MUNISI: Military Mathematics and Natural Sciences
e-ISSN: xxxx-xxxx; p-ISSN: xxxx-xxxx
Vol. 1, No. 1, June 2023, pp. 7-16
Available online at https://jurnal.idu.ac.id/index.php/munisi

The Influence of The Biochemical Components of Marijuana on Several Systems in Human Body: Review

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Abstract

Marijuana is a substance that has the same effect as opium, which has a decreased or altered function of consciousness, loss of taste, intoxication and can lead to addiction. History has recorded a long road to the relationship between humans and cannabis plants. Nowadays, Marijuana affects the brain, influences Genetic alveolar macrophages, sperm health, Cardiovascular system, and oral health. However, a little review discussed the effect of Marijuana on the human body even though the compound can dramatically influence almost the whole human body. Therefore, this review article is important to study the effect of Marijuana on the human body.

Keywords: *Cannabis sativa L.; drugs; marijuana; phytochemicals.*

Introduction

Marijuana (*Cannabis sativa* L.) is an annual plant, which can grow and spread in tropical or sub-tropical areas with a tree height of one to five meters (Rosani 2013). We often know marijuana as a substance that has the same effect as opium, which has a decreased or altered function of consciousness, loss of taste, intoxication, and can lead to addiction. History has recorded a long road of the relationship between humans and cannabis plants since thousands of years ago, i.e., experiencing euphoria (prolonged feeling of pleasure without cause). The cannabis plant is usually made into marijuana cigarettes. Fingering leaves with male and female flowers in different plants (having two houses). The flowers are small in groups at the end of a twig. Marijuana only grows in tropical mountains.

The active substances found in marijuana to date are 60 cannabinoids, including Δ9-THC (Delta 9 Tetrahydrocannabinol), CBD (Cannabidiol), CBN (Cannabinol), CBC (Cannabichromene), CBG (Cannabigerol), and others (Rudolf 2007). The main active constituent in marijuana is Δ9-THC, which has hallucinogenic and depressant effects. When marijuana is used like a cigarette, Δ9- tetra-hydro cannabinoid acid (Δ9-THCA) is only partially converted to THC. The conversion temperature was dependent on the decarboxylation of THCA under analysis and smoking conditions. The average

conversion rate to THC under the analysis conditions is around 70%. Meanwhile, when it is made into cigarettes, it is around 30% (Siegel et al. 2000). Another main active substance possessed by the cannabis plant is CBD. This cannabis plant has anxiolytic and antipsychotic properties and to improves some of the side effects of THC. THC and CBD have been shown to have opposite effects on regions of brain activation in various cognitive tasks (Sabrina 2014). CBD is a plant non-psychotropic constituent, generally found in relatively high concentrations in cannabis (Skoog et al. 1991; Sabrina 2014). CBD is a component of cannabis and is 40% of the plant extract. However, CBD concentrations vary widely and depend on growing conditions, different phenotypes of illegal cannabis, and the plant parts analyzed (Bruci et al. 2012). CBN was the first natural cannabinoid to be isolated and purified. Saito (2011) reported the isolation of a compound known as CBN by distillation (Sabrina. 2014). THC and CBD have been shown to have opposite effects on regions of brain activation in various cognitive tasks (Rudolf 2007). CBD is a plant non-psychotropic constituent, generally found in relatively high concentrations in cannabis (Rudolf 2007). CBD is a component of cannabis and is 40% of the plant extract. However, CBD concentrations vary widely and depend on growing conditions, different phenotypes of illegal cannabis, and on the plant parts analyzed (Siegel et al. 2000). CBN was the first natural cannabinoid to be isolated and purified. CBN was the first natural cannabinoid to be isolated and purified.

Marijuana is a dried leaf and flower bud of a plant that has the scientific name *Cannabis sativa*. Techniques that are usually used to consume them are by smoking, vaporizing, or drinking directly (Mehmedic et al. 2010). The physiological effects of consuming marijuana will peak 30 minutes after inhalation and reach 2-4 hours after drinking (Winstock et al. 2010). The use of marijuana is widely used for public medical treatment. However, some people use cannabis to take advantage of its therapeutic properties in medicinal ingredients. Biochemically, marijuana contains about 60 cannabinoids. This substance can cause various pharmacological effects (Izzo et al. 2009). Marijuana content was found in the presence of exogenous ligands and endogenous ligands such as anandamide and 2-arachidonic-glycerol (Borrelli et al. 2013). Activation of 2 G-protein-coupled receptors, CB1 and CB2, has several functions that directly inhibit the response to neurotransmitters such as acetylcholine, dopamine, and glutamate. In addition, marijuana can indirectly affect the receptors of γ-aminobutyric acid, N-methyl-D-aspartate, opioids, and serotonin (Pazos et al. 2005; Pagano et al. 2015). CB1 receptors are located in the basal ganglia, which is the place for motor control, the cerebellum, which is the hub for cognition and coordination, the hippocampus which is the center of concentration and memory, the cortex which is where cognitive function and sensory integration work, the hypothalamus which is a place for regulating appetite, hormones, and sexual activity, the amygdala which is the site of regulation of anxiety, emotions, and fear,

CB2 receptors are found in the immune system. These receptors play a role in controlling the effects of pain, inflammation, the hematopoietic system, and so on. The biochemical content of marijuana can cause cannabinoid receptor activation disorders

which include euphoria, psychosis, memory, cognitive, reduction of locomotor function, appetite, antiemetics, pain relief, and sleep induction (Radwan et al. 2015).

Result and Discussion

Marijuana chemical ingredients

The active substances found in cannabis (*Cannabis sativa*) include Δ9-THC (Delta 9 Tetrahydrocannabinol), CBD (Cannabidiol), CBN (Cannabinol), CBC (Cannabichromene), CBG (Cannabigerol), and others (Tayyap and Durre, 2014). Some of the active substances found in marijuana are as follows Δ9-Tetrahydrocannabinol and Δ9-Tetrahydrocannabinolic Acid. The main active constituent in marijuana is Δ9-THC, which has hallucinogenic and depressant effects. When marijuana is used like a cigarette, Δ9- tetra hydro cannabinoid acid (Δ9-THCA) is only partially converted into THC. The conversion temperature was dependent on the decarboxylation of THCA under analysis and smoking conditions. The average amount of conversion to THC under the analysis conditions is around 70%. Meanwhile, when it is made into cigarettes, it is around 30% (Herkenham et al. 1991). The half-life of THC in the plasma ranges from 20–36 hours. When used by inhalation/smoking, the effect appears for 7–10 minutes at 2–3 hours in fixed users with a Δ9-THC half-life of about 2 hours, Δ9-THC 11 oic acid about 120 hours. In non-permanent users, the half-life of Δ9-THC is about 1.5 hours, Δ9-THC 11 oic acid is about 144 hours (Siegel et al. 2000).

Cannabichromene, The CBC content in marijuana ranges from 0.7-0.8%, besides that the abundance is relatively very small. There have been very few pharmacological studies of CBC. CBC functions as an anti-microbial, anti-implantology effect and has analgesic properties. Cannabigerol (CBG) is a type of Cannabinoid that has no psychoactive properties. Has anti-tumor activity in vitro, is antibacterial (Christian 1994). CBG was the first cannabinoid identified and the acid precursor CBG proved to be the first biogenic cannabinoid produced in the factory. Propyl side chains and monomethyl ether derivatives are other cannabinoids from this group (Christian 1994).

Marijuana Effects on The Brain

Based on neuroimaging studies the effects of long-term marijuana use on the brain cause neuroplastic changes in the reward system, stress, and major brain functions involved in emotional processing and decision making. (Koob and Valcow, 2016). Based on the results of chronic cannabis THC exposure tests in animals, it is proven that there is a collection of DA responses to DA stimulants in the stadium with both [11 C] - (+) PHNO and [11 C] PET raclopride imaging (Christian 1994) and to decrease DA synthesis through PET imaging with [18 F] DOPA (Bloomfield et al. 2014). The presence of THC exposure causes neurological changes that affect various cognitive processes that can effect changes in neural architecture. Emerging research has shown a link between brain structure and connectivity. For example, Van den Heuvel et al. and Greicius et al. demonstrated a strong structural connection between the white matter index and the strength of functional connectivity in a default mode network (van den Heuvel et al

2008; Wilson et al. 2000). Similarly, others have reported correlated patterns of gray matter structure and connectivity that in many respects reflect the underlying intrinsic network (Segall et al. 2012). Thus, the literature suggests a direct relationship between structural and functional connectivity, it is likely that changes in connectivity will also be present where changes in brain volume result from marijuana use. The existing literature on the long-term effects of marijuana on the brain provides an inconsistent picture (that is, the presence or absence of structural changes) due to methodological differences across studies. Thus, a methodology was used to collect multimodal measures in a large group of chronic cannabis using a broad age range of adults that allowed characterization of changes throughout life without developmental or maturation bias as in other studies. An MRI scan was performed on a Siemens 3 Tesla Trio scanner with uses standard 12-channel phased-array head coils. We use technique Different MRIs to investigate brain changes between marijuana users and groups control: (i) high-resolution T1-weighted images to measure gray matter volume, (ii) resting-state functional MRI scan collected to assess connectivity functional brain, and diffusion tensor imaging scans were collected for provides an assessment of structural connectivity between brain regions via white matter channels.MRI data processing and voxel-based morphology (VBM) techniques were used to investigate structural abnormalities of the brain as a whole. High-resolution T1 image processed by using Diffeomorphic Anatomical Registration Through Exponentiated Li Algebra (DARTEL), an improved VBM method that achieves image registration brain between subjects with greater accuracy at SPM 8. The fMRI resting state (rsfMRI) image was analyzed using the AFNI (NIMHS Scientific and Statistics Computing Core) and the internal MATLAB script. Functional connectivity is measured using a seed-based approach by selecting the apex of the bilateral orbitofrontal cluster gyri from VBM analysis, [+26 + 54 - 8] and [- 16 +58 - 10] in the MNI template. The cross-correlation coefficient between these seed voxels and all other voxels is computed to produce a correlation map. The correlation map then was converted to a z-score map using Fisher's inverse of the hyperbolic tangent transformation.

The study provided evidence that chronic marijuana heavy users had lower gray matter volumes of OFC compared to controls. This effect on OFC is not surprising given that OFC is a major region in the reward network, is enriched with CB1 receptors, and is heavily involved in addictive behavior (Schacht et al. 2012) as associated with disturbances in motivation (Kringelbach et al. 2003; Filbeya et al. 2014) and retrieval decisions (Wilson et al. 2000). While others have reported changes in various CB1-enriched areas such as the amygdala, hippocampus, ventromedial prefrontal, OFC, insula, and striatum, our findings are specific to OFC.

Genetic Alveolar Macrophages

Pulmonary alveolar macrophage cells can be collected using bronchoalveolar lavage. The analysis was used to compare healthy alveolar cells and alveolar cells that have DNA damage. In someone's lungs who doesn't smoke may appear to have a fair amount of DNA injuries like the ones they had, on average, 41% of the DNA was double-

stranded after base release. This percentage is explained by a deficiency of macrophages in the enzyme responsible for the recovery of the DNA double-strand, poly (ADP) -ribose polymerase. We have shown that poly (ADP) -ribose polymerase activity remains low in newly isolated alveolar macrophages exposing ex vivo to hydrogen peroxide, while concurrently treated lymphocyte cell lines have an instant increase in poly-polymerase (ADP) -ribose activity. Adult alveolar macrophages are end-stage cells, and rarely replicate (Kringelbach et al. 2003).

We conclude that the low percentage of double-stranded DNA seen in macrophages of nonsmokers after base release is an expected phenomenon. The low poly (ADP) -ribose polymerase activity in alveolar macrophages was a possible disadvantage in this study as it disadvantage in low values for double-stranded DNA in control cells. In other words, this means that non-smoker macrophages have smaller differences when the percentage of DNA is double-stranded compared to smoker's cells. For this reason, a sample size larger than that used in this initial study is needed to show a significant difference in DNA damage between cells in nonsmokers and smokers. Nevertheless, this study demonstrated a trend in which macrophages from marijuana smokers had a lower mean percentage of double-stranded DNA after alkaline release than macrophages recorded in nonsmoking cells. Additionally, macrophages from subjects who smoke and marijuana or cocaine appear to have additional DNA damage (Sherman et al. 1995).

The reason for this additive effect was not evident from the evaluation of the inhalation explosion or nitrite content of macrophages because these parameters did not differ between the smoking groups. However, these two parameters may be interactive because oxygen radicals potentiate single-stranded DNA damage induced by tobacco-specific nitrosamines. In this study, we did not assess whether the nitrate content of macrophages correlated with smoke-specific nitrosamines. Based on our preliminary findings, the additive mechanisms, detrimental effects of marijuana and tobacco smoke on the DNA of macrophages and other lung cells remain fertile areas for future research. Evaluating single-strand DNA damage in alveolar macrophages may not be the only method for assessing DNA modification in these cells.

Rhesus monkeys have been exposed to marijuana smoke every day for one year and then their carcinogenic DNA was measured in their lungs. Although the mean and median stirring rates were not statistically different, 15 of the 22 stir sizes were highest in the experimental group, while they were lowest in 12 of the 22 mistreated animals. Thus, primate studies using this carcinogenic adduct DNA in lung tissue show a trend similar to our study of using single-stranded DNA cleavage in alveolar macrophages to delineate the role of cannabis in lung cancer. Another marker of DNA damage that can be evaluated in the future is 8-hydroxy-2'-deoxyguanosine which increases when lymphocytes are exposed to reactive intermediate oxygen. In contrast, PMA-stimulated granulocytes did not show an increase in 8-hydroxydeoxyguanosine when DNA damage was examined. The different types of leukocytes may have an intermediate reactive oxygen response resulting in varying degrees of DNA damage. The search for an ideal marker of DNA injury concerning oxidant injury is important because of our observation

that increased superoxide production by smokers' macrophages is associated with decreased double-strand DNA content. Future studies should use more than one method to measure DNA modification in macrophages flushed from smokers to determine which procedure has the best sensitivity for detecting damage. We also postulated that examining the nitrite content of alveolar macrophages would correlate with DNA damage. This assumption is based on the premise that nitrite will function as a marker for inhaled nitric oxide or marijuana / tobacco-specific nitrosamines (Matsuda et al. 1990).

Nitrite does function, however, as a marker for smoking plant material because it is the highest in macrophages from cannabis and tobacco smokers and lowest in the cells of cocaine smokers and nonsmokers. This also attests to the fact that the absence of hemoglobin in the alveoli causes inhaled nitric oxide to not be fully oxidized to nitrite rather than being completely detoxified to nitrate. The role of nitrites in the lungs and the pathogenesis of cancer has received further attention. In conclusion, we describe lavaged alveolar macrophages as a source for determining adverse biochemical events associated with marijuana, tobacco, and/or smoking cocaine. In this initial study, macrophages from marijuana smokers tended to have more single-stranded DNA than cells from nonsmokers, and concurrent tobacco use added to this effect. DNA damage measurements also appeared to correlate with macrophage stimulated oxidant release, but there was no association between the nitrite content of macrophages and DNA aberration.

Effects of Marijuana on Sperm Health

Many researchers support marijuana's role in reducing sperm count and concentration, causing abnormalities in sperm morphology, reducing sperm motility and viability, and inhibiting fertilization capacity. Research to date has extensively demonstrated the presence of cannabinoid receptors in sperm, suggesting that marijuana has the potential to impair sperm function. The decreased sperm concentration was observed in a sample of adult male rats subjected to 16 puffs of marijuana per day for 75 days, so the sperm count was significantly suppressed ($p < 0.05$). Demonstrations in these animals cause decreased libido and sexual function but have not been replicated in human studies. Subsequent research has been aimed at humans and found that the monthly sperm count showed that marijuana users for at least 4 days for 6 months had significantly lower sperm counts than men who smoked 5 to 9 cigarettes of marijuana per week. This suggests a reversal between marijuana use and sperm count. Subsequent research has been aimed at humans and found that the monthly sperm count showed that marijuana users for at least 4 days for 6 months had significantly lower sperm counts than men who smoked 5 to 9 cigarettes of marijuana per week. This suggests a reversal between marijuana use and sperm count. Subsequent research has been aimed at humans and found that the monthly sperm count showed that marijuana users for at least 4 days for 6 months had significantly lower sperm counts than men who smoked 5 to 9 cigarettes of marijuana per week. This suggests a reversal between marijuana use and sperm count (Cadola et al. 2013).

Cardiovascular System Effects of Marijuana

Marijuana smoking by people with cardiovascular disease poses health risks because of the consequences of the resulting increased cardiac work, increased catecholamine levels, carboxyhemoglobin, and postural hypotension. Once it became apparent that THC probably accounted for much of marijuana's effects in humans and THC became available, the better control over delivered dose offered by THC made it a desirable choice for many investigators (Clarke and David 2007).

In this review, the findings from experiments using marijuana and experiments that used pure THC will be intermixed, but the reader should keep in mind that experiments with THC in many ways involve simpler conditions than the same experiment administering a mix of substances from smoked marijuana. .Thus, most of what is known about cardiovascular effects in animals is from experiments with THC or other cannabinoids given by routes other than smoking..Very few experiments describe the cardiovascular effects of marijuana on older people, people with cardiovascular or cerebrovascular disease, or females of any age. Acute cardiovascular effects In humans, an easily measured, fairly consistent, and rapid effect of smoking marijuana is a 20% to 100% increase in heart rate, starting during the 10 minutes or so it takes to smoke a marijuana cigarette and lasting 2 to 3 hours.2 "5 When sitting or supine while smoking, blood pressure increases slightly and decreases slightly while standing. 2 Cardiac output increases 30% or more; 6 "10 cardiac work increases (Richard et al. 1988; Clarke and David 2007).

Effects of Marijuana on Oral Health

According to the journal entitled "Analysis of Stimulated Saliva Volume in Cannabis Addicts at the 2014 Medan Insyaf Rehabilitation Center" work, consuming marijuana can cause health problems in the human oral cavity, such as xerostomia, periodontal disease, caries, candidiasis, and changes in the epithelium of the oral cavity, even oral cancer. This is due to the lack of saliva volume in marijuana addicts which functions as protection, mucosal lubrication, and antimicrobial for the human oral cavity.

In vivo studies conducted on mice by Prestifilipo, it was found that THC decreased flow from the submandibular glands. In addition to direct activity, THC which accumulates in nerve cells can inhibit the work of the parasympathetic nervous system, thereby reducing the volume of stimulated saliva secretion in the ex-cannabis addict group compared to the group without a history of consuming cannabis (control). In addition, there was a very significant difference in the volume of stimulated saliva between the ex-marijuana addicts and the control group (not consuming cannabis), where the p-value was <0.05.

Cannabis sativa, also known as marijuana, is the most commonly used drug worldwide among all PAS. Generally, marijuana users had worse oral health than nonsmoking, with higher dental scores, higher plaque scores, and less healthy gingiva. An important side effect of cannabis is xerostomia. Thus, chronic marijuana use can increase the risk of caries. Smoking and chewing marijuana cause changes in the oral epithelium called 'cannabis stomatitis'; these include buccal mucosal leukoedema and

hyperkeratosis. Acute signs and symptoms include irritation and superficial anesthesia of the oral epithelium, and xerostomia. With chronic use, 'cannabis stomatitis' appears as chronic inflammation of the oral epithelium and leukoplakia, which can progress to neoplasia. Marijuana can cause variable parasympathetic effects, which are associated with a stress response, such as a visit to the dentist, which can be associated with episodes of syncope. Dental treatment in patients who are poisoned can cause the patient to experience acute anxiety, dysphoria, and paranoid thoughts such as psychosis.

Oral cancer disorders or lesions diagnosed from the lesions found in drug addicts consist of aphthous stomatitis, frictional keratosis (of the sharp edges of the teeth), candidiasis, traces of tooth extraction, and epilepsy of the tongue. In a previous study, a group of 64 legal and illegal drug users presented with lesions, such as candidiasis, angular cheilitis, ulcers, leukoplakia, mucositis, herpes, papilloma, and gingivitis (O'Doherty et al. 2003). Regarding oral health, drug users showed a decrease in SFR and an increase in the number of mucosal lesions compared to the control group, but no association was found with oral cancer or potentially malignant disorders.

Conclusion

Marijuana has adverse effects on health, including the health of the womb, brain, alveolar genetics, sperm, cardiovascular, female reproduction, and mouth. Of all the research conducted in this journal, it has no benefits for the health of the body.

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