Breaking the mental shackles - The magic mushroom way

By

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DECLARATION

I, Alby John (2018-11-022), hereby declare that the seminar report entitled **'Breaking the mental shackles - The magic mushroom way'**, has been completed by me independently after going through the reference cited herein and I have not copied from any of the fellow students or previous seminar reports.

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Certified that the seminar report entitled **'Breaking the mental shackles - The magic mushroom way'** for the course Pl. Path. 591 has been prepared by Alby John (2018-11-022), after going through various references cited herein under my guidance, and she has not copied or borrowed from any of her fellow students.

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1. Introduction

Man's interest in fungi started with the observation of beautiful umbrella shaped mushrooms or toad stools appearing on the ground. Mushrooms are the fleshy spore bearing fruiting bodies of a fungus growing above ground on soil or on other substrates. Generally, the edible one are called mushrooms and the poisonous type toadstools. From the prehistoric time onwards mushrooms have an inevitable role in human's life. Our ancestors were fascinated by their characters. Based on the human use generally mushrooms can be classified as edible, toxic, hallucinogenic, medicinal and other uses. Hallucinogenic mushrooms (also called psychotropic fungi) are a very special category of poisonous mushrooms, which in tolerable doses aren't discomforting (Singer, 1978). These can become poisonous in case of an overdose and even death may cause by the presence of additional poisonous substance present in the fungus, together with hallucinogenic alkaloids. It acts on the central nervous system which results in alteration of normal functioning of brain i.e., there will be distortion to the sensation and vision. Magic mushrooms are hallucinogenic mushrooms. They are wild or cultivated mushrooms that contain psilocybin, a naturally occurring psychoactive and hallucinogenic compound. Psilocybin is the active principle. It can cause hallucination or psilocybin syndrome which means they can cause you to see, hear and feel sensations that seem real but aren't. (Hartney, 2019). They are also known as psychedelics, shrooms, liberty cap, sacred mushroom, teonanacatl (God Fungus). The term Psychedelics is derived from the Greek word '*Psyche'* meaning mind and '*Deloun'* to reveal i.e., mushrooms which helps in mind revealing.

2. Tripping through time: The fascinating history

Magic mushrooms have been used since prehistoric times all over the world. This mind enhancing sacraments were used by cultures widely separated by time and space and have influenced religions and philosophies of the world. Mushroom stones and motifs were discovered from Mexico and Guatemala region of Central America. These are estimated to be of age 1000-500 B.C. i.e., Mayan civilization period. This excavations of Mayan temple ruins strongly underscores the important cultural role played by these mushrooms. Our present day understanding of the historical use of psilocybin mushrooms largely arises from the works of ancient ethnomycologists.

On June 29, 1995 R Gordon Wasson (vice president of the prestigious banking firm J.P Morgan) together with his friend Allan Richardson (New York fashion photographer) made history by becoming the first whites to participate in a mushroom velada. The nocturnal mushroom ceremony took place in a remote village in the North east region of Oaxaca, Mexico under the guidance of Maria Sabina who is known as the **Saint Mother of the Sacred Mushrooms**. On May 13, 1957 Wasson published an article about these psychoactive mushrooms "Seeking the Magic Mushroom" in Life magazine which gave the first popular media coverage of their existence. Wasson gave a well clear picture about the use of psilocybin mushrooms in shamanic ceremonies by indigenous Mesoamerican people and their personal experience after uptake of these mushrooms. During these exploration studies about hallucinogenic mushrooms, Wasson was accompanied by Prof. Roger Heim (one among the world's leading mycologist and director head of France national museum of natural history). Heim made water color paintings of the psilocybes they explored during their trip and it was accurate enough for field identifications.

Heim and Wasson collected and identified various species of family Strophariaceae and genus *Psilocybe*. They would supply these mushrooms to several chemical laboratories for analysis. On 1958, Albert Hofman at Sandoz laboratories in Basle, Switzerland isolated and characterized the compound psilocybin from the Central American mushroom *Psilocybe Mexicana* (Erowid, 1995).

So, Wasson and his colleagues can be considered as first generation of ethnomycologists. They not only studied the ethnographic origins of mushroom rituals, but also used these mushrooms and had personal knowledge of their power. They laid a foundation stone for the further studies and research on magic mushrooms.

3. Magic (Psilocybin) mushrooms

Mushrooms containing psilocybin mainly belong to families

1. Strophariaceae (Eg: *Psilocybe*)
2. Bolbitiaceae (Eg: *Conocybe*)
3. Cortinariaceae (Eg: *Galerina*)
4. Coprinaceae (Eg: *Panaeolus*)

Among these *Psilocybe* sp. are the most diverse and those with the widest geographical distribution (Singer, 1978).

Classification of *Psilocybe* spp. (Kirk *et al*., 2008)

Kingdom : Fungi

Phylum : Basidiomycota

Class : Agaricomycetes

Order : Agaricales

Family : Strophariaceae

Genus : *Psilocybe*

World distribution of *Psilocybe* mushrooms

Psilocybe are the most important in ethnomycology. They probably were used in many ethnic groups in the world. More than 150 species of *Psilocybe* are reported throughout the world (Guzman et al., 2005). However, Mexico is the country with the highest no. of species i.e. more than 55, while Europe has only 16 and US & Canada 22. In Latin America, excluding Mexico, there are around 50 sp. Africa has only 4 sp. In Asia and Australia there are 15 sp. It is clear that, tropics and sub tropics in the world have majority of the species with more than 100 in comparison with temperate regions which have around 40 species. Another important observation is that the majority were found in hygrophytic or mesophytic forests, also known as subtropical cloud forests and grew in humid mountains at 900-

1400 m altitude close to the sea. In Mexico it was observed that more than 90 percent of the known species are in this kind of vegetation.

Table. 1. World distribution of *Psilocybe* mushrooms

Countries	**No. of species**
Mexico	55
Latin American	50
U S and Canada	22
Europe	16
Asia	15
Australia	15
Africa	4

Characteristics of *Psilocybe*

All the Psilocybes and other psilocybin producing mushrooms are saprophytes, so that they can exploit a broad range of ecological niches and hence are geographically widely distributed. They are found in a wide range of habitats like dung deposits, mosslands, grasslands and decaying wood debris. They are hygrophanous in nature i.e. fading of the mushroom color upon drying. Bluing reaction is a common feature to many of the psilocybe mushrooms, i.e. the mushrooms will turn bluish or bluish green when they are bruised. This happens as a normal response to growing conditions or while they are handled as they are picked. Spore print of the mushroom is purplish brown to black in color. Besides the spore print and bluing reaction, the most representative character is the presence of a separable gelatinous pellicle (Stamets, 1996).

Important Psilocybes

a) *Psilocybe azurescens* (flying saucer mushroom)

It occurs naturally along a small area of the west coast of the United States. Pileus is conic to convex expanding to broadly convex and eventually flattening with age with a pronounced persistent broad

umbo. Surface is smooth, viscid when moist, covered by a separable gelatinous pellicle. It is chestnut brown to caramel in color. Gills attachment is sinuate (smoothly notched and running briefly down the stem) to adnate (attached widely to stem). Stipe is silky white, brown from base and hollow at maturity. Extremely bitter in taste. Generally found on deciduous wood chips or in sandy soils rich in lignicolous debris.

b) *Psilocybe Cubensis* (golden tops)

It is distributed throughout the tropical and subtropical environment. Pileus is conic-companulate often with an acute umbo at first, becoming convex and finally plane in age without any umbo. Reddish cinnamon brown in young fruiting bodies, becoming lighter with age to more golden brown. Gills attachment is adnate to adnexed (gills attachment narrowly to stem). Stipe is white in color having a persistent annulus. It is a coprophilic fungus which prefers to grow on humid grasslands and having a farinaceous taste (freshly ground flour).

c) *Psilocybe cyanescens* (Wavy capped)

It is chestnut brown in young stage and becomes caramel colored with age. Pileus is conic convex at first soon expanding to broadly convex to nearly plane in age with a wavy margin. Gills attachment is adnate to subdecurrent (gills running briefly down stem). Stem is whitish smooth and hairy. Bitter in taste and found in wood chips, saw dust and fields rich with rotting wood.

d) *Psilocybe semilanceata* (Liberty cap)

The mushroom get its common name from its resemblance to the phyrgian cap, also known as the liberty cap because of its resemblance with the cap worn by people in the Eastern Europe during the French revolution to signify freedom. Pileus is conic to companulate with an acute umbo. Gills attachment is adnexed. Stipe is slender and flexuous. Farinaceous taste and commonly found around cool temperate and artic regions of northern hemisphere.

Plate.1. Important Psilocybes

Psilocybe cubensis

Psilocybe cyanescens

Psilocybe semilanceata

Psilocybe azurescens

4. Cultivation of *Psilocybe* spp.

Commonly adopted technique for the cultivation of *Psilocybe* spp is PF TEK (Psilocybe Fanaticus Technique) developed by Mc Pherson (Fanaticus, 1991). Main steps involved are

1. Substrate Preparation
2. Sterilization
3. Inoculation
4. Incubation
5. Fruiting and harvesting (Nicholas and Ogame, 2006)

1. **Substrate Preparation**

Materials required in this step are vermiculite, brown rice flour, jars, spoon, strainer and water. Pour water slowly over the vermiculite (140g per jar of 250 ml size) while stirring with a spoon. Stir it well so that all the vermiculite is uniformly soaked with water. If there is too much water in the bowl, pour the wet vermiculite in a strainer and let the excess water drain for a minute. Put the required amount of brown rice flour (40 g per jar of 250ml size) into the wet vermiculite and mix it with a spoon. The goal is to uniformly coat the wet vermiculite particles with a layer of brown rice flour. Fill the mixture in jars. It is very important to fill the substrate in the jars without tapping it down at all. It should stay very airy and loose to provide optimum conditions for the growth of the mycelium. Fill up the jars with dry vermiculite to the top. This layer hinders air borne contaminants reaching the underlying substrate during the inoculation and incubation. Take a wide strip of aluminium foil and wrap them tightly over the mouth of the jar. Loosely screw lids onto the jars, taking care not to tear the foil below. The use of lids in the PF Tek is optional, but does provide an additional layer of protection.

2. **Sterilization**

Load the jars into pressure cooker, along with the appropriate amount of water, and sterilize the jars at 15 psi for 45 minutes on a medium flame. If the cooker get heat up too fast this cause the jar to crack. After 45 minutes take the cooker from the flame and cool for at least five hours.

3. **Inoculation**

Materials required: Spore syringe, alcohol lamp, sterilized jar containing substrates.

When the jars have cooled to room temperature, place them onto a clean surface, along with the spore-water syringe and alcohol lamp. Remove the lids, and loosen the top layer of foil. Remove the cover from the syringe, wipe the needle with an alcohol moistened cotton ball and then hold the tip of the needle in the flame of the lamp until it just begins to glow red (be careful to keep the plastic end of the needle away from the flame, and be sure to exercise caution when using alcohol near an open flame.) Allow it cool for a few seconds before using. Working one jar at a time, remove the top layer of foil, shake the syringe gently to disperse the spore solution, and inject a small amount into the jar at four equally spaced points just inside the inner rim. Insert the needle 1 inch (2 cm) into the jar so that its point is past the dry vermiculite layer, and then squeeze out a few drops. We should be able to see the solution run down the sides of the jar. Repeat at the other three points. Each jar should get a total of 1 - 1.5 ml of solution. So one 10 ml syringe is sufficient for 6-10 jars. Inject all of the jars in the same

way, and then replace the top layer of foil and lid on each of them. Mark the outside of the jars with relevant information (inoculation date and the species or strain information) and place in a clean, warm spot to incubate.

Preparation of spore syringe: Place 25 ml water in a jar fitted with a filter disc and lid, along with 2 drops of dishwasher rinse agent (to prevent spores from clumping and sticking to the sides of the jar and syringe). Seal and sterilize for 30 minutes at 15 psi. Allow to cool completely before using. To guarantee sterility, this method is best performed in front of laminar air flow. Wipe the work area well with alcohol. Light the alcohol lamp, and heat the inoculation loop until red hot. Unscrew the lid, lift it slightly from the jar, then cool the loop in the sterile water. Replace the lid loosely on the flask and then use the loop to pick up some spores from the print. Lift the lid, swirl the loop in the water, and then replace the lid. Repeat once or twice for good measure. Individual spores are minute, we won't necessarily be able to see them in the water. Draw some spore suspension into the syringe, gently filling and emptying the syringe two or three times to ensure an even distribution of spores. Replace the needle cover, label the syringe with the strain and date, and place it in a clean Ziploc bag until needed. Syringes prepared in this way can be stored in the refrigerator for a month or two, but are best if used as soon as possible.

4. Incubation

The jars should be stored at 75-85^0 F (24-29^0 C). If the temperature is consistently within this range, then simply storing them in a clean box should be sufficient. If not, an incubator box will ensure healthy and rapid growth. Within a week we will begin to see the first signs of spore germination in the jars. Tiny pinpoints of bright white fuzzy growth can be seen usually near the base of the jar directly below the injection points. In time, these tiny colonies will radiate outward to form individual spheres of mycelium. In 10 days to a few weeks, the spheres inside each jar will join one another, and the jar will be fully colonized. Depending on the temperature and viability of the spore syringe it takes 14-28 days for the mycelium to colonize the whole jar.

5. Fruiting and harvesting

Once the jars are completely colonized, they are ready to be fruited. At this point we will remove the lids and foil, moisten the top layer of vermiculite and place the jars below a light source, either artificial light provided by a dedicated fluorescent "grow" light or a brightly lit window. Because *P. cubensis* requires light to stimulate fruiting, and we want to limit fruiting to the upper surface of the cakes, you need to somehow restrict light exposure to only that area of the jars. You can do this in a number of ways, such as wrapping the jars in aluminum foil or strips of thick, opaque paper. One simple method we have used is to place the jars inside short pieces of cardboard tubing, like the type used to store posters, cut to come just above the rim.

Preparing the Jars for Fruiting

Remove the lids and foil from each jar. Wipe a clean fork with some alcohol, allow it to evaporate, and then gently scrape (not scrape off) the dry vermiculite layer all the way down to the top of the cake below, to break up and evenly distribute the mycelial fragments within. Take a spray mister of clean water and mist the vermiculite until it is saturated (it will darken slightly in color; as soon as we can see free flowing water, that is enough.) Repeat with each jar, cleaning the fork each time to avoid inadvertently spreading contaminants. When all of the jars are ready, place them in individual cardboard tubes inside an enclosed container, such as a large clear plastic bag (cut or punch several holes in it to provide some gas exchange) or a clear plastic storage tub. If you are using a fluorescent grow light, set your timer to an 8-hour on / 16 hour off cycle; otherwise, simply locate the jars in a well-lit area, such as near a sunny window. The ideal temperature of your growing area should be in the 65-75°F (18-24^0 C) range, slightly lower than that required during colonization. Mist the casing lightly once or twice each day to replace any water lost to evaporation. In a few days to two weeks you should see primordia begin to form. Most likely, they will form inside the casing layer and will not be visible until they are already well-formed miniature mushrooms. Once they have achieved this size, they tend to grow astoundingly fast, and can seem to reach full size almost overnight. As they grow, they will draw water from the cake and the casing layer, so be sure to increase misting as needed to keep the vermiculite saturated, always taking care not to over water.

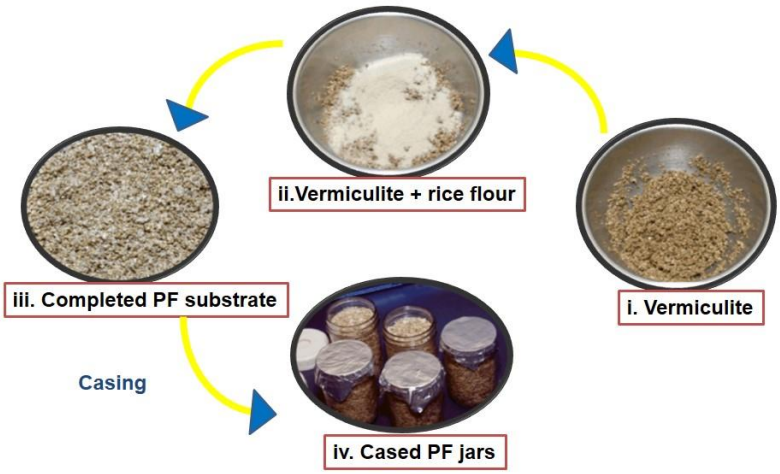
Harvesting

Once the mushroom has reached an appropriate size for efficient spore dispersal, it ceases growing and its cap widens to expose its spore-producing gills to the atmosphere. The best time to harvest the

mushrooms is just prior to this point i.e. when the cap is completely inrolled and the partial veil is hidden. Ideally, you have to pick your mushrooms as soon as the partial veil is visible, or at the latest, before it begins to break. Usually, a fair amount of vermiculite will be stuck to the base of the harvested mushrooms, leaving behind a divot in the casing layer. Once you are done harvesting, simply fill these holes with fresh vermiculite, mist the casing thoroughly and return the jars to their fruiting area. During the period immediately following a harvest, increase misting frequency significantly, in order to replace the substantial amount of moisture removed from the cakes. Each jar should produce three to five crops, or flushes, of mushrooms, with about a week of recovery time between each harvest. During the later flushes, when the nutrients of the substrate are substantially depleted, the cakes will shrink. After the fourth or fifth flush, the jars will be pretty much fully depleted, and the number of mushrooms that form will be minimal. At this point, the cakes should be discarded, since the mycelium in them will begin to die and will eventually rot, becoming a vector for contamination.

Plate. 2. Cultivation of *Psilocybe* spp.

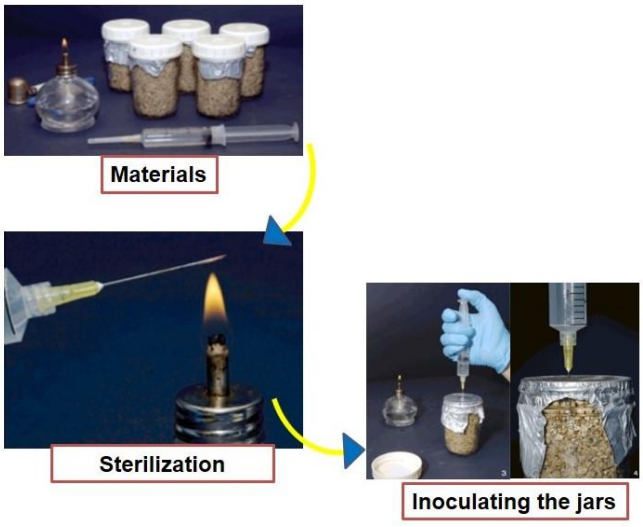
1. Substrate preparation



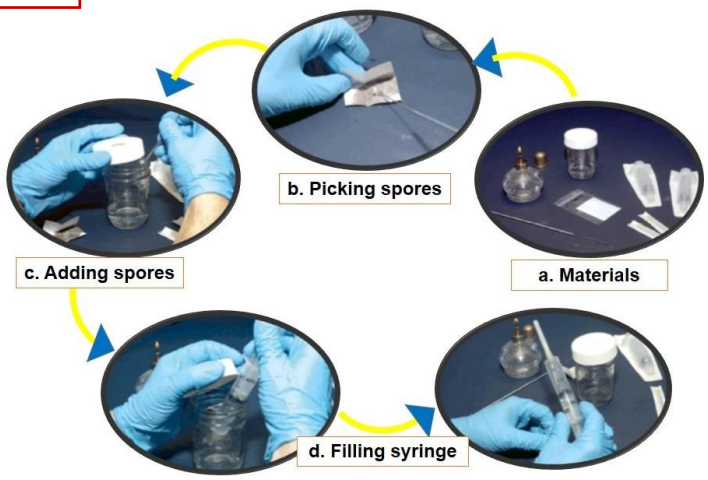
2. Sterilization

Sterilization - 15 psi for 45 min

3. Inoculation



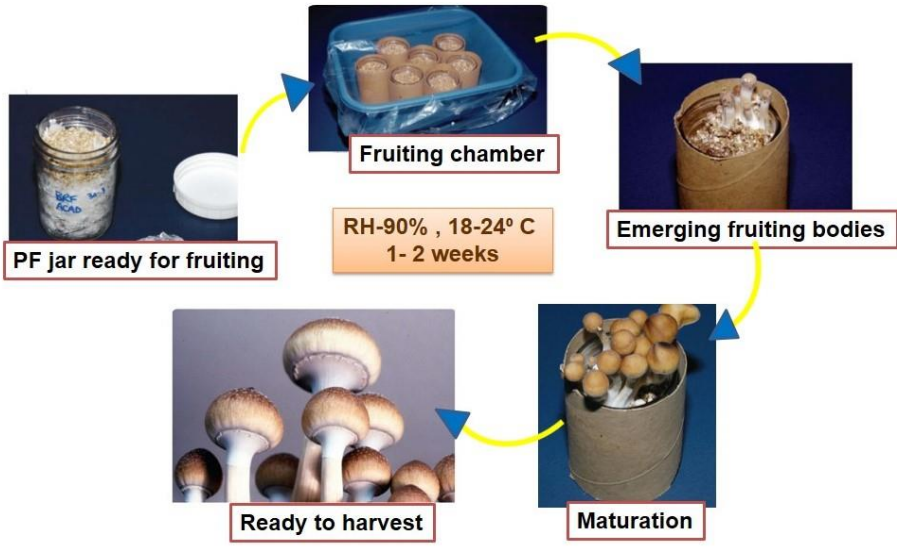
Spore syringe preparation



4. Incubation

Spore germination (within a week) | Colonization (After 10 days) | Fully colonized PF jar (14-28 days)

5. Fruiting and harvesting



5. Chemistry behind *Psilocybe* spp.

Chemical Characters

Psilocybin is the active principle or the major psychoactive agent in magic mushrooms. Chemical structure of psilocybin is N,N – dimethyl - 4 – Phosphoryloxytryptamine. Inside the body psilocybin get dephosphorylated to psilocin which is pharmacologically active. This psilocybin and psilocin are indole tryptamine derivatives. i.e. these compounds are closely related to the common amino acid L-tryptophan which is an indole derivative and precursor of the neurotransmitter serotonin. In nature the psilocin often occurs in small amounts along with psilocybin. In some species such as *P. baeocystis* and *P. semilanceata* two other substances are also known to occur baeocystin and norbaeocystin. Psilocybin and psilocin in their pure forms are white crystalline powder. Both drugs are unstable in light and their stability at low temperatures in the dark under an inert atmosphere is very good (Tyls *et al*., 2014). Psilocin is more lipid soluble than psilocybin and readily crosses the blood brain barrier. Psilocybin is heat stable and water soluble. So steeping dried mushrooms in boiling water to make a decoction or tea is a common way to extract these drugs.

What magic mushrooms do to our brain?

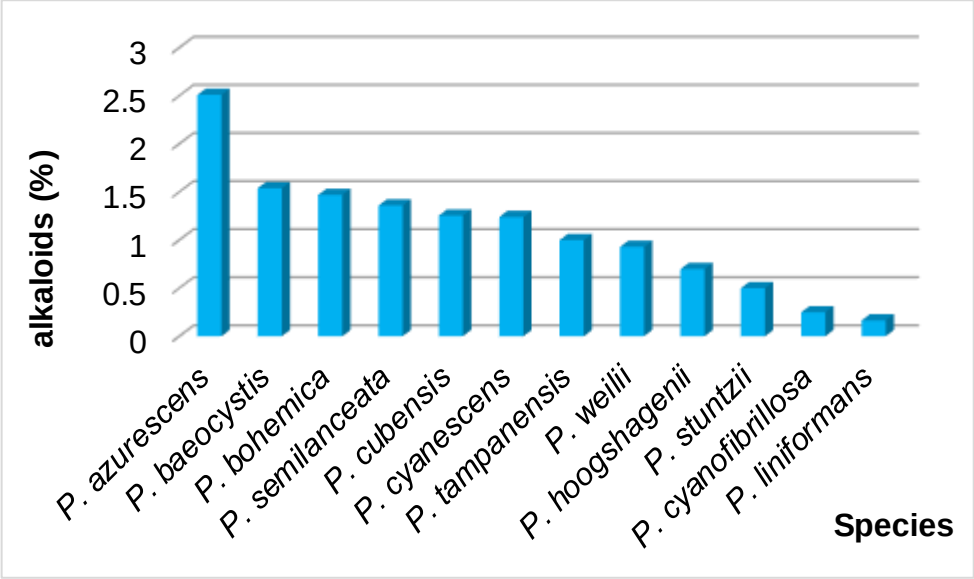
When we consume a psychoactive (magic) mushroom psilocybin breaks down in our stomach and psilocin is what does the magic. Psilocin is more lipid soluble than psilocybin and it readily crosses the blood brain barrier. Because of its structural similarities to serotonin, psilocin exerts its effect on the CNS (Central Nervous System) by stimulation of the serotonin receptors. Serotonin chemically 5 – hydroxy tryptamine or 5- HT is an important neurotransmitter in the human body. It is mainly found in our intestine and CNS (brain and platelets). It helps to regulate our mood, behavior, appetite, digestion, sleep etc. There are different serotonin receptors in our body. Psilocin binds with the serotonin receptor 2A which are located within the thalamus and cortex region of our brain. This will lead to reduction in blood flow to the Default Mode Network (DMN). It is the region that is responsible for your thoughts of self, others, future, past and overthinking. The blood flow to that area was severely reduced and the brain was put down in a sort of sedated dream like state. Parallel to this decrease in blood flow there was also a decrease in neuronal activity within the DMN. The neurons of the DMN which have to perform are also in a deactivated state. But they should still need to process while we are under the effects of this substance. Our brain is pretty awesome, it has got this quality called neuroplasticity. Whenever a signal in our brain (an emotion or a thought) which normally runs

down a specific path isn't able for some reason to run down the same path (in this case DMN), our brain will automatically create new connections. It will create new connections or new junctions between neurons and we will find alternative ways to exchange information. The same information that DMN would normally process was now being processed through alternative paths and the overall communication of neurons within your brain was spectacularly enhanced. The interesting fact is that the areas of the brain separated from each other which don't normally cooperate to process information are now establishing new connections under the effects when the DMN was deactivated. There is a dramatic temporary reorganization of the communication and great enhancement in the neuronal activity, which finally results in hallucinogenic effect. The combination of these effects that make psilocybin so useful for combating depression and addiction. For example when new areas in the brain start talking to each other you might have new insights into old problems and that's why some experts describe tripping as a condensed version of talk therapy and dissolving ego (Carhart-Harris *et al.*, 2014)

Effect of psilocybin on consumption

Total duration of psilocybin activity in our body is 4-7 hrs. After ingesting psilocybin mushrooms, it will take 20-40 minutes to start feeling the effects. By then, psilocybin will have broken down into psilocin which acts on the serotonin receptors in the brain. The effects peak at about 60-90 minute. Then the effect will gradually decrease and the main effects disappear entirely within 6-8 hr. No more effects will be there after 24 hrs.

Fig.1. Concentration of alkaloids in *Psilocybe* spp.



Dosages of mushroom intake

Recommending a dosage for mushroom ingestion is complicated because of the great variability in the potency of mushrooms, both among different species and between the strains of the same species. In addition to the great variation in potency among different mushrooms, there is also a very real and often wide variation in individual sensitivity to psilocybin.

Table. 2. Dosages of mushroom intake

Species	Alkaloids (%)	Low Dose (5-10 mg)		Medium Dose (12-25 mg)		High Dose (30-40 mg)	
		g/kg Body weight	g/ 80 kg male adult	g/kg Body weight	g/ 80 kg male adult	g/kg Body weight	g/ 80 kg male adult
P. azurescens	2.51	0.0045	0.36	0.011	0.9	0.214	1.8
P. bohemica	1.47	0.007	0.6	0.018	1.5	0.036	3
P. cubensis	1.25	0.006	0.7	0.0204	1.7	0.04	3.4
P. cyanescens	1.24	0.0125	1.0	0.03	2.5	0.06	5
P. cyanofibrillosa	0.25	0.05	4.0	0.012	10	0.24	20

The table given shows the recommended dosage by different *Psilocybe* species. This helps to figure out an amount in grams for each species at any one of three dose levels.

Symptom expression

Effects produced by psilocybin include

1. Sensory effects
2. Physical effects
3. Mental effects

1. Sensory effects

- Hallucinations – Seeing, hearing, touching or smelling things in a distorted way or perceiving things that don't exist
- Intensified feelings & sensory experiences – feeling brighter colors and sharper sounds
- Mixed senses – seeing sounds or hearing colors
- Perception of time – changes in sense of time

2. Physical effects

- Nausea
- Drowsiness
- Muscle weakness
- Head ache
- Rise in heart rate, blood pressure

3. Mental effects

- Euphoria – a feeling or state of immense excitement and happiness
- Panic reactions – sudden feel of intense fear or anxiety
- Nervousness
- Paranoia – believing that other people are trying to harm you
- Psychosis – it's a condition at which your thought and emotions are so impaired and contact is lost with external reality

Factors that hold psilocybin in our body

Time taken for eliminating the psilocybin from our body depends on factors like

- Age – people aged above 65 tend to have reduced blood flow to their kidney and liver which can delay the excretion of psilocybin
- Body mass – people with higher Body Mass Index (BMI) tend to excrete psilocybin faster than those with lower BMI
- Being active – psilocybin is excreted faster in active people with high metabolic rates

- Drinking water – water can speed up the excretion of psilocybin
- Liver and kidney function – having liver or kidney disease can slow down the time it takes for psilocybin to pass through the body (Buddy, 2019).

Psilocybin Vs caffeine

By knowing the powerful human psychological effects we might reasonably think whether the compounds found in these magic mushrooms might be in any way toxic to human health. In fact, there is no evidence to suggest that they are at all poisonous. First of all they are unlikely to be toxic because they have such a long history of human use without a single attributed death. In addition these molecules have been subjected many times to toxicological tests, which showed them to be not harmful. Psilocybin has an LD 50 of 280 mg/kg in rats, which means that you need to give the test animals 280 mg of psilocybin for every 1 kg body weight inorder to kill half of them. In case of an average 80 kg adult male, he need to ingest 22g of pure psilocybin or something like 500g of dried *Psilocybe cubensis* mushrooms, inorder to earn a 50 % chance of dying. While comparing it with caffeine, which is widely considered to be a benign human drug, has an LD 50 of 192 mg/kg making it around 1.5 times as toxic as psilocybin (Nicholas and Ogame, 2006).

6. Case studies

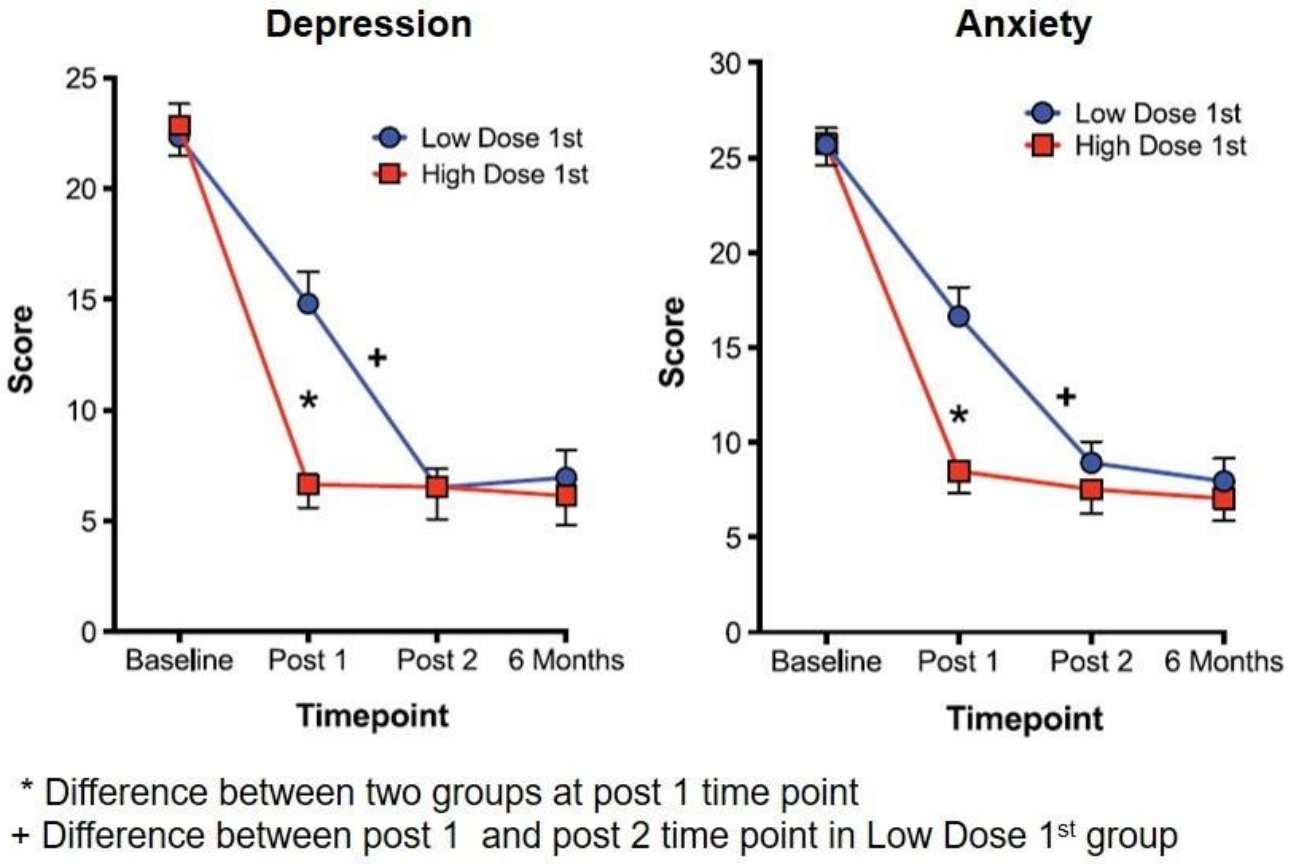
Case Study: 1

Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial (Griffiths *et al*., 2016)

Cancer patients often develop chronic, clinically significant symptoms of depression and anxiety. The effects of psilocybin were studied in 51 cancer patients with life-threatening diagnoses and symptoms of depression and/or anxiety. This randomized, double-blind, cross-over trial investigated the effects of a very low (placebo-like) dose (1 or 3 mg/70 kg) vs. a high dose (22 or 30 mg/70 kg) of psilocybin administered in counterbalanced sequence with 5 weeks between sessions and a 6-month follow-up. Instructions to participants and staff minimized expectancy effects. High-dose psilocybin produced large decreases in clinician- and self-rated measures of depressed mood and anxiety, along with increases in quality of life, life meaning, and optimism, and decreases in death anxiety. At 6-month

follow-up, these changes were sustained, with about 80% of participants continuing to show clinically significant decreases in depressed mood and anxiety.

Fig.2. Effect of psilocybin on depression and anxiety



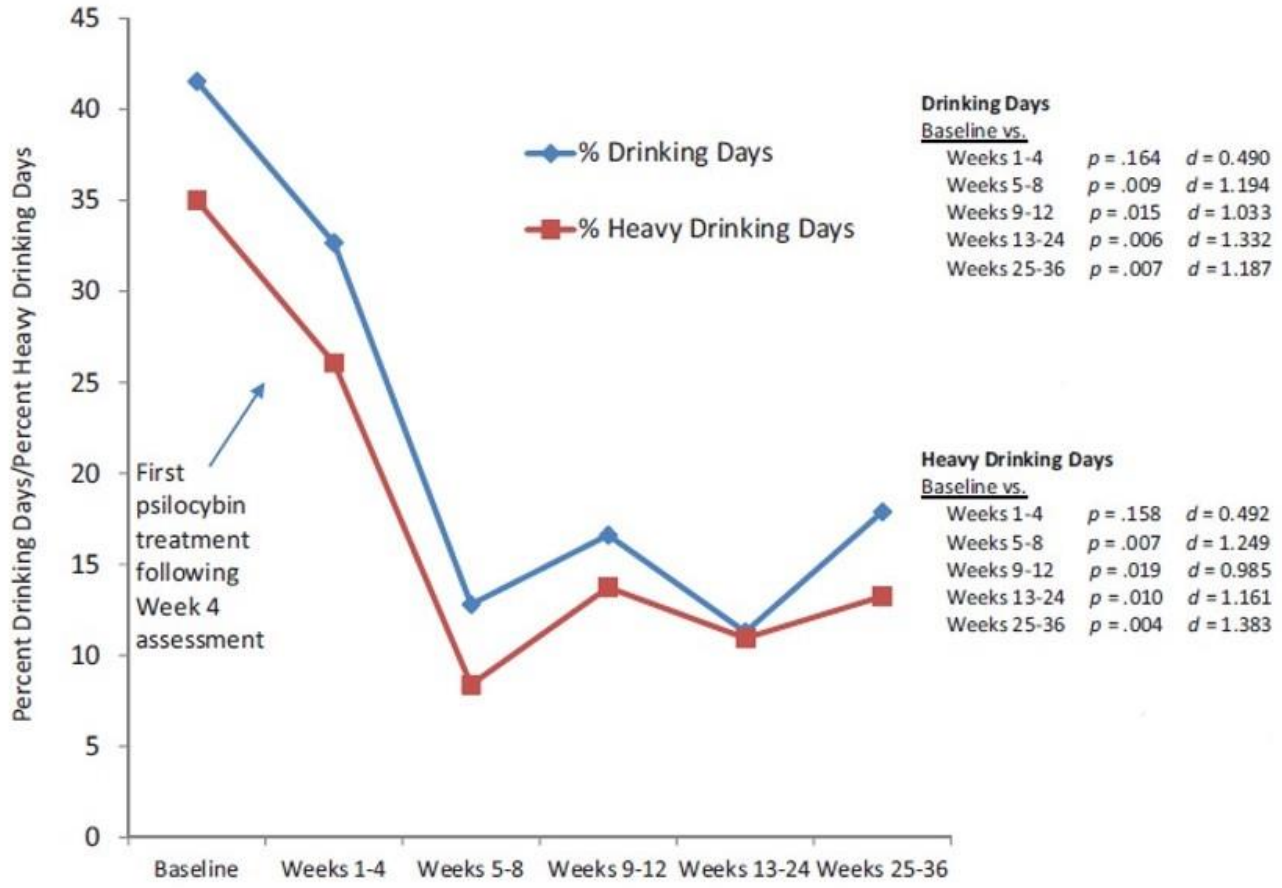
Case Study: 2

Psilocybin-assisted treatment for alcohol dependence: A proof-of-concept study (Bogenschutz *et al*., 2015)

A single group proof-of-concept study was conducted to quantify acute effects of psilocybin in alcohol-dependent participants and to provide preliminary outcome and safety data. Ten volunteers with DSM-IV alcohol dependence received orally administered psilocybin in one or two supervised sessions in addition to motivational enhancement therapy and therapy sessions devoted to preparation for and debriefing from the psilocybin sessions. Participant's responses to psilocybin were qualitatively similar to those described in other populations. Abstinence did not increase significantly in the first 4 weeks of treatment (when participants had not yet received psilocybin), but increased

significantly following psilocybin administration. Gains were largely maintained at follow-up to 36 weeks. The intensity of effects in the first psilocybin session (at week 4) strongly predicted change in drinking during weeks 5–8 and also predicted decreases in craving and increases in abstinence self-efficacy during week 5.

Fig.3. Psilocybin-assisted treatment for alcohol dependence



Case Study: 3

Pilot study of the 5-HT2AR agonist psilocybin in the treatment of tobacco addiction (Johnson *et al*., 2014)

To determine the safety and feasibility of psilocybin as an adjunct to tobacco smoking cessation treatment they conducted an open label pilot study administering moderate (20 mg/70 kg) and high (30 mg/70 kg) doses of psilocybin within a structured 15-week smoking cessation treatment protocol.

Participants were 15 psychiatrically healthy nicotine-dependent smokers (10 males; mean age of 51 years), with a mean of six previous lifetime quit attempts, and smoking a mean of 19 cigarettes per day for a mean of 31 years at intake. Biomarkers assessing smoking status, and self-report measures of smoking behavior demonstrated that 12 of 15 participants (80%) showed seven-day point prevalence abstinence at 6-month follow-up. After 6 months 80 % of them have kicked the habit and it was compared with the best smoking cessation drugs i.e abstinence rate of bupropion (24.9-26.3 %) and varenicline (33.5-35.2 %). These results highly promises the therapeutic potential of psilocybin.

7. Recent advancements

1. **John Hopkins University School of Medicine opens center for psychedelic and consciousness research (Sep, 2019)**

Johns Hopkins School of Medicine announced the launch of the Center for Psychedelic and Consciousness Research in Baltimore, Maryland. Funding for the center comes from $17 million given from private donors. One of the first studies the center is undertaking is evaluating the effects of psilocybin-assisted therapy on the eating disorder anorexia nervosa. This pilot study clinical trial is in the early stages with a targeted completion date in December 2022 (Bauer, 2019).

2. **Jamaica is home to the first magic mushroom research center (Oct, 2019)**

The center will be located on the campus of the University of the West Indies in Mona, Jamaica. It is funded by Field Trip Ventures of Toronto, Canada. Objective of the center is to study the genetics of magic mushrooms and develop methods for extracting the compounds from the mushrooms (Bauer, 2019).

3. **Engineering *E. coli* to produce psilocybin**

This is the first time psilocybin has been produced from a prokaryotic organism (Adams *et al.*, 2019). They achieved a 32-fold improvement in psilocybin titer (concentration), reaching 1.16 g/l. This is the highest psilocybin production titre achieved so far from a recombinant organism. The authors say this work is a significant step towards demonstrating the feasibility of industrial production of biologically-derived psilocybin.

8. Legal status

Since the Controlled Substance Act (CSA) of 1970, clinical studies using psychedelics ceased. Much of the research completed on these agents in the 1950s and 1960s was not taken seriously due to the small nature of the studies or methodology inconsistent with current research standards. However, interest in understanding the neuropsychiatric effects of these agents and their potential role in medical therapy persisted. Because of the CSA Schedule I status of these agents, clinical research in humans seemed unlikely and locating funding sources virtually impossible. In 1992, the National Institute on Drug Abuse worked with a Food and Drug Administration advisory committee that ultimately allowed for the resumption of research of psychedelic agents. The Heffter Research Institute, founded in 1993 by Nichols and colleagues, is the only institute solely dedicated to clinical research of the medicinal value of psychedelic agents such as psilocybin (Daniel and Haberman, 2017). In 2018, researchers from John Hopkins University recommended reclassification of the drug from Schedule I to Schedule IV in order to allow its use in medicine. In most of the countries the use of this psilocybin containing mushroom is illegal, table below shows the list of countries where these mushrooms doesn't have any legal barrier. In 2019, Denver became the first city in US to permit the use of magic mushrooms.

Table.3. Legal status of magic mushrooms

Country	Possesion	Sale	Transport	Cultivation
Austria	✓	×	×	✓
Bahamas	✓	✓	✓	✓
Brazil	✓	✓	✓	✓
Jamaica	✓	✓	✓	✓
Netherlands	✓	✓	✓	✓
Samoa	✓	✓	✓	✓
India	×	×	×	×

9. Future prospects

Detection of mode of action of alkaloids other than psilocybin i.e, baeocystin and norbaeocystin. Identifying the cause of bluing reaction in *Psilocybe* sp. Development of effective drugs for mental disorders after due research study and legal recognition of the medical use of psilocybin.

10. Conclusion

Man's quest for substances which provide ease of mind resulted in the discovery of magic mushrooms. Global health estimates revealed that people suffering from mental illness such as anxiety or depression have crossed 300 million (WHO, 2017). As the search for novel treatments for mental illness grows, the focus at present is on psilocybin and its potential as a treatment for mental health problems. Recent studies have revealed its medicinal use which make a boon for many a patient having mental disorder. So the time for magic mushroom to break the mental shackles isn't far away, it's on the way.

11.Discussion

1. In which geographical region the psilocybin mushrooms are seen abundantly?

   More than 55 species across the world are reported from Mexico. Majority were found in hygrophytic or mesophytic forests, also known as subtropical cloud forests and grew in humid mountains at 900- 1400 m altitude close to the sea. In Mexico it was observed that more than 90 percent of the known species are in this kind of vegetation.

2. Any magic mushrooms reported from kerala?

   Psilocybe wayanadensis and *Psilocybe keralensis* are reported from forest regions of wayanad and idukki.

3. Is there any plants showing this hallucinogenic property?

   Plants like cannabis, tobacco, opium poppy etc are psychoactive in nature

4. Is there any chance for addiction if we consume these magic mushrooms?

   Yes, it can cause addiction if it is consumed without proper guidance. During 2016 there was news reports like selling of the magic mushrooms in omelettes from munnar region of kerala. Recently, shroom tourism is emerging in kodaikanal region, where these mushrooms are sold by adding in various food items. But, if it is used under the supervision of well-known clinician, it can have enormous mental health benefits.

5. What is the mechanism of action of magic mushrooms as a treatment for alcohol dependence?

   Psilocin is more lipid soluble than psilocybin so it readily crosses the blood brain barrier. Because of of its structural similarity with the serotonin, psilocin exerts its effect on the CNS (Central Nervous System) by stimulation of the serotonin receptors. Serotonin helps to regulate our mood, behavior, appetite, digestion, sleep etc. Activation of this receptors in the thalamus, the area of the brain responsible for sensory input, appears to decrease thalamic activity, thus leading to sensory alterations commonly referred to as hallucinations. The combination of these effects that make psilocybin so useful for combating depression and addiction. For example when new areas in the brain start talking to each other we might have new insights into our problems and that’s why some experts describe hallucinogenic effect as a condensed version of talk therapy.

12. References

Adams, A.M., Kaplan, N.A., Wei, Z., Brinton, J.D., Monnier, C.S., Enacopol, A.L., Ramelot, T.A. and Jones, J.A. 2019. In vivo production of psilocybin in E. coli. *Metabolic Eng*. 56: 111-119.

Bauer, B. 2019. Jamaica is home to the first magic mushroom research center [on-line]. Available: https://psychedelicreview.com [05 Nov. 2019].

Bauer, B. 2019. Johns Hopkins Medicine opens center for psychedelic and consciousness research [on-line]. Available: https://psychedelicreview.com [05 Nov. 2019].

Bogenschutz, M. P., Forcehimes, A. A., Pommy, J. A., Wilcox, C. E., Barbosa, P., and Strassman, R. J. 2015. Psilocybin-assisted treatment for alcohol dependence: A proof of concept study. *J. Psychopharmacol*. 29 (3): 289-299.

Buddy, T. 2019. How long does psilocybin stay in your system? [on-line]. Available: https://www.verywellmind.com [30 Oct. 2019].

Carhart-Harris, R.L., Leech, R., Hellyer, P.J., Shanahan, M., Feilding, A., Tagliazucchi, E., Chialvo, D.R., and Nutt, D. 2014. The entropic brain: a theory of conscious states informed by neuroimaging research with psychedelic drugs. *Front. Human Neurosci*. 8: 20.

Daniel, J. and Haberman, M. 2017. Clinical potential of psilocybin as a treatment for mental health conditions. *Ment. Health Clin*. 7(1): 24-28.

Erowid. 1995. Psilocybin mushrooms [on-line]. Available: https://erowid.org/plants/mushrooms [27 Oct. 2019].

Fanaticus. 1991. Psilocybe fanaticus [on-line]. Available: http://www.fanaticus.com [30 Oct. 2019].

Griffiths, R. R., Johnson, M. W., Carducci, M. A., Umbricht, A., Richards, W. A., Richards, B. D., Cosimano, M. P., and Klinedinst, M. A. 2016. Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *J. Psychopharmacol*. 30 (12): 1181-1197.

Guzman, G. 2009. The hallucinogenic mushrooms: diversity, traditions, use and abuse with special reference to the genus Psilocybe. In: Misra, J. K. and Deshmukh, S. K. (eds), Fungi From Different Environments. Science Publishers, Enfield, New Hampshire, pp. 256-277.

Hartney, E. 2019. What to know about magic mushroom use [on-line]. Available: https://www.verywellmind.com [01 Nov. 2019].

Johnson, M.W., Garcia-Romeu, A., Cosimano, M.P., and Griffiths, R.R. 2014. Pilot study of the 5-HT2AR agonist psilocybin in the treatment of tobacco addiction. *J. Psychopharmacol*. 28(11): 983-992.

Kirk, P. M., Cannon, P.F., Minter, D.W., and Stalpers, J.A. 2008. Dictionary of the Fungi (10th Ed.). Wallingford CABI, Oxfordshire, 759p.

Nicholas, L. G. and Ogame, K. 2006. *Psilocybin Mushroom Handbook*: *Easy Indoor and Outdoor Cultivation*. Quick American, Canada, 209p.

Singer, R. 1978. Hallucinogenic mushrooms. In: Rumack, B. H. and Salzman, E. (eds), *Mushroom poisoning: Diagnosis and treatment*. CRC press Inc., Florida, USA, pp.201-203.

Stamets, P. 1996. *Psilocybin Mushrooms of the World*. Ten Speed Press, California, 245p.

Tyls, F., Palenícek, T., and Horacek, J. 2014. Psilocybin–summary of knowledge and new perspectives. *Eur. Neuropsychopharmacol*. 24(3): 342-356.

Wasson, R. G. 1957. Seeking the magic mushroom. Life, 13 May 1957, pp. 102-120.

WHO [World Health Organization]. 2017. Depression and other common mental disorders: Global health estimates [on-line]. Available: https://apps.who.int>iris>handle [28 Oct. 2019].

KERALA AGRICULTURAL UNIVERSITY

COLLEGE OF HORTICULTURE, VELLANIKKARA

Department of Plant Pathology

Pl. Path 591: Master's Seminar

Name : Alby John

Admission No : 2018-11-022

Major Advisor : Dr. Reshmy Vijayaraghavan

Venue : Seminar Hall

Date : 28-11-2019

Time : 11.30 am

Breaking the mental shackles – The magic mushroom way

Abstract

Man's interest in fungi started with the observation of beautiful umbrella shaped mushrooms appearing on the ground. Mushrooms are the fleshy spore bearing fruiting bodies of a fungus growing above ground on soil or on other substrates. Based on the human use, mushrooms can be classified as edible, toxic, hallucinogenic, medicinal and others. Magic mushrooms are hallucinogenic mushrooms that contain the psychoactive and hallucinogenic compound psilocybin. They act on the Central Nervous System (CNS) and cause hallucination syndrome. Magic mushrooms are also known as psychedelics and has derived its name from two Greek words '*Psyche'* meaning mind and '*Deloun'*- to reveal.

Psilocybe spp. belonging to the family Strophariaceae are saprophytes and found in a wide range of habitats. They are hygrophanous in nature and exhibit bluing reaction. Spore print of the mushroom is purplish brown to black in colour and the most representative character is the presence of a separable gelatinous pellicle (Stamets, 1996). Main steps involved in the cultivation of *Psilocybe* spp. are substrate preparation, sterilization, inoculation, incubation, fruiting and harvesting (Nicholas and Ogame, 2006).

Psilocybin is the active principle in magic mushrooms. Inside the body, psilocybin gets dephosphorylated to psilocin which is pharmacologically active. Because of its structural similarities to neurotransmitter serotonin, psilocin exerts its effect on the CNS by stimulating the serotonin receptors. Activation of the serotonin receptors in the thalamus, which is the area of the brain responsible for sensory input, appears to decrease thalamic activity, thus leading to sensory alterations commonly referred to as hallucinations.

Global health estimates revealed that people suffering from mental illness such as anxiety or depression have crossed 300 million (WHO, 2017). As the search for novel treatments for mental illness grows, the focus at present is on psilocybin and its potential as a treatment for mental health problems. A study on the effects of psilocybin administration in patients with life-threatening cancer showed a significant reduction in depression and anxiety, along with increase in optimism and quality of life (Griffiths *et al.*, 2016). Moreover, it was reported that psilocybin has clinically relevant effects in reducing alcohol and drug addiction (Bogenschutz *et al.*, 2015)

In most of the countries, psilocybin is illegal and is listed as schedule I drug under the US Controlled Substance Act (CSA) of 1970. However, these magic mushrooms have an enormous therapeutic potential against drug addiction and other mental instabilities. In 2018, researchers from John Hopkins University recommended reclassification of this drug from schedule I to schedule IV, in order to allow its use in medical field. As a next step, John Hopkins University School of Medicine opened 'Center for Psychedelic and Consciousness Research' in September 2019 following which world's first magic mushroom research center was launched in Jamaica. So the time for magic mushroom to break the mental shackles isn't far away, it's on the way.

References

Bogenschutz, M. P., Forcehimes, A. A., Pommy, J. A., Wilcox, C. E., Barbosa, P., and Strassman, R. J. 2015. Psilocybin-assisted treatment for alcohol dependence: A proof of concept study. *J. Psychopharmacol*. 29 (3): 289-299.

Griffiths, R. R., Johnson, M. W., Carducci, M. A., Umbricht, A., Richards, W. A., Richards, B. D., Cosimano, M. P., and Klinedinst, M. A. 2016. Psilocybin produces substantial and sustained decreases in depression and anxiety in patients with life-threatening cancer: A randomized double-blind trial. *J. Psychopharmacol*. 30 (12): 1181-1197.

Nicholas, L. G. and Ogame, K. 2006. *Psilocybin Mushroom Handbook*: *Easy Indoor and Outdoor Cultivation*. Quick American, Canada, 209p.

Stamets, P. 1996. *Psilocybin Mushrooms of the World*. Ten Speed Press, California, 245p.

WHO [World Health Organization]. 2017. Depression and other common mental disorders: Global health estimates [on-line]. Available: https://apps.who.int>iris>handle [28 Oct. 2019].