



ANTIPSYCHOTIC ACTIVITY OF AQUEOUS ETHANOLIC EXTRACT OF *TINOSPORA CORDIFOLIA* IN AMPHETAMINE CHALLENGED MICE MODEL

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Received: 21st January 2010 Revised: 25th February 2010 Accepted: 13th March 2010

Abstract

Tinospora cordifolia is reported to have CNS active principle and is used for the treatment of various neurological disorders. Hence, the effect of aqueous ethanolic extract of *Tinospora cordifolia* was investigated for its putative antipsychotic activity using amphetamine challenged mice model. Haloperidol (1 mg/kg i.p.) was administered acutely to mice as standard drug. Control animals received vehicle (10% DMSO). The in vivo receptor binding studies were carried out to correlate the antipsychotic activity of the extract with its capacity to bind to the DAD₂ receptor. The results in SLA showed that the hydro alcoholic extract of the stems of *Tinospora cordifolia* at a dose level of 250 mg/kg and 500 mg/kg showed no significant antipsychotic activity in amphetamine induced hyperactivity in mice when compared to standard. Extract alone treated group at a dose level of 250 mg/kg and 500 mg/kg showed a decreased in locomotor activity when compared to the control. The plant extract increased the DAD₂ receptor binding in a dose dependent manner in treated mice compared to the control group.

Key words: *Tinospora cordifolia*, amphetamine, locomotor activity, ethanolic extract.

Introduction

Up to half of current drugs are derived from natural products. Less developed countries: 80% of people rely on plant-based medicine for primary health care (1). The

natural products often serve as chemical models or templates for the design and total synthesis of new drug entities. Because of modern isolation techniques and pharmacological testing procedures, new plant

drugs usually find their way into medicine as purified substances rather than in the form of older galenical preparations. The species *Tinospora cordifolia* (Family: Menispermaceae) is a traditional plant used in *ayurvedic medicine* for its general tonic, anti-periodic, anti-spasmodic, anti-inflammatory, anti-arthritic, anti-allergic and anti-diabetic properties and in the treatment of various other diseases. In the present study, an attempt has been made to explore the psychoactive potential of the aqueous ethanolic extract of *Tinospora cordifolia* in amphetamine challenged mice model. The *in vitro* receptor binding studies were also done to correlate the antipsychotic activity of the plant extract with its capacity to bind to the DA-D2 receptors.

Guduchi [*Tinospora cordifolia* (Wild.) Miers ex Hook. F. & Thoms] is a large, glabrous, deciduous climbing shrub belonging to the family Menispermaceae (2). It is distributed throughout tropical Indian subcontinent and China, ascending to an altitude of 300m. Propagated by seeds and vegetative method. It was large extensively spreading glabrous, perennial deciduous twiner with succulent stems and papery bark; leaves simple, alternate, cordate, entire, glabrous, 7-9 nerved, flowers yellow in lax racemes, flowers usually solitary; fruits drupe, red when ripe. The surface of the stems appears to be closely studded with warty tubercles and the surface

skin is longitudinally fissured. On removal of the surface skin, the dark greenish mucilaginous stem is seen. A variety of constituents has been isolated from *Tinospora cordifolia* plant and their structures were elucidated. They belong to different classes such as alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoids, phenolics, aliphatic compounds and polysaccharides (3).

Materials and Methods

Collection of the plant material

The plant material (stem), *Tinospora cordifolia*, was collected from National Botanical Research Institute, Lucknow in the month of November, 2008 and the identity of the plant was confirmed by Dr. A.K.S Rawat, Scientist, Pharmacognosy, NBRI, Lucknow.

Extraction

Dried and powdered stems were extracted by cold percolation method using 50% aqueous ethanol as solvent.

Pharmacological Studies

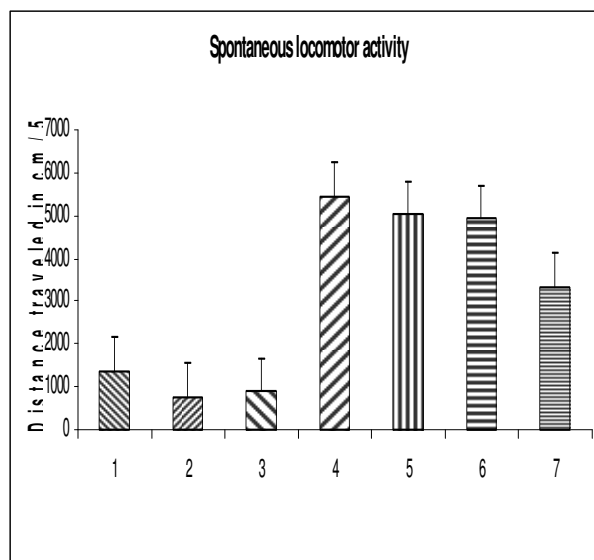
1. Assessment of spontaneous locomotor activity (4).
2. Receptor Binding Assay (5).

Administration of drug

Female albino mice of Wistar strain (28 ± 2 , body weight) were divided into seven groups of six animals each. Animal experimentation procedures were approved by Institutional Animal Ethics Committee and

care of laboratory animals was taken as per CPCSEA guidelines

Group I (Sham), Group II (Plant extract, 250 mg/kg), Group III (Plant extract, 500 mg/kg), Group IV (Amphetamine, 5.5 mg/kg), Group V (Plant extract and Amphetamine), Group VI (Plant extract and Amphetamine), Group VII (Haloperidol and Amphetamine).










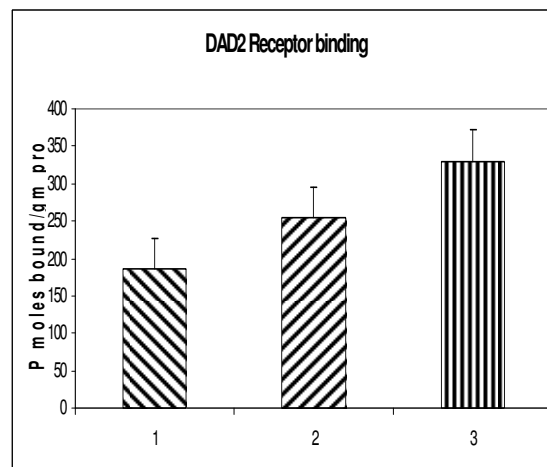
-  Control
-  Extract (250 mg/kg)
-  Extract (500 mg/kg)
-  Amp (5.5 mg/kg)
-  Amp (5.5 mg/kg) + Extract (250 mg/kg)
-  Amp (5.5 mg/kg) + Extract (500 mg/kg)
-  Amp (5.5 mg/kg) + Hal (1 mg/kg)

Figure 1: Effect of extract on Spontaneous Locomotor Activity in control and treated animals.






-  Control
-  Extract (250 mg/kg)
-  Extract (500 mg/kg)

Figure 2: Effect of the extract on *In vivo* DAD₂ receptor binding

Results and Discussion

1. Spontaneous Locomotor Activity

The hydroalcoholic extract of the stems of *Tinospora cordifolia* (Menispermaceae) at a dose level of 250 & 500 mg/kg showed no significant antipsychotic activity in amphetamine induced hyperactivity in mice when compared to the standard. Extract alone treated group at a dose level of 250 & 500 mg/kg showed decrease in locomotor activity when compared to sham. This suggests that *Tinospora cordifolia* has no significant antipsychotic activity at a dose level of 250mg/kg and 500 mg/kg.

2. *In vivo* Receptor Binding Studies

In order to correlate the antipsychotic activity of the drug with its capacity to bind to the receptors under study the *in vivo* receptor

binding studies were carried out. The results were expressed in p moles bound/g protein. Results of DA-D₂ receptor binding studies indicate that *Tinospora* increases the DA-D₂ receptor binding in a dose dependent manner in treated mice as compared to sham group. Thus, it may be concluded that possibly it acts through the dopaminergic DA-D₂ receptors.

Conclusion

The CNS acting drugs are invaluable therapeutically; because they can produce specific physiological and psychological effects. All critical analysis on commercial and other information available on traditionally known CNS active herbal remedies indicate that the most popular amongst such remedies are those which are clinically and preclinically the most well studied ones, and which are also recommended for therapeutic purposes by the health authorities of many Western and other countries outside the USA. The action of the nervous system and its subtle disruptive functioning caused by xenobiotics could be evaluated through the performance of animals in several behavioral tests (6). On the basis of the results it may be concluded that the aqueous ethanolic extract of *Tinospora cordifolia* possess no psychoactive potential at the given dose levels.

References

1. Agarwal A.K., Chaturvedi R.K., Shukla S., Sheth K., Chauhan S., Ahmed A., Sheth P.K.. Restorative potential of dopaminergic grafts in presence of antioxidants in rat model of Parkinson's disease. *J. Chem. Neuroanat.* 2004a; 8: 253-264.
2. Anonymous, The Wealth of India 'Raw Materials' (Revised Ed. Vol.-X), Council of Industrial and Scientific Research, New Delhi.2003. pp 70-71.
3. Dixit S. N., Khosa R. L. Chemical investigation on *Tinospora cordifolia*; *Indian Journal of Applied Chemistry.* 1971; 34(1): 46-47.
4. Powell C.M., Miyakawa T. Schizophrenia-Relevant Behavioral Testing in Rodent Models: A Uniquely Human Disorder? *Biological Psychiatry.* 2006; 59 (12): 1198-1207.
5. Hamblin M., Creese L. Receptor Binding and the discovery of psychotherapeutic drugs. *Drug Development Research.* 1999; 1(4): 343-372.
6. Sethiya N. K., Thakore S. G., Mishra S. H. Comparative evaluation of commercial sources of indigenous medicine shankpushpi for anti-stress potential a preliminary study. *Pharmacology online.* 2009; 2: 460-467.