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REVIEW ARTICLE

Cannabis and its influence on cellular stability and tissue integrity: analysis of cell lysis and cell death markers

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ABSTRACT

Introduction: cannabis consumption has been the subject of growing scientific interest due to its effects on cellular stability and tissue integrity, with relevant implications for public health.
Objective: to analyze the available evidence on the effects of cannabis on cell lysis, inflammation, and tissue degeneration in vital organs.
Methods: a systematic review of the scientific literature was conducted across various databases. The search was carried out using an algorithm with keywords and Boolean operators, allowing the identification of relevant sources. The selected studies, after applying inclusion and exclusion criteria, were critically analyzed considering timeliness, methodological quality, and thematic relevance, and integrated into the final synthesis of the review.
Development: tetrahydrocannabinol affects neuroplasticity and neuronal homeostasis, generating cognitive and structural alterations in the brain. In the liver, CB1 receptor activation promotes inflammatory processes and fibrosis, while in the cardiovascular system arrhythmias, orthostatic hypotension, and risk of heart failure have been reported. Findings also show an increase in reactive oxygen species and endothelial dysfunction, compromising cell viability. Although some studies suggest beneficial immunomodulatory effects, the prevailing evidence highlights negative consequences on organ function and tissue integrity.
Conclusions: cannabis exerts adverse effects on cellular stability and the integrity of essential organs, promoting inflammatory and degenerative processes. These findings reinforce the need for further research and preventive strategies that consider neurological, cardiovascular, and hepatic risks.

Keywords: Marijuana Abuse; Cannabis; Inflammation; Substance-Related Disorders; Cell Death.

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INTRODUCTION

Cannabis sativa, commonly known as marijuana, is an illegal drug in Ecuador and a chemical substance that causes mental alterations.[1] Abuse of this substance can lead to severe consequences at the tissue level in the human body. It is well established that cells—the fundamental biological units—are primarily affected. Marijuana use remains a highly controversial issue today: some view it as a medicinal drug, while others classify it as a psychotropic substance.

Marijuana can cause either permanent or, in some cases, reversible harmful effects. A key factor is the cellular response—defined as the reaction of our cells to foreign agents such as marijuana. Cannabinoids, from the perspective of host defense, increase cellular immunity while decreasing humoral immunity. [2] This shift is associated with a significant increase in Th2-derived cytokines (e.g., IL-4) and a reduction in Th1-derived cytokines (e.g., IFN-γ and IL-12), driven by these compounds.

Beyond its impact on immune response, marijuana significantly influences tissue lysis, as any toxic substance can cause irreversible damage to affected tissues. The most affected system is the nervous system; marijuana acts primarily on the limbic system, where learning, information processing, and memory formation occur.[3] Importantly, cannabis directly affects cerebral gray matter, thereby altering its functions. This substance can also damage the liver—a vital organ responsible for regulating blood chemistry and producing bile for fatty acid degradation.[4]

The harmful effect of marijuana on the liver is considerable: CB1 receptor activation may lead to abnormal tissue scarring, particularly in individuals with preexisting hepatic injury. Additionally, a study demonstrated certain hepatotoxic potential of marijuana in mice, though this finding is not considered fully relevant since it has not been observed in humans.[5]

Regarding the cardiovascular system, marijuana use can cause serious harm, including exacerbation of orthostatic hypotension associated with vasovagal reactions.[6] Given this context, the present review was conducted to analyze the available evidence on the effects of cannabis on cell lysis, inflammation, and tissue degeneration in vital organs.

METHODS

This study was designed as a systematic literature review following PRISMA guidelines to ensure transparency and reproducibility in the search, selection, and analysis of evidence. The search period spanned from 2000 to 2024 to include recent and relevant research on cannabis effects on cellular stability and tissue integrity. Both experimental and clinical studies were considered, along with prior reviews providing complementary information on mechanisms of cell lysis, apoptosis, and tissue damage.

Information sources included major biomedical databases: PubMed, SciELO, ScienceDirect, Google Scholar, LILACS, and BVSALUD. Secondary references from selected article bibliographies and gray literature—including technical reports and institutional documents—were also reviewed to broaden the evidence base. This strategy enabled identification of studies published in indexed journals and academic repositories, ensuring a comprehensive overview of the topic.

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The search strategy employed an algorithm combining keywords and Boolean operators. Terms included: "cannabis" OR "marijuana" AND ("apoptosis" OR "cell death" OR "lysis" OR "oxidative stress" OR "inflammation"), adapted to each database. Articles in Spanish, English, and Portuguese were included, as these languages represent a large portion of biomedical scientific output. Searches were refined using corresponding DeCS/MeSH descriptors to ensure precision and exhaustiveness.

Inclusion criteria encompassed studies published within the defined timeframe, with full-text access, directly addressing the relationship between cannabis and cellular stability, inflammation, apoptosis, or tissue damage. Duplicates, articles without full access, irrelevant studies, those outside the temporal range, and purely theoretical publications lacking empirical data were excluded.

The selection process occurred in several phases. Initially, 330 sources were identified; 200 were removed due to duplication or irrelevance. The remaining 130 entries were screened against eligibility criteria, yielding 40 articles. Of these, 38 underwent full-text review, and ultimately, 28 studies were included in the qualitative analysis.

Data extraction and analysis were performed systematically, collecting key variables: author, publication year, methodological design, studied population/sample, main findings, and conclusions. Comparative tables were developed to organize information and facilitate interpretation. Given the heterogeneity of study designs and outcomes, a qualitative synthesis was conducted instead of a quantitative meta-analysis. Nevertheless, narrative synthesis allowed identification of common patterns, discrepancies, and knowledge gaps, providing a critical and structured perspective on cannabis effects on cellular stability and tissue integrity.

DEVELOPMENT

Marijuana use has become a topic of increasing scientific interest, particularly regarding its effects on various biological systems. The analysis focused on marijuana's impacts on immune, hepatic, and cardiovascular function, as well as on cellular integrity and neuronal health, as summarized in Table 1.

Table 1. Effects of marijuana on different tissues.

Tissue/System	Effects
Cardiovascular	• Vascular function is impaired, causing vasodilation and potentially disrupting normal blood flow regulation. • Marijuana use can cause transient increases or decreases in blood pressure, with unpredictable variations depending on dose and individual response. • Cases of myocardial infarction and hypertensive crises associated with cannabis use have been reported.
Hepatic	• Excessive marijuana use may contribute to hepatitis and fibrosis in at-risk individuals, although a direct causal relationship remains unclear. • Marijuana may interfere with the metabolism of certain liver-processed medications, altering their levels and efficacy. • Chronic use may be associated with an increased risk of non-alcoholic fatty liver disease (NAFLD).
Cerebrovascular	• Drug dependence induces psychological processes that translate into neuronal changes in the brain. • Tetrahydrocannabinol (THC) is the primary psychoactive compound, binding to specific chemical structures on neuronal membranes. • Dependence develops within seconds due to pharmacokinetic factors.

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Immune Function Alterations
Marijuana use can modulate the activity of immune cells such as macrophages and lymphocytes, reducing proinflammatory cytokine production and altering inflammatory responses. This immunomodulatory effect may impair the body's ability to combat infections and promote relative immunosuppression, increasing vulnerability to pathogens and chronic inflammatory processes. (7,8)

Cannabinoids interact with CB1 and CB2 receptors on immune cells, modulating signaling pathways such as NF-κB and JAK/STAT. This interaction regulates transcription of genes associated with cytokines like IL-2, TNF-α, and IFN-γ, and induces redox imbalances, increasing oxidative stress and compromising immune homeostasis. (9,10)

Hepatic Apoptosis
Cannabinoids can either induce or inhibit apoptosis in liver cells depending on cell type and exposure context. In hepatocytes, CB1 receptor activation promotes apoptosis, whereas in hepatic stellate cells, CBD may induce programmed cell death with potential antifibrotic effects.(11,12)

Mechanisms include caspase activation, endoplasmic reticulum stress, and mitochondrial dysfunction. THC and CBD can modulate cytochrome c release and caspase-3 activation, triggering apoptosis. In other contexts, CB2 signaling may exert protective effects by inhibiting proapoptotic pathways and modulating hepatic inflammatory responses. (3,13)

Cell Membrane Damage
Marijuana exposure can compromise hepatocyte membrane integrity, leading to serum release of liver enzymes such as ALT and AST—indicators of cellular damage. These changes reflect altered membrane permeability and structural instability in liver cells.(2,14)

At the molecular level, cannabinoids can induce lipid peroxidation in cell membranes, altering fluidity and membrane protein function. Increased reactive oxygen species (ROS) contribute to disruption of the lipid bilayer and loss of cellular integrity, promoting enzyme leakage and progression toward fibrosis. (1,3,15)

Alterations in Hepatic Biochemical Markers
Cannabis use has been associated with elevated transaminases (ALT, AST), alkaline phosphatase, and bilirubin, reflecting negative impacts on liver function. These biochemical changes are consistent with hepatocellular damage and cholestasis, as reported in clinical and experimental studies. (5)

Mechanisms include CB1 receptor activation in hepatocytes, promoting inflammation and fibrosis, as well as altered cytochrome P450 enzyme activity. This leads to accumulation of toxic metabolites and impaired bilirubin excretion, resulting in detectable abnormalities in liver function tests.(16)

Drug Metabolism Interference
The liver metabolizes THC and CBD primarily via the CYP450 enzyme system. Marijuana use can alter the activity of isoenzymes such as CYP2C9 and CYP3A4, modifying the pharmacokinetics of concomitant medications and increasing the risk of adverse interactions.(17,18)

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Mechanisms include competitive inhibition of cytochrome P450 enzymes and induction of other isoforms, altering the metabolism rate of drugs such as anticoagulants, antiepileptics, and antidepressants. This may cause plasma accumulation or reduced therapeutic efficacy, depending on the interaction type.[19,20]

Endothelial Dysfunction

Chronic marijuana use has been linked to endothelial dysfunction, characterized by reduced nitric oxide bioavailability and increased vascular oxidative stress. These changes predispose individuals to hypertension, atherosclerosis, and higher cardiovascular event risk.[21,22]

Mechanisms involve CB1 receptor activation in endothelial cells, promoting ROS production and inflammatory pathways like NF-κB. This impairs endothelial function, reduces nitric oxide–dependent vasodilation, and enhances monocyte adhesion, contributing to cardiovascular disease development. [23,24]

Neuronal Damage

Prolonged cannabis use is associated with structural and functional brain alterations, evidenced by MRI studies and neuronal damage biomarkers. Chronic users show deficits in memory, attention, and executive functions. [2,4,25]

Mechanisms include THC interaction with CB1 receptors in cortical and hippocampal neurons, altering neurotransmitter release (e.g., glutamate and GABA). Additionally, synaptic plasticity dysfunction and reduced functional connectivity have been observed, compromising neuroplasticity and promoting cognitive decline. [26,27]

CONCLUSIONS

Based on the bibliographic analysis, marijuana exerts systemic effects in humans. Neurologically, it has a pronounced impact, classifying it as a psychotropic substance. Cardiovascularly, evidence suggests marijuana users face an increased risk of heart failure. Hepatically, limited studies report hepatotoxic effects observed in animal models, though these have not yet been confirmed in humans. These findings underscore the need for continued research and preventive strategies addressing neurological, cardiovascular, and hepatic risks associated with cannabis use.

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