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HERBAL DRUG ADDICTION: LATEST INFORMATION ON TRENDS AND OUTLINES

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ABSTRACT

Herbal drugs of abuse are being practiced for ages. Old-fashioned addictive substances, such as opium, and cannabis are mainly imitated or altered from the ingredients likely based on crude drugs. Cannabinoids and cathinone are derived from natural derivatives. Safety and efficacy altogether is a matter of concern that needs to be discussed and awareness related to that must be spread. In this review, we briefly, discuss some plants such as khat, kratom, salvia, and mandrake, with the perception that experts and common people alike are aware of the possible glitches caused by regular and synthetic derivatives, and appropriate resistor procedures will be taken. Some "herbal plants" should be termed as injurious drugs since chronic management has been connected with addiction and cognitive deficiency, and findings inspecting these features are deficient**.** This paper discusses toxicity issues and main safety concerns regarding plant-derived products. Safety persists as the major concern with the use of herbal remedies, it becomes imperious, to ensure that all herbal constituents are safe and reliable.

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Introduction

Plant parts containing psychoactive have exhibited new inclination observed in users, regarding the ingestion of plant parts. In the past, these substances were employed at the center of religious ceremonies of ancient civilizations. In the present times, these herbal products are easily available on websites and some of them have no allowable restrictions [1]. The custom of herbal medications and their derivatives endures increasing rapidly across the world for the management of various health challenges. This past decade has perceptibly observed natural therapies, incorporated with these herbal remedies. The developing world mainly relies on herbals as the main resource of healthcare and conventional medical exercise [2]. The use of herbal remedies has also been widely embraced with complementary and alternative medicines, with the belief in healthy living. Herbal medicines are a balanced and moderate approach to healing, but their safety concerns are a major issue. Many of the herbs and extracts obtained from them are untested and their use is also not monitored. The protection of most herbal products is compromised by a deficit of quality control methods; therefore, improved consideration of the risks associated with these products is crucial [3]. The exploitation of plant-based drugs is also a serious matter of concern, and this matter is as old as the history of human beings, as with Coca, Opium, and Cannabis that were utilized in religious rituals and for relieving the pain [4]. In the market, these materials have been recognized as 'designer drugs' or 'herbal highs'. Many examples are available for such types. To avert reversion to long-lasting drug dependence *Rhizoma Corydalis* can be used. Derived from *Uncaria rhynchophylla*, Alkaloids, seem to be effective on addictive results caused by ketamine and methamphetamine. *Radix Pueraiae* and *Salvia miltiorrhiza* can effectively inhibit the intake of alcohol. On opioid dependence, it has been observed that Sinomenine has therapeutic impacts. An alkaloid extract of *Stephania intermedia*, l-Stepholidine, weakens the acquisition, of morphine-induced conditioned place preference [5]. Though the majority of psychoactive are synthetic chemicals, most of them are derived naturally. As man-made cannabinoids are counterparts of cathinone and Δ9-tetrahydrocannabinol from khat

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and cannabis, respectively; the plant-based substances, their toxicity aspects remain to be unelucidated [6]. To serve the purpose, the traditional plant-based drugs, such as coca, opium, and cannabis, have been methodically reconnoitered, as in **Figure 1** and **Table 1** some "herbal highs" should be categorized as harmful drugs since long-lasting management has been connected with dependence and rational damage; for some others, the recent trends of abuse, studies investigating these aspects are lacking [7]. Some herbal products and supplements are used for recreation purposes, and they serve huge clinical effects ranging from euphoric to hallucinogens. Despite having huge potential for abuse, addiction, and adversities, still incorrect perception persists that these products are all safe, and legal for use. Health-related professionals must be conscious of this problem as increased marketing and media resources have made these products accessible to many young adults and teenagers. This review will focus on plant-based Psycho-actives obtained from different plants.

Figure 1. Plants known for drug abuse

Salvia divinorum is full of brief psychoactive possessions, its leaves usually are disbursed by munching, burning, as an infusion, or tea. When in liquid form, Salvia can be combined with other liquids. Its leaves are crushed and mixed with drinks or it is smoked into vapors. The leaves are rich in opioid-like derivatives that persuade hallucinations [8]. Salvinorins are a group of natural chemical compounds and their structural analogs. Many have been isolated from Salvia. Chemically, they are termed diterpenoid furanolactones. Salvinorin A, the neoclerodane diterpene, resylts in the psychoactive effect of the plant [9]. Salvinorin A, is a hallucinogen, is known for its dissociative effects, and is under survey for its conceivable application as a framework to progress in the path of new drug development for discussing psychiatric diseases, for example, addiction from cocaine dependence [10]. It is active at the low dose of 200 μg, being a powerful and sensitive κ-opioid receptor agonist, as guaranteed by the possessions in mice clogged by κ-opioid receptor antagonists. The leaf extracts, dried leaves, and pure salvinorin A are constant at ambient temperature. In humans, salvinorin A induces short-lived, profound hallucinations [11]. A cigar-like 'quid' is made by rolling the fresh leaves of the plant, which is then chewed or sucked to enhance the active ingredient absorption. The most common way for recreation use it is by smoking the crushed dried leaves from a pipe providing hallucinations on an instant basis [12]. 200–500 microgram doses of salvinorin A, on inhalation, results in being unable to control physical movements; or film-like hallucinations [13, 14]. When Salvia is chewed, the leaves secrete chemical components of salvinorin A. It is an even more potent D2 receptor partial agonist [15]. The concentration of salvinorin A travels from oral mucosa or the respiratory area and gets converted to salvinorin B, i.e. its main inactive metabolite, after swallowing. Salvinorin A is rapidly metabolized [16]. Short-term effects of Salvia include hallucinations, uncontrolled laughter mood and emotional swings, detachment from self, lack of coordination, and slurred speech.

Table 1. Details of Plants known for drug abuse

S.No.	Plant name	Common name	Part used	Chemical constituent	Commonly used as
1.	Salvia divinorum	Khat	dried leaves	Salvinorin A	Hallucinogen
2.	Cannabis sativa	Hemp	leaves	delta9-tetrahydrocannabinol and cannabidiol	Psychoactive
3.	Mitragyna speciosa	Kratom	leaves	mitragynine and 7-hydroxy mitragynine	Stimulant
4.	Piper methysticum	Kava	dried root and rhizome	Kava lactones	Euphoric
5.	Aconitum carmichaeli	Aconite	Roots	Aconitine	Analgesic

Cannabis sativa has two main constituents; delta9-tetrahydrocannabinol and cannabidiol. THC accounts for the addictive property of cannabis due to its psychoactive properties. THC-induced dopamine release was not specified in one study, as probably THC persuades less Dopamine release, as compared to stimulants like methylphenidate or amphetamine [17]. The main psychoactive compound in cannabis producing a high sensation is THC. It is also available in oils, edibles, tinctures, capsules, etc. On the interaction of both the compounds with the endocannabinoid system of the body, they exhibit different effects. They are widely used to alleviate symptoms of certain diseases, but their efficacy in some cases is not well established [18]. 113 distinct cannabinoids have been isolated from cannabis as phytocannabinoids, and tetrahydrocannabinol. The FDA has approved many drugs that contain individual cannabinoids; however, it has not certified the cannabis plant for any medical use. They are used for nausea and vomiting associated with cancer chemotherapy, specific rare forms of epilepsy, and loss of appetite and weight loss [19].

Kratom: is a concentrated, dried version of *Mitragyna speciosa* leaves, and is further processed in pill or powdered form. It is chewed for its stimulant properties. It is consumed as a gel capsule or brewed as a tea, and has similar impacts to opioid drugs like heroin in high doses [12]. Food and Drug Administration are imposing a strict check on supplements derived from it. Adverse effects of it are nausea, itching, dry mouth, and insomnia. The drug is addictive on its own, originally common among people who suffer from some serious effects from the usage of opioid painkillers [13, 14]. The leaves of the tree, contain the main ingredients in the form of indole alkaloids, such as mitragynine and 7-hydroxymitragynine [15]. mitragynine and 7-hydroxymitragynine have been the focus of multiple pharmacological investigations as they bind to the human ƙ-opioid and μ-opioid receptors with nanomolar affinity, and function as partial agonists at the μ-opioid receptor.7-Hydroxymitragynine shows almost fivefold greater affinity at the μ-opioid receptor han mitragynine [16]. The content of mitragynine and other alkaloids in kratom differ among specific plant strains. Kratom extracts are often accelerated by being mixed with other psychoactive compounds to strengthen the impacts of the concentrated contents of mitragynine. The use of the conditioned place preference test, indicated the possibility to misuse mitragynine and related alkaloids, as documented in animal studies, which indicated a distinct reward-effect for 7-hydroxymitragynine

Kava: It is derived from the plant *Piper methysticum*. A relaxing drink is made from it, similar to that of alcohol, in the terms of liver damage. FDA has elevated apprehensions about safety. Since 2002, the FDA has released consumer advisories related to kava's potential dangers [17]. Powdered and gel capsule obtained from the plant is used as nutraceuticals or dietary supplements. The sedative impacts of kava have been used for epilepsy, alleviate anxiety, depression, and withdrawal symptoms. It is known for its sleep-inducing, properties and they have been reported as well [18]. Kava lactones, or kava pyrones, are the resultant of the dried root and rhizome of *Piper methysticum* [19]. Kava may also enhance the effects of benzodiazepines and alcohol [20]. Kava consumption seems to be non-addictive. It also causes improvements in recognition memory tasks and accuracy [21]. On regular usage, it causes calming sensation same as alcohol and benzodiazepines. It mainly causes euphoria, which is a feeling of wellness, and also causes relaxation. Kava acts through GABA receptors in the central nervous system and stimulates dopamine in the brain. Over usage of the substance is practiced, to cause relaxing effects at a faster pace. Overdosing increases the risk of abdominal cramping, and breathing-related complications.

Aconitum: Aconitum carmichaeli and *kusnezoffii* are known for their analgesic effects. Existing diester diterpene alkaloids including hypaconitine, aconitine, and mesaconitine in both species, accounts for the toxicity caused by the plant [22, 23]. Poisoning cases due to homemade liquor obtained from aconite used for some medicinal applications were reported in China. Cardiac toxicity from consumption of the derived preparations leads to tachycardia and eventually, some cases of death have been reported. As reported in a case study, a combination of A. carmichaeli and A. kusnezoffii overdose results in hypotension and bradycardia. The contents of aconitine measured by HPLC-DAD in the urine and post-mortem femoral blood were 264 and 10.8 micrograms/L, respectively. Hence, accidental, or suicidal poisoning due to the intake of plant-derived material on investigating sudden or unexplained death should be considered and kept in mind [24, 25].

Khat: is a plant indigenous to Arabian Peninsula. Khatin, cathine, and cathinone are the potent alkaloids present in them. It is used by chewing its shoot and leaf. After chewing, alkaloids such as cathine and cathinone are emerged to cause psychoactive impacts. Alcoholic extracts of khat are also being used on the large scale for the same effects. Khat is the popular plant-based substance after *Salvia divinorum*. Khat and its alkaloids like cathine and cathinone are listed in schedules III and I in many places worldwide [26, 27].

Mandrake: it belongs to the perennial plants in the genus Mandragora. *Mandragora officinarum* is the most common one. Word "mandrake" is applicable to plant roots with poisonous alkaloids. It is known for its hallucinogenic, healing, and poisonous specifications. Its fruits has fertility-enhancing properties [28, 29].

Conclusion

This work appraised plant-based materials, mainly the ones categorized as psycho-actives used in illicit drugs of abuse. Naturally derived psychoactives are easily accessible, and the constituents present in them can be chemically reformed modify their possessions, and obtain new synthetic moieties from them on a faster basis. They are used further to synthesize the basis for synthetic and semi-synthetic derivatives. Therefore, they should be properly dealt with the documentation purposes. Some of still in the category, where they have not been properly classified to which category of abuse or addiction, they fully belong. Their doses and availability are something that has to be intervened to make sure might even be lethal if not properly used.

Therefore, it is believed essential to cultivate a standard screening appliance for early detection of Natural based psycho-actives for regulatory purposes.

Future Prospects

Based on natural lead compounds, an impressive number of chemicals have been isolated either from medicinal plants or synthesized. Plant-based medicine act as the most used raw material for developing novel healing agents and this trend will be continued in the future. In an era of quickly developing technology and science, people tend to ignore traditional knowledge and values, and also traditional medicines [30-33]. In general, for developing new medicinal agents, the synthetic route's success rate can be 1/10,000; nevertheless, with searching for new therapeutic moieties based on medicinal plants used in the traditional medicinal system it can be as high as 1/4 or more. Last but not least, the ecological ethics principle should be upheld by preserving biodiversity while using natural resources for drug discovery [34-38].

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