOR pathway and increasing cellular proliferation (Heinlein and Chang 2004, Murray 2021).

Moreover, the tumor microenvironment also plays a pivotal role in PCa pathogenicity, with studies suggesting interactions between tumor cells and immune cells (Krammer 2000). Apoptosis regulation is disrupted in aggressive PCa, involving intrinsic and extrinsic pathways (Debatin and Krammer 2004). Dysregulation of apoptosis, including overexpression of anti-apoptotic factors like *Bcl-2*, contributes to chemoradiotherapy resistance (McKenzie and Kyprianou 2006, McCarty 2004).

## 3. Current Therapeutic Agents, Strategies, and Associated Challenges

Over the past two decades, there have been noteworthy advancements in the understanding



**Figure 1: Histopathological and molecular progression of human prostate cancer.**

and treatment of metastatic PCa, particularly in metastatic CRPC (mCRPC). Fortunately, this progress has led to extended survival and improved quality of life for affected individuals. However, challenges persist, including tumor heterogeneity and acquired resistance, which hinder the achievement of lasting remissions and cures (Yamada and Beltran 2021).

PCa, primarily androgen-driven, has been treated with ADT since the 1940s. ADT involves lowering testosterone production through surgical or medical castration. However, certain challenges are associated with ADT, warranting a risk-benefit analysis (Yamada and Beltran 2021). A 14-member panel comprised of urologists, urologic oncologists, and medical oncologists recommended vigilant monitoring of PCa patients undergoing ADT to detect the shift from castrate-sensitive to CRPC early. Moreover, they emphasized on identification and management of ADT side effects, along with quality of life. This becomes crucial as combinatorial therapeutic approaches with ADT become more prevalent, necessitating optimized patient care (Shore et al. 2020).

In solid tumors, the first demonstration of an improvement in overall survival was provided by olaparib in patients with mCRPC harboring homologous recombination repair deficiencies. Despite a major breakthrough, a number of issues relating to Poly (ADP-ribose) polymerase (PARP), inhibitors remain (Teyssonneau et al. 2021). However, response to PARP inhibition is influenced by specific homologous recombination DNA repair genes HR gene alterations, with higher responses observed in *BRCA* and *PALB2* compared to *CDK12* or *ATM* (de Bono et al. 2020). *ATM*-mutated PCa may be less responsive to PARP inhibitors and could be more amenable to ATR (Ataxia Telangiectasia and Rad3-Related) inhibition or combined ATR and PARP inhibition (Neeb et al. 2021). *CDK12* alterations may be less responsive to PARP inhibition but have shown associations with immunotherapy responses (Antonarakis et al. 2020). Moreover, in situations where PARP inhibitors are not available or not suitable, platinum chemotherapy can be considered, especially in patients with *HR* gene deficiency. Furthermore, a trial investigated the combination of abiraterone, enzalutamide,

docetaxel, and cabazitaxel showing a significant radiographic PFS benefit in patients with *PTEN* loss (Welti et al. 2018). However, serious adverse events were observed, emphasizing the need for careful consideration of risks and benefits (Yamada and Beltran 2021).

On the other hand, the growing array of drugs for metastatic PCa raises questions about the optimal sequence of therapies. For patients previously treated with docetaxel and androgen receptor pathway inhibitors (ARPIs), the CARD trial provides level one evidence supporting the use of cabazitaxel. This trial demonstrated improved progression-free survival and overall survival with cabazitaxel compared to another ARPI in patients who had progressed after docetaxel and ARPI therapy (de Wit et al. 2019). However, routine sequential use of ARPIs may not be supported, especially if other life-prolonging therapies are available. The earlier use and longer exposure to ARPIs in metastatic hormone-sensitive PCa and non-metastatic CRPC settings may also influence downstream resistance patterns, including the development of AR-independent variants (Yamada and Beltran 2021).

#### 4. Plant-Based Anti-Prostate Cancer Treatment

Plants continue to play a pivotal role in discovering novel drugs, drug leads, and chemical compounds. The field of plant-based drug discovery has predominantly yielded advancements in the development of anti-cancer and anti-infectious agents. Moreover, ongoing efforts in this area persistently generate promising leads that advance into clinical trials. Expanding on this trajectory, the following examples highlight plants and Phytocompounds with the potential to contribute to PCa therapeutic strategies.

##### 4.1. *Tamarix articulata*

A study conducted by (Alnuqaydan et al. 2022, Skelton 2023) investigated the anti-cancer potential of *Tamarix articulata* (Tamaricaceae), commonly known as Athel tamaris. In vitro

evaluation *T. articulata* leaf extract exhibited a significant decrease in cell viability and clonogenic properties, as well as abrogated the motility and invasive properties of PCa cell model (LnCaP cells). The methanolic extract of *T. articulata* demonstrated these effects at the dose of 245-289µg/ml. In addition, the extract of *T. articulata* down-regulated the protein expression P13K-Akt, TGF-β-SMAD2/3 and its downstream proteins MMP-2, MMP-9, and MET-associated proteins snail and vimentin. Moreover, the results showed an up-regulation of tight junction protein expression, such as E-cadherin and TIMP1. The study concluded that *T. articulata* possesses anti-PCa properties (Alnuqaydan et al. 2022).

##### 4.2. Hesperidin

Hesperidin is a plant-based molecule that is usually derived from citrus fruits. It is known to have numerous medicinal properties, including efficacy against human PCa cells. In a study with the objective of evaluating hesperidin's anti-proliferation potential, the evaluation revealed that in vitro treatment of PCa cells led to significant cell growth and viability reduction in a dose-dependent manner. Furthermore, this inhibition occurred due to cell cycle arrest and necrosis-like apoptotic cell death induced by reactive oxygen species generation, following hesperidin treatment (Ning et al. 2020).

##### 4.3. *Castanea sativa*

In another study, two prostate cell lines (DU145 and PC3) were used to assess the apoptosis-mediated anticancer activity of tryptophan-derived endogenous metabolite kynurenic acid (KYNA) and of the lactam form of 3-2'-pyrrolonidinyl-kynurenic acid (3-PKA-L) from *Castanea sativa* (Fagaceae). Notably, in all experiments, 3-PKA-L exhibited anticancer activity in the high concentration range (0.01 mM – 1 mM) from 24 to 72 h. Moreover, the results revealed an extrinsic apoptosis-mediated cell death, induced by 3-PKA-L. This study concluded that 3-PKA-L has more potent anti-proliferation qualities than KYNA, which is why it should be

further tested for PCa treatment (Beretta et al. 2021).

#### 4.4. *Paris forrestii*

*Paris forrestii*, belonging to family Melanthiaceae, is a unique plant found in Tibet and Yunnan, China. In a study by (Xia et al. 2020), the antitumor activity of *P. forrestii* on PCa cells was evaluated. The extract displayed a potent anticancer activity toward PCa, similar to that of pure saponins from *P. forrestii*. However, it was less effective in suppressing the human normal prostate epithelial cell line RWPE. Furthermore, at 4 µg/mL *P. forrestii* significantly decreased proliferation and induced apoptosis in cancer cells. At the dose of 2 µg/mL, the *P. forrestii* rhizome extract significantly suppressed the migration and invasion of cancerous prostate cells. To explore the molecular mechanisms, PCa cells (LNCAP and PC3 cell lines) were treated with a 5 µg/mL *P. forrestii* dose and analyzed using transcriptomics. By using q-PCR, the expression levels of *NEAT1*, *MALAT1*, *TIPIN*, *LYAR*, *IQGAP3*, *GINS2*, and *ZGRF1* were validated as consistent with microarray data, suggesting that these genes might participate in the anticancer effect produced by the extract (Xia et al. 2020).

#### 4.5. *Crateva adansonii*

*Crateva adansonii* (Capparaceae) is a shrub used to treat tumors in Cameroon. A study was done to establish the ethnopharmacological basis of this shrub by determining the bioactive components and elucidating the underlying mechanism involved. Following the treatment of pancreatic cancer cell lines by *C. adansonii* Dichloromethane-methanol extract, daucosterol (steroid saponin) was identified as a major anticancer principle. It significantly inhibited LNCaP, DU145, and PC3 prostate carcinoma cell growth and proliferation at a concentration of 1 µg/mL. Notably, it increased the number of late apoptotic (DU145) and apoptotic (PC3) cells. Moreover, cell cycle proteins (cdk1, pcdk1, cyclin A and B) were down-regulated in DU145 and PC3 cells. However, only cdk2 was down-regulated in PC3 cells. Moreover, the anti-apoptotic Akt, pAKT and Bcl-2 proteins

were also down-regulated, while up-regulating the pro-apoptotic protein Bax. Additionally, daucosterol decreased chemotaxis and cell migration, while it increased cell adhesion to fibronectin and collagen matrix, inducing anti-metastasis effects (Zingue et al. 2020).

#### 4.6. *Biarum bovei*

The *Biarum* species (Kardeh) has been a part of Middle Eastern and Persian traditional functional food and medicine for decades. An investigation into medicinal properties, including anti-cancer activities of methanol extracts of *B. bovei* leaves and corm, was conducted by (Wahab et al. 2023). In-vitro evaluation showed that the extracts exhibited significant anticancer activity against DU-145 (PCa cells) with IC<sub>50</sub> values ranging between 22.73–44.24 µg/ml. Moreover, rats fed on a 2000 mg/kg dosage of the extract showed no toxicological sign or serum biochemical changes. These results make *B. bovei* an attractive candidate for further chemotherapeutic explorations (Wahab et al. 2023).

#### 4.7. *Curcuma Longa*

*Curcuma longa* (Zingiberaceae) has a long list of therapeutic uses. A study explored the anti-PCa efficacy of *C. longa* components via a systematic approach to reveal the integration effect mechanisms of multiple anticancer compounds against PC3 cells. Three curcuminoids from *C. longa* (curcumin, CUR; demethoxycurcumin, DMC; bisdemethoxycurcumin, BDMC) showed significant synergistic anticancer activities. Moreover, the combination index analysis revealed an additive effect of CUR combined with DMC or BDMC, while a combination of all three curcuminoids at a ratio of 1:1:1 led to superior synergistic effects. Furthermore, glycoproteomics and proteomics demonstrated that different curcuminoids regulate various protein pathways, such as ribosome, glycolysis/gluconeogenesis, biosynthesis of amino acids, and a combination of CUR, DMC, and BDMC exhibited the most powerful effects on down-regulation of protein expression (Wei et al. 2021).

**Table 1: Medicinal plants and phytochemicals with activity against prostate cancer.**

Plant	Family	Common Name	Part Used	Chemical Constituent	Dose/Binding Energy	Extract	Study Type/Target	Citation
<i>Tamarix articulata</i>	Tamaricaceae	Athel Tamaris/Athel	Leaves	NA	245-289 µg/ml	Methanolic	In vitro	(Alnuqaydan et al. 2022)
<i>Citrus sinensis</i>	Rutaceae	Citrous fruits	Fruit peel	Hesperidin	150 µM	NA	In vitro	(Ning et al. 2020)
<i>Castanea sativa</i>	Fagaceae	Sweet chestnut	Chestnut honey	3-PKA-L	NA	NA	In vitro	(Beretta et al. 2021)
<i>Paris forrestii</i>	Melanthiaceae	Takht	Dry Rhizome	Saponins glycosides	and 2-5 µg/ml	Ethyl acetate	In vitro	(Xia et al. 2020)
<i>Crateva adansonii</i>	Capparaceae	Garlic pear/Varun	shrub	Daucosterol	1 µg/mL	Dichloromethane-methanol	In vitro	(Zingue et al. 2020)
<i>Biarum bovei</i>	Araceae	Kardeh	Leaves and corms	Fatty phyosterols, alcohols, etc	In vitro: 22.73–44.24 µg/mL In vivo: 2000 mg/kg	Methanolic	In vitro and in vivo	(Wahab et al. 2023)
<i>Curcuma Longa</i>	Zingiberaceae	Turmeric	Rhizome	Curcuminoids (CUR, DMC, BDMC)	NA	NA	In vitro	(Wei et al. 2021)
<i>Ipomoea batatas</i>	Convolvulaceae	Morning-glories	Aerial part	Triterpenoid (Nummularic Acid)	In vitro: 3–50 µM In vivo: 10 mg/kg	Ethyl acetate	In vitro and in vivo	(Majid et al. 2022)
<i>Moringa oleifera</i>	Moringaceae	Sohanjan	Leaves	NA	198.53 µg/mL	Methanolic	In vitro	(Khan et al. 2020)
<i>Dracocephalum palmatum</i>	Lamiaceae	Dragonhead	Dried leaves	Flavonoids phenols	and NA	-	In vitro	(Lee et al. 2020)
<i>Salvia miltiorrhiza</i>	Labiatae	Red sage	Whole plant	NA	In vitro: 6.25–12.5 µg/mL In vivo: 500 mg/kg	Ethanollic	In vitro and in vivo	(Bae et al. 2020)
<i>Euodia ruticarpa</i>	Rutaceae	Wu Zhu Yu	NA	Rutaecarpine	7 mg, 35 mg, and 70 mg/kg b.w./day	NA	In vivo	(Lin and Yeh 2021)
<i>Erythrina excelsa</i>	Fabaceae	NA	Stem bark	Excelsanone	1, 10, and 20 µg/mL	Ethyl acetate	In vitro	(Cbaweng et al. 2020)

#### 4.8. *Ipomoea batatas*

*Ipomoea batatas* (Convolvulaceae) is a medicinal food plant used in ethnomedicine for centuries. In an in vitro study, the antiproliferative potential of nummularic acid from *I. batatas* was studied against PCa cells (DU145 and PC3). Moreover, Sprague Dawley rats were used to gauge the in vivo anti-cancer ability of nummularic acid. The findings of the study revealed a significant time- and dose-dependent reduction in proliferation of PCa cells, reduced migration, invasion, and increased apoptotic cell population, following the treatment (3–50 µM). After 72 h of nummularic acid treatment, a significant IC<sub>50</sub> of 21.18 ± 3.43 µM against DU145, and 24.21 ± 3.38 µM against PC3 cells in comparison to the controls cabazitaxel (9.56 ± 1.45 µM and 12.78 ± 2.67 µM) and doxorubicin (10.98 ± 2.71 µM and 15.97 ± 2.77 µM) were observed. In Sprague Dawley rats, nummularic acid treatment exhibited a potential increase in prostate weight compared to the control. Multi-dose treatment with nummularic acid (10 mg/kg) significantly reduced the prostate size in comparison to the control. Moreover, nummularic acid-treated groups exhibited

substantial restoration of hematological and histological parameters, all point to nummularic acid as a novel small molecule with a strong pharmacokinetic and therapeutic profile. The mechanistic probe revealed that nummularic acid treatment considerably increased the cleavage of caspases and downstream PARP, up-regulated BAX and P53, and down-regulated BCL-2 and NF-κB, inducing apoptosis in PCa cells (Majid et al. 2022).

#### 4.9. *Moringa oleifera*

In a study conducted by (Khan et al. 2020) *Moringa oleifera* (Moringaceae) methanolic leaves extract was evaluated for its role in Notch signaling pathway inhibition in human PCa cell (DU145) line. The leaf extract induced marked morphological and nuclear alterations in a concentration-dependent manner, significantly inhibiting cell survival. The IC<sub>50</sub> value of the extract for DU145 cells was observed to be 198.53µg/mL, 24 h post-treatment. Furthermore, an up-regulation of *Bax* expression with concurrent down-regulation of the *Bcl-2* gene induced apoptosis. Moreover, the extract suppressed the abnormal Notch signaling

pathway via down-regulation of *Notch-1* and *Hes-1* expression (Khan et al. 2020).

**4.10. *Dracocephalum palmatum*** *Tamarix Dracocephalum palmatum* (Lamiaceae) is an eastern Russian medicinal plant traditionally used by nomadic people; however, research on this plant remains limited. A study on the anticancer potential of the dried leaves of *D. palmatum* using PC-3 cells revealed that the extract caused apoptosis, in addition to intracellular ROS-independent anticancer effects on PCa cells. The molecular mechanism assessment exhibited an increased SOD-2, cleaved caspase-8, and cleaved-PARP expression and inhibited p-AKT signaling. These results make *D. palmatum* a promising candidate for further research and development (Lee et al. 2020).

**4.11. *Salvia miltiorrhiza*** To assess the anti-proliferative activity of *Salvia miltiorrhiza* (Labiatae), the CRPC cell line DU-145, in vitro and in vivo models were utilized by (Bae et al. 2020). After treatment with the ethanol extract *S. miltiorrhiza* plant, a dose-dependent decrease in cell number of DU-145 cells was observed, as DNA laddering analysis indicated DU-145 cell apoptosis. Moreover, the *S. miltiorrhiza* extract increased p53 and reduced Bcl-2 protein expression. The levels of prostate-specific antigen were also considerably reduced in *S. miltiorrhiza-treated* group compared to the controls. Similarly, a decrease in androgen receptor expression was observed in the extract-treated cells. For in vivo evaluation, Six-week-old male BALB/c nude mice were randomly divided into a normal control group (n=101) and a treated group (n=101) administered 500 mg/kg *S. miltiorrhiza* for 2 weeks, and their tumor volumes were measured. The one-dose-per-day treatment with the extract, given over 2 weeks, significantly inhibited tumor growth (Bae et al. 2020).

**4.12. *Euodia ruticarpa*** *Euodia ruticarpa* (Rutaceae), a Chinese herbal medicine used for treating various cancers, is a rich source of the alkaloid rutaecarpine. With the

aim of evaluating rutaecarpine effects in vivo in PCa cells, a study was done. For this purpose, C57BL/6J male mice (8 weeks old) were randomly grouped (n = 9), subcutaneously loaded with TRAMP-C1 PCa cells. This was followed by rutaecarpine administration, dissolved in soybean oil, at 7 mg (low dose), 35 mg (medium dose), and 70 mg/kg b.w./day (high dose) for successive 39 days, given by gavage. In a dose-dependent manner, rutaecarpine reduced both tumor volume and solid PCa weight in allogenic TRAMP-C1 male mice. Notably, it increased (TNF- $\alpha$ +IFN- $\gamma$ ) (Th1-)/IL-10 (Th2-) cytokine secretion ratios by splenocytes and TNF- $\alpha$  (M1-)/IL-10 (M2-) cytokine secretion ratios by macrophages as compared to those of the dietary control group, suggesting that in vivo rutaecarpine regulated the immune balance toward Th1- and M1-polarized characteristics. After rutaecarpine treatment, CD19+, CD4+, and CD8+ lymphocytes in the peripheral blood of allogenic TRAMP-C1 mice were significantly elevated. Tumor weights in mice positively correlate with TNF- $\alpha$  secretion, indicating tumor cachexia. Conversely, there's a negative correlation with Th1-antibody (IgG) levels, suggesting that a stronger Th1-polarized immune balance may inhibit PCa cell growth. The study concluded that rutaecarpine inhibits PCa cell growth in mice, and correlated the anti-cancer effects with Th1-polarized immune balance in vivo (Lin and Yeh 2021).

**4.13. *Erythrina excelsa*** The stem bark of *Erythrina excelsa* (Fabaceae) yielded a novel isoflavonoid, excelsanone (2), which were further studied by (Gbaweng et al. 2020). Excelsanone, from the ethyl acetate fraction of *E. excelsa*, induced significant concentration-dependent inhibition of DU145 cell growth at 1, 10, and 20  $\mu$ g/ml. The study underscored *Erythrina* species as rich sources of secondary metabolites, highlighting the cytotoxic potential of excelsanone and its potential as an active principle. Further research is warranted to elucidate the mechanism behind excelsanone's cytotoxic effects (Gbaweng et al. 2020).

## 5. Recommendations and Conclusions

This review underscores the promising role of anticancer phytochemicals and medicinal plants in PCa management, highlighting their multifaceted mechanisms including apoptosis induction, cell cycle arrest, anti-angiogenesis, and androgen receptor modulation. Compounds such as kynurenic acid and the lactam form of 3-2'-pyrrolonidinyl-kynurenic acid, hesperidin, and medicinal plants such *Tamarix articulata*, *Castanea sativa*, *Paris forrestii*, *Crateva adansonii*, *Biarum bovei*, *Curcuma Longa*, *Ipomoea batatas*, *Moringa oleifera*, *Dracocephalum palmatum*, *Salvia miltiorrhiza*, *Euodia ruticarpa*, and *Erythrina excelsa* demonstrate the potential of attenuating resistance and toxicity. Preclinical and early-phase clinical evidence support their efficacy in reducing prostate-specific antigen levels, tumor burden, and metastasis in PCa models. However, translational gaps persist: bioavailability limitations, variable dosing, and heterogeneous patient responses necessitate optimized formulations (e.g., nanoparticles, liposomes) for enhanced delivery. We recommend prioritizing large-scale, multicenter randomized controlled trials to validate efficacy and safety profiles, stratified by Gleason score and genetic markers (e.g., BRCA mutations). Integration into personalized medicine frameworks, guided by pharmacogenomics, could optimize therapeutic outcomes. Regulatory bodies should expedite approval pathways for standardized phytopharmaceuticals.

In conclusion, phytochemicals and medicinal plants offer a cost-effective, low-toxicity adjunct to the PCa armamentarium, fostering holistic, integrative oncology. Sustained interdisciplinary research will bridge bench-to-bedside divides, potentially revolutionizing PCa prognosis and quality of life for millions worldwide.

### Conflict of Interest

The authors declare that they have no competing interests.

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### Consent Forms

NA

### Authors' Contribution

NS and GL performed the literature search and manuscript preparation. GL conceptualized the study and supervised it. NS & GL refined the manuscript for publication. The authors read and approved the final manuscript for publication.

### Data Availability

All the relevant data of this manuscript is available from the authors.

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