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Ethnopharmacology – From Mexican Hallucinogens to a Global Transdisciplinary Science

[Keynote]

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ABSTRACT

Psychoactive natural substances have been reported from practically all regions of the world, but Mexican indigenous cultures have played a crucial role having influenced medical, toxicological, biological, chemical, pharmaceutical, and, of course, anthropological research.

Especially in the 1950's and 1960's peyotl, teonanacatl and other psychoactives came to the attention of researchers and revelers alike. In this overview we highlight the developments of ethnopharmacology from the initial development of the term until today using one psychoactive species as an example - *Salvia divinorum*. In 1962 "ethnopharmacologists", Albert Hofmann and R. Gordon Wasson, documented and collected a flowering specimen of *Ska Maria Pastora* allowing the species botanical description as *Salvia divinorum* Epling & Játiva. Five years later Efron et al. (1967) organised a symposium "Ethnopharmacologic search for psychoactive drugs" which over the next decades would give its name to a discipline which today is much more broadly defined, dealing with local and traditional medicines, their biological activities and chemistry. Globalisation has resulted in a world-wide commodification of many traditional medicines and psychoactives, as exemplified by *S. divinorum*. This fascinating Lamiaceae has become globally recognized for its best known active constituent salvinin A, a kappa-opioid antagonist which has a unique effect on human physiology.

While today ethnopharmacology is a thriving discipline, the interest in psychoactive substances is no longer central to the discipline. The search for anti-cancer agents (which also started in earnest in the 1960's) had been of particular relevance and today includes among its many foci:

- The scientific study of local and traditional knowledge not only in remote regions, but for example, also in urban immigrant communities
- Research linking ethnopharmacology to biodiversity research both in terms of a sustainable use of natural resources (ecosystems)
- Pharmacological studies with the aim of understanding the effects of complex mixtures on specific diseases or disease targets

- The safety of herbal medicines
- Anthropological and historical approaches on the use of medicinal and food plants and the link between food and medical uses of plants and fungi.

50 years on ethnopharmacology is very different from what D. Efron and colleagues had envisioned.

INTRODUCTION

To the best of our knowledge, the term “ethnopharmacology” was first published in 1967 by Efron and colleagues who used it in the title of a book on hallucinogens: “Ethnopharmacological Search for Psychoactive Drugs” (Efron, et al., 1970; Holmstedt, 1967). Thus with this book, we celebrate both 50 years of a ground-breaking symposium and the introduction of a new term. This introduction is much later than, for example, the term ethnobotany which in 1896 was coined by the US-American botanists William Harshberger describing the study of human’s plant use. Both ethnopharmacology and ethnobotany investigate the relationship between humans and plants in all its complexity. “Ethnopharmacology” also replaced the many other terms which had been used previously like “Pharmakoëthnologie” used already by Tschirch (1910) in his classic “Handbuch der Pharmakognosie” or pharmacoetnologia or Aboriginal botany. (cf. Heinrich, 2014).

However, there is considerable variation in terms for what constitutes ethnopharmacology. In a book edited in 2015 by the first author and Prof. Anna Jaeger (Heinrich and Jaeger, 2015), we compiled definitions of ethnopharmacology as they were given by the contributors to this book. The range from definitions which are very much embedded in the:

- Sociocultural sciences [e.g. Dan Moerman (USA): Ethnopharmacology is the study of the way people use plants, informing us about the varying ways people create meaning about these living objects.];
- Biomedical research [eg. Pravit Akarasereenont (Thailand): “A science dealing with the study of the pharmacology of traditional medicine and focusing on the active substances and their pharmacological action.” or Thomas Efferth (Germany): “Ethnopharmacology focuses on research on efficacy, safety, and modes of actions of traditional medicines with pharmacological methods.”]

In general the multidisciplinary of the field is highlighted very well clearly recognized by [e.g. Tony Booker (UK): The study of the historical and modern interactions between humans and flora, fauna and minerals and how these substances, their extracts and the chemical compounds derived from them, may be utilised to prevent and treat ill-health in people and their dependent animals]. Others stress the link between local and traditional knowledge with research conducted by academically trained investigators, with – in our view – Graham Jones (Australia) expressing it most eloquently and clearly: “Ethnopharmacology constituting a respectful marriage between modern science and ancient wisdom with much to be gained in both directions.”¹

Consequently, ethnopharmacology is not a very sharply circumscribed field of research and is heavily influenced by the academic, cultural and political background of a researcher.

In the beginning, the discipline of ethnopharmacology was focused primarily on the study of the traditional use psychoactive substances. However, the trajectory of this discipline has expanded in to an array of studies. We explore one of the early ethnopharmacological studies, the discovery, description and chemical elucidation of the Mexican Lamiacea *Salvia divinorum*. While this species is not as famous as other Mexican psychoactives such as *Psilocybe* mushrooms, it does demonstrates one of the earliest ethnopharmacological studies, as well as a 50 year trajectory of discovery, from the description of the plant to its genetic profiling.

There can be no doubt that in 2018 ethnopharmacology is a thriving discipline, embedded in a range of larger disciplinary contexts like botany, pharmacy, anthropology, and medicine. Estab-

1. Note added by Editor, Dennis McKenna. My personal favourite definition is that proposed by Holmstedt and Bruhn (1983): “The interdisciplinary scientific exploration of biologically active agents traditionally employed or observed by humans.” In my opinion this definition is succinct, specific and sufficient, in that it notes that ethnopharmacology is not restricted to medicines, nor to plants, or to substances ingested, but also correctly restricts the discussion to “traditional use.”

lished journals now publish thousands of articles in this field of research and while there are not many institutes that have the term in their name, many groups based in the pharmaceutical, biological, chemical and other schools publish in the field. This is impressive for a field that has had a surprisingly short history.

THE EARLY YEARS

While research on local and traditional plants dates back many centuries and includes, for example, the many explorers “discovering” exotic treatments, the modern history is a post-World-War II development. The 1950’s and 1960’s saw a dramatic socio-cultural change in “Western” societies. As part of the opening up of the rigid post-WW2 societies, numerous new developments in the cultures including music, the performing, and visual arts, but also tremendous socio-cultural conflicts formed new societal perspective. A key element of this was a fast developing interest in psychedelic substances, most importantly hallucinogenic plants. For example, in the 1960’s and 1970’s the psychologist and prolific writer Timothy Leary (1920 - 1996) impacted on the political and societal thinking on mind-altering drugs including most notably LSD and those which were derived from traditional and local knowledge (especially *Psilocybe* spp.). With the group’s experiments on psychedelic substances during his “Harvard Years” (1960 – 1963), Timothy Leary may have had more impact on what later one was called ethnopharmacology, than we are aware of.

Cannabis and products derived from it became an important element of this (counter-)culture. A key role in this context played research on and experiences with hallucinogenic plants and fungi from modern day Mexico, The highly toxic *Toloatzin* or Jimson weed *Datura stramonium* L. (Solanaceae) is one of the main and widely distributed hallucinogenic plants and fungi of Mesoamerica (together with peyotl - *Lophophora williamsii* (Lem. ex Salm-Dyck) J.M. Coult., ololihqui - *Turbina corymbosa* (L.) Raf. and the mushrooms teonanacatl - *Psilocybe* spp.); all have long traditions of use as hallucinogens. The following example, however, was only discovered by Western societies in 1962 - *Salvia divinorum*. It sparked great interest both in scientific terms and by those interested in its use. While no detailed historical information is available, it is clear that this discovery also contributed to the interest in holding the symposium at the University of California, San Francisco Medical Center (January 28-30 1967) and, therefore, to the book by Efron et al (1967, republished 1970)

SALVIA DIVINORUM

In 1962, ethnopharmacologists, Albert Hofmann and R. Gordon Wasson, undertook an expedition to Oaxaca, México (Hofmann, 1980; Wasson, 1962). Their main informants in the region became a curandera – Maria Sabina – who later became first persecuted and then famous. She provided the essential link between Mazatec traditional culture and the ‘explorers’. On this trip, they recorded several different plants and their use by Mazatec healers. As well as recording the cultural uses, they attended ceremonies, which incorporated the use of *S. divinorum* Epling & Jativa, a member of the Lamiaceae (Labiatae). This expedition contributed much to the early understanding of the cultural role and use of this species. Wasson and Hofmann were also able to obtain a flowering specimen of this plant, making the scientific description of *S. divinorum* possible (Epling and Jativa 1962; Casselman et al 2014). This “discovery” was met with great excitement and led to a flurry of research in ethnopharmacology, phytochemistry, neuropharmacology and other disciplines.

Many years later, in 1982, Ortega and his team (Ortega, Blount, and Manchand, 1982) isolated and identified the main active compound in *S. divinorum*, salvinorin A. In the early 1990s, the psychoactive properties of salvinorin A were elucidated (Siebert, 1994). With the confirmation of its psychoactivity, the cultural adoption of *S. divinorum* as a “new” psychoactive, outside of Mexico, gained considerable momentum.

THE BOTANY OF SALVIA DIVINORUM

All recorded native populations of *S. divinorum* are in Oaxaca, southern Mexico. This state is bordered by the Pacific Ocean to the west and, in the north, the Sierra Mazateca mountain range. Much of this mountain range is covered by tropical montane cloud forest (Ott, 1995, 1996; Reisfield, 1993), an ecosystem typified by high humidity and persistent cloud cover. Growing in the understory of the forest, *S. divinorum* has been found in several locations between 500 and 1500 meters altitude (Ott, 1995, 1996). Populations of this plant are mostly found near water courses in partial or full shade and

grow in moist, nutrient-rich soil. In these conditions, *S. divinorum* grows and reproduces primarily vegetatively, flowering sporadically when enough sun penetrates the forest canopy (Reisfield, 1993).

S. divinorum grows up to 1.5 m in height and has a hollow, quadrangular stem, which is green, translucent and crisp (Ott, 1996; Reisfield, 1993). The leaves are 10–25 cm long, 5–10 cm wide, and are opposite on the stem, elliptic in shape and have serrated margins (Epling and Jativa 1962; Ott 1996; Reisfield 1993). Numerous glandular and non-glandular trichomes are present on the leaf surface (Kowalczyk, et al., 2013; Siebert, 2004). The flowers have white corollas with purple calices. The flowers are three to four centimeters in length and grow on panicles of 20 to 30 flowers. According to reports on wild populations, as well as laboratory experiments, *S. divinorum* does not produce flowers on a regular, seasonal basis (Reisfield, 1993; Valdés, et al., 1987). In Oaxaca, this plant is observed to flower between October and June (Reisfield, 1993). Flowering is initiated by set durations of uninterrupted darkness greater than 12 hours (Reisfield, 1993). In laboratory experiments, it has been found that if plants are exposed to light during a dark period, flowering is aborted and the plant returns to vegetative growth (Reisfield, 1993).

There is limited information on the sexual reproduction of *S. divinorum*, however, it is very adept at clonal propagation both naturally and anthropogenically. On the basis of the reported reproductive behaviour of *S. divinorum*, it has been suggested that the more recent evolutionary trajectory of this plant may have been influenced by humans (Reisfield, 1993). It is hypothesized that *S. divinorum* may have been translocated from its original environment at some point in history, however, this has not been confirmed nor have other populations of *S. divinorum* been discovered in the Americas (Reisfield, 1993). The pollination vector for *S. divinorum* is also uncertain. It has been suggested that the pollination may be ornithophilous (Reisfield, 1993). This is corroborated by the dimensions of the corolla as well as the sugar content and the volume of nectar produced (Reisfield, 1993).

HISTORY OF SALVIA DIVINORUM

Until 1964, the use of *S. divinorum* appears to have been confined to the Mazatecs, an indigenous Mexican group located in northeast Oaxaca. The name Mazatec or Mazateca is said to mean “Lords of the Deer,” and was the name given to this group by the Aztec (Mooney, 1911). After Spanish colonization in the 1500s, the Dominicans and Jesuits began to convert indigenous peoples to Catholicism (Mooney, 1911). Although Spanish attempts at conversion were largely successful, the Mazatec also maintained their traditional beliefs, which are still practiced today (Hofmann, 1990, 1980; Mooney, 1911; Ott, 1996). The Mazatec employ three main plants with psychoactive properties as part of their spiritual practices. These include *Psilocybe* spp. mushrooms, the seeds from *Ipomoea violacea* L. (morning glory) and the leaves of *S. divinorum* (Allen, 1994, 1997; Foster, 1984; Schultes, 1969). Mazatec use of *S. divinorum* takes place primarily during healing and divination ceremonies, as well as in the training of medical practitioners (Giovannini and Heinrich, 2009).

There are four illnesses for which Mazatecs are known to have used *S. divinorum* (Johnson, 1939; Ott, 1996; Prisinzano, 2005; Valdés, Diaz, and Paul, 1983). First, this plant is often employed to cure eliminatory dysfunction such as diarrhoea. Secondly, people who are near death can be given an infusion of the plant’s juices as a palliative, after which it is reported that the patient often recuperates for a short time. Thirdly, *S. divinorum*, in small doses, is used to cure headaches and rheumatism. Finally, it is given to cure a Mazatec illness known as *panzón de arrego* or a swollen belly. This Mazatec illness is believed to be caused by a curse from a brujo, (male witch) someone who practices black or evil magic (Prisinzano, 2005; Ott, 1996; Valdés, Diaz, and Paul, 1983; Johnson, 1939).

S. divinorum is tended in secret groves, deep within the forest, by medicinal practitioners known as a *curandero* (male) or *curandera* (female) (Reisfield, 1993). It is planted in rich, black soil at the bottom of a gully, usually in close proximity to a stream (Diaz, 2013). Cuttings can be taken from the mother plant and planted directly into the moist soil, however, this plant will also root itself, if a branch breaks off and falls on the ground (Beifuss, 1997). Although these *S. divinorum* groves may be natural, it is difficult to determine the extent of human influence (Ott, 1996; Reisfield, 1993). The locations are well-protected by each individual *curandero* or *curandera* to avoid theft, and more importantly, contamination by malicious magic (Johnson, 1939). The large, mature leaves of *S. divinorum* are harvested by pinching the petiole of the leaves close to the main stem of the plant. The leaves are either eaten or crushed into a fine pulp using a mortar and pestle, and then infused in water (Campbell, 1997; Valdés, 2001).

Mazatec *curanderos* and *curanderas* are trained through an informal apprenticeship, during which they are led through a series of progressive visions by an experienced teacher (Valdés, Diaz, and Paul, 1983; Diaz 1979). These visions are initiated by the three psychoactive plants mentioned

previously and are an integral part of training. Over a period of two years, *curanderos* and *curanderas* ingest these plants at regular intervals to integrate the knowledge from their experiences into their practice (Valdés, Diaz, and Paul, 1983). Initially, trainees ingest increasingly larger doses of *S. divinorum* leaves, which show them the way to heaven, where the initiated learn from the tree of knowledge (Valdés, Diaz, and Paul, 1983).

During consumption of *S. divinorum*, either the leaves are chewed or the juice from crushed leaves is infused in water and ingested as a liquid (Diaz, 2013, 1979; Valdés, 2001). These ceremonies are led by a *curandero* or *curandera*, and last approximately two to three hours, during which time the participants, who ingested the plant, are guided through different states of consciousness (Schultes, Hofmann, and Rättsch, 2001; Ott, 1996; Valdés, Diaz, and Paul, 1983; Hofmann, 1980, 1990; Estrada, 1977; Schultes, 1976). These ceremonies take place at night in a dark and remote location to prevent disruptions (Valdés, 2001; Valdés, Diaz, and Paul, 1983; Diaz, 1979), as absolute quiet is considered essential to the success of the ceremony. Several leaves are rolled into cigar-shaped tubes, chewed and swallowed. If the participant is unable to chew the leaves or manage the bitter taste, he or she is permitted to drink juice-infused water instead (Estrada, 1977). During each ceremony, there is one person present who does not ingest *S. divinorum*. It is the role of this person to watch over the ceremony and prevent any harm to participants (Diaz, 1979; Valdés, Diaz, and Paul, 1983). After the effects of *S. divinorum* have worn off, the *curandero* or *curandera* will often bathe the participant in the juice of the leaves (Valdés, 2001), which is said to end the effects of the experience (Valdés, Diaz, and Paul, 1983). After the ceremony, participants are “debriefed”; this dialogue helps to explain the meaning of their visions and ensure the success of the ceremony (Diaz, 1979; Estrada, 1977; Hofmann, 1990; Valdés, Diaz, and Paul, 1983).

The Spanish chronicled many of the rituals, which employed psychoactive plants, but very little about *S. divinorum* was recorded. One reason for this could be that the Mazatecs have several names for *S. divinorum*. In their native language it is referred to as Ska Maria Pastora, Ska Maria, Ska Pastora, and in Spanish it is called Hojas de Maria Pastora, Hojas de la Pastora, Hoja de adivinación, Hierba Maria or La Maria (Valdés, 2001; Valdés, Diaz, and Paul, 1983; Schultes, 1972; Wasson, 1962). The Mazatecs associate this plant with the Christian saint, Mary (Valdés, Diaz, and Paul, 1983), however, the reference to her as a shepherdess is not consistent with Christian mythology (Wasson, 1962). This name may reflect an interpretation of a pre-contact description of the plant that was later incorporated into Christian beliefs (Ott, 1995).

In the scientific literature, *S. divinorum* has not received as much attention as the other plants used by the Mexican indigenous peoples including the Mazatec; the seeds of the morning glory *Ipomoea violacea* and hallucinogenic mushrooms *Psilocybe* spp. (Valdés, 2001; Valdés, Diaz, and Paul, 1983; Schultes, 1970). *S. divinorum* was first mentioned in western academic literature in 1939 by anthropologist J. Johnson (Johnson, 1939). In 1945, B. Reko reported a “magic plant” used by the Mazatecs called “hoja de adivinación” or “the leaf of the prophecy”, indicating that the indigenous people used this plant to produce visions (Valdés, Diaz, and Paul, 1983; Diaz, 1979; Schultes, 1967). Seven years later in 1952, R. Weitlander reported “yerba de Maria” used by *curanderos* in Oaxaca (Weitlander, 1952). The first botanical specimen of *S. divinorum* was collected by A. Pompa, a Mexican botanist. He described this plant as “xka [sic] Pastora” however, he was unable to collect a flowering specimen at the time leaving his collection only identified to the genus level (Pompa, 1957).

R. Gordon Wasson was a very important ethnopharmacologist and chronicler of psychoactive plants, especially those used by the Mazatec people. Wasson is best known for his research on the traditional Mexican use of *Psilocybe* spp. mushrooms. In July 1961, during his second expedition to Mexico, Wasson participated in an *S. divinorum* ceremony along with Albert Hoffman, known for his discovery of lysergic acid diethylamide or LSD (Reisfield, 1993; Hofmann, 1980; Wasson, 1962). In doing so, Wasson and Hoffman were the first western academics to participate in, and record, this ceremony. In December 1962, Wasson and Hoffman successfully collected a flowering sample of *S. divinorum*, which was classified by Carl Epling as a new species (Epling and Jativa, 1962). Contrary to popular belief, the first living *S. divinorum* specimen to be propagated outside Mexico was not collected by Wasson and Hoffman, but by psychiatrist and ecologist, Sterling Bunnell, who, in 1962, brought back a living *S. divinorum* specimen to UCLA Davis from an expedition to Oaxaca (Siebert, 2003).

Research on the effects of salvinorin A on its molecular target, the kappa-opioid receptor, has been extensive since it represents the only known non-nitrogenous kappa-opioid receptor selective agonist (Casselmann, et al., 2014).

In conclusion, *S. divinorum* was “discovered” just five years prior to the symposium on ethnopharmacology. We have no information on the links between these “discoveries” and the developing

plans for such a symposium. It may well be timely, to start a historical project on academic and social developments in the USA and beyond driven by the ethnopharmacologic search for psychoactive substances .

ETHNOPHARMACOLOGY 50 YEARS ON

Returning to the ethnopharmacology at the end of the 2nd decade of the third millennium, ethnopharmacology today has a very different focus and interest. In the years after the symposium, it seems that only limited research was going on, aside from studies on psychoactive plants and fungi as exemplified by *S. divinorum*.

The next key event was the launch of the *Journal of Ethnopharmacology* in 1979, which was founded by Laurent Rivier and Jan G. Bruhn. Here the scope shifted to “a multidisciplinary area of research concerned with the observation, description, and experimental investigation of indigenous drugs and their biological activity” (Rivier and Bruhn, 1979). Eleven years later the 1st International Congress on Ethnopharmacology was held in Strasbourg, France (5-9 June 1990) and since then 18 conferences have been held on four continents, all organized by the International Society for Ethnopharmacology (ISE - <http://www.ethnopharmacology.org/>), which was originally founded in 1990 in Strasbourg. In 2013 the Society for Ethnopharmacology, India was founded affiliated to the ISE.

Research is conducted in numerous institutions and most active are many of the fast emerging economies especially in Asia (most notably China, but also India, South Korea, Thailand, and other ASEAN countries, some African (South Africa) and American countries (esp. Brazil). Clearly, the *Journal of Ethnopharmacology* is the leading journal in the field today. In its first year (1979) 29 articles were published, ten years later (1989) this had risen to 85, in 1999 to 205, and in 2009 to 465, with 2016 seeing 649 published articles. Overall, at the time of writing (August 2017) just over 9600 articles have been published in the *Journal of Ethnopharmacology* alone.

The main areas of research today are on antioxidant, anti-inflammatory and anticancer agents (Table 1). The vast majority of these are *in vitro* or *in vivo* studies. In recent years more clinical studies on traditional preparations (often small and not well designed) have also been conducted. Studies describing the use of medicinal and other useful plants are another element of research in the field of ethnopharmacology, and these are often conducted with the goal that they lead to an experimental study of some of these botanical drugs (cf. Heinrich, et al., 2017). At the same time, it is noteworthy that psychoactive and other effects on the CNS have not been of that much importance (Yeung et al 2018). However, one must also acknowledge that this measure (i.e. keywords used in Medline) is a relatively crude one, most importantly, because research which later on focuses on pure compounds or well-defined extracts may not be coded in such a way that it is visible in this comparison.

Antioxidant	2057	Malaria	588
Inflammation	2054	Urinary	411
Cancer	2026	Central nervous system	310
Infecti\$	1971	CNS	165
Food	1600	psychoactive	62
Diabetes	1546	hallucinogen\$	64
Skin	1089	Cosmetic\$	188
Gastrointestinal	826	Fertility	156
Respiratory	638	aphrodisia\$	111

Table 1 Main topics covered in ethnopharmacological research (number of hits): Medline database search (13/05/2017) combing “Ethnopharmacology or traditional medicine” with specific therapeutic areas as specified. (Ethnopharmacology or traditional medicine): 21,697 [Ethnopharmacology only: 11,607] and

CORE CHALLENGES

Plants (and animal) based medicines are an integral part of indigenous medical systems in many regions of the world, and form a part of the traditional knowledge of a culture. While the focus of the symposium which gave ethnopharmacology its “modern” name and the current areas of research

differ, it is the conviction of the authors of this paper, that the commonality is in the hope that this research will not only provide scientific evidence both in socio-cultural as well as in biomedical terms but that it will help in empowering people, recognising their autochthonous traditions and enabling them to make the best use of such knowledge.

A key criticism the field had to engage with is the accusation of exploiting local and traditional knowledge without fair and appropriate benefits to the regions of origin and the original keepers of this knowledge and practice. However, scientists have been the first to highlight the inextricable link between cultural and biological diversity. In 1988 a group of dedicated scientists involved in research on local and traditional uses of plants and biodiversity conservation and with strong interest in supporting indigenous and local peoples called for the recognition of indigenous rights and for increased support for research on ethnobiological inventories, on conservation and management programmes – resulting in the *Declaration of Belem* (Posey and Dutfield, 1996). Four years later, in 1992, the Convention on Biological Diversity (Rio Convention) was signed and has since been amended in numerous treaties and protocols, most recently (2010) the Nagoya Protocol (*Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization (ABS) to the Convention on Biological Diversity*). This development is both driven by the historical experience of many countries, and as importantly, indigenous peoples in exploitative extractions of biodiversity. Ethnopharmacology was one of the disciplines both involved in the debate and affected by the resulting legal changes. 25 years after the Convention on Biological Diversity and 50 years after San Francisco conference that led to a named new field of research, there are still no examples where research and the requirements for benefit sharing have resulted in concrete and long term benefits to the regions or countries of origin.

In the last 25 years, numerous efforts have focused on translating the principles of this treatise into best practice. However, examples of problematic or poor practice also abound. We continue to have a very complex and critical debate about who benefits from this research and on how we best follow the ethical guidelines which in this field are most prominently, based on the Convention on Biological Diversity (the Rio Convention, 1992) and subsequent agreements. An understanding of these efforts needs to be based on the fast changing framework, and for example, the Sustainable Development Goals directly impact on the research and development needs globally. Consequently, modern ethnopharmacological research provides new evidence for old preparations and contributes to primary health care (Heinrich 2010). How to best achieve this is still in its infancy and we – as scientists – have still not achieved large scale contributions to improving healthcare globally.

In this regard ethnopharmacology is embedded in a wider debate about the historical and future role of traditional medicines and medical systems globally. In 2016 some systems of traditional medicine (TM) were included in the 11th edition of the International Classification of Diseases (ICD-11), providing a strong impetus both for closer links between traditional medicines and biomedicine, but also adding new responsibilities to practitioners of TM and to those who investigate such medical systems

Ongoing debates relate to best practice in the field (e.g. Cos, et al., 2006, Heinrich, et al., 2017). Here concerns about what constitutes best practice in terms of concepts and methods are addressed and clearly, there is a need to improve the methods we use in data acquisition and analysis. These debates are shared with many other fields of research, and, for example, best practice in pharmacological research is an important concern in many areas of the discipline. Biomedical research that cannot be reproduced or which is of poor quality or which is poorly reported will ultimately undermine the credibility, relevance, and sustainability of the research process in general (e.g. Mullane, et al., 2015).

CONCLUSION

This volume celebrates the fiftieth anniversary of a very important conference, and in this paper, we have looked beyond the scope “ethnopharmacology” covered at its start. While one must acknowledge that psychoactive natural substances are no longer at the center, the detailed look at the history of the discovery of *Salvia divinorum* by Western science and society has been an important driving force not only leading the conference (Schultes, 1967), but has continued with a flurry of neuropharmacological research on the species and its active metabolites. As such it exemplifies how ethnopharmacology links the study of local knowledge and practices and bio-scientific and biomedical investigations. Today’s research is thriving but also the conflict exemplified in the history of “discovering” and researching *Salvia divinorum* are a part of the current scenario. Research

in ethnopharmacology must, by definition be interdisciplinary, or preferably transdisciplinary, and applying these findings in prevention and treatment should be an element of such research.

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