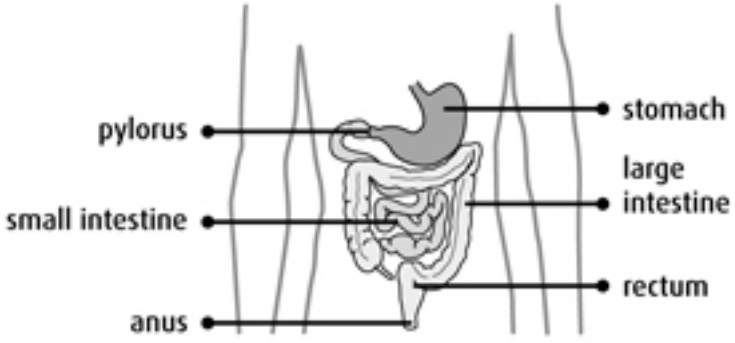
Stomach Cancer

Excerpt from www.cancer.ca:

The stomach is a muscular sac-like organ in the upper abdomen. It is part of the digestive system. Organs of the digestive system change food into energy and help pass waste out of the body.

Food moves from the mouth through the esophagus to the stomach. In the stomach, the food is mixed with digestive juices (enzymes and acids), which are made by the glands in the lining of the stomach. The semi-solid mixture leaves the stomach through a muscular ring called the *pylorus* and passes into the small intestine. From there, food goes to the large intestine, where digestion is finished.



The wall of the stomach has four layers. Stomach cancer begins in the cells of the inner layer, which is called the *mucosa*. It can spread through the other layers of the stomach as it grows.

Stomach cancers that start in the lymphatic tissue (*lymphoma*), in the stomach's muscular tissue (*sarcoma*) or in the tissues that support the organs of the digestive system (*gastrointestinal stromal tumour*) are less common and are treated in different ways.

J Cell Biochem. 2011 Apr;112(4):1192-205. doi: 10.1002/jcb.23041.

Antiproliferative mechanism of a cannabinoid agonist by cell cycle arrest in human gastric cancer cells.

Park JM, Xian XS, Choi MG, Park H, Cho YK, Lee IS, Kim SW, Chung IS.
Source

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Abstract

For gastric cancers, the antineoplastic activity of cannabinoids has been investigated in only a few reports and knowledge regarding the mechanisms involved is limited. We have reported previously that treatment of gastric cancer cells with a cannabinoid agonist significantly decreased cell proliferation and induced apoptosis. Here, we evaluated the effects of cannabinoids on various cellular mediators involved in cell cycle arrest in gastric cancer cells. AGS and MKN-1 cell lines were used as human gastric cancer cells and WIN 55,212-2 as a cannabinoid agonist. Cell cycles were analyzed by flow cytometry and western blotting. Treatment with WIN 55,212-2 arrested the cell cycle in the G0/G1 phase. WIN 55,212-2 also upregulated phospho-ERK1/2, induced Kip1/p27 and Cip1/WAF1/p21 expression, decreased cyclin D1 and cyclin E expression, decreased Cdk 2, Cdk 4, and Cdk 6 expression levels, and decreased phospho-Rb and E2F-1 expression. ERK inhibitor decreased the proportion of G0/G1 phase which was induced by WIN 55,212-2. Inhibition of pAKT led to cell cycle arrest in gastric cancer cells. Cell cycle arrest preceded apoptotic response. Thus, this cannabinoid agonist can reduce gastric cancer cell proliferation via G1 phase cell cycle arrest, which is mediated via activation of the MAPK pathway and inhibition of pAKT.

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Loss of cannabinoid receptor 1 accelerates intestinal tumor growth

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Abstract

Although endocannabinoid signaling is important for certain aspects of gastrointestinal homoeostasis, the role of the cannabinoid receptors (CB) in colorectal cancer has not been defined. Here we show that CB1 expression was silenced in human colorectal cancer due to methylation of the CB1 promoter. Our genetic and pharmacologic studies reveal that loss or inhibition of CB1 accelerated intestinal adenoma growth in *ApcMin*/+ mice whereas activation of CB1 attenuated intestinal tumor growth by inducing cell death via downregulation of the anti-apoptotic factor survivin. This downregulation of survivin by CB1 is mediated by a cAMP-dependent PKA signaling pathway. These results indicate that the endogenous cannabinoid system may represent a potential therapeutic target for prevention or treatment of colorectal cancer.

Pharmacological research the official journal of the Italian Pharmacological Society (2009)
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Abstract

Emerging evidence suggests that cannabinoids may exert beneficial effects in intestinal inflammation and cancer. Adaptive changes of the endocannabinoid system have been observed in intestinal biopsies from patients with inflammatory bowel disease and colon cancer. Studies on epithelial cells have shown that cannabinoids exert antiproliferative, antimetastatic and apoptotic effects as well as reducing cytokine release and promoting wound healing. In vivo, cannabinoids - via direct or indirect activation of CB(1) and/or CB(2) receptors - exert protective effects in well-established models of intestinal inflammation and colon cancer. Pharmacological elevation of endocannabinoid levels may be a promising strategy to counteract intestinal inflammation and colon cancer.

J Pain Symptom Manage. 1997 Nov;14(5):311-4.

Intractable nausea and vomiting due to gastrointestinal mucosal metastases relieved by tetrahydrocannabinol (dronabinol).

Gonzalez-Rosales F[1], Walsh D.

Author information

Abstract

Four years following resection of a Clark's level IV malignant melanoma, a 50-year-old man developed widespred metastatic disease involving the liver, bones, brain, gastrointestinal mucosa, and lungs. One week after whole brain radiation therapy, he was admitted to the hospital for nausea, vomiting, and pain. He was treated with several antiemetic drugs, but it was not until dronabinol was added that the nausea and vomiting stopped. Dronabinol was an effective antiemetic used in combination with prochlorperazine in nausea and vomiting unresponsive to conventional antiemetics.

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9392925

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J Surg Res. 2009 Jul;155(1):40-7. doi: 10.1016/j.jss.2008.06.045. Epub 2008 Aug 9.

Pharmacological synergism between cannabinoids and paclitaxel in gastric cancer cell lines.

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Author information

Abstract

Orally applicable Delta9-tetrahydrocannabinol and its synthetic derivatives have been used as antiemetic drugs during chemotherapy in cancer patients. However, it is not well known how cannabinoids influence the effects of chemotherapeutic agents on malignant tumors. In this study, we investigated how the endogenous cannabinoid anandamide (AEA) changes the effect of paclitaxel on gastric cancer cell lines. In the human gastric cancer cell line, HGC-27, which express cannabinoid receptor 1 (CB1), AEA stimulated proliferation at concentrations under 1 microM, while it strongly suppressed proliferation through the induction of apoptosis at 10 microM. This bimodal effect was reproduced by a selective CB1 agonist, arachidonyl-2-chloroethylamide, although the effects were less marked. When AEA was used with paclitaxel, AEA at 10 microM synergistically enhanced the cytotoxic effect of paclitaxel, whereas it showed no significant effect at lower concentrations. Flow cytometric analysis revealed that addition of 10 microM AEA synergistically enhanced paclitaxel-induced apoptosis, possibly through the activation of caspase-3, -8, and -9. Our results suggest that cannabinoids could be a good palliative agent for cancer patients receiving paclitaxel.

Comment in

- Upper gastrointestinal tumors. [Endoscopy. 2010]

PMID:
19394652

[PubMed - indexed for MEDLINE]

http://www.ncbi.nlm.nih.gov/pubmed/19394652

J Cell Biochem. 2010 May 15;110(2):321-32. doi: 10.1002/jcb.22540.

Effect of a synthetic cannabinoid agonist on the proliferation and invasion of gastric cancer cells.

Xian XS[1], Park H, Cho YK, Lee IS, Kim SW, Choi MG, Chung IS, Han KH, Park JM.

Author information

Abstract

Although cannabinoids are associated with antineoplastic activity in a number of cancer cell types, the effect in gastric cancer cells has not been clarified. In the present study, we investigated the effects of a cannabinoid agonist on gastric cancer cell proliferation and invasion. The cannabinoid agonist WIN 55,212-2 inhibited the proliferation of human gastric cancer cells in a dose-dependent manner and that this effect was mediated partially by the CB(1) receptor. We also found that WIN 55,212-2 induced apoptosis and down-regulation of the phospho-AKT expression in human gastric cancer cells. Furthermore, WIN 55,212-2 treatment inhibited the invasion of gastric cancer cells, and down-regulated the expression of MMP-2 and VEGF-A through the cannabinoid receptors. Our results open the possibilities in using cannabinoids as a new gastric cancer therapy.

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