The Past, Present and Future of Psychedelic Medicines

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When people hear the word “psychedelic,” it may conjure up memories of hippies adorned in bellbottoms and love beads, rock music, acid trips and social unrest. Yes, that was all part of the drug culture back in the 60’s and 70’s.

Today we are going to revisit psychedelics, also known as hallucinogens or psychoactive substances, both the natural plant-based and synthetic man-made varieties and their future potential.

The history of man’s use of natural psychedelics goes back to when humans consumed only the foods they could forage in nature. They would eat what they happened across and if it tasted good and did not make them sick or kill them, they would continue to seek it out as a form of sustenance. On the other hand, if they tried something new and it tasted bad, made them sick or killed them, then they would not be eating that again. Along their path in search of a gastronomical discovery, early man inevitably wandered across a plants or fungi that did more than fill their bellies. Some researchers have even suggested that the ingestion of psychoactive foods may have had an influence on the evolution of early humans.

Reliable evidence indicates that intentional human use of psychedelics began in the Neolithic Period in Mesopotamia and South America.

A recent study of ancient Greek pottery has proven that psychedelics were used in what are believed to be “incubation rituals.”
“incubation rituals were religious practices where people slept in a sacred space to receive a dream from a deity that may provide healing or prophecy. In the Greek Cult of Asklepios, god of medicine, sick worshippers had to spend the night in the sanctuary and wait to be visited by the god curing them during their dreams. Those dreams were triggered by drugs dispensed by priests. So, research confirms an earlier use of hallucinogens, then later comparisons in a number of other cultures.” (1)

In Europe, during the Middle Ages, men and women who practiced witchcraft learned to use psychoactive plants such as herbane, Thorn apple, and belladonna. They learned that by combining these compounds with oils they could be applied to the skin and absorbed into the bloodstream, however, without the deadly results of consuming them orally.
R.E.L. Masters and Jean Houston in their book, *The Varieties of Psychedelic Experience,* described, “That the witches’ ointment already was known in the fifteenth century…”
Many of the medieval practitioners using these plants would likely have experienced extremely vivid hallucinations involving flying off to destinations where many emotional states and

physical activities were experienced. Eyewitness accounts stated that the force and intensity of these hallucinations, especially the vivid imagery, left the witches with memories that to them were as real as any other memory. (2)

Shamans, or witch doctors of indigenous tribes having discovered how to use these special plants and mushrooms, would pass this knowledge down to subsequent generations of shamans. With the use of psychoactive plants, shamans had the power to enter trances, combat evil spirits and disease, and to communicate with ancestors. For instance, hallucinogenic cacti, plants, mushrooms, and seeds that contain mescaline, psilocybin, and lysergic acid amide, respectively, were used to induce altered states of consciousness in healing rituals and religious ceremonies throughout pre-Columbian Mesoamerican cultures. (3)

Psychedelic plants and fungi had been used in medicinal and spiritual traditions for millennia. It would take until the beginning of the 20th century for researchers to inadvertently discover how to synthesize psychoactive drugs. One such researcher was Anton Kollish, a research scientist working for the German chemical company Merck. Kollish was attempting to formulate an appetite suppressant. What he ended up discovering was methylenedioxymethamphetamine or MDMA (ecstasy) and its derivatives. However, his experiments had failed to produce the appetite suppressant, so the formula was shelved. (4)

It was not until the early 60's that the American chemist, Alexander Shulgin, began doing research on synthesizing psychoactive drugs, after having been inspired by a personal experience with mescaline. In 1965 he was successful at synthesizing MDMA but did not conduct any trials at that time. In 1975 Shulgin was again able to synthesize MDMA, but he did not conduct self-trials until 1976. In 1977 Shulgin gave it to psychotherapist, Leo Zeff, who distributed it enthusiastically to hundreds of therapists. Shulgin, and others involved, did not share their knowledge of MDMA until a presentation at a public conference in 1983. (5)

Years before the successful synthesis of MDMA, pharmaceutical firms began investigating the fungus, ergot, finding that it contained valuable medicinal compounds such as ergotamine, which was used to treat migraines. A Swiss chemist named Albert Hoffman became especially interested in this field and in November of 1938, he created a derivative of ergot called lysergic acid diethylamide, commonly known as LSD.

It was not until five years later that Hoffman returned to his discovery and inadvertently experienced its effects. His discovery of the new drug's profoundly psychoactive effects was one of the more famous accidents in the history of science. (6)

According to an article by Erica Dyke in the Canadian Medical Association Journal," Hofmann's drug opened a new era of hallucinogenic research. Over the next 15 years, more than a

thousand articles on the use of LSD appeared in medical and scientific publications. In 1957, that work gave rise to the term “psychedelic” to describe a mind-manifesting response, described by some as an experience that brought to light – ‘matters that had previously been part of the unconscious’. (7)

During the 1950s and into the early 1960s, LSD was used successfully to treat alcoholism, arguably by compressing years of psychotherapy into a single, intensive and self-reflective session that helped patients with alcohol dependence achieve a new self-image and the willpower to move beyond their disease. Others explored LSD as an adjuvant to psychotherapy for addressing trauma; still others used it to model psychosis and to generate interest in studying schizophrenia as a chemical reaction in the brain.” (8)

Unfortunately, by the mid-1960s, research into LSD, psilocybin, MDMA and other psychedelics came to a halt, largely because it had become synonymous with countercultural activities, hedonism, and drug abuse. By the 1970’’s Nixon had declared a War on Drugs and all research on mind-altering drugs came to an end when they became illegal under the federal Controlled Substance Act.

Currently psychedelic compounds are still classified as schedule 1 controlled substances. This classification is based upon the substance’s medical use, potential for abuse, and safety or dependence liability. However, with the ever-growing global mental health crisis and the shortage of effective therapeutic treatments, there has been a reconsideration of the therapeutic benefits of psychedelic compounds in recent years.

With the aid of innovative technology, such as functional neuroimaging techniques, researchers have been better able to understand the impact of psychedelics on brain connectivity and neuroplasticity.
As of 2022, there were hundreds of clinical trials recruiting participants for assessing the therapeutic effects of psychedelics. The evidence from these trials suggests that psychedelic drugs may employ some of their long-lasting therapeutic effects by generating structural and functional neural plasticity. (9) In other words, the ability to literally change your mind. However, the benefits of psychedelics are more achievable when paired with professional behavioral intervention.

As stated earlier, psychoactive drugs show great potential for treating conditions such as severe depression, PTSD, and addiction. Consequently, investors have been piling into this burgeoning field, and a host of medications based on MDMA, LSD, psychedelic mushrooms, ketamine, the South American plant mixture ayahuasca, and the African plant ibogaine are now under development, and in some cases vying for approval by the Food and Drug Administration.

The FDA has what is called a “breakthrough therapy” designation, which is a process designed to speed up the development and review of drugs that may show significant improvement over currently available treatments. Several psychedelic-related compounds have been given this designation, which reflects a growing optimism that these compounds might be useful for treating certain neuropsychiatric disorders. This designation was granted for ketamine in 2013 for treatment-resistant depression, for MDMA in 2017 for post-traumatic stress disorder (PTSD), and for psilocybin in 2019 for treatment-resistant depression. In 2019, S-ketamine, with the brand name of SPRAVATO nasal spray, was granted FDA approval for treatment-resistant depression, potentially paving the way for MDMA and psilocybin to follow suit. The SPAVATO is currently the only “breakthrough therapy” of the three to be given FDA approval. (9)

The first MDMA-assisted therapy appeared to be on track for FDA approval by August of 2024, but a report from an independent review committee challenged the integrity of the trial data from the drug’s maker, so the FDA convened a panel of independent investigators on June 4, 2024, to determine whether to recommend the drug’s approval.
On September 9th, the FDA denied approval of MDMA for the treatment of PTSD stating that there was not enough evidence that the therapy was safe or effective.

Due to the challenging nature of testing psychedelic drugs, the FDA must ensure the safety and well-being of human test subjects and therefore recommends guidelines for clinical trials.

In June of 2023, the U.S. Food and Drug Administration (FDA) issued its first draft guidance entitled Psychedelic Drugs: Considerations for Clinical Investigations Guidance for Industry. This guidance highlights considerations for sponsors who are developing psychedelic drugs for treatment of medical conditions such as psychiatric disorders and substance use disorders as well as for the clinical trials that will be conducted under an investigational new drug application. “Psychedelics” as used in the Guidance, specifically limited to psilocybin, LSD and MDMA. (11)

Unlike many other drugs, psychedelic drugs cannot be self-administered. In these trials, the duration of treatment may be as long as 12 hours. In the FDS’s proposed guidelines Safety monitory should include observation by two monitors for the duration of the treatment session. The lead monitor would consist of a healthcare provider with graduate-level professional training and clinical experience in psychotherapy, licensed to practice independently. An assistant monitor with a bachelor’s degree and at least 1 year of clinical experience in a licensed mental healthcare setting. If the lead monitor is not a physician, then there would need to be a licensed on-call physician available who would be able to reach the clinical site within 15 minutes in the event of a medical emergency. (10)

What can also complicate these trials is the need for follow-up psychotherapy to aid the patient in utilizing the insights they have gained from their drug-induced therapy, which is not controlled by the FDA.

Two of the key factors of psychedelic assisted psychotherapy are *set and setting*. Set refers to how the patient is feeling mentally at the time of therapy and setting is the environment where the therapy is taking place, often overnight. The patient is administered the drug in a comfortable bed in a clinical setting with two clinicians always monitoring the patient. Follow-up psychotherapy may be done immediately after treatment has concluded or the following day. Depending on the diagnosis and treatment, additional treatments may be required.

According to a story on CBS news, Lori Tipton is among the growing number of people who say that MDMA, also known as ecstasy, saved their lives.
Raised in New Orleans by a mother with untreated bipolar disorder who later killed herself and two others, Tipton said she endured layers of trauma that eventually forced her to seek treatment for crippling anxiety and hypervigilance. For 10 years nothing helped, and she began to wonder if she was "unfixable."
Then she answered an ad for a clinical trial for MDMA-assisted therapy to treat post-traumatic stress disorder. Tipton said the results were immediate, and she is convinced the drug could help a lot of people. But even as regulators weigh approval of the first MDMA-based treatment, she's worried that it won't reach those who need it most.

I have personally interviewed several individuals who have used psylocibins, not in a clinical setting. They expressed to me that it made them feel calmer, a feeling of clarity and a oneness with the world. It was also stated that it did not make them feel the need to keep doing it and that the improvement of their mental condition continued for several months or more. Psychedelics are not considered to be addictive. Most deaths resulting from the use of psychedelics are the result of suicide or dangerous behavior causing accidents.

Several of these novel modalities have been utilized for palliative care in terminally ill and dying patients. They are said to elicit an experience of peace and alleviate the fear of dying as well as the pain and agitation that can accompany end of life. (12)

Scientific researchers have now tapped into ancient psychedelic remedies, and if investigated correctly, these drugs could have exciting potential to alleviate much suffering and to help people overcome mental conditions brought on by traumatic life experiences and situations. If psychedelic psychotherapy has the potential to "cure" mental illnesses by getting to the core issues residing in the subconscious, I believe that many of these people would have the opportunity to live stable, productive lives and be assets rather than burdens to society.

Citations

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