

THE EFFECT OF ARTIFICIAL BEZOAR (BOVINE GALLSTONE POWDER) ON PROLIFERATION OF HUMAN PANCREATIC CANCER

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Introduction

Bile pigments, including bilirubin and biliverdin, contribute importantly to the defense against oxidative stress. Moreover, recent clinical studies suggest that mildly elevated serum bilirubin levels might protect from certain forms of cancer. Artificial bezoar (powdered bovine gallstones, also known as Niu Huang, or Calculus bovis) is used in traditional Chinese medicine for centuries for its antipyretic and anti-inflammatory properties (1,2). In the present experimental study, we investigated the effect of artificial bezoar on proliferation of human pancreatic cancer.

Methods

The *in vitro* study focused on growth inhibitory effects of artificial bezoar (Biopharma, Australia) was performed on human pancreatic adenocarcinoma cell line Pa-Tu-8902 (DSMZ, Germany). The *in vivo* experiments were carried out on nude mice (strain CD-1, n=5 in each group) xenotransplanted sc. with the same cancer cells. After successful attachment and growth initiation of cancer cells, the mice were treated with daily oral administration of water suspension of powdered bovine gallstones (50 mg/kg b.wt.) containing more than 50% of calcium bilirubinate. The control group did not receive any treatment. The primary endpoints were the survival time (assessed by Kaplan-Meier survival analysis) as well as tumor size progression during the first 24 days (measured every 3 days) (evaluated by repeated measures ANOVA with Holm-Sidak post-hoc testing).

Results

According to preliminary *in vitro* data, even very low concentrations of artificial bezoar were able to substantially inhibit growth of Pa-Tu cancer cells (Fig. 1). Higher doses of bezoar were probably less efficient due to its improper solubilization. As compared to controls, mice treated with artificial bezoar survived significantly longer (38.0 ± 7.6 vs. 48.2 ± 5.5 , $p=0.003$) and this was confirmed also by Kaplan-Meier survival analysis (Fig. 2). Furthermore, both groups differed significantly in tumor size already since 14th day after initiation of artificial bezoar therapy (Fig. 3). The most pronounced difference in tumor size was detected at 24th day of therapy (0.88 ± 0.4 vs. 3.29 ± 2.2 cm³, $p=0.03$ in artificial bezoar vs. control group, respectively, Fig. 3).

Fig. 1. The effect of artificial bezoar on growth of PaTu human pancreatic cancer cells after 24 hrs

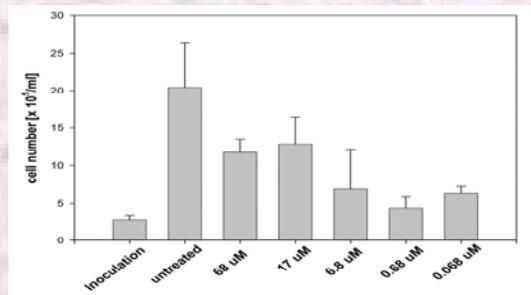


Fig. 2. The effect of artificial bezoar on survival of mice transplanted with Pa-Tu-8902 cancer cells

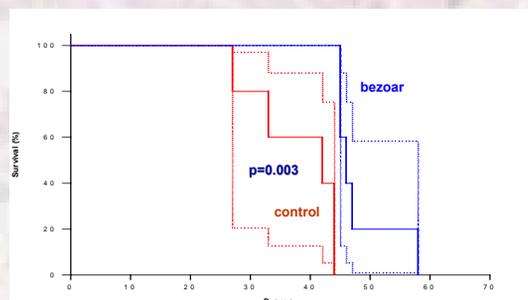
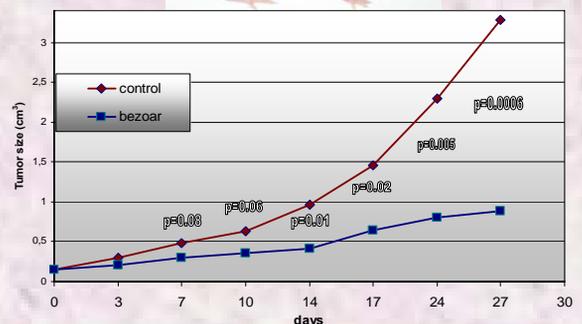
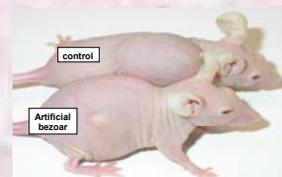


Fig. 3. The effect of artificial bezoar on tumor size 24th day after cancer cell transplantation



CONCLUSIONS

In our experimental *in vitro* and *in vivo* model of human pancreatic cancer, substantial antiproliferative effects of orally administered artificial bezoar were demonstrated. These results suggest that components of bovine gallstones, presumably bilirubin, might contribute to the protection from pancreatic cancer.

Literature

1. McGeary RP, Szczyzew AJ, Toth I. Biological properties and therapeutical potential of bilirubin. *Mini Rev Med Chem* 2003; 3:253-256.
2. McDonagh AF. Is bilirubin good for you? *Clin Perinatol* 1990; 17:359-369.

Acknowledgement

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