Psilocybian Mycetismus With Special Reference To Panaeolus

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A SEQUENCE OF "PECULIAR" CASES

Mushroom intoxications have been noted throughout history. One 11th Century episode in Japan allegedly involved some Buddhist nuns who became lost in the forest. After eating some wild mushrooms, they felt compelled to dance. Some woodcutters who were also lost happened along, indulged in the peculiar fungus and joined the nuns in dancing. This tale has been handed down in the *Konjaku Monogatari* ("Tales of Long Ago") and the legendary toadstools became known first as dancing mushrooms *(maitake)* and later as laughing mushrooms *(waraitake)* (Sanford 1972; Wasson 1973). While the identity of the causative fungus is unknown, *Panaeolus papilionaceus* (Fries) Quélet has been suggested as one possible candidate (Sanford 1972; Wasson 1973). Sanford (1972) notes that Seichii in his *Genshoku Nihon kinrui zukan* (Icones of Japanese Fungi) quotes a 1917 episode from a newspaper article:

> Mr. Taniguchi (age 31), Mrs. Taniguchi [age 35], and Mrs. Taniguchi's brother, Buntsuke (age 41), treated themselves to two bowls of mushroom soup while the elder Mrs. Taniguchi (age 71) ate one bowl with only two or three mushrooms in it. They had hardly eaten when first Mrs. Taniguchi and then Mr. Taniguchi began to feel odd. Mr. Taniguchi then went next door to ask someone to fetch a doctor. When he got back home he found his wife dancing around stark naked, playing an imaginary *shamisen,* and laughing raucously. Even as he stood there amazed at all the uproar he found that he too was falling into the same crazed state. The older brother also eventually began to dance crazily. The intoxication of Taniguchi's mother was weaker, however, and though she became muddled she never lost complete control of her senses. She did, however, keep repeating the same words over and over and went to every house in the neighborhood apologizing throughout the night for "preparing such a poor meal" and thanking everyone "for putting up with it."

Dr. Seichii was "able to obtain samples of the mushrooms involved and solidly identify them as none other than *Panaeolus papilionaceus"* (Sanford 1972).

In 1816 a poor man gathered what he believed to be common ordinary meadow mushrooms in Hyde Park, London. Soon after commencement of his stewed mushroom meal, "he was, to use his own expressions suddenly seized with a dimness or mist before his eyes, lightness and giddiness of his head, with general trembling and sudden loss of power,—so much so, that he nearly fell off the chair; to this succeeded, loss of recollection; he forgot where he was, and all the circumstances of his case." Later it was observed that the patient "suffered much from giddiness, and was greatly inclined to sleep; his pulse was slow and feeble." The mushrooms were identified as *Agaricus campanulatus* Linnaeus, the cause of a similar case that had been reported in the September 1815 issue of *Gentleman's*

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Magazine (Glen 1816). *A. campanulatus* later become known as *Panaeolus campanulatus* (Fries ex Linnaeus) Quélet and its reputation of possessing sedative properties persisted into the 20th Century (McIlvaine 1973). Thus Krieger (1911) suspected this species to have caused an intoxication following ingestion of what the victim presumed were shaggy manes *(Coprinus comatus). Panaeolus papilionaceus,* in contrast, had gained quite a different reputation in North America (McIlvaine 1973):

> I have seen it produce hilarity in a few instances, and other mild symptoms of intoxication, which were soon over, and with little reaction. But I have seen, at table, the same effects from eating preserved peaches and preserved plums which had fermented. Many personal testings have been without effect. Testings upon others vary with the individuals. The fungus seems to contain a mild stimulant. It is not dangerous, but should be eaten with caution. Being of small size, and not a prolific species, quantities of it are difficult to obtain. Moderate quantities of it have no effect whatever.

In 1914, a classic case of psilocybian mycetismus occurred in Maine after Mr. W., a middle-aged avid mycophile, "strictly temperate in his habits," and his adult niece consumed mushrooms (perhaps a pound fresh weight) fried in butter and which he had identified as the butterfly *Panaeolus, i.e., P. papilionaceus* (Verrill 1914).

> Next, say about half an hour after eating, both of us had an irresistible impulse to run and jump, which we did freely. Soon both of us became very hilarious, with an irresistible impulse to laugh and joke immoderately, and almost hysterically at times. The laughing could be controlled only with great difficulty; at the same time we were indulging extravagantly in joking and what seemed to us funny or witty remarks. Mr. Y., who was with us, said that some of the jokes were successful; others not so, but I can not remember what they were about.

Later during the experience Mr. W.

> had a very disagreeable illusion. Innumberable human faces, of all sorts and sizes, but all hideous, seemed to fill the room and to extend off in multitudes to interminable distances, while many were close to me on all sides. They were grimacing rapidly and horrible and undergoing contortions, all the time growing more and more hideous. Some were upside down.

Eidetic imagery was very prominent as the

> faces appeared in all sorts of bright and even intense colors – so intense that I could only liken them to flames of fire, in red, purple, green and yellow colors, like fireworks.

Macropsia was also evident as Mr. W. felt his body "elongate upward to the ceiling. . .like Jack's beanstalk. . ." Soon he experienced his body collapse to its natural height. "The entire experience lasted six hours. No ill effects followed" (Verrill 1914).

In 1916, a *Panaeolus* species appeared in a New York mushroom house and surprisingly was consumed unnoticed amongst commercial *Agaricus.* Murrill (1916), believing this "dangerous" mushroom to be a new species, designated it *P. venenosus* Murrill. Shortly thereafter, Douglass (1917), a surgeon, described the experience resulting after his maid, wife, and he himself had eaten some *Panaeolus* (later determined by Murrill to be *P. semiglobatus* Murrill *nomen nudum)* gathered in a cucumber bed in Maine. Despite the fact that Douglass attempted management with intravenous morphine and atropine, he later concluded that the "pilzatropin" contained in *Panaeolus companulatus, retirugis, semiglobatus,* and *venenosus* produced symptoms that were "purely those of a stimulated nervous system" and could not "conceive that a full meal of these mushrooms could cause death" (Douglass 1917). Without citing any specific cases and apparently unaware of the mushroom poisoning classification proposed by Douglass, Ford (1973) coined the categorical term "Mycetismus Cerebralis" for this "peculiar poisoning" and mentioned *P. campanulatus* and *P. papilionaceus* as being responsible.

Reports of accidental *Panaeolus* poisonings have not been limited to Europe and the U.S. In the early 1940's a rash of such intoxications occurred in Australia. *Panaeolus ovatus* Cooke & Massee became known as the "hysteria fungus" since patients were sometimes admitted to the hospital after beginning "to feel numbness in arms and legs, to see coloured lights and to become almost hysterical" (Trotter 1944). One patient was quoted as having felt as if he "had been on a bender." Treatment generally consisted of administration of an emetic such as zinc sulfate and hospitalization was for never more than overnight.

In 1957, between a half and one hour after enjoying some little dung-inhabiting mushrooms, a victim of mushroom poisoning in Bremen, Germany began to notice "glimmers" before his eyes. Three attempts at vomiting were unsuccessful and he felt weak with occasional shortness of breath. He was hospitalized and

given charcoal in four glasses of water and an injection of apomorphine to induce vomiting. He received gastric lavage and intravenous fluids. After a two day stay, all was in order. The fungus responsible was identified afterwards as *P. papilionaceus* (Bull. ex Fr.) Quélet (von Neuhoff 1958).

In August, 1965, an important case was documented from the French Mediterranean (Heim; Hoffman & Tscherter 1966). It involved a woman and her two children (ages 11 and 14). After unsuspectingly eating a meal of *Panaeolus cyanescens* (Berkeley & Broome) Saccardo, the mother experienced terrifying hallucinations and was treated with gastric lavage and sedatives. While the elder child experienced visual echo patterns and was incapable of raising himself from an armchair, the younger convulsed and lost consciousness, thus exhibiting "an extreme neurophysiologic manifestation of the cerebral excitation syndrome" (Pollock 1974).

PANAEOLIAN CHEMO-TAXONOMY

On the basis of some of the preceding scattered reports implicating *Panaeolus* species as the provokers of cerebral mycetisms, the suggestion by Schultes (1939; 1940) that *Panaeolus campanulatus* Linnaeus var. *sphinctrinus* (Fr.) Bresadola (now considered to be a separate species, *sphinctrinus)* was the *teonanácatl* of the Aztecs seemed quite convincing. Ethnobotanical studies by the Wassons, Heim, and other collaborators, however, suggested that *Psilocybe* species, *Stropharia* cubensis Earle, and possibly even *Conocybe siligineoides* Heim, rather than *Panaeolus* were employed for magico-religious purposes (Heim, Wasson & Collaborators 1958). Guzmán (1959) even referred to *P. sphinctrinus* as the "false" *teonanácatl.* Nevertheless, the isolation of crystalline psilocybin from *P. sphinctrinus* mushrooms (RP1 strain) grown on compost certainly established the hallucinogenic potential of that species (Heim, Wasson & Collaborators 1958). Soon afterwards, Hofmann, Heim & Tscherter (1963) were not able to substantiate their findings by analysis of other samples of *P. sphinctrinus.* Unfortunately, neither the specimen sources nor herbarium reference numbers were cited in either study. Although serotonin (5-hydroxytryptamine) was found to be present in carpophores of *Panaeolus campanulatus* (Fr.) Quélet—from Washington and Idaho, *P. foenisecii* (Fr.) Kühner—from Washington and Michigan, *P. acuminatus* (Schaeff. ex Fr.) Quélet—from Washington, *P. fontinalis* Smith—from Michigan, *P. semiovatus* (Fr.) Lundell-from Michigan, *P. subbalteatus* (Berkeley & Broome) Saccardo—from Michigan, and *P. texensis* Tyler & Smith—from Texas; no 4-hydroxytryptamine derivatives such as psilocin were detected in these species (Wier & Tyler 1963; Tyler & Smith 1963). Later studies with Argentinian specimens of *P. sphinctrinus* also revealed the presence of serotonin but no 4-hydroxytryptamine derivatives (Tyler & Gröger 1964). One point was clear — *Panaeolus sphinctrinus* was certainly a "mystifier."

Ola'h (1970) thus undertook a systematic study of the genus *Panaeolus,* chemically analyzing various samples which consisted of: a) wild carpophores, mycelia and carpophores obtained in culture; b) wild carpophores and mycelia; c) mycelia and carpophores obtained in culture; or d) mycelia only. This investigator assayed twenty-three samples of *P. sphinctrinus* twenty of which were from Quebec and one of which was the RP1 strain, revived from spore after seven years. Thirteen samples, including mycelia of the RP1 strain, were found to contain psilocin and seven of these also contained psilocybin. Five samples of *P. foenisecii* (four from Quebec and one from Paris) were studied chemically. Two from Quebec contained both psilocin and psilocybin, whereas the one from Paris and one of the two other Quebec samples contained psilocin. Of ten samples of *P. fimicola* (Fr.) Quélet, five were found to contain both psilocin and psilocybin. A smmple of *P. microsporus* Ola'h & Cailleux was shown to produce psilocin but not psilocybin in carpophores derived from culture and neither compound was detected in the mycelia. This characteristic was transmitted into two successive generations also studied. A sample of *P. castaneifolius* (Murr.) Smith from Quebec contained psilocin in the wild carpophores, mycelia and carpophores obtained in culture, but psilocybin occurred only in the mycelia. This same pattern was found also in the next generation of this sample. Four samples of *P. africanus* Ola'h were capable of synthesizing psilocin and psilocybin in the mycelial stage and one of these was shown to produce psilocin in carpophores from culture. Because of these irregularities in psilocin and psilocybin biosynthesis, *P. africanus, castaneifolius, fimicola, foenisecii, microsporus,* and *sphinctrinus* were classified as "latent psilocybian" species (Ola'h 1969; Ola'h 1970).

A sample of *P. ater* (Lange) Kühner & Romagnesi from the East Indies was found to contain psilocin and psilocybin in mycelia and carpophores obtained in culture. Wild carpophores were not chemically examined and these findings were consistent in the next generation. Four samples of *P. cambodginiensis* Ola'h & Heim, consisting of mycelia and fruiting bodies from culture, contained both psilocin and psilocybin. Both of these indoles were also detected in wild carpophores, mycelia and carpophores from culture of *Panaeolus cyanescens* (Berkeley & Broome) Saccardo from

Menton, France and an additional source. The same pattern was observed also in the next generation of the Mediterranean source. A sample of *P. subbalteatus* (Berkeley & Broome) Saccardo from Quebec was determined to possess both psilocin and psilocybin in wild carpophores and mycelia from culture. Likewise, *subbalteatus* from Paris synthesized psilocin and psilocybin in the mycelia, and psilocin was found in wild carpophores of that sample (data on psilocybin not presented for those carpophores). Neither psilocin nor psilocybin could be detected in mycelial cultures of *subbalteatus* from two other sources, one of which is the American Type Culture Collection. Three samples of *P. tropicalis* Ola'h were found to contain psilocin and psilocybin in wild and cultivated carpophores and mycelia. As a result of these findings, Ola'h (1969; 1970) placed *P. ater, cambodginiensis, cyanescens, subbalteatus* and *tropicalis* in the category of frankly "psilocybian."

Three samples of *P. acuminatus* (Schaeff. ex Fr.) Quélet were negative for psilocin and psilocybin. Seven samples of *P. campanulatus* (Fr. ex L.) Quélet were also found to be negative for psilocin and psilocybin. One sample of *P. leucophanes* (Berkeley & Broome) Saccardo and its next generation were also lacking psilocin and psilocybin. Mycelia and cultivated carpophores of two samples of *P. retirugis* (Fr.) Quélet and their next generations were negative for psilocin and psilocybin as was one sample of *P. semiovatus* (Fr.) Lundell & Nannfeldt. These species were thus classified as "non-psilocybian." *P. fontinalis* Smith, *fraxinophilus* Smith, *guttulatus* Bresadola and *phalaenarum* (Fr.) Quélet were also included as "non-psilocybian" since there were no reports alleging hallucinogenic effects from these species (Ola'h 1969; Ola'h 1970).

Since the completion of Ola'h's monograph, additional studies have been reported on the chemistry of *Panaeolus* species. Psilocybin has been detected (0.08 percent dry weight) in an Italian collection of *P. retirugis* (Fiussello & Ceruti Scurti 1971-1972). Psilocybin has also been detected in Italian collections of *P. foenisecii* (one of two samples), *subbalteatus* (one sample) and *campanulatus* (one sample) (Fiussello & Ceruti Scurti 1972). Furthermore, psilocin has been detected in two Italian collections of *P. cyanescens* and psilocybin in one of these (Fiusselo & Ceruti Scurti 1972). Mycelia and cultivated carpophores of Italian *P. subbalteatus* have been shown to be capable of producing psilocybin (Ceruti Scurti, Fuissello & Jodice 1972). One Italian collection of *P. guttulatus* and *P. sphinctrinus* lacked psilocybin and psilocin (Fiusselo & Ceruti Scurti 1972) and a collection of Czechoslovakian *P. campanulatus* was devoid of these indoles (Semerdzieva & Nerud 1973). Finally, an additional sample of *P. foenisecii* from Quebec was reported to be positive for psilocybin, and although a sample of carpophores of this species from Washington was determined to be devoid of psilocybin, this indole was detected in carpophores of *foenisecii* from Indiana (0.17 percent dry weight) (Robbers, Tyler & Ola'h 1969).

Since *P. venenosus* was known only, sometimes in great numbers, from mushroom-growing houses in New York, the "problem of its origin or occurrence in the wild state" was unresolved (Levine 1919). *P. venenosus* Murrill has been determined to be conspecific with *P. subbalteatus* (Berk. & Br.) Sacc. (Ola'h 1970; Singer & Smith 1958a), but the true identity of *P. semiglobatus* Murrill has been a mystery. Despite the fact that type material was described as *Campanularius semiglobatus* Murrill from New York (growing on manure in 1910 in Murrill's garden) (Murrill 1911; Saccardo & Trotter 1925), and that this species was later cited as occurring in Virginia (Murrill 1920), contemporary mycologists seem to have been unaware of these reports and suggested the causative species of the intoxication described by Douglass (1912) may even have been a *Stropharia* (Heim 1958; Ola'h 1970; Tyler & Smith 1963). The type material was thus obtained, examined microscopically by Ott and the author and determined to be *P. subbalteatus*. A professional mycological determination was then kindly provided by Guzmán stating that *P. semiglobatus* is conspecific with *P. subbalteatus*. Although *P. subbalteatus* may have a rubescent tinge (hence once even described as *P. rufus* Overholts), it is quite variable in color and morphology (on one occasion even cited as *P. variabilis* Overholts). Some strains mimic *P. papilionaceus*. Although various authors still refer to this "butterfly" *Panaeolus* as a distinct species (Ceruti Scurti & Bianco 1973; Guzmán 1972), Ola'h (1970) regards *papilionaceus* to be conspecific with *P. campanulatus*. The single citing of psilocybin in *campanulatus* by Fuissello and Ceruti Scurti (1972) has not yet been verified and it is certainly possible that the collection may have contained more than one species. Thus there is great probability that at least some intoxications attributed to *P. papilionaceus* or *P. campanulatus* were actually due to *subbalteatus* or other closely related species such as *sphinctrinus*.

The true identity of *P. ovatus* Cooke & Massee remains unknown. The only researchers to have studied the problem seem to be Aberdeen and Jones (1958) who state that "a detailed examination of *Panaeolus ovatus* Cke. & Mass. showed it to be closely related to, and possibly identical with *Anellaria sepulchralis* (Berk.)

Sing." which is generally considered "edible." *A. sepulchralis* is believed by Ola'h (1970) to be identical with *Panaeolus phalaenarum* (Fries) Quélet for which no chemical studies have been reported. It is possible that Aberdeen and Jones collected *P. phalaenarum* rather than *ovatus,* for *phalaenarum* had been cited from Australia in *Grevillea* even before the original description of *ovatus* (Cooke 1889). A more recent description of *ovatus* by Cleland (1934) is still insufficient in microscopic detail to be useful in distinguishing between the two species. The problem is further complicated by the fact that *A. sepulchralis* may be conspecific with *P. antillarum* (Fr.) Dennis rather than *P. phalaenarum,* if these latter two species are really distinct (Guzmán 1972). It may very well be that *Panaeolus cyanescens* was the cause of at least some of the intoxications attributed to *P. ovatus.* It was only quite recently, in fact, that the presence of *P. cyanescens* in Australia was first noticed (Hall 1973) and now it is known to be widespread there (Southcott 1974).

The biosynthesis of psilocin and psilocybin are enzyme mediated and the enzymes involved would be expected to have both genetic and environmental regulation. From the limited data available in case reports, chemical studies and metabolic considerations pertaining to psilocin (to be discussed in the next section), it appears that the frequency of genes allowing psilocin and psilocybin biosynthesis within some *Panaeolus* species, such as *foenisecii* and *sphinctrinus,* may vary greatly from one population to the next, whereas for other species such as *cyanescens* the complex of psilocybian alleles appears to be relatively stable and consistent. *Panaeolus* has long been a difficult problem for the fungal taxonomist and under the classification by Ola'h (1970) there are notable inconsistencies. The genus is basically divided into two subgenera: *Eu-Panaeolus* and *Pseudo-Panaeolus.* But even in the "true" *Panaeolus* there are species without pleurocystidia such as the "psilocybian" *subbalteatus,* the "latent psilocybian" *sphinctrinus,* and the "non-psilocybian" *acuminatus* as well as species with these facial cystidia such as the "psilocybian" *ater* and the "latent psilocybian" *fimicola.* In the "false" *Panaeolus* there are species such as the "psilocybian" *cyanescens,* "latent psilocybian" *foenisecii* and "non-psilocybian" *semiovatus.*

A more recent classification by Guzmán (1972), based on microanatomical characteristics, recognizes four subgenera. A chemotaxonomic classification, nevertheless, might be of greater utility in view of modern interest in psychoactive fungi. It is thus proposed that those *Panaeolus* species which are capable of synthesizing psilocin and/or psilocybin be considered as belonging to Section *Copelandia* Pollock, *sectio nov.* of the genus *Panaeolus* (Fries) Quélet. This section includes species with various probabilities of possessing these 4-hydroxytryptamine derivatives: a) high probability – *cyanescens* (Berkeley & Broome) Saccardo, *cambodginiensis* Ola'h & Heim and *tropicalis* Ola'h b) intermediate probability – *subbalteatus* (Berkeley & Broome) Saccardo and *ater* (Lange) Kühner & Romagnesi; and c) low to moderate probability – *africanus* Ola'h, *castaneifolius* (Murrill) Smith, *fimicola* (Fries) Quélet, *foenisecii* (Fries) Kühner, *microsporus* Ola'h & Cailleux, *sphinctrinus* (Fries) Quélet, *retirugis* (Fries) Quélet and *campanulatus* (Fries ex Linnaeus) Quélet. Those species with a high probability of possessing 4-substituted indole hallucinogens comprise Guzmán's subgenus *Copelandia,* whereas those which appear to have "intermediate" probability of containing these compounds fall into his subgenus *Panaeolus.* Those with low to moderate probability of producing hallucinogenic constituents are found in Guzmán's subgenera *Anellaria (africanus), Panaeolina (foenisecii)* and *Panaeolus.* Species not included in Section *Copelandia* would be expected to have very low or unknown probability of producing psychotropic 4-substituted indoles.

THE BLUING PHENOMENON AND OTHER METABOLIC CONSIDERATIONS

"The blue color of the sclerotia and of the base of one single specimen" of *Panaeolus subbalteatus* appeared "to be of the same nature as the bluing in *Copelandia cyanescens* (Berk. & Br.) Sing." *(Panaeolus cyanescens)* "and the bluing *Psilocybes"* (Singer & Smith 1958a). Thus Singer and Smith surmised:

> If this assumption is correct, it must become quite clear that a direct or indirect relation must exist between the bluing capacity of a species and its capacity to provoke cerebral mycetisms. On the basis of this hypothesis it is actually possible to predict which genera and species might be significant for the research on cerebral mycetisms of the type represented by *Panaeolus subalteatus [sic]* and *Psilocybe caerulescens.*

It seems that Guzmán may have contributed to the origin of this bluing hypothesis, for Singer (1958) related "that there are a *Psathyrella* and copelandias from Santa Cruz which Guzmán, who collected them there, is inclined to think may be hallucinogenic." While *Psathyrella sepulchralis* Singer, Smith & Guzmán does not blue and was probably confused by some Zapotecs

with *Psilocybe zapotecorum* (Singer, Smith & Guzmán 1958). Singer (1962) soon began to refer to the Copelandia *(Panaeolus cyanescens),* an ardent bluer, as "apparently hallucinogenic."

While the bluing reaction has not been studied in hallucinogenic mushrooms *per se,* a number of studies shed light on this phenomenon. Blaschko and Levine (1960a) found that the gill plates of the mussel *Mytilus edulis* Linnaeus possess an enzyme which readily converts psilocin to a blue product with the consumption of oxygen. This reaction occurs more rapidly with psilocin (4-OH-N,N-DMT) than with either its 6-hydroxy isomer or 5-hydroxy isomer bufotenin. Since it was known that both the bivalve molluscan enzyme and ceruloplasmin, a copper containing oxidase of mammalian plasma, could utilize 5-hydroxytryptamine (serotonin) as a substrate, Blaschko and Levine (1960b) performed a comparative study. Both the *Mytilus* enzyme and ceruloplasmin from pig plasma convert psilocin and 4-hydroxytryptamine to a blue product, whereas bufotenin and its 6-hydroxy analog as well as serotonin, 6-hydroxytryptamine and 7-hydroxytryptamine are oxidized to brown pigments. Some important differences in the two enzyme systems were also noticed. For instance, whereas the mollusk enzyme could also utilize 4,5 and 7-hydroxytryptophan (the former yielding a blue pigment and the latter two brown pigments), these amino acids were not suitable substrates for porcine ceruloplasmin.

When Horita and Weber (1961a) were studying the dephosphorylation of psilocybin by alkaline phosphatase of various mammalian tissues, they discovered that in some of their preparations, especially heart and kidney, the liberated psilocin was oxidized so rapidly to a blue metabolite that they were unable to measure the formation of psilocin. By inhibitor studies and the tissue distribution of the oxidase activity, they were able to conclude that monoamine oxidase, an enzyme very important in serotonin and dopamine metabolism, was not the enzyme acting on psilocin.

Weber and Horita (1963) then determined that cytochrome oxidase, a mitochondrial enzyme, is responsible for the rapid oxidation of psilocin by tissue homogenates. Using a preparation of cytochrome oxidase derived from pig heart, these investigators found that while psilocin is oxidized to a dark blue product and the synthetic hallucinogen 4-hydroxy-N,N-diethyltryptamine to a bluish-green metabolite, 4-hydroxytryptamine becomes a blackish-brown pigment. Bufotenin, 5-hydroxytryptamine and 5-hydroxytryptophan are converted to brown compounds. Furthermore, "the 4-hydroxyindoles are consistently better substrates for the cytochrome oxidase than are the 5-hydroxyindoles" (Weber & Horita 1963).

Kalberer, Kreis & Rutschmann (1962) synthesized ^{14}C-psilocin and studied its *in vivo* metabolism in rats. After oral or intravenous administration of 10 mg/kg psilocin, at least 80 percent of the radio-psilocin was excreted during the first 24 hours. About 25 percent of the psilocin was passed unaltered in the urine and only about 4 percent underwent demethylation and subsequent oxidative deamination to 4-hydroxyindoleacetic acid. The largest portion of urinary metabolites were unidentified non-glucuronide hydrophilic substances.

In vitro studies with purified calf intestinal phosphatase and homogenates of brain, heart, kidney, liver and small intestine from various mammalian species have shown that psilocybin is an excellent substrate for alkaline phosphatase (Horita & Weber 1961b). Additional studies have shown that psilocybin is rapidly dephosphorylated *in vivo* in mice (Horita & Weber 1962). Furthermore, pretreatment with β-glycerophosphate, a competitive substrate for alkaline phosphatase, not only diminished tissue concentrations of psilocin but also "reduced the intensity of the reaction as compared to normal mice treated with psilocybin (Horita & Weber 1962). Parallel measurements of psilocybin tissue concentrations were not attempted due to lack of a suitable assay (Horita 1975). Depression, exophthalmos, piloerection and some hindleg ataxia were noted as major symptoms of the psilocybian reaction in mice. These studies along with some ancillary observations, such as the lipid solubility of psilocin being greater than that for psilocybin, strongly suggest that psilocin is the pharmacologically active metabolic form of psilocybin (Horita 1963).

Returning to the bluing phenomenon, Gilmour and O'Brien (1967) noticed that a subfraction of rat brain mitochondria produced a dark blue color in the presence of psilocybin with prolonged incubation and that oxygen was not required. This as pointed out by Levine (1967) resulted from the action of a phosphatase liberating psilocin and a subsequent oxidation by the ferric ions present, for among other considerations the chelating agent EDTA markedly inhibited the production of the blue color. Bocks (1967a) discovered that *para*-diphenol oxidase (laccase) derived from the fungus *Polyporus versicolor* is capable of oxidizing psilocin to a blue product which has a similar ultraviolet spectrum to the compound obtained by ferric chloride oxidation of psilocin.

Laccases, first isolated from lacquer trees and responsible for the blackening of lacquer tree juices, possess certain properties similar to ceruloplasmin

("animal laccase"). For instance, they are copper-containing and share many substrates such as *para*-phenylenediamine and hydroquinone (Peisach & Levine 1965). An unusually stable laccase has been isolated from a mushroom known as *Russula foetens* (Gregg & Miller 1940). In addition to acting on usual substrates, this *Russula* enzyme has been demonstrated to catalyze the oxidation of an inorganic salt, potassium ferrocyanide (Gregg & Miller 1940). Laccase is essentially a *para*- diphenol oxidase in contrast to the copper containing phenolase complex (tyrosinase), which not only is responsible for *ortho*-hydroxylation of phenols but also is an *ortho*-diphenol oxidase (Mason 1955). Furthermore, *para*-diphenol oxidases are blue copper proteins in which there is a valency change in the copper from 2^+ to 1^+ during the oxidation of substrates, whereas *ortho*-diphenol oxidases are colorless with the copper remaining at 1^+ valence and thus suggesting a different mechanism of action (Bocks 1967b). Nevertheless, there is some overlapping of substrate specificity. The *Russula* laccase as an example may oxidize catechol "at nearly the same rate as *p*-phenylenediamine and hydroquinone" (Gregg & Miller 1940). *Para*-cresol and catechol have been routinely used to measure the aerobic oxidation of monohydric and *o*-dihydric phenols by tyrosinase. It is noteworthy that these two activities have been partially separated in enzyme preparations derived from the common commercial edible mushroom (Adams & Nelson 1938; Mallette & Dawson 1949; Mallette *et al.* 1948) *(Psalliota campestris* as it used to be called in Europe, *Psalliota bispora* as it is now called in Europe and *Agaricus bisporus* as it is now usually called in the Americas).

Furthermore, a mycelial extract of the commercial mushrooms was shown to catalyze the oxidation of *p*-phenylenediamine at about twice the rate as that of catechol and an extract from carpophores of this mushroom oxidized catechol but not *p*-phenylenediamine. Rhizomorphs ("stings of hyphae which transport substances from the absorbing mycelium to the fruitbodies") catalyze the oxidation of both *p*-phenylenediamine and catechol, the latter more rapidly (Lindeberg 1950). It was suggested that the oxidation of the catechol was partly due to laccase and partly to polyphenoloxidase (tyrosinase). Thus the mycelia may produce laccase and the carpophore a tyrosinase, "whereas in the rhizomorphs a mixture of both enzymes is formed" (Lindeberg 1950).

Adventitious browning is well known to occur in the flesh of certain ripe fruits (such as apples, pears and avocados) and some vegetables (such as eggplant) as well as in the hyphae of mushrooms following injury during harvesting, storage or preparation for the table. This rapid browning seems to result from the oxidation of endogenous phenols catalyzed by enzymes having laccase and phenolase activity, but other enzymes such as peroxidases and catalases, which require the presence of hydrogen peroxide for activity, might also make a contribution (Mason 1955). The bluing reaction most likely is mediated by the same enzymes.

Singer (1948) first observed that the bluing reaction of *Stropharia cubensis* Earle could be enhanced by the use of metol *(para*-methylaminophenol). He later stated that "a chemical character which accompanies the bluing phenomenon is that of metol, which gives a constant strongly positive reaction with the context of the stipe in the bluing psilocybes, becoming deep purple after a few minutes" (Singer 1958). Although the "metol test" later became popularized for the rapid identification of psilocybian mushrooms (Enos 1970), it is entirely nonspecific. I have applied small aliquots of a fresh saturated solution of *p*-methylaminophenol sulfate to sections of the brown and white varieties of commercial *Agaricus bisporus* and observed the rapid development of purple staining. A simultaneous experiment was run employing *p*-aminophenol sulfate which promptly produced dark brown staining. After about 5-10 minutes, a purple tinge could be observed on these darkened mushroom pieces. Both compounds eventually produce a blackish-brown discoloration. Controls brown very slowly and the color is not as intense. *Para*-aminophenol is a known laccase substrate (Peisach & Levine 1965) and *p*-methylaminophenol must also serve as a substrate for such phenol oxidases.

MODERN USE OF PANAEOLUS MUSHROOMS

The recreational and spiritual use of psilocybian mushrooms has become a worldwide transcultural phenomenon (Pollock 1975). Although much new information has been gathered on the use of cyanescent *Stropharia* and cerulescent *Psilocybe* species, the present discussion will focus primarily on *Panaeolus.*

The most widely utilized *Panaeolus* appears to be the coprophilous *P. cyanescens.* This predominantly tropical species, commonly called a "copelandia" and originally described from Ceylon, is also known from the Philippines *(Copelandia papilionacea* sensu Bresadola), Indonesia, Australia, Cambodia, Malagasy Republic, Florida *(Campanularius westii* Murrill), Mexico, Jamaica *(Panaeolus anomalus* [Murrill] Sacc. & Trott.), Hawaii, Brazil, Bolivia and even as far north as France and Italy. The author has received personal communications suggesting the use of this species in Chiapas, where

Panaeolus cyanescens is a common psilocybian species. By the fall of 1972, it had become obvious to college students that psilocybin mushrooms were abundant in Florida (Kimbrough 1975) and word-of-mouth stories told of fraternity parties with bushel-basket quantities of magic fungi. With a widespread reputation that "Gainesville is Kingsville" for psilocybin mushrooms, it is entirely possible that some mycophagists sampled *Panaeolus cyanescens* in addition to the ubiquitous *S. cubensis* Earle. By 1972, the use of this cyanescent *Panaeolus* had become well established in the Hawaiian Islands (Pollock 1974) and it appears that other psychoactive fungi might occasionally be employed there as well. For instance, *Panaeolus tropicalis,* a species reported on dung of cattle and wild animals from Cambodia, the Republic of Central Africa and Mexico, has now also been identified from Hawaii (Rhoades 1975). During recent field studies in the Pacific Northwest, it came to the author's attention that a few years ago entrepreneurs in Hawaii exported some small psilocybin mushrooms (probably *Panaeolus)* on dry ice to an eagerly awaiting California street market. It seems that this psychotropic merchandise had spoiled and lost activity due to delays in unloading and distribution. Although knowledge that drying is the best way to preserve these mushrooms had not generally reached the public, folk knowledge that the mushrooms could be stored for short periods of time in honey was available in Hawaii and elsewhere. Thus, the mushrooms were allegedly exported in honey with satisfactory results, except perhaps for the taste which was quite unpalatable to the consumer from whom this information was elicited.

Bali, Indonesia has gained a worldwide reputation as an exotic mushroom paradise. Almost three years ago a former Peace Corps worker who had traveled to Bali recounted to the author her experience after a psychedelic mushroom omelet, the mushrooms having been purchased from native children on the beach. Although Heim (1973) suspected the use of *Panaeolus cyanescens* in Bali after a report from a Dutch correspondent, no specimens were available. Recently, however, a sample from Bali arrived in Mexico containing carpophores of a yet unidentified *Conocybe* species and *Panaeolus cyanescens* (Ott 1975). The Caribbean has also become quite a mushroomic Elyseum. In Jamaica, for example, island inhabitants eagerly collect and dry magic fungi to brew in delectable teas for personal use and to sell to mycophilic tourists. *Panaeolus cyanescens* is certain to be one of the species utilized.

"Copelandias" are now often collected, utilized and sometimes even sold for their psychedelic effects in Australia, where users refer to them as "blue meanies" (Southcott 1974). This name may refer not only to their bluing, but also to their potency. It has been said "that about six of the blue meanies were enough for a good trip, and they were sometimes eaten straight, or in curry, etc." (Southcott 1974). A case has been cited in which a 17 year old female "with a history of use of cannabis and LSD, on one occasion, about 1971, partook of some *Copelandia cyanescens* obtained in the vicinity of Adelaide. She became frightened when her hallucinatory attack came on and sought medical attention. She stated that she thought she was a banana and somebody was skinning her" (Southcott 1974). Despite the growing use of *Panaeolus cyanescens,* it appears that "Gold Tops" (a composite term for *S. cubensis* Earle, *Psilocybe subaeruginosa* Cleland and presumably also *Psilocybe collybioides* Singer and Smith [Southcott 1974]) are more widely employed in Australia (Hall 1973; McCarthy 1971; Southcott 1974).

Panaeolus cambodginiensis, another coprophilous species, had been known only from Cambodia. Material originating from Colombia in June, 1974 had been tentatively identified by Ola'h as the same species (Pollock 1975). Guzmán has now established the identity of this species as *cambodginiensis.* With mushroom consciousness as high as it is in Colombia, chances are good for the occasional use of this fungus.

Panaeolus subbalteatus was first described as collected in a tare field in Apethorpe, England in 1860 and was next observed in the botanical garden in Brussels, Belgium. Although this coprophilous and occasionally terricolous species had been noted from additional sites in Europe, Massachusetts, Michigan, Missouri, Ohio, Ontario, New York, Quebec and Washington; as well as from Mexico, Argentina, Japan and Africa, no deliberate nonmedical use of this fungus for the alteration of consciousness has been reported. In the last few years many people in Oregon have become very much aware of the presence of psilocybian mushrooms (Ott in publication; Weil 1975). Liberty Caps have become well known on rich pasture land soil, for it has been observed by the author that herbarium collections from all over Oregon were identified by Alexander Smith as *Psilocybe semilanceata.* It is possible, however, that Smith was confusing this species with *Psilocybe pelliculosa* (Smith) Singer and Smith. Unfortunately, disrespectful mycophagists have stolen all of this material from the herbarium in question, and it is not possible to verify his identifications. Another species widely employed is a *Panaeolus* which occurs not only in the garden (on manure) but also on composting

hay piles. Mycologists in Oregon examined such specimens and identified them as *Panaeolus subbalteatus* (Denison 1975; Rhoades 1975). It seems that there is another coprophilous *Panaeolus* which is much less frequently employed in Oregon. Users had supposedly been ingesting up to 250 carpophores of a species which was later determined by chemical analysis to contain traces of psilocybin and identified by Guzmán as *Panaeolus sphinctrinus* (Ott 1975). This latter species is cosmopolitan. It is probably ingested deliberately in Colombia where unfortunately like elsewhere the standard cliché is "if it grows on cow dung, it is hallucinogenic." A trial by the author of a soup containing 50 specimens of *P. sphinctrinus* gathered in Texas was without noticeable psychic effects, a sample of this collection later having been identified positively by Guzmán.

Although indications are that *Panaeolus campanulatus* may be generally "inactive," it seems to be employed in southern California where 40 to 60 little brown lawn mushrooms are said to constitute a dose. Lawn inhabiting *Panaeolus* is usually foenisecii but the identity of a sample of such material obtained by the author has been determined by Guzmán to be *P. campanulatus* sensu Hora. The extent of its use elsewhere has not yet been ascertained.

Panaeolus ater, originally described from Denmark as a variety of *P. fimicola,* has also been reported elsewhere in Europe and from the East Indies. Alaskan herbarium material, one collection of which had been tentatively identified by Kempton as *Panaeolus ater,* was obtained by the author for further study. Guzmán has now keyed out not only a 1963 southcentral Alaskan collection from a grassy area in mixed woods but also another collection from Anchorage as *Panaeolus ater.* No bluing was noted when the Alaskan specimens of *ater* were collected (in contrast to *P. ater* from the East Indies). Thus, aside from being rare, the Alaskan strains may be inactive. Furthermore, although authenticated *P. foenisecii* and *P. sphinctrinus* were found by the author to be quite common on lawns and soil enriched with horse dung in Anchorage, there has been no indication of attempted use of these inconsistently psilocybin-containing species by the Alaskan populace. Nevertheless, it seems that psilocybin mushrooms are sometimes employed even as far north as Alaska since the author was told of an occasion in which dried, yellow-colored magic mushrooms sent from Louisiana were enjoyed there. The mushrooms in that instance presumably were *S. cubensis,* a species so plentiful in Louisina and other Gulf Coast states that it served as the basis for a bogus field guide (Ghouled 1972). That publication, like others (Enos 1970; Fisher 1973) of its kind, was filled with misinformation. Ghouled (1972) even referred to a photograph of *cubensis* primordia as depicting the "young state of *Pn. subbalteatus.* Choice and edible." Furthermore, Jacobs (1975) who suggests in a medical journal that "Mississippi and adjacent states are rapidly receiving a reputation in the drug culture as the 'mushroom capital' of the United States," believes that *Panaeolus subbalteatus* is "the second native hallucinogenic mushroom" in Mississippi. He based his identifications and much of his misinformation on Ghouled's misleading guide.

It has been alleged by Sanford (1972) that "a rather well known mycologist in the Boston area has seen *Panaeolus papilionaceus* deliberately gathered in both Maine and Louisiana. Interestingly enough, in the case of New England, it was thrifty farmers taking advantage of an opportunity to get 'drunk for nothing,' while in Louisiana the gatherers were rather more modern sophisticates looking for a psychedelic thrill." The psychoactive mushrooms eaten in Louisiana probably were not *Panaeolus* at all but rather *S. cubensis,* whereas in Maine *Panaeolus* does seem to be employed. Blackington (1958) describes an experimental trial of *Panaeolus papilionaceus* by Brother Bacon of Norway, Maine to achieve a"mental jag." The results of the first "tasting were so unusual, Mr. Bacon ate them many times again." It has also been reported in a Maine newspaper that a group of French Canadian fishermen consumes *Panaeolus campanulatus* for its intoxicating properties when they fish in Maine, the identification having been provided by a state botanist (Schultes 1974). Bacon's amateur identification was based on McIlvaine's *One Thousand American Fungi* which is entirely inadequate for *Panaeolus* identification and it is not known what guide was employed in the latter identification. It is noteworthy that Wasson (1974), who was, of course, interested in the use of *Panaeolus* in Maine, could not extract a letter from Blackington. Most likely the *Panaeolus* employed there is *subbalteatus,* but other species such as *sphinctrinus* and *fimicola* are possibilities as well.

THE TRIP BEYOND ECSTASY: PSYCHO-MYCOLOGICAL FRONTIERS

When a mind-altering substance is suddenly unleashed on a population already accustomed to using an array of psychoactive compounds, mass media may foster a rampant escalation of use. Such was the case with methaqualone, once heralded as a "downer with a difference," for "luding out" rapidly became a popular pastime in the United States (Agar 1972). The overall

recreational use of methaqualone, however, soon declined. The use of psilocybian mushrooms for ecstatic experiences, in contrast, generally continues to become incorporated into the fabric of modern society.

When Hofmann traveled to Huautla de Jiménez, where these mushrooms have been traditionally employed since ancient times, the renowned *curandera* María Sabina enthusiastically accepted his offering of manufactured psilocybin (Kreig 1964), but after a synthetic dose she did not seem to prefer the tablets to the mushrooms themselves (Wasson 1976). Mass media reports have greatly stimulated public consciousness of these fungi. But in technologically advanced societies, where psychotropic substances of all sorts can be purchased illicitly (usually in adulterated form) from street markets, genuine hallucinogenic fungi have usually not been available. Although wild psilocybian mushrooms are much more widespread than ever appreciated, interested persons have by and large gradually had to learn how to recognize the locally available species. Tourists have been traveling to Huautla for a long time, and the resemblance of Liberty Caps to *Psilocybe mexicana* Heim could not have gone unnoticed in such areas as British Columbia.

Misinformation has surrounded psychedelic mushroom use in British Columbia as well. Liberty Caps have been employed there since the early 1960's, despite later misnomers that in Canada "several varieties of psilocybin mushrooms" growing untended "would appear" to "have been ingested by only a few exceptional experimenters" (Canadian Report 1973). From Vancouver to the Queen Charlotte Islands the use of Liberty Caps has become such an integral part of subcultural living that the season is announced in the popular press (Oakenbough 1974). Even a seven year old girl in Vancouver was observed by the author to maintain her own "stash." She had developed a fondness and respect for these mushrooms plus a tremendous inquisitiveness toward them. Whenever adults would employ Liberty Caps (the usual dose being 20-25), she would usually eat one or two and claimed to experience a mild effect.

The identity of the British Columbia Liberty Caps has been presumed to be *Psilocybe semilanceata* (Dawson & Morelli 1975). This identification may have been based on a public awareness publication (British Columbia Access 1972) which duplicated most of its material from Enos (1970) to serve as a hallucinogenic mushroom guide for British Columbia. From examination by Guzmán of collections in the fall of 1975, it has now been determined that Liberty Caps refer to two species, *Psilocybe pelliculosa* and *P. semilanceata.* Furthermore, field studies have now turned up additional species in use such as authentic *Psilocybe cyanescens* in Washington. The annulated *"cyanescens"* referred to by Weil (1975) actually represents a new species.

Psychomycological field studies are needed in other areas of the world as more species remain to be discovered. Since *Panaeolus texensis* specimens are no longer available (Smith 1975) and the Latin description is insufficient in detail to be useful, this species entity must be disregarded. Nevertheless, there are species of *Panaeolus* and other psilocybian genera which remain in need of chemical analysis. Although strain differences in alkaloid production have already been observed chemically, there may be differences in the spectrum of biosynthetic alkaloids produced by different species. Such differences may well be important psychopharmacologically and it would be erroneous to presume that the psychotropic actions of psilocybian fungi can be predicted entirely based on studies with pure psilocybin or psilocin. Just as additives to new world hallucinogenic preparations may be important (Schultes 1972) so might other constituents present in the mushrooms. So little clinical study has been attempted comparing the psychoneurophysiologic effects of different psilocybian species (Stein 1959; Stein, Closs & Gabel 1959), that this area of investigation is virtually unexplored.

Although psilocybin is generally considered to be equipotent to psilocin on a molar basis, this actually may not be true. Wolbach, Miner & Isbell (1962) compared the effects of psilocin and psilocybin after intramuscular injection in human subjects, autoclaving the compounds in a solution containing vitamin C prior to administration. It was believed that the "addition of Vitamin C effectively prevented the alteration of psilocin to a compound with a deep-violet hue." Vitamin C, however, has been shown to reduce the blue oxidation product of psilocin (possibly a dimeriquinone) to a colorless compound (Bocks 1967a). Thus, it is unknown what the dosages of psilocin employed by these investigators actually were.

While psilocin, psilocybin, mescaline and LSD are generally considered to produce the same clinical manifestations in people, there are probably important neuropharmacologic differences which have yet to be explored. It is known, for instance, that while psilocybin, LSD and muscimol increase body temperature toward normal in mice pretreated with reserpine, mescaline causes a further decrease and ibotenic acid has no significant effect (Waser 1967). LSD (300 ug/kg i.v.) has been shown in unrestrained rats to increase blood flow to the frontal and parietal lobes as well as to the cerebellum (Goldman *et al.* 1975a). Furthermore,

whereas in rats delta-9-tetrahydrocannabinol (1 mg/kg i.v.) significantly decreases blood flow to the cerebellum, hypothalamus, basal ganglia and dorsal hippocampus (Goldman *et al.* 1975b), the only significant effect of psilocybin (10 mg/kg i.v.) on brain blood flow was a decrease to the dorsal hippocampus (Fischer 1975). Data on mescaline are not yet available (Fischer 1975). Although it is suggested that autoradiographic studies with ^{3}H-LSD "strengthen the hypothesis that the action of LSD in the brain is linked in some way to serotonergic neurons (Diab, Freedman & Roth 1971), more extensive studies have been done with ^{14}C-psilocin. No correlations could be found between the distribution pattern of ^{14}C-psilocin in rat brain "with the numerical nerve and glial cell density, the volume cell density, the capillary density, the contents of oxidative enzymes, the uptake of labelled amino acids, the lipid contents and other patterns known through chemical or histochemical studies" (Hopf & Eckert 1969). Psilocin uptake is low in the hypothalamus (serotonin rich) but very high in the neocortex (serotonin poor). Furthermore, it is high enough in the serotonin-rich hippocampus, an important part of the limbic system, to suggest that "a main site of action on this structure could explain some of the behavioral effects" of psilocin (Hopf & Eckert 1969). Hallucinogenic substances would reasonably be expected to have multiple sites and mechanisms of action. There is already some evidence that in addition to central serotonergic pathways, dopaminergic pathways may be involved in the complex action of LSD (Horita & Hamilton 1973; Pieri, Pieri & Haeferly 1974; Roszell & Horita 1975; von Hungen, Roberts & Hill 1974). Dubansky and Vyhnankova (1967) administered psilocybin to healthy volunteers and to brain-damaged patients. They observed that complex hallucinations and other visual psilocybin manifestations tended to be almost completely suppressed in persons with lesions involving central optic pathways. In contrast, while the absence of complex hallucinations was observed in patients with brain lesions but intact central optic pathways, other visual manifestations of psilocybin were observed. No studies have yet been attempted to determine what central nervous system pathways are actually essential for other manifestations of psilocybin intoxication such as the prominent tendency toward laughter and the frequent yawning.

Field observations are that psilocybian mushrooms are often employed with *Cannabis* species and/or alcoholic beverages. Furthermore, the author has observed the concomitant use of *Psilocybes* with *Amanita muscaria* in British Columbia and the Pacific Northwest. The pharmacologic interaction between psilocin or psilocybin and other psychoactive compounds such as delta-9-THC, ethanol, ibotenic acid and muscimol has not yet been investigated. Such studies would certainly be worthwhile not only because these compounds are often employed together but also because of the great potential for obtaining important new information on central nervous system neuropharmacology.

There may well be mushroom hallucinogens of an entirely different chemical nature than the tryptamines and isoxazoles. Numerous species in various genera have reputations, albeit some most obscure, of being psychoactive (Heim 1963). One notable example is *Pholiota spectabilis* (Fries) Kummer, in North America now usually designated as *Gymnopilus spectabilis* (Fr.) Smith. In 1942, a Cleveland, Ohio resident "had taken a few nibbles from a mushroom that she found" in the woods. Later she experienced "the most glorious visions of color and sounds of music, but with no feeling of discomfort whatever" (Waters 1965). The hallucinations soon passed and this victim of mycetismus "added that if this were the way one died from mushroom poisoning, she was all for it." The fungal identification seems to have been reliable and this species had been reported from Japan as producing such effects (Romagnesi 1964). The Japanese name for this fungus is even *o-waraitake* ("big-laughing mushroom") (Sanford 1972; Wasson 1973). A mycetism case involving three persons occurred in Boston in 1966, and indole derivatives other than psilocin and psilocybin were reported to occur in a sample of the *spectabilis* (Buck 1967). It was later determined that a false positive reaction for indoles was produced by *bis*-noryangonin present in this spectacular species (Hatfield & Brady 1969). Such styrylpyrones are widely distributed in *Gymnopilus* species (Hatfield & Brady 1971), some of which are "edible." Thus the psychoactive principles in *spectabilis* remain unknown.

Although the natural distribution of fungal psychotropogens is still largely unknown, even less is known about their neuropharmacologic mechanisms of action. The natural tendency of human beings to partake of "mind-altering" substances is so well documented (Efron, Holmstedt & Kline 1967; Schultes & Hofmann 1973) that one can easily perceive why arbitrary legislation and enforcement procedures are entirely useless in preventing such social pharmacological behavior in modern societies. The sanctioning of some modulators of "escape" such as ethanol with the disapproval, or legal taboo, of other more efficacious substances is sheer nonsense. When a human being experiences a drug induced alteration of consciousness there occurs a simultaneous change in psychic free

energy, thermal energy and entropy. A chemical reaction is accompanied by the liberation or absorption of heat energy (enthalpy) and a change in entropy. Entropy (ΔS) pertains not only to the randomness of the system but is the final form into which heat energy dissipates. This change in the "state of chaos" (ΔS) together with the change in enthalpy (ΔH) results in a change in free energy (ΔF). These changes can be accurately measured for chemical reactions *in vitro* (Kitzinger & Benzinger 1960), but the complex electro-chemical changes which occur as one experiences a chemical catalytic alteration of consciousness are not accessible to such measurement. The "escaping" tendency of matter and other forms of energy toward entropy is so well known thermodynamically that an attempt to maintain a single homeostatic state of consciousness would have to be an entirely unnatural act. Exploration of the potential usefulness of alternate states of consciousness has certainly begun (Drug Abuse Council 1975), but is still in its infancy.

One obvious promising field for use of hallucinogens as mediators of pathways to alternate states of consciousness is, of course, medicine. It has been proposed both in Europe (Leuner 1968) and the United States (Fischer & Goldman 1975) that psilocybin or a related substance be used in psychotherapy rather than mescaline or LSD. While LSD may be extremely useful (Grof 1975), clinical observation from well over a thousand controlled hallucinogenic drug sessions is that psilocybin is shorter acting, seems to produce very few adverse reactions, is associated with fewer flashbacks and is accompanied by less post session depression than the hallucinogens LSD and mescaline (Fisher & Goldman 1975; Leuner 1968). Although psilocybin is substantially more efficious than LSD or mescaline, various other hallucinogens as well as natural dosage forms of these compounds deserve such testing.

The efficacy of psilocybin is further demonstrated by the paucity of adverse reactions occurring from the use of psilocybian mushrooms. Although "bad trips" are occasionally reported from these fungi (McCarthy 1971; Stein 1958), they are much easier to manage than are those often produced by various synthetic street drugs. Although it was suggested that *P. candidipes* Singer & Smith may be "poisonous" rather than just hallucinogenic (Singer 1958), recent studies suggest that this is not the case (Ott 1975). Furthermore, Singer and Smith (1958b) not only allege that Imai (1932) reported cases of death caused by *S. caerulescens* Imai (later changed to *S. venenata* Imai for nomenclatural reasons) but also that this Japanese species is conspecific with Höhnel's Javanese species *subaeruginascens* and *aerugineomaculans. S. Venenata* was not reported to have caused any deaths (Imai 1932) and is regarded as a hallucinogenic mushroom in Japan, no different essentially from any other Japanese psilocybian species (Matsuda 1960; Sanford 1972; Wasson 1973; Yokoyama 1976). There are no rumors in Japan of *venenata* being deadly (Yokoyama 1976) and its name is *shibiretake* ("benumbing mushroom"). Authentic *venenata* was kindly supplied by Hongo and Yokoyama and type material of *subaeruginascens* and *aerugineomaculans* was obtained for comparison. Microscopic examination by the author with McLain suggested that *venenata* is a distinct species. Although we must await definitive determinations by Guzmán to be sure, it appears that Singer and Smith were mistaken in all matters pertaining to the *venenata* problem.

Psilocybian mushroom use in Australia has generally reached socio-pharmacologic equilibrium. Although more fungal "abuse" cases are being detected now, there has been no additional legislation, and the phenomenon of psychoactive mushroom use in Australia has generally not changed over the last few years (Hall 1976). Although no additional psilocybian species have been reported from Australia, there is a white fungus being employed there that resembles the deadly *Amanita verna.* It is called "white "frenzy" or "white death," but no deaths seem to have been attributed to its use (Hall 1976). In the United States, genuine psilocybian mushrooms and possibly extracts prepared from them are occasionally sold as street drugs to meet the tremendous demand. Such a practice may be expected to continue until duly licensed and inspected commercial sources of supply become available for distribution through legitimate channels to provide the consumer protection that is indicated. Although use of these fungi is still growing in the U.S., drug abuseologists and drug "scapegoaters" as discussed by Szaz (1975) cannot reasonably consider this phenomenon a major problem. Between July 1973 and June 1975, the DEA confirmed the psilocybin content of nine exhibits (one from Arkansas, one from Oregon, five from Louisiana, one from Missouri and one from Washington) and the psilocyn *[sic]*content of two exhibits from North Dakota (Johnson 1975), and in January 1975, PharmChem Labs (1975) reported the presence of psilocin in four street samples and both psilocin and psilocybin in another, sources noted from California and Oregon. These figures compare rather meagerly to 978 exhibits of LSD, 930 of PCP and 70 of "other" hallucinogens such as 4-bromo-2,5-dimethoxyamphetamine, the thiophene analog of PCP, etc. confirmed by the Drug Enforcement Administration for the fiscal year 1975 alone (Johnson 1975). In 1970, LSD constituted 9 percent of the total

DEA analytical work load, whereas "all hallucinogens" (a category that includes the sympathomimetic but not hallucinogenic compound MDA) constituted 11 percent. By the end of fiscal 1975, confirmed LSD exhibits comprised 2 percent and "all hallucinogens" (including 25 MDA exhibits) comprised only 5 percent of their total analytical workload (Johnson 1975).

Psilocin or a suitable congener may well prove to be of great utility in psychoanalysis and psychotherapy. It may certainly be efficacious for therapy of opiate dependent patients, alcoholics and certainly abusers of street hallucinogens. The potential for detecting some organic brain lesions by the use of such compounds has also been observed (Dubansky *et al.* 1963), and their potential for assisting with the alert terminally ill should also be considered. Since LSD has already been shown to be of benefit in some of these patients, might not psilocybian mushrooms, with their tradition of use in medico-religious rites since ancient times, be a more natural, psychologically aesthetic medicinal sacrament in the preparation of these patients for a death with dignity?

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