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### Cancer Therapy

## Boswellic acid inhibits growth and metastasis of human colorectal cancer in orthotopic mouse model by downregulating inflammatory, proliferative, invasive and angiogenic biomarkers

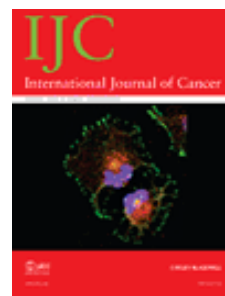
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**Keywords:**

AKBA; colorectal cancer; NF- $\kappa$ B; growth; metastasis

**Abstract**

Numerous cancer therapeutics were originally identified from natural products used in traditional medicine. One such agent is acetyl-11-keto-beta-boswellic acid (AKBA), derived from the gum resin of the *Boswellia serrata* known as Salai guggal or Indian frankincense. Traditionally, it has been used in Ayurvedic medicine to treat proinflammatory conditions. In this report, we hypothesized that AKBA can affect the growth and metastasis of colorectal cancer (CRC) in orthotopically implanted tumors in nude mice. We found that the oral administration of AKBA (50–200 mg/kg) dose-dependently inhibited the growth of CRC tumors in mice, resulting in decrease in tumor volumes than those seen in vehicle-treated mice without significant decreases in body weight. In addition, we observed that AKBA was highly effective in suppressing ascites and distant metastasis to the liver, lungs and spleen in orthotopically implanted tumors in nude mice. When examined for the mechanism, we found that markers of tumor proliferation index Ki-67 and the microvessel density cluster of differentiation (CD31) were significantly downregulated by AKBA treatment. We also found that AKBA significantly suppressed nuclear factor- $\kappa$ B (NF- $\kappa$ B) activation in the tumor tissue and expression of proinflammatory (cyclooxygenase-2), tumor survival (bcl-2, bcl-xL, inhibitor of apoptosis (IAP-1) and survivin), proliferative (cyclin D1), invasive (intercellular adhesion molecule 1 and matrix metalloproteinase-9) and angiogenic C-X-C (CXC) receptor 4 and vascular endothelial growth factor) biomarkers. When examined for serum and tissue levels of AKBA, a dose-dependent increase in the levels of the drug was detected, indicating its bioavailability. Thus, our findings suggest that this boswellic acid analog can inhibit the growth and metastasis of human CRC *in vivo* through downregulation of cancer-associated biomarkers.

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