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Coffee diterpenes kahweol acetate and cafestol synergistically inhibit the proliferation and migration of prostate cancer cells

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Abstract

Background: Coffee inhibits the progression of prostate cancer; however, the direct mechanism through which coffee acts on prostate cancer cells remains unclear. This study aimed to identify the key compounds of coffee that possess anti-cancer effects and to investigate their mechanisms of action.

Methods: The anti-proliferation and anti-migration effects of six potentially active types of coffee compounds, including kahweol acetate, cafestol, caffeine, caffeic acid, chlorogenic acid, and trigonelline hydrochloride, were evaluated using LNCaP, LNCaP-SF, PC-3, and DU145 human prostate cancer cells. The synergistic effects of these compounds were also investigated. Apoptosis-related and epithelial-mesenchymal transition-related proteins, androgen receptor in whole cell and in nucleus, and chemokines were assessed. A xenograft study of SCID mice was performed to examine the *in vivo* effect of coffee compounds.

Results: Among the evaluated compounds, only kahweol acetate and cafestol inhibited the proliferation and migration of prostate cancer cells in a dose-dependent manner. The combination treatment involving kahweol acetate and cafestol synergistically inhibited proliferation and migration (combination index < 1) with the induction of apoptosis, the inhibition of epithelial-mesenchymal transition, and decrease in androgen receptor, resulting in the reduction of nuclear androgen receptor in androgen receptor-positive cells. Moreover, kahweol acetate and cafestol downregulated CCR2 and CCR5 without an increase in their ligands, CCL2 and CCL5. The xenograft study showed that oral administration of kahweol acetate and cafestol significantly inhibited tumor growth.

Conclusion: Kahweol acetate and cafestol synergistically inhibit the progression of prostate cancer. These coffee compounds may be novel therapeutic candidates for prostate cancer.

Keywords: androgen receptor; apoptosis; cafestol; kahweol; prostate cancer.

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