

The Potential of *Psilocybe* Genus Fungi to Treat Depression and Some Addictions

VLAIC Vanessa Eveline*, Andreea ONA

University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca,
Faculty of Agriculture, Department of Crop Science,
3-5 Calea Mănăştur, 400372, Cluj-Napoca, Romania

*Correspondence: vanessa-eveline.vlaic@student.usamvcluj.ro

Abstract: The therapeutic use of the substance psilocin produced by the fungi from the genus named *Psilocybe* has been an interesting but also controversial topic of discussion among researchers since the 1950s until now. These fungi can synthesize several alkaloids such as psilocybin, which has hallucinogenic properties, but also muscarine, which is a toxic substance that stimulates that part of the nervous system called parasympathetic. The use of psilocybin in therapy has been spreading for several decades from America, spreading all over the western world. For the first time, the substance was isolated from a species called *Psilocybe mexicana* mushroom, but then more than 30 such species were discovered. Psilocybin mushrooms were used by the Aztec shamans in healing, religious and divinatory rituals, but also by the Mesoamerican populations. This natural organic compound is derived from the substance dimethyltryptamine phosphate which is known to be a brain stimulant, and which is found in more than 200 species of mushrooms of the *Psilocybe* genus. The liver breaks down psilocybin through the phosphorylation process resulting in psilocin, the substance that causes the psychoactive effect. Because the substance is used for relaxing the nervous system, its introduction into medicine and psychotherapy has brought great controversies until now.

Keywords: alkaloids, hallucinogenic, psychoactive effect, *Psilocybe* genus, psilocybin, therapy.

Introduction

Since the 1950s until now, the therapeutic use of the substance psilocin produced by the fungi of the genus *Psilocybe* has been an interesting but also contentious topic of debate among researchers (Van Court, 2022).

Psilocybe genus is spread all over the globe and is part of the

family Hymenogastraceae. These fungus are capable of producing a variety of alkaloids, including psilocybin, which has psychedelic effects, as well as muscarine, a poisonous chemical that activates the parasympathetic nervous system (Kosentka et al., 2013). The compound was initially discovered in a species of mushroom known as *Psilocybe mexicana*, but more than 30 other similar species have since been identified (Ohenoja et al., 1987). Fungi form small fruiting bodies that look like the perfect picture of a small, brown mushroom. The colour of the mushrooms can have shades of yellow to brownish yellow, and their spores are easily recognized by their purple to blue colour (Yachaj, 2003). However, their appearance varies from one species to another, but most of them show the warning colour that denotes the fact that they are species with hallucinogenic substances, such as the appearance of a blue colour when the spore-producing part of fungi is broken or the appearance of a blue discolouration at the base of the mushroom stem. Like the substance lysergic acid diethylamide (LSD), mushrooms' effects are similar to mescaline but have a shorter duration (Rosalind, 2016). There are also known individuals belonging to this genus that does not have a lethal or toxic effect on the body, but some poisonous species such as *Conocybe*, *Galerina*, and *Inocybe* have also been identified and the similarity between them is very high. These fungi grow best and are often found on substrates consisting of soil, moss, dung or even wood (Paul, 1996). The substance produced by these mushrooms was also used to reduce the symptoms of people addicted to alcohol and other addictions, anxiety, depression, migraines, post-traumatic stress disorder, and many other conditions, unfortunately, there are still no sufficient scientific researches that proof its efficiency (<https://www.webmd.com/vitamins/ai/ingredientmono1654/psilocybin>). Among all the elements that have an action on the brain, psilocybin is among the safest variants (Hendricks et al., 2015). Therefore, the current work aims to review the beneficial effects that this substance can have on some types of addictions, but also on depression, one of the biggest problems that humanity is facing today.

Chemical structure and synthetic production of psilocybin

5-HT receptor or hydroxy tryptamine or serotonin is a monoamine neurotransmitter mediated by at least 13 different G

proteins from the de A family. They act through the receptor membrane in the central part of the nervous system and in its peripheral part, but also in non-neuronal tissues such as blood, endocrine or cardiovascular. The structure of serotonin and psilocybin is very similar and for this reason, the action of psilocybin is dependent on 5-HT receptors and has the greatest affinity with them (figure 1) (Carhart-Harris et al., 2012; Carhart-Harris et al., 2016).

Depending on the density of receptors located in the brain area responsible for emotional and cognitive processes, the action of psilocybin can be influenced, and its action can vary. What is even more important is the fact that constant negative states can influence the emergence of psilocybin addiction. Swendsen et al. (2000) observed this phenomenon in patients suffering from depression.

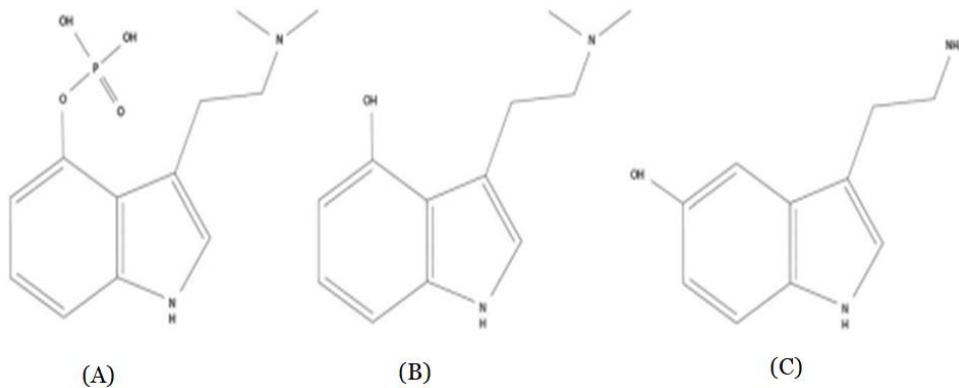


Figure 1. The chemical structure of psilocybin (A), psilocin (B), and serotonin (C) (After Stebelska, 2013)

Because the very high demand has increased a lot in recent years for experiments and different research, the market has increased a lot and the synthesis of this substance must be done differently than the extraction directly from the fungi (Fricke et al., 2020). After several researches, it was concluded that it can be synthesized at low cost even from glucose or other fungi such as *Aspergillus nidulans* that have a much faster growth and development (Fricke et al., 2017). *Saccharomyces cerevisiae*, the well-known yeast, is an element from which psilocybin and certain compounds such as tryptophan can be extracted and synthesized (Borodina and Nielsen, 2014).

Psilocybin therapy for depression

Depression is a disease that is known to the majority of the population and also the most common condition around the world and the intensity of the symptoms is influenced by age, gender, or nationality (World Health Organization, 2017). Some of the symptoms of this disease that affects from the youngest to the oldest are fatigue, a constant feeling of upset, nervousness, irritability, frustration, concentration problems, anxiety and restlessness, unexplained body pains or constant headaches and many others (Chand and Arif, 2022). Among other medicinal treatments, psilocybin can be one of the new therapeutic methods. These, because they are metabolized into psilocin after ingestion, must be taken as a prodrug (Brown et al., 2017). Following some studies conducted, psilocybin does not present a substance with high risks of addiction or serious adverse reactions, but its consumption for therapeutic purposes is indicated to be done under the observation of a doctor (Barrett et al., 2018). However, some limitations must be overcome before it can be established as part of psychiatric treatment. These boundaries include the global history and the negative overview of psychedelic substances, predominantly in the United States, due to challenges with federal regulations (Johnson et al., 2017). On the contrary, other countries, from example in Jamaica, these mushrooms can be used, consumed and decriminalized, and there is developing a budding medical psychedelic tourism industry (Lowe, 2021).

Psilocybin therapy for tobacco and alcohol addiction

As is already known, addiction to tobacco and alcohol-based drinks has a very high degree of spread throughout the globe. The mortality rate from these factors is huge, after a lot of research in this field, it was concluded that approximately 400,000 people die from excess alcohol consumption and approximately 100,000 from cigarette consumption, implicitly tobacco, every year (Miller and Mark, 1998). The combination of the two substances is the key factor in treating or reducing their use. These being correlated, the researchers found out that those individuals who smoke are much more susceptible to having problems with excessive alcohol consumption and vice versa (<https://pubs.niaaa.nih.gov/publications/aa71/aa71.htm>). As is already known, smoking does not mean only the consumption of tobacco; cigarettes have a high content of other substances harmful to the body. The most important

element is nicotine, which, after a multitude of studies, is the factor that creates addiction. Nicotine has a short-term action on the brain of mammals, that's why smokers feel the need to consume this substance at very short intervals (Swan and Lessov-Schlaggar, 2007). After some research, it was demonstrated that alcohol addiction is a combination of the genome of each individual and the biotic and abiotic factors in the environment, the most important of which is the excessive consumption of tobacco. Most of the diseases caused by excessive alcohol consumption appear in the brain, more precisely in the frontal lobe and in the vicinity of the cerebellum. Some consequences of using this substance are behavioural, emotional, and sometimes cognitive problems (Oscar-Berman and Marinković, 2007).

Researchers have discovered the effect that psilocybin has on alcohol addiction, and this is based on the 5-HT receptor therapies with these mushrooms that could improve or even treat this very common addiction in the future (Bogenschutz et al., 2015). Considering that these two substances are correlated, in the case of tobacco addiction, the 5-HT receptor present in the chemical composition of psilocybin is the one that can be used to treat psychological addiction. Since the 1950s, researchers have made these connections between tobacco addiction and its treatment with the help of substances that have a psychedelic effect on the brain of mammals (Johnson, 2022). Having already been demonstrated by researchers, the mechanism by which this substance can intervene and improve alcohol and tobacco addiction is a simple and easy-to-understand one correlated with the 5-HT receptor; the psilocybin molecule is very similar to the hormone serotonin, thus replacing the pleasure of smoking and consuming alcohol with the consumption of psilocybin, the effect is the same but without resulting in a dependence on this substance (Michael and Ben, 2019; Rush, 2022).

Conclusions

Psychedelic-assisted therapies may provide new vital occasions to current issues in the controversial treatment of psychiatric disorders. This may be feasible, toxicologically safe, psychologically well-endured, and may have enormous potential in medicine. It is also necessary to research whether psilocybin interacts with other medications that cause hallucinations in the brain or not. Based on the results of these studies, very powerful drugs based on psilocybin may be created.

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