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Holy Basil leaf extract decreases tumorigenicity and metastasis of aggressive human pancreatic cancer cells *in vitro* and *in vivo:* Potential role in therapy

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ABSTRACT

There is an urgent need to develop alternative therapies against lethal pancreatic cancer (PC). *Ocimum sanctum* (“Holy Basil”) has been used for thousands of years in traditional Indian medicine, but its anti-tumorigenic effect remains largely unexplored. Here, we show that extracts of *O. sanctum* leaves inhibit the proliferation, migration, invasion, and induce apoptosis of PC cells *in vitro*. The expression of genes that promote the proliferation, migration and invasion of PC cells including activated ERK-1/2, FAK, and p65 (subunit of NF-κB), was downregulated in PC cells after *O. sanctum* treatment. Intraperitoneal injections of the aqueous extract significantly inhibited the growth of orthotopically transplanted PC cells *in vivo* ($p < 0.05$). Genes that inhibit metastasis (*E-cadherin*) and induce apoptosis (*BAD*) were significantly upregulated in tumors isolated from mice treated with *O. sanctum* extracts, while genes that promote survival (*Bcl-2* and *Bcl-xL*) and chemo/radiation resistance (*AURKA*, *Chk1* and *Survivin*) were downregulated. Overall, our study suggests that leaves of *O. sanctum* could be a potential source of novel anticancer compounds in the future.

1. Introduction

Pancreatic cancer (PC) has a dismal prognosis with a median 5-year survival of about 5% [1]. This is in large part due to the intrinsic resistance of PC cells to chemo and radiation therapy [2,3]. Thus, there has been a concerted effort towards the development of newer drugs that can overcome this inherent resistance. Plant-derived chemicals (phytochemicals) have emerged as a potential source of novel anticancer compounds. Several natural products including curcumin [4], fisetin [5] and thymoquinone [6] have been demonstrated to enhance the sensitivity of PC cells to chemotherapeutic agents. Although initially promoted as chemopreventive drugs, they have also shown significant pro-apoptotic, anti-proliferative and anti-metastatic effects on cancer cells, prompting a call for their introduction as therapeutic agents.

Ocimum sanctum (commonly known as “Holy Basil”) is a medicinal herb found in the semitropical and tropical parts of India. It has been used for thousands of years in the Ayurvedic and Siddha systems of medicine to treat diverse ailments including infections, skin and liver disorders and as an antidote for snake and scorpion bites [7]. It has been used as an anti-inflammatory, immunomodulatory, anti-infective, anti-stress, antipyretic, antitussive, anti-diabetic [8], cardioprotective, neuroprotective and hepatoprotective agent [9,10]. Although every part of the plant has been suggested to have therapeutic uses, the leaves (and leaf extracts) have been most extensively studied. The leaves of *O. sanctum* are the source of an essential oil which has numerous medicinal properties. Both ethanolic and essential oil basil extracts have previously been shown to have antioxidant effects [10–15]. Ethanolic extracts have been shown to promote epithelialization of wounds and to counteract the healing suppressant effect of dexamethasone in albino rats [16]. Eye drops containing *O. sanctum* leaf extract protected against ferric chloride-induced lipid peroxidation and exhibited significant

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