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CHEMISTRY AND PHARMACOLOGY OF THE «SACRED MUSHROOMS» OF MEXICO

Abstract - A. HOFMANN - Chemistry and Pharmacology of the «Sacred Mushrooms» of Mexico.

The use of special mushrooms in a magical and religious context by the Indians of Central America has been reported already in the chronicles of the naturalists who came in the country soon after the conquest of Mexico by Cortes in 1521. But it was only in the thierties of our century that american ethnologists discovered a still existing mushroom cult in the mountains of Southern Mexico, which was later investigated extensively by Valentina Pavlova and R. Gordon Wasson. After the botanical identification of the «sacred mushrooms» as several species of the genus *Psilocybe*, by the french mycologist Roger Heim, the mushrooms were chemically investigated in the pharmaceutical laboratories of the Sandoz Company in Basel. Two new alkaloids, named psilocybin and psilocin, were found to be psychoactive principles of «teonanacatl», which was the Aztec name of the «sacred mushrooms».

Psilocybin and psilocin belong to the large group of indole alkaloids, representing a special type characterised by a substitution at the position 4 of the indole skeleton. This special structural charachteristic relates the teonanacatl alkaloids with the ergot alkaloids ad with LDS, wich are also substituted in the position 4.

The picture of the pharmacological properties of psilocybin and psilocin is very similar to that of LSD, wich may be summarised as forming a syndrom of ergotropic stimulation. Antagonism to serotonin and low toxicity are additional common pharmacological properties.

The effects on the human psyche and consciousness of psilocybin and psilocin represent a typical psychedelic spectrum.

In the chronicles of the naturalists and explorers who came to Mexico soon after the conquest of the country by Cortez in 1521 inebriating mushrooms are mentioned which were used by the Indians in religious ceremonies and magical medicinal practices. The most important of these witnesses is the Franciscan Friar Bernardino de Sahagun who describes the magic mushrooms and their use in

his famous historical work, Historia General de las Cosas de Nueva España, written between the years 1529 and 1590. These mushrooms, which were called in the Aztec language «Teonanacatl», what means «God's Flesh», played an important part in the pre-Columbian cultures of Central America. To the Christian missionaries, the inebriating, vision- and hallucinations-producing effects of these mushrooms seemed to be Devil's work. They therefore tried by all the means of their power to extirpate their use. But they succeeded only partially, for the

Fig. 1 - Mushroom Stone.

Indians have continued sectretly down to our time to use «Teonanacatl», which was sacred to them.

The mushroom-cult must be very old. So-called mushroom stones have been found in El Salvador, Guatemala and the contiguous districts of Mexico. These are stone sculptures in the form of a pileate mushroom, on whose stem the face or the form of a god or demon is carved. Most are about 30 cm high. The oldest pieces date back to before 500 B.C., which means that the ceremonial-religious use of the magic mushrroms is more then two thousand years old.

Strange to say, the reports in the old chronicles about the use of sacred mushrooms remained unnoticed during the following centuries, probably because they were regarded as extravagances of a superstitious age. However, between 1936 and 1938 American investigators, Robert J. Weitlaner, Blas Pablo Reko, Jean Basset Johnson and Richard E. Schultes, ascertained, that mushrooms were still eaten in our day for magic purposes by natives in certain districts of South Mexico.

Systematic studies of the mushrooms cult in its present form were then made later, betwenn 1953 and 1956, by the amateur ethnomycologists R. Gordon Wasson and his wife Valentina Pavlovna. On one of their expeditions to the remote mountainous districts of South Mexico the Wassons were accompanied by the well-known mycologist Professor Roger Heim, from Paris. Heim succered in identifying and classifying the most important types of mushrooms used for magic purposes by the Indians. These were foliate mushrooms (Agaricales), from the family *Strophariaceae*, mostly new species of the genus *Psilocybe*, e.g. *Psilocybe mexicana* Heim, *P. caerulescens* Murr. var. *mazatecorum* Heim, et al. Subsequently Heim was able to grow cultures of some of these species in the laboratory. Artificial cultivation provided a very good yield especially with *P. mexicana*.

As chemical investigations of the Mexican mushrooms carried out in Paris and in the USA remained unsuccessful, Professor Heim addressed the Pharmaceutical Research Laboratories SANDOZ in Basel, Switzerland, because he felt that there, where LSD had been discovered, a substance with psychotropic properties similar to those of the mushrooms, special experiences and knowledge useful for the isolation experiments could be available. Thus it was LSD that showed Teonanacatl the way into our laboratories.

In our isolation studies we first tested the extracts in animals. But the results were not clear-cut and doubts arised wether the musrhooms cultivated and dried in Paris were still pharmacologically active at all.. In order to settle this fundamental question I decided to test the mushrooms on myself. I ate 32 dried specimens of *P. mexicana*, a medium dose, used by the Mexican shamans. The mushrooms exerted a marked psychedelic effect as the following laboratory records show: «Thirty minutes after taking the mushrooms the exterior world began

to undergow a strange transformation. Evertything assumed a Mexican character. As I supposed that my knowledge of the Mexican origin of the mushrooms would lead me to imagine only Mexican scenery, I tried consciously to look at my environment as I knew it normally. But all voluntary efforts to look at things in their costumary forms and colors proved ineffective. Wether my eyes were closed or open I saw only Mexican motifs. When the doctor supervising

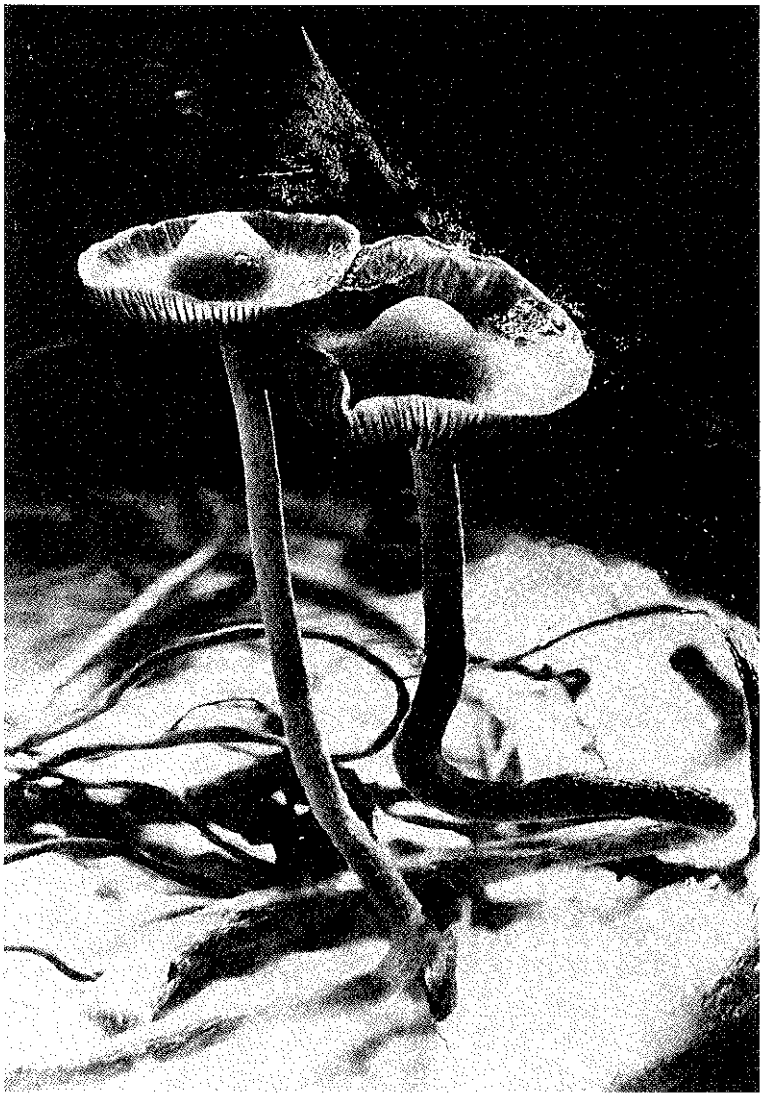

Fig. 2 - *Psilocybe mexicana* Heim (Photo A. Brack).

the experiment bent over me to check my blood pressure, he was transformed in an Aztec priest and I would not have been astonished if he had drawn an obsidian knife. In spite of the seriousness of the situation it amused me to see how the Germanic face of my colleague had acquired a purely Indian expression. At the peak of the experiment, about 1 1/2 hours after the ingestion of the mushrooms, the rush of the interior picturs, mostly abstract motifs changing rapidly in chape and colour, reached such an alarming degree that I feared to be torn into this wirlpool of forms and colours and would dissolve. After about six hours the dream come to an end. Subjectively I had no idea how long the strange condition had lasted. I felt my return to everday reality to be a happy return from a strange, fantastic but quite really experienced world into the old familiar home».

This self-experiment showed that the negative results of the tests in animals must be attributed to a much lower sensitivity of animals compared with that of humans against substances which influence the higher psychic functions. With the aid of the reliable test in human beings, which means that my colleagues and myself tested the extract fractions on ourselves, we succeeded to isolate the psychoactive principles of the mushrooms, and finally to purify and cristallise them.

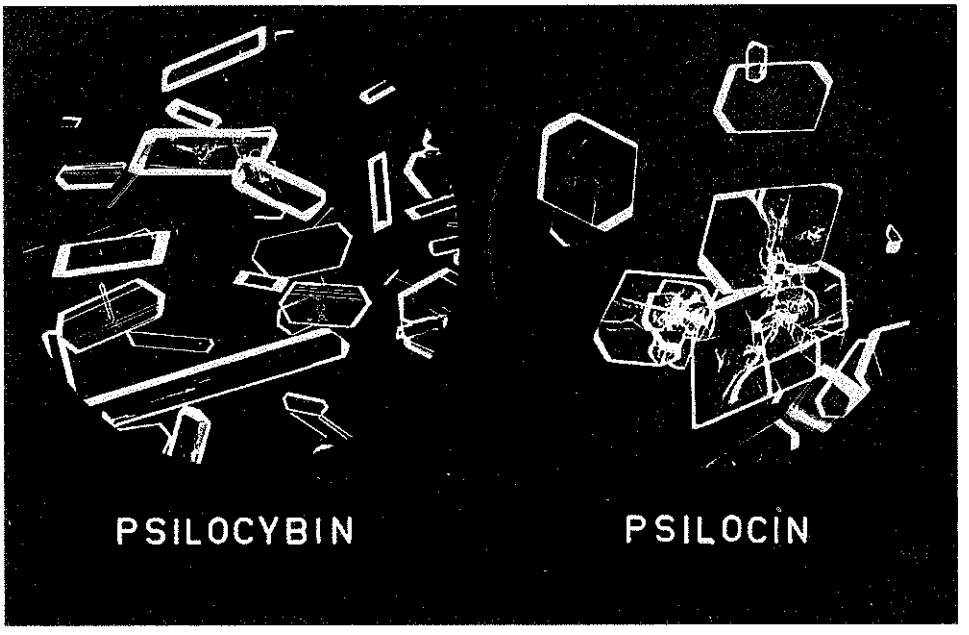

Fig. 3 - Psilocybin - Psilocin cristals.

The main active principle from the psilocybe mushrooms was called psilocybin and a second active substance, which occurs in lower quantity was named psilocin.

The extraction and isolation of psilocybin and psilocin was carried out with my laboratory assistant Hans Tscherter, and in the following elucidation of the structure and the synthesis participated my coworkers the Drs. A. Frey, H. Ott, Th. Petrzilka and F. Troxler.

Degradation studies and spectral data allowed to attribute to psilocybin and psilocin the structuralformulae represented in fig. 4.

Mild hydrolysis transformed psilocybin into psilocin and phosphoric acid. Psilocybin is the phosphoric acid ester of psilocin, of 4-hydroxy-N,N,-dimethyltryptamin, which means that the psychoactive principles of teonanacatl belong

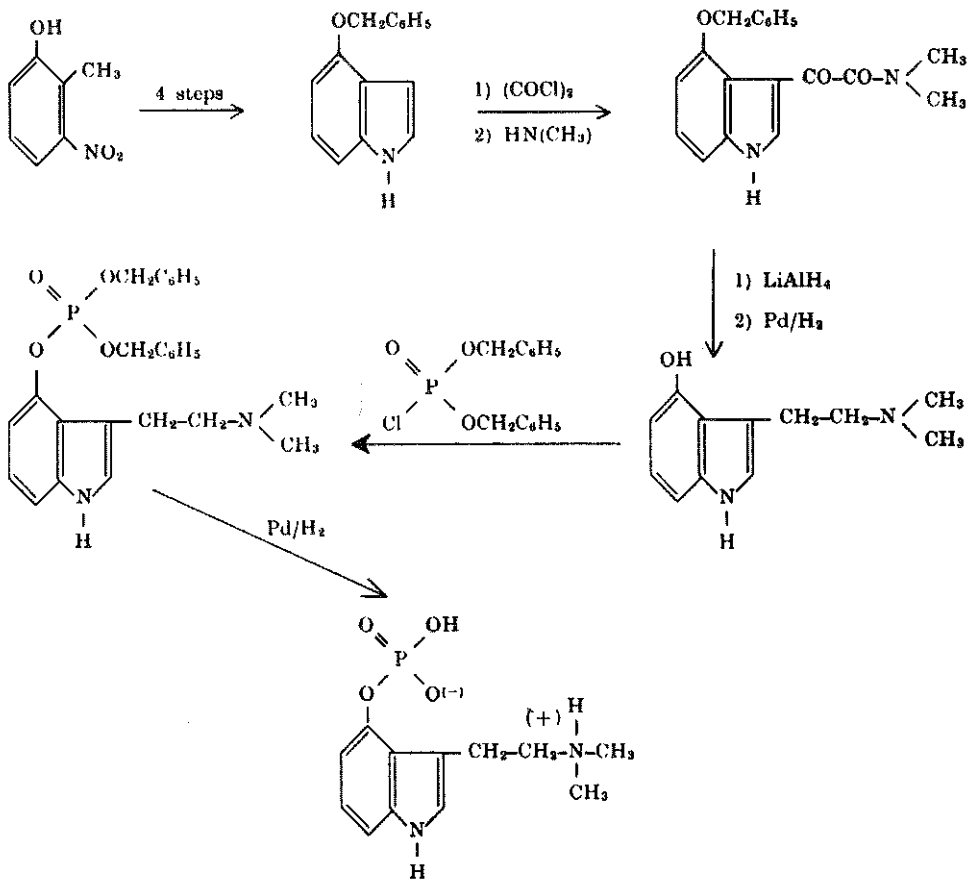

Fig. 4 - Synthesis of Psilocybin.

to the biological important class of indol, and more specific tryptamin compounds, widely distributed in the plant and animal kingdom. Psilocybin is novel inso far as it is the first natural indol compound which contains a phosphoric acid radical. Psilocybin and psilocin belong together with the ergot alkaloids to the rare natural indol compounds which are substituted in the 4-position of the indol skeleton.

These structural formulae of psilocin and psilocybin were confirmed by the totalsynthesis of these compounds. The scheme in fig. 4 demonstrates the procedure. The synthesis of psilocybin, which starts with o-nitrocresol comprises 10 stages. Psilocybin can be produced by this way in an industrial scale.

It was in this way that the mystery of Teonanacatl, the magic mushroom was solved. The substance that's magic effects led the Indians to believe for centuries that a god was residing in the mushroom, was identified and can even been prepared in glass flasks.

In later investigations psilocybin and psilocin have been detected also in mushrooms botanically related to the Mexican Teonanacatl species, e.g. in *Stropharia cubensis* Earle growing not only in Central America but also in Cambodia and Thailand, furthermore in North American *Psilocybe* species, namely in *P. pelliculosa* A. H. Smith, in *P. cyanescens* Wakefield, in *P. baeocystis* Singer and Smith. *P. semilanceata* occurying in Europe was found to contain the same quantity of psilocybin and psilocin as *P. mexicana*. Also *Copelandia cyanescens* Berk et Br. which grows in Indonesia and is cultivated in the island of Bali contains psilocybin and psilocin. The natives grow this mushroom on the excrements of cows and buffalos in their gardens. It is reported that they eat it at certain festivals and that they sell this mushrooms to foreigners travelling through the country. *Copelandia cyanescens* makes an exception among the other hallucinogenic mushrooms regarding the content of psilocybin and psilocin. Whereas in the *Psilocybe* mushrooms psilocybin represents the main constituent and psilocin is mostly found only in traces, the opposite is tru for *Copelandia*. The dried mushrooms of the *P.* species contain 0,2 to 0,4 percent of psilocybin and less than 0,1 percent of psilocin. In a sample of dried *C. cyanescens* we found 1,2 percent psilocin and 0,6 percent psilocybin.

Psilocin is a very unstable compoud, it is easely destroyed by the oxigen of the air which is due to its para-amino-phenolic structure. The phosphoric acid radical acts as a protective group.

Mental Effects

Psilocybin and psilocin produce psychic effects in man which are similar to those produced by mescaline or LSD. The medium oral dose is 10 mg, which elicits the same symptoms as the consumption of about 2 g of dried *P. mexicana* mushrooms.

The first analysis of the effects of psilocybin in man was made at the Psychiatric Clinic of the University of Basel and was based on personal studies carried out by several members of the staff of the Sandoz research laboratories. As a result of these and many others investigations, the effects of psilocybin, which are qualitatively identical with those of psilocin, can be described as follows: Oral doses of a few milligrams lead after 20 to 30 minutes to changes in the psychic sphere.

The psychic symptoms produced by small doses, up to 5 mg comprise effects on mood and environmental contact, in that there is frequently a subjectively pleasant sensation of intellectual and bodely relaxation and detachment from the environment. These effects are often associated with a pleasant feeling of physical tiredness and heavyness, but sometimes, by contrast, with a feeling of extraordinary lightness and bodely hovering. With higher doses, up to 10 to 20 mg, more profound psychic changes are prominent and are associated with alterations in spatial and temporal perception and with changes in the awareness of the self and body image. Visual and acoustic hypersensitivity is present and may lead to illusions and hallucinations. In this dreamlike state long forgotten memories, even such from early childhood, are often recalled. Visionary experiences and states of cosmic consciousness may also occur. The symptoms last 4 to 6 hours.

The development of «cross» tolerance between LSD and psilocybin supports the concept that these two substances cause psychic effects by acting on the same brain mechanisms.

The influence of mood and expectations of the subject on responses to psilocybin has been studied. It was found that positive expectations mostly lead to positive experiences; anxiety or preoccupation lead to unpleasant or even terrifying experiences. Unpleasant, depressed, anxious mood before the session results in general to an intensification of these states, as is the case with pleasant mood. Mystical and religious experiemces are often reported after respective expectations and in supporting surroundings.

Pharmacological Properties

Psilocybin does not exhibit typical effects on isolated organs (intestine, uterus, heart) with the exception of a pronounced inhibition of the effects of serotonin on these organs. On the entire animal however, it has characteristic autonomic effects, namely dilatation of the pupils, contraction of the nictitating membrane, piloerection, temperature increase. This is an ergotropic excitation syndrom, which results from a central stimulation of sympathetic structures. In the electroencephalogram an activation is detected which is characterized by a practically complete disappearance of the slow wawes.

A very characteristic effect of psilocybin is the enhancement of monosynaptic spinal reflexes, for example, the patellar reflex of cats.

The pharmacological effects of psilocin correspond amply to those of psilocybin qualitatively and, on molecular basis, also quantitatively, wich means that the phosphoric acid radical does not contribute to the pharmacological activity of psilocybin.

The toxicity of psilocybin in animals is very low in comparison to its effective dose in man. The LD_{50} for the mouse is 280 mg/kg, which means, that psilocybin is 2,5-times less toxic in this test than mescalin while it exhibits a 50-times higher psychedelic effect in man than this alkaloid.

Biochemical Data

Psilocybin is readily dephosphorylated by purified calf intestinal phosphatase to give psilocin and phosphoric acid, inorganic phosphate respectively. The same happens, if psilocybin is exposed to mammalian tissue homogenates. There is some evidence, that the effects in the central nervous system by psilocybin are only exerted after its transformation to psilocin.

Absorption, distribution, excretion and metabolism of psilocin in the rat were studied quantitatively with the C^{14}-labeled compound. Psilocin and its metabolites are excreted mainly in the urine, approximately 65% within 24 hours, whereas 15-20% appear in the bile and feces.

Medicinal Use of Psilocybin

Before closing my lecture some remarks on the use of psilocybin in psychiatry and in the drug scene.

Psilocybin has been used in the same way as LSD, as a pharmacological adjuvant in psychoanalysis and psychiatry. This use is based on the capacity of these substances to further the recollection of forgotten or repressed traumatic experiences and to improve the psychiatrist-patient relationship by the inhibition reducing effects of psilocybin. In brain research psilocybin is a useful tool due to its faculty to intervene in a specific way with neurotransmitters. This effect can be explained by the close relationship between the chemical structure of psilocybin and the neurotransmitter serotonin, which plays an important role in the biochemistry of the brain.

This promising medicinal application of psilocybin, like that of LSD, came to an end, when production, possession and use of psychedelic substances were prohibited by the international health authorities. This prohibition took place after these substances had found the interest of the drug scene, where they produced accidents and psychotic reactions due to uncautious, irresponsible application.

The Indians of Mexico still use the teonanacatl mushrooms, but they dont have drug problems. Respecting the deep, overwhelming mental effects of these mushrooms they have put a tabu on them. They remain in the hands of the curanderos o curanderas, the priestdoctors of the Indians. This attitude should also be ours. In the hands of the priest-doctors of our society, in the hands of psychiatrists and psychologists the teonanacatl medicine could find a convenient beneficial application.

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From these two standard publications references to other publications on the subject can be found.

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