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EXPERIMENTAL STUDY ON POLYHERBAL EXTRACT AS A EFFECTIVE REMEDY FOR PREMATURE EJACULATION

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ABSTRACT

The Present research was designed to evaluate the effect of Poly herbal extract (PHE) in the treatment of premature ejaculation (PME) in albino rats. PME is a serious concern of the current society. Male's suffering from PME fails to enjoy sexual pleasures. Poly herbal extract (a 1:1 combination of *Syzgium aromaticum* & *Elettaria cardamomum* extracted in ethanol) at a dose of 200 mg/kg orally was administered to sexually active male rats for a period of 14 days. The sexual behavior was studied on day 1 and day 7 and it was found that the mount latency and intromission latency was faster in PHE treated male rats when compared to Control group. There is also an increase in mount frequency, intromission frequency and ejaculation latency herbal extract treated group compared to control rats. The results are comparable with the standard aphrodisiac Sildenafil citrate (5 mg/kg,p.o). The present findings indicate that PHE has a significant PME inhibitory effect and thereby prolongs ejaculation time. The phytoconstituents reported in the herbal extract such as tannins and flavonoids may be responsible for inhibiting PME in rats.

INTRODUCTION

Ejaculation disorders are the most common sexual dysfunctions in male that can result in infertility [1-3]. Inability to perform sexual function is a major problem of the reproductive process known as sexual dysfunction [4,5]. Sexual dysfunction is further classified in to sub types including premature ejaculation, delayed ejaculation, retrograde ejaculation and anejaculation [6]. Factors such as alcoholism, diabetes mellitus, arterial hypertension and tobacco can also cause ejaculation problems. Premature ejaculation and sexual desire disorders were the frequent problems reported in young adult males with adverse familial relationship [7].

Dopamine plays a prominent role in the control of ejaculation at brain and spinal levels and stimulation of dopamine receptors by dopamine can provoke the ejaculation process [8,9].There are several natural herbs that are effective and may have quick onset of action in the treatment of PME [10]. One such herbal formulation is PME which is a complex mixture of effective herbs such as Clove and Cardamom that are traditionally used in the treatment of sexual dysfunction. Hence the current research was planned with an objective to explore the effectiveness of PHE in the treatment of PME by using albino rats.

Materials and methods

Fresh Clove flower buds and Cardamom seeds were purchased from a nearby herbal store. They were shade dried and mechanically pulverized to a coarse powder and weighed. Clove powder 50 g and Cardamom powder 50 g were mixed in the ratio 1:1 and further subjected to hot continuous successive extraction in a Soxhlet apparatus with ethanol. Extractive was concentrated below 40 °C and further drying was carried out under reduced pressure. The extractive was stored in a dessicator for further evaluation. The obtained extract was subjected to phytochemical tests for detection of phytoconstituents present in it viz. alkaloids, carbohydrates, glycosides, phytosterols, fixed oils & fats, phenolic compounds & tannins, proteins and free amino acids, gums & mucilages, flavanoids, lignins and saponins.

Animals: Wistar rats of either sex (150-200 g) were obtained from Sainath agencies, Musheerabad, Hyderabad (282/99/CPCSEA) and housed in animal facility of Marri Laxman Reddy College of Pharmacy, Hyderabad (1567/PO/RE/S/11/CPCSEA). After randomly arranging the animals in to different groups and before commencement of experiment, for 30 days period the rats were acclimatized. Rats were kept in cages made up of polypropylene and preserved under standard environmental setting such as temperature (26 ± 2ºc), relative moisture (45-55%) and 12hr dark/light cycle. The rats were supplied with rat diet made up of pellets (Golden Mohur Lipton India Ltd.) with water *ad libitum.*

Single dose oral acute toxicity with gross behavioral study in Mice for 14 days [11,12] **:** The Acute toxicity evaluation of ethanolic extract of poly herbal formulation was performed on the principle of OECD guidelines 423 by using mice and fixed dose studies were selected where the limit dose is 2000 mg/kg.The given herbal extract was also studied oral acute toxicity in albino mice at doses 5, 50, 300 & 2000 mg/kg (OECD 423). Mice were observed for 4 hrs for behavior, autonomic and neurological symptoms or mortality. Body weights were recorded 6 hrs post dosing. Following next day, every day (for 1 hr) behavioral changes, toxic symptoms or mortality was recorded for one week & body weights were documented on 8^{th} & 14^{th} day after drug administration. If rats are devoid of lethality, then a cut off dose of $1/5^{th}$ and $1/10^{th}$ of higher dose was choosen as therapeutic dose.

Preparation of male rats: The male rats were trained, for sexual behavior, two times a day for a period of minimum of 10 days. The male rat which did not show any sexual interest during the test period was considered as an inactive male. The sexually active male rats were selected for testing aphrodisiac activity of the polyherbal formulation.

Preparation of female rats: Female rats were housed in separate cages with food and water *ad libitum*. The female rats were brought in oestrous phase by treating them with estradiol valerate 10µg/kg for 48 hours prior to experimentation, respectively, to make them sexually acceptable and were selected for the study.

Experimental Procedure: The sexually active male were separated and divided into 3 groups; each group consisting of 6 animals. The animals in the divided groups received the treatment orally. Control rats received 2% acacia (vehicle), test group rats received Polyherbal extract (200 mg/kg, p.o) and Standard group rats received Sildenafil Citrate (5mg/kg, p.o) for 14 days.

Sexual Behavior Study: The sexual behavior of the experimental rats was observed in a dim light at 10 a.m. in a specially designed cage that has glasses and wood. The male experimental rat was first placed in the cage and then one female rat in estrous phase was introduced. An initial period of 10 minutes was considered as acclimatization period. After 10 minutes activity of male rat in each group was recorded individually for 30 minutes. In the aphrodisiac activity of the Polyherbal extract, several parameters were observed on day 1 and day 7.

These include

1. **Mount latency (ML)** (amount of time it takes for a male to mount the female for the first time)

2. **Mount frequency (MF) (**No. of mounts observed in 30 minutes)
3. **Intromission latency (IL):** Time taken for first intromission following introduction of the female.
4. **Intromissionfrequency (IF) (**No. of intromission observed in 30 minutes)
5. **Ejaculation latency (EF)** (amount of time taken for a male rat to ejaculate)

Statistical Analysis:

All the results were expressed as Mean ± SEM .Interpretation of the result was supported by statistical analysis. Results of the same group of different days of treatment were analyzed by one way analysis of variance (ANOVA) followed by Dunnett's test to calculate the level of significance. Statistical analysis of data was performed using Graph Pad Prism 5.

Results and discussion: The ethanolic PHE studied for oral acute toxicity in albino mice at doses 5, 50, 300 & 2000 mg/kg and was found non toxic at 2000 mg/kg. Hence oral LD_{50} of given extract was found to exceed 2000 mg/kg. Therefore 2000 mg/kg was regarded as safest higher therapeutic dose for the ethanolic extract and $1/10^{th}$ i.e 200 mg/kg was preferred for the further studies. In the present study the influence of PHE on premature ejaculation was examined. Albino rats were used as subjects as there are several homologies between human sexual behaviors and that of the rat such as ejaculation. Both male and female rats were trained for sexual behaviour especially males house with females two times a day for a duration of 10 days and female rats were brought to oestrous phase by the administration of estradiol valerate 10 µg/kg for 48 days before the experimentation. Pre treatment with PHE 200 mg/kg , p.o significantly decreased the time of onset of mount latency (124.8 ± 9.17 seconds) and Intromission latency (19.5 ± 0.073 seconds) when compared to control male rats (ML 175 ± 13.41 seconds, IL 26.3 ± 0.175 seconds). Sildenafil citrate treated rats exhibited a significant decrease in the time of onset of mount latency (96.3 ± 15.11 seconds) and Intromission latency (12.66 ± 1.864 seconds). PHE treatment has shown an increase in mount frequency (6.28 ± 0.04), Intromission frequency (1.96 ± 0.114) and Ejaculation latency (1.586 ± 0.476 sec) when compared to control group male rats (MF 4.12 ± 0.17, IF 1.54 ± 0.125 & EL 0.175 ± 0.192 seconds). Sildenafil Citrate has shown a remarkable increase in MF, IF & EL when compared to control. These results indicate that PHE at a dose of 200 mg/kg p,o has a significant effect in delaying the ejaculation time as well as acts as an effective aphrodisiac. Hence it can be effectively used in the treatment of PME. The results are depicted in tables 1-5, figures 1-3 and graphs 1-5.

Table 1: Mount latency (ML) in seconds of Polyherbal extract and Sildenafil citrate treated rats

Groups	Day 1	Day 7
Control	175 ± 13.41	231.5 ± 6.12
Polyherbal extract 200 mg/kg, p.o	124.8 ± 9.17**	158.3 ± 14.65**
Sildenafil citrate 5mg/kg, p.o	96.3 ± 15.11***	107.4 ± 11.85***

Values are expressed in Mean ± SEM. One way ANOVA with *P<0.05, **P<0.01, ***P<0.001 by using Dunnett's test.

Table 2: Mount frequency (MF) of Polyherbal extract and Sildenafil citrate treated rats

Groups	Day 1	Day 7
Control	4.12 ± 0.17	4.76 ± 1.15
Polyherbal extract 200 mg/kg, p.o	6.28 ± 0.04*	6.15 ± 0.08*
Sildenafil citrate 5mg/kg, p.o	9.64 ± 1.25**	8.34 ± 0.19**

Values are expressed in Mean ± SEM. One way ANOVA with *P<0.05, **P<0.01, ***P<0.001 by using Dunnett's test.

Table 3: Intromission latency (IL) in seconds of Polyherbal extract and Sildenafil citrate treated rats

Groups	Day 1	Day 7
Control	26.3 ± 0.175	24.11 ± 1.764
Polyherbal extract 200 mg/kg, p.o	19.5 ± 0.073*	21.34 ± 0.159
Sildenafil citrate 5mg/kg, p.o	12.66 ± 1.864***	14.35 ± 0.181***

Values are expressed in Mean ± SEM. One way ANOVA with *P<0.05, **P<0.01, ***P<0.001 by using Dunnett's test.

Table 4: Intromission frequency (IF) of Polyherbal extract and Sildenafil citrate treated rats

Groups	Day 1	Day 7
Control	1.54 ± 0.125	2.31 ± 0.654
Polyherbal extract 200 mg/kg, p.o	1.96 ± 0.114*	4.85± 1.719**
Sildenafil citrate 5mg/kg, p.o	3.19 ± 1.72**	5.35 ± 1.628***

Values are expressed in Mean ± SEM. One way ANOVA with *P<0.05, **P<0.01, ***P<0.001 by using Dunnett's test

Table 5: Ejaculation latency (EL) in seconds of Polyherbal extract and Sildenafil citrate treated rats

Groups	Day 1	Day 7
Control	0.715 ± 0.192	1.176 ± 0.256
Polyherbal extract 200 mg/kg, p.o	1.586 ± 0.476*	2.965± 1.382*
Sildenafil citrate 5mg/kg, p.o	3.05 ± 1.263**	3.612 ± 0.354**

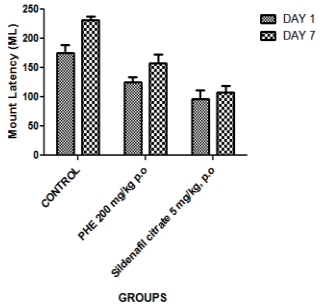
Values are expressed in Mean ± SEM. One way ANOVA with *P<0.05, **P<0.01, ***P<0.001 by using Dunnett's test

Figure 1: Attraction of male rat towards a female rat after treatment with polyherbal extract 200 mg/kg, p.o

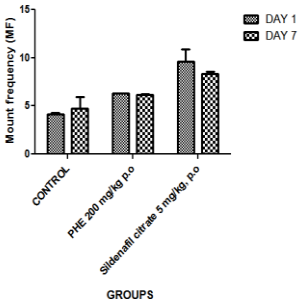
Figure 2: Mount latency of male rat after treatment with polyherbal extract 200 mg/kg, p.o

Figure 3: Intromission latency of male rat after treatment with polyherbal extract 200 mg/kg, p.o

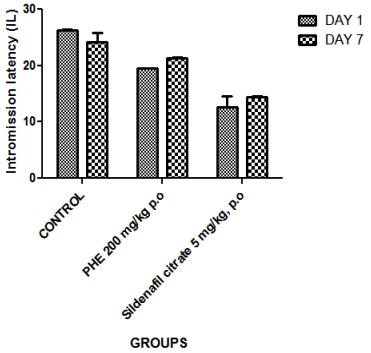
Graph 1: Mount latency of Control, PHE and Sildenafil Citrate treated rats on day 1 and day 7 of treatment



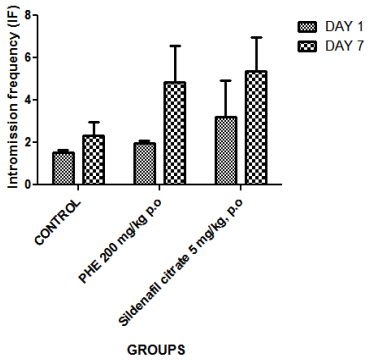
Graph 2: Mount frequency of Control, PHE and Sildenafil Citrate treated rats on day 1 and day 7 of treatment



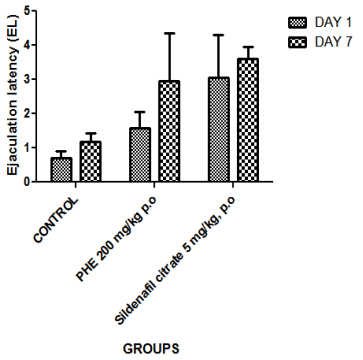
Graph 3: Intromission latency of Control, PHE and Sildenafil Citrate treated rats on day 1 and day 7 of treatment



Graph 4: Intromission frequency of Control, PHE and Sildenafil Citrate treated rats on day 1 and day 7 of treatment



Graph 5: Ejaculation latency of Control, PHE and Sildenafil Citrate treated rats on day 1 and day 7 of treatment



CONCLUSION

Phytochemical analysis of PHE has confirmed the presence of flavonoids, tannins, alkaloids and glycosides. Single dose oral acute toxicity studies have shown the safest therapeutic dose as 200 mg/kg. Sexual behaviour studies has demonstrated the effect of PHE on ML, IL, MF, IF and EL and found to be highly effective in delaying ejaculation time in male rats.

It is well known that dopaminergic and cholinergic pathways in brain control ejaculation process. The synergistic interactions between the constituents of clove and cardamom in the PHE may alter the dopaminergic and cholinergic pathways in brain and hence may result in the inhibition of rapid ejaculation. However further studies are required to determine the exact mechanism of the ingredients in the PHE on sexual behaviors such as ejaculation.

Conflict of interest: This is to inform that the authors declare that they have no conflicts of interest regarding this article.

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