Review > Pharmaceutics. 2021 Aug 3;13(8):1195. doi: 10.3390/pharmaceutics13081195.

Inhibitors of the PI3K/Akt/mTOR Pathway in Prostate Cancer Chemoprevention and Intervention

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PMID: 34452154 PMCID: PMC8400324 DOI: 10.3390/pharmaceutics13081195

Free PMC article

Abstract

The phosphatidylinositol 3-kinase (PI3K)/serine-threonine kinase (Akt)/mammalian target of the rapamycin (mTOR)-signaling pathway has been suggested to have connections with the malignant transformation, growth, proliferation, and metastasis of various cancers and solid tumors. Relevant connections between the PI3K/Akt/mTOR pathway, cell survival, and prostate cancer (PC) provide a great therapeutic target for PC prevention or treatment. Recent studies have focused on small-molecule mTOR inhibitors or their usage in coordination with other therapeutics for PC treatment that are currently undergoing clinical testing. In this study, the function of the PI3K/Akt/mTOR pathway, the consequence of its dysregulation, and the development of mTOR inhibitors, either as an individual substance or in combination with other agents, and their clinical implications are discussed. The rationale for targeting the PI3K/Akt/mTOR pathway, and specifically the application and potential utility of natural agents involved in PC treatment is described. In addition to the small-molecule mTOR inhibitors, there are evidence that several natural agents are able to target the PI3K/Akt/mTOR pathway in prostatic neoplasms. These natural mTOR inhibitors can interfere with the PI3K/Akt/mTOR pathway through multiple mechanisms; however, inhibition of Akt and suppression of mTOR 1 activity are two major therapeutic approaches. Combination therapy improves the efficacy of these inhibitors to either suppress the PC progression or circumvent the resistance by cancer cells.

Keywords: PI3K/Akt/mTOR pathway; natural compounds; prostate cancer; small-molecule mTOR inhibitors.

Figures

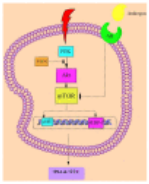

Figure 1 Possible mechanisms from clinical studies...

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