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HUMAN

Hypnotic effect of methanolic extracts of *annona senegalensis* bark and *ficus thonningii* leaves in mice and chicks

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ABSTRACT

Annona senegalensis and *Ficus thonningii* are indicated for the management of ailments ranging from stomach disorders, veneral disease, toothache, psychosis and snake envenomation. Methanolic extracts of these plants was investigated for hypnotic effect in adult mice and day old chick models of hypnosis. Results obtained showed that the extract of *Annona senegalensis* has pronounced central nervous system depressant effect, which manifested inform of sedation followed by sleep. It also potentiated the central nervous system depressant effect of phenobarbitone. These effects were dose dependent, 1,000 mg/kg of the extract showed higher activity than 500mg/kg. *Ficus thonningii* did not demonstrate significant central nervous system effect, but it potentiated central nervous system depressant effect of phenobarbitone. The results obtained supports the use of combinations of these plants for the management of psychosis.

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INTRODUCTION

Annona Senegalensis Pers of the family *Annonaceae* is locally called wild custard apple in English and ocha (Igbo), abo or arere (Yoruba) in local languages, (Burhill, 1985). It is a small tree or shrub found in the savannah, but can grow up to 6m. Its bark infusion is used for the relief of toothache, root bark as antidote to snake bite, the wax as a larvicidal agent, and leaf infusion as an eye lotion (Dalziel 1937). The lotion and infusion are used for the management of leprosy in male, (Chevalier 1937). Mixture of perforated leaves with lattices of *Caloropis procera* (Asclepiadaceae) and *Euphorbia batsamifera* (Euphobiaceae) are applied as a droning for the management of yaws in horses (Dalziel 1937). The root is used as ingredients in the preparation of arrow poison (Jackson, 1973). Stem and root barks are used for diarrhea and gastrointestinal troubles (Kerharo and Adam 1964). The roots are used in Northern Nigeria for the treatment of veneral disease, (Dalziel 1937). The Bark is chewed in Senegal for Stomachache and its infusion with other plant bark is used for treatment of skin Eruption, (Dalziel 1973). The fruit when eaten in much quantity give favorable treatment for guinea worm infestation, (Dalziel 1937). The bark of the trunks, branches and roots are used extensively, as vermifuge (Dalziel 1937).

Phyto-chemical analysis of the root powder showed the presence of tannin, wax, glycosides, proteins and amino acids. Seed, bark, leaves and fruits contain a minor alkaloid of Aporplime known as annonaine, (Oliver 1960).

Ficus Thonningii is called cediya in Hausa. It is commonly found in town where it is grown for its shade.

The study seeks to determine the hypnotic effect of *A. senegalensis* and *F. thonningii* in adult mice and day old chicks.

MATERIALS AND METHODOLOGY

Collection and extraction of plant materials

The leaves of *Ficus thonningii* and bark of *Annona senegalensis* were obtained by herbalist on 16th September 2008 in Jos and identified by Mr abdukareem of school of forestry, Jos. Collected plant materials were dried under the shade for about 6 weeks. The leaves and bark were reduced and sieved individually. Each powder was soxhlet extracted with methanol for 72 hours. The obtained methanol extract was collected into a pre-weighed beaker and evaporated to dryness at 40° C. The process was repeated for the second powder. The concentration of the stock solution obtained was prepared by reconstituting the appropriate amount of the extract in a measured volume of distilled water.

Hypnotic effect of *A. senegalensis* and *F. thonningii*

Wister rats were divided into four groups of five each, group A received 40 mg/Kg of phenobarbitone, group B received distilled water, while groups C and D received 500 and 1000mg/Kg of *A. senegalensis* and groups E and F received 500 and 1000mg/Kg of *F. thonningii*. After 30 minutes, the rats were observed for reduced activity and hypnosis. The same procedure was repeated using day old chicks.

Effect of *Annona senegalensis* and *Ficus thonningii* extracts on phenobarbitone induced sleep

The chicks were divided into four subgroups I, II, III and IV of five each. Each groups received 500 mg/kg and 1000 mg/kg each of *A. senegalensis* and 500 mg/kg and 1000 mg/kg *F. thonningii* respectively. Thirty minutes after the administration of the extract, the chicks were injected with 40 mg/Kg of phenobarbitone (I.P), and observed for hypnosis.

RESULT

Table 1: Hypnotic effect of A. senegalensis and F. thonningii in adult mice

Treatment	Onset of sleep (min)	Duration of sleep (min)
Phenobarbitone (40 mg/Kg)	34.20±1.72	87.60±3.88
A. senegalensis (extract):		
500 mg/kg	49.20±1.20*	62.20±4.37*
1000 mg/kg	41.40±4.12*	79.60±12.35*
F. thonningii (extract):		
500mg/kg	–	–
1000mg/kg	–	–
Distilled water (10 ml/kg)	–	–

KEY:

*****P<0.05 significant difference when test is compared with phenobarbitone.

Table 2: Hypnotic effect of A. senegalensis and F. thonningii in day old chicks

Treatment (ml)	Onset of sleep (min)	Duration of sleep (min)
Phenobarbitone (40 mg/Kg)	7.00±0.32	496.20±13.08
A. Senegalensis (extract);		
500 mg/kg	24.00±1.14^{++}	122.40±8.86**
1000 mg/kg	18.60±1.73^{+}	169.40±20.19**
F. Thonningii (extract);		
500 mg/kg	–	–
1000 mg/kg	–	–
Distilled water (10 ml/kg)	–	–

**KEY: ****P<0.001, $^{+}$P<0.05, $^{++}$P<0.001, significant difference when compared with phenobarbitone

Table 3: Effect of A. senegalensis and F. thonningii on phenobarbitone-induced sleep in day old chicks

Treatment	Onset of sleep (min)	Duration of sleep (min)
Phenobarbitone (40 mg/Kg)	7.00±0.32	496.20±13.08
A. Senegalensis		
Extract + Phenobarbitone (40 mg/Kg)		
500 mg/Kg	6.60±0.25	793.80±19.55**
1000 mg/kg	5.80±0.66	1034.00±38.58***
F. Thonningii		
Extract + phenobarbitone (40 mg/Kg)		
500 mg/kg	7.40±0.37	739.00±30.69**
1000 mg/kg	6.80±0.49	788.60±81.75**
Distilled water (10 mg/Kg)	_	_

**KEY: ***P<0.05, **P<0.001, ***P<0.0001 significant difference when compared with phenobarbitone.

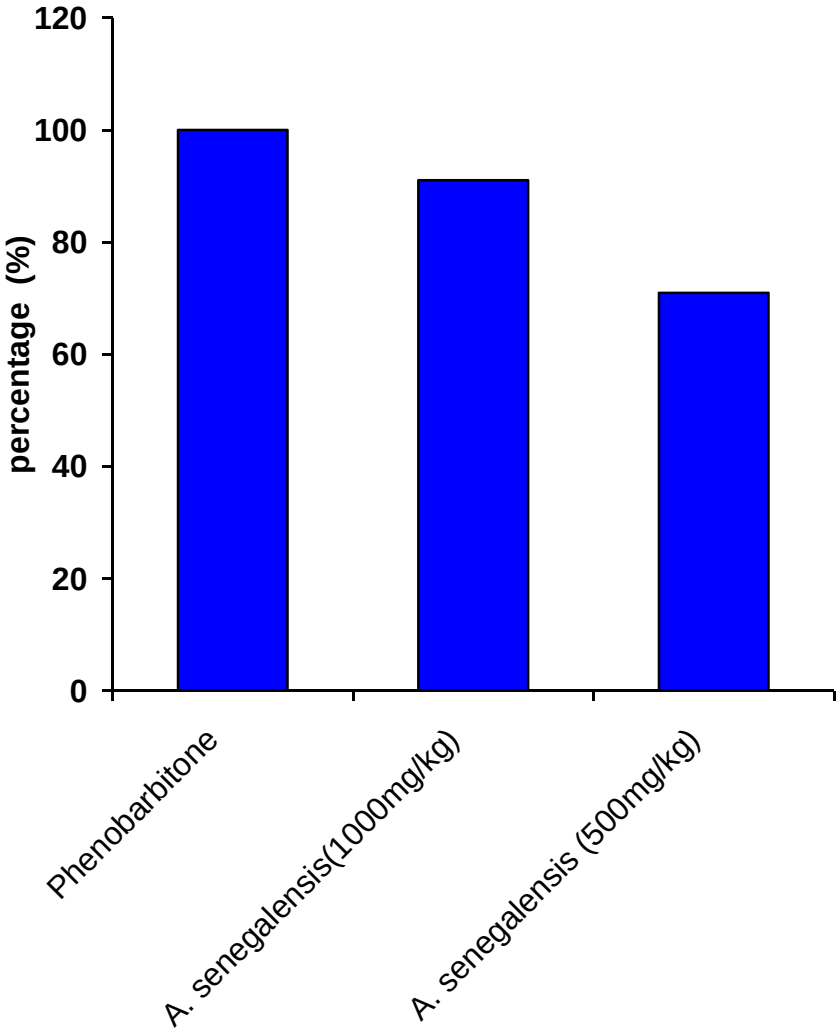

FIG. 1: PERCENTAGE DURATION OF SLEEP BY A. senegalensis IN MICE

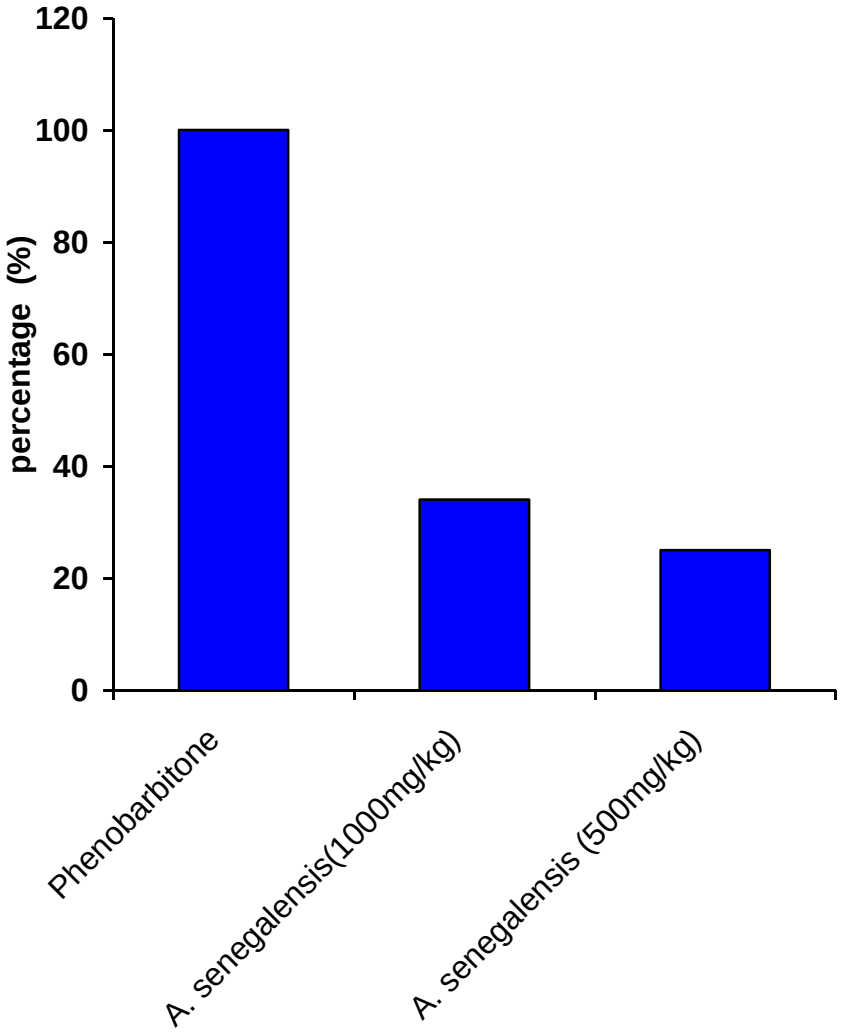

FIG. 2: PERCENTAGE DURATION OF SLEEP BY A. senegalensis IN DAY OLD CHICKS

DISCUSSION

Ancient people used different methods and procedures to treatment of psychiatric disorders and very often, herbal concoctions are used in the procedures. Numerous scientific discoveries in the industrial age have revealed that most of the medicinal plants used in the management of psychosis possess sedative-hypnotic activity. Chemical agents discovered from these herbal medicines have made massive contribution to the development of modern day medicine and significantly improved quality of life of psychiatric patients in the last century. Large numbers of patient still use natural medicinal plants for self-treatment of different psychiatric disorders (Babic, 2007).

Many of today's synthetic drugs originated from the plant kingdom, and until only about two centuries ago, major pharmacopoeias were dominated by herbal drugs. Herbal medicine went into rapid decline when basic and clinical pharmacology established themselves as leading branches of medicine. Nevertheless, herbal medicine is still of interest in many diseases, in particular psychiatric and neurological disorders. Although very many pharmaceutical agents are available for the treatment of mental disorders, physicians find that many patients cannot tolerate the side effects, do not respond adequately, or eventually stop responding to these drugs. In comparison to orthodox medicines, many therapeutic herbs have far fewer side effects. They can provide an alternative treatment or be used to enhance the effect of prescription medications (Seyedeh-Atefeh *et al.,* 2013, Akhondzadeh, and Maleki, 2006).

Results from this study revealed that the extracts of *A. senegalensis* and *F. thonningii* had effect on phenobarbitone-induced sleep. *Ficus thonningii* alone did not alter the behavioural activities of the animals (mice and day old chicks). Changes such as increased/decreased locomotor activity, depression, aggressive tendency, pecking at selves or at foot, withdrawal syndrome or sleeping effect was not observed. The effects observed was similar to that obtained with distilled water (test control).

A. senegalensis extract induced hypnosis in mice and day old chicks, it reduced the onset of sleep induced by phenobabitone (i.e. onset of hypnosis), as observed by loss of writing reflex. The onset of sleep was shorter in day old chicks than in adult mice. The effect

observed was similar to that obtained when phenobarbitone (standard control) was administered. Hypnosis induced by *A. senegalensis* is dose related as the group of mice that received 1000 mg/kg had more potent effect than the group that received 500 mg/Kg. The same dose dependent effect was observed in day old chicks. The onset of action observed on administration of phenobarbitone was shorter in both species of animals compared with the extract and was more pronounced in the chicks. The variation in the time of onset of sleep is due to the fact that the mice are matured with well-developed blood brain barrier (BBB) that interferes with the kinetics of both the extract and drugs leading to delayed onset of sleep. On the contrary the chicks are too young and have not yet fully developed their blood brain barrier. Implying that there will be little or no obstruction in the movement of drugs into the brain, hence faster onset of sleep. The duration of action (sleep duration) in mice and day old chicks was dose dependent, with 1000 mg/Kg showing more activity. Phenobarbitone also produced dose dependent activity in both species.

The results obtained from this study also showed that *A. senegalensis* and *F. thonningii* potentiated the hypnotic effects of phenobarbitone. *A. senegalensis* and *F. thonningii*, decreased onset of sleep and increased the duration of sleep induced by phenobarbitone. The potentiating effect of the extracts on phenobarbitone induced-sleep was observed in day old chicks and adult mice. *A. senegalensis* produced the most potent dose related effects in mice and day old chicks. The effect observed was more pronounced in day old chicks than in adult mice. This findings supports the use of these herbs for the management of insomnia and psychosis,

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