Emodin inhibits invasion and migration of prostate and lung cancer cells by downregulating the expression of chemokine receptor CXCR4.


Source

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Abstract

Emodin (ED), an anthraquinone derivative, has been found to inhibit proliferation, induce apoptosis, suppress angiogenesis, impede metastasis, and enhance chemotherapy. However, the detailed mechanism of ED related to the regulation of CXC chemokine receptor-4 (CXCR4) gene expression that affects cellular migration and invasion in prostate and lung cancer cells are not fully understood. Recent evidence indicates that the CXCR4/CXCL12 axis is involved in promoting invasion and metastasis in tumors. Thus, novel agents that can downregulate CXCR4 expression have therapeutic potential in repressing cancer metastasis. Among ED and its derivatives, it is found that ED downregulated the expression of both CXCR4 and HER2 without affecting cell viability in tumor cells. The suppression of CXCR4 expression by ED was found to correlate with the inhibition of CXCL12-induced migration and invasion of both DU145 and A549 cells. Besides, neither proteasome inhibition nor lysosomal stabilization had any effect on ED-induced decrease in CXCR4 expression. The basic molecular mechanisms unveiled that the downregulation of CXCR4 was at the transcriptional level, as indicated by downregulation of mRNA expression and suppression of NF-κB activation. Overall, our findings suggest that ED is a novel blocker of CXCR4 expression and, thus, has enormous potential as a powerful therapeutic agent for metastatic cancer.

PMID:22299827