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Plant hallucinogens: springboards for psychotherapeutic drug discovery

Dennis J. McKenna*

Botanical Dimensions[1], *P.O. Box 807, Occidental, CA 95465, USA*

Abstract

Medicinal chemists have traditionally looked to the biosynthetic diversity found in nature to provide structural templates for the development of novel therapeutic agents, and the field of hallucinogen chemistry is similar to other fields in this respect. Even LSD, for many psychopharmacologists the prototype hallucinogen, is not itself a natural compound but rather is a semisynthetic analogue of alkaloids found in plants and fungi. A similar statement could be made about the other major structural classes of hallucinogenic agents: the phenylethylamine derivatives, the tryptamine derivatives, and the β-carboline derivatives. In each case, compounds occurring naturally in some plant, usually associated with a long tradition of ethnomedical or ceremonial use, have been the starting point for the synthesis of numerous analogues. Some of these, such as the methoxylated amphetamine derivatives, display a pharmacological profile that differs in important respects from their natural product templates. In some instances the analogues have proven to be useful tools in the hands of neurobiologists characterizing the structure and function of brain neurotransmitter systems; in other cases, they have led to the development of new psychopharmacological agents with realized or potential clinical utility. This paper gives a brief historical overview of the role of natural products in the history and development of medicinal chemistry and experimental pharmacology, particularly with respect to the development of psychopharmacology and the discovery of CNS-active agents. It discusses the potential for the discovery of new medications with psychotherapeutic and/or research applications though the investigation of plants and natural compounds with serotonergic activities. Finally, consideration is given to some lesser known plant hallucinogens which may provide further useful leads for psychotherapeutic drug discovery.

Keywords: Hallucinogen; Medicinal plant; Ethnomedicine; Natural product; Serotonin; Drug discovery; Psychopharmacology; Medicinal Chemistry

1. Introduction

The utilization of plants as therapeutic medicines is an ancient tradition, far older than the contemporary sciences of medicine, pharmacology, or chemistry; it is a tradition that can claim both historical and prehistoric precedent, having its origins in an era when medicine, magic, religion, and pharmacology were facets of a single empirical discipline. In many indigenous cultures, plant-based, traditional medicine has remained essentially unchanged from the form practiced by our ancestors 5000 or more years ago. Even in our contemporary era of sophisticated medicinal chemistry and pharmacological 'magic bullets', plant-derived medicines remain significant. The World Health Organization has estimated that over 75% of the world's population still relies on plant-derived medicines, usually obtained from traditional healers, for their basic health-care needs [1]. According to recent estimates, as many as 25% of currently available prescription drugs contain plant extracts or naturally occurring compounds, while at the same time, less than 10% of the earth's 400,000 to 750,000 plant species have been scientifically investigated for possible pharmacological activity [2]. Clearly the 90% of the world's flora that remains uninvestigated comprises a rich trove for the discovery of new therapeutic compounds, including those with neuropharmacological and psychopharmacological activity. The contributions to this discovery process that could be made through the systematic investigation of the chemistry and pharmacology of plant hallucinogens is the subject of the present paper.

*Corresponding author. Fax: (1) (612) 433 5104;
E-mail: djmckenna@aol.com.

[1] Botanical Dimensions is a non-profit, 501(c)3 Organization dedicated to the investigation and preservation of plants of ethnomedical significance and their lore. Recently, Botanical Dimensions sponsored an interdisciplinary biomedical investigation of hoasca, a hallucinogenic beverage used throughout the Amazon Basin.

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