Original Research Article

Effects of a Herbal Sex Enhancer (Vigpower) and Zinc Supplementation on Sex Hormones, Hepatic and Renal Function in Male Albino Rats

ABSTRACT

Aim: This study evaluated the effects of a herbal sex enhancer (Vigpower) and zinc supplementation on sex hormones, hepatic and renal function in male albino rats.

Methodology: A total of 49 male Albino rats weighing between 150 to 180g were used for the study. Vigpower, Viagra and zinc were orally administered to the rats daily for 28 days. Testosterone and estradiol were quantitatively determined using a rat-specific sandwich-enzyme linked immunosorbent assay (ELISA) method. The liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were determined using the Reitman-Frankel method. Alkaline phosphatase (ALP) was determined using the Colorimetric endpoint method. Sodium (Na^+), potassium (K^+) and chloride (CL^-) were determined using ion selective electrode (ISE) method. Urea was determined using Urease bertholet method. Creatinine was determined using Jaffe-Slot method and qualitative phytochemical analysis was done on Vigpower capsule using classical methods.

Results: Phytochemical analysis revealed the presence of flavonoids, protodioscin, saponins and phenols in the herbal capsule Vigpower. Testosterone levels were significantly higher in all the treatment groups compared to the negative control, with group 7 (Vigpower + Viagra + zinc) having the highest value. Estradiol levels were significantly lower, whereas testosterone-estradiol (T/E) ratio was significantly higher in all the treatment groups compared to the negative control, except for group 4 (zinc) which showed no significant difference compared to the negative control. ALT levels in the treatment groups were not significantly different from the negative control, except for groups 6 (Viagra + zinc) and 7 (Vigpower + Viagra + Zinc), which had significantly higher levels. AST and ALP levels in the treatment groups were not significantly different from the negative control, except for group 7 (Vigpower + Viagra + Zinc), which was significantly higher than the negative control and all other treatment groups. There was no significant difference in sodium (Na^+), chloride (Cl^-) and urea levels in the treatment groups, compared to the negative control. Potassium (K^+) and creatinine levels were significantly higher in group 7 (Vigpower + Viagra + zinc), compared to the negative control and all other treatment groups.

Conclusion: Singular administration of Vigpower, Viagra and zinc increased testosterone levels of the male rats. Vigpower and Viagra had equipotent effects on the sex hormones and also increased the testosterone-estradiol ratio. Vigpower, Viagra and zinc as singular treatments, had no impact on liver enzymes and renal function. However, the combination treatment of Vigpower, Viagra and zinc was hepatotoxic and elevated potassium and creatinine levels. Herbal sex enhancers and their combination with other medications could provoke the desired sexual effect, but may damage other organ systems and pose serious public health challenges.

***Keywords**: Sex hormones; Sex enhancers; Herbal aphrodisiacs; Vigpower (Vigueur power); Viagra (Sildenafil citrate); Liver enzymes; Renal function*

1. INTRODUCTION

"Aphrodisiacs or sex enhancers are foods or drugs that arouse the sexual instinct, induce venereal desire, increase pleasure and performance. They could be classified by mode of action into three types: those that increase (1) libido, (2) potency, or (3) sexual pleasure. They bring about their desired effect by modulating hormonal, neurological and other biochemical pathways. Sex enhancers are usually taken to meet sexual needs or demands and to improve sexual health" [1]. The search for effective aphrodisiacs is as old as the history of man, as different natural and synthetic products have been used over the years to improve sexual

behaviour. This is because enhanced sexual behaviour improves relationship satisfaction and self-esteem in humans [2].

Furthermore, with an increase in the prevalence of erectile dysfunction, one of the most common forms of sexual dysfunction and an increase in male infertility, the use of sex enhancers is on the rise. Herbal sex enhancers are sought after the most, as they are less expensive, considered to be natural and safe compared to orthodox drugs. Herbal sex enhancers are also easily acquired without prescriptions, with authorities not regulating their use, nor evaluating their efficacy and safety profiles [3, 4, 5]. This study looks at the efficacy and safety of a herbal sex enhancer, thus evaluates the effects of Vigpower and zinc supplementation on sex hormones, hepatic and renal function in male albino rats.

2. MATERIALS AND METHODS

2.1 Experimental Animals

A total of forty-nine male Albino rats weighing between 150 to 180g were used for the study. The rats were housed in standard cages at regulated room temperature, with controlled 12-hour light-dark cycles, and allowed access to feed and water *ad libitum*. The rats were allowed to acclimatize for two weeks prior to the commencement of study.

2.2 Drugs

A commonly used polyherbal sex enhancer capsule Vigpower (Vigueur Power) was used for the study. Vigpower is manufactured by Green World Inc., USA and World (Tianjin) Nutrition & Health Food Co., Ltd., China. Sildenafil citrate tablets (Viagra) was also used for the study. Viagra (Vega 100) is manufactured by Hab Pharmaceuticals & Research Ltd, India. The Zinc supplement used was manufactured by Nature's Field Company, Nigeria.

2.3 Acute Toxicity Study

"Acute toxicity study was done by the fixed dose procedure, using a group of 3 rats. 2000 mg/kg body weight of Vigpower was orally administered to each of the rats. The rats were then observed for signs of toxicity for 48 hours. After observation, there were no signs of toxicity, hence the polyherbal capsule Vigpower was deemed safe up to a dose of 2000 mg/kg body weight". [6] Viagra and Zinc are standard drugs, and the doses were translated from the human dose.

2.4 Dose Calculation

2.4.1 Vigpower

The administered rat dose was extrapolated from the human daily dose [7] as shown below:

Human daily dose is 2 capsules (300 mg each) daily, which is 600mg/day.

Rat dose (mg/kg) = Human daily dose × 0.018 × 5

=600 × 0.018 × 5

= 54mg/kg/day

2.4.2 Viagra (Sildenafil Citrate)

The administered rat dose was extrapolated from the human daily dose [7] as shown below:

Human daily dose is 1 tablet (100mg) daily, which is 100mg/day.

Rat dose (mg/kg) = Human daily dose × 0.018 × 5

= 100 × 0.018 × 5

= 9mg/kg/day

2.4.3 Zinc

The administered rat dose was extrapolated from the human daily dose [7] as shown below:

Human daily dose is 1 tablet (50mg) daily, which is 50mg/day.

Rat dose (mg/kg) = Human daily dose × 0.018 × 5

= 50 × 0.018 × 5

= 4.5mg/kg/day

2.5 Experimental Design

After acclimatization, the rats were weighed and grouped into 7 groups of 7 rats each. Treatments (drugs) were administered daily according to the groups by means of oral gavage for 28 days.

Group 1: Negative control group.

Group 2: Administered Vigpower

Group 3: Administered Viagra

Group 4: Administered Zinc

Group 5: Administered Vigpower and Zinc

Group 6: Administered Viagra and Zinc

Group 7: Administered Vigpower, Viagra and Zinc

2.6 Reagents and Biochemical Analyses

"All reagents were commercially purchased and the manufacturer's standard operating procedures strictly followed. Quality control (QC) samples were run together with the biochemical analysis. Testosterone and estradiol were quantitatively determined using a rat-specific sandwich-enzyme linked immunosorbent assay (ELISA) method as described by Elabscience Biotechnology Company limited, China". [8] The liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were determined using the Reitman-Frankel method [9], as modified by Randox laboratories limited (UK). Alkaline phosphatase (ALP) was determined using the Colorimetric endpoint method [10] as modified by Randox laboratories limited (UK). The electrolytes, sodium (Na^+), potassium (K^+) and chloride (CL^-) were determined using ion selective electrode (ISE) method [11]. Urea was determined using Urease bertholet method [12], as modified by Randox laboratories limited (UK). Creatinine was determined using the Jaffe-Slot method [13], as modified by Randox laboratories limited (UK). Qualitative phytochemical analysis was done on the herbal capsule using classical methods [14].

2.7 Statistical Analysis

Data was analysed using Graph Pad Prism version 8.0.2. Differences between groups were compared using one way analysis of variance (ANOVA), followed by Tukey's multiple comparison test. Results were considered statistically significant at 95% confidence interval ($p \leq 0.05$). Values are expressed as Mean ± SD.

3. RESULTS AND DISCUSSION

Table 1: Qualitative Phytochemical Analysis of the Herbal Capsule Vigpower.

Phytochemicals	Presence

Flavonoids	+
Protodioscin	++
Saponins	+
Tannins	-
Phenols	+
Alkaloids	-
Terpenes	-

+ Present, - Not present

Table 1 shows the results of phytochemical analysis. The results revealed the presence of the phytochemicals flavonoids, protodioscin, saponins and phenols in the herbal capsule Vigpower in variable amounts. This agrees with the work of da Cruz *et al*. [15], in which they reported that flavonoids and saponins are some of the main bioactive components of herbal sex enhancers. "Plant products have been shown to contain different bioactive phytochemicals or secondary metabolites which have nutritive value, but also possess the ability to affect several biochemical pathways and bring about drug-like responses. This forms the basis for their use and application in medicine" [16, 17].

Table 2: Effects of Treatment on Sex Hormones of the Male Rats.

Groups n = 7	**Testosterone (ng/mL)**	**Estradiol (pg/mL)**	**Testosterone/Estradiol Ratio****
Group 1 (Neg. Control)	2.34 ± 0.13	9.88 ± 0.16	247.0 ± 14.56
Group 2 (Vigpower)	2.53 ± 0.09[a]	8.43 ± 0.51[a]	300.6 ± 22.26[a]
Group 3 (Viagra)	2.63 ± 0.10[a]	8.33 ± 0.43[a]	316.1 ± 22.26[a]
Group 4 (Zinc)	2.70 ± 0.10[a]	9.83 ±0.15 [cgkLm]	274.7 ± 13.24
Group 5 (Vigpower + Zinc)	2.80 ± 0.07[ad]	8.60 ± 0.42[a]	326.2 ± 18.17[ak]
Group 6 (Viagra + Zinc)	2.73 ± 0.06[a]	8.00 ± 0.11[a]	341.7 ± 7.22[aL]
Group 7 (Vigpower + Viagra + Zinc)	2.85 ± 0.07[af]	7.75 ± 0.50[a]	368.2 ± 14.39[afjm]
P-value	< 0.0001	< 0.0001	< 0.0001
F-value	8.967	19.12	18.77
Remark	S	S	S

***-Converted to similar units, n – Number of rats, NS – not significant, S – significant, [a] – significantly different from control, [b] –significant difference between, groups 2 vs 3, [c] – significant difference between, groups 2 vs 4, [d] –significant difference between, groups 2 vs 5, [e] – significant difference between, groups 2 vs 6, [f] –significant difference between, groups 2 vs 7, [g] – significant difference between, groups 3 vs 4, [h] - significant difference between, groups 3 vs 5, [I] - significant difference between, groups 3 vs 6, [j] - significant difference between, groups 3 vs 7, [k] -*

significant difference between, groups 4 vs 5, [L]- significant difference between, groups 4 vs 6, [m] - significant difference between, groups 4 vs 7, [n] - significant difference between, groups 5 vs 6, [o] - significant difference between, groups 5 vs 7, [p] - significant difference between, groups 6 vs 7

Table 2 shows the results of the sex hormones after treatment. Testosterone levels were significantly higher ($p< 0.05$) in all the treatment groups compared to the negative control, with group 7 (administered Vigpower + Viagra + zinc) having the highest value. This implies Vigpower, Viagra and zinc as singular treatments significantly increased testosterone levels. Also, zinc in combination with the sex enhancers effectively increased the testosterone levels in the rats in a synergistic manner.

Estradiol level was significantly lower ($P< .05$) in all the treatment groups compared to the negative control, except for group 4 (administered zinc) which showed no significant difference ($P> .05$) compared to the negative control. Also, the estradiol level in group 4 (administered zinc) was significantly higher than the other treatment groups. This implies the sex enhancers Vigpower, Viagra and their combinations reduced estradiol levels in the male rats.

Testosterone-estradiol (T/E) ratio was significantly higher ($P< .05$) in all the treatment groups compared to the negative control, except for group 4 (administered zinc) which showed no significant difference ($P> .05$) compared to the negative control. This indicates the sex enhancers Vigpower, Viagra and their combinations increased T/E ratio, in the male rats. This could be due to the inhibition of the enzyme aromatase, responsible for converting testosterone to estradiol by Vigpower and Viagra.

Testosterone, the male sex hormone and estradiol play critical roles in male sexual function and behavior. They modulate erectile function, libido, sexual potency and also have reproductive functions in the hypothalamus-pituitary-gonadal axis. The balance or ratio between these hormones gives a measure of sexual function [18]. The results of this study are in consonance with the works of Janjic *et al*. [19], in which they reported increased testosterone levels in male adult rats after sildenafil administration. Kotta *et al*. [2], reported that the herbal plant *Tribulus terrestris* increased the levels of testosterone, leutinizing hormone and dihydrotestosterone in male rats. They also reported that protodioscin a phytonutrient found in Vigpower, showed androgenic effects. In another study, administration of tadalafil decreased serum estradiol levels, increased testosterone levels, resulting in an increase in the T/E ratio [20]. Egwurugwu *et al*. [21], reported a dose dependent increase in testosterone levels, but no significant effect on the

levels of estradiol after zinc administration for six weeks in male rats. Other studies have also reported an increase in testosterone levels, improved sexual competence, sexual desire and sexual function in both human and animal models [22, 23, 24].

Table 3: Effects of Treatment on Liver Enzymes of the Male Rats

Groups n = 7	**ALT (IU/L)**	**AST (IU/L)**	**ALP (IU/L)**
Group 1 (Neg. Control)	8.00 ± 1.73	46.20 ± 6.69	56.60 ± 4.89
Group 2 (Vigpower)	12.50 ± 3.32	49.00 ± 9.63	62.00 ± 6.32
Group 3 (Viagra)	8.25 ± 0.50	48.00 ± 4.15	62.00 ± 9.71
Group 4 (Zinc)	9.33 ± 2.31	48.33 ± 6.36	59.33 ± 5.03
Group 5 (Vigpower + Zinc)	9.80 ± 2.05	47.60 ± 6.66	61.60 ± 8.78
Group 6 (Viagra + Zinc)	14.50 ± 3.54[a]	50.00 ± 9.73	52.00 ± 5.00
Group 7 (Vigpower+Viagra+Zinc)	67.50 ± 2.12 [afjmop]	89.00 ± 7.87 [afjmop]	103.0 ± 8.41 [afjmop]
P-value	< 0.0001	< 0.0001	< 0.0001
F-value	205.9	10.68	10.76
Remark	S	S	S

n – Number of subjects, NS – not significant, S – significant, [a] – significantly different from control, [b] –significant difference between, groups 2 vs 3, [c] –significant difference between, groups 2 vs 4, [d] –significant difference between, groups 2 vs 5, [e] –significant difference between, groups 2 vs 6, [f] –significant difference between, groups 2 vs 7, [g] –significant difference between, groups 3 vs 4, [h] - significant difference between, groups 3 vs 5, [I] - significant difference between, groups 3 vs 6, [j] - significant difference between, groups 3 vs 7, [k] - significant difference between, groups 4 vs 5, [L]- significant difference between, groups 4 vs 6, [m] - significant difference between, groups 4 vs 7, [n] - significant difference between, groups 5 vs 6, [o] - significant difference between, groups 5 vs 7, [p] - significant difference between, groups 6 vs 7

Table 3 shows results of the liver enzymes after 4 weeks of treatment. ALT levels in the treatment groups were not significantly different (p>0.05) from the negative control, except for groups 6 (administered Viagra + zinc) and 7 (administered Vigpower + Viagra + Zinc), which had significantly higher (*P*< .05) levels. The combination group of Vigpower, Viagra and zinc had significantly higher (*P*< .05) ALT levels than all the other treatment groups. AST and ALP levels in the treatment groups were not significantly different (*P*> .05) from the negative control, except for group 7 (administered Vigpower + Viagra + Zinc), which was significantly higher than the negative control and all other treatment groups. This implies the singular treatments with Vigpower, Viagra and zinc had no impact on the liver enzymes. However, their combination (Vigpower + Viagra + zinc) was hepatotoxic and grossly elevated the liver enzymes. This shows a clear mechanism of drug-herb reaction elevating the levels of the liver enzymes, and adversely affecting liver function.

Various researchers citing different mechanisms have reported hepatoprotective effects of sildenafil, including the improvement of the cytoarchitecture of the liver [25, 26, 27]. However, Okpalakunne *et al*. [28], reported hepatotoxic effects, and elevation of liver enzymes when sildenafil was administered at higher doses (100mg/kg). The herbal testosterone booster teasel at doses of 10 and 15mg/kg was found to be hepatoprotective in rats [29]. On herb-drug combinations, Briggs *et al*. [30], reported hepatotoxic outcomes, as the combination of Ruzu bitters and glibenclamide worsened liver parameters, with elevated aminotransferases and alkaline phosphatase levels. Zinc, an important component of different enzymes was found to confer hepatoprotective effects and improved liver parameters in different animal and human studies [31, 32].

Table 4: Effects of Treatment on Renal Function Parameters of the Male Rats

Groups n = 7	**Na^+ (mmol/L)**	**K^+ (mmol/L)**	**Cl^- (mmol/L)**	**Urea (mmol/L)**	**Creatinine (mg/dL)**
Group 1 (Neg. Control)	141.6 ± 5.13	4.26 ± 0.49	94.60 ± 0.89	6.56 ± 0.36	2.92 ± 0.28
Group 2 (Vigpower)	140.5 ± 4.20	4.83 ± 0.94	93.75 ± 0.96	5.90 ± 0.78	2.63 ± 0.26
Group 3 (Viagra)	139.8 ± 2.50	5.03 ± 0.95	94.50 ± 0.56	5.38 ± 0.89	2.78 ± 0.33
Group 4 (Zinc)	137.3 ± 2.52	4.73 ± 0.70	92.67 ± 0.58	4.97 ± 0.47	2.33 ± 0.25
Group 5 (Vigpower + Zinc)	135.6 ± 2.07	4.52 ± 0.31	93.60 ± 0.47	5.60 ± 0.65	2.42 ± 0.19
Group 6 (Viagra + Zinc)	140.0 ± 2.0	7.60 ± 0.87^{aeILn}	93.67 ± 0.52	6.40 ± 0.87	2.43 ± 0.42
Group 7 (Vigpower + Viagra + Zinc)	140.0 ± 5.66	9.10 ± 1.27^{afjmo}	95.00 ± 1.01	6.05 ± 0.21	5.20 ± 0.42^{afjmop}
P-value	0.4147	< 0.0001	0.5020	0.0582	< 0.0001
F-value	1.069	16.20	0.9206	2.657	25.99
Remark	NS	S	NS	NS	S

n – Number of subjects, NS – not significant, S – significant, [a] – significantly different from control, [b] –significant difference between, groups 2 vs 3, [c] –significant difference between, groups 2 vs 4, [d] –significant difference between, groups 2 vs 5, [e] –significant difference between, groups 2 vs 6, [f] –significant difference between, groups 2 vs 7, [g] –significant difference between, groups 3 vs 4, [h] - significant difference between, groups 3 vs 5, [I] - significant difference between, groups 3 vs 6, [j] - significant difference between, groups 3 vs 7, [k] - significant difference between, groups 4 vs 5, [L]- significant difference between, groups 4 vs 6, [m] - significant difference between, groups 4 vs 7, [n] - significant difference between, groups 5 vs 6, [o] - significant difference between, groups 5 vs 7, [p] - significant difference between, groups 6 vs 7

Table 4 shows results of renal function parameters after 4 weeks of treatment. The results reveal there were no significant differences (*P*> .05) in sodium (Na^+), chloride (Cl^-) and urea levels in the treatment groups, compared to the negative control. Potassium levels were significantly

higher ($P< .05$) in groups 6 (Viagra +zinc) and 7 (Vigpower + Viagra + zinc), compared to the negative control and all other treatment groups. There were no significant differences ($P> .05$) in creatinine levels in all the treatment groups compared to the negative control, except for group 7 (Vigpower + Viagra + zinc), which was significantly higher ($P< .05$) than the negative control and all other treatment groups. This indicates singular administration of Vigpower, Viagra and zinc was innocuous, non-toxic to the kidney and did not impact any of the renal function parameters. However, treatment with the combination of Vigpower, Viagra and zinc elevated potassium and creatinine levels.

Studies have reported Viagra administration to be reno-protective in both human and animal studies, as it improved kidney function, attenuated markers of acute kidney injury, reduced electrolyte derangement and improved general kidney histology. This was attributed to anti-inflammatory, antioxidant and anti-apoptotic pathways [33, 34, 35]. Other studies reported acute kidney injury due to overdose of sildenafil administration [36]. Researchers have reported different effects of herbal aphrodisiacs on renal function. Kpomah & Arhoghro [37], reported that the polyherbal Jalin Herbal Mannex Liquid (JHML) increased testosterone, but had no significant effect on urea, creatinine and serum electrolytes of wistar rats, which is in agreement with the results of this study. Asuquo *et al*. [38], reported that the leaves of *Spondias mombin*, were relatively safe, but prolonged usage could cause nephrotoxicity. There have also been documented cases of renal failure, following the consumption of *Tribulus terrestris* [39, 40].

4. CONCLUSION

Vigpower contains flavonoids, protodioscin, saponins and phenols. Singular administration of Vigpower, Viagra and zinc increased testosterone levels of the male rats. Vigpower and Viagra had equipotent effects on the sex hormones, increased testosterone levels, reduced estradiol levels and increased the testosterone-estradiol ratio. Vigpower, Viagra and zinc administered singularly, had no impact on liver enzymes, was non-toxic to the kidney and did not impact renal function. However, treatment with the combination of Vigpower, Viagra and zinc was hepatotoxic and elevated potassium and creatinine levels. Use of herbal sex enhancers and their combination with other medications could bring about the desired sexual effect, but may damage other organ systems and pose serious public health challenges.

Ethical Approval:

Animal Ethic committee approval has been collected and preserved by the author(s)

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