

## Review Article

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## Cannabis Wrong Way to be Employed

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### Introduction

The history of medical cannabis spans millennia, with the plant playing a role in various cultures and civilizations for therapeutic purposes. The use of cannabis for medicinal reasons can be traced back to ancient times, when it was employed by different societies for a range of health-related applications. One of the earliest documented instances of medical cannabis use dates to ancient China. The Chinese emperor Shen Nung is credited with the compilation of the “Pen Ts’ao,” a pharmacopoeia that documented the medicinal properties of various plants, including cannabis. Shen Nung is believed to have recommended cannabis for a variety of ailments, including rheumatism and malaria, highlighting its perceived healing properties.

In ancient India, cannabis found a place in traditional Ayurvedic medicine. The sacred Hindu text, the Atharvaveda, mentions cannabis as one of the “five kingdoms of herbs,” emphasizing its potential therapeutic value. Cannabis was used to treat a range of conditions, from anxiety and insomnia to digestive issues.

Moving westward, ancient Egypt is another civilization where evidence of medical cannabis use exists. The Ebers Papyrus, an ancient Egyptian medical text, references cannabis as a treatment for conditions such as inflammation and glaucoma. The plant’s analgesic properties were recognized, and it was often prescribed to alleviate pain.

The ancient Greeks also embraced the medicinal properties of cannabis. The renowned physician Dioscorides included cannabis in his pharmacopoeia, “De Materia Medica,” around the 1st century CE. The Greeks utilized cannabis for treating earaches and suppressing sexual desire, among other purposes.

As history unfolded, cannabis continued to be employed for medical reasons in various parts of the world. In medieval Islamic societies, scholars like Avicenna recognized cannabis for its potential in treating a range of ailments. The plant’s use persisted through the Middle Ages in Europe, where it was recommended for conditions such as pain and insomnia.

In the 19<sup>th</sup> century, cannabis began to attract attention in Western medicine. The Irish physician William O’Shaughnessy conducted studies in India and introduced cannabis to Western medicine as a treatment for conditions like muscle spasms and pain. Cannabis-

based medications were widely available in the United States and Europe during this period.

However, as the 20<sup>th</sup> century dawned, the perception of cannabis underwent a significant shift. Regulatory measures and legal restrictions were implemented in many countries, leading to the decline of cannabis as a mainstream medicinal option. The United States implemented strict regulations with the Marihuana Tax Act of 1937, effectively criminalizing cannabis.

From Main Phyto-Cannabinoid [1-3].

### Phyto-Cannabinoids

|   |   |
|---|---|
| Phyto-cannabinoids  | (THC, Δ <sup>9</sup> -THC) Psychotropic |
| 9-Δ-Tetrahydrocannabinol  |   |
| Cannabidiol   | (CBD) Psychotropic                      |
| Tetrahydrocannabivarin  | (THCV) Psychotropic                     |
| Cannabichromen  | (CBC) Psychotropic                      |
| Psychotropic Cannabicylol   | (CBL) Non psychotropic                  |
| Cannabielsoin   | (CBE) metabolite synthesizes            |
| Cannabigerol  | (CBG) Non-psychotropic                  |
| Cannabinydiol   | (CBND) Non-psychotropic                 |
| Cannabitol  | (CBT) precursor cannabidiol acid        |
| Cannabivarin  | (CBV) Non-psychotropic                  |
| Cannabidivarin  | (CBDV) Non-psychotropic                 |
| Cannabichromevarin  | (CBCV) Psychotropic                     |
| Cannabigerovarin  | (CBGV) Non-psychotropic                 |
| Cannabigerol monomethylate  | (CBGM)                                  |
| The main precursors of most cannabinoids are (Nachnani R, Raup-Konsavage WM, Vrana KE, 2021) three cannabinoids recently discovered |   |
| 19 Δ tetra-hydro-cannabiforol   | (THCP)                                  |
| 2.Cannabidiforol  | (CBDP)                                  |
| 3 Cannabidibutol  | (CBDB)                                  |

## Furtherly an Endogenous Cannabinoid System Exists. It is the Endocannabinoid System

|                              |                  |
|------------------------------|------------------|
| Anandamide                   | (AEA)            |
| 2-arachidonilglicerole       | (2-AG)           |
| 2-arachidonil-gliceril-etero | (noladin, 2-AGE) |
| Virodamine                   |                  |
| N-arachidonildopamine        | (NADA)           |
| Palmitoiletanolamide         | (PEA)            |

It wasn't until the latter part of the 20<sup>th</sup> century that a renewed interest in medical cannabis emerged. In the 1970s, synthetic cannabinoids were developed for medical use, and research on the plant's therapeutic properties resumed. In the 1990s, California became the first U.S. state to legalize medical cannabis for certain conditions, marking a turning point in the modern history of medical cannabis.

Since then, there has been a growing recognition of the potential medical benefits of cannabis. Many countries and states have implemented medical cannabis programs, allowing patients to access cannabis-based treatments for conditions such as chronic pain, epilepsy, and cancer-related symptoms. Scientific research continues to explore the various compounds in cannabis, such as THC and CBD, and their potential therapeutic applications.

In recent years, an increasing number of countries have moved towards decriminalization and legalization of medical cannabis, acknowledging its potential as a valuable tool in healthcare. As the stigma surrounding cannabis diminishes and scientific understanding deepens, the history of medical cannabis continues to evolve, with the plant reclaiming its place in the pharmacopeias of the world.

The objective of this article is to identify the disadvantages and prospects of cannabis abuse against appropriate laboratory test use. Moreover, in past decades of research, the retrieval of components in Cannabis has made feasible the study of several psychotropic and non-psychotropic compounds that this herb and their variants contain. Non-medical products have appeared on the market and this article aims to assess the pharmacological impact of these on a wide population of consumers. Nowadays, a broad variety of cosmetics, food, supplements, and many other products attract wide-ranging consumption on the market [4].

Over the past decades, Cannabis abuse has raised interesting possibilities for research cues. The discovery of its various compounds could have led to research on its endogenous components. What about its endogenous human variants? In the end, the development of several legal products brought cannabis far from research branches and close to consumers who hadn't any deep knowledge of its effects [5,6].

The variety of products produced cannot ascertain deeply several molecules' pharmacological aspects. In the end, legalization got close to cannabis and isotropic derivatives and so it got close to consumers to products that had no precise limitation in the list of its components within the products. E.g., in cosmetics, food products, in the products and consumer goods in general this is a serious mistake. The consumption of these new fashion products can be a serious mistake by unaware consumers because it makes it possible that the Cannabis contained may reach a toxic level after several applications or ingestion. Cannabis contains a varied number

of substances; some are psychotropic and part of them are non-psychotropic. Which are devoid of chemical and clinical studies using free-marketed products. Nevertheless, it makes possible the identification of effects on humans, even in small doses. As it can be in consumer products. A good perspective can derive from proper Pharmacovigilance control of the broad consumption of new-fashionable and new-taste products. Indeed, passed collected data can delineate a strategy for a correct prevision on Cannabis effects. It would be necessary to improve the management of sometimes harmful side effects as it represents a step forward in public health management. Pharmacovigilance properly asset data. Analysis strategy possible to obtain an innovative guide to correct use. Safety and efficacy would improve the general quality of consumption by pharmacovigilance-corrected skills definitively [7].

## Cannabinoids

A pharmacovigilance system could ensure the health of all consumers of these novel and free fashion products. In the absence of specific descriptions, it is noteworthy that overdose incidents can occur easily. Manifestation of effects beyond personal idiosyncrasies could pose a secondary health concern. However, it is possible to pinpoint hospital visits and enhance intoxication data through information obtained from emergency care services.

The cannabinoid system operates through two receptors, CB1 and CB2. CB1 is centrally located in the body-brain system, particularly in the nervous system, while CB2 is predominantly found in the bowel and heart. During both the phases of use and abuse of various substances within cannabis, which number several dozen, each acts according to its unique pharmacodynamics and pharmacokinetics. An illustrative example of adsorption is presented in the following table.

Numerous types of substances with psychotropic effects have been identified, potentially signifying neuropsychiatric implications in their abuse. Some of these substances contribute to permanent abstinence, leading to enduring psychiatric disorders. These disorders can be classified based on the degree of abuse and corresponding behaviors. Nevertheless, the introduction of free cannabis products represents a novel approach to engaging with the substances present in Cannabis sativa and Cannabis indica. A thorough pharmacovigilance assessment can significantly contribute to our understanding of these substances, which are present in varying densities across different Cannabis varieties, incorporating the latest findings from contemporary scientific research on the subject [8].

In recent years, there has been growing attention and interest in the innovative uses of cannabis in medicine, prompting numerous researchers and healthcare professionals to explore its potential therapeutic applications. Cannabis, a plant also known as hemp, has been used for medicinal purposes since ancient times, but recent scientific discoveries are revealing new horizons in the field of medicine.

One of the most studied uses involves the treatment of chronic pain. Cannabis contains compounds called cannabinoids, including THC (tetrahydrocannabinol) and CBD (cannabidiol), which act on pain receptors in the nervous system. Numerous clinical studies have demonstrated that cannabinoids can be effective in managing pain associated with conditions such as arthritis, fibromyalgia, and other chronic illnesses. This has led to a growing interest in the development of cannabis-based therapies to improve the quality of life for patients with chronic pain.

Another area where cannabis is showing promise is in the management of neurological disorders. CBD, in particular, has demonstrated potential neuroprotective and anti-inflammatory effects. Clinical studies are underway to assess the efficacy of cannabis in treating epilepsy, multiple sclerosis, and other neurological conditions. Preliminary results are encouraging, suggesting that cannabis could be a valuable resource to enhance the quality of life for patients with neurological disorders.

Cannabis has also been studied for its use in managing mental illnesses. Several studies indicate that certain cannabinoids may have positive effects on conditions such as anxiety, depression, and post-traumatic stress disorder (PTSD). Some patients report an improvement in psychological symptoms with controlled cannabis use, paving the way for new therapeutic options for those who do not respond adequately to conventional therapies.

An area where cannabis has shown particular efficacy is in managing symptoms associated with cancer therapies. Cancer patients undergoing chemotherapy or radiation often experience nausea, loss of appetite, and pain. Some cannabinoids, such as THC, have been shown to be helpful in alleviating these symptoms, improving the quality of life for cancer patients. This has spurred further exploration of potential applications of cannabis in the field of oncology, aiming to improve outcomes and mitigate the side effects of anticancer therapies.

However, it is important to emphasize that research on cannabis in medicine is still in a relatively early stage, and there are many issues to address, such as standardizing doses and fully understanding the long-term effects. The use of cannabis for medical purposes is also the subject of debate in many societies, with ethical and legal considerations influencing its acceptance and regulation.

In conclusion, the innovative uses of cannabis in medicine represent an exciting and evolving field of research. The scientific evidence gathered so far suggests that cannabis could play a significant role in managing various medical conditions, offering new perspectives and therapeutic options. However, it is crucial to continue with in-depth research, adhering to rigorous scientific protocols, to fully understand the therapeutic potential of cannabis and ensure that patients benefit from it safely and effectively.

## Discussion

Undoubtedly, Cannabis and its derivatives can be used more intelligently for the exploitation in the laboratory of substances called therapeutic leads for the development of drugs against pain: both the chemical variation and the pharmacodynamic variation that leads to the effect of the interaction with the receptor and its binding power are two characteristics that can modulate the effect and be decisive in the therapeutic demand that the therapies require. In addition, the pharmacodynamic aspects are evaluated, which in turn are influenced by the PKa and pH of the molecule on its absorption. The distribution of the newly formed molecule is based on its lipophilic, as well as its chemical and metabolic characteristics, which depend in any way on the chemical characteristics that attribute not to the newly formed molecule through its synthesis. Nevertheless, its excretion depends on these chemical characteristics. Many other data can reach the prospective to lead the modification of Cannabis therapeutic leads and be the future of drug discovery from natural derivatives [8].

## Conclusion

Clinical evaluation of different dosages of cannabinoids and innovative delivery systems.

The clinical reference is to be clear on Cannabis's effects and safety.

- Ophthalmic delivery of cannabinoids is now used for glaucoma therapy. Furthermore, clinical safety and efficacy are a broad therapeutic spectrum, thanks to innovative formulations.
- APH-1403 CBD is encapsulated in biodegradable polymer nanospheres as a lyophilised formulation, administered orally. The Phase II clinical assessment is indicated for Opioid addiction and Multiple sclerosis at a dose of 400–800 mg BID.
- The EudraCT2015-004227-31 trial is a clinical pilot study that aimed to assess the impact of perioperative administration of synthetic cannabinoid nabilone in the context of spinal fusion surgery, coping with surgery, and the pain perception of patients with severely reduced quality of life. The primary endpoints in Placebo (K-Gruppe) versus Nabilone (V-Gruppe) versus Intention-to-treat groups evaluated the anxiety, depression, low back pain disability, and pinprick pain. They re-evaluated them as secondary endpoints by different methods. The study assessed nabilone favourably.
- The EudraCT2017-004253-16 trial aimed to assess Nabilone for non-motor symptoms in Parkinson's disease by an open-label study to evaluate long-term safety and efficacy. The study's primary endpoint was safety. The parameter assessed in this category was the C-SSRS describing suicidality. No patient experienced suicidality. Therefore, the count was 0. The secondary efficacy criteria were measured as the change in the different clinical scales and questionnaires regarding motor symptoms and other domains of non-motor symptoms in Parkinson's Disease between V 1 and V 3; arithmetic means (standard deviation) Part 1  $1.58 \pm 13.87$ ; Part 2  $-0.58 \pm 3.49$ ; Part 3  $-1.89 \pm 6.88$ ; Part 4  $-0.16 \pm 2.14$ ; Motor Sum Score  $-2.47 \pm 7.88$ ; Sum Score Part 1 – 3  $-0.89 \pm 14.99$ . Secondary endpoints were arithmetic mean (standard deviation) MMSEn  $0.42 \pm 1.84$  MoCA-0.11  $\pm 1.94$  and change in scores for cognition.
- THC and CBD standardized extract formulations are Oro-mucosal preparations, that treat painful spasticity and neuropathic pain in multiple sclerosis. Dosage: Each 100 microlitre spray contains 2.7 mg delta-9-tetrahydrocannabinol (THC) and 2.5 mg cannabidiol (CBD) from Cannabis L. sativa.
- THC and CBD and their volume of distribution allow their storage for four weeks in fatty tissues from which they lowly deliver their therapeutic effect. Modified release formulations on non-compartmental pharmacokinetic analysis show a first-order terminal elimination.

Among all Cannabis the Phyto derivatives Cannabidiol, it seems to be the most appropriate to start the transformation into new potential candidates for human tests. It is not a psychotropic-deprived product, and its adsorption gets a favourable pharmacokinetic parameter. Further steps in drug development demonstrated endocannabinoids or Ali amides PEA palmitoylethanolamide to be efficient in chronic pain management. Future prospective molecular studies can assess the appropriate modification of these important phytotherapy drug leads by human tests. Molecular modification and drug modelling can start from this therapeutic lead to ensure new pharmaceutical goals as well as ADRs (Adverse Drug Reactions) reduction. Definitively drug design improvement

and active principles substitution can reduce side effects and improve their therapeutic action. Indeed, this consideration can lead to a step forward in chronic pain management [1-9].

#### Conflict of Interest

The author discloses from any conflict of interest, that he solely contributed to outlining the poster., no funding was used. Furthermore, to realize this article.

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