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Hypnotic , Muscle Relaxant , Anticonvulsant and Endocrine Effects of *Myristica fragrans*

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ABSTRACT:-

Ethanolic extracts of M. fragrans induced dose dependent muscle relaxant, anticonvulsant and hypnotic effects in rats . Aqueous extracts were less potent. Both ethanolic and aqueous extract had no effects on LH, FSH, testosterone levels, sperm content of epididymal head and sexual desire of the treated male rats.

INTRODUCTION

The dried ripe seed of Myristica fragrans (Nutmeg)contains fixed oil25-40%and volatile oil 8-15%.Myristica oils include safrole, myristica (metoxy safrole) , methoxyeugenol, caphene, B-terpineol,B-pinene, myrcene, limonene and sabinene [(1).] Myristica possessed platelet anti–aggregating activity, this could be completely contractions of rat stomach strips produced by prostaglandin E2,an diminishes synthesis of prostaglandin like material produced by isolated human colon. In traditional medicine eugenol was used against gastrointestinal upset and chronic diarrhea as well as in controlling diarrhea associated with certain carcinomas such as medullar carcinoma of thyroid. Prostaglandin doses of nutmeg powder have been reported to cause atropine like side effects (tachycardia and absence of salivation) [(1,2)] .

Myristica being the responsible component for the central action of nutmeg. Nutmeg oils also decrease fertility in rat and some nutmeg constitutes possess carcinogenic properties[(2)]. The intoxication dose of nutmeg for human is 15 gm., flushing of skin tachycardia, and absence of salivation were the main side effects[(1)]

MATERIALS& METHODS

Plants and extraction:-

Ripe seeds of Myristica fragran s were brought from local market.250gm. of the seeds powdered and divided into2 equal parts. Then extracted in ethanol 80%and distilled water by soxholet. The solvents were removed by rotary evaporator (30°C).The final aqueous and alcohol residues were 6.6 and 42gm.respectivelly.

Distilled water was used to dissolve the residues to give the required concentration. The injected volume of the extract solution was 0.2-0.3ml\rats.

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Central nervous effects:-

Sleeping test :-

Potentiation of hypnotic effect of pentobarbital :-

Each extract was injected intraperitoneally in two dose levels 100 and 200mg\kg. 18 rats were used for each dose level and 18 rats were used for each dose level and 18 rats injected with normal saline to serve as control. The extracts were administered 30 minutes after injection of 35mg\kg of sodium pentobarbital intraperitoneally. Then the animals were tested for righting reflex . By this test animal are placed on their backs, the failure to regain their normal posture 3 conecutive times in the one minute was taken as onset of sleep, while time interval between loss and recupturation of reflex was considered as sleep duration[3]

Anticonvulsant test:-

Five groups of rats of both sexes(18 rats per group)were treated intraperitoneally with 100 and 200mg\kg of the extracts and a group of rats were injected with normal saline .30 minutes later animals were injected with strychnine 2mg\kg.

The occurrence of convulsion was recorded. rats devoid of convulsion for 60 minutes were considered protected[3].

Muscle relaxation test:-

The effect of extract on the muscle tone was assessed by using the test De La traction described by Courvoisier[4]. In this test, rats are hung by the fore paws on a thin wire placed over a bench, Normal rats pull themselves immediately with the aid of their hind paws ,failure of the rats to pull within10 seconds, or dropping down 3 consecutive time in 60 seconds was taken as the criterion for the presence of muscle relaxation.

Endocrine effects:-

Ninety adult male rats were housed in cages at25°C((light\darkness 14:10 hours).They were divided into 5 groups(18rats in each group).The first four groups were given aqueous and ethanolic extracts of Myristica fragrans 100 and 200mg as a single oral dose for 60 days. The fifth group was given normal saline by the same route and for the same period . After 60 days, blood samples were collected from 12 males from each group. The blood samples were centrifuged at 2500 PRM for 30minuts.

The prepared sera were stored in deep freeze .L.H., F.S.H. and testosterone were estimated by radioimmunoassay. Sperm content of the epididymal head of the same males were estimated according to the method of Sakamoto and Hashimoto (1986)[5]. The rest 6 males in each group were matted with 24 females during the pro estrus and estrus period . Recovery of sperm in the vaginal smears was considered as day (one) of pregnancy. All females were killed at day 14 of gestation . Fetuses were counted, weighted, examined for fetal resorption and fixed either in Bouin´s solution for subsequent gross and histological observation ,or in 95% alcohol for skeletal staining by alizarin-red method[6]. For gross and histological work ,fixed fetuses were dehydrated in ascending grades of alcohol.Uponrecahing70% alcohol, they were examined for external malformation. Some of fetuses were further processed for routine histological procedures. Serial sections,7µm thick, were stained with hematoxylin and eosin[5].

RESULTS

Central nervous system:-

As shown in the table 1, ethanolic extract of M. fragrance induced muscle relaxant activity . The extract was effective at a dose of 200mg\kg body weight .The rates of muscle relaxant effect induced by this dose was 50%.However water extracts exerted weak muscle relaxant effects at both dose levels. Ethanolic and water extracts of M. fragrances induced dose related increase in sleeping time induced by pentobarbital .Ethanolic extract was more effective than water extract(table2). Ethanolic extracts of M. fragrans also showed dose related antiepileptic activity. A low antiepileptic activity was recorded with aqueous extract(table3)

Endocrine effects:-

Neither the ethanolic nor the aqueous extracts change the serum L.H., F.S.H. and testosterone levels.(table1).Both extracts did not affected sperm count in the epididymal head (table2),and sexual desire of males .Litter size \dam was not significantly changed , no gross and histological teratogenic effect , and no skeleton deformities were recorded in the progeny of the treated male rats.

DISCUSSION:-

Central nervous effects of nutmeg may be related to its contents of mescaline , myristicine, and elimicin. Mescaline inhibit release of serotonin via its effect on presynaptic serotonin receptors[3],on the other hand nutmeg inhibit monoamine oxidase which is responsible for metabolism of catecholamine [7].While some theories postulate that elemicine and myristicin metabolized finally to amphetamine like nitrogen containing metabolites, the agent which increase releasing of catecholamine in the central nervous system[1].further more ,nutmeg also contains eugenol which possess anesthetic effect[1],usually via interfering with central transmitter or central trans membrane exchange of ions. On other hand tachycardia, flushing of skin, pupils dilatation, absence of salivation, abortion in pregnant female and other atropine like effects appear after ingestion of nutmeg [1,7],clearly show that nutmeg possess anticholinergic activity. Therefore central effect of nutmeg in our study may be elated to its interfering with many central nervous system transmitters.

Although M.fragrans contain elemicine and myristcin which increase the central catecholamine level, the mediators which essential for maintaining the rise in L.H. , F.S.H[8],but in the other hand M.fragrans exerts atropine like effect.. Atropine was able to block ovulation in rats by antagonizing the stimulatory effect of acetylcholine [9],therefore the endocrine stimulatory effect of M.fragrans could be abolished by its acetylcholine blocking effects.

Table (1):- Muscle relaxant effect of ethanolic and equous extract of M.fragrans

Treatments	Type of extract and dose	No. of animals	Animals with muscle relaxation	%	Signifincancy Compared with control
M.fragrans	Ethanolic extract l00mg/kg	18	4	22.2	P<0.01
	Ethanolic extract 200mg\kg	18	9	50	P<0.001
	Aqueous extract 10Omg/kg	18	2	11.1	P<0.05
	Aqueous extract 200mg/kg	18	2	11.1	P<0.05
control		18	0	0	

Table (2) ::Prolongation of hypnotic effect of pentobarbital by ethanolic and aquous extracts of M,fragrans.

Treatments	Type of extract and dose	No. of animals	Duration of sleep\min. potentiation of hypnotic effect of pentobarbital	Signifincancy Compared with control
M.fragrans	Ethanolic extract l00mg/kg	18	32±2.4	P<0.01
	Ethanolic extract 200mg\kg	18	36.2±2.1	P<0.001
	Aqueous extract 10Omg/kg	18	27.6±	P<0.05
	Aqueous extract 200mg/kg	18	28.2±1.2	P<0.05
control		18	22.6±1.4	

Table (3):-percenage of animals protected from the convulsant effect of strychnine by ethanolic and aqueous extracts of M. fragrans.

Treatments	Type of extract and dose	No. of animals	No.of animals protected from the convulsant effect of strychnine	%	Significancy Compared with control
M.fragrans	Ethanolic extract l00mg/kg	18	6	33.3	P<0.001
	Ethanolic extract 200mg\kg	18	8	44.4	P<0.001
	Aqueous exract 10Omg/kg	18	1	5.5	P<0.05
	Aqueous extract 200mg/kg	18	1	5.5	P<0.05
Control		18	0	0	

Table(4) effects of M.fragrans on the serum L.H., F.S.H., testosterone and sperm content of epididymal head in adult male rat.

Treatments	Type of extract and dose	Serum LH MIU\ml.	Serum FSH MIU\ml.	Serum testosterone MIU\ml.	Sperm content $\times 10^6$mg.of epididymal head
M.fragrans *	Ethanolic extract l00mg/kg	1.12±0.16	1.49±0.62	3.18±0.36	3.12±0.98
	Ethanolic extract 200mg\kg	1.18±0.18	1.53±0.51	3.21±0.71	3.11±0.76
	Aqueous extract 10Omg/kg	1.21±0.29	1.56±0.43	3.31±0.73	3.08±0.72
	Aqueous extract 200mg/kg	1.17±0.32	1.59±0.73	3.29±0.86	3.14±0.92
Control		1.19±0.20	1.61±0.92	3.40±0.96	3.06±0.88

*All effects were not significant

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التأثير المنوم والمرخي للعضل والمضاد للصرع والتأثير الصماوي لجوز الطيب

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الخلاصة

دراسة صممت لبيان تأثير المستخلص الكحولي والمائي لجوز الطيب. أظهرت هذه الدراسة أن المستخلص الكحولي له تأثير مرخي للعضلات ومضاد للصرع ومنوم وبشكل يتناسب طرديا مع كمية الجرعة المعطاة للجرذان بينما المستخلص المائي كان ذو فعالية قليلة.

ولم يسجل تأثير ذو أهميه احصائيه لكلا المستخلصين على مستويات الهرمون المحرض للجريب و الهرمون اللوتيني و الشحمون االخصوي كما لم يسجل تأثيرا للمستخلصين على كمية الحيامن في الاقنية الخصوية و الرغبة الجنسية لدى ذكور الجرذان المعالجة .

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