Study on the toxicological effect of synthetic marijuana, it's compounds and derivatives in society

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ABSTRACT
In Brazil, there was a more than significant increase in the use and commercialization of synthetic marijuana over an average of 5 years. Also known as "K2", "K9" or "Spice", it's a chemical substance that simulates the effects of Cannabis Sativa, but is produced in the laboratory and may contain different chemical compounds. The reason for it's increase has been mainly due to its relatively low price and the lack of traditional drug tests, making it attractive to vulnerable groups such as the poor, people below the poverty line, children and adolescents who see the opportunity to enter the world of drugs. In this way, the work seeks to elucidate the toxicology of synthetic marijuana and its dangers for human use, focusing on possible compounds and their consequences.

Keywords: Cannabis sativa, Spice, K2, Toxicology.

1 INTRODUCTION

Cannabis sativa has pharmacological importance due to its therapeutic potential and its effects within toxicology (MLOST, BRYK & STAROWICZ, 2020). This exposed the plant as a therapeutic compound for pain, anxiety, and depression (GILMAN, SCHISTER, POTTER, SCHMITT, WHEELER, PACHAS & EVINS, 2022).

In the years between 2000 and 2008, synthetic derivatives of *Cannabis sativa appeared* in Europe and the United States . As of July 2012, synthetics have been considered phytocannabinoids through their chemical structures, inhibition constant (Ki) and major discoveries by the *Drug Enforcement Administration* (DEA). In its commercialization, it is common to come across a mixture of herbs, commonly known as "*Spice*" or "K2", as a consequence of its rapid growth as a drug of abuse, it was banned in 2010 (BUKKE, ARCHANA, VILLANI, SERVIDDIO & CASSANO, 2021).

Spice or K2 contains a combination of several types of highly potent synthetic cannabinoid agonists, as well as other psychoactive components, many of which are unknown. Its effects are similar to those of cannabis, usually causing relaxation, euphoria, perceptual disturbances, and changes in cognitive abilities, however, the adverse effects are more intense and long-lasting than those of natural cannabis that range from nausea to symptoms such as psychomotor agitation, sweating, palpitations (COHEN, MAMA, ROSCA, PINHASOV & WEINSTEIN, 2020).

Due to the lack of any qualitative report of the substances, all K and Spice drugs are classified as synthetic cannabinoids. In recent years, there has been a considerable increase in the use of synthetic drugs, with the percentage of consumption that was previously approximately 5% tripling to 15%, showing that the use and trafficking of these substances are not future trends, but rather a present reality that is intensifying in a worrying way, mainly affecting the young, poor and vulnerable population (PAIVA & BRANCO, 2023).

In order to clarify information and aggregate facts, this project was conceived and developed, seeking to raise through an analysis of synthetic marijuana, its derivatives and compounds, evaluating its harmful effects on the human body and understanding the implications of its use.

2 METHODOLOGY

This is a bibliographic and observational review, which used research and studies related to the toxicology involved in the use of synthetic marijuana, popularly known as Spice/K2, which is in emergency in Brazil, compromising health from children to adults. Such data were extracted through scientific publications found on the PUBMED and Google Scholar article search platforms, news in online newspapers and disclosures (initially used as information consultation) from the National Health Surveillance Agency and the World Health Organization.

As an inclusion criterion, we used current articles, in the period from 2019 to 2023, in English and Portuguese, which portrayed the proposal of the chosen theme, found through the descriptors "Cannabis sativa", Spice/K2 and Toxicology. As exclusion, articles that did not have the descriptors, predecessors to 2019 and unrelated to the theme were excluded.

In order to select the articles found, a previous analysis of the titles was carried out, to which they were related, the abstracts were also analyzed and, after the application of the inclusion and exclusion criteria, the full reading of the works was carried out to choose the articles with greater affinity to the theme.

In total, 90 articles were found in the searches with the descriptors, however, after the criteria described above, only 8 articles were chosen to start this project.

3 THEORETICAL FRAMEWORK

3.1 *CANNABIS SATIVA*

The medicinal virtues of Cannabis Sativa were first documented in the pharmacology textbook Materia Medica by Greek and Roman physicians in the first century A.D. However, a more accurate description of the physiological effects was recorded by ancient Asian writers (BUKKE ET AL., 2021).

The Cannabis Sativa plant contains more than 100 types of phytocannabinoids, chemical compounds capable of interacting with the cannabinoid receptors present in our bodies, they are best known and predominant are tetrahydrocannabinol (THC) and cannabidiol (CBD). THC is found in the largest amount and it is responsible for its popular psychoactive effects, such as euphoria, dizziness, impaired coordination and recent memory, however, it also has benefits in controlling pain, nausea, anxiety, insomnia, anorexia and spasticity. CBD has antiepileptic, analgesic, anxiolytic and sedative properties, with less pronounced psychoactive effects. Both phytocannabinoids have anti-inflammatory effects, and the effect is enhanced when THC and CBD act together (CHAVES, BITTENCOURT & PELGRINI, 2020).

Subsequently, THC has been the subject of studies related to its pharmacology, toxicity and therapeutic potential as cannabinoids, research has resulted in the discovery of an entire endocannabinoid system. Unlike CBD, which has been a difficult substance to study and understand, as it does not have the typical behavioral effects of cannabis, it is believed that it is not responsible for psychotropic effects (MLOST, BRYK & STAROWICZ, 2020).

3.2 SYNTHETIC MARIJUANA

Synthetic cannabinoids are an emerging class of psychoactive substances that have propagated globally through structural alterations of existing molecules, generating new analogues with potentially serious adverse health effects. They represent the predominant category of drugs identified by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), with 207 substances identified as of October 2020. Acting as total agonists on receptors confers a much greater potency than natural cannabis, which has led to acute and chronic intoxication, including deaths (BUKKE ET AL., 2021).

These products can also be identified as herbal or liquid incense, mimicking the effects of marijuana by acting on the same synthetic receptors as THC, the psychoactive component of marijuana. Although they are labeled as "not for human consumption," these products are often smoked, resulting in a marijuana-like feeling of euphoria along with other effects. They are marketed as "legal" and "safe" alternatives, but they are dangerous and can affect the brain more intensely than marijuana itself, with variable and, in some cases, fatal effects (BASAVARAJAPPA & SUBBANNA, 2019).

3.3 EPIDEMIOLOGY IN BRAZIL

During an extensive scan of several databases of the Toxicological Information Centers across the country, in the period from 2010 to 2019, no records of notifications related to poisoning by synthetic cannabinoids, such as Spice and other similar substances, were found. Of the centers that responded, some reported that they did not have data on notifications of poisoning by synthetic cannabinoids, however, the Belo Horizonte center stressed that the absence of registration does not necessarily mean the non-existence of cases, but rather that these cases may not have been identified by the patients or professionals who performed the care. In addition, other databases, such as the SUS Department of Informatics (DATASUS) and the Oswaldo Cruz Foundation (Fiocruz), also did not present notifications or epidemiological data related to any type of drug (SILVA & MOURA, 2022).

Synthetic marijuana has spread throughout Brazil, especially in the city of São Paulo, expanding its presence in relation to traditional drugs. In the last five years, there has been a significant increase in the seizure of these substances, which now accounts for 15% of seizures, previously the number of seizures was 5%. Drugs are predominantly impacting poor and vulnerable young people, representing a worrying and accelerated presence in the epidemiological context of K drugs (G1, 2023).

4 FINAL THOUGHTS

There is a complexity of the therapeutic and psychoactive properties *of Cannabis Sativa*, mainly through its main components, THC and CBD, has aroused a growing interest in the scientific community as alternative routes for the treatment of diseases because it has a high therapeutic potential in a variety of medical conditions. The emergence of the "K drug" has proven to be a serious threat to public health, the substance that is marketed as a "safe" and cheap alternative to marijuana, has demonstrated a toxcicological potential and adverse effects incomparable to the natural plant, leading to worrying consequences, including cases of acute and chronic intoxication.

Although the study is about its incidence, because its chemical composition is extremely variable, the "K drug" makes it highly dangerous, especially among young and more vulnerable people, thus highlighting the urgent need for regulation and public education to try to mitigate as much as possible the damage associated with its increasing consumption.

The present study exposed that the imminent public health crisis raises issues such as the need for further studies and research involving the subject, in order to obtain solutions, as well as the promotion of discussion among young people, who are the main risk group.

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