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Improvement of Sexual Behavior in Male Rats via Dietary Supplementation with *Panax ginseng* Extract Standardized with Ginsenoside Rg3

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Korean ginseng (*Panax ginseng* CA Meyer) is important traditional medicinal plants whose ginsenosides are generally accepted as serving to improve sexual functions, such as penile erection. The aim of the current study was to utilize *panax* ginseng extract standardized with ginsenoside Rg3 (PGRg3) to improve the sexual behavior in rats. Male rats were categorized on the basis of seven consecutive mating pre-tests as Sexually-Active (SA) and Sexually-Inactive (SI); and stretching-yawning, penile erection, sedation and stereotyped behavior of the same animals. The results indicated that PGRg3 at three tested doses (50, 150 and 450 mg kg^{-1} b.wt.) enhanced the copulatory pattern of both SI and SA rats, ejaculation mechanisms, increase the sexual drive of SI rats. The two groups of rats, exhibited different behavioral responses to PGRg3. Moreover, PGRg3 was effective in SA rats at dose as low as 50 mg kg^{-1} b.wt. however it was effective in SI rats at the higher doses (150 and 450 mg kg^{-1} b.wt.). It could be concluded that PGRg3 succeeded to enhance sexual behavior and has beneficial effects as traditional medicinal herbal plant in male with sexual dysfunction.

Key words: *Panax ginseng*, sexual behavior, male, penile erection, sexual dysfunction, traditional medicine

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INTRODUCTION

The sexual dysfunction is a common disease and with an increasing incidence as a result of the longer lifespan, the increasing prevalence of degenerative diseases as well as the increase in injuries and stress associated with industrialized lifestyles. Both medical and surgical treatment modalities are available for treating sexual dysfunction. Inspite of the availability of conventional medical treatments, people are still seeking for alternative natural recourses derived from plants and herbs to improve their sexual life (Rowland and Tai, 2003). However, the efficiency of these agents in the treatments of sexual dysfunction in not clear.

In recent years, the use of dietary supplements has been increased dramatically (Ervin *et al*., 2004; Noonan and Noonan, 2006). Supplements are becoming more important and more commonly used by consumers in their personal healthcare regimens (Marinac *et al*., 2007; Timbo *et al*., 2006). Numerous products are currently promoted for enhancing erectile function and sexual performance in men and are marketed with the implied assumption that they are safe and natural. Yet reports of adulteration for products in this category abound. Adulterants found in dietary supplements include, but aren't limited to, Active Pharmaceutical Ingredients (APIs) such as the PDE-5 inhibitors sildenafil (Viagra®), vardenafil (Levitra®), tadalafil (Cialis®) and, in an attempt to avoid detection, the unapproved analogues of these drugs (FDA, 2007a-c, 2009; Reepmeyer *et al*., 2007). This practice is illegal and places consumers at risk for potentially serious side effects from these drugs such as abnormal vision, headaches, myalgia, dizziness, flushing and dyspepsia (Fink *et al*., 2002; Sunwoo *et al*., 2004). Of further concern is that these APIs may interact with prescription medications such as nitrates, erythromycin and protease inhibitors (Langtry and Markham, 1999). Interaction between PDE-5 inhibitors and nitrates, for example, can dangerously lower blood pressure. Patients treated with nitrates for medical conditions often concomitantly suffer from erectile dysfunction. Due to the potential for life-threatening drug interactions, these patients may turn to ''natural" products as alternatives and unknowingly become exposed to pharmaceutical drugs (FDA, 2006).

Korean red ginseng is widely used in traditional medicine for the treatment of many disorders (Goldstein, 1975; Bahrke and Morgan, 1994). The root or root extract of *P. ginseng* has been demonstrated to induce vasodilation (Chen *et al*.,, 1984), inhibit platelet aggregation (Kimura *et al*., 1988; Teng *et al*., 1989), enhance learning and memory (Abe *et al*., 1994), produce anxiolytic effects (Bhattacharya and Mitra, 1991) and facilitate male rat copulatory behavior (Kim *et al*., 1976). Previous studies have investigated the physiological effects of ginsenoside saponins, the biologically active constituents of ginseng (Soldati and Sticher, 1980) and determined that specific ginsenosides can elicit significant effects on nitric oxide synthesis (Chen and Lee, 1995), acetylcholine induced catecholamine secretion (Tachikawa *et al*., 1995), maternal aggression (Yoshimura *et al*., 1988) and glycemic activity (Ng and Yeung, 1985). Although over 30 different ginsenosides have been identified overall (Soldati and Sticher, 1980; Tachikawa *et al*., 1995), the ginsenoside content between different strains of ginseng is vastly different (Bahrke and Morgan, 1994), suggesting that distinct ginseng strains may produce different physiological effects. The aim of the current study was to utilize P*anax ginseng* extract standardized with ginsenoside Rg3 (PGRG3) to improve the sexual behavior in active and inactive male rats.

MATERIALS AND METHODS

Chemicals and hormones: Ketamine, xylazine (Bayer, Cairo, Egypt) was freshly dissolved in saline at a concentration that allowed the administration of 1 mL kg^{-1}, subcutaneously (s.c.) for the females. Estradiol benzoate and progesterone (Sigma Chemical Co., St. Louis, MO, U.S.A.) were dissolved in corn oil and both injected S.C. in a volume of 0.2 mL/ female rat.

Ginseng materials: The standarized *Panax ginseng* extract EFLA400 (Phoenix ginseng) (Batch No. 303298) of *Panax* ginseng C.A. Mayer was prepared according to the published procedure (Korean patent 0425022, PCT/KR2003/000003) and was supplied by Lotte Group R&D Center (Seoul, Korea). The content of ginsenoside Rg3 (PGRg3), a pharmacologically active ingredient of Phoenix ginseng, was 3.6 % (w/w) (Panwar *et al*.,, 2005) as determined by HPLC (i.e., 36 μg mg^{-1} *P. ginseng* extract). PGRG3 was dissolved just before treatment in a certain amount of saline to make 50, 150 and 450 mg mL^{-1} solutions. The solutions were sterilized by membrane filtration and administrated orally to the rats at a volume of 1 mL kg^{-1} b.wt.

Experimental animals: Three months old male and female Sprague-Dawley rats (140-150g.) were purchased from Animal House Colony, NRC, Giza, Egypt. The animals were maintained on standard lab diet (Protein: 16.04%; Fat: 3.63%; Fiber: 4.1% and metabolic energy: 0.012 MJ) and water *ad libitum* at the Animal House Lab., National

Research Center. After an acclimation period of 2 weeks, animals were maintained on a 12-h light cycle; from 7 am to 7 p.m. The females were ovariectomized under intraperitoneally injection (i.p.) with ketamine plus xylazine anesthesia (120±2 mg kg^{-1} b.wt.) and were used as mating stimulus in the copulatory experiments. The experimental protocol was approved by National Research Center Review Committee for the use of human or animal Subjects.

Behavioral procedure: All the experiments were performed between 9 a.m. and 2 p.m. in a soundproof, air-conditioned room, where the animals were monitored by trained observers unaware of the experimental design. Sixty male rats were divided into four treatment groups and treated orally with only one dose day^{-1} of PGRg3 for a period of one month as follow: (1) the control group, (2) the group treated orally with PGRg3 at low dose (50 mg kg^{-1} b.wt), (3) the group treated orally with PGRg3 at medium dose (150 mg kg^{-1} b.wt.) and (4) the group treated orally with PGRg3 at high dose (450 mg kg^{-1} b.wt.).

Evaluation of male sexual behavior: Evaluation of male sexual behavior was carried out using the ovariectomized females which were brought into estrus by subcutaneously (s.c.) injection with 30 μg estradiol benzoate and after 48 h they were injected with 0.5 mg progesterone and were used 4-5 h thereafter. All females were screened with non-experimental sexually experienced males and only those exhibiting good sexual receptivity (solicitation behavior and lordosis in response to mounting) and no rejection behavior were used. The males were transferred singly to an observation cage (40×30×34 cm) and after a 3-min adaptation period, a receptive female were introduced. Male copulatory behavior was evaluated according to the method described by Dewsbury (1972) by calculating the (1) The time from the introduction of the female until the first mount and intromission [mount latency and intromission latency (ML and IL)], (2) The number of mounts and intromissions preceding ejaculation [mount and intromission frequency (MF and IF)], (3) The interval between the first intromission and ejaculation [ejaculation latency (EL)] and (4) The time between the first ejaculation and the next intromission [post-ejaculatory interval (PEI)]. After the PEI, the test was considered complete.

Tests were discontinued when IL or PEI was >15 min or EL was>30 min. Only those animals which were completed at least the last five or four mating tests out of the seven conducted at 4-day intervals were considered Sexually Active (SA) (n = 28). Whereas, those which never mounted or intromitted during the training tests were considered Sexually Inactive (SI) (n = 25). Animals which were displayed discontinuous activity were discarded (n = 7). In addition, the following parameters were evaluated in the 6 and 7th test: (1) Latency to the first contact (CL) as the time from the introduction of the female on the opposite side of the cage until the first voluntary contact by the male and (2) Total time spent in genital exploration by the male (GET), which were recorded from the introduction of the female until the first ejaculation or the end of the test in the event of its being discontinued.

Evaluation of sex penile erection (PE), sedation and stereotyped behavior (SB): Stretching-Yawning (SY) and PE episodes were counted up for each animal. Sedation and Stereotyped Behavior (SB) were scored as described by Ferrari and Giuliani (1993). In brief, every 5 min, starting immediately in the test period (30 min), each rat was observed for 30 sec sedation was graded: 0 = absent, 1 = immobility of the animal for at least 25 sec with open eyes, 2 = immobility of the animal for at least 25 sec with closed eyes. SB was graded: 0 = absent, 1 = low (intermittent or continuous sniffing), 2 = high (continuous sniffing and/or intermittent or continuous licking and biting). Sedation and SB values were represented for each rat by the sum of all the scores attributed to the animal during the test period.

Experimental protocol: After having verified the consistency of the SA rats copulatory behavior in the 6 and 7th tests, twenty four animals from the selected SA rats were divided into four groups (6 rats/ group; not statistically different for any of the parameters considered), which were orally received saline, PGRg3 at 50, 150 and 450 mg kg^{-1} b.wt. Another twenty four of the selected SI rats were randomly divided into four groups and were treated orally as previously described. SA and SI rats were transferred in groups of three homogeneous as regards treatment and sexual typology to the glass observation cages which they were accustomed singly. The tests (Experiment 1) were started immediately after the oral treatment with PGRg3 and were lasted 30 min. During this period, SY, PE, sedation and SB were evaluated for each rat. Immediately after the completion of the recording of the above behavioral parameters, the second experiment was started and the male rats were placed singly in other cages where their sexual behavior towards a receptive female, presented 3 min later, were observed.

Statistical analysis: All data were subjected to statistical analyses using the General Linear Models (GLM) Procedure of the Statistical Analysis System (SAS, 1982). The significance of the differences among treatment groups with variable means was determined by

Waller-Duncan k-ratio T test (Waller and Duncan, 1969). All statements of significance were based on a probability level of $p \leq 0.05$.

RESULTS

Experiment 1: The effects of oral administration of PGRg3 (50, 150 and 450 mg kg^{-1}) on SY, PE, sedation and SB are depicted in (Fig. l, 2, 3 and 4), respectively. These results indicated that SY episodes of the control animals in SA and SI groups were sporadic during the test period and did not differ significantly. Treatment with PGRg3 at 50 mg kg^{-1} b.wt. stimulated SY in all rats however, no significant difference was observed between the two types of animal. On the other hand, at 150 or 450 mg kg^{-1} b.wt., PGRg3 showed to be effective in SA rats, whereas, SI animals received PGRg3 at 450 mg kg^{-1} showed a significant increase in SY compared to those of control SI (Fig. 1).

The current results also indicated that PE was similar in the control SA and SI animals (Fig. 2). However, stimulation of PE was apparent after PGRg3 treatment at all doses only for SI animals in dose dependent fashion (Fig. 2). On the other hand, both SA and SI rats displayed significant increased sedation after PGRg3 treatment (Fig. 3). The comparative analysis between SI and SA rat sedation observed in the control animals and after the oral administration of PGRg3 at the three tested doses showed that sedation was significantly different in the two types of animal. Moreover, the sedation was found to be increased in SI and SA rats in a dose dependent manner although this increase was pronounced in the SI than the SA animals. A similar degree of SB was also scored in SI and SA rats only after PGRg3 administration (Fig. 4).

Experiment 2: Data presented in Table 1 revealed that all SI rats scored a higher CL (185 ±75) compared to those values for SA rats (4.3±0.9) in the 7th test. On the other hand, in the 8th test, oral treatment with PGRg3 at the three tested doses (50, 150, 450 mg kg^{-1} b.wt.) resulted in significant decreases in both CL (175±62, 130±22, 90±12, respectively) and GET (50±2.1, 42±3.9, 30±0.9, respectively) for SI animals. This decrease was

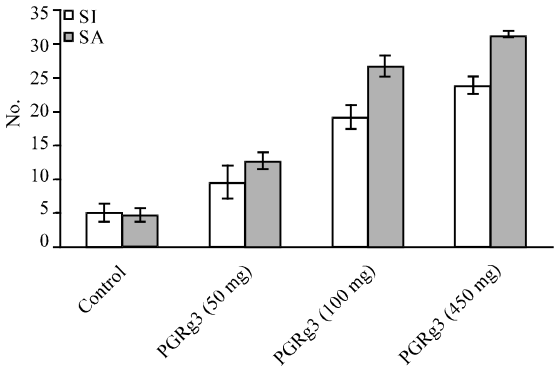

Fig. 1: Stretching-Yawning (SY) in SI and SA rats treated orally with PGRg3 extract (n)

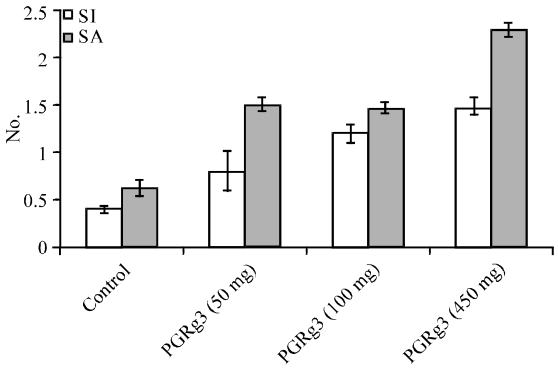

Fig. 2: Penile Erection (PE) in SI and SA rats treated orally with PGRg3 extract (n)

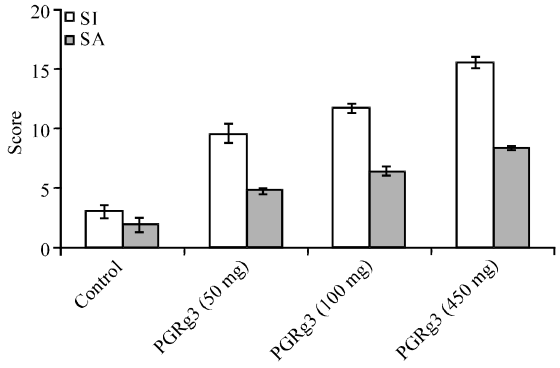

Fig. 3: Sedation in SI and SA rats treated orally with PGRg3 extract (score)

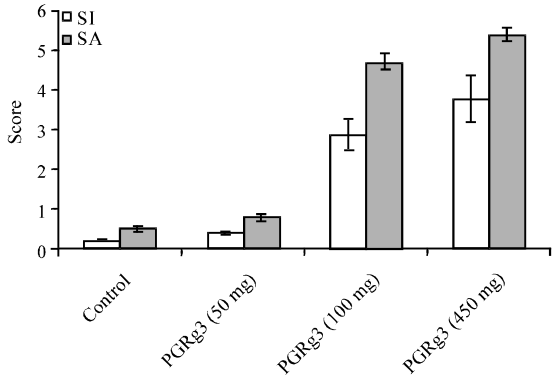

Fig. 4: Stereotyped Behavior (SB) in SI and SA rats treated orally with PGRg3 extract (score)

Table 1: Effect of oral treatment with different doses of PGRg3 on contact latency (CL) and genital exploration (GET) of sexually inactive (SI) and active (SA) male rats

	CL (s)		GET (s)	
Treatment (Test)	SI	SA	SI	SA
Control (7)	185±75[a]	4.3±0.9[a]	70±3.6[a]	7.3±1.2[a]
Saline (8)	196±24[a]	4.9±1.2[a]	74±4.2[a]	7.1±1.6[a]
Control (7)	186±32[a]	4.2±0.8[a]	72±5.1[a]	7.2±1.1[a]
PGRg3 (50 mg kg^{-1} b.wt.) (8)	175±62[b]	4.2±0.9[a]	50±2.1[b]	3.8±1.1[b]
Control (7)	187±34[a]	5.2±1.3[a]	73±4.2[a]	7.4±0.9[a]
PGRg3 (150 mg kg^{-1} b.wt.) (8)	130±22[c]	3.1±0.9[b]	42±3.9[c]	2.1±0.2[c]
Control (7)	188±35[a]	4.9±0.3[a]	77±4.6[a]	7.7±1.6[a]
PGRg3 (450 mg kg^{-1} b.wt.) (8)	90±12[d]	2.6±0.4[c]	30±0.9[d]	1.6±0.7[d]

Within each column, means superscript with different letters (a, b, c, d) are significantly different (p = 0.05), CL: Contact latency; GET: Genital exploration; SA: Sexual active; SI: Sexual inactive

Table 2: Effect of oral treatment with PGRg3 extract on copulatory behavior of sexually inactive (SI) rats

Treatment (Test)	ML (s)	IL (s)	MF (No.)	IF (No.)	EL (s)	PEI (s)
Control (7)	250±55[a]	300±58[a]	3±0.3[a]	2±0.2[a]	540±30[a]	553±30[a]
Saline (8)	242±45[a]	304±77[a]	3±0.2[a]	2±0.3[a]	558±40[a]	548±33[a]
Control (7)	247±43[a]	306±65[a]	3±0.3[a]	2±0.1[a]	545±65[a]	549±25[a]
PGRg3 50 mg (8)	200±12[b]	260±29[b]	5±1.6[b]	3±0.8[b]	450±32[a]	430±25[b]
Control (7)	251±33[a]	301±46[a]	3±0.4[a]	2±0.1[a]	540±32[a]	549±48[a]
PGRg3 150 mg (8)	170±22[c]	195±18[c]	8±1.8[c]	5±1.5[c]	340±26[b]	340±32[c]
Control (7)	248±39[a]	304±43[a]	3±0.8[a]	2±0.3[a]	540±28[a]	543±53[a]
PGRg3 450 mg (8)	98±14[d]	123±16[d]	15±3.4[d]	11±2.5[d]	204±45[c]	201±39[d]

Within each column, means superscript with different letters (a, b, c, d) are significantly different (p = 0.05), ML: mount latency; IL: Intromission latency, MF: Mount frequency; IF: Intromission frequency; EL: Ejaculation latency; PEI: Post-ejaculatory interval

Table 3: Effect of oral treatment with PGRg3 extract on copulatory behavior of sexually active (SA) rats

Treatment (Test)	ML (s)	IL (s)	MF (No.)	IF (No.)	EL (s)	PEI (s)
Control (7)	21±5[a]	48±8[a]	17±3[a]	12±2[a]	412±30[a]	421±30[a]
Saline (8)	20±4[a]	48±7[a]	17±2[a]	11±3[a]	408±40[a]	418±33[a]
Control (7)	21±3[a]	36±5[b]	16±3[a]	12±1[a]	405±35[a]	419±25[a]
PGRg3 50 mg (8)	14±2[b]	60±9[c]	26±6[b]	16±1[b]	430±42[a]	411±35[b]
Control (7)	19±3[a]	47±6[a]	18±3[a]	12±2[a]	407±33[a]	422±38[a]
PGRg3 150 mg (8)	10±2[c]	75±8[d]	32±7[c]	19±3[c]	440±20[b]	405±22[c]
Control (7)	18±3[a]	42±3[a]	16±8[a]	11±3[a]	409±38[a]	423±36[a]
PGRg3 450 mg (8)	8±4[d]	116±9[e]	46±3[d]	22±1[d]	460±38[c]	317±28[b]

Within each column, means superscript with different letters (a, b, c, d, e) are significantly different (p = 0.05), ML: Mount latency; IL: Intromission latency, MF: Mount frequency; IF: Intromission frequency, EL: Ejaculation latency; PEI: Post-ejaculatory interval

pronounced in the animals received the higher doses of PGRg3 which indicated that the PGRg3 is effective on SI rats. In SA rats, these parameters were also affected by the treatment with PGRg3 at the three tested doses and the recorded CL values were 4.2±0.9, 3.±0.9 and 2.6±0.4 for 50, 150 and 450 mg kg^{-1} b.wt., respectively. However, the recorded GET values for the SA rats were 3.8±1.1, 2.1 ±0.2 and 1.6±0.7 for the three tested doses, respectively. It is clear from the data presented in Table 1 that CL and GET were significantly decreased by the treatment with PGRg3 in a dose dependent manner which also indicate that PGRg3 was also effective in SA rats although these effects were pronounced in SI rats than SA group.

Daa presented in Table 2 showed the effects of PGRg3 on copulatory behavior in SI rats and indicated that PGRg3 have a significant improvement in the copulatory behavior in SI rats. The results revealed that these parameters were decreased significantly in the three tested doses and the recorded values were 200±12, 170± 22 and 98 ±14, respectively for ML; 260±29, 195±18 and 123±16, respectively for IL; 450±32, 340±26 and 204±45, respectively for EL and 430±25, 340±32 and 201±39, respectively for PEI. Whereas, MF and IF were significantly increased in this group in the 8th test compared to the same parameters in the same SI rats in the 7th pre-test and the recorded values for MF in this test were 5±1.6, 8±1.8 and 15±3.4 for the three tested doses respectively. However, the recorded V of IF were 3±0.8, 5±1.5 and 11±2.5 for the tested doses, respectively. In the same concern, data presented in Table 3 showed that PGRg3 had a significant improvement on the various parameters regarding the copulatory behavior for SA rats in a dose dependent manner. The results also suggested that PGRg3 enhanced libido and copulatory performance as indicated by the increased of IL (60 ±9, 75±8 and 116±9), MF (26±6, 32±7 and 46±3), IF (16±1, 19±3 and 22±1) and EL (430±42, 440 ±20 and 460±38) with the significant decrease in ML (14±2, 10±2 and 8±4) and PEI (411±35, 405±22 and 317±28) for the three tested doses, respectively. Moreover, there were significant differences

between the data collected in the 7th per-test and those collected in the 8th test for the same SA group of rats.

DISCUSSION

Ginseng is well known herb used for the treatment of sexual dysfunction. Several studies on laboratory animals have shown that ginseng enhance libido and copulatory performance. These effects of ginseng may not be due to changes in hormone secretion, but to the direct effects of ginseng, or its ginsenoside components, on the central nervous system and gonadal tissues (Kang *et al*., 2002; Tsai *et al*., 2003). Indeed, there is good evidence that ginsenosides can facilitate penile erection by directly inducing the vasodilatation and relaxation of penile corpus cavernosum (Hong *et al*., 2002). Moreover, the effects of ginseng on the corpus cavernosum appear to be mediated by the release and/or modification of release of nitric oxide from endothelial cells and perivascular nerves (Murphy and Lee, 2002). Treatment with ginseng extract also affects the central nervous system and has been shown to significantly alter the activity of hypothalamic catecholamines involved in the facilitation of copulatory behavior and hormone secretion. The findings that ginseng treatment decreased prolactin secretion also suggested a direct nitric oxide-mediated effect of ginseng at the level of the anterior pituitary (Kang *et al*., 2002). Thus, animal studies lend growing support for the use of ginseng in the treatment of sexual dysfunction and provide increasing evidence for a role of nitric oxide in the mechanism of ginsenoside action.

The present study demonstrated that PGRg3 exerts a sexual stimulation in both SI and SA rats which seems to involve ejaculation mechanisms and sex-arousal. It has already been shown that these independent aspects of sexual behavior are variously modulated by pharmacological agents (Beach, 1956). In the current study, all sexual parameters tested including CL, GET, which reflect interest towards the female (Ferrari and Giuliani, 1995) and certain measures of copulatory pattern (mount and intromission latencies, post ejaculatory interval), which resemble human 'libido', were significantly affected by the PGRg3 treatment.

The modulatory effect of PGRg3 on sexual drive was further confirmed in SI rats by the enhancement effects of the extract to stimulate copulatory behavior, to modify GET or to reduce CL. Moreover, CL was significantly decreased in these animals after PGRg3 treatment at the three tested doses although these effects were pronounced in the groups received the higher doses (i.e 450 mg kg^{-1} b.wt.), probably as a consequence of the anti-sedative effects exerted by PGRg3 at high doses.

A previous study showed that CL and GET are useful indicators of rat copulatory activity (Ferrari and Giuliani, 1995). But while it seems obvious that CL will be different in SA and SI rats, one would hardly expect a similarly low GET in the two types of rat. However, it has been demonstrated that, after repeated copulatory training tests, low GET reflects opposite situations in SI and SA rats, namely, sexual indifference in the former and high sexual drive culminating in copulation in the latter (Ferrari and Giuliani, 1995). The second significant finding which emerges from the current study was that the animals categorized as SA and SI on the basis of their sexual behavior were also markedly different in their behavioral response to the same doses of the PGRg3. In the SA rats, treatment with PGRg3 induced a moderate sedation that was significantly lower than that induced in SI rats. Moreover, PGRg3 stimulated PE and SY to a great extent. As regards SY, an impressive effect was seen in SI animals not only at the low dose but also at the high dose.

It is well documented that SY is stimulated by certain receptors including the dopamine receptors. If SY is evoked by a selective stimulation of a particular dopamine receptor subtype, namely the DA D_2 autoreceptor (Ferrari, 1985) or alternatively the DA D_3 receptor (Kostrzewa and Brus, 1991), it may be hypothesized that this kind of receptor is particularly sensitive in SI rats. Although, any interpretation regarding the underlying mechanisms is at present highly speculative, several possibilities can be proposed. The first possibility is that there are basic, a priori, behavioral and biochemical differences between the animals classified as SA and SI. The second possibility is that in SA rats the sensitivity of DA receptors is changed by repeated copulatory tests because of the release of DA into certain brain area during the copulation (Damsma *et al*.,, 1992).

The sexual-stimulant properties of PGRg3 are not surprising, as one of the major actions of the extract may be the block of the reuptake of dopamine (DA) and so increase its synaptic availability (Oh *et al*., 1997; Nah *et al*., 2009; Hwang and Jeong, 2010). The key role of DA in sexual behavior is well documented (Ferrari and Giuliani, 1995; Lee *et al*., 2008). Other mechanisms for the sexual properties enhancement of the PGRg3 may be involved the improvement of the testicular function and the increase of testosterone secretion as well as increase the sperm counts (Kim *et al*., 1999; Hassan *et al*., 2006; Qinna *et al*., 2009). In this regards, Hwang *et al*. (2004) reported that ginseng improves the survival rate and sperm quality in guinea pigs exposed to TCDD and stimulates the spermatogenesis (Yamamoto *et al*., 1977). This action may be attributed to the increase in LH

secretion which acts directly on the pituitary gland (Tsai *et al*., 2003). Furthermore, the current study revealed that treatment with PGRg3 resulted in a significant decrease in mount and intromission latency (ML and IL). These results were in agreement with those reported by other investigators (Murphy *et al*., 1998). Similar to these findings, Hong *et al*. (2002) reported that erectile function scores were significantly higher in patients treated with Korean red ginseng than in those who received placebo. Moreover, Wang *et al*., (2010) proved that ginsenoside Rg1 from *panax* ginseng could be a promising new drug for erectile dysfunction and low libido.

Although, ginseng's exact mechanism of action remains elusive, its physiological effects are thought to be due to the presence of tetracyclic triterpenoid saponins known as ginsenosides in the *Panax* species (Murphy and Lee, 2002). These ginsenosides appear to have an effect both on the neurotransmitters involved in sexual arousal and on the NO/cGMP pathways involved in erection (Park *et al*., 2006; Lin *et al*., 2007). Although there is also a possible impact on the Hypothalamus-Pituitary-Adrenal (HPA) axis with a corresponding impact on cortisteroid and prolactin levels (Kim *et al*., 1976).

The big question is does ginseng live up to its reputation as a male sexual tonic? From the obtained data, the answer appears to be a qualified yes, but dosage and length of administration appear to be important (Choi *et al*., 1995). In a sixteen week, double-blind study using three grams of ginseng per day versus a placebo in men suffering from erectile dysfunction, the ginseng treatment offered significant improvement in erectile quality over placebo (Hong *et al*., 2002). Another study also found a significant improvement over placebo only after several weeks of administration (Choi *et al*., 1999). The same study also found no changes in sexual response after acute, short-term ginseng administration. Moreover, Shamloul (2010) recommended ginseng as an effective aphrodisiac.

It would appear; therefore, that PGRg3 has the potential to be useful as a sexual enhancer in SA rats at dose as low as 50 mg kg^{-1} b.wt. However, in SI rats the dose should be increased to at least 150 mg kg^{-1} to induce a significant sexual enhancement. Similar to the current observations were reported by Ellis and Reddy (2002) and Coleman *et al*. (2003) however, they recommended a higher dose reached 1 g per day for a period of several weeks.

CONCLUSION

From the current study, we can conclude that PGRg3 succeeded to improve male sexual behavior in both active and inactive rats. Moreover, these results demonstrated that PGRg3 significantly facilitates male copulatory behavior and lend growing support for the use of PGRg3 extract as traditional medicinal in the treatment of male sexual dysfunction.

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