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Cannabinoids and its disease targeting mechanisms for Parkinson's Disease and Cancer

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Abstract
Background: Endocannabinoids, Phyto-cannabinoids and synthetic cannabinoids are the three categories of cannabinoids. The way that various cannabinoids attach to endocannabinoid receptors determines the physiological effects that they have.
Cannabinoids treatment: Enzymes that catalyse the synthesis and degradation of endocannabinoids, together with cannabinoid receptors, comprise the endocannabinoid system. The placement of the receptor within neurons is consistent with the well-known motor activities of cannabis. The main organ where the cannabis CB_1 receptor is connected is the nervous system. CB_2 and CB_1 are currently the two recognized cannabinoid receptors. Bradykinesia, or slowness of movement, is another symptom that people with Parkinson's disease (PD) may have in addition to fatigue, forgetfulness, tense muscles, and strange vocal tones. It stems from the degeneration of the basal ganglia, which can be brought on by gene mutations, inflammatory stress, misfolded protein aggregation, or the production of free radicals. It mostly impacts the body's neuromuscular coordination. A group of diseases collectively referred to as cancers are distinguished by abnormal cell growth that has the potential to invade or spread to other body parts.
Conclusion: More than 100 distinct forms of cancer that affect the body and can affect humans. By building a common connection in the main secondary messenger that may interact with the target protein, we have attempted to establish a linkage between Parkinson's disease and cancer. Cannabinoids are thought to be the basis of cure for both the disorders.

Keywords: Cannabinoid, endocannabinoid, Phyto-cannabinoid, Parkinson's Disease, Cancer

Introduction
Cannabinoids are a group of structural compounds that are mostly found in the cannabis plant, most animals, and synthetic drugs category and is for the main active ingredient found in marijuana plants (*Cannabis sativa*) [1]. The main psychoactive ingredient in cannabis and Phyto-cannabinoid is tetrahydrocannabinol (THC) (Δ^9-THC), which is the most well-known cannabinoid [2]. Only 4 of the at least 113 different Phyto-cannabinoids that have been isolated from cannabis: THCA, CBDA, CBCA, and their common precursor CBGA, have been shown to have a biogenetic origin [3]. It was removed from the 12th edition of the U.S. Pharmacopeia by the American Medical Association after approximately making it available as a licensed medicine in the country [4]. Cannabinoids can be classified into endocannabinoids, Phyto- cannabinoids and synthetic cannabinoids. With every new finding about the properties and uses of this intriguing plant, as well as research into how it affects human health, the usage of medical cannabis is expanding. Different cannabinoids have different physiological effects depending on how they bind to endocannabinoid receptors [5]. The endocannabinoid system is made up of cannabinoid receptors, endocannabinoids, and the enzymes that catalyse their manufacture and breakdown. The endocannabinoid system has garnered a great deal of attention as a possible therapeutic target in a variety of clinical disorders in recent decades. It is well known that it plays a role in a number of physiological processes, including energy balance, immune response, blood pressure regulation, appetite stimulation, memory, learning, and embryogenesis. It is also known to play a protective role in pathological conditions where it prevents the development of certain disorders [6]. Cannabinoids are a class of chemicals named after the primary active ingredient of the marijuana plant (*Cannabis sativa*). Δ^9-tetrahydrocannabinol was found as the active principle

in this plant [7]. It is well recognized that cannabinoids cause a wide range of physiological effects, including strong impacts on locomotion. These well-known motor actions of cannabinoids are compatible with the receptor's location within neurons. Cannabinoid CB_1 receptor expression in the brain is patterned and is primarily found in regions that regulate motor behaviour, such as the cerebellum and basal ganglia. On the other hand, the brainstem has modest amounts of cannabinoid CB_1 receptors, which could account for the low toxicity of cannabinoid receptor agonists: a desirable property for potential medicinal applications [8, 9, 10].

Although it is expressed in other organs, the nervous system is the primary organ where the cannabinoid CB_1 receptor is linked. There are now two known cannabinoid receptors: CB_2 and CB_1 (with the isoform CB_{1a} arising from alternative splicing). While it is expressed in other organs as well, the nervous system is the primary organ linked to the cannabinoid CB_1 receptor. The CB_2 receptor is not expressed in neurons and is primarily linked to the immune system [11].

Materials and Methods

This review is based on the collected information of the phyto-constituent i.e. cannabinoids, which were available on the internet, were considered for this study. A web-based literature search was conducted using computerized database search engines, such as Google Scholar, PubMed, ScienceDirect, Elsevier, Web of Science, etc. for cannabinoids and how it is related to PD and Cancer. The search has also led up to a hypothesis which was concluded from that how some proteins interfere in the signaling mechanism of PD and Cancer along with the role of prevention pathway of PD and Cancer by cannabinoids.

Parkinson Disease

Parkinson's disease (PD) is a chronic neurological illness that affects 1-2 percent of people over 65 percent worldwide. Classical motor symptoms such bradykinesia, rest tremor, postural abnormalities, and rigidity are its primary characteristics. In addition to motor symptoms, people with Parkinson's disease (PD) frequently experience non-motor symptoms such as dyspepsia, anxiety, melancholy, constipation, sexual dysfunction, orthostatic hypotension, sleep difficulties, and cognitive impairments. A gradual loss of dopamine-containing basal ganglia neurons, particularly in the pars compacta region of the substantia nigra, is a pathophysiological feature of Parkinson's disease (PD). The nigrostriatal tract degeneration (which may be the cause of mot motor symptoms) and the accumulation of Lewy bodies in surviving neurons (which is the hallmark of Parkinson's disease) are the results of this neuron degeneration, which appears to be linked to mitochondrial dysfunction, oxidative stress, and decreased protein degradation [12]. Levodopa (L-DOPA) and dopamine degradation inhibitors, such as dopamine decarboxylase inhibitors, monoamine oxidase (MAO) inhibitors and catechol-O-methyl transferase (COMT) inhibitors, are the mainstays of pharmacological therapies for Parkinson's disease (PD). L-DOPA is the primary drug used to treat motor symptoms in Parkinson's disease (PD), yet some people do not react to it. Furthermore, long-term usage of L-DOPA causes significant motor side effects (dyskinesia), which gradually reduces the drug's therapeutic benefit. In addition, people with Parkinson's disease (PD) also take additional drugs such as antidepressants, anxiolytics, sedatives and antipsychotics, to treat non-motor symptoms. These drugs have a limited therapeutic window and can have serious side effects. Managing these non-motor symptoms is one of the most challenging current issues in the pharmacological treatment of Parkinson's disease (PD). These non-motor symptoms do not respond to dopaminergic medications [13]. Parkinson's disease (PD), which affects 1% of the world's elderly population, is one of the most common neurodegenerative illnesses after Alzheimer's disease. It primarily affects the body's neuromuscular coordination and results from the destruction of the basal ganglia. In the substantia nigra pars compacta (SNpc), there is severe deprivation of dopaminergic neurons affecting the striatum, which ultimately results in dopamine depletion. This deprivation can be caused by mutations in genes, inflammatory stress, misfolded protein aggregation or the formation of free radicals [14]. Parkinson's disease (PD) sufferers may also have bradykinesia or slowness of movement, in addition to other symptoms like weariness, forgetfulness, stifled muscles and voice abnormalities. The symptoms that the sufferer experiences are caused by a variety of noradrenergic, serotonergic and cholinergic mechanisms. These mechanisms work in concert to cause a significant percentage of dopamine-forming nerve cells to disappear throughout the nigral area. Additionally, the generation of two compounds: free reactive radicals and hydrogen peroxide; leads to the damage and eventual death of neurons [15].

Cancer

A collection of disorders known as cancers are characterized by aberrant cell proliferation that has the capacity to infiltrate or spread to other bodily regions. In contrast, benign tumors do not metastasize. A lump, unusual bleeding, protracted cough, unexplained weight loss and altered bowel movements are among the possible warning signs and symptoms. Although cancer may be the cause of these symptoms, there are other possible explanations. Humans can suffer from more than 100 different types of cancer [16, 17, 18]. About 22% of cancer-related deaths are related to tobacco usage. An additional 10% can be attributed to being overweight, having a poor diet, not exercising or drinking too much alcohol. Additional contributing factors are certain illnesses, radiation exposure and exposure to environmental contaminants. Infections including Helicobacter pylori, hepatitis B, hepatitis C, human papillomavirus infection, Epstein-Barr virus and human immunodeficiency virus (HIV) cause 15% of cancer cases in underdeveloped nations. These elements work, at least in part, by altering a cell's genetic makeup. Usually, a great deal of genetic alterations is needed prior to cancer developing. 5–10% of cancer cases are caused by hereditary abnormalities. Certain indications and symptoms, as well as screening tests, can identify cancer. Next, medical imaging is usually used to look into it more and a biopsy is usually used to confirm it [17, 20, 24]. Lung, prostate, colorectal and stomach cancers are the most prevalent cancer types in men [25, 26]. The most prevalent forms in females are colorectal, lung, cervical and breast cancer [22, 26]. Skin cancers other than melanoma would make up about 40% of all new cancer cases annually if they were counted [27, 28]. Acute

lymphoblastic leukaemia and brain tumors are the most frequent childhood diseases with the exception of non-Hodgkin lymphoma in Africa [29]. Ninety to ninety-five percent of cancer cases are caused by genetic abnormalities resulting from environmental and lifestyle factors. The remaining 5-10% are the result of genetic inheritance [19]. Environmental does not only mean pollution; it also includes any non-inherited source such as economic, behavioural or lifestyle issues [30]. Tobacco usage (25–30%), food and obesity (30–35%), infections (15–20%), radiation (both ionizing and non-ionizing, up to 10%), inactivity and pollution are common environmental variables that cause cancer death [19, 31].

Cannabinoids in Parkinson Disease

Akinesia, tremor and stiffness are examples of Parkinsonian motor disorders. The pathological hallmark of this illness is the degeneration of nigrostriatal dopaminergic neurons. Unbalances in basal ganglia physiology, including elevated subthalamic nucleus neuron activity, are brought on by dopamine deprivation. Lesions in the subthalamic nucleus or its inhibition with the GABA agonist muscimol lessen stiffness, tremor and akinesia, but they can cause contralateral dyskinesias [32]. It appears that cannabinoids prevent neurotransmitter release from the SNr's subthalamic terminals [33, 34, 35]. Moreover, cannabinoids exhibit far stronger effects in the SNr in an animal model of Parkinson's illness, potentially through their action at subthalamic terminals. In other regions of the basal ganglia, the effectiveness of cannabinoids is mostly unaffected by this impact. This discovery, along with the large safety margin of this pharmacological class, points to the possibility that cannabis could be included in the development of novel therapeutic strategies for the management of Parkinson's disease and associated movement disorders [36].

The common and debilitating nature of non-motor symptoms in Parkinson's disease (PD) is exacerbated by the poor efficacy of current treatments and their significant adverse responses. Given that the ECS (Endocannabinoid system) plays a role in the etiology of Parkinson's disease (PD), cannabis may be able to treat the disease's symptoms. However, to the best of our knowledge, only four RCTs have been conducted in which CB_1 receptor agonists (nabilone, cannabis extract) or antagonists (rimonabant) have been administered to patients with Parkinson's disease (PD), and only one of those trials (n=7) has shown statistically significant positive effects (significant reductions in levodopa-induced dyskinesia). Crucially, every cannabinoid was well tolerated [37].

Cannabinoids in Cancer

The Controlled Substances Act of 1970 classified medicinal cannabis as a schedule I agent, which limited research into it as a possible medical product and contributed to the dearth of clinical data on the drug's use for treating cancer pain. However, the results of the limited studies that were conducted on the use of medicinal cannabis for managing cancer pain indicate that it may have therapeutic promise and is, deserving of more research to be carried out [38]. According to recent studies, medicinal cannabis may be useful in the treatment of cancer discomfort. The scope and caliber of research done up to this point, however, are quite small. Therefore, further study is required to determine the effectiveness of medical cannabis as a therapeutic adjunct or as a substitute for opiates. It is also necessary to determine the best ways to administer the drug in order to achieve maximum therapeutic efficacy with the fewest possible adverse effects [39, 40]. Currently, one of the most fascinating and promising areas of study on cannabinoids is their capacity to regulate a cell's decision to survive or die [41].

Literatures on Parkinsons Disease

Project Title	Major Findings	Reference No.
Activational role of cannabinoids on movement	The systemic effects of Δ^9-tetrahydrocannabinol on motor behaviour is discussed in this study. The cannabis receptor agonist reduced movement at extremely low dosages by having an auto receptor-like action. This was followed by a dose-dependent stimulating impact on activity that was broken up by the onset of stiffness and catalepsy. Here it suggests that the main modulatory effects of cannabis, which balance opposing systems, override their activational function in movement at greater dosages.	[11]
Is cannabidiol the ideal drug to treat non-motor Parkinson's disease symptoms?	Better treatment alternatives are required since the pharmaceutical therapy for these symptoms has poor effectiveness and causes serious side responses. Preclinical and early clinical research on cannabidiol (CBD), a Phyto cannabinoid that lacks the euphoric and cognitive effects of tetrahydrocannabinol, indicates that this chemical may be useful in treating non-motor Parkinson's disease (PD) symptoms. Here the examination of preclinical and clinical research on CBD in particular, as well as clinical studies on cannabinoids in Parkinson's disease was done.	[13]
Therapeutic Potential of Cannabinoids in CNS Disease	This review identifies CNS illnesses that may benefit from the therapeutic benefits of cannabis therapy and emphasizes recent developments in our understanding of the endocannabinoid system. Ongoing clinical trials using marijuana to treat the symptoms of various illnesses are mentioned here when appropriate.	[42]
Cannabis in Parkinson's Disease: the patient's perspective versus clinical trials: a systematic literature review	Parkinson's disease (PD) is a condition that is frequently treated with cannabis and cannabinoids. In particular, placebo control is needed to provide adequate assessment of the efficacy of cannabinoids in PD therapy. This should include placebo substitutes of both CBD and cannabis administered by inhalation, with careful monitoring of the doses administered to patients. Based on the literature review, it was concluded that non-motor symptoms of PD such as pain, anxiety and sleep seem to respond better to cannabis treatment than do motor signs was observed.	[43]

Cannabis and its derivatives for the use of motor symptoms in Parkinson's disease: a systematic review and meta-analysis.	There is now more interest in researching cannabis's potential benefits for Parkinson's disease due to recent changes in the drug's legal status in some nations. Pre-clinical research on the use of cannabis to relieve motor symptoms has been done in great detail. Analysis was done on fifteen studies, six of which were RCTs. Overall, there was good tolerance for the intervention. Randomized controlled trials were all very susceptible to bias was observed.	[44]
Cannabinoid effects in basal ganglia in a rat model of Parkinson's disease	In line with their well-known impacts on motor behaviour, the brain's basal ganglia have a high concentration of cannabinoid receptors. In this work, cannulae in the striatum, globus pallidus, and substantia nigra were implanted into rats that had 6-hydroxydopamine lesions of the nigrostriatal pathway. The results of this study, along with the large safety margin of this pharmacological class, point to the possibility that cannabis might be included in the development of novel therapeutic strategies for the management of Parkinson's disease and other movement disorders was discussed here.	[36]
Cannabinoids in Late Life Parkinson's Disease and Dementia: Biological Pathways and Clinical Challenges.	Tetrahydrocannabinol and CBD may have neuroprotective therapeutic-like effects on dementias, according to emerging research. Cannabinoids are being used off-label in clinical practice to treat Parkinson's disease (PD) and Alzheimer's disease (AD) symptoms. Larger sample sizes and controlled studies with longitudinal designs are needed to investigate the long-term effectiveness of these medications in PD, AD, and dementia. All things considered, cannabis compounds are well accepted and seem to be safer than the majority of psychiatric medications; nonetheless, because dementia patients are more susceptible, the doctor must monitor them appropriately.	[45]
Cannabidiol and Cannabinoid Compounds as Potential Strategies for Treating Parkinson's Disease and L-DOPA-Induced Dyskinesia.	According to the studies we've discussed here, cannabinoids may have an impact on how Parkinson's Disease and L-DOPA-Induced Dyskinesia develop and show up. There appear to be a number of processes at work, from direct modifications in important neurotransmitters like glutamate and dopamine to indirect anti-inflammatory actions. Preclinical experiments indicate that CBD is one of the most promising medications among the cannabinoids that have been studied thus far.	[46]

Literatures on Cancer

Project Title	Major Findings	Reference No.
Cannabinoid Receptor as a Novel Target for the Treatment of Prostate Cancer	A growing number of people are interested in cannabinoids, the active ingredients in *Cannabis sativa* and its derivatives, because of its wide range of pharmacologic properties, which include tumors regression, anti-inflammatory actions, and the suppression of cell proliferation. Treatment of androgen-responsive human prostate cancer LNCaP cells reduced the amounts of PSA released and inside the cell, while also inhibiting the development of the cells, inducing apoptosis, and inhibiting the androgen receptor treating prostate cancer.	[47]
Cannabinoids and cancer: causation, remediation, and palliation.	THC and other cannabinoids may be beneficial adjunct therapies for cancer patients receiving palliative care. These cannabinoids increase appetite, lessen nausea and vomiting, and ease mild neuropathic pain; however, it is unclear if these effects outweigh the current pharmacological therapies for these symptoms. Creating safer, non-smoking delivery techniques for cannabinoids and cannabis extracts that enable users to titrate dosages and attain intended therapeutic effects while avoiding unfavourable psychoactive effects is a significant problem for their palliative usage was studied.	[48]
Cannabinoids and Cancer Chemotherapy: Associated Adverse Effects	Cannabis has long been used to treat cancer pain as well as pain, nausea and cachexia brought on by cancer therapies, so many patients are not new to using it. The US Food and Drug Administration has approved two cannabis-based pharmacotherapies so far to treat adverse effects associated with cancer chemotherapy: dronabinol and nabilone. Strong preclinical data is provided by this study, among others suggesting that cannabinoid-based medicinal methods may be able to reduce the negative effects of chemotherapy for cancer can be observed.	[49]
Cannabinoids for Symptom Management and Cancer Therapy: The Evidence	In addition to traditional receptors (CB_1 and CB_2), cannabinoids can bind to ion channels (transient receptor potential vanilloid), specific orphan receptors (GPR55 and GPR119), and peroxisome proliferator-activated receptors. It has been shown that cannabinoids somewhat lessen cancer discomfort. Although there are many studies supporting the potential benefits of cannabis in the treatment of cancer, no randomized trials have been carried out. Additionally, there is evidence that cannabinoids promote tumors migration and proliferation and that malignancies may be dependent on cannabinoid receptors for survival.	[50]
Cannabinoids in cancer treatment: Therapeutic potential and legislation	Cannabinoids have mostly been utilized in palliative care for cancer patients in order to reduce pain, reduce nausea, and increase appetite. A vast and significant family of intricate molecules known as cannabinoids shows promise as a therapeutic agent for the treatment of a number of illnesses, including cancer. Different *in vitro* and *in vivo* cancer models showed that cannabinoids might effectively control tumors development; however, the kind of cancer and medication dose appear to be related to these anticancer effects.	[51]
UPLC-MS Analysis of *Cannabis sativa* Using Tetrahydrocannabinol (THC), Cannabidiol (CBD), and Tetrahydrocannabinol Acid (THCA) as Marker Compounds: Inhibition of Breast Cancer Cell Survival	Using tetrahydrocannabinol (THC), cannabidiol (CBD) and tetrahydrocannabinolic acid (THCA) as marker molecules, ultra performance liquid chromatography-mass spectrometry (UPLC-MS) was used to characterize extracts from *Cannabis sativa* L. Different extracts were shown to have inhibitory effects on the growth and survival of highly metastatic breast cancer cells. The dichloromethane extract included a greater concentration of CBD, which was shown to be useful in preventing the development of breast cancer cells *in vitro* and in angiogenesis. All things considered, it can be said that the African strain of *C. sativa* contains CBD, THC, and THCA, which may be utilized as marker components in UPLC-MS analysis. The plant's	[52]

and Progression	capacity to impede the growth and survival of breast cancer cells may support the medication's long-standing usage as an anticancer treatment.	
Preclinical and Clinical Assessment of Cannabinoids as Anti-Cancer Agents	This review concentrated on analysing the overall efficacy of these compounds in research involving humans and animals in order to provide insight into the translational and therapeutic potential of cannabis. Most of the *in vivo* animal research covered here suggests that endogenous, synthetic, and plant-derived cannabinoids can successfully inhibit the development and invasion of tumors.	[53]
Potential Use of Cannabinoids for the Treatment of Pancreatic Cancer	Through cannabinoid receptor-dependent or receptor-independent mechanisms, endogenous cannabinoids: synthetic or cannabis extracted from plants can suppress tumor angiogenesis, cause tumor cell death, and decrease tumor invasion and growth. Compared to normal pancreatic tissue, cannabinoid receptors seem to be abundantly expressed in pancreatic cancer. Both THC and CBD seem to have proapoptotic and antiproliferative properties. When coupled with gemcitabine, CBD enhanced survival results in a pancreatic cancer model that is relevant to clinical practice and so there is a severe need for clinical research on the use of cannabis in the treatment of pancreatic cancer.	[54]

Impact of Cannabinoid in Cancer and PD patients
Proteins which act with cannabinoid and have impact on both Parkinson's disease and cancer are as follows

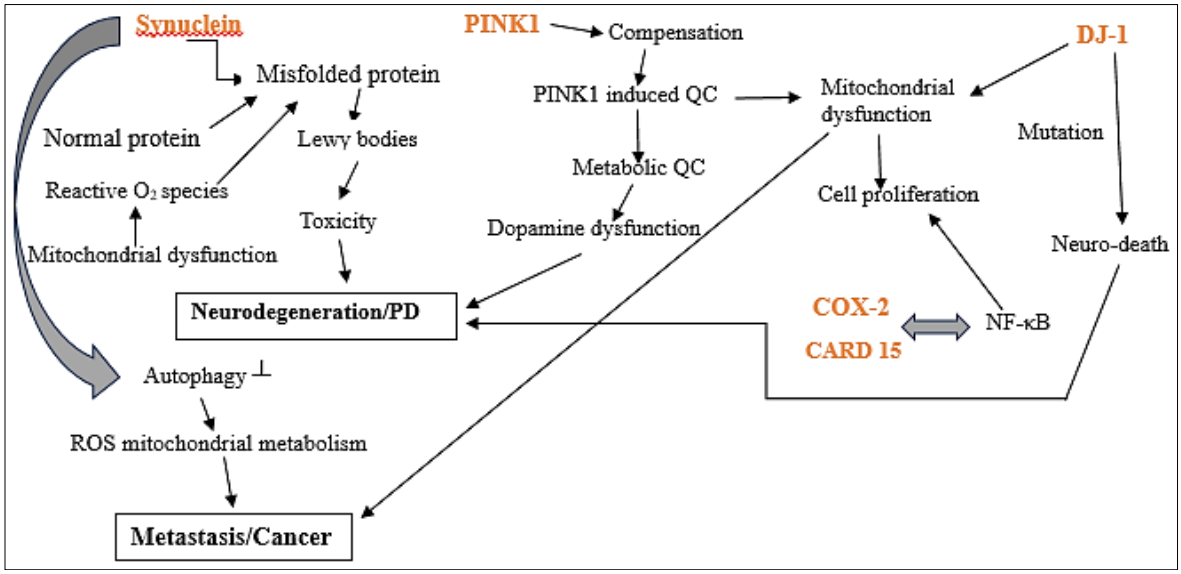

Fig: Interrelation between Parkinson's Disease and Cancer

Role of cytokines, oxidative stress and glial cells with cannabinoids to prevent PD and malignancy

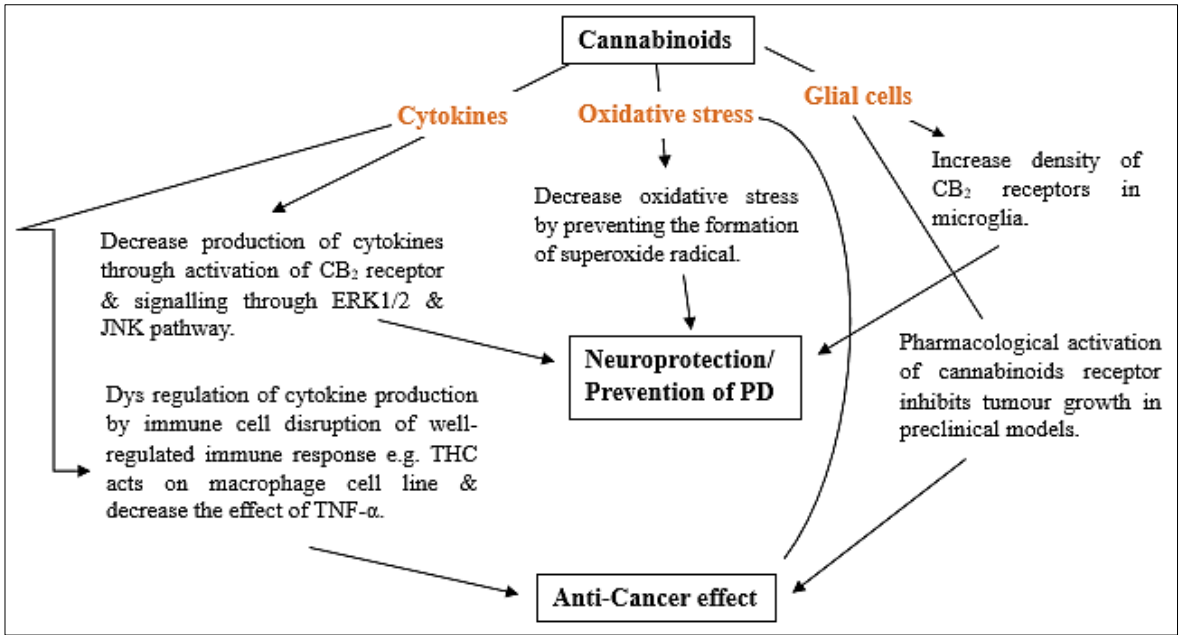

Fig: Prevention pathway of Parkinson's Disease and Cancer

Discussion

Overall, Parkinson's disease affects individuals independently and does not depend on age. However, the opposite is not true for a person who already has cancer is not likely to be affected by Parkinson's disease because cancer is an age-related condition that strikes people at the appropriate age. Parkinson's disease and cancer are caused by chronic inflammation, cell proliferation and other neuronal loss; cannabinoids operate through the endocannabinoid system to alleviate these conditions.

Conclusion

One explanation for the similarities between Parkinson's disease (PD) and cancer is the inflammation hypothesis, which states that different reactions take place in the different cellular backgrounds of cell division and cell death. The immune factors and free radicals released from chronic inflammatory reactions not only promote the occurrence of disease but also make it easier for cellular DNA to accumulate mutations, forming proteins with aberrant functions.

PINK1 and *DJ-1* mutations result in the overproduction of free radicals and oxidative stress in the mitochondria, which causes neuron defects and stimulates cell proliferation. *COX2* and *CARD15* mutations activate the NF-**κ**B pathway and induce chronic inflammation, leading to a wide range of genetic mutations and abnormal cellular signalling. The different cellular backgrounds of cancer cells and neurons (mitotic vs. post-mitotic cells) bring completely distinct reactions to external stimuli and internal changes: some undergo cell proliferation, and others neuron death. The final rsesult is two serious diseases: cancer and PD.

Abbreviations

ROS= Reactive O_2 species**,** PINK1= PTEN-induced putative kinase 1**,** DJ-1= Protein deglycase 1**,** COX2= Cyclooxygenase 2**,** NF-κB= Nuclear factor kappa B**,** ERK1/2= Extracellular signal regulated protein kinase 1&2**,** JNK= Jun N-terminal kinase**,** THC= Δ^9 tetrahydrocannabinol**,** TNF-α= Tumour necrosis factor-α, CARD15- Caspase recruitment domain- containing protein 15.

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Ethical Approval

This article does not contain any studies with human participants or animals performed by any of the authors.

Author Contributions

Conceptualization, data collection, data analysis, manuscript writing and manuscript revision was done by Rajnandan Borah and Manoleena Sarkar.

References

1. Marijuana, also called: Cannabis, Ganja, Grass, Hash, Pot, Weed. Medline Plus. 2017 Jul 3.
2. Pertwee R, ed. Cannabinoids. Springer-Verlag; c2005. p. 2. ISBN 978-3-540-22565-2.
3. Aizpurua-Olaizola O, *et al*. Evolution of the Cannabinoid and Terpene Content during the Growth of Cannabis sativa Plants from Different Chemotypes. J Nat Prod. 2016 Feb;79(2):324-331. DOI: 10.1021/acs.jnatprod.5b00949. PMID: 26836472.
4. IOM (Institute of Medicine). Marijuana and medicine: Assessing the science base. Washington, DC: National Academy Press; c1999.
5. Camargo Palladini M. Indications for the use of cannabinoids. Braz J Pain. October 2023. DOI: 10.5935/2595-0118.20230054-en.
6. Fraguas-Sanchez, *et al*. Medical Use of Cannabinoids. Drugs. 2018;78:1665-1703. https://DOI.org/10.1007/s40265-018-0996-1.
7. Mechoulam R, *et al*. Chemical basis of hashish activity. Science. 1970;169:611-612.
8. Herkenham M, *et al*. Neuronal localization of cannabinoid receptors in the basal ganglia of the rat. Brain Res. 1991;547:267-274.
9. Herkenham M, *et al*. Characterization and localization of a cannabinoid receptor in rat brain: a quantitative *in vitro* autoradiographic study. J Neurosci. 1991;11:563-583.
10. Tsou K, *et al*. Immunohistochemical distribution of cannabinoid CB1 receptors in the rat central nervous system. Neuroscience. 1998;83:393-411.
11. Sanudo-Pena MC, *et al*. Activational role of cannabinoids on movement. Eur J Pharmacol. 2000;391:269-274.
12. World Health Organization (WHO). Neurological disorders: public health challenges. WHO Press, Geneva; c2006.
13. Crippa JAS, *et al*. Is cannabidiol the ideal drug to treat non-motor Parkinson's disease symptoms. Eur Arch Psychiatry Clin Neurosci. 2019;269:121-133. DOI: 10.1007/s00406-019-00982-6.
14. Sevcík J, *et al*. Potential role of cannabinoids in Parkinson's disease. Drugs Aging. 2000;16:391-395. https://DOI.org/10.2165/00002512-200016060-00001.
15. More SV, *et al*. Promising cannabinoid-based therapies for Parkinson's disease: motor symptoms to neuroprotection. Mol Neurodegener. 2015;10:1-26. https://DOI.org/10.1186/s13024-015-0012-0.
16. Cancer-Signs and symptoms. NHS Choices. Archived from the original on 2014 Jun 8. Retrieved 2014 Jun 10.
17. World Health Organization. Cancer. 2018 Sep 12. Retrieved 2018 Dec 19.
18. National Cancer Institute. Defining Cancer. 2007 Sep 17. Retrieved 2018 Mar 28.
19. Anand P, *et al*. Cancer is a preventable disease that requires major lifestyle changes. Pharm Res. 2008 Sep;25(9):2097-116. DOI: 10.1007/s11095-008-9661-9.
20. National Cancer Institute. Obesity and Cancer Risk. 2012 Jan 3. Archived from the original on 2015 Jul 4. Retrieved 2015 Jul 4.
21. Jayasekara H, *et al*. Long-Term Alcohol Consumption and Breast, Upper Aero-Digestive Tract and Colorectal Cancer Risk: A Systematic Review and Meta-Analysis. Alcohol Alcoholism. 2016 May;51(3):315-30. DOI: 10.1093/alcalc/agv110. PMID: 26400678.
22. World Cancer Report 2014. World Health Organization. 2014. Chapter 1.1. ISBN 978-92-832-0429-9. Archived from the original on 2017 Jul 12.
23. American Cancer Society. Heredity and Cancer. Archived from the original on 2013 Aug 2. Retrieved 2013 Jul 22.

24. American Cancer Society. How is cancer diagnosed? 2013 Jan 29. Archived from the original on 2014 Jun 14. Retrieved 2014 Jun 10.
25. World Cancer Report 2014. World Health Organization. 2014. Chapter 1.1 ISBN 978-92-832-0429-9.
26. Siegel R, *et al*. Cancer statistics, 2023. CA Cancer J Clin. 2023;73(1):17-48. DOI: 10.3322/caac.21763. ISSN: 0007-9235.
27. Dubas LE, Ingraffea A. Nonmelanoma skin cancer. Facial Plast Surg Clin North Am. 2013 Feb;21(1):43-53. DOI: 10.1016/j.fsc.2012.10.003. PMID: 23369588.
28. Cakir BO, *et al*. Epidemiology and economic burden of nonmelanoma skin cancer. Facial Plast Surg Clin North Am. 2012 Nov;20(4):419-22. DOI: 10.1016/j.fsc.2012.07.004. PMID: 23084294.
29. World Cancer Report 2014. World Health Organization. 2014. Chapter 1.3. ISBN 978-92-832-0429-9. Archived from the original on 2017 Jul 12.
30. Manton K, *et al*. Cancer Mortality and Morbidity Patterns in the U.S. Population: An Interdisciplinary Approach. Springer Science & Business Media; 2008 Dec 28. ISBN 978-0-387-78193-8.
31. Islami F, *et al*. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. CA Cancer J Clin. 2018 Jan;68(1):31-54. DOI: 10.3322/caac.21440. PMID: 29160902.
32. Wichmann T, *et al*. The primate subthalamic nucleus. III. Changes in motor behavior and neuronal activity in the internal pallidum induced by subthalamic inactivation in the MPTP model of Parkinsonism. J Neurophysiol. 1994;72:521-530.
34. Sanudo-Pena, *et al*. Role of the subthalamic nucleus on cannabinoid actions in the substantia nigra of the rat. J Neurophysiol. 1997;77:1635-1638.
35. Sanudo-Pena, *et al*. Effects of intrapallidal cannabinoids on rotational behavior in rats: interactions with the dopaminergic system. Synapse. 1998;28:27-32.
36. Sanudo-Pena MC, *et al*. Cannabinoid effects in basal ganglia in a rat model of Parkinson's disease. Neurosci Lett. 1998;248:171-174.
37. Crippa JAS, *et al*. Is cannabidiol the ideal drug to treat non-motor Parkinson's disease symptoms? Eur Arch Psychiatry Clin Neurosci. 2019;269:121-133. DOI: 10.1007/s00406-019-00982-6.
38. Borgelt LM, *et al*. The pharmacologic and clinical effects of medical cannabis. Pharmacotherapy. 2013;33:195-209.
39. Whiting PF, *et al*. Cannabinoids for Medical Use: A Systematic Review and Meta-analysis. JAMA. 2015;313:2456-73.
40. Blake A, *et al*. A selective review of medical cannabis in cancer pain management. Ann Palliat Med. 2017;6(Suppl 2):S215-S222.
41. Guzman M. Cannabinoids: potential anticancer agents. Nat Rev Cancer. 2003;3:745-55.
42. Croxford JL. Therapeutic Potential of Cannabinoids in CNS Disease. CNS Drugs. 2003;17(3):179-202. DOI: 1172-7047/03/0003-0179.
43. Figura M, *et al*. Cannabis in Parkinson's Disease-the patient's perspective versus clinical trials: a systematic literature review. Polish Journal of Neurology and Neurosurgery. 2022;56(1):21-27. DOI: 10.5603/PJNNS.a2022.0004.
44. Thanabalasingam SJ, *et al*. Cannabis and its derivatives for the use of motor symptoms in Parkinson's disease: a systematic review and meta-analysis. Ther Adv Neurol Disord. 2021;14:1-22. DOI: 10.1177/17562864211018561.
45. Costa AC, *et al*. Cannabinoids in Late Life Parkinson's Disease and Dementia: Biological Pathways and Clinical Challenges. Brain Sci. 2022;12:1596. DOI: 10.3390/brainsci12121596.
46. Ferreira Junior NC, *et al*. Cannabidiol and Cannabinoid Compounds as Potential Strategies for Treating Parkinson's Disease and L-DOPA-Induced Dyskinesia. Neurotoxicity Research. 2020;37:12-29.
47. Sarfaraz S, *et al*. Cannabinoid Receptor as a Novel Target for the Treatment of Prostate Cancer. Cancer Res. 2005;65(5):March 1, 2005.
48. Hall W, *et al*. Cannabinoids and cancer: causation, remediation, and palliation. Oncology. 2005;6:35-42.
49. Ward SJ, *et al*. Cannabinoids and Cancer Chemotherapy-Associated Adverse Effects. J Natl Cancer Inst Monograph. 2021;2021(58):lgab007. DOI: 10.1093/jncimonographs/lgab007.
50. Davis MP. Cannabinoids for Symptom Management and Cancer Therapy: The Evidence. JNCCN-Journal of the National Comprehensive Cancer Network. 2016;14(7):915-922.
51. Daris B, *et al*. Cannabinoids in cancer treatment: Therapeutic potential and legislation. Bosn J Basic Med Sci. 2019;19(1):14-23. DOI: 10.17305/bjbms.2018.3532.
52. Bala A, *et al*. UPLC-MS Analysis of Cannabis sativa Using Tetrahydrocannabinol (THC), Cannabidiol (CBD), and Tetrahydrocannabinolic Acid (THCA) as Marker Compounds: Inhibition of Breast Cancer Cell Survival and Progression. Natural Product Communications. 2019;1-5. DOI: 10.1177/1934578X19872907.
53. Ladin DA, *et al*. Preclinical and Clinical Assessment of Cannabinoids as Anti-Cancer Agents. October. 2016;7(Article 361).
54. Sharafi G, *et al*. Potential Use of Cannabinoids for the Treatment of Pancreatic Cancer. Journal of Pancreatic Cancer. 2019;5(1). DOI:10.1089/pancan.2018.0019.