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Marijuana & Mental Health: Therapeutic effects and risks of medicinal and hedonistic uses

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Eduardo Pinto e Silva
PhD in Education, Federal University of São Carlos

ABSTRACT
The paper addresses the therapeutic effects and risks of the medicinal and hedonistic uses of cannabis on mental health. Preliminary historical and psychosocial aspects of marijuana use and the right to health are preliminarily considered. It points below to the complexity and diversity of medicinal therapy in different situations: epilepsy; Alzheimer 's; anxiety; depression; psychosis and autism; chemical dependence. And finally, the hedonistic use of marijuana, considering psychosocial aspects, sociability and sensitivity.

Keywords: Mental health, Medical cannabis, Psychosocial aspects, Therapeutic effects and risks, V Medical Cannabis Course of UNIFESP.

1 INTRODUCTION

The present text, final work of the V Course of the Medical Use of Cannabis (2021), was elaborated based on the records of the classes and the systematization of readings of bibliographic survey carried out by this author, psychologist and doctor in education, with emphasis on those related to the theme *Marijuana & Mental Health*. We seek to focus on the therapeutic effects and risks of the medicinal and hedonistic uses of cannabinoids and/or marijuana (MALCHER-LOPES; RIBEIRO, 2007; ZUARDI; CRIPPA; GUIMARAES, 2008).

After this Introduction, we address, in the following items, separately, the medicinal and hedonistic use, although, to a certain extent, the boundary between the medicinal therapeutic effects and those related to well-being is not so clear. The latter are usually related to what is conventionally called "recreational use". But here we prefer to adopt the term "hedonistic use", because we consider it more comprehensive and consistent with an equally comprehensive conception of health.

1.1 HISTORICAL AND PSYCHOSOCIAL ASPECTS OF MARIJUANA USE

There is a huge variety of historical aspects reported about the properties, use, and domestication of the plant commonly termed marijuana. The same can be said for the contexts and psychosocial effects of its use (CASTILLA, 2007).

There are several denominations of cannabis, and a long historical process of domestication of the plant and its uses in different countries and times, as well as in different religious orders: Hinduism, Taoism, Buddhism, Rastafari. And yet, in rituals of the Mexican tribes (Tepehua) and Candomblé (Aula 2 – 10/03/2021 - Profa. Renata Monteiro -pharmacist).

It is recorded that in 1899 the Merck Manual already contained clinical indications of marijuana use (Class 4 – 03/23/2021 – Prof. Eliane Nunes). There is a history of the use of the plant and some of its medicinal uses (Epilepsy, Parkinson's, Glaucoma, Chronic Pain, Alzheimer's, Cancer, Sclerosis, Autism, and even Depression, Anxiety and AIDS Symptoms). Then there was strong propaganda against, from the end of the 1920s until years later, with the influence of the racist perspective of the American Anslinger (1937) (Aula 3 – 16/03/2021 – Prof. Paulo Morais).

The historical and cultural representations of the cannabis plant are diverse. As an example in the literature, we can mention Schultes and Hofmann, who refer to marijuana as "Plantas de los dioses". Historical aspects are very old. You can take us back to the year 770 BC. The Brahmins made use of marijuana in the meditative processes of sacred texts. In Mesopotamia there was the religious use of "sacred incense." The use as an anesthetic for minor surgeries, mixed with other products such as datura and wine was also characterized as an ancient historical practice. In Nepal there had since time immemorial the cult of God Shiva, venerated, pointed out as the one who discovered and taught the recipes of *Cannabis.* In India, marijuana was consumed by shamans in the form of a drink to induce trance states. Marijuana is given different names throughout the ages and spaces. It is used and termed as ganja in the Rastafarian cult. This religious-cultural practice or psychosocial phenomenon is relatively well known to other cultures. *Reggae and* some musicians such as Peter Tosh and Bob Marley, are world-famous icons or symbols of Rastafarian culture (Lecture 6 – 06/04/2021 – Profa. Eliana Rodrigue). Hence the correct designation of the existence of a "cannabis culture" (CASTILLA, 2007).

Some studies bring detailed reports on the history of marijuana in the world and in Brazil (CARLINI, 2019; 2006), of marijuana consumption in Brazil (PEREIRA; SHAH; SHIGAKI; LARA, 2018) and about social representations and stigmas in relation to its users (SOUSA, 2013), often mixed with structural racism (ALMEIDA, 2019) (Aula 10 – 04/05/2021 – Prof. Michael Dantas). It is known that the motto of prohibitionism and the politics of wars in Brazil was historically related to racism, police violence and the mass incarceration of the poor, black and peripheral; and that when such social conditions intersect with that of the female gender, other aggravating elements are presented, both historical and current (Aula 8 – 20/04/2021 – Profa. Luciana Boiteux; Class 10 – 04/05/2021 – Profa. Breeze Lima). This meant and means, in addition to a prejudiced attitude, a simplification about the multiplicity of motives and forms of use by different social segments, as diverse as they are difficult to be circumscribed to certain particularities and singularities of classes, groups, age group, or even of social circumstances and influences, the media and government campaigns, among others, even by researchers who tried to do so (PEREIRA; SHAH; SHIGAKI; LARA, 2018). Sousa (2013) points out that negative if not stigmatized narratives of marijuana prevail, despite being conveyed, in daily life and in the media, through a multiplicity of references, from that of merchandise of trafficking, through

that of object of use of celebrities, to its mention and debate as a pharmacological, therapeutic or even "recreational" or "entertainment" product. What is perceived is that the wealth of narratives and references, despite the predominant, degrading if not moralistic character, indicate a polemical and polysemic social construction of marijuana, compatible with its undeniable historical, cultural and psychosocial diversity (CASTILLA, 2007).

Raphael Mechoulam, an Israeli researcher, in the article "Early phytocannabinoid chemistry to endocannabinnoids and beyond", contrary to the myths and prejudices surrounding the plant, revealed, in 1964, from the isolation of delta 9 tetrahydrocannabinol (THC), its therapeutic and anticonvulsant effects. Mechoulan synthesized CBD and THC (Lecture 4 – 23/03/2021 – Prof. Eliane Nunes). In Brazil, the physician and researcher Eliseu Carlini, began his studies on marijuana in 1952, by the Escola Paulista de Medicina. Since then, and in numerous subsequent studies (CARLINI, 2019; 2006; CARLINI; ROBERTS; GALDURÓZ 2004; CARLINI; MASUR, 2004), indicated the anticonvulsant property of cannabis, among others. In the 80's there was interruption of studies (prohibition). UNIFESP, however, develops research on medicinal use in its Observatory. The Journal Observes Marijuana can be an important access to information, as can the episodes of the Miniseries "Marijuana Through Time." One of them deals with the political aspects of marijuana (Class 6 – 06/04/2021 – Profa. Eliana Rodrigue).

In 1992 there was a remarkable discovery: that of the endocannabinoid anandamide, the "substance of happiness", produced by the brain. And in 1993, the identification of CB1 and CB2 receptors. These discoveries could revalue, but always in the midst of all kinds of ebbs and flows, and oppositions of all kinds (moralistic, prejudiced, unjust/legalistic), the historical aspects of the use of the plant for medicinal purposes (MALCHER-LOPES; RIBEIRO, 2007).

We understand that the health of the individual is linked to the health of the social being, to modes of sociability in which human rights are non-negotiable. But the history of civilization and societies rigs welfare conditions for economic interests, and relations of power and domination create a series of obstacles to healthy psychosocial conditions, or worse, engender pathogenic psychosocial conditions. in which subjects in conditions of vulnerability and poverty, or ethnic-racial and gender conditions, are predominantly harmed.

1.2 FROM HUMAN RIGHTS TO CIVIL DISOBEDIENCE

Human Rights are basic and indispensable rights for human life on the planet. Such rights do not admit of any distinction of social class, color, gender, nationality, religion, sexual orientation or of any other kind that nullifies the fundamental rights of a person. The articles of the Universal Declaration of Human Rights express them accurately. It is an official document prepared and approved by the UN Commission on Human Rights in 1948. Composed of a preamble and 30 articles,

they aim to guarantee the social well-being and dignity of humanity. We indicate some of the fundamental rights, such as the right to life, liberty, health, which are mixed with others, such as political, legal, educational and freedom of expression rights.

Article 1 reads that "all human beings are born free and equal in dignity and rights"; Article 2 states that "every human being has the capacity to enjoy rights and freedoms," "without distinction of any kind, whether of race, color, sex, language, religion, political or other opinion, national or social origin, wealth, birth, or any other condition." Article 3 is short and dense: "every human being has the right to life, liberty and personal security." Articles 4 and 5 repudiate slavery and any cruel condition that human beings may be subjected to. Article 11 points out that "every human being accused of a criminal act has the right to be presumed innocent" and that "no one shall be guilty of any action or omission which, at the time, did not constitute an offense under national or international law." Article 12 asserts that "no one shall be subject to interference with his or her private life." Articles 19 and 20 indicate, respectively, that: "every human being has the right to freedom of opinion and expression" or "freedom to have opinions without interference and to seek, receive and transmit information and ideas"; and the "right to freedom of peaceful assembly and association." Article 25 points out that "every human being has the right to a standard of living capable of ensuring for himself and his family health, well-being, including food, clothing, housing, medical care and the indispensable social services." And it is also worth highlighting a complement to Article 27, given the purposes of this text: "every human being has the right to participate freely in the cultural life of the community, to enjoy the arts and to participate in scientific progress and its benefits." We will not dwell on it, because this set of solid propositions is enough to justify how plausible civil disobedience can be in the face of the unscientific and restrictive prohibitions of the medicinal and/or hedonistic use of cannabinoids and/or marijuana.

Prohibitionism hurts fundamental rights. International drug policy instituted a global regime of control from the second world war, but we can refer to a "prehistory" of the "war on drugs", exemplified by the "Temperance League" in the US, of a moralistic character and religious orientation. Before the institutionalization of this policy, there was the force, in the USA, of Prohibition (1919-1936). The global politics or regime of control characterizes a model of moral and ideological social control that aims to persecute producers, sellers, and consumers. There are countries with total control, such as Japan. In Brazil, the user is distinguished from the trafficker. In the Netherlands there is a de facto legalization. And Canada and Uruguay are legalization *in jure*. The Shanghai Commission was the landmark of international control or policy. Prohibitionist control starts from the presumption of trafficking (aprioristic condemnation). In this case, in Brazil, it characterizes violation of the Federal Constitution. And we reiterate, it goes against the Declaration of Human Rights. The rigidity of the prohibitionist model ignores scientific studies on the medical therapeutics of cannabis. The UN, it is

worth noting, fights prohibitionism and defends regulation (Lecture 8 – 20/04/2021 - Prof. Cristiano Maronna).

The National Drug Act is not restricted to the issue of crime. It institutes a national system of drug policy. Establishes norms for the repression of production and trafficking. And it indicates drugs as dangerous. This is opposed to the principles of freedom, autonomy and citizenship, that is, to the principles or values proclaimed in the law itself; principles contradictory to the core of the law (repression) and its criminal nature. The purpose of the law refers to misuse and inclusion – which could refer us to due use (and exclusion). It provides for involuntary hospitalization (by a family member or legal guardian, or even by a health professional, in the absence of one of these). Quite contradictory to the issue of autonomy and freedom of the user. It removes fundamental rights and considers the user as a devoid or unreasonable being. The unconstitutionality of the cultivation ban prescribed by the National Drug Law is being discussed. Distributing without marketing can carry a criminal penalty of 5 to 15 years. Sowing can also be considered a crime, if so discretioned its distribution by the police authority. The law implies a high rate of incarceration due to the framing as traffickers of many who could be considered users. There are sentences whose duration supplants that decided by the late trial. There is a high cost of prohibitionism that could be invested in social policies (GORDHANDAS, 2014). Prohibition still implies low quality of drugs, which tends to further burden the public health system (Aula 8 – 20/04/2021 - Prof. Ítalo Coelho de Alencar).

Prohibitionism or "drug crime" can be considered historically recent (early twentieth century). There are several examples of criminalization in Brazilian history, even when medical use was admitted. Drug addiction was progressively considered as a disease, under the focus of the user as a patient to be criminalized. The so-called "sanitary", "hygienist" model was constituted, which advocated mandatory hospitalization, in the name of the sick and public order. A medical-police system. A stigmatizing and exclusionary control. International conventions have been accumulating and overlapping since approximately 1940, with sanctions, reprimands and civil interdictions. The sanitary model was later replaced by the war model, even before the dictatorial period. In this, the user was then equated with the trafficker. A vision of an authoritarian "social danger of drugs" was naturalized. And addiction was conceived as "mental illness." Many studies point to such criticisms, such as those of Luisa Saad ("Fumo de negro: a criminalização da marijuana no pós-abolição"), Nilo Batista ("Critical introduction to Brazilian Criminal Law"), Saulo de Carvalho ("The criminal drug policy in Brazil: criminological and dogmatic study of Law 11.343/06") and Luciana Boiteux ("The Brazilian antimodel: prohibitionism, incarceration and penal selectivity in the face of drug trafficking") (Aula 8 – 20/04/2021 - Prof. Dr. Luciana Boiteux).

In the face of prohibitionism, the confrontations of fundamental human rights and pertinent questions of the unconstitutionality of some laws in Brazil in the face of the Federal Constitution, civil

disobedience presents itself as a justifiable prerogative. And this struggle for the right (denied) is also a struggle for health. Civil disobedience can be understood as a tool to overcome unjust laws. Thoreou was the originator of the term (USA, 1949). Historical personalities fought them, such as Gandhi in India (struggle for independence) and Luther King in the USA (struggle for civil and black rights). This is a right of resistance. A right of exception. Or still, a legitimate act, because it was erected on the principle of what is just, and which became famous in King's phrase about the "moral duty to disobey unjust laws" (Lecture 5 – 30/03/2021 – Prof. Patricia Milani)

1.3 HEALTH IS RIGHT, RIGHT IS HEALTH

Health problems are socially determined. It is not possible to isolate the disease as something circumscribed to a biological organism, as if it existed in an environment devoid of economic, political, moral, cultural and social clashes. As if there were no conflicts and antagonisms in a class society. Mercantile values often overlap with pro-life values. There are such problems in all areas. Even the struggle and civil disobedience in favor of the health and freedom of the cultivation of cannabis for medicinal purposes are interposed industrial interests, which forge the production of the synthetic cannabinoid, even though the extracted cannabinoid phytopharmaceutical has greater safety of use. The point is that rights are a condition for health. Hence the maxim that health is right, and right is health.

Legalization is necessary under several arguments. And the prohibition compromises three dimensions of use: substance (which can be degraded), body (inadequate dosages) and society (with increased violence). Legalization and regulation can protect at-risk groups and respect users. The use of medical cannabis in some diseases and the reasons and arguments that support its advocacy for science are expressed by the Movement for the Regulation of Medical Cannabis (MOVRECAM). There is a relationship that can be established between prohibition and the absence of regulation that stimulates the illegal market, violence, repression and corruption. Planting can favor the best use of the active ingredient and the "committee" or "entourage" effect of marijuana. In addition, it can correct the social imbalance of access to cannabis. The prohibitionist policy and the war on drugs historically falls on the poor, blacks and peripherals (Aula 1 – 02/03/2021 – Prof. Sidarta Ribeiro).

Health problems of different origins could benefit from the medicinal use of cannabis, as well as avoiding medications with unwanted side effects. This is the case with sportsmen, for example. Or Cannabidiol (CBD) can act in the prevention of injury in high-performance athletes. Many athletes prefer the use of CBD over painkillers and anti-inflammatories. It is necessary to debate what is or is not harmful to the athlete. In 2018 the World Anti-Doping Agency (WADA) withdrew CBD as doping. We emphasize that there is chemical dependence and side effects of analgesics and anti-inflammatory drugs and heart and kidney health risks. Cannabidiol is an alternative to ibuprofen. It can be used not

only in chronic pain, but also for ostearthritis and fibromyalgia. Or even, to accelerate recovery after physical exercises of athletes. CBD assists in the maintenance of homeostasis. Several athletes of different modalities have made or are making medicinal use: Andrew Flansky, triathlete, for injury to the hip flexor tendon (athlete reported improvement in hip, anxiety and sleep); Martellus Bennet, American football; Billy Kemper, Company *EcoScience*, which he sells (he used it for his mother with cancer, initially, and then for himself, in place of painkillers, and referred to improvement for usual problems of flight routines and time zones, as it helps with sleep). Bob Burniquitis, skateboarder; Nate Diaz, MMA fighter, for healing and inflammation (vaporized use); The NBA's Kareem Abdul-Jabbar. And yet, the case of Ross Rebagliati, *snowboarder*, who lost a gold medal on charges of use/doping, but was later proven to have been passive inhalation and regained the medal. CBD can be considered a mild remedy and of low acute toxicity, indicated as anxiolytic, analgesic, antioxidant and active neuroproducer (Aula 4 – 23/03/2021 - Prof. Raul Thame de Toledo Almeida)

There are a diversity of social and contextual issues related to the social and medicinal use of cannabis. Health is a question of citizenship, of struggle for rights, and not a practice circumscribed to medical-biological expertise. Health involves social, medicinal and legal aspects. Civil and political rights can be related to citizenship and identity of the social being. Social and health rights are provided for in the Federal Constitution. The WHO's notion of health is related to full well-being. There are collective interests related to the popular medical cannabis movement. It is important to recognize the authenticity of the popular cause, popular education and the black and women's movements. The work of Paulo Freire highlights the importance of social action aimed at emancipation from oppression (Aula 5 – 30/03/2021 – Profa. Patricia Milani). The aforementioned civil disobedience and the moral duty to fight unjust laws is also articulated to an educational practice by Mandela, in a phrase equally famous to that of Luther King: "education is the most powerful weapon of changing the world." Father Ticão (deceased, one of the protagonists of the Course that gives rise to the present work) was moved by social ideals such as this, as well as those previously mentioned, Luther King and Gandhi. And Sidarta Ribeiro considers the prohibition of the therapeutic use of cannabis a colossal historical error on a planetary scale. In the country we have more than 10 thousand patients registered with ANVISA and more than 20 thousand linked to some cannabis association. The WHO indicates the safety and efficiency of the medical use of cannabis and defended its removal from the list of proscribed or prohibited substances. Domestic cultivation and extraction of oil from the plant is a right to health and life. And the cultivation itself does not materialize crime (Lesson 5 – 30/03/2021 - Profa. Deborah Garcia).

PL 399/2015 does not contemplate domestic cultivation. It is important, for the movement to decriminalize the cultivation of cannabis sativa for personal therapeutic use, the signing of PLS 4514/2017. A survey by SBEC in Brazil points to the following data: 79% in favor of medicines from

the plant; 87% aware of the possibility of use as a remedy for diseases; but only 41% know which diseases and 9% know someone who has used them; 91% of respondents without religion support the distribution by SUS (percentiles of 81% for Catholics and 70% for evangelicals). A total of 27 countries removed cannabis from Annex IV of the 1961 Convention on Narcotic Drugs (against 25 and 1 abstention, Brazil among them). The reclassification had been recommended by the WHO. Brazilian regulations are restrictive. And there is a high cost of medication (Mevatyl at 2,800 reais a box). In this way, the struggles for the inseparable right-health pair proliferate, such as those of the manifesto of support for cannabis research, which can be done by the link http://bit.ly/2LBiK5O (Aula 4 – 23/03/2021 - Profa. Eliana Nunes).

2 THE THERAPEUTIC EFFECTS AND RISKS OF THE MEDICINAL USE OF CANNABINOIDS AND/OR MARIJUANA FOR MENTAL HEALTH

2.1 THE COMPLEXITY AND DIVERSITY OF THERAPEUTICS AND CANNABINOID PROPERTIES

The therapeutic-medicinal use of cannabinoids in mental health should be selective and parsimonious, that is, one should select well the oil or product according to the behavioral issue to be treated, and always with caution regarding the dosage so that it is neither insufficient nor beyond what is necessary. The selectivity refers us to the multiple cannabinoid properties of the plant and the different medicines derived from them, as well as to the attention to the "entourage" effect that may or may not be present in the chosen drug. And due to this selection occur the variations regarding the dosage, or evolution and management of the dosage.

There are many diseases in which the medicinal use of cannabis can be beneficial, some of them from the field of mental health (epilepsy, Alzheimer's) and public health (cancer) of great interest. Benefits and risks should be investigated and directed to selectivity and dosage. In the case of epilepsy, for example, traditional treatment leads to the reduction of "neuronal firings," but at the expense of drowsiness. In this disease one can use the cannabinoid, which produces dissynchrony, without generating the lethargy of the torpor of the traditional treatment. Studies are not assertive in frequent pathologies, as in the case of cancer. Although such a health problem does not integrate the field of mental health, it should be noted that a discussion focused on the issue of mental health problems cannot fail to point out that there is no pathology that does not involve the behavioral and psychodynamic factor. In the case of cancer, the medicinal use can mitigate side effects of chemotherapy (pain, lack of appetite, sleep problems), and some studies even point to antitumor properties, although there are controversies, and this neuroprotective aspect is very important in the approach to mental health pathologies (Aula 1 – 02/03/2021 - Prof. Sidarta Ribeiro).

The effects of the different drugs, properties and forms of use should always be taken into account on the basis of selectivity and parsimony. An important question is whether it would be better to allow planting so that there is the use of the whole plant and its "entourage" effect or only use of the active principles. It is considered that the whole plant can further expand the range of research and uses. At the same time, in the field of mental health, caution must be exercised, according to the pathology, in the use of the drug whose THC principle is operative. It is also worth considering that the legalization of active ingredients could maintain greater control of some risks. There are risks of use and risk groups. Early and abusive use in adolescents and young people is not recommended. And the use in the elderly tends to be more beneficial than in other age groups (Aula 1 – 02/03/2021 - Prof. Sidarta Ribeiro).

There are differences between the isolated cannabinoids and those from the extract. Ethnopharmacology addresses the perception of communities of substances that interact with their organisms. The *Cannabis sativa* is from the family *cannabacea*. There are two subspecies: sativa and indic. In relation to the various types of plants, there are hybrids (male and female in the same plant). Hermaphrodites are rarer, such as C99 or Cinderella 99. The male plant has a low concentration of THC (e.g., hemp, which is rich in fiber). The female plant has a large amount of resins with medicinal richness. There are 3,000 varieties of the same family. There are narcotic properties (hedonistic use) and therapeutic properties (medicinal use) (Lecture 6 – 06/04/2021 - Prof. Dr. Eliana Rodrigues).

The prescription, use and management of cannabis-derived products should be carried out with the aid of pharmacogenetics. Pharmacogenetic testing is useful for treatment choices. The chronic and abusive use of THC can generate psychotic symptoms or schizophrenia in predisposed individuals (polymorphism in a reduced portion of individuals). In this pathology the question of the selectivity of the property of the drug is fundamental. In the case of anxiety, THC can be beneficial, and dosage is key. A former marijuana smoker before treatment whose medicinal oil is used for pain, for example, may benefit from pain reduction but feel more anxious if THC metabolism is reduced. The hypothesis of behavioral and metabolic polymorphism should be considered. The finding of such a condition leads to adjustments or management of treatment in order to avoid adverse effects of anxiety. Pharmacogenetics improves clinical decision-making and optimizes benefits. It helps to avoid adverse effects and saves time and money with treatment (AULA 15 – 08/06/2021 – Prof. Dr. Fabrício Pamplona).

The properties of the drugs vary according to plant, form of cultivation and extraction. Only the discussion of trichomes and terpenes would lead us to a series of considerations that are beyond the scope of this work. Parthenocarpic infrutescence is the scientific name for the fruit of marijuana. Trichomes are secretory glands rich in THC. Terpenes (a substance present in the plant that has taste and smell) are secondary metabolites, and flavonoids, bioactive compounds. At UFRJ, a

standardization of the extraction process was developed (the first regulated and standardized extraction in Brazil). It was sought to obtain at each harvest an extraction with the same concentration of cannabinoids and terpenes (standardization of the product). The purest extract is golden in color. Despite the diversity of drugs we can consider, generically, that by influencing the activity of the cannabinoid system we can interfere in almost all diseases that affect humans. But we must highlight possibilities of contraindications, and in the focus of this work, the need for caution in the administration in cases of tendency to psychosis, bipolar disorder, anxiety, phobia, paranoia, adolescence (amotivational syndrome) and schizophrenia (CLASS 19 – 06/06/2021 – Prof. Renata Monteiro).

Terpenes (secondary metabolites) are volatile and aromatic chemical compounds. Myrcene is one of the most common terpenes in marijuana. It is a natural oleofinic organic compound that associated with CBD reduces pain. Linalool has therapeutic potential in the case of Alzheimer's. Terpenes are produced by plants, animals, microbes and fungi, with the most diverse purposes. More than 40,000 species are known. They are arguably the largest and most diverse class of naturally occurring organic products (class of natural hydrocarbons). In plants they are part of the natural or specialized metabolites. Medicinal properties such as: inhalation of certain terpenes associated with improved mood and emotional well-being stand out; antitumor, anti-inflammatory, antifungal, antibacterial, antioxidant effects, as well as pain relief, bronchodilation, muscle relaxation and neuroprotection (AULA 19 – 06/06/2021 – Prof. Lu Cannabier) (AULA 19 – 06/06/2021 – Prof. Lu Cannabier).

Marijuana has 1500 compounds and 177 cannabinoids. Cannabis sativa of the female gender during the reproductive phase produces parthenocarpic infrutescences. We can highlight two compounds: THC and its therapeutic action: bactericidal, anti-inflammatory, analgesic, corticosteroid, immunoregulatory, neuroprotective, brain regeneration and proliferation of neurons in the hippocampus; and CBD: serotonin balancer (Lecture 2 – 10/03/2021 - Profa. Renata Miller)

As demonstrated by Israeli researchers Raphael Mechoulan and Shimon Bem-Shabbat on the "entourage" effect, all the natural components found in cannabis (cannabinoids, terpenes) combine synergistically with increased beneficial effects. That's because the effects of cannabis compounds alone aren't as effective as when they act synergistically. About Myrcene, in addition to the anti-inflammatory properties (which help in reducing swelling in lesions and improving the immune system response) there is aid for relaxation, sleep quality and anxiolytic and antidepressant effects (increased dopamine), providing positive feelings and reducing excessive (anxiogenic) activity of the nervous system (AULA 19 – 06/06/2021 – Prof. Lu Cannabier).

As already mentioned, one of the great discoveries after the effects of THC in the history of marijuana studies (especially the anticonvulsant), was the existence of the endocannabinoid system.

Its action is referred to by the metaphor of the "maestro of the organism" (diverse, metabolic, immune systems) and its neuroprotective potential is discussed in the field of application to mental health pathologies.

The endogenous cannabinoid system (ECS) includes receptors, endogenous ligands, or endocannabinoids themselves (such as anandamide, AEA and 2-arachdonoyl glycerol, 2-AG), and enzymes. The cannabinoid molecule is recognized by a receptor. The receiver produces responses that generate ion channel opening and effects. THC is a partial agonist of CB1, like other cannabinoids or phytocannabinoids. The synthetic cannabinoid is a full agonist and has a response of greater amplitude. The safety range of cannabinoids is wide (Lecture 3 – 03/16/2021 - Prof. Paulo Morais). The theme is vast and includes biochemical knowledge that goes beyond the limits of the systematized knowledge for the elaboration of this work.

The discussion on the use of marijuana for mental health benefits includes relevant contributions, such as those of Malcher-Lopes and Ribeiro (2007), "Marijuana, brain and health", and of studies organized in the collection "Cannabis and Mental Health: a review on the drug of abuse and the drug" (ZUARDI, CRIPPA, GUIMARÃES, 2008). In this collection, we highlight Part IV, dedicated to Cannabis and Psychopathology (includes texts on anxiety, psychosis, mood, post-traumatic stress), and Part V, in which cannabis is made explicit as a drug of abuse, which differs from hedonistic use, to be considered in the next item.

The broadest and most basic discussion on drugs is carried out by Carlini and Masur (2004), and on cannabinoid substances in medicine we have the relevant systematization of Carlini, Rodrigues and Galduróz (2004), but because of the limitations of this work, they will not be presented.

Malcher-Lopes and Ribeiro (2007) present a table entitled "Pharmacological properties of cannabinoids present in marijuana", as well as a Glossary at the end of the book that "translates" technical-scientific terms. We extracted from the table only the pharmacological properties of the two most well-known cannabinoids: THC and CBD. We present: which are only THC; which are from THC and CBD; and which ones are just from CBD. We highlight in bold those directly related to mental health-disease processes:

THC Antipyretic

Antiviral THC

THC Appetite Stimulator

Hipotensor THC

Psicotrópico THC

Analgésico THC e CBD

Ansiolítico THC e CBD

Anticonvulsivo THC e CBD

Antiemético THC e CBD

Antiinflamatório THC e CBD

Antioxidante THC e CBD

Antitumorígeno TCH e CBD

Imunodepressor THC e CBD

Neuroprotetor THC e CBD

Sedative THC and CBD

CBD Antipsychotic

Antispasmodic CBD

If the use of cannabis in mental health problems deserves to be discussed with regard to the specificities of such problems, it is worth mentioning that the issue of anxiety and depression, just to stay in two aspects, affects numerous other pathologies in which cannabis can be administered (either in the treatment of the disease or the symptom). Thus, we consider it important to mention possible biopsychic benefits of the use of cannabis in a pathology that does not concern mental health (although it can be considered a psychosomatic disease) and that is responsible for the death of a significant number of individuals and populations: cancer. Cannabis in cancer can act as: appetite stimulant; antitumor effects; anti-nausea and anti-vomiting action (induced by chemotherapy). For some patients can act as protective action in peripheral neuropathy, analgesic (reduces doses of opioids); for others, they may have a beneficial effect on anxiety, depression and sleep. The dosages and known composition of the oils should be well observed, to avoid risks in place of responsive effects (Class 9 – 27/04/2021 – Prof. Dr. Paula Dall'Stellaasil).

Given the general considerations presented here, with emphasis on the issue of selectivity, parsimony and propriety of the uses and management of cannabinoid drugs, we will present, albeit synthetically, some of their characteristics in specific mental health issues, such as: the anticonvulsant effect in epilepsy; the neuromodulatory action and on memory in the use in Alzheimer's; the possibilities and precautions of use as an anxiolytic; the challenges and risks of use in depression; and the use of CBD as a medicinal cannabinoid in psychosis and autism.

2.2 THE ANTICONVULSANT EFFECT IN EPILEPSY

The anticonvulsant effect is characterized as the best known and perhaps best proven in medicinal studies of cannabinoids. It was discovered in 1839. The treatment of epilepsy with cannabinoids can be considered an ancient promise for a better future. Records of cannabis use for epilepsy (seizures, seizures), pains etc., date back to 2700 BC in China and 1000 BC in India. Irish physician Brook discovered the use for pain, cholera, tetanus, and seizure in 1843. In 1973, Brazilian physician Carlini discovered the anticonvulsant property of CBD in rats. And a clinical trial in 1980

(Cunha et. al.) finally confirmed this property. There is increased endocannabinoid neural action and limitation of the spread of epileptiform neuronal activity. In the long term, there is also, in theory, a neuroprotective role of phytocannabinoids. Lutz et. al. indicate increased endocannibinoids in response to epileptiform activations, corresponding to a "natural" containment of hyperarousal. Geffrey pointed to a positive interaction of cannabidiol with clobazan. There are many studies with CBD and need for more studies with *Full Scream*. Holanda and Polona (2017) pointed out in a double-blind randomized study a reduction of 43.95% of seizures. The high number of patients refractory to conventional treatments shows that the search for new treatments is essential and that these are essential to increase the quality of life. The high incidence of side effects, added to the high costs/difficult accessibility, drives the search for new therapeutic strategies that increase patient adherence (AULA 13 – 05/25/2021 – Prof. Ortale Trainotti). Since it is necessary to expand studies and that can be more detailed, which is valid for most studies on the medicinal use of cannabis, an unfortunate legacy of the senseless prohibitionism in relation to the plant and scientific research.

The pharmacological effects on epilepsy were addressed by Israeli researcher Mechoulan in "*Cannabinoids in health and disease*." This, together with Prof. Dr. Carlini (former professor of UNIFESP, deceased, renowned and widely recognized reference in marijuana research,), published, in 1978, a study of the effects of CBD for epilepsy (Aula 4 – 23/03/2021 - Profa. Eliana Nunes).

Epilepsy should be distinguished from epileptic seizure. While epileptic seizure refers to abnormal neuronal activity, epilepsy concerns a heterogeneous group of neurological disorders that have a chronic tendency to epileptic seizures. The (acute) crises demand a therapeutic approach to the triggering factor. Whereas epilepsy has as its object of treatment the seizure threshold. There are epileptic seizures of different types: focal (neuronal networks of a single cerebral hemisphere) and generalized (2 hemispheres) that are more exuberant (e.g., tonic-clonic crisis; absence crisis) (AULA 13 – 25/05/2021 – Prof. Giovanni Ortale Trainotti).

Epilepsy affects all ages. It is the second neurological disease in young adults (the first is migraine). Worldwide, it affects 1% of the population. It is higher in developing countries where there are, among others, a higher number of prenatal diseases. The goal (not always achieved) of conventional treatment is seizure control without side effects. There are 25 antiepileptic drugs (which is an indicator of the difficulties of treatment that achieves the indicated goal). The following problems are identified in conventional treatment: high incidence of side effects (sleep, drowsiness, changes in appetite and weight, mood swing, paresthesia or "tingling", visual changes and variations in neuroendocrine axes); high cost; poor accessibility and low adherence; frequent drug interactions (AULA 13 – 25/05/2021 – Prof. Giovanni Ortale Trainotti).

Regarding the prognoses, it is known that the longer periods of uncontrolled crises and the greater durability of the crises have negative prognostic effects. The higher incidence of crises

generates psychosocial losses and a higher risk of depression and mortality. Sudden death occurs in 1 in 1000 patients/year, especially in young adults. Even with a wide range of medications, 1 in 3 patients continue to have seizures. "Resistant epilepsy" (denomination for cases in which maximum doses of 2 drugs have already been tried without success) affects 35% of cases. These are the so-called "refractory cases" (AULA 13 – 25/05/2021 – Prof. Giovanni Ortale Trainotti). So what's the option? Cannabis medicines. Throughout the course, mothers whose children suffered from several epileptic seizures on the same day and who did not obtain results with conventional treatment, made their testimonies about the very positive results of cannabis treatment.

The therapeutic medicinal use of cannabis in epilepsy is discussed in a scientific article by Mattos et.al. (2017). The authors conducted a survey of studies from 1940 to 2015. They indicate, based on such systematization, the use of CBD for seizures. They point out that the improvements vary from total to partial. They argue that it is an effective treatment, without adverse and toxic effects. And yet, without creating tolerance, dependency or abstinence. Finally, they emphasize that the control of seizures prevents brain damage, in order to modify what would be the natural history of the disease.

2.3 THE ACTION ON MEMORY AND QUALITY OF LIFE AND THE USE IN ALZHEIMER'S

Alzheimer's is a neurodegenerative disease and the most common of the dementias related to senility or pathological aging. It affects more women than men and affects mainly in the 75 to 80 years, 80 to 85 years (MANZARO, 2017).

There is a forecast of the increased longevity of the world's population that indicates that by 2050 there will be twice as many elderly people as in 2010. From the age of 85 there is a 40% chance of having Alzheimer's. There are 50 million demented people in the world. And by 2050 that number could be 152 million. The disease is more common than you might think: 1 in 10 people over the age of 65 has Alzheimer's. The use of cannabis medicine can act from favoring better quality of life (restorative sleep, better appetite, improvement of common pains in old age), through its modulating action of the body and its metabolism, to neuroprotective effects that can slow down mnemic or memory losses. The effects of cannabis use are not antagonistic to those of conventional drugs and the necessary deepening of research seems quite promising for the prevention and treatment of the disease.

The term "dementia" is a generic name. In order to be able to fit in case of dementia requires at least 2 of the following symptoms: memory problem, language problem, executive dysfunction, attention dysfunction and social cognition abnormality. Alzheimer's is not a sudden disease, on the contrary, it is progressive and insidious. It involves progressive synaptic and neuronal loss, as well as plaque accumulation of beta-amyloid proteins. We can indicate 10 signs, namely: memory impairment that disrupts everyday life, difficulties in planning and problem solving, difficulties in completing familiar tasks, confusion with time and place, difficulty in understanding visual information and spatial

relationships, problems with words in speech or writing, not knowing where to put things (losing the ability to "redo steps"), difficulty judging, withdrawal from work or social activities, change in mood and personality. And the following risk factors: age (highest risk factor), family history (mainly first-degree relatives), genetics (risk genes; deterministic genes), head trauma, diabetes, hypertension, cardiovascular disease, hypercholesterolemia, sedentary lifestyle and smoking. Prevention factors are: reduction of risk factors (e.g., control of the diseases mentioned), regular physical exercise, healthy eating (whose guideline may be based on the *slogan* "peel more, unwrap less"), social connections, keeping mentally healthy, regular sleep, avoiding tobacco and avoiding excess alcohol (AULA 13 – 25/05/2021 – Prof. Denise Lufti Pedra).

There are other neurodegenerative dementias with some converging symptoms, but with distinct characteristics, such as: frontotemporal dementia, corticobasal degeneration, traumatic encephalopathy syndrome, Huntington's disease, Lewy body dementia, progressive supranuclear palsy. And yet, non-degenerative dementias: vascular dementia, normal pressure hydrocephalus, vitamin B12 deficit, hypothyroidism, depression, infectious dementias (AULA 13 – 25/05/2021 – Prof. Denise Lufti Pedra) (MANZARO, 2017).

Regarding the possible beneficial effects of the use of cannabinoid medication, in addition to well-being (quality of life, sleep, appetite), it is worth mentioning some considerations about the endocannabinoid system, albeit briefly. It is a system of homeostasis that regulates our entire organism. Cannabis replaces the deficient endocannabinoid (e.g., anandamide; aracdonoyl ethanolamine). The actions of what are called receptors are known: CB1 in the central nervous system (modulation of neurotransmitter activity) and CB2 (reduces inflammation and preserves bone mass). The neuromodulation of the endocannabinoid system amplifies or attenuates the action of neurotransmitters (AULA 13 – 25/05/2021 – Prof. Denise Lufti Pedra).

There are common or specific properties of cannabidiol and THC, as well as CBD. CBD is: antibacterial, antitumor, anticonvulsant, anti-inflammatory, antioxidant, antipsychotic, neuroprotective, bone growth promoter, anxiety and depression reducer, nausea and vomiting reducer, intraocular pressure reducer, spasticity and muscle spasm reducer, and relieves chronic pain. And THC is: antitumoral, anti-inflammatory, antioxidant, neuroprotective, reducer of anxiety and depression, reducer of nausea and vomiting, stimulator of appetite, reducer of intraocular pressure, favorer of sleep (reparative), sedative, reducer spasticity and muscle spasm, and relieves chronic pain (AULA 13 – 25/05/2021 – Prof. Denise Lufti Pedra).

In relation to Alzheimer's, CBD: reduces the formation of beta-amyloid protein and blocks the pathway that leads to the accumulation of the TAU protein. And THC: reduces amyloid beta protein. Synthetic cannabinoids also have a positive effect; through activation of CB2 receptors help remove beta-amyloid protein from human brain cells; through CB1 receptors block the formation of

neurofibrillary tangles of TAU protein. In rats, synthetic cannabinoids blocked the release of pro-inflammatory substances and TAU protein targeting CB2 receptors. In mice with AD (Alzheimer's disease), the combination of CBD and THC results in memory preservation and improves learning capacity. The therapeutic effects of THC and CBD may be indicated, even with studies still advancing. THC reduces agitation and aggressiveness, competitively inhibits acetylcholinesterase (such as conventional drugs used in the early/mildly moderate phases), decreases glutamate release with decreased neurotoxicity in the neurodegenerative cascade (such as conventional medications used in the moderate/severe phases), improves depression and fatigue, increases hunger and improves taste, decreases pain and disconnects pain and suffering. And CBD: improves memory, anxiety and sleep, decreases neuroinflammation (has antioxidant and neuroprotective effect) and has antipsychotic (reduces agitation) and anticonvulsant effects (AULA 13 – 25/05/2021 – Prof. Denise Lufti Pedra).

Linalool, as previously mentioned, is potentially effective for Alzheimer's. Article published in the journal Neuropharmacology indicates reversal of mental and emotional degradation: "reverses histopathological features and restores cognitive and emotional functions through an anti-inflammatory effect." Being touted as a "candidate" for Alzheimer's prevention for preclinical studies. Researcher Elthan Russo points to the following synergistic effects of Linalool: Linalool + THC: sedative and analgesic effects; Linalool + CBD + THCV + CBVD: anticonvulsant effect; Linalool + CBG: anxiolytic effect; Linalool + CBD: analgesic effect. (CLASS 19 – 06/06/2021 – Prof. Lu Cannabier).

It is worth mentioning that the use of cannabis, from the perspective of integrative health, should always consider contextual aspects, as well as the before and after the prescription. Patients who are refractory or have ineffective results from the treatment of Alzheimer's and other pathologies (autism, epilepsy) tend to benefit, in different ways and degrees, from the medicinal use of cannabis. But we should not pay attention only to the signs and symptoms of the disease, nor should we consider it as an isolated problem. It is necessary to contextualize it, to take its set and context. It is important to consider the environment in which the problem/disease is situated. It is very important that the patient is involved with the strategies of his treatment and, in the case of Alzheimer's, the role of the family is fundamental, given the cognitive weakness and discernment that affects the patient. The initial use of cannabis should be cautious: "start low, go slow", are slogans (Lecture 7 – 13/04/2021 - Profa. Carolina Nocetti). Self-care and body awareness are important aspects to enhance the benefits of medicinal use, and despite the challenges for such a condition in AD, the systematic care of the patient by family members and professionals, as well as cognitive stimulation activities, combined with exercise practices (consistent with the physical and psychological state of the patient) are recommended and greatly favor quality of life (MANZARO, 2017).

Nocetti and Ribeiro (2020) point to cannabis as an adjuvant drug in the treatment of AD. In general, the review articles, and the insufficiency if not lack of studies with humans, or even the very complexity of the elements involved (genetic and individual/singular aspects; the endocannabinoid system; the paradoxical effects of drugs and their interactions with the organism, its systems and brain – see later discussion on the use of anxiety and depression) prevent more assertive indications. Nevertheless, authors such as Carvalho and Mello (2020) tend to highlight more possible benefits, and in this case, indicate the use of cannabidiol for AD. In a literature review article, they point out that the limited efficacy of drugs used in AD in combating the degeneration of neurons, senile plaques and neurofibrillary tangles, motivate research on the identification of the therapeutic potential of cannabidiol. They point out that improvements are observed in "social recognition" and "learning", and although they emphasize that "studies with human beings" are necessary to "evaluate the safety and efficacy" of this "phytocannabinoid", they even mention that there is "reduction and recovery of memory deficit" (in this case, in the treatment of mice) (CARVALHO; MELLO, 2020). The perspective of Carvalho and Mello (2020) is based on the line of research integrative and complementary health practices. Systematized studies indicate symptom relief, predominantly, but also refer to the reduction of neuronal inflammation that may have broader ramifications. Although they indicate promising aspects, they recognize even in reference to animal studies, that the damage caused to memory is not reversed.

Camargo Son et. al. (2019) in a review article from 2007 to 2017 address the use of cannabidiol and delta 9-TH in Alzheimer's and Parkinson's. Promising therapeutic effects indicate: reduction of motor and cognitive symptoms; neuroprotective action. The results are explained by the antioxidant, CB1 receptor antagonist and activation of PPAR-gamma receptors. They consider adverse effects such as drowsiness and dry mouth. Further research on therapeutic and adverse effects is recommended, with higher doses and periods of exposure so that substances can be considered a more effective and safe therapeutic option.

Marsicano et.al (2002) focus on the endogenous cannabinoid system in the extinction of aversive memory. It is known that AD patients have very significant recent memory impairments, and as we have seen, not reversible, only potentially attenuated in their progressive rate of degradation (by conventional and cannabis drugs, which act in a relatively similar or non-antagonistic way, as previously exposed), and that curiously some memories and negative emotional conditioning tend to persist. It is about such memories and conditionings that Marsicano et. al. refer to the same pointed out by Malcher-Lopes and Ribeiro (2007):

> The amygdala acts on the emotional response, the formation of aversive (negative) memories, and the perception of fear and stress. The presence of CB1 in the amygdala is responsible for the erasure of traumatic memories and this helps to explore the relaxing effects and decreased anxiety caused by marijuana. In some people, depending on the dose and emotional state, the

> action of marijuana on the amygdala can generate opposite effects, with the transient emergence of paranoid thoughts (MALCHER-LOPES; RIBEIRO, 2007, p.55).

Malcher-Lopes and Ribeiro (2007) address many aspects related to marijuana and the brain, from its natural history and in Brazil, to considerations about the endocannabinoid system and marijuana as both medicine and toxic. The mental and neurobiological effects are explained, the "cascades of biochemical reactions (p.44), the effects on sleep and dream, "sexual appetite" (p.72), "immune effects" (p.74), "anticonvulsants" (p.82) and neuroprotective (p.83). Regarding the administration of THC in animal models of Alzheimer's, they indicate that there is inhibition of neurodegenerative and its symptoms, in addition to having beneficial effects on the behavioral disorders and lack of appetite present in this disease (p.84).

Malcher-Lopes and Ribeiro (2007, p.135), who refer to the neuroprotective aspects and anti-inflammatory effects, among others, understood as constitutive of numerous possibilities and therapeutic potentialities and well-being of the use of cannabinoids, mention that there is a "flexibilization" of "neuronal groups", in a passage in which they indicate "typical mental effects" of marijuana:

> The antiepileptic action, the short-term memory deficits, the perceptual alteration that converts even the most common stimuli into novelty, the loss of attention, the altered sensation of the passage of time, laziness, the increase in creativity and contemplative attitude, all these mental effects typically caused by marijuana may derive directly from the flexibilization of coordination between neuronal groups (MALCHER-LOPES; RIBEIRO, 2007, p.135).

For our part, we emphasize that in the most diverse studies on cannabis and mental health (ZUARDI, CRIPPA; GUIMARÃES, org., 2008), the consideration of the need for more research with human beings, and the deepening of existing ones, despite the prohibitionism that hinders them, are recurrent. It is necessary to recognize, under the necessary rigor of scientific caution, that, while some findings are consolidated, others increasingly seem to be plausible in the short, medium and long term. Thus, we align ourselves with Malcher-Lopes and Ribeiro (2007, p.63) who, when they argue that the "endocannabinoid system" is one of the "main conductors in the orchestration of vital functions", or even when they consider that marijuana produces "complex" effects and indicative of the "fantastic potential of the endocannabinoid system as a target for new remedies"; being challenging the task of directing its effects and using them selectively (MALCHER-LOPES; RIBEIRO, 2007, p.64).

2.4 POSSIBILITIES AND PRECAUTIONS OF USE AS AN ANXIOLYTIC

The use of medical cannabis in psychiatry is controversial in cases of psychosis and depression, more so in the former than in the latter. Admissibility in all cases must be well understood and analysed. The precaution in the use of cannabis in anxiety, whether as a specific behavioral disorder or as a problem related to other diseases and health conditions, also deserves to be highlighted. One of the

aspects known to be important to be properly considered is the dosage. Nevertheless, it can be pointed out that the anxiolytic (anxiety-reducing) property of cannabis is undoubted, provided that it is well managed and properly managed.

We can consider the use of cannabis medication in cases of anxiety and obsessive-compulsive disorders (OCD). Anxiety can be considered an adaptive response to a threat. When excessive (in itself, or depending on the objective situation), it becomes problematic.

As in all discussions about the use of cannabis in mental health problems (as well as in other health-disease processes), it is worth some considerations about the endocannabinoid system, this time in relation to receptors and retrograde lipid neurotransmitters, especially 2-AG and anandamide. The CB1 and CB2 receptors are coupled to the G protein, and act respectively on the nervous and immune systems (and others). The receptivity of CB2 can be amplified by different substances (e.g. pepper). Enzymes such as amide hydrolysis and COX-2 synthesize and degrade endocannabinoids (AULA 12 – 18/05/2021 - Prof. Eduardo Perin).

Regarding anxiety disorders, the DSM-5 separated them from OCD and post-traumatic *stress* . Anxiety disorders affect 29% of the population in the USA. The action of CBD and THC on anxiety is already relatively well studied. CBD provides a decrease in anxiety in its action on the CB1 receptor, is anti-inflammatory in its action on CB2, and decreases pain and anxiety in its action on serotonin. THC acts to decrease anxiety through the CB1 receptor. It is noteworthy that this occurs with low doses, which provide a decrease in anxiety and pain, as well as provide metabolic gains of the autoimmune system and bone growth. The vanilloid receptor is biphasic and anxiogenic when hyperactivated. At low dose it is anxiolytic. The reversal of high- and low-dose effects is valid for both THC and CBD, that is, it is beneficial at low dose (decreases anxiety) and harmful at high dose (increases anxiety). Acting on CB1 can extinguish fear memory and decrease responsiveness to *stress*. THC and CBD reduce the anxious behavior of rodents after conditioned fear. In humans the effect under basal anxiety is limited, and more effective in situational anxiety. Study of the U inverted in 5 groups, one of them placebo and others with different dosages of CBD to evaluate effects of anxiety (in this case, specific to the act of public speaking of people without problems) demonstrated that CBD is best in moderate doses (neither high nor low). The action of CBD and THC may be beneficial for anxiety, sleep, social anxiety disorder ("social phobia") and obsessive-convulsive disorders (OCD) and obsessive-convulsive symptoms (OCS) (CLASS 12 – 05/18/2021 - Prof. Eduardo Perin).

There are clinical case reports of patients who did not get answers and/or suffered side effects with traditional medications and who obtained improvements with the use of different types and doses of cannabis oils. In one of the classes, Professor Eduardo Perin reported a case of a patient with anxiety crises, which occurred when he migrated to the state of São Paulo. The patient had used clomipramine (tricyclic antidepressant), with worsening, and sought medical attention. The psychiatrist used *Full*

Screem with this patient (with a predominance of CBD), started with a few drops, and gradually increased until 12, when then the seizures ceased, but the patient then still did not leave the house. With yet another slight increase in the dose this improved, without the aid of psychotherapy. The professor also mentioned clinical cases described by Shindler et al., from 2008: a case of OCD and major depressive disorder, which obtained benefit with THC; and another, weighted as risky treatment, with symptom or trace of psychosis and OCD, in which THC improved OCD and did not worsen "psychosis." It was inferred from the clinical descriptions of the professor that there are different symptoms associated with anxiety disorders as the case may be, and that treatments should be zealous in terms of dosages and composition, having favorable results when well administered in terms of their anxiolytic effects and associated symptoms (such as sleep/insomnia) (AULA 12 – 18/05/2021 - Prof. Eduardo Perin).

The discussion about the use of cannabis in anxiety occurs in conjunction or articulated with the discussion about its use in depression, so that in the following item we present some systematizations that we made based on some scientific articles selected by us.

2.5 THE CHALLENGES AND RISKS OF USE IN DEPRESSION

The therapeutic use of cannabinoids in psychiatry and its main advances was systematized in an article by Crippa, Zuardi and Hallack (2010), researchers at USP in Ribeirão Preto. The authors, whose analyses are also developed in the aforementioned collection "Cannabis and Mental Health", Part IV "Cannabis and Psychopathology" (ZUARDI, CRIPPA, GUIMARÃES – org., 2008), made a survey of studies and literature reviews on the therapeutic use of the following cannabinoids: cannabidiol, rimonabant, delta-9-tetrahydrocannabinol and analogues. Cannabidiol has therapeutic potential as an antipsychotic, anxiolytic and antidepressant. Delta-9-tetrahydrocannabinol (THC) and analogues have anxiolytic effects on cannabis dependence and are adjuvants in the treatment of schizophrenia, although more studies are needed. Rimonabant, on the other hand, was effective in the symptoms (physiological and subjective) of cannabis intoxication, besides being an adjuvant in the treatment of smoking. But the potential side effects of this antagonist – induction of depression and anxiety – limit its clinical use. That is, if in epilepsy the anticonvulsant effect is already well accepted and the clinical responsiveness positive, and if in anxiety the dosage of cannabinoids is known to be a fundamental element to generate therapeutic effect (and avoid risk of potentiating it), in the different forms or pictures of depression and psychosis, other issues are (re)posed and demand greater caution. As we pointed out, selection and parsimony are part of the psychiatric clinic, and are not recommendations that are limited only to the use of cannabis. It is therefore necessary to point out that, although the "cannabinoids" have "demonstrated that they may have broad therapeutic interest in

psychiatry", "more controlled studies" are needed to conform the "findings and determine the safety of these compounds" (CRIPPA; ZUARDI; HALLAK, 2010, p.56).

The indication of cannabidiol or CBD presents, according to Crippa, Zuardi and Hallak (201, p.59), strong evidence (controlled clinical trials in humans) in schizophrenia, and moderate evidence in psychoses associated with Parkinson's or induced by cannabis, being the same valid for anxiety in healthy subjects, anxiety induced by cannabis or derived from social anxiety disorder; And yet, there is "some evidence," based on animal studies, on cannabis withdrawal syndrome and depression.

Animal studies suggest that the antidepressant and mood-stabilizing effect present in CBD is mediated by activation of the 5-HT receptor. This cannabinoid, Like the standard antidepressant imipramine, it decreases the immobility time of animals submitted to the forced swim test. According to the authors, "since CBD has been shown to have anticonvulsant, anxiolytic and antidepressant effects, it was hypothesized that this cannabinoid would have a pharmacological profile similar to mood-stabilizing drugs" (CRIPPA; ZUARDI; HALLAK, 2010, p.61). But studies of patients with bipolar affective disorder (BAD) have suggested, in turn, that "CBD is not effective for the treatment of manic episodes in BAD" (CRIPPA; ZUARDI; HALLAK, 2010, p.61).

The use of the cannabis plant is referred to as a reliever by patients with anxiety and depression, but controlled clinical trials with delta-9-THC and analogues have not been sufficiently conducted. If in anxiety one dosage can be beneficial and another can intensify it, in depression euphoria can also be induced in certain doses. For Crippa, Zuardi and Hallak (2010, p.62), the "paradoxical findings" of delta 9-THC "could be explained by the observation that its effects on anxiety and mood seem to be dose-dependent", with "low to moderate doses" demonstrating "anxiolytic and euphoric properties", and "higher doses" being "anxiogenic". Genetic and individual factors still need to be better understood; despite "promising indications" for the relief of "psychotic and mood symptoms," "it is prudent to discourage the use of these cannabinoids in these conditions": "an alternative could be the cautious exploration of the beneficial effects of the mixture of delta 9-THC and CBD, which is already used in some neurological disorders" (CRIPPA; ZUARDI; HALLAK, 2010, p.61).

Saito, Wotjak and Moreira (2010) address the pharmacological exploration of the endocannabinoid system and the new perspectives for the treatment of anxiety disorders and depression. These are literature review studies. The authors point out that studies on the pharmacological profile that led to the discovery of the endocannabinoid system in mammals indicate that endocannabinoids modulate a "diversity of brain functions, including anxiety, fear, and mood", so as to exert "effects of the anxiolytic and depressive types" (SAITO; WOTJAK; MOREIRA, 2010, p.7). The conclusion they present refers to experiments with animals, in which it is indicated that "drugs that facilitate the action of endocannabinoids may represent a new strategy for the treatment of anxiety disorders and depression" (SAITO; WOTJAK; MOREIRA, 2010, p.7).

Endocannabinoids are "endogenous binding substances" and the "development of novel pharmacological compounds" that target "receptors or the synthesis and degradation of ligands has revealed several complex brain functions" (SAITO; WOTJAK; Moreira, 2010, p.8). The authors argue that "drugs that amplify endocannabinoid action" imply a "more subtle strategy" for "pharmacological interventions" than "direct activation of cannabinoid receptors" (SAITO; WOTJAK; MOREIRA, 2010, p.9). Some compounds that interfere with the endocannabinoid system have potential advantages and disadvantages. Among the pros for depression, CB1 and CB2 agonists, TRPV1 antagonists, endocannabinoid uptake inhibitors AM404, VDM11, UCM707, OMDM and AM1172 stand out (SAITO; WOTJAK; Moreira, 2010, p.10). The authors report that in the so-called "major depression" the levels of endocannabinoids AEA and 2-AG, in the few studies that were measured, were reduced: "from a set of few exceptions, most of the preclinical and clinical data support a scenario in which attenuated endocannabinoid signaling promotes the occurrence of symptoms similar to those of anxiety and depression" (SAITO; WOTJAK; Moreira, 2010, p.11). Low doses of delta 9-THC and synthetic analogues have properties similar to anxiolytics and depressants, and at the behavioral level, they alleviate the "consequences of inevitable stressors and animal models of depression": "in addition, cannabinoids increased neutrofin levels, induced hippocampal neurogenesis, and suppressed stress hormone secretion" (SAITO; WOTJAK; Moreira, 2010, p.11). The paradoxical effects of cannabis use and The action of cannabinoid receptor agonists are explicitly mentioned by the authors:

> Although therapeutic applications for these substances can be envisioned, there are major obstacles that limit their applicability in the clinic. For example, treatment with cannabinoids can cause addiction and tolerance, induce sedative effects, and impair learning and memory. In general, low doses tend to induce anxiolysis [behavioral state of tranquility], whereas higher doses may induce opposite effects. The reasons for these differences are yet to be determined. They could be attributed to dose-dependent actions in different brain regions and neural populations. In addition, high concentrations of cannabinoids can lead to desensitization/internalization of CB1 receptors, thus resulting in lower endocannabinoid signaling. It is tempting to assume that such processes are responsible for the paradoxical effects of cannabis use on emotional responses such as episodes of anxiety and panic. To work around these problems, future studies may try to target the allosteric site of the CB1 receptor (SAITO; WOTJAK; Moreira, 2010, p.11).

TaThis considerations, however, do not prevent them from pointing out that the "uptake and/or hydrolysis of anandamide represents promising pharmacological targets", whether for the therapeutics of "depression" or for "anxiety disorders", since the effects induced by these "endocannabinoid enhancers" differ "from those of direct CB1 agonists, especially by avoiding "ubiquitous activation" (endocannabinoid action is restricted, temporally and spatially); nor to conclude that the "malfunction of the endocannabinoid system may promote the development and maintenance of psychiatric disorders such as depression, phobias and panic disorder"; thus, the expectation remains that "CB1 agonists or anandamide hydrolysis inhibitors exert antidepressant and anxiolytic effects", which should be better considered by other studies (SAITO; WOTJAK; Moreira, 2010, p.12).

2.6 THE USE OF CBD AND THE MEDICINAL CANNABINOID IN PSYCHOSIS AND AUTISM

As mentioned before, the endocannabinoid system governs and modulates body and behavior. The deficiency of the same can be suppressed and by the use of cannabis medicine. Phytocannabinoids are neurostabilizers that act on the problems arising from endocannabinoid deficiency. Among the uses in clinical practice can be highlighted those related to pain, mood disorders and insomnia, as well as lack of appetite and nausea. This is true in psychosis and autism. In the case of psychosis the indication is only of the drug based on CBD, because the use of THC can be harmful and stimulate typical symptoms of this pathology, such as delirium and hallucinations. In the case of autism, careful management does not rule out whole oil. The renowned researcher, Russo, was one of the pioneers in considering the aforementioned "collective effect" or "*entourage effect*", which concerns the collective action of cannabinoids, arguing that the use of whole oil is better than synthetic (cannabinine oil). Regarding the therapeutic use in psychiatry, there is an important group from USP in Ribeirão Preto, focusing on synthetic CBD. There are analgesic, antidepressant and antipsychotic effects, similar to those of "atypical antipsychotics" (Lecture 4 – 03/23/2021 - Profa. Eliana Nunes).

Autism or ASD (Autism Spectrum Disorder) is a pathology whose studies have had remarkable development and in which the use of cannabinoids seems to be promising, acting positively on the quality of life, food and interactivity of its carriers.

There is a multifactorial complexity and cause of autism, expressed in the film's title "Autism Riddles." We highlight the importance of food in the treatment of autism, which can make it one of the indicative aspects of cannabis use. There are several comorbidities of ASD (Autism Spectrum Disorder). The use of cannabinoids in autism, as in epilepsy, is justified mainly because of their action as a neurostabilizer (Lecture 6 – 06/04/2021 - Profa. Eliana L. Guerra Nunes)

There are reports of significant improvements in marijuana use in cases of autistic children in several studies. It is worth mentioning the need to treat inflammation together, as well as microdosing for beginners; or the need for precaution with psychoactive effects. Low doses can have good effects. The first oil indicated, is the rich in CBD. This can be replaced by the complete oil at a later stage. ASD includes many syndromes and use of different oils. There is a need for live pharmacies in addressing autism and other diseases that can benefit from the use of *cannabis* (Lecture 6 – 06/04/2021 - Profa. Eliana L. Guerra Nunes).

2.7 THE USE OF LOW THC CBD IN TREATMENT FOR CRACK ADDICTION

The University of Brasilia (UnB) conducts scientific studies with cannabis at the Center for Drugs and Associated Vulnerabilities. The use of CBD with low THC content in the treatment for crack addiction is investigated and recommended. Therapeutic use is indicated both in acute crises and in withdrawal. A work is developed in the CAPS of Ceilândia. Treatment of addiction can be crack,

alcohol, and marijuana itself. In the case considered here, we focus on the report of the study and clinical experience of the treatment of crack addiction presented in one of the classes by Profa. Andrea Galassi (Class 11 – 11/05/2021- Prof. Andrea Galassi).

Some delusional symptoms, difficulty sleeping and lack of appetite, present in the acute crack crisis, are attenuated with the use of marijuana. Crack users themselves have noticed such an effect. Thus, this mobilized clinical studies. The use of CBD can provide longer periods of abstinence and improve quality of life, by providing better sleep and nutrition. Chronic user anxiety and depression can also be treated with CBD. The medicinal use can also provide resumption of daily social and work activities, and decrease the frequency of crack use and the side effects of the drugs that are used in its conventional treatment (Aula 11 – 11/05/2021- Profa. Andrea Galassi).

In the research carried out, two groups were compared: one made use of cannabidiol; and another of the traditional medicines (antidepressant, anxiolytic and mood stabilizer). The research was conducted with non-hospitalized patients. That is, with people in a situation of routine life preserved. Unlike, therefore, double-blind randomized studies with patients disconnected from their context (inpatients). This professor highlighted the importance of the research being carried out in the real context of the user's life. And he pointed out that it is consistent with the health care model whose basis is the territory. He criticized the idea that marijuana is the "gateway" to other drugs, and referred to it being the "exit door" of crack. He also criticized the segments of Psychiatry that point to crack addiction as a "disease of the brain", because dependence is contextual and multifactorial, he argued. He also reported that the study showed positive results. The cannabinoid use group had benefits. He considered that different clinical pictures demand applicability of different cannabinoids. But that in the research had only one type: CBD low THC. Questions remain open as to whether a drug with a higher THC content could not increase the benefits, or even be better for some clinical cases and not for others. Distinct applicability exists for different contexts and clinical conditions. It is necessary to be able to take into account these adjustments and specificities. Thus, we point out the need for advances and deepening on the use of cannabis in the treatment of crack addiction (Aula 11 – 11/05/2021- Profa. Andrea Galassi).

We also consider it important to consider the importance of the medical use of cannabis in harm reduction, referred to in one of the classes by Profa. Sheila Dantas (Coordinator of the Federation of Therapeutic Cannabis Associations in Brazil and President of the Cannabis League in Paraíba), user of medical cannabis for rheumatic pain, as well as for refractory epilepsy and autism of her child (Aula 11 – 11/05/2021- Profa. Sheila Dantas).

Harm reduction is a strategy to minimize harm from substance use. It does not aim at prohibition or abstinence, but also at the promotion of health, dignity and respect for the human person. The harm reduction policy emerged in the 1980s when HIV was transmitted by injecting drug users.

The positive results achieved with the distribution of syringes and guidelines allowed an expansion of the harm reduction policy for other problems related to mental health (Aula 11 – 11/05/2021- Profa. Sheila Dantas).

The right of associativism entails the exchange of information and discussion on the reform of drug policy, a need pointed out in the introductory item of this work when we consider cultivation through the right of civil disobedience. When supported by associations, users of medical cannabis have greater guarantees of using more appropriate oils and dosages, as well as better quality substances. We must face the dismantling of harm reduction policies and the defense of the current Bolsonaro government of a diametrically opposed policy, of compulsory hospitalizations and forced abstinence. There is restriction on freedoms and "therapeutic communities" that are characterized as spaces of mistreatment. Associations are a form of organization of people with common goals and benefits; are governed by Civil Law, private law associations, non-profit, which does not prevent them from having revenues (community of associated property). The Associations enable support for patients and harm reduction. Support for patients, especially in regions where there are no doctors and access to cannabis therapy. Associations reduce misuse and misinformation. Reduce risks such as: inadequate dosages; inappropriate type of oil (e.g., contaminated oils, made from "pressed marijuana"; counterfeit oils); violence to which the buyer can be subjected in trafficking. And benefits: orientation to cultivation; "solidarity or associative cultivation"; "covering" lack of medicine from growers at home who have eventual crop problems; dissemination of knowledge and experiences. And finally, but not last, they play an important social role in breaking prejudices and paradigms, in the critical discussion about the reform of drug policy and in the reception of users (Aula 11 – 11/05/2021- Profa. Sheila Dantas).

3 THE HEDONISTIC USE OF MARIJUANA

3.1 SOCIABILITY AND PSYCHOSOCIAL ASPECTS

Historical and psychosocial dimensions related to the use of marijuana were treated in the Introduction of this work, and now we resume them in the sense of discussing the hedonistic use, a term considered more comprehensive and engaged than the "recreational use". We understand hedonistic use as beyond individual or narcissistic pleasures, even if it also involves them. We have preliminarily addressed some of the class reports to indicate the marijuana-sociability relationship. And then other systematizations, especially those inspired by the work of Malcher-Lopes and Ribeiro (2007)

The "Green Prophet", founder of the Cannabis Cultural Association of São Paulo (ACuCA-SP), made mention, in his report in one of the classes of the course, to the "recreational use" (which in his case later expanded to the religious and therapeutic uses). The speaker mentioned participations in 2009 in the Marijuana March (legitimized in 2011 by the Supreme Court), in the creations of the "Pain

Collective" (Unnumbing Reason, in 2010) and "Breathe Harm Reduction: Green Prophet" (2011), which denotes the imbrication of hedonistic use with different forms of sociability. This aspect was also evident in the following years. In 2012, he promoted the foundation of the Cannabis Association of São Paulo (ACuCa). In 2015 he participated in the Cannabis (Online Congress on Cannabis). And yet, in 2016, he ran for alderman; which was repeated in 2018 and 2020, this time in a collective candidacy ("Ganja Coletiva") (Aula 11 – 11/05/2021 - Prof. Fernando "Profeta Verde").

ACuCa was considered the first and perhaps only cannabis association in Brazil with cultural bias, that is, not related to therapeutic medicinal use. There is evidence of a cannabis social movement that seeks the modification of the drug law and the participation of the "voices of cannabists" in the laws. The communitarian character in favor of balance in the game of social forces is characterized as a counterpoint to economic interests. The socialist perspective merges, in the trajectory of the speaker, with cannabis associations, considered a tool for the construction of a new drug policy that invites participation, solidarity, cooperation and collective decisions, in the sense of a transforming force of society (Aula 11 – 11/05/2021 - Prof. Fernando "Profeta Verde").

The imbricated relationship between marijuana and sociability was also made explicit in the mention of the history of cannabis associations and clubs, such as the "Hashish Club" in France, which proclaimed the use of cannabis as a way to give light to artistic productions. He also referred to the "Diambistas Club" in Maranhão. In this one they make wheels in which they smoke and sing. In the group's sayings: "they invigorate the soul", "they bring the joy of living". He also mentioned the social cannabis clubs in Spain, in order to indicate the clubs as a fusion between associations, production, distribution and consumption. He indicated that there are different types of cannabis associations: activist, cultural, medicinal, political, professional and religious. They make different social actors interact and mobilize critical opinions on marijuana, prohibition, regulation and legalization, among others (Aula 11 – 11/05/2021 - Prof. Fernando "Profeta Verde").

The issue of marijuana and sociability was also made explicit in the participation of professors Angela Aboin (Mãesconha) and Prof. Keka Richie (ACuCa) in the Course.

Professor Keka Richie addressed the theme Associativism and Sociocracy. He presented associativism as an instrument for a community to come out of anonymity and gain social, legal and political expression in favor of the collective. Reported on organizational and financial aspects of an association. He mentioned the work of collective construction of the Statute of an association. He pointed to diversity as the great richness of the collective. He pointed out rules of sociocracy as the consideration of the interest of all people and the unanimous acceptance of all people in the decisions. The decisions have a popular basis. And there is collective power and intelligence. Consent is of the whole. Sociocracy obeys the following principles: effectiveness, evidence, consent, continuous improvement, equivalence, total transparency and accountability. Its benefits are inclusive governance,

adaptability, flexibility, engagement and stimulation of creativity. The speaker concluded her presentation by pointing out that the activist soul of sociocratic associativism acts in favor of the collective and common good, being critical of white, elitist and sexist society (Aula 12 - 18/05/2021- Profa. Keka Richie).

Prof. Angela Aboin, known for being a mother of an autistic child, in turn, emphasized the importance of the anti-asylum struggle and the deleterious effects of the institutionalization of different clinical conditions of different complexities, and under which there are prejudices and mistreatment in diverse social environments. He mentioned *the slogan* "to lock up is not to treat", recalling the commemoration of the day of the anti-asylum struggle. He pointed out that an articulation between the struggle for medical cannabis and anti-asylum is important. He defended the humanization of CAPS and mental health. He described and criticized the history of asylums, asylums and hospitals and their "strategy" of withdrawal from social life. He mentioned the importance of movements for inclusion. He compared the holocaust and dictatorship to asylums as spaces of mistreatment. He argued about the need for welcoming and human contact for mental health. He referred to the well-known case of 60,000 deaths in the Barbacena Hospital, as well as to the occurrence of cases of rape, abuse, starvation and doping in patients in numerous situations of institutionalization. And yet: of "loss of identity" and curtailment of freedom. He reiterated criticism of institutionalization and mechanical restraints (use of helmets, straitjackets, bindings), lobotomy and electroshock. He argued that there is safe, well-tolerated and effective use of cannabis in ASD, according to recent studies. He pondered that there is no treatment for central issues of autism, but rather a better neurological environment for the development of the child, modulation of neurons, decrease in anxiety, anguish and depression, improvements in mood, sleep, communication, or even stereotypy and management behavior in ASD. He concluded by pointing out that cannabis medicine opens new perspectives of life to autistic patients and children and to others who have been institutionalized and treated inhumanely for years (Aula 12 - 18/05/2021- Profa. Angela Aboin).

3.2 SENSITIVITY AND CREATIVITY

The discussion about the sensitivity and creativity sharpened through the use of marijuana is reported by users and we can point out subjective and objective aspects related to this perception. As Gabeira (2007) points out, there are many myths surrounding marijuana and its use, nonsensical effects and attacks and defenses that indicate that this habit, disseminated throughout the world, has relations with the social reality (specificities of the use and vision of marijuana in Brazil) and the most diverse dimensions and political positions.

We consider that chronic and abusive use can lead to distortions of users' perceptions. But on the other hand, there are numerous reports of artists and users, whose controlled or moderate hedonistic

use refers to the sharpening of sensitivity and creativity, which should not be neglected. Thus, we will consider, albeit briefly, some scientific aspects addressed in the book "Marijuana, brain and health" (MALCHER-LOPES; RIBEIRO, 2007).

Malcher-Lopes and Ribeiro (2007, p.53) address the action of THC on "brain circuits" called "base nuclei" and the presence of CB1 in the cerebellum. They explain that in the "nucleus *accumbens*" the CB1 receptor is abundant; it is the region of the brain that participates in the "anticipation and processing of the sensations of pleasure and reward" (MALCHER-LOPES; RIBEIRO, 2007, p.54). The "action of the active principles of marijuana" in this region "may be behind the amplification of the pleasures that marijuana causes, including the pleasure of eating, laughing and the pleasure of an affective or sexual relationship" (MALCHER-LOPES; RIBEIRO, 2007, p.54). But such pleasures, he warns, can also contribute to the case of "abusive use and psychological dependence of the drug" (MALCHER-LOPES; RIBEIRO, 2007, p.54; p.95; Melman, 1992; FIRMINO; QUEIROZ, 2009).

Malcher-Lopes and Ribeiro (2007) consider that the most immediate mental effect of marijuana is the "relief of mental and physical stress", and also indicate: "inner peace" and "empathy", facilitation in "interpersonal relationships", intensification of "emotions and perceptions" and enrichment of "visual perception" (p.104); "more flexible associations of concepts, ideas and emotions" that favor creativity" and "elaboration of metaphors" (but which can also hinder "logical and objective reasoning") (p.105).

The authors present a detailed characterization of marijuana as a "tonic": cannabinoids promote a "disorganization of neuronal processing" that has as a consequence a "facilitation of the restructuring of memory traits", thus making it easy to understand that their use "facilitates the creative process and the generation of *insights*" (p.141-142). The tonic thus acts as an "appetite stimulator", "relaxing" and aphrodisiac", while allowing the "deepening of the sensory experience", "enriches the appropriation and production of the arts" and "favors states of low anxiety", reducing "social tensions" in different contexts (in "prisons" and "dance parties") through its "anti-stressful action" (p.142)

3.3 THE DISTINCTION BETWEEN THE WELL-BEING OF HEDONISTIC USE AND ENJOYMENT AS A SYMPTOM

The hedonistic use of a socializing and engaged character, which promotes well-being, can develop, however, an unwanted facet, in which it is characterized as dependence and abuse. As Malcher-Lopes and Ribeiro (2007, p.56) point out, "the abusive and chronic use of marijuana can generate reversible memory deficit, lack of motivation and depression."

According to the psychoanalytic perspective, pleasure and displeasure are inseparable and related to the contradictions of the subject of the conflict and to the antithetical pair: life drives and death drives. As Melman (1992) points out, the use-symptom of marijuana is related to subjective and

social issues, such as the death drive and delinquency, which is understood rather as a social symptom related to abandonment than to a deformation of character, as conservative and uncritical discourses insist on the social inequalities of the capitalist order. The author resorts to the Lacanian concept of enjoyment, in which there is a differentiation and opposition to the common use of the word, usually related to pleasure.

Freudian and psychoanalytic discussions about the pleasure principle are well known, which is not only related to the pursuit of pleasure, but also to avoiding displeasure; and yet, we emphasize, to what lies beyond the pleasure principle, which refers us to the repetition compulsion and the death drive directed to the self itself (FREUD, 1985). It is to this situation that the notion of an unbearable excess of pleasure that reaches the social and erotic body is related, or even a kind of violated pleasure, although divorced from its rule and principle, by giving in to displeasure. The discussion is complex and involves the understanding of the cleaved subject and its conflicts and ambivalences, aspects that should not be unduly "psychologized", since the separation between individual psychology and social psychology is a great misconception, as Freud (1985) considers in his classic text of 1921, "Psychology of the Masses and Analysis of the Self" (title that receives different translations according to editions/translations that are used).

The discussion of this dimension of the use-symptom or use-enjoyment of marijuana leads us to the issue of abusive and chronic use, addressed by several authors, such as in Part V of the collection organized by Zuardi, Crippa and Guimarães (2008), as well as by Malcher-Lopes and Sidarta (2007) who, as previously exposed, differentiate marijuana as a tonic from marijuana as a toxic and drug that can generate psychological dependence. Chronic use and dependence can also cause, especially in adolescents and young people, the amotivational syndrome. But chronic and dependent use should not be confused with hedonistic use and the search for experiences by adolescents and young people, since the notion that such a search necessarily leads to the "ladder of drugs" or to an inexorable pathological destiny, contrary to the hedonistic use that promotes sensitive experience and well-being, as previously addressed, it is a gross error, which integrates the myths about marijuana and its use, eloquently addressed by Gabeira (2007, p.28).

Fermino and Queiroz (2009) refer to the frequent view that the use of marijuana would be related to obtaining pleasure or relief from the conflicts or ills of existence. And they consider that the Freudian reading situates marijuana as a "palliative" or "vehicle that produces a certain refuge" (FERMINO; QUEIROZ, 2009, p.253). And they question about such a function, its validity and effectiveness.

The authors mention studies that indicate that "psychoactive substances" are consumed "in various cultures for therapeutic, religious purposes and, due to the hedonistic character present in the history of humanity, as a way of obtaining pleasure" (FERMINO; QUEIROZ, 2009, p.253).

They ponder or problematize this possibility of "pleasure", because, by seeking the "relief" of the "situation that bothers them, it corners the subject" (FERMINO; QUEIROZ, 2009, p.254). And they also mention the conception that "drugs reveal a symptom, denounce problems of our society"; and they take up Freud's comment, in "The Malaise of Civilization," about the soothing effect of "toxic substances" (FERMINO; QUEIROZ, 2009, p.254).

The authors consider, without moral judgment, that the drug, in theory, could increase pleasure and decrease displeasure. But they problematize such a view. And they argue that in practice consumption assumes a "very contradictory character" (FERMINO; QUEIROZ, 2009, p.255). They exemplify cases in which one user reported that without the drug he was sad, and another who could only face the work in which he felt discriminated against when he smoked a joint. From "worry buffer" or "relaxing and anxiolytic mechanism", they ponder, the use is diluted in everyday life, changing "mood", "working capacity" and even "reasoning" (FERMINO; QUEIROZ, 2009, p.255). The issue of abstinence, psychological dependence and amotivational crisis are indicated under the metaphor of the "car without fuel" (FERMINO; QUEIROZ, 2009, p.255).

As we have pointed out, the authors reject the moralistic bias. They point out the inevitability of suffering. And they argue about another way of dealing with it than the use – dependent, we point out – of marijuana. Reason is then argued as a more effective form of suffering relief or even possible recourse in the pursuit of happiness (plausible, not idealized) (FERMINO; QUEIROZ, 2009, p.255).

According to Fermino and Queiroz (2009, p.257), the "reflective understanding, that is, reason", is what allows an experience in which there is the possibility of discernment between an idealized happiness and another plausible. As they argue, this possibility of being happy, under the mediation of reason, is distinguished from "naïve hedonism" (FERMINO; QUEIROZ, 2009, p.257).

There would then be another enjoyment distinct from the symptom-enjoyment, referred to by the authors as a satisfaction, or experience of the meaning of life in its course, and not as something essentialized. Therefore, a living of a "continuous reflective and active exercise, in search of a good living that implies moments of connection to projects, ideas and people" (FERMINO; QUEIROZ, 2009, p.258).

Therefore, based on the reflections presented here, we can indicate the pertinence of distinguishing between a symptomatic narcissistic-hedonism, which ranges from an inability to deal with frustrations to as a refuge from social issues of fact of difficult acceptance, from an objectifying, binding hedonism, entangled in the collective struggle, since the individual struggle against social hardships is in fact too costly. As well as distinguishing interactive and creative (not merely "recreational") hedonistic uses from uses that, although liable to be considered hedonistic, assume as their main mark dependence or chronicity.

4 FINAL CONSIDERATIONS

In the present work, we seek to articulate the content of the classes to the systematizations of readings carried out under the focus of mental health and the benefits and risks of the therapeutic-medicinal and hedonistic uses of cannabis.

In Introduction we address the historical and psychosocial aspects of marijuana use and human rights and civil disobedience. We proclaim that cannabis health is a right and the right is a social and institutional aspect that promotes biopsychosocial health.

We were able to present a series of considerations about the therapeutic effects and risks of the medicinal use of cannabinoids and/or marijuana for mental health. This item was the one that we highlighted the most in the present study. When addressing the complexity and diversity of therapeutics and cannabinoid properties, we advocate the parsimonious and selective use of medications. We develop analyses on neurological pathologies: the anticonvulsant effect on epilepsy and the cannabis action on memory and quality of life in Alzheimer's disease. Next, we consider the use of cannabis in mental-behavioral disorders, namely: the possibilities and precautions of use as an anxiolytic; the challenges and risks of use in depression; the use of CBD and the medicinal cannabinoid in psychosis and autism; and use of CBD low THC in the treatment of crack addiction.

We indicate the importance of management and caution in the prescriptions and dosages of the different compositions of cannabinoids according to pathologies and individual, psychosocial and genetic conditions of patients, according to scientific knowledge. We consider that there are paradoxical effects of cannabis, some consolidated scientific knowledge and others to be better investigated. And we regret that the medicinal potential of cannabis in the endocannabinoid system has not been as developed as it could be due to a narrow-minded if not prejudiced prohibitionism.

We end with the discussion of the hedonistic use of marijuana, in order to consider the marijuana relationship, sociability and psychosocial aspects. We also indicate several aspects of the hedonistic use of marijuana related to well-being, social interactions, sensitivity and creativity. We highlight marijuana as a tonic. Consideration of such aspects did not prevent us from considering the unwanted facet of abusive use and dependence. It is necessary to make clear the distinction between the well-being of hedonistic use and narcissistic-pathologizing hedonistic use; distinguish marijuana as a tonic from marijuana as toxic; or even, the social-subjective well-being of what we call self-absorbed enjoyment, a kind of symptom of social and psychosocial malaise.

We conclude that the use of marijuana and cannabinoid drugs holds promise in promoting good social, psychosocial and subjective being, and the existing risks elements to be always considered, being a challenge to society and science to better know them, in a multi, inter and transdisciplinary perspective (ABRAMD, 2006), always far from the marks of prejudice, moralism, prohibitionism, structural racism and stigmas.

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