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Review

Understanding the Anti-Cancer Effects of Phytochemicals on Prostate Cancer: A Promising Leads for Drug Discovery in Medicine

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Abstract

Prostate cancer is a common tumor and is mainly found in the prostate tissue. Prostate cancer was the second most frequent cancer after lung cancer, and in 2020 it was the fifth cause of cancer in men around the world. Phytochemicals are natural compounds found in many types of medicinal plants, vegetables, and fruits. The aim of this review is to collect and analyze scientific information on phytochemicals with potential on prostate cancer and to highlight their therapeutic role in the treatment of prostate cancer with their underlying molecular mechanisms of action. In this study, we searched the PubMed, Google Scholar, Google, and Scopus databases to gather scientific information about phytochemicals with medicinal properties for prostate cancer using the terms prostate cancer, phytochemical, herbal medicine, medicine, and biological activity. The scientific analysis of the data in this review has shown that the medicinal importance of auriculasin, calycopterin, crebanine, denbinobin, irigenin, isolinderalactone, neobavaisoflavone, nodakenin, obacunone, pachypodol and tectochrysin are medically important due to their antiproliferative activity against cancer of the prostate. However, analysis of scientific data has also revealed other molecular mechanisms in medicine related to its effectiveness on prostate cancer. The scientific data in this review revealed the anticancer effects of a large number of phytochemicals in medicine against prostate cancer.

Keywords: Prostate cancer, medicine, pharmacological, phytochemical

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Plants and plant-based products derived from them have always been excellent sources of natural antioxidants. Numerous dietary supplements, nutraceuticals and cosmetic products are prepared from plants and their pure phytochemicals. In addition, many modern drugs, such as morphine, papaverine, vinblastine, vincristine, and ephedrine, are also derived from natural products.[1–3] We use different types of plant products in our daily life as food and medicine.[4] The development of a new class of natural products including food products in the field of food science and technologies for the treatment of human disorders is constantly increasing.[5,6] Clinicians and researchers have discovered the biological applications of traditional medicine in global health. Populations in Africa and Asia used traditional medicine for their primary health care.[7,8] Plants contain many active phytochemicals, commonly known as secondary metabolites, which occupy a special place in modern medicine.[9,10] Phytochemicals are present in various parts of vegetables, herbs, fruits and seeds and are considered to be the most advanced source of mol-

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ecules against human diseases.[11,12] Phytochemicals have been used for the treatment and prevention of human health complications and are equally important for plants. Plant compounds can be used as medicine for medicine due to higher biological activity and low toxicity.[13–15] The chemical diversity of phytochemicals has attracted the attention of scientists in the development of newer and more effective medicines against human diseases.[16] Alkaloids, phenols, flavonoids, terpenes, steroids, and volatile oils are good examples of secondary metabolites and their derived by-products that have been discovered to exist in plants.[17–19] The health benefits of consuming polyphenols have been suggested to be due to their antioxidant properties.[20]

Prostate Cancer

Prostate cancer is the second leading cause of cancer deaths among men in the US, and incidence and mortality rates are highest in men of African ancestry. An estimated 268,000 new cases of prostate cancer were diagnosed in 2022 in the United States alone.[21–23] Prostate cancer has caused a huge health burden on the Chinese population.[24] The incidence of prostate cancer varies widely across different regions, with the most heightened rates reported in North America, Australia, and Northern Europe.[25] Worldwide, an estimated 1,414,259 new cases and 375,304 deaths were linked to prostate cancer in 2020. The prevalence of prostate cancer varies across different countries, with higher rates found in Eastern countries.[26] Prostate cancer is the most common type of cancer in men and is the second leading cause of death among males after lung cancer.[27–30] According to the latest World Health Organization (WHO) classification of tumors, prostate cancer can be subclassified according to histological types, subtypes, and growth patterns. While approximately 95% of patients are diagnosed with conventional acinar adenocarcinoma, commonly called conventional prostate cancer.[31] Radical prostatectomy (RP) is one of the main treatment options for men with localized prostate cancer.[32] Prostate cancer is the most common cancer and the second leading cause of cancer-related deaths among Australian males. Prostate cancer is more prevalent in older men, who also have more multimorbid conditions than younger men.[33] Prostate cancer is a common male malignant tumor that mainly occurs in the prostate tissue. Prostate cancer usually grows slowly, with early symptoms being unclear and may lead to symptoms such as frequent urination, urgency, and pain. Currently, small molecule drugs for the treatment of prostate cancer mainly include three categories: androgen receptor (AR) antagonists, targeted therapy drugs, and chemotherapy drugs.[34] Prostate cancer is one of the most serious diseases threatening the health of elderly men, and it is also the second deadliest cancer in men. The diagnostic process of prostate cancer relies on clinical evaluation, laboratory tests, and medical imaging techniques.[35] There is also evidence that environmental or occupational exposure to pesticides may increase risk of prostate cancer.[36] Prostate cancer is a malignant epithelioid tumor with a high risk of bone metastasis. The molecular mechanisms underlying prostate cancer development are complex, whose basic reason is a genetic imbalance.[37] Currently, Prostate-Specific Antigen (PSA) is commonly used as a diagnostic marker for prostate cancer assessment, together with digital rectal examinations (DRE) and Magnetic Resonance Imaging (MRI).[38] During advanced stages of the disease skeletal metastasis is common.[39] Current treatment options for prostate cancer include surgical removal, radiation therapy, hormonal therapy, or chemotherapy.[40]

Biological Potential of Phytochemicals on Prostate Cancer

Calycopterin

Calycopterin is an important phytochemical purified from *Dracocephalum kotschyi*. The cytotoxic property of calycopterin in HepG2 cells has been investigated and revealed its cytotoxicity via mitochondrial dysfunction and PI3K/Akt and Mitogen-activated protein kinase (MAPK) signaling.[41] Calycopterin can induce preferential antiproliferative effects on cancer cells, including leukemia, colon carcinoma, gastric adenocarcinoma, osteosarcoma, and fibrosarcoma.[42] The biological potential of calycopterin was investigated based on its apoptotic effects on two prostate cancer cell lines *in-vitro*. Calycopterin treatment reduced to 50% cell viability compared to the control group. However, calycopterin treatment of healthy human umbilical cord endothelial cells (HUVECs) did not cause any significant reduction in cell viability. Moreover, after 14 days, colony size and numbers reduced significantly in calycopterin treated cells. A significant decrease in the migration ability was also observed in both lines subjected to calycopterin after 48 h suggesting the apoptotic and anti-metastatic effects of calycopterin in both hormone-dependent and independent prostate cancer cell lines.[43]

Irigenin

Irigenin is an active phytochemical of *Belamcanda chinensis* and Rhizoma Belamcandae.[44–47] RWPE-1, LNCaP and PC-3 cells were treated with or without an extract of *Belamcanda chinensis*, irigenin and tectorigenin. Irigenin alone decreased the cell number in all 3 cell lines. Irigenin inhibited the proliferation of RWPE-1, LNCaP and PC-3 cells, causing G1 arrest and the induction of p21WAF1 or p27 protein expression. Studies signified the role of irigenin in regulating prostate cancer cell number by inhibiting proliferation through cell cycle regulation.[48]

Isolinderalactone

Isolinderalactone showed anticancer potential on A549 lung cancer cells.[49] Isolinderalactone could induce apoptosis in the human breast cancer MDA-MB-231 cell line.[50] Biological potential of isolinderalactone isolated from the dried root of *Lindera aggregate* for their antitumor activities in human ovarian cancer cells has been investigated. Isolinderalactone caused cell death in SKOV-3 and OVCAR-3 cells and increased the cell proportion in the subG1 phase. Additionally, isolinderalactone significantly induced mtSO production and reduced reactive oxygen species (ROS) production. Moreover, isolinderalactone downregulated mitochondrial membrane potential and the expression levels of anti-apoptotic Bcl-2 family proteins and superoxide dismutase (SOD). Isolinderalactone induces cell death by upregulation of mtSO, downregulation of mitochondrial SOD2, and inactivation of the STAT3-mediated pathway.[51]

Tectochrysin

Biological potential of tectochrysin at the concentrations of 0-20 µg/ml on prostate cancer cell line 22Rv.1 and normal prostate cell RWPE-1 have been investigated. Tectochrysin significantly inhibited the proliferation activity of 22Rv.1 cells and induced their apoptosis, and promoted the expressions of genes dr4, dr5, trail, p53, caspase-3, caspase-8, caspase-9, bid, bax and foxo3. Further, it also inhibited the expressions of akt, pi3k and bcl-2. Tectochrysin can induce prostate cancer cells apoptosis through affecting tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) and PI3K/AKT signaling pathways, which signified their anti-prostate cancer activity.[52]

Crebanine

Chemo-sensitizing effects of crebanine in ovarian cancer cells have been investigated. Crebanine increased the sensitivity of cisplatin in intrinsic cisplatin resistant SKOV3 cells, but not in cisplatin sensitive A2780 cells. Chemo-sensitizing effects of crebanine in SKOV3 cells were mediated via activating apoptosis-induced cell death through caspase-3, -8 and cleaved poly ADP-ribose polymerase (PARP). Akt/NF-κB signaling was blocked by crebanine leading to increased sensitization to cisplatin.[53]

Pachypodol

Pachypodol is found to be present in *Pogostemon cablin*.[54] Biological potential of pachypodol (10 mg/kg) against perfluorooctane sulfonate (PFOS)-induced testicular toxicity in adult male rats has been investigated on Sprague-Dawley rats. Pachypodol treatment potently alleviated all the impairments in testes against PFOS-induced testicular toxicity. Further, free-radical scavenging potential of pachypodol against the PFOS-instigated testicular dysfunctions signifying its biological potential in the medicine.[55]

Denbinobin

Biological potential of denbinobin from *Dendrobium nobile* for their inhibitory potential on prostate cancer cell migration has been investigated. Denbinobin inhibited Rac1 activity which prevented lamellipodial formation. Cortactin phosphorylation and translocation to the lamellipodia were also impaired, and PC3 cells were unable to migrate which indicate that denbinobin prevents CXCL12-induced PC3 cell migration by inhibiting Rac1 activity.[56]

Neobavaisoflavone

Biological potential of neobavaisoflavone and psoralidin for their cytotoxic and apoptotic effects have been investigated in combination with TRAIL on LNCaP prostate cancer cells. Neobavaisoflavone and psoralidin sensitized TRAIL-resistant cells and markedly augmented TRAIL-mediated apoptosis and cytotoxicity in prostate cancer cells. Cotreatment of LNCaP cells with 100 ng/ml TRAIL and 50 µM neobavaisoflavone or 50 µM psoralidin increased the percentage of the apoptotic cells which revealed its potential role in prostate cancer.[57]

Auriculasin

Auriculasin is a major components of the *Maclura pomifera* and *Flemingia philippinensis*.[58–60] Auriculasin is isolated from *Flemingia philippinensis* Merr. and Rolfe. Auriculasin induced DNA fragmentation and chromatin condensation in lymph node carcinoma of the prostate (LNCaP) prostate cancer cells.[61] Auriculasin induces ROS-mediated apoptotic cell death, suppresses angiogenesis and sensitizes TRAIL-resistant primary prostate cancer cells to TRAIL-mediated apoptosis.[62] Auriculasin, has been associated with anticancer effects in humans and mice.[63] Auriculasin demonstrated a potential biological effect on dopamine activity.[64] Combined treatment with auriculasin and TRAIL at optimal concentrations resulted in tumor-specific apoptotic cell death in RC-58T/h/SA#4 cells.[65] Auriculasin derived from *Flemingia philippinensis*, induces significant cell death and apoptosis via ROS generation in prostate cancer cells. Auriculasin treatment resulted in selective apoptotic cell death in LNCaP prostate cancer cells, in addition to inhibiting tumor growth in a xenograft mouse model.[66]

Nodakenin

Nodakenin is found to be present in *Angelica gigas* Nakai. Multidrug-resistant phenotype-reversal activities of *Angelica gigas* and its compounds decursin and nodakenin in doxorubicin-resistant NCI/ADR-RES ovarian cancer cells have been investigated. Combination of doxorubicin with either *Angelica gigas* or decursin inhibited a proliferation of NCI/ADR-RES cells.[67]

Obacunone

A non-targeted cell metabolomics strategy has been adopted to reveal the proliferation inhibition mechanism of obacunone on 22RV1 prostate cancer cells. Metabolic description network of obacunone to defense prostate cancer was built. In addition, morphological observation, cell proliferation and apoptosis analysis of 22RV1 human prostate cancer cells were performed to better understand physiopathologic changes after obacunone treatment.[68]

Conclusion

This review was collected and analyzed scientific information on the many classes of phytochemical substances with a drug potential in prostate cancer, and highlighted their therapeutic significance in the treatment of prostate cancer in medicine. All the scientific information of auriculasin, calycopterin, crebanine, denbinobin, irigenin, isolinderalactone, neobavaisoflavone, nodakenin, obacunone, pachypodol and tectochrysin have been collected and analyzed in the present review in order to investigate their therapeutic potential in medicine against prostate cancer. However, the molecular mechanisms of their underlying actions on prostate cancer are also summarized in this review. Scientific data of the present review revealed the biological role of auriculasin, calycopterin, crebanine, denbinobin, irigenin, isolinderalactone, neobavaisoflavone, nodakenin, obacunone, pachypodol and tectochrysin in the medicine for their anti-proliferative activities on prostate cancer (Figure 1-3). However, the scientific evidence in this review also revealed different molecular mechanisms in medicine for efficacy against prostate cancer. However, scientific data on safety profiles must be investigated by scientific research to apply clinical use in medicine. Based on the presented scientific information, it is possible to conclude that these botanical chemicals have potential medicinal applications for prostate cancer. This can be concluded that it can be used for treatment of prostate cancer in the future for its medicinal advantages.

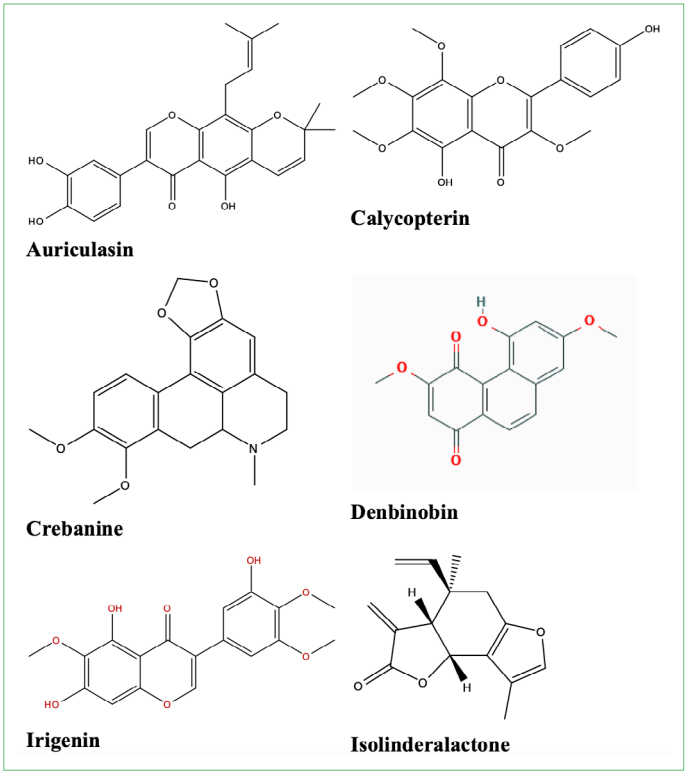

Figure 1. Chemical structure of phytochemicals.

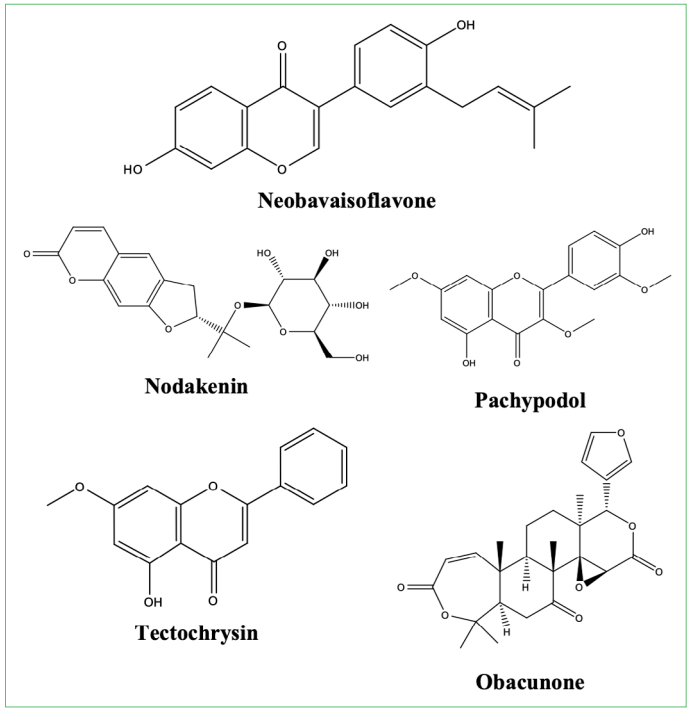

Figure 2. Chemical structure of phytochemicals.

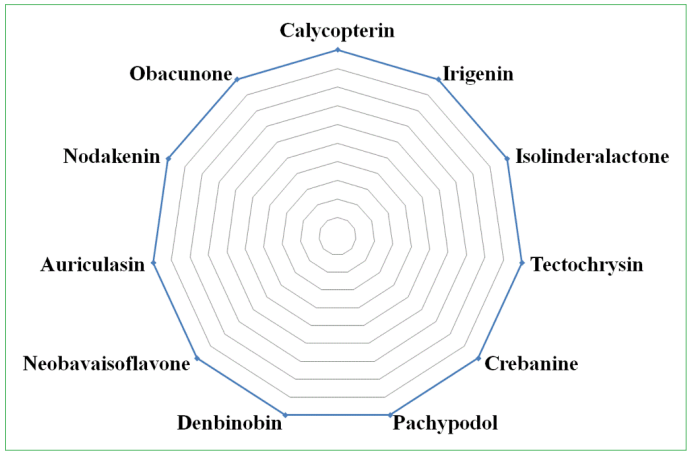

Figure 3. Phytochemicals having effectiveness on prostate cancer.

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References

1. Patel DK, Patel K. An overview of medicinal importance, pharmacological activities and analytical aspects of fraxin from cortex fraxinus. Curr Tradit Med 2023;9:109–115.
2. Patel DK, Patel K. Herbal medicines genkwadaphnin as therapeutic agent for cancers and other human disorders: A review of pharmacological activities through scientific evidence. Curr Tradit Med 2024;10:e230523217251.
3. Patel K, Patel DK. Therapeutic benefit and biological importance of ginkgetin in the medicine: Medicinal importance, pharmacological activities and analytical aspects. Curr Bioact Compd 2021;17:e190721190770.
4. Patel DK. Health benefits, therapeutic applications, and recent advances of cirsilineol in the medicine: Potential bioactive natural flavonoids of genus artemisia. Endocr Metab Immune Disord Drug Targets 2023;23:894–907.
5. Patel K, Patel DK. Health benefits of ipecac and cephaeline: Their potential in health promotion and disease prevention. Curr Bioact Compd 2021;17:206–213.
6. Patel K, Jain A, Patel DK. Medicinal significance, pharmacological activities, and analytical aspects of anthocyanidins 'delphinidin': A concise report. J Acute Dis 2013;2:169–178.
7. Patel DK, Patel K. Biological potential and pharmacological activity of columbianetin in chronic diseases. Drug Metab Bioanal Lett 2023;16:50–58.
8. Patel K, Gadewar M, Tahilyani V, Patel DK. A review on pharmacological and analytical aspects of diosmetin: A concise report. Chin J Integr Med 2013;19:792–800.
9. Patel DK. Therapeutic role of columbianadin in human disorders: Medicinal importance, biological properties and analytical aspects. Pharmacol Res - Mod Chinese Med 2023;6:100212.
10. Patel DK. Biological importance, therapeutic benefits, and analytical aspects of active flavonoidal compounds 'corylin' from psoralea corylifolia in the field of medicine. Infect Disord Drug Targets 2023;23:e250822208005.
11. Patel DK. Health beneficial aspect and therapeutic potential of cirsimaritin in the medicine for the treatment of human health complications. Curr Bioact Compd 2022;18:27–38.
12. Patel DK, Patel K. Potential therapeutic applications of eudesmin in medicine: An overview on medicinal importance, pharmacological activities and analytical prospects. Pharmacol Res Mod Chinese Med 2022;5:100175.
13. Patel DK, Patel K, Dhanabal SP. Development of quality control parameters for the standardization of gymnema sylvestre. J Acute Dis 2012; 1:141–143.
14. Patel DK. Biological importance, therapeutic benefit, and medicinal importance of flavonoid, cirsiliol for the development of remedies against human disorders. Curr Bioact Compd 2022;18:e240821195804.
15. Patel DK. Medicinal importance, pharmacological activities, and analytical aspects of engeletin in medicine: Therapeutic benefit through scientific data analysis. Endocr Metab Immune Disord Drug Targets 2023;23:273–282.
16. Patel DK. Biological importance of bioactive phytochemical 'Cimifugin' as potential active pharmaceutical ingredients against human disorders: A natural phytochemical for new therapeutic alternatives. Pharmacol Res Mod Chinese Med 2023;7:100232.
17. Patel DK. Biological potential and therapeutic benefit of Chrysosplenetin: An Applications of polymethoxylated flavonoid in medicine from natural sources. Pharmacol Res Mod Chinese Med 2022;4:100155.
18. Patel K, Patel DK. Medicinal importance and therapeutic benefit of bioactive flavonoid eriocitrin: An update on pharmacological activity and analytical aspects. Nat Prod J 2024;14:e100723218583.
19. Patel DK, Patel K, Gadewar M, Tahilyani V. Pharmacological and bioanalytical aspects of galangin-a concise report. Asian Pac J Trop Biomed 2012;2:S449–S455.
20. Patel DK, Kumar R, Laloo D, Hemalatha S. Evaluation of phytochemical and antioxidant activities of the different fractions of Hybanthus enneaspermus (Linn.) F. Muell. (Violaceae). Asian Pac J Trop Med 2011;4:391–396.
21. Darst BF, Shen J, Madduri RK, Rodriguez AA, Xiao Y, Sheng X, et al. Evaluating approaches for constructing polygenic risk scores for prostate cancer in men of African and European ancestry. Am J Hum Genet 2023;110:1200–1206.
22. Khan MA, Acharya S, Anand S, Sameeta F, Pramanik P, Keel C, et al. MYB exhibits racially disparate expression, clinicopathologic association, and predictive potential for biochemical recurrence in prostate cancer. IScience 2023;26:108487.
23. Duenweg SR, Brehler M, Lowman AK, Bobholz SA, Kyereme F, Winiarz A, et al. Quantitative histomorphometric features of prostate cancer predict patients who biochemically recur following prostatectomy. Lab Investig 2023;103:100269.
24. Kong F, Wang C, Zhang J, Wang X, Sun B, Xiao X, et al. Chinese herbal medicines for prostate cancer therapy: From experimental research to clinical practice. Chinese Herb Med 2023;15:485–495.
25. Chen D, Hu Y. Approaches for boosting antitumor immu-

nity in prostate cancer therapy: A comprehensive review on drugs, products, and nanoparticles. J Drug Deliv Sci Technol 2023;89:105048.
26. Akhtar S, Hassan F, Ahmad S, El-Affendi MA, Khan MI. The prevalence of prostate cancer in Pakistan: A systematic review and meta-analysis. Heliyon 2023;9:e20350.
27. Khamesi SM, Salehi Barough M, Zargan J, Shayesteh M, Banaee N, Haji Noormohammadi A, et al. Combined anticancer effects of neutron radiation and genistein on prostate cancer cells. J Radiat Res Appl Sci 2023;16:100731.
28. Ayati M, Shiraghaee M, Amini E, Rakhshani N, Sharifi L. A rare case report of muscular metastasis of prostate cancer. Urol Case Reports 2023;51:102619.
29. Dakir EH, Gajate C, Mollinedo F. Antitumor activity of alkylphospholipid edelfosine in prostate cancer models and endoplasmic reticulum targeting. Biomed Pharmacother 2023;167:115436.
30. Xia QD, Zhang SH, Zeng N, Lu YC, Qin BL, Wang SG. Novel androgen receptor inhibitors for metastatic hormone-sensitive prostate cancer: Current application and future perspectives. Biomed Pharmacother 2023;168:115806.
31. Marra G, van Leenders GJLH, Zattoni F, Kesch C, Rajwa P, Cornford P, et al. Impact of epithelial histological types, subtypes, and growth patterns on oncological outcomes for patients with nonmetastatic prostate cancer treated with curative intent: A Systematic review. Eur Urol 2023;84:65–85.
32. van der Slot MA, Remmers S, van Leenders GJLH, Busstra MB, Gan M, Klaver S, et al. Urinary incontinence and sexual function after the introduction of NeuroSAFE in radical prostatectomy for prostate cancer. Eur Urol Focus 2023;9:824–831.
33. Tiruye T, Roder D, FitzGerald LM, O'Callaghan M, Moretti K, Beckmann K. Prognostic value of comorbidity measures among Australian men with non-metastatic prostate cancer. Cancer Epidemiol 2023;87:102482.
34. Zhang JY, Zhao LJ, Wang YT. Synthesis and clinical application of small-molecule drugs approved to treat prostatic cancer. Eur J Med Chem 2023;262:115925.
35. Teng Y, Li W, Gunasekaran S. Biosensors based on single or multiple biomarkers for diagnosis of prostate cancer. Biosens Bioelectron X 2023;15:100418.
36. Hurwitz LM, Beane Freeman LE, Andreotti G, Hofmann JN, Parks CG, Sandler DP, et al. Joint associations between established genetic susceptibility loci, pesticide exposures, and risk of prostate cancer. Environ Res 2023;237:117063.
37. Teng H, Yang B, Su Y, Chen J, Cui L, Sun R, et al. Aminooxyacetic acid hemihydrochloride leads to decreased intracellular ATP levels and altered cell cycle of prostate cancer cells by suppressing energy metabolism. Biomed Pharmacother 2023;167:115605.
38. Spick M, Muazzam A, Pandha H, Michael A, Gethings LA, Hughes CJ, et al. Multi-omic diagnostics of prostate cancer in the presence of benign prostatic hyperplasia. Heliyon 2023;9:e22604.
39. Jimenez-Andrade JM, Ramírez-Rosas MB, Hee Park S, Parker R, Eber MR, Cain R, et al. Evaluation of pain related behaviors and disease related outcomes in an immunocompetent mouse model of prostate cancer induced bone pain. J Bone Oncol 2023;43:100510.
40. Grover P, Nunez-Cruz S, Leferovich J, Wentz T, Bagchi A, Milone MC, et al. F77 antigen is a promising target for adoptive T cell therapy of prostate cancer. Biochem Biophys Res Commun 2023;680:51–60.
41. Esmaeili MA, Farimani MM, Kiaei M. Anticancer effect of calycopterin via PI3K/Akt and MAPK signaling pathways, ROS-mediated pathway and mitochondrial dysfunction in hepatoblastoma cancer (HepG2) cells. Mol Cell Biochem 2014;397:17–31.
42. Moradi M, Gholipour H, Sepehri H, Attari F, Delphi L, Arefian E, et al. Flavonoid calycopterin triggers apoptosis in triple-negative and ER-positive human breast cancer cells through activating different patterns of gene expression. Naunyn Schmiedebergs Arch Pharmacol 2020;393:2145–2156.
43. Lotfizadeh R, Sepehri H, Attari F, Delphi L. Flavonoid calycopterin induces apoptosis in human prostate cancer cells invitro. Iran J Pharm Res 2020;19:391–401.
44. Li S, Li S, Tang Y, Liu C, Chen L, Zhang Y. Ultrafiltration-LC-MS combined with semi-preparative HPLC for the simultaneous screening and isolation of lactate dehydrogenase inhibitors from Belamcanda chinensis. J Sep Sci 2016;39:4533–4543.
45. Li J, Li WZM, Huang W, Cheung AWH, Bi CWC, Duan R, et al. Quality evaluation of rhizoma belamcandae (Belamcanda chinensis (L.) DC.) by using high-performance liquid chromatography coupled with diode array detector and mass spectrometry. J Chromatogr A 2009;1216:2071–2078.
46. Peng C, Liang Y, Wang X, Xie H, Zhang T, Ito Y. Preparative isolation and purification of flavonoids from the Chinese medicinal herb belamcanda by high-speed countercurrent chromatography. J Liq Chromatogr Relat Technol 2009;32:2451–2461.
47. Kang SW, Kim MC, Kim CY, Jung SH, Um BH. The rapid identification of isoflavonoids from belamcanda chinensis by LC-NMR and LC-MS. Chem Pharm Bull 2008;56:1452–1454.
48. Morrissey C, Bektic J, Spengler B, Galvin D, Christoffel V, Klocker H, et al. Phytoestrogens derived from belamcanda chinensis have an antiproliferative effect on prostate cancer cells in vitro. J Urol 2004;172:2426–2433.
49. Abu-Izneid T, Rauf A, Shariati MA, Khalil AA, Imran M, Rebezov M, et al. Sesquiterpenes and their derivatives-natural anticancer compounds: An update. Pharmacol Res 2020;161:105165.
50. Chuang C, Wang L, Wong Y, Lin E. Anti-metastatic effects of isolinderalactone via the inhibition of MMP-2 and up regulation of NM23-H1 expression in human lung cancer A549 cells. Oncol Lett 2018;15:PMC5835907.
51. Rajina S, Kim WJ, Shim JH, Chun KS, Joo SH, Shin HK, et al.

Isolinderalactone induces cell death via mitochondrial superoxide- and STAT3-mediated pathways in human ovarian cancer cells. Int J Mol Sci 2020;21:7530.
52. Wang Y, Ke RJ, Jiang PR, Ying JH, Lou EZ, Chen JY. The effects of tectochrysin on prostate cancer cells apoptosis and its mechanism. Zhongguo Ying Yong Sheng Li Xue Za Zhi [Article in Chinese] 2019;35:283–288.
53. Mon MT, Yodkeeree S, Punfa W, Pompimon W, Limtrakul P. Alkaloids from stephania venosa as chemo-sensitizers in SKOV3 ovarian cancer cells via Akt/NF-κB signaling. Chem Pharm Bull 2018;66:162–169.
54. Zhang J, Zhu M, Zhang J. Pachypodol protects newborn rats from anaesthesia-induced apoptosis in the developing brain by regulating the JNK/ERK pathway. Int J Dev Neurosci 2021;81:633–642.
55. Umar Ijaz M, Rauf A, Mustafa S, Ahmed H, Ashraf A, Al-Ghanim K, et al. Pachypodol attenuates perfluorooctane sulphonate-induced testicular damage by reducing oxidative stress. Saudi J Biol Sci 2022;29:1380–1385.
56. Lu TL, Han CK, Chang YS, Lu TJ, Huang HC, Bao BY, et al. Denbinobin, a phenanthrene from dendrobium nobile , impairs prostate cancer migration by inhibiting Rac1 activity. Am J Chin Med 2014;42:1539–1554.
57. Szliszka E, Czuba ZP, Sedek Ł, Paradysz A, Król W. Enhanced TRAIL-mediated apoptosis in prostate cancer cells by the bioactive compounds neobavaisoflavone and psoralidin isolated from psoralea corylifolia. Pharmacol Reports 2011;63:139–148.
58. Ribaudo G, Vendrame T, Bova S. Isoflavones from maclura pomifera: Structural elucidation and in silico evaluation of their interaction with PDE5. Nat Prod Res 2017;31:1988–1994.
59. Lv HW, Wang QL, Luo M, Zhu MD, Liang HM, Li WJ, et al. Phytochemistry and pharmacology of natural prenylated flavonoids. Arch Pharm Res 2023;46:207–272.
60. Shi X, Zhang G, Ge G, Guo Z, Song Y, Su D, et al. In vitro metabolism of auriculasin and its inhibitory effects on human cytochrome P450 and UDP-glucuronosyltransferase Enzymes. Chem Res Toxicol 2019;32:2125–2134.
61. Noh S, Choi E, Hwang CH, Jung JH, Kim SH, Kim B. Dietary compounds for targeting prostate cancer. Nutrients 2019;11:2401.
62. Fofana S, Ouédraogo M, Esposito RC, Ouedraogo WP, Delporte C, Van Antwerpen P, et al. Systematic review of potential anticancerous activities of erythrina senegalensis DC (Fabaceae). Plants 2021;11:19.
63. Hashemi S, Sharifi A, Zareei S, Mohamedi G, Biglar M, Amanlou M. Discovery of direct inhibitor of KRAS oncogenic protein by natural products: A combination of pharmacophore search, molecular docking, and molecular dynamic studies. Res Pharm Sci 2020;15:226.
64. Wang T, Liu Y, Liu H, Li C, Wang Y. Auriculasin from Flemingia philippinensis roots shows good therapeutic indexes on hyperactive behavior in zebrafish. Biochem Biophys Res Commun 2018;503:1254–1259.
65. Cho HD, Gu IA, Won YS, Moon KD, Park KH, Seo KI. Auriculasin sensitizes primary prostate cancer cells to TRAIL-mediated apoptosis through up-regulation of the DR5-dependent pathway. Food Chem Toxicol 2019;126:223–232.
66. Cho HD, Lee JH, Moon KD, Park KH, Lee MK, Seo KI. Auriculasin-induced ROS causes prostate cancer cell death via induction of apoptosis. Food Chem Toxicol 2018;111:660–669.
67. Choi HS, Cho SG, Kim MK, Kim MS, Moon SH, Kim IH, et al. Decursin in Angelica Gigas Nakai (AGN) enhances doxorubicin chemosensitivity in NCI/ADR-RES ovarian cancer cells via inhibition of p-glycoprotein expression. Phyther Res 2016;30:2020–2026.
68. Xie J, Zhang A, Qiu S, Zhang T, Li X, Yan G, et al. Identification of the perturbed metabolic pathways associating with prostate cancer cells and anticancer affects of obacunone. J Proteomics 2019;206:103447.