Chapter 14
An Evolutionary Perspective on the Use of Hallucinogens*

Washington Soares Ferreira Júnior, Margarita Paloma Cruz, Fábio José Vieira, and Ulysses Paulino Albuquerque

14.1 Introduction

Hallucinogens have been used by human communities since ancient times. For example, records of the use of the plant *Sophora secundiflora* (Gomez-Ortega) Lag. ex DC. dating from between 8440 and 8129 BC have been found in the state of Texas in the southern USA (Furst 2004). Psychoactive drugs are capable of causing not only visual but also auditory, tactile, and gustatory hallucinations (Schultes and Hofmann 1993). Because of these characteristics, they are often believed to mediate communication with gods or spirits (Schultes and Hofmann 1993; Rodrigues and Carlini 2005; De Feo 2004), earning them the name "entheogens." This term, coined by Gordon Wasson (1992), means "god within me," a reference to the fact that, when such substances are ingested, they establish a closer connection between the person who consumes them and the gods. The term entheogen is arguably more appropriate when we want to refer to the use of psychotropic drugs in the religious, shamanic, or spiritual context. The fact that some hallucinogenic plants induce a certain health condition of well-being may have favored their learning and use by human beings

W.S. Ferreira Júnior (✉) • U.P. Albuquerque
Laboratory of Applied and Theoretical Ethnobiology (LEA), Department of Biology,
Federal Rural University of Pernambuco, Av. Dom Manoel de Medeiros, s/n,
Dois Irmãos, Recife, Pernambuco 52171-900, Brazil
e-mail: kba.bio@hotmail.com

M.P. Cruz
Colombian Society of Ethnobiology, Bogotá, Colombia

F.J. Vieira
Department of Biology, State University of Piauí, Av. Senador Helvídio Nunes de
Barros, s/n, Junco, Picos, Piauí 64607-760, Brazil

(Johns 1990). Obviously, as suggested by Johns (1990), the cultural context mediates this use and importance in a culture. A relevant issue for an understanding of the relationship between humans and natural chemicals is how a culture's relationship with these substances originated and developed. In this sense, the following question may be of high importance: is there a hallucinogen–medicine continuum that is similar to the food–medicine continuum discussed elsewhere in this book?

In an article entitled "Mescaline Cactus Used in Folk Healing," Dobkin de Rios (1968) reports the hallucinogenic and medicinal use of *San Pedro* cactus (*Trichocereus pachanoi* Britton & Rose) in a rural community in Peru, suggesting that psychoactive substances are effective in treating diseases. However, the author shows that although the use of hallucinogenic plants in curing disease has been noted by several authors, the use of such plants in medicinal contexts has not been adequately discussed. The fact that there is an overlap between medicinal and hallucinogenic uses may indicate that humans discovered the hallucinogenic uses from the selection of medicinal plants. Rodriguez et al. (1982) suggest that the local people in the Amazon incorporated plants in their rituals that have antiparasitic properties due to the presence of alkaloids. Recent evidence reinforces the interpretation of these authors. Data from Roulette et al. (2014) support the hypothesis that the use of tobacco may protect against parasites.

In this chapter, we present some considerations for developing the hypothesis that hallucinogenic substances are effective in the treatment of diseases, which often does not appear clearly in the literature, and we discuss how the hypothesis can provide insights into human evolution that involve the use of these substances. We then present previous findings on the treatment of diseases using hallucinogens, including the different actions of psychoactive drugs and other elements that may interact in the treatment of diseases. We refer to the use of hallucinogens in the context of traditional or local communities, not as recreational drugs.

14.2   Hallucinogenic and Medicinal Uses

The use of hallucinogenic substances as medicines has been recognized in local medical systems, but little academic study has been undertaken on this relationship. Many studies combine the medicinal and hallucinogenic properties of plants into the same category, recognizing hallucinogens as a secondary feature of some species used in traditional medicine (see Schultes 1938; Rodriguez et al. 1982). For example, Weiner (1971), working in a rural community in Tonga (a country located east of Australia), discussed the strange absence of hallucinogenic plants in traditional medicine, which shows a close relationship between the hallucinogenic and medicinal uses for this author.

We believe that this strong relationship between hallucinogenic and medicinal uses may be due to experimentation with medicinal plants, which led to the development of a culture of traditional hallucinogens. Many authors have shared this idea (Weil 1965; Rodriguez et al. 1982; Etkin 1988; Brussell 2004), proposing that

the hallucinogenic effects of plants were discovered subsequent to their medical applications when users of these drugs took higher doses than recommended. This application seems to have been the case with *nutmeg*, according to a report by Weil (1965). Rodriguez et al. (1982) suggest that many hallucinogenic plants were initially used for the treatment of diseases due to their antiparasitic properties. The fact that many cultures around the world have developed entire systems of belief and practice around hallucinogenic plants may suggest the existence of an adaptive component in such practices.

Given the evidence, there seems to be a belief among researchers that these substances may alter the mind, not only in terms of their hallucinogenic effects but also in a medicinal context (Randolph 1905). However, we must separate the two perspectives that seem to emerge from the works of these authors. The cure can be interpreted from the perspective of the researcher (the biomedical model) or from the perspective of the culture studied. For example, when an investigator witnesses a shamanic ritual that includes the ingestion of a psychoactive substance and records testimony that it healed the patient, we must distinguish whether the cure was actually achieved at a physiological level or in the sphere of "cultural diseases," those related to the worldview and beliefs of a particular people.

Determining the moment when medicinal plants were also considered to be hallucinogens is no easy task because the concept of illness for traditional cultures often differs from what "disease" means to Westernized or modern people (Hurrell 1991; Herndon et al. 2009). This subject has been extensively studied (Coelho 1976; Monod 1970; Rodriguez et al. 1982; Fackelmann 1993; Menéndez 1994; Agosta 1997; Shepard Jr. 2002; De Feo 2004; Toledo 2006; Bourbonnais-Spear et al. 2007). Most of these authors indicate that, in addition to recognizing what we might call physiological diseases (diseases that would be accepted by modern medical science), many traditional communities also recognize diseases caused by supernatural agents (for example, see Garro 2000).

Schultes and Hofmann (1993) argue that non-industrialized cultures do not differentiate between physiological and supernatural causes of disease. Rather, disease is the result of "interference with the spiritual world." Therefore, the best medicine to treat diseases would be entheogens, which enable contact with the spiritual world, where an effective cure for the disease can be identified. This complex process is difficult to explain without systematic and specific case studies. A hallucinogenic plant may have medicinal properties that treat some (but not all) physical infirmities. If a particular healing ritual always uses the same plants to treat a complex consisting of several diseases, then it would be reasonable to assume that the cure operates not at a physical level but rather at a "supernatural" level, according to the worldview of the culture. Considering the cause of a disease to be other than physiological or even to be supernatural typically means that the cure is also not "conventional" and that it does not fit the types of treatments recognized by modern medical science.

Agosta (1997), in a review of plant compounds used as medicines, notes that in traditional communities, diseases are often thought to be caused by evil spirits. Therefore, healers should administer psychotropic drugs and use their influence to communicate with the spirit world and achieve the patient's healing. According to

Schultes (1979), healers and shamans take hallucinogens (in this case, entheogens) to make contact with deities through visions or dreams. These visions provide knowledge about the disease afflicting the patient and tell the healers the proper treatment for the condition (see also Rodrigues and Carlini 2005; De Feo 2004). In this case, the entheogen becomes a vehicle that allows the healer to explore aspects of the disease and treat the patient. Thus, the entheogen has an indirect effect because it is ingested by the healer, not by the patient.

In other situations, the treatment is indirect not because the hallucinogens allow contact with the gods to determine the cure for the disease but instead because healers can use hallucinogens to confront and combat a disease through symbolic battles with the cause of the disease (Rivier and Lindgren 1972). In the case presented by Dobkin de Rios (1968), the *San Pedro* cactus is used to cure diseases indirectly through a ritual treatment in which the healer drinks the entheogen and receives information about the cause of the disease. However, Dobkin de Rios explains in his description of the ritual that both the patient and the healer drink the infusion from the *San Pedro* cactus, an act that leads to hallucinations and vomiting in the patient who ingested the substance. Dobkin de Rios (1968) and Rodriguez et al. (1982) suggest that this action may have a curative effect.

This example shows that sometimes the treatment can produce indirect contact between the deities and the healer who ingests the drink, in addition to a direct effect on the patient who also ingests the drink. A similar report on the hallucinogenic cigarette *tira-capeta*, used in healing rituals in Maroon communities in Brazil, can be found in Rodrigues et al. (2008). According to the authors, the cigarette is used by both the healer and the patient and may exert a direct effect on the latter in the treatment of disease. The key issue in these examples is that the act of vomiting or smoking may have more of a symbolic effect than a strictly physiological effect in fighting a specific disease.

However, we regard these actions as a direct treatment because the patient came into direct contact with the hallucinogenic substance, which could have had played a role in curing the disease. Healing through direct treatment is in line with Western biomedical concepts. That is, the patient takes the hallucinogen, which has one or more bioactive compounds with medicinal properties. In addition, the vehicle used (e.g., powder, beverage, or cigarette) and how the substance is consumed contribute to the effect of the active principle in the body.

These examples show that hallucinogens can play both a direct and an indirect role in curing diseases while also facilitating communication with deities, thus allowing healers to decipher the origins of diseases or to symbolically battle diseases. In contrast to the types of treatments already noted, Schultes and Hofmann (1993) have discussed a ritual in which only the patient drinks a hallucinogenic substance while the shaman observes the behaviors and responses to the drink and diagnoses the patient's maladies. This example presents a third type of disease treatment involving hallucinogens but does not suggest any medicinal properties. Thus, there may be a cultural placebo effect in which particular cultural expectations cause a member of the culture to attain the desired effect even without pharmacological elements. For example, Albuquerque and Chiappeta (1994) describe a ritual with the plant *Jurema* (*Mimosa tenuiflora* (L.) Poir.) in which a person consumed

the drink offered but did not have the same reactions that the others had (see also Souza et al. 2008).

In addition to the situations presented above, there are other cases, as documented by Dobkin de Rios (1968), Rivier and Lindgren (1972), and Albuquerque and Chiappeta (1994), in which both the healer and the patient (and even other people in the ritual) took the plant to hallucinate. In addition to other factors, the combination of various elements of the ritual (songs and dances, for example) can cause a synergism that leads to the patient's "cure."

Some authors have suggested that healing in rituals is accomplished through a combination of plants with entheogenic properties, songs, and prayers (Monod 1970; Bourbonnais-Spear et al. 2007). This idea is supported by Albuquerque and Andrade's (2005) study on African-Brazilian cults. They argue that, for the remedies to be complete, their administration must be accompanied by an enchantment to facilitate the healing process. Thus, one must consider the complete set of ritual elements that create a contagious atmosphere among participants, leading to emotional states that can produce states of trance (Camargo 1998).

One of the most striking elements in rituals is music, which may consist of whistling or magical songs that accompany the entire ritual. Katz and Dobkin de Rios (1971) provided an important contribution in this area with their analysis of the role of whistling in the *ayahuasca* healing rituals of Peruvian Amazon natives. They concluded that the ingestion of hallucinogenic plants and the whistles produced by healers during the period of intoxication were the method for invoking the forces of nature and the guardian spirits. Dobkin de Rios and Katz (1975) subsequently elaborated on their findings and established a link between musicality, religious rites, and healing. They questioned the importance of music in ceremonies with hallucinogenic plants in Western societies, finding that different types of music can evoke particular moods and may regulate the hallucinogenic effect of the drug administered. Monod (1970), studying the Piaroa Indians in South America, believed that the songs sung during the rituals had curative and preventive effects. Other authors corroborated the assertion that music is essential to ritual divination of diagnoses and healing. Mentally, rhythmic singing with a drumbeat seems to support the flow of visions and minimize fear (see Albuquerque and Chiappeta 1994). Metzner (1998) reported that Western psychotherapy and the healing systems of shamanic indigenous peoples use plants or psychoactive drugs to cure or obtain knowledge and that these objects are invariably essential to the success of healing.

If our goal is to investigate whether hallucinogens are effective in the treatment of diseases, then we must consider the distinct views of disease between human groups and biomedicine as well as the different forms of treatment with hallucinogens (direct or indirect). In this text, however, we adopt an approach based on the biomedical model to evaluate the effectiveness of both medicinal and hallucinogenic applications, focusing on direct treatment.

As weak evidence for direct treatment, some studies have isolated and identified substances with hallucinogenic and medicinal properties in the same plant, which corroborates the idea that plants with hallucinogenic properties also have medicinal properties. However, we must discern whether these substances can actively treat targeted diseases. For example, Mackie et al. (1955) prove the efficacy of the sub-

stance *thujone*, a constituent of essential oils from various plants, as an anthelmintic. Albert-Puleo (1978) also reports this substance to be a hallucinogen, demonstrating that a substance may in fact have both hallucinogenic and medicinal properties.

Table 14.1 presents species of plants and fungi with compounds that have proven hallucinogenic and/or medicinal pharmacological properties. As shown in the table, there are substances that have confirmed hallucinogenic properties but where no studies have demonstrated their medicinal properties, for example, muscimol and ibotenic acid in the *Amanita muscaria* species. Other substances, however, have already been proven to have both medicinal and hallucinogenic properties (see Table 14.1). Indeed, this evidence seems to indicate that the initial consumption of a plant for medicinal purposes may lead to the discovery of its use as a hallucinogen.

Table 14.1 List of species with recorded hallucinogenic uses and their substances with hallucinogenic and/or medicinal properties proven in pharmacological studies

Species	Substances	Properties	References
Amanita muscaria (L. Fr.) Lam.	*Muscimol*	Hallucinogenic	Perry and Perry (1995); Satora et al. (2005)
	Ibotenic acid	Hallucinogenic	Satora et al. (2005)
Atropa belladona L.	*Atropine*	Medicinal and hallucinogenic	Rates (2001); Schultes and Hofmann (1993)
	Hyoscyamine; *hyoscine*	Hallucinogenic	van Dongen and Groot (1995); Schultes and Hofmann (1993)
Brugmansia arborea (L.) Lagerh.	*Tropane alkaloids (atropine and scopolamine)*	Hallucinogenic	van der Donck et al. (2004)
Cannabis sativa L.	*Cannabinoids ("arachidonoylethanolamide"; "2-arachidonoyl glycerol"); bioactive fatty acids ("palmitoylethanolamide" and "oleamide")*	Medicinal	Petrocellis et al. (2000)
	Cannabinoids ("4-acetoxy-2-geranyl-5-hydroxy-3-n-pentylphenol"; "8-hydroxycannabinol" and "5-acetyl-4-hydroxycannabigerol")	Medicinal	Radwan et al. (2009)
	Cannabinoids (Cannabicromano)	Medicinal	Ahmed et al. (2008)
	Cannabinoids	Medicinal	Velasco et al. (2004); Beaulieu and Rice (2002)
		Medicinal and hallucinogenic	Ashton (2001); Honório et al. (2006); Bonfá et al. (2008); Ameri (1999)

(continued)

Table 14.1 (continued)

Species	Substances	Properties	References
Claviceps purpurea (Fr.) Tul.	*Ergot alkaloids (ergotamine and ergometrine)*	Medicinal	Komarova and Tolkachev (2001); Lorenz et al. (2009)
	Ergot alkaloids (ergolines)	Medicinal and hallucinogenic	Eadie (2003)
	Ergot alkaloids (ergotamine)	Medicinal and hallucinogenic	van Dongen and Groot (1995)
Datura spp.	*Tropane alkaloids (atropine and scopolamine)*	Hallucinogenic	Perry and Perry (1995)
Datura stramonium L.	*Atropine*	Medicinal	Irambakhsh et al. (2010)
	Atropine	Medicinal and hallucinogenic	Rates (2001)
Digitalis spp.	*Digoxine*	Medicinal	Rates (2001)
Nicotiana sp.	*Harmine*	Hallucinogenic	Davis et al. (1969)
Papaver somniferum L.	*Codeine*	Medicinal	Rates (2001)
Psilocybe spp.	*Psilocybin, psilocin*	Hallucinogenic	Schultes (1998); Huhn et al. (2005)
Salvia divinorum Epling & Játiva	*Salvinorin A*	Medicinal and hallucinogenic	Capasso et al. (2006)
Tabernanthe iboga Baill.	*Ibogaine*	Hallucinogenic	Kubiliené et al. (2008); Sheppard (1994)
	Ibogaine	Medicinal and hallucinogenic	Popik and Wróbel (2001)
Trichocereus pachanoi Britton & Rose	*Mescaline*	Hallucinogenic	La Barre (1979)
Trichocereus williamsii (Lem. Ex Salm-Dyck) Coult.	*Mescaline*	Hallucinogenic	La Barre (1979)

14.3 Adaptive Significance of the Use of Hallucinogens

Based on the evidence we present, it is very likely that the use of hallucinogens, especially in ritual contexts, has arisen from the selection of medicinal or food plants by humans. One possible scenario is that the initial trial plants (for medicine) led humans to encounter the natural chemicals that cause altered states of

consciousness, to which different cultures have attributed different meanings. Most likely, the same plant can be taken to act as both a medicine and a hallucinogen (from a biomedical perspective), or the use has focused solely on its hallucinogenic properties. In this sense, we may considerer that the use of hallucinogens is a by-product of the human active search for plant chemicals. Obviously, cultures that assign a meaning to the positive experiences provided by the use of hallucinogens may have started, after the accidental discoveries, an active search for such products.

In many cultures, natural hallucinogens are reported to have a property by which the eyes of the "experimenter" (shamans, in some cultures) are opened to a spiritual world. The hallucinogenic experience allows access to this world because it brings together knowledge and power. Many healers and shamans claim that they have access to different types of knowledge because they were taught by the plants they used. These plants are called by many Amazonian societies "plants with the mother" (see Luna 1984; Jauregui et al. 2011), but they are not necessarily psychotropic. Such plants are used to guide initiation processes and the transmission of traditional knowledge, as noted by Jauregui et al. (2011:747) for *ayahuasca* (a South American psychotropic):

> (…) visions are an expression of the initiates' journey to their inner world and to the spirit world, where different scenes and spiritual entities may appear, depending on the initiate's religious, cultural, and social imprint. In the case of the ethnic Amazonian groups, the entire framework of their cosmovision is expressed. Therefore, it is common among indigenous people to have visions of serpents, jaguars, Amazon river dolphins, and eagles.

Different ethnographic and non-scientific (based on reports of individual experiences) records illustrate the role of hallucinogen consumption as a learning strategy for beginners, not only for the knowledge transmission of traditional rituals and medical practices but also for other aspects of life, including the identification of plants and animals in the local environment (see Lamb 1993). In these reports, the beginner's hallucinogenic experience, guided by a healer or shaman, acts as a key learning strategy (Albuquerque 2001). In such cases, psychoactive plants can play an important role in the adaptation of the human groups in their respective environments. We call this hypothesis the "psychotropic hypothesis of the adaptation" (Albuquerque 2001). If in fact plant hallucinogens play an important role in human adaptation (improving learning and knowledge transmission), then, at the least, we need pharmacological evidence to support this claim. However, experimental studies using rats with psilocin (from hallucinogenic mushrooms) and salvinorin A (from *Salvia divinorum*) have found deleterious effects on learning and memory acquisition (Braida et al. 2011; Rambousek et al. 2014). Other investigations with different animal models and substances (for example, see Molinengo et al. 1986; Koupilova et al. 1989), including humans in a double-blind controlled study (MacLean et al. 2013), reinforce these findings. These findings may suggest that the use of hallucinogens by traditional human groups does not have an adaptive character, particularly affecting learning processes. However, we need more evidence to verify the adaptive role in the use of hallucinogens in human evolutionary history.

Just as evidence of coevolution between humans and plant chemicals used as food and medicine has been presented in other chapters of this book, we can also

assume a long coevolutionary process with psychotropics. Sullivan and Hagen (2002) suggest that this coevolutionary history may have been motivated by the scarcity of high-quality food in the ancestral environment, which led hominids to consume these allelochemicals to save energy. Obviously, both the accidental encounter with these plants in search of medicinal substances and the need to save energy in famine situations may have led to this scenario. In particular, we believe that the lack or complete scarcity of high-quality food may have resulted in the consumption of psychotropics either accidentally or intentionally. For example, many modern cultures have a set of foods that are basically consumed only in times of scarcity called famine foods or emergency foods. They are typically highly toxic plants that must undergo detoxification processes to be consumed. We suggest that these scenarios in ancestral environments may have put hominids in contact with these substances as famine foods.

Chemical-ecological evidence, such as the presence of adaptations in mammals to defend themselves against plant chemicals, reinforces this interpretation. Perhaps the most remarkable adaptation is the evolution of liver enzymes (cytochrome P450) that metabolize many plant chemicals, clearly indicating that humans were exposed to plant toxins throughout their evolution (Sullivan and Hagen 2002; Sullivan et al. 2008). There is a large polymorphism in genes coding cytochrome P450 enzymes (named CYP genes), and the frequency varies in different populations, which indicates that the ability of different individuals to metabolize xenobiotics varies across these populations (Sullivan and Hagen 2002; Sullivan et al. 2008). Considering that the deleterious effect on learning and memory acquisition is dependent on the dose of the hallucinogen, as observed for salvinorin A (MacLean et al. 2013) and psilocin (Rambousek et al. 2014), some individuals can ingest a hallucinogen and witness the desired effect without necessarily having a deleterious effect on memory. By presenting multiple copies of the CYP genes, some individuals may have a high metabolic rate for the hallucinogenic compound. Thus, the individual may experience hallucinations because some amount of the compound is not metabolized, but not enough to have a deleterious effect on memory. However, this idea needs empirical verification, as may be the case for other studies on human populations that have undergone positive selection for CYP genes and simultaneously interact with entheogens as part of their culture.

14.4   Final Considerations

According to the discussions raised by this chapter, we can conclude the following points:

1. There is an association between the use of hallucinogenic and medicinal substances. This association is related to the properties of these substances, which may be hallucinogenic or medical, depending on the dosage. However, no systematic study linking ethnographic data with pharmacological uses has been found. For example, have hallucinogenic substances been used pharmacologically in a healing ritual activity for all diseases?

2. To discuss the possible roles of the adaptive use of hallucinogens, we present studies that assess the effect of hallucinogens on learning and memory. We note that many of these studies use isolated substances. An interesting study could assess how traditional hallucinogenic preparations, not simply an isolated hallucinogen, can affect learning and memory.

3. When substances have different properties depending on dosage, researchers tend to assume that the medicinal effects were discovered before the hallucinogenic effects. This idea has been suggested by different studies, but to the best of our knowledge, it has not been studied and tested. Thus, there is a tendency among researchers to consider the hallucinogenic effects to be secondary to the medical effects.

4. The different disease treatments using hallucinogens can be grouped into three types. In the indirect treatment, only the healer takes the hallucinogen and receives contact with deities and insights into the causes of the disease to diagnose and/or obtain treatment for the patient. In the second type, direct treatment, the patient takes the hallucinogen, which may have active ingredients with the desired properties that have a direct effect in curing the disease. In the third type, the patient takes the hallucinogen, but it does not have active compounds for the treatment of the disease in question. Thus, healing can be considered a case of "cultural placebo."

5. In addition to hallucinogens, other elements present in rituals also serve an important function in the healing process. Hallucinogenic substances may have the ability to influence the types of visions experienced. There is evidence of the positive effect of plant hallucinogens on attitude, mood, and behavior in humans. Doblin (1991: 23) discussing the famous "Good Friday Experiment" conduced with psilocybin asserts that "psychedelic drugs can help facilitate mystical experiences when used by religiously inclined people in a religious setting." Recent studies have found similar conclusions (Griffiths et al. 2006, 2011).

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