SPECIAL ARTICLE

PSYCHOTOMIMETICS, CHEMICAL, PHARMACOLOGICAL AND CLINICAL ASPECTS

By

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The psychotomimetics, also termed "mind changing drugs" differ from other groups of psychotropic substances in producing very profound psychic changes associated with changes in the perception of reality, of space and time, and of the body image. They transfer the subject into a sort of dream world, which is experienced as quite real. Consciousness is always retained. Hallucinations occur only after very high doses ; they are not a characteristic feature of these substances, it would therefore be more correct to call them not hallucinogens, but psychotomimetics ; they mimic a sort of psychosis. Most of them are known as magic or esoterical drugs.

After a brief review of the psychotomimetics listed in the table, the drugs derived from the author's own investigations, (LSD 25), psilocybin and the active principles of ololiuqui) are discussed in greater detail.

Psychotomimetics

Anhalonium Lewinii (peyotl) :	mescaline
Cannabis indica (hashish) :	tetrahydrocannabinols, etc.
Peganum harmala	harmine (banisterine), yageine,
Banisteria caspi (yage)) ;	telepathine), harmaline
Piptadenia peregrina (cohoba) :	bufotenin, dimethyltryptamine
Piper Methysticum (kawa-kawa) :	active principles uknown
Amanita muscaria :	active principles unknown
d-lysergic acid diethylamide (LSD) 25)	
Psilocybe spec. } (Teonanacatl) :	psilocybin, psilocin
Stropharia cubensis }	
Rivea corymbosa (ololiuqui) :	alkaloids of the ergot type

LSD 25

d-Lysergic acid diethylamide, known as LSD 25 (formula I) a semi-synthetic compound from ergot, is by far the most active and most specific psychotomimetic known. The effective oral dose in human beings is 0.02—0.05 milligrams.

LSD proved to be a valuable tool in experimental psychiatry in producing so-called model psychosis. Further more it offers new possibilities for the experimental study of psychosomatic relationships.

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The distribution in the body and the excretion was studied in mice with the aid of LSD labelled with ^{14}C. Surprisingly enough the concentration is lowest in the brain. Excretion is mainly, i.e., about 80%, through the liver, bile and intestinal tract.

A comprehensive study of the pharmacological properties on the one side and of the psychic activity on the other side of LSD and of a large number of derivatives of this compound showed that there exists a relationship between psychotomimetic activity and the syndrome of a general central sympathicotonic stim ulation.

Another important pharmacological property of LSD is its antagonism to serotonin. In extremely low concentrations LSD blocks the peripheral effects of this neurohumoral agent—(formula VII).

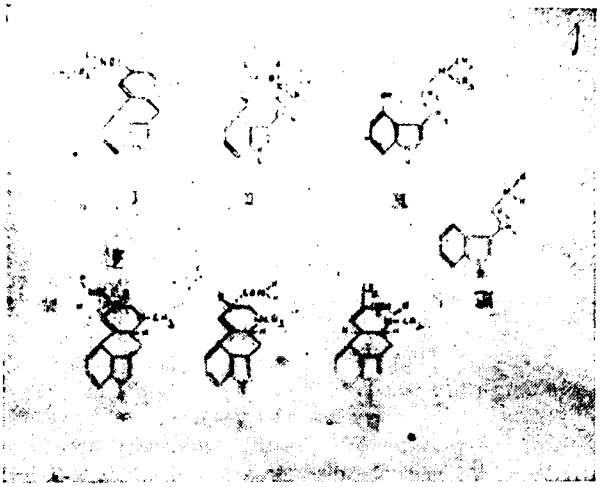
Psilocybin

The sacred mushroom (teonanacatl) played an important role in the pre-columbian cultures of Central America. It was eaten by the Indians at their feasts and religious ceremonies and also by soothsayers to acquire clairvoyance. Sacred mushrooms are still used in our day for magic purposes by certain Indian tribes in the remote mountains of South-Mexico, as reported by R. G. Wasson and the well-known mycologist, R. Heim. In 1958 A. Hofmann and colleagues succeeded in isolating the active principles of Psiclocybe mexicanna Heim, and of other "Sacred mushrooms". The main component was named psilocybin, which is accompanied by small amounts of a related compound named psilocin.

The chemical constitution of psilocybin (formula II) and psilocin (formula III) could be confirmed by the total synthesis of these compounds.

Ololiuqui

Very recently the riddle of "Ololiuqui" another ancient magic drug of the Aztecs and other Indian tribes of South Mexico, has been elucidated. "Ololiuqui" are the seeds of certain convolvulaceous plants such as Rivea corymbosa (L.) Hall. f. and Ipomea tricolor Cav. The active principles have been found to be alkaloids of the ergot type. Three of the components could be crystallized and identified so far, i.e., lysergic acid amide (isoergine) (formula IV), isolysergic acid amide (ergine (formula V) and chanoclavine (formula VI.)



Observations on the chemical structure of psychotomimetics.

A review of the structural formulae of the natural psychotomimetics shows that with the exception of the non-nitrogenous active principles of hashish and of mescaline, they are all indole derivatives or more accurately tryptamine derivatives. The structural relationship of the psychotomimetics with the brain factor serotonin which all are tryptamine derivatives, suggest that certain idole structures are of importance in the biochemistry of psychic functions.

The use of psychotomimetics in experimental and practical psychiatry

The resemblance borne by the effects of psychotomimetic substances to the symptoms of certain mental disorders led to the term "model psychosis" being coined. Such model psychoses are of value in the experimental study of the biochemical processes involved in mental disorders.

In recent years promising results have also been obtained with the use of psychotomimetics as drug aids in psychotherapy. Mainly two effects of drugs such as LSD and psilocybin are of value :

(1) their ability to release the patient from his autistic fixation and isolation by shattering and transferring his customary setting. As a result, the patient can re-establish rapport with the therapist.

(2) these drugs reactivate forgotten or repressed memories. Even experiences of very early childhood may be reactivated. This is of major importance for the success of psychotherapy, particularly when the experiences are those which have led to psychic trauma.

Agents such as the psychotomimetics with their profound and unforseeable effects may not be taken by patients without medical supervision. But in the hands of the skilled capable psychotherapist these substances are new drug aids which facilitate the task of the doctor in his objective recognition of the conflicts involved and subjectively enable the patient to attain self-awareness and gain insight into his disease.