

Answer 1:

Bibliographic Information

Loxiglumide (CR1505), a cholecystokinin antagonist, specifically inhibits the growth of human pancreatic cancer lines xenografted into nude mice. Nio Y; Tsubono M; Morimoto H; Kawabata K; Masai Y; Hayashi H; Manabe T; Imamura M; Fukumoto M First Department of Surgery, Shimane Medical University, Japan Cancer (1993), 72(12), 3599-606. Journal code: 0374236. ISSN:0008-543X. Journal; Article; (JOURNAL ARTICLE); (RESEARCH SUPPORT, NON-U.S. GOV'T) written in English. PubMed ID 8252474 AN 94073802 MEDLINE (Copyright (C) 2008 U.S. National Library of Medicine on SciFinder (R))

Abstract

BACKGROUND. Cholecystokinin is thought to be an important factor regulating the growth of human pancreatic cancers. The study was designed to evaluate the effects of the cholecystokinin antagonist loxiglumide (CR1505) on the growth of human pancreatic cancer. **METHODS.** Human gastrointestinal cancer xenografted tumors (one esophageal, one gastric, two colorectal, two biliary tract, and two pancreatic cancers) were transplanted into nude mice. The mice were given CR1505 at 250 mg/kg daily for 14 days, either subcutaneously or intragastrically, and the tumor volumes before and after treatment were compared. In vitro effects of CR1505 were assessed by measuring the DNA synthesis (3H-thymidine incorporation). **RESULTS.** CR1505 inhibited the growth of the two pancreatic cancer lines but did not inhibit the growth of the other lines. CR1505 also inhibited in vitro DNA synthesis in the two pancreatic cancer lines at lower concentrations than in the other lines. This pancreatic cancer-specific inhibitory effect of CR1505 was retarded by exogenously administered cholecystokinin in one pancreatic cancer line but was augmented in the other line. The effect of CR1505 was inhibited by oral administration of the trypsin-inhibitor camostatate (FOY-305) in both pancreatic cancer lines. **CONCLUSIONS.** These results suggest that CR1505 may specifically inhibit the growth of human pancreatic cancers and may be suitable for clinical study. However, its antiproliferative effect may not necessarily be dependent on its cholecystokinin-antagonism but may be mediated through the proteolytic enzymes found in the lysosomes of the pancreatic cancer cells.