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Research Article **Clinical Research in Brain and Neurological Disorders** **Open Access**

Case Report: Clinical Responses of Cannabinoids in Treatment of Patients with Brain Cancer

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Received Date: February 13, 2022; **Accepted Date:** February 26, 2022; **Published Date:** February 28, 2022

Citation: Taylor T. Case Report: Clinical Responses of Cannabinoids in Treatment of Patients with Brain Cancer, J Clinical Research in Brain and Neurological Disorders, V(1)1.

Abstract

Phyto cannabinoids are a structurally diverse class of naturally occurring chemical constituents in the genus Cannabis (Cannabaceae). This chemical classification is broadly based on their derivation from a common C21 precursor (cannabigerolic acid, CBGA), or its C19 analog (cannabigerovaric acid, CBGVA), the predominate phytocannabinoid precursors formed through the reaction of geranyl pyrophosphate with olivetolic and divarinic acid.

Keywords: Cannabinoids; clinical responses; brain cancer

Introduction

Cancer is a complex family of diseases affecting millions of people worldwide. Gliomas are primary brain tumors that account for ~80% of all malignant brain tumors. Glioblastoma multiforme (GBM) is the most common, invasive, and lethal subtype of glioma. Therapy resistance and intra-GBM tumoral heterogeneity are promoted by subpopulations of glioma stem cells (GSCs). *Cannabis sativa* produces hundreds of secondary metabolites, such as flavonoids, terpenes, and phytocannabinoids. Around 160 phytocannabinoids have been identified in *C. sativa*. Cannabis is commonly used to treat various medical conditions, and it is used in the palliative care of cancer patients. The anti-cancer properties of cannabis compounds include cytotoxic, anti-proliferative, and anti-migratory activities on cancer cells and cancer stem cells. There is evidence that malignant solid tumors contain a subpopulation of cancer stem cells (CSCs) that have a clonogenic and tumorigenic potential. Similar to stem cells, CSCs are characterized by a capacity for self-renewal, in which one cell generates more stem cells. CSCs also possess an ability for multi-lineage differentiation, which increases genetic heterogeneity within the tumor mass.

Case Presentation

Pre-Clinical Studies

Studies have demonstrated that phytocannabinoids potentially possess anti-cancer properties, including the inhibition of cell migration, proliferation, and angiogenesis and the induction of apoptosis in skin, lung, breast, prostate, and glioma cancer cellsOne of the most abundant phytocannabinoids, THC, was shown to inhibit the growth of some tumors, inhibit angiogenesis, and induce apoptosis in various cancers cells in vitro and in vivo. THC and CBD exhibited synergistic inhibition of cell proliferation in GBM cell lines. Furthermore, CBD was found to inhibit the invasiveness of breast cancer cells and GBM cells at sub-lethal concentrations by downregulating matrix metalloproteinases (MMPs) and their inhibitors (TIMPs).

Cannabinoid receptors can be activated by interaction with endo-, phyto- or synthetic cannabinoids. The cannabinoid receptors type 1 and type 2 (CB1 and CB2) belong to the seven-transmembrane G-protein coupled receptor (GPCR) superfamily and are among the most abundant subtype in the body.

The endocannabinoid system (ECS) is a signaling network that consists of cannabinoid receptors, endogenous ligands (termed endocannabinoids), and metabolic enzymes. The ECS is widely distributed in the body, and it has an important role in maintaining a homeostatic balance and in the regulation of various physiological processes, such as synaptic transmission and immunomodulation.

Summary

Conceptual perspective of the anti-cancer activity of phytocannabinoids. Cannabis compounds and phytocannabinoids, in particular, by activating cannabinoid receptor-dependent mechanisms, may interact synergistically in some of the cases and target malignant cells by inducing, e.g., cell apoptosis and inhibition of cancer cell migration. Moreover, phytocannabinoids may target CSCs, in some cases leading to an improved outcome, e.g., by inhibiting the characteristic self-renewal and drug resistance of CSCs.

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