

## PSYCHOACTIVE SUBSTANCES IN NATURAL PRODUCTS AND THEIR MANAGEMENT\*

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The subject of substances had received great attention compared to other substances. This is because of their characteristics to produce drug dependence which has led to public health and social problems. This resulted in international drug control treaties to reduce the harm produced by these substances. It is also true that some of the most useful medicines have been derived from these plants, e.g. morphine and codeine.

It was in 1909 that the Shanghai Conference recommended the creation of a mechanism at the international level for control of dependence-producing substances. There are three international treaties which are available to countries to use (1):

1. **Single Convention on Narcotic Drugs, 1954 and its revising Protocol of 1972.** This convention covers principally substances derived from *Papaver somniferum*, *Erythroxylon coca* and *Cannabis sativa*. Many synthetic substances similar to opiates are also controlled under this convention. This convention has been ratified by about 125 countries and controls about 100 substances.

2. **Convention on Psychotropic Substances of 1971.** This covers a wide range of psychotropic substances including tetrahydrocannabinol derived from *Cannabis sativa* plant. This convention has been ratified by about 95 countries and controls about 90 substances.

3. **1988 UN Convention Against Illicit Trafficking on Narcotic and Psychotropic Substances.** This new convention was adopted in November 1988 and controls primarily precursors which are used in the manufacture of narcotic drugs and psychotropic substances.

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## Development of behavioural pharmacology.

It was important to investigate these substances and a new discipline of behavioural pharmacology has been developed. This deals with investigation of the dependence liability, abuse potential and actual abuse of these substances. A Committee on Problems of Drug Dependence in the U.S.A. meets every year where researchers meet to exchange their views and suggest interventions. The WHO also had to establish an Expert Committee on Drug Dependence where problems of drug dependence are reviewed. Substances requiring international control are recommended to the Secretary-General of the United Nations and the decision to control this taken by a 40-member UN Commission on Narcotic Drugs in Vienna.

I would like to speak of my personal contributions to the subject since I had been in charge of the responsibilities under international treaties at WHO Headquarters.

I began my professional career in pharmacology at the University of Edinburgh under Professor J.H. Gaddum in 1956. At the Department of Pharmacology the group led by Gaddum had identified serotonin in the dog's brain. Gaddum also had demonstrated that LSD antagonizes the stimulant actions of serotonin on smooth muscles and thus the hallucinatory effects of LSD may be due to this antagonism. It was Hoffman who earlier shown that LSD produces hallucination (2).

On my arrival at Edinburgh in 1956, Dr R.B. Barlow had synthesized about 25 analogues of serotonin and tryptamine hoping that I would find potent antagonists of serotonin and that these may find a place in treating some diseases.

At WHO headquarters, I remained responsible for this programme for 14 years (1976-1990). The following are the highlights of my activities:

*Papaver bracteatum*. I inherited from Dr George Ling a project to investigate the pharmacology of thebaine, a principle constituent in *Papaver bracteatum*. The purpose of the project was to be able to use *Papaver bracteatum* for obtaining the world's legitimate needs of opiates. Professor Schuster of Chicago, Professor L. Harris of Richmond, Virginia and Professor Yanagita of Japan collaborated with WHO in this project (3). Buprenorphine, an opioid agonist and antagonist, obtained from thebaine was also reviewed and recommended for international control.

*Cannabis sativa*. The Single Convention on Narcotic Drug controls the plant while seven analogues THC are controlled under the 1971 Convention. While formulating the 1971 Convention they included all isomers of THC un-

Schedula I of the 1971 Convention. WHO collaborated with Professor Salemink of Utrecht and reviewed the subject. A subsequent WHO Expert Committee (TRS 618) identified only 7 isomers of THC which were placed under control.

The US Government had requested that controls on dronabinol, an isomer of Delta-9-THC be reduced as it was a useful medicine in preventing vomiting induced by cancer chemotherapy. The WHO Expert Committee (S 787) had agreed with this recommendation but the case is still not accepted by the UN Commission on Narcotic Drugs.

*Erythroxylon coca.* Cocaine is the most active alkaloid in this plant. It is used as a local anaesthetic. Coca leaf is used in the Andean region for a number of indications. WHO with Professor Salemink has reviewed substances other than cocaine present in this plant. Their pharmacological properties were reviewed and is published in the Journal of Ethnopharmacology. My personal view is that coca leaf can hardly contribute to modern therapeutics but has created numerous drug abuse problems in many societies.

*Catha edulis.* The UN Narcotics Laboratory and in particular, Dr Andrei have been responsible for the isolation of many substances from the plant: in particular, cathinone and cathine. The WHO has investigated the pharmacological properties of these two substances and the associated public health and social problems associated with khat chewing. Based on these investigations, WHO has recommended cathinone, the most active principle in khat, and cathine for control under the 1971 Convention (TRS 618, (5,6)). The UN Commission has accepted this recommendation. The decision whether and when to control khat as a plant still remains for the authorities in countries to decide. Notification to the Secretary-General of the Convention by a Member State party to the 1971 Convention will enable WHO to regulate the plant material and seek advice of an Expert Committee on Drug Dependence. (7-9)

## REFERENCES

1. REXED, B. et al. (1984). Guidelines for the control of Narcotic and Psychotropic Substances in the Context of the International Treaties. WHO publication.
2. KHAN, I., (1959) Ph.D. Thesis University of Edinburgh.

3. KETTENES - VAN DER BOSCH, J. J., SALEMINK, C.A., KHAN, I., (1981) Biological Activity of the Alkaloids of *Papaver bracteatum* Lindl. *Journal of Ethnopharmacology* **3**, 21-38
4. NOVAK, M., SALEMINK, C.A., KHAN, I. (1984) Biological activity of the alkaloids of *Erythroxylon coca* and *E. novogranatense*. *Journal of Ethnopharmacology* **10**, 261-274
5. KHAN, I., and KALIX, P. (1984) Khat, a plant with amphetamine-like effects. *Trends in Pharmacological Sciences including Toxicological Sciences*.
6. KALIX, P., KHAN, I. (1984) Khat, an amphetamine-like plant material. *Bulletin of the World Health Organization* **62** (5), 681-6
7. WHO (1978) Expert Committee on Drug Dependence -21 st Report. Technical Report Series (618).
8. WHO (1985) Expert Committee on Drug Dependence-22 nd Report Series (729)
9. WHO (1989) Expert Committee on Drug Dependence-26 th Report. Technical Report Series (787).