# Psilocybin

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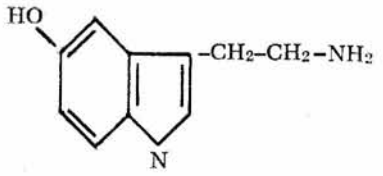
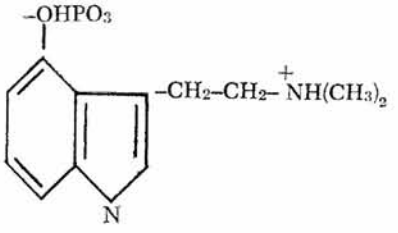
*Psilocybin is a naturally occurring indole alkylamine found in various species of new world mushrooms. It enjoyed widespread use among the pre-Columbian cultures of Central America and has recently found its way into the present youth drug culture. The pharmacologic properties and physiologic effects of psilocybin are similar to those of LSD-25 as are the psychologic changes induced by the ingestion of the drug. The primary differences between psilocybin and LSD-25 are those of duration of action and potency. Details of the biochemistry, physiologic effects and metabolism as well as history of social usage and legal status of psilocybin are discussed.*




serotonin




*1.* psilocybin

**INTRODUCTION:** Psilocybin is an indolealkylamine found in the mushroom species *Psilocybe mexicana* Heim, and others of the new world. It is structurally related to several other naturally occurring compounds possessing a psychopharmacologic action. Fig 1 shows the structural resemblance of psilocybin to serotonin, the naturally occurring neurotransmitter substance.

Fig 1 shows psilocybin to possess an indole nucleus substituted at the four position with a phosphoric acid grouping. This makes psilocybin unique among the naturally occurring indole-alkyl-amines. No other compound of this class possesses a phosphoric acid grouping, and no other related compound with hallucinogenic properties is substituted at the four position.

Psilocybin was isolated and subsequently synthesized by Hoffman at the Sandoz Laboratories in 1958. Since that time psilocybin, along with the other hallucinogens such as LSD, STP, and DMT has gained wide public recognition as an "abused" drug.

**History, Current Social and Legal Studies:** The use of psilocybin as a social intoxicant can be traced back four centuries to the legendary "magic mushroom" of Mexico and Central America. Also known as the "food of the gods," it was the sacred mushroom of the pre-Columbian cultures. Stone artifacts dating back to 1500 BC indicate that the mushroom culture extended at least from the Aztecs in Mexico to the Mayas in Guatemala.

Used in the ceremonial setting with religious overtones, the partaking of the mushroom was presided over by a priestess.[8] Conducted by candle-light, the ceremony is said to be a blend of both Christian and pagan elements, at times including a curing ritual. History also records the intoxicating mushroom as having been among the delicacies of the coronation feast of Montezuma in 1502.

The coming of the Europeans and their rapid exploration of the new world contributed to the disintegration of the Indian culture as a separate entity. Missionaries, attempting to convert the pagans to the Christian way of life, often

persecuted members of the mushroom cult, thus forcing them into hiding.

It was not until 1953 that the magic mushroom was rediscovered. It was at this time that Gordon Wasson, an eastern banker, brought the mushroom cult into the 20th century. Wasson, who is an amateur ethnologist, and his wife Valentina Pevlovnia, a student of mushrooms, journeyed to a remote Mexican village to observe the ancient rituals of the Oaxacan Indians. He persuaded the Indians to give him a few samples of a mushroom used in their ceremonies. These samples were identified later by Heim as a previously unknown species of the genus *Psilocybe*. The proper name has since been given as *Psilocybe mexicana* Heim.[8]

In 1958, Dr. Albert Hofman isolated two materials from the mushroom. The main component was psilocybin, the first phosphorylated indole to be discovered. The other component was psilocin, not phosphorylated, but equally active. These compounds were then synthesized and made available to the scientific community for research purposes.[16] Psilocybin and psilocin are now licensed by the USFDA for research purposes only. Its distribution is confined to scientists receiving federal or state grants to specifically study the biological effects of the drug.

The modern day controversy over the use of hallucinogens including psilocybin perhaps dates back to the early experiments of Dr. Timothy Leary. Leary and Richard Alpert began experimenting with psilocybin in 1960 by testing the effects of the drug on prisoners. By the fall of 1962 they had dispensed more than 3,500 doses of the drug to some 400 volunteers. They found that 73% of their subjects had a "very pleasant" experience.

However, as they expanded their research, criticism began to mount and in the fall of 1962 the university decided that the dangers of psilocybin might be too great to allow the kind of admittedly nonmedical experimentation that Leary and Alpert were conducting. They were asked to stop the experiments or leave Harvard.

Thus psilocybin has left the research lab and entered the hallucinogenic subculture. However, LSD is generally preferred over psilocybin by those who indulge in the use of hallucinogenic drugs. Although LSD and psilocybin have essentially the same physiological and psychological effects, at the same dosage, LSD is about 100 times as potent as psilocybin. Moreover, LSD is much more available on the black market than is psilocybin and it is commonly said that most of the capsules sold as psilocybin are largely LSD.

Legally, psilocybin is covered by the Drug Abuse Control Amendments of the Federal Food, Drug, and Cosmetic Act of 1965. The penalties for first offense of illegal production or sale of psilocybin is one year in prison or a $10,000 fine, or both. For giving psilocybin to persons under age 21 the penalties range from two to six years in prison or $5,000 to $15,000 in fine, or both. This federal law has no provisions for possession only, thus the penalties for possession are covered by state laws, which are highly variable and range from misdemeanor to lengthy prison terms.

**Biochemical Synthesis:** Recent research has revealed a possible synthetic pathway for psilocybin and psilocin. According to Agurell,[1] experimental data suggest the following sequence from tryptophan to psilocybin: tryptophan → tryptamine → N-methyltryptamine N, N, → dimethyltryptamine → psilocin → psilocybin.

**Clinical Syndrome:** In general, the physiological

effects of psilocybin resemble those of the sympathomimetic drugs. These effects include, among others: (1) increased pulse rate and blood pressure, (2) dilated pupils, (3) tremors, and (4) cold sweaty palms (Rieffer, 1968). With low doses of 5 to 10 mg, the effects are generally mild. There are usually some alterations of mood consisting of either mild euphoria or dysphoria.[8] Tests of psychologic functioning usually show some degree of impairment. However, this finding is usually attributed to alterations in concentration and attention. Nausea, dizziness, weakness, and sensitivity to light may be somatic symptoms of consequence. The threshold dose is usually around 60 μg/kg. Clinical doses usually range from 115 to 160 μg/kg. Both frequency and intensity of clinical effects increase with dosage.

Hollister[10] relates the following pattern of the clinical syndrome. During the first 30 minutes, his subjects became dizzy, light-headed, or giddy. Nausea and abdominal discomfort accompanied by anxiety, tension, or restlessness were also reported. Some subjects also experienced weak, aching muscles accompanied by twitching and shivering. Also described was numbing of the tongue, lips, and mouth.

The second 30 minutes were experienced with blurred vision, brighter colors, longer afterimages, sharp definition of objects, and visual patterns with the eyes closed. Increased auditory acuity was noted. Physiological symptoms included yawning, tearing, facial flushing, and sweating. Most subjects also experienced a state with loss of attention and concentration, slow thinking, feelings of unreality, and depersonalization. Incoordination or difficult and tremulous speech were also noted.

The effects occurring between 60 and 90 minutes after ingestion were predominantly visual. Colored patterns and shapes were generally described as pleasing, although at times they were frightening. Most often these patterns occurred with the eyes closed, although occasionally they were superimposed upon objects in the field of vision. Many subjects reported undulation or wavelike motion of viewed surfaces. Distance perception was impaired and there was a slowed passage of time. Nearly all subjects experienced an introspective state of mind.

The syndrome from 90 to 120 minutes was marked by a continuation of many of these effects in varying degrees, especially the introspective state. Also noted were increased bodily sensations and neutral processes. From 120 to 180 minutes there was a waning of the previously described effects. By 180 to 300 minutes after ingestion there was a nearly complete resolution of the drug-induced effects.

*Psychologic Changes:* Psilocybin produces a variety of psychologic changes. Certain of these changes appear to be rather constant findings in numerous clinical studies. However, most psychic changes coincident with the use of psilocybin are extremely variable and are attributed by most workers to be the result of differences in personality structure.

Some of the most constant psychic changes are those of perception, primarily visual. Visual changes often vary from multicolored, nondescript patterns to frank visual hallucinations. Psilocybin decreases the spatial distortion threshold.[7]

Auditory perception may be altered, but frank auditory hallucinations apparently are quite rare.[14] More often, increased auditory acuity is reported.

Tactile sensation appears to be variable. Some subjects report decreased sensitivity. Perception of size, direction and distance is altered by psilocybin. In addition, there may be dis-

tortion of the body image. The subject may feel long and drawn out or short and stubby. A feeling of lightness or heaviness of the extremities has also been noted.[14]

Perhaps the most frequently noted psychic change has been a distortion of time sense. According to Hollister,[8] some subjects think time is passing more slowly, while others think the reverse.

Studies of the effects of psilocybin on cognitive functions and psychomotor performance are somewhat confusing. However, most researchers agree that psilocybin should not be considered to produce a state of organic intoxication because memory and orientation are spared and gross confusion is absent. However, intoxication is sufficient to cause impairment in the performance of a perceptual-cognitive-motor test.[3] Solomon states that psychological testing of subjects on psilocybin generally, although not consistently, shows slight decrements in performance.[16] Hollister finds impaired performance of complex discrimination tasks but not so much with simple tasks.[8] He also states that immediate memory as well as simple problem solving are impaired.

Much clinical evidence suggests that critical judgement is impaired. Hollister and Solomon believe that at least some of the impairment shown in intellectual functioning may be due to an altered state of attention.[8,16] However, the possibility still exists that there is a primary effect on brain mechanisms for cognitive thinking.

Although it is a popular conception that drugs such as psilocybin increase the users' powers of creativity, Hollister states that all evidence points to impaired artistic technique.[8] He points out that there is no concrete evidence of increased artistic abilities or performance either during or after the drug experience.

A great variety of subjective effects of psilocybin have been reported. Psilocybin nearly always produces a dreamy, introspective state of mind. Hollister emphasizes that this is nearly always without notable impairment of faculties.[10] (This cannot be said of LSD-25.) Some subjects taking psilocybin reexperience the past; others have described déjà vu experiences. It is not unusual for a subject to believe that he has an unusual ability to perceive the feelings and motivations of people around him. At times, subjects will express great empathy. Misinterpretation of environmental stimuli is not uncommon.

The visionary experience which many people assume is synonymous with a drug-induced state is not common. However, it is well-known that a few subjects actually achieve a transcendental state while taking hallucinogenic drugs, and apparently extra-drug variables (such as personality structure and state of mind prior to taking the drug) are the primary determinants of this effect.

Concerning the relation of psilocybin to LSD and mescaline, it is not believed that the subjective effects of mescaline, LSD, and psilocybin are similar, equivalent, or indistinguishable. Furthermore, recent studies indicate that cross-tolerance between LSD and psilocybin does develop. This indicates the possibility of a similar mode of action. Hollister states three primary differences between LSD and psilocybin: shorter duration of action, more agreeable response, and production of introspection without marked impairment of faculties.[8]

No major or significant toxic effects of psilocybin are known at the present time. Chronic administration results in the development of tolerance which will eventually disappear during several weeks of abstinence.

**Metabolism:** The metabolism of psilocybin is

believed to begin with dephosphorylation by alkaline phosphatase to produce psilocin. From this point it is believed that the body treats psilocin in much the same manner as it does $\alpha$-methyltryptamine, which has a related structure.

Studies indicate significant uptake of psilocybin into the kidney, pancreas and intestinal tract. Low concentrations are found in brain, spleen, liver, heart, and lungs. Concentrations present in plasma, allowing for equilibration in the brain, correlate well with the onset and decrescence of clinical effects.

**Theories on the Mechanism of Action:** Psilocybin is relatively unstable, the phosphoric acid grouping being lost soon after ingestion. It is thus likely that all activity is caused by the resultant 4-hydroxy dimethyltryptamine, or psilocin. The chemical resemblance of this compound to the biogenic amine, ~~serot~~ serotonin, is quite evident.

Thus it would seem that the majority of researchers now favor the view that psilocybin acts by interference with the metabolism of the catecholamines or serotonin. The anatomical sites of this interference are probably multiple. However, the primary neurological impact of most hallucinogens is thought to be on afferent impulses entering the ascending reticular formation through collaterals from the sensory pathways, whereas the physiologic or autonomic effects of psilocybin may stem from an action on the hypothalamus.[18]

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The author's reference list is available on request from *Texas Medicine*, 1801 N Lamar Blvd, Austin, Texas 78701.