Overview of Salvia divinorum – Substance-induced psychosis

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As per the literature, humans ingest a comprehensive range of food materials including drugs along with dietary supplements which are mainly derived through medicinal plant products and modifying the purpose of the central nervous system (CNS). These psychoactive based properties are mainly attributable to the existence of plant-derived secondary metabolites. Most of the cases or studies showed the effects of these phytochemicals derived from secondary metabolites on the human CNS might be linked either to their ecological roles or molecular along with biochemical based properties are reported in case of plants along with higher animals. One of the mental health disorders, psychosis where person losses its capacity of critical thinking, they perceive things differently as compared to the people around. They see or hear things that other people cannot see or hear (hallucination) or even believe things that are not true (delusion). There are so many synthetic psychosis inducer synthetic cannabinoids (SCs) as well as semi-synthetic and natural. Psychosis is a disorder which shows the effect for long-term or sometimes for the short term on an individual. In this review we will mainly look for natural psychosis inducers like Salvia divinorum and this plant may produce some secondary metabolites. Still, many of these are found to show an effect on human health in some or the other way which may range from hallucination to organ failure. These secondary metabolites affect the hippocampus region of the human brain, which is linked with memory. It is interesting to note how one chemical is used for an organism for protection and that one chemical act as a mind-altering chemical for the higher class of organism – the humans.

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INTRODUCTION

Drug-induced psychosis is also called a substance-induced psychotic disorder where people’s reality is mainly distorted through the use of a substance, and it is difficult to see the world how it is. The primary symptoms of drug-induced psychosis which includes hallucinations, delusions, anti-social behaviour, depersonalisation, lack of emotion, violent behaviour etc. (Fergusson et al., 2003). In other words, psychosis is the condition when our mind is not in our control. They visualise things or hear that other people cannot see or hear which we call hallucination or believe things that are not true. (delusion) (Glasner-Edwards et al., 2008). Hallucinations exist in various forms, e.g. seeing a person that doesn’t exist, hearing voices etc. because delusions considering as beliefs but without any logical basis, e.g. Paranoia (someone believes they are being watched or stalked without any evidence). In short, certain drugs or any stimulant (Crebbin et al., 2009) consumed in a substantial amount (amphetamines
and methamphetamine; Cannabis; Alcohol; Cocaine; Psychedelics) and do some changes in brain chemistry which cause psychosis (Chen et al., 2005). Various substances were reported related to psychosis should be either short-term or long-term effect. But the most notable thing is that few drugs somehow cut the burden of psychosis when the drug leaves the body while some of them may live for days, months, or years. In literature, multiple reasons related to drug-induced psychosis were reported, e.g. some of the drugs showed mimic with other types of mental disorders, i.e. schizophrenia or bipolar disorder (Chen et al., 2005). In this regard, we focused on psychosis-inducing plants, especially Salvia.

Salvia is considered as one of the largest class of plants, especially mint family, Lamiaceae, with about 1000 types of herbs, shrubs, herbaceous perennials, and annuals. Salvia (family Mentheae; subfamily Nepetoideae). This variety is widely distributed with three specific areas of assorted variety: Central and South America have approx. Six hundred species; Central Asia and the Mediterranean have 250 species; Eastern Asia has 90 species (Epling and Jativa, 1962). Besides being the most extensive family, it is also the rarest species of mint / Lamiaceae family. As per the literature, Salvia is undoubtedly not a characteristic genus—a part of its branches have a closer relationship to other genera in the ethnic group Mentheae than to other Salvia species (Hanes, 2001). This review aims to discuss the effects of Salvia divinorum's psychoactive property and the way it is used by traditional Mazatec people (Linde et al., 1996) and other Salvia species found till date (Casselman and Heinrich, 2011).

One of the species of Salvia, i.e. Salvia divinorum is the one who can create hallucination and delusion in an individual who smoke or chew the divinorum's leaves. This is the only plant found in the mint family that causes psychosis (Chartoff et al., 2008). Other species of Salvia are used in various purposes; for example- S. cavaleriei is used for treating boils, hemoptysis since S. desoleria is used to treat menstrual diseases, central nervous system disease (Currie, 2013). A study using DNA sequencing of Salvia species showed that, in any case, there are various forms of lever mechanisms in Salvia in three different situations. This eventually makes the variety non-monophyletic, which implies that people from the family have evolved from various progenitors, rather than common ancestors (Ebner et al., 2010). The DNA investigation has demonstrated that the family may consist of three unique clades, or branches (Fichna et al., 2012). The study presumed that Salvia is undoubtedly not a characteristic genus—a portion of its branches have a closer relationship to other genera in the ethnic group Mentheae than to other Salvia species (Ford et al., 2011). This genus has been reported to have antioxidant properties which are due to the rosmarinic acid and its derivatives, and they also show the cytotoxic activity tested against the human cancer cell lines. Various Salvia species are famous for their use like- S. apiana (white sage), S. azurra (blue sage), S. hispanica (produce edible seeds; high in protein) etc. (Ford et al., 2011).

One of the Salvia species, i.e. Salvia divinorum (perennial herb belonging to the mint family or Lamiaceae) with the psychosis-inducing property. Salvia divinorum develops around 3 feet tall with a leaf spread of 2 feet, which is more significant than other Salvia plants. The Salvia sage develops in tropical forests at altitudes of 300 to 1800 meters (Ebner et al., 2010). Salvia divinorum has large green oval shape (regularly likewise dentate) leaves, with a yellow undertone that arrive at 10 to 30 cm (4 to 12 in) long. The leaves have no hairs on either surface, and practically no petiole with light green veins along the surface S. Divinorum delivers not very many seeds, with no pollen tube inside the style. Some leaves become exceptionally huge, nearly the size of a hand. Thus it is known that it does not have a pollen tube, so we use the hybridisation method or selective breeding method repeatedly to increase the number of Salvia divinorum. This species, i.e. S. Divinorum, is a close relative of other primary American plants, including sage (Ford et al., 2011).

Mazatec is local inhabitants of Sierra Mazateca (also called as the Sierra Madre) in district Northern Oaxaca, known for their practice of consuming psychoactive plants, seeds and mushrooms. However, they use many psychoactive plants, especially Salvia divinorum. In Mazatec, people chew Salvia leaf before going for their prayer or any ritual ceremony. They take Salvia leaves with tea, alcohol in one out of two ceremonies which they regularly consume during prayer, whose effect lasts for about couple of hours because they take 13 pairs of leaves to roll or six leaves roll even the Mazatec give three leaves before going for their prayer or any other ritual ceremonies (Chartoff et al., 2008). An individual’s weight determines the portion of S. Divinorum taken. Salvia divinorum is of interest as a psychedelic plant found in the mint or Lamiaceae family, containing psychoactive chemical salvinorin-A (Ebner et al., 2010). Besides, psychotropic terpenoid (divinorin A) also reported and its structure closely resemblance to salvinorin-A.

In contrast, phytochemical studies were conducted...
and reported several diterpenes from salvinorin-A to salvinorin-F. According to the literature, the concentration of Salvinorins may vary from salvinorin-A to salvinorin-F and also reported in different stages of plant growth. When we look into the chemical profile of *Salvia* plant components, i.e. leaves and stems where it will be mentioned that ratio of salvinorin C to salvinorin A is higher in case of mature leaves and stems as compared to young leaves. Out of these salvinorins, only one active diterpene, i.e. salvinorin-A, is reported and considered as one of the most powerful naturally occurring hallucinogen.

In general, leaves of *Salvia* species are smoked or chewed for long periods or even brewed in tea. The mind gets hallucinated at an intense level, describing the plant’s caretaker or the wise man/women’s practical knowledge, after the prayer gets over (Ford et al., 2011). Some of the countries like Denmark, Ireland, Italy, Japan, Armenia, Latvia, Lithuania, Philippines, Romania, Portugal, Poland, Singapore, Switzerland etc. prohibit the funding or proliferation of *Salvia divinorum*.

Salvinorin A, active part of *Salvia divinorum*, inhibits intestinal motility, and it may occur due to the activation of kappa-opioid receptors (KORs) (Grilli et al., 2009). In contrast, this compound directly targets other than KORs in the inflamed gut (González et al., 2006). Normally, intestinal inflammation mainly upregulates cannabinoid receptors along with endogenous cannabinoids. As per the literature, curanderos may use *S. Divinorum* leaves of cure or recover from several ailments among the Mazatec people (Hofmann, 1990). Usage of these leaves at a low concentration may be applied and cure all ailments, i.e. headaches, arthritis, anaemia, digestive problems diarrhoea etc.

Similarly, consumption of these leaves at higher doses to treat alcoholism. Besides, several reports were reported related to Salvia and used successfully to treat depression in patients that we’re unable to find relief from standard treatments and antidepressant drugs [6]. In contrast, consumption of Salvia may also lead to changes in the brain structure and showed mental health issues, i.e. psychosis, depression, etc. due to consumption. It may also damage other organ systems (lungs, liver, and kidneys) as well (Sheffler and Roth, 2003). Generally, the effect of *Salvia* after consumption may reach their peak or showed side effects after 5 to 25 minutes and mainly depended on the method of ingestion and how much quantity should be used (Steru et al., 1985). According to the US survey (Substance Abuse and Mental Health Services Administration, SAMHSA) published in the year 2008 and reported approximately 1.8 million people (ages 12 and older) consumed Salvia at least once in their lifetime (Rubino et al., 2008).

Similarly, another survey conducted in the US by Monitoring the Future (MTF) in the year 2012 and reported students of different age groups (about 1.4 per cent population, 8th-grade students; 2.5 per cent, 10th-grade students, and 4.4 per cent, 12th-grade students) consumed Salvia at least once in the earlier year. One of the studies conducted where it will be mentioned that salvinorin A mainly attached with specific opioid neurons, i.e. kappa opioid receptors and is mainly known for inducing the euphoria and is generally associated with particular narcotic drugs (i.e. heroin or morphine) (Roth et al., 2002). In short, plants can produce a variety of chemical compounds called secondary metabolites (Pfeiffer et al., 1986). So, these metabolites mainly protect against pathogens and can cut the effect of radiation. Generally, chemical compounds extracted from plants (Ukai et al., 2002) which may react with human bodies in a specific way, i.e. organ failure/death to reactions which may inspire a synthesis of lifesaving pharmaceuticals (Zhang et al., 2005) finally. Various plants (Figure 1), i.e. Opium poppy (*Papaver somniferum*), Peyote (*Lophophora williamsii*), Cannabis (*Cannabis sativa*), Ayahuasca (*Banisteriopsis caapi*), Betel nut (*Areca catechu*), Tobacco (*Nicotiana tabacum*), Jimsonweed (*Datura stramonium*) and Coca (*Erythroxylum coca*) were reported which may affect the brains and mental states of the humans who ingest them (Yadav et al., 2015).

**CONCLUSION**

Psychosis is linked with mental illness because an individual loses its control over themselves. an individual is reported with long term or short term effect on the human brain. No such cure is still reported but is treated with antidepressant drugs and some natural remedies. We here mainly talked about the natural psychosis inducers which are developed by the plants for their protection which we call secondary metabolites, and these secondary metabolites affect the human brain in such a way that an individual loses its senses. *Salvia* is the natural psychosis inducer which is native to Mexico. More botanical information is required for a better understanding of this species as the use of *Salvia divinorum* is increasing worldwide. There is no harmful effect seen in humans of its use, but before large scale use for the human benefit, its toxicology must be well studied.

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Figure 1: Plants inducing psychosis

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Conflict of Interest

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