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Curcumin: Ancient Drug, Modern Challenges, Malignant Pancreatitis

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Curcumin is the yellow biphenolic pigment isolated from turmeric, a curry spice that has been used as a therapeutic agent in human health system for centuries. Ever since then this dietary agent has attracted the interest of health practitioner and research oncologist for the treatment of various cancers [1]. In recent years the number of research publication on the therapeutic efficacy of curcumin has been expanding at a significant pace, as reflected by a web www.clinicaltrials.gov in November 2013 "curcumin" generating over 20 clinical trials in a wide variety of chronic diseases, particularly in cancer.

Pancreatic cancer is a complex and count one of the life-threatening disease of the solid malignancies. The American Cancer Society estimates that a total of 45,220 (22,740 men and 22,480 women) new cases and 38,460 (19,480 men and 18,980 women) deaths related to pancreatic cancer will occur in the United States in 2013. Despite decades of effort utilizing adjuvant and neoadjuvant therapies, the 5-year survival rate remains at only 5%. Therefore, a valuable approach is needed to prevent the progression and metastasis of pancreatic cancer [2].

Curcumin treatment has been shown to block human pancreatic cancer cells growth by inhibiting NF-kB-regulated targets such as COX-2, PGE2, and IL-8 [1]. In a clinical trial, curcumin (8 g) was orally administered to 25 patients per day for 2 months. Circulating curcumin was detected as the glucuronide and sulfate conjugate forms, albeit at low steady-state levels, suggesting poor oral bioavailability. Only two patients showed clinical biological activity and one had ongoing stable disease for more than 18 months [3]. In this study, one patient showed marked tumor regression accompanied by significant increases in levels of serum cytokines such as IL-6, IL-8, IL-10, and IL-1 receptor antagonists. Curcumin administration blocks activation of NF-ĸB, COX-2, and STAT3 [3].

In aforementioned clinical trials the plasma concentrations of curcumin is very low in patients taking relatively high oral doses of curcumin. This underpins the reduced cytotoxicity of oral administered curcumin outside the gastrointestinal tract. In another trial curcumin enhances the efficiency of gemcitabine in patients with locally advanced or metastatic adenocarcinoma of the pancreas (NCT00192842). Although a daily dose of 1 g/kg of curcumin increased the antitumor effects of gemcitabine in pancreatic cancer model, if we take this dose of curcumin in average weight patients (70 g/70 kg individual), it will be higher as compared to the dose (8 g) in the clinical trial investigating the concomitant effect of curcumin and gemcitabine. Any anticancer drug requires absolute systemic bioavailability to achieve an efficient therapeutic response in pancreatitis, and curcumin lack this quality [4].

Several strategies have been proposed to overcome the low bioavailability of curcumin. A clinical trial addressing the effect of orally administered curcumin and piperine in human patients with tropical pancreatitis resulted in reduced erythrocyte MDA levels with significant increases in glutathione (GSH) levels in the curcumin treated group [5]. As we know that piperine is a potent inhibitor of drug metabolism and may cause toxicity in people taking specific drugs [6]. Recently, two clinical trials (NCT01982734, NCT01925287) completed, which reported that incorporation of curcumin into micelles improved the bioavailability of curcumin.

It is essential to understand that different strategies not only increase the retention time and effectiveness of curcumin, but also its toxicity. The improved bioavailability of the novel formulations should establish safety issues. Even though such problems have not been documented, but attention is urgently needed. A comparative study also required to investigate most suitable formulation of curcumin to advance to large ultimate clinical trials. It is also important to insights some of the novel formulations for the ingestion of curcuminoids. These are the important questions which should be addressed before curcumin translated to the clinics for the treatment of pancreatic disorders, particularly pancreatic cancer.

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