

## Abstract

# Celastrol Modulates Lipid Synthesis via PI3K/Akt/mTOR Signaling Axis to finalize Cell Death Response in Prostate Cancer Cells <sup>†</sup>

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**Abstract:** FASN is key enzyme during lipid biogenesis is associated with prostate cancer. In this study, we aim to investigate the potential role of celastrol, root extracts of *Tripterygium wilfordii* on modulation of lipid biosynthesis-associated PI3K/Akt signaling. To determine the effect of celastrol on cell viability, prostate cancer cells were exposed with celastrol in dose dependent manner. AR (+) LNCaP and AR (−) DU145 and PC3 cell viability were inhibited by celastrol with IC<sub>50</sub> in the range of 0.05–1  $\mu$ M. To address the role of celastrol on cell death mechanism, celastrol-treated prostate cancer cells were evaluated with immunoblotting and flow cytometric analysis. Celastrol significantly upregulated PARP and caspase 9 cleavage also increased sub-G1 population. Celastrol also inhibited cell migration and invasion. These effects were associated with decreased PI3K/Akt signaling axis and downregulation of epithelial mesenchymal transition in prostate cancer cells. Likewise, lipid biosynthesis was downregulated with celastrol, however inhibition of PI3K/Akt signaling axis via LY294002 further decrease the cell migration and proliferation rate in prostate cancer cells. Our data suggest that, celastrol suppressed cell proliferation via inhibition of lipid biosynthesis through downregulation of PI3K/Akt signal axis. Targeting lipid metabolism-related enzymes in prostate cancer may offer new avenues for therapeutic approaches.

**Keywords:** celastrol; FASN; prostate cancer



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