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Full Length Research Paper

Effects of the methanol extract of *Erythrina abyssinica* on hot flashes in ovariectomized rats

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We investigated the estrogen-like properties of the methanol extract of *Erythrina abyssinica* in ovariectomized rats. Climaterix was induced in female rats by surgically removing the ovaries. Data loggers implanted in the abdominal cavity during the procedure recorded core temperatures at predetermined time intervals for 72 h. 6 h after the onset of temperature recording, animals were treated with estrogen (1 mg/kg), methanol extract of *Erythrina abyssinica* (200 mg/kg) or an equivalent volume of 5% ethanol. Rats treated with extract had significantly fewer hot flashes (171 ± 11 vs. 264 ± 21) which were of shorter duration (683 ± 137 min vs. 1935 ± 345 min) compared to untreated animals. Treated animals had lower core temperature during periods of high activity indicating that the methanol extract of *E. abyssinica* reduced frequency and duration of hot flashes.

Key words: Ovariectomized, extract, *Erythrina abyssinica,* climaterix.

INTRODUCTION

The majority of peri-menopausal women develop symptoms associated with reduced estrogen secretion. Associated symptoms such as insomnia, loss of libido, depressions, vaginal dryness and hot flashes may greatly affect their life styles. Some of these symptoms may be severe enough to require therapy. Hormone replacement therapy was for a long time the treatment of choice for the management of menopausal symptoms until after Women's Health Initiative published its findings on combined therapy showing that the risks associated with the use of combined estrogen and progesterone therapy (HRT) outweighed the benefits (Rossouw et al., 2002). As a result of this publication, the use of HRT has greatly decline especially, in the USA (Hersh et al., 2004). Even before the publication of these results, women were cautious about the use of HRT and preferred to use various forms of alternative therapies to treat menopausal symptoms (Pitkin, 2012, Azizi et al., 2011). Recently, plant based compounds with estrogenic effects have come to the lime light. These phytoestrogens as they are known have been isolated from a variety of plants ranging from foods to medicinal plants (Setchell, 1998; Khaodhair et al., 2008; Al-Anazi et al., 2011). Several plants from the *Erythrina* genus have reportedly shown estrogen-like effects in rats – examples include *Erythrina lysistemon* (Tanee et al., 2007), *Erythrina poepigiana* (Djiogue et al., 2009) and *Erythrina variegata* (Shirwaikar et al., 2010). *Erythrina abyssinica* is a common plant in sub-Saharan Africa where it is used to treat inflammation, gonorrhoea, wounds, stomach problems, diarrhoea and viral infections (Agroforestry Center, ND; Bekalo et al., 2009; Vlietinck et al., 1995). Although, many studies have investigated the medicinal properties of *Erythrinas* and their constituent compounds, very few studies have looked at *E. abyssinica* (Cui, 2007). In this paper, we investigated whether *E. abysinnica* like most *Erythrinas* has estrogen-like properties in ovariectomized (OVX) rats.

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MATERIALS AND METHODS

E. abyssinica was collected in Yaoundé, Cameroon and authenticated at the National Herbarium (No: 50458/HNC). After drying and grinding, stem barks were soaked in methanol for 72 h. Methanol was recovered using a rotator evaporator. Obtained extract was air dried for three months until all traces of solvent had evaporated. Methanol extract of *E. abysinnica* (MEEA) was prepared in 5% ethanol and administered at a dose of 200 mg/kg.

Drugs used

The drugs included estrogen (a mixture of estrone, equilin and 17 α-dihydroequilin, 17 α-estradiol, equilenin and 17 α-dihydroequilenin) (Bodene (PTY) Limited), penicillin (Bodene (PTY) Limited) and diclofenac (Austell Laboratories (PTY) Ltd).

Measurement of hot flashes

Smart Button Data loggers (ACR systems, Canada) were used to monitor the core temperature changes in the animals at 2 min intervals for 72 h. Data loggers were preset to start measuring core temperatures on the 8th day after ovariectomy. Mature female Wistar rats (200 to 250 g) underwent bilateral ovariectomy and data loggers protected in sterilized neutral wax were implanted into their abdominal cavities.

Animals received a single intramuscular dose of long acting penicillin and diclofenac (10 mg/kg and 3.2 mg/kg respectively) before recovery from the procedure. On day 8 after surgery animals were randomly assigned to one of three groups and treated orally with one of the following; group 1 was treated with 200 mg/kg MEEA, group 2 was treated with 1 mg/kg estrogen while group 3 received 5% ethanol in distilled water. 66 h after administration of drugs, all rats were terminated with a high dose of ether and data loggers recovered. Data was retrieved from loggers unto excel spreadsheets and analyzed.

Total number of hot flashes after treatment

The mean number of hot flashes was determined by counting all temperature recordings ≥ 38°C for each animal and the average for six animals per group calculated. The mean number of hot flashes was calculated at 6 h intervals to determine the frequency of hot flashes before drug administration and frequency at different time intervals after drugs have been administered.

Determination of the duration of hot flashes

The duration of each hot flash was obtained by calculating the difference between the onset and the end of a hot flash. The mean of these hot flash durations was determined by calculating the mean of hot flashes in animals of the same group at a specific time interval.

Statistical analysis

Graph Pad InStat was the software used to analyze the data. ANOVA was used to compare the means and standard deviations of treated groups to that of controls. Results were expressed as the mean ± standard deviation.

RESULTS AND DISCUSSION

Total number of hot flashes

A hot flash was defined as core temperature ≥38°C. All OVX animals had hot flashes as per definition of hot flashes. The oral administration of MEEA and estrogen significantly ($p<0.05$) reduced the total number of hot flashes in treated animals compared to controls (171 ± 11/154 ± 12 vs. 264 ± 21) while the plant extract and estrogen produced comparable numbers of hot flashes (Figure 1).

Core temperatures were consistently higher in untreated rats compared to treated groups. Ovariectomy is a good model of menopause as hot flashes are one of the early signs of menopause. It is believed that hot flashes are caused by the shrinking of the brain's thermoneutral zone (Freeman, 2001; Grady, 2002) such that minor changes in core temperature which would otherwise not elicit a thermoregulatory response become sufficient to produce sweating and peripheral vasodilation. Freeman (2001) suggested that minor core temperature elevations triggered hot flashes in individuals with reduced or non-existent thermoneutral zones. It is also known that sympathetic activation plays an important role in the generation of hot flashes by further narrowing the thermoneutral zone. Importantly, sympathetic activation is increased in menopausal women experiencing hot flashes (Freedman, 2001).

Number of hot flashes per six hour intervals

Treated groups showed persistently lower numbers of hot flashes at 6-h intervals as compared to controls (Figure 2). There was a decrease in the number of hot flashes from 16:00 to 22:00 in all three study groups. The temperature highs and lows occurred in all groups of animals at the same time though the highs in treated animals were much lower than for untreated animals. Core body temperature peaked between 16:00 to 22:00 h on both days 1 and 2 in all experimental groups. However, the extract and estrogen treated rats had lower temperature peaks compared to the control animals. These peaks could reflect the effect of ovariectomy on the normal temperature circadian cycle which peaks during periods of high activity (Christinal et al., 2004). Estrogen and extract treated animals had fewer numbers of hot flashes compared to the controls. Extract and estrogen treatment would seem to protect OVX rats from reacting to small temperature rises which trigger hot flashes in untreated animals.

Duration of hot flashes

Animals treated with either extract or estrogen had significantly ($p< 0.05$) reduced durations (683 ± 137 min/869 ± 53 min vs. 1935 ± 345 min) of hot flashes (Figure 3). Although, both estrogen and MEEA significantly reduced the duration of hot flashes, yet, the effect of MEEA extract on duration of hot flashes was more pronounced than the effect of estrogen.

The onset of hot flashes was noted 8 days after ovariectomy and although, all the ovariectomized animals

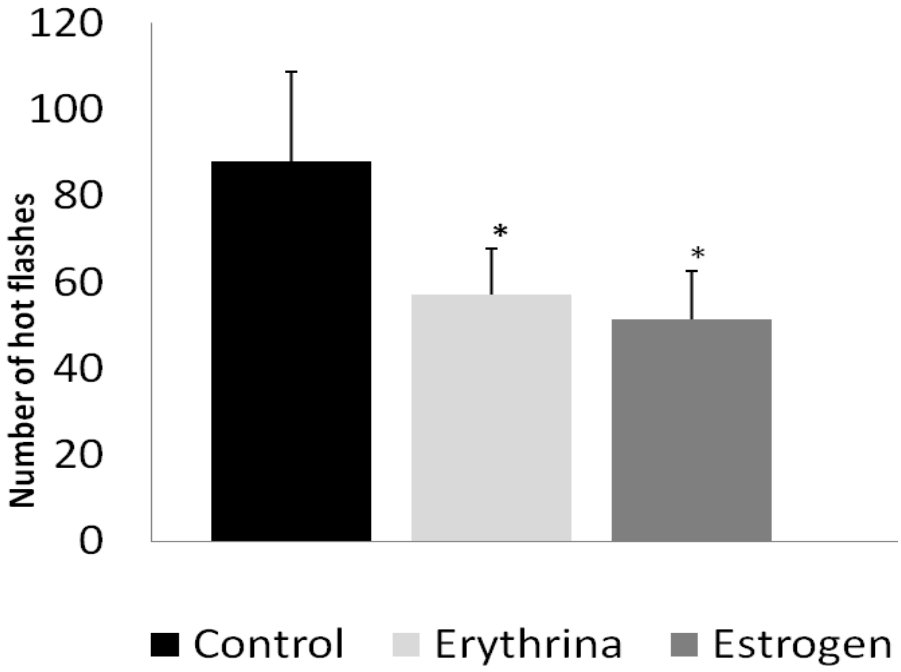

Figure 1. Number of hot flashes in treated and untreated ovariectomized rats. *p< 0.05, n=6.

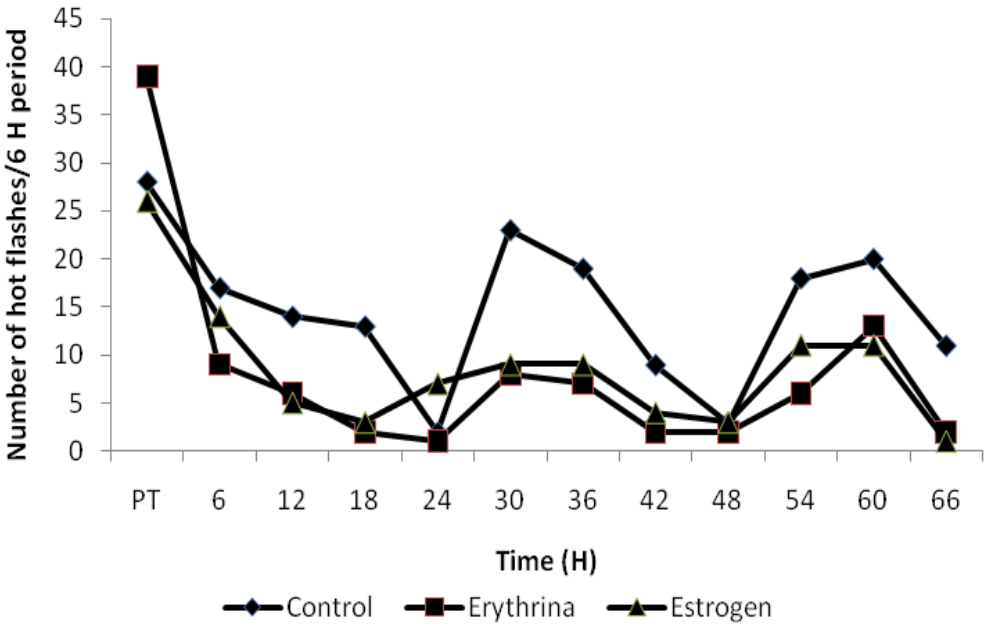

Figure 2. Variation in number of hot flashes per 6 h intervals in treated and untreated ovariectomized rats; PT = 6 h period preceding drug treatment. n= 6 rats per group.

showed an increase in core temperatures and presented with hot flashes, the untreated group had significantly higher core temperatures as well as, numbers and duration of hot flashes compared to both treatment groups. Freeman and Blacker (2002) reported that estrogen supplementation raises the body's threshold for thermoregulation thereby, preventing responses to small changes in core temperature. Like estrogen, MEEA also reduced the numbers, duration and frequency of hot flashes in OVX rats indicating that MEEA may also prevent thermoregulatory responses to small fluctuations in core temperatures.

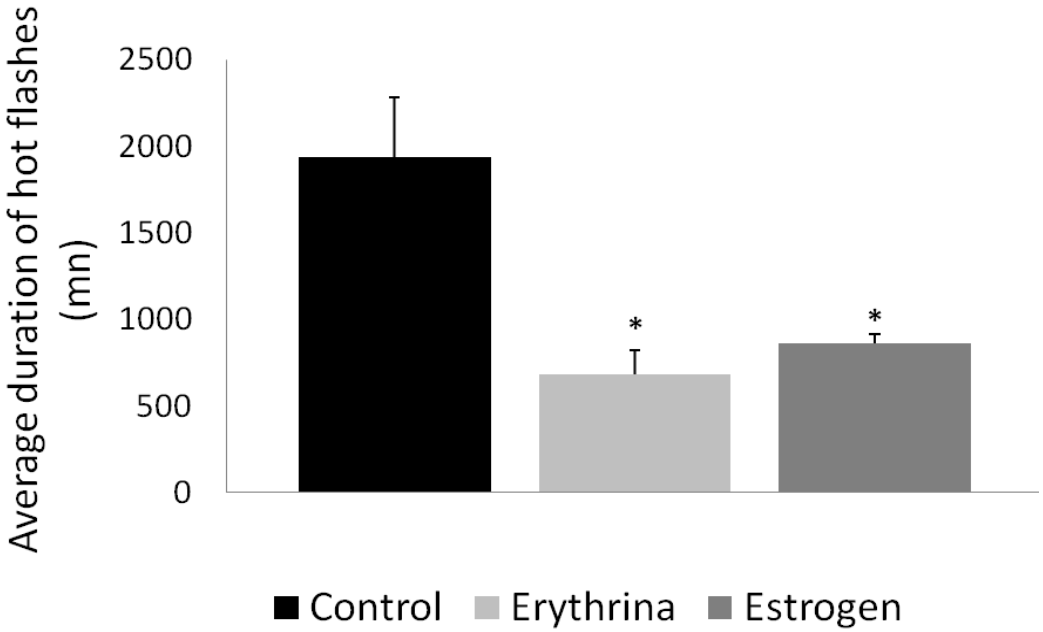

Figure 3. Duration of hot flashes in treated and untreated ovariectomized rats, *p< 0.05, n=6.

The effects of estrogen on hot flashes are not yet fully understood but it is speculated that estrogen increases the size of the thermoneutral zone and raises the sweating threshold thus, reducing the frequency of hot flashes (Freedman and Blacker, 2002; Daks and Rance, 2010).

Conclusion

The methanol extract of *E. abyssinica* reduces the number and duration of hot flashes in ovariectomized rats in a comparable fashion to a small dose of estrogen and may therefore, be useful in the prevention of hot flashes in perimenopausal women.

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