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Does Boswellia Have a Role in Cancer Therapy?

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Research conducted over the past few years has suggested a possible role for the Ayurvedic herb *Boswellia serrata* in the management of edema associated with brain tumors. Malignant brain tumors produce highly active forms of leukotrienes and this causes localised fluid build up in the brain around the tumor which damages healthy nerve cells.

Twelve patients with malignant glioma, a type of brain tumor, were given 3600 mg/day of Boswellia extract (standardised to 60% boswellic acids) for 7 days prior to surgery.[1] Ten patients showed a decrease in fluid around the tumor, with an average reduction of 30% in 8 of the 12 patients. Signs of brain damage decreased during the treatment; 1 patient became worse. Vomiting as a side effect was observed in 1 patient. This resulted in the European Commission declaring Boswellia as an orphan drug (a drug with no sponsors to fund the registration process) for the treatment of edema resulting from brain tumors.[2]

Nineteen children and adolescents with intracranial tumors received palliative therapy with Boswellia extract at a maximum dose of 126 mg/kg/day.[3] All patients were previously treated with conventional therapy. An antiedematous effect was demonstrated by MRI in one patient. Five of the 19 children reported an improvement of general health (perhaps a placebo effect). Some objective improvement, sometimes transient, was observed in 7 patients. Twelve patients with brain tumors and progressive edema caused by either the tumor or treatment were given Boswellia extract.[4] Edema was reduced in 5 patients. Of 5 patients with treatment-related leukoencephalopathy, clinical improvement following Boswellia was sustained for several months.

In addition Boswellia extract and boswellic acids have shown anticancer activities in cell cultures, including inhibition of cell growth and DNA synthesis.[5,6] The induction of differentiation and apoptosis (possibly due to topoisomerase I inhibition) suggests that boswellic acid may be useful in the treatment of leukemia.[7-9]

The ability of boswellic acids (such as boswellic acid acetate and acetyl-11-keto-β-boswellic acid (AKBA)) to induce *in vitro* apoptosis has been demonstrated in the following tumor cell lines: myeloid leukemia cells,[10] metastatic melanoma and fibrosarcoma cells,[11] various leukemia, hematological and brain tumor cell lines,[12] colon cancer cells,[13] liver cancer Hep G2 cells[14] and malignant glioma.[15] In addition AKBA was found to be cytotoxic towards meningioma cells *in vitro*.[16,17]

Topical application of Boswellia extract with the tumor promoter TPA inhibited the expected formation of skin tumors in mice.[18,19] Boswellic acids have also been shown to inhibit tumor growth *in vivo* using a rat brain tumor model (glioma), albeit at quite high doses (720 mg/kg boswellic acids).[20] The effect was dose dependent. In mice carrying prostate cancer cell tumors, systemic doses of AKBA inhibited tumor growth and triggered apoptosis in the absence of systemic toxicity.[21]

Commentary

While Boswellia shows promise in the management of peritumoral edema, its clinical value in the management of other cancers is uncertain. The promising *in vitro* results suggest that further investigations are warranted. Of particular interest is the observation that the *in vitro* concentrations of boswellic acids required for inhibition of cell growth were a similar order of magnitude to the plasma concentrations seen in human pharmacokinetic studies (particularly if Boswellia is taken with food). The specific studies are as follows.

Twelve healthy adult men were given capsules containing 333 mg of Boswellia extract after a 7-day washout period.[22] Venous blood samples, drawn at various times after administration of the herb, were analysed for 11-keto-beta-boswellic acid (KBA). A mean peak plasma level of 2.72 ± 0.18 x 10^3 µmol/mL was reached at 4.50 ± 0.55 hours, with an elimination half life of 5.97 ± 0.95 hours. These results suggested that Boswellia is best taken orally every 6 hours and that this should achieve steady state plasma levels after approximately 30 hours.

In a randomized, open, single-dose, two-way crossover study, 12 healthy male volunteers received 786 mg of Boswellia extract either with or without a standard high-fat meal.[23] Plasma concentrations of boswellic acids were

measured up to 60 hours after the oral dosing. Administration in conjunction with a high-fat meal led to a substantial improvement in the bioavailability of the boswellic acids. For example, the maximum concentration for AKBA was 6.0 ng/mL for the fasted conditions versus 28.8 ng/mL with food. However, as might be expected the time that this and other maxima were reached was delayed by the meal. Boswellic acids have also been shown to cross the blood-brain barrier in rats.[24]

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