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Chemotherapy-induced adverse effects in the gastrointestinal tract and role of cannabinoids

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Chemotherapy, intended to kill cancerous cells, is also toxic to healthy cells. In the gastrointestinal tract, three main types of adverse effects may be induced: nausea/emesis; diarrhea; constipation. Each kind of antineoplastic drug may induce one or more of these effects. For example, cisplatin is considered highly emetogenic and induces both acute and delayed nausea and vomit, associated to alter gastric emptying and gastric distension. 5-fluorouracil induces diarrhea, potentially fatal due to dehydration. Finally, constipation is typically induced by drugs like vincristine, with the development of paralytic ileus. The three drugs alter the gut wall architecture, with the development of mucositis of different degrees and evolution after treatment finalization. Several lines of evidence, mainly in experimental animals, have shown that manipulating the endo-cannabinoid system may be beneficial to prevent/treat the effects on gastrointestinal motility. Thus, although their effects are not that clear in rodents, which do not vomit, cannabinoid agonists have been shown to reduce signs of nausea/emesis in animals capable of vomiting and they are actually used in the clinic as antiemetic adjuvants. Cannabinoid agonists may be useful, even at low, non-psychoactive doses, to reduce chemotherapy-induced diarrhea. Finally, cannabinoid antagonists were shown to reduce paralytic ileus induced by vincristine in a rat model, suggesting that endo-cannabinoid activity is increased by this antineoplastic drug. Thus, cannabinoid-based drugs could be used to relieve and prevent chemotherapy-induced adverse effects in the gastrointestinal tract and could then contribute to better preserve quality of life of cancerous patients during treatment.

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