Table 3: Effects of super7 polyherbal drug formulation on body weight

Groups	Mean basal body weight (g) ± SEM	Mean final body weight (g) ± SEM	Mean weight gain (%) ± SEM	p-value
I	79.20 ± 1.36	147.62 ± 3.24	46.35 ± 1.51	0.026
II	80.91 ± 3.61	148.20 ± 6.28	45.41 ± 1.07	0.026
III	76.54 ± 1.78	133.17 ± 4.10	42.53 ± 1.99	0.045
IV	89.24 ± 2.72	159.31 ± 2.73	43.98 ± 1.35	Control
V	74.41 ± 2.37	135.69 ± 4.45	45.16 ± 1.48	0.040
VI	77.80 ± 1.42	122.63 ± 3.54	36.56 ± 1.04	0.068

Values were expressed as mean ± standard error of mean (S.E.M), n = 7.

From Table 3, there were significant differences ($p < 0.05$) in body weight gains of animals in all the groups except group VI when compared with controls in group IV.

Table 4: Effects of super 7 polyherbal drug formulation on feed intake

Groups	Week 1 Mean feed intakes (g) ± S.E.M	Week 2 Mean feed intakes (g) ± S.E.M	Week 3 Mean feed intakes (g) ± S.E.M	Week 4 Mean feed intakes (g) ± S.E.M	Mean Mean ± S.E.M	P - value
I	115.79 ± 17.04	98.29 ± 7.22	126.84 ± 10.84	128.49 ± 2.78	117.35 ± 9.47	0.02
II	118.23 ± 8.81	109.73 ± 6.06	122.54 ± 8.62	137.33 ± 5.96	121.96 ± 7.36	0.02
III	128.43 ± 15.61	100.63 ± 14.29	138.01 ± 15.00	135.17 ± 4.19	125.56 ± 12.27	0.02
IV	144.67 ± 17.01	176.93 ± 8.29	145.24 ± 11.84	115.74 ± 14.51	145.65 ± 12.91	-
V	103.77 ± 8.40	97.84 ± 5.92	138.40 ± 11.47	122.40 ± 13.78	115.60 ± 9.89	0.03
VI	137.40 ± 10.54	97.73 ± 9.26	143.51 ± 5.37	96.80 ± 15.99	118.86 ± 10.29	0.02

Values were expressed as mean ± standard error of mean (S.E.M), n = 7.

The means of the weekly mean feed intakes had statistically significant decreases (P < 0.05) in all the groups when compared with the control group IV.

Table 5: Effects of super 7 polyherbal drug formulation on water intake

Groups	Week 1 Mean water intakes (ml) ± S.E.M	Week 2 Mean water intakes (ml) ± S.E.M	Week 3 Mean water intakes (ml) ± S.E.M	Week 4 Mean water intakes (ml) ± S.E.M	Mean Mean ± S.E.M	P-value
I	151.10 ± 15.64	151.67 ± 12.78	153.01 ± 11.28	223.24 ± 9.61	169.76 ± 12.33	0.01
II	173.56 ± 15.21	162.14 ± 12.09	175.76 ± 9.71	228.57 ± 14.21	185.01 ± 12.81	0.01
III	127.27 ± 14.36	151.13 ± 7.61	188.97 ± 20.80	232.86 ± 10.85	175.06 ±13.41	0.01
IV	158.84 ± 9.30	184.26 ± 9.96	197.87 ± 10.47	245.71 ± 16.74	196.67 ±11.62	-
V	132.94 ± 7.33	148.51 ± 8.91	181.23 ± 12.37	221.43 ± 12.04	171.03 ±10.16	0.02
VI	147.59 ± 18.21	174.10 ± 19.30	165.41 ± 17.46	222.86 ± 8.65	177.49 ±15.91	0.01

Values were expressed as mean ± standard error of mean (S.E.M), n = 7.

From Table 5, all the groups had statistically significant decreases (P < 0.05) in mean of weekly mean water intakes when compared with the control group IV.

Table 6: Effects of super 7 polyherbal drug formulation on FSH level

Groups	Mean FSH levels (mIU /ml)			
	Baseline (B) ± S.E.M	**After treatment (AT) ± S.E.M**	**(AT - B) ± S.E.M**	**P-values**
I	2.13 ± 2.13	0.00 ± 0.00	- 2.13 ± 2.13 ≡ 0.00 ± 0.00	0.01
II	4.40 ± 2.75	0.00 ± 0.00	- 4.40 ± 2.75 ≡ 0.00 ± 0.00	0.03
III	0.02 ± 0.02	0.27 ± 0.27	0.25 ± 0.27	0.04
IV	5.20 ± 1.79	0.05 ± 0.05	- 5.15 ± 1.79 ≡ 0.00 ± 0.00	Control
V	6.96 ± 6.31	0.13 ± 0.13	- 6.83 ± 6.31 ≡ 0.00 ± 0.13	0.003
VI	5.20 ± 4.01	0.27 ± 0.16	- 4.93 ± 4.01 ≡ 0.00 ± 0.00	0.001

Values were expressed as mean ± standard error of mean (S.E.M), n = 7. P < 0.05 implies statistically significantly difference from baseline value; only group 3 recorded increase in FSH level.

Negative values were considered to be equivalent to zero.

Table 7: Effects of Super 7 polyherbal drug formulation on LH level

Groups	Mean LH levels (mIU /ml)			
	Baseline (B) ± S.E.M	**After treatment (AT) ± S.E.M**	**(AT - B) ± S.E.M**	**P-values**
I	34.20 ± 12.71	43.58 ± 9.54	9.38 ± 11.67	0.01
II	14.40 ± 10.01	51.88 ± 18.31	37.48 ± 19.17	0.02
III	63.30 ± 38.60	18.64 ± 5.91	0.00 ± 2.50	0.01
IV	15.00 ± 7.65	12.64 ± 6.74	0.00 ± 1.24	Control
V	16.50 ± 10.21	10.98 ± 4.84	0.00 ± 2.35	0.003
VI	33.90 ± 16.16	0.04 ± 0.04	0.00 ± 0.00	0.02

Values were expressed as mean ± standard error of mean (S.E.M), n = 7. P < 0.05 implies significantly different from group IV. There were significant increase (P < 0.05) in LH levels of animals in group I and II after treatment when compared to their baseline levels.

Negative values were considered to be equivalent to zero.

Table 8: Effects of super7 on mlondialdehyde (MDA) and Super oxide dismutase (SOD)

Groups	Mean MDA concs (nm/ml) ± S.E.M	MDA P-values	Mean SOD concs (µ/ml) ± S.E.M	SOD P-values
I	2.85 ± 0.49	0.02	3.64 ± 2.78	0.01
II	3.36 ± 0.23	0.01	28.48 ± 20.31	0.04
III	4.26 ± 0.31	0.06	35.15 ± 6.15	0.06
IV	3.24 ± 0.34	Control	6.06 ± 6.06	Control
V	3.37 ± 0.23	0.01	22.43 ± 12.66	0.04
VI	4.18 ± 0.21	0.06	21.21 ± 21.21	0.002

Values were expressed as mean ± standard error of mean (S.E.M), n = 3 for both MDA and SOD.

Effects on MDA level:

There were significant alterations ($p < 0.05$) in mean MDA level of animals in groups I, II and V when compared with controls group IV. Only group I recorded less MDA concentration than the control group IV.

Effects on SOD level:

There were significant differences ($p < 0.05$) in mean SOD levels of animals in all the groups except group III which recorded non-significant increase ($P > 0.05$) when compared with control group IV. Super7 had dose dependent increases in SOD enzyme.

Discussion

In accordance with the results of the phytochemical analysis, the positive gonadotropin effects of Super7 might be mainly due to the presence of flavonoids, saponins and tannins. This is due to the following reasons: flavonoids and tannins had been reported to improve the serum levels of gonadotropins (FSH and LH) significantly [30]. Flavonoids and saponins have positive effects on androgen bioavailability [31]. On the other hand, alkaloids, cardiac glycosides and anthraquinones reduced significantly the serum level of FSH, LH, progesterone and estradiol [32]. Steroids including anabolic steroids and corticosteroids (cortisone, prednisone) could have a serious effect on fertility [33]. Some components of terpenoids (essential oils) have a high ovicidal activity [34].

The results of the acute toxicity tests implied that the drug have high safety profile. However, higher doses should be used with caution. A previous study on *Carica papaya*, a component of the test drug (Super7) had an LD_{50} above 5,000 mg/kg body weight with no signs of autonomic or other symptoms of toxicity [35]. But in the sub-acute study, the levels of alkaline phosphatase, gamma glutamyl transferase and bilirubin increased in a dose-dependent fashion, suggesting a possible damage to the hepato-billiary system [35]. The increased body weights was attributed to anabolic effects which caused increased metabolism, tissue generation and muscle building which resulted in general increases in body mass index [36]. Many factors might have been responsible for the decrement in feed intakes. Some of these factors include: possibility of side effects such as anorexia. The feed might contain some thermogenic ingredients which might have caused early satiety in the rats [37]. There might have also been drug – feed interaction which might have resulted in slowing down the gastrointestinal tract motility. Increased LH implied successful ovulation and formation of corpus luteum which will in turn produce estrogen and progesterone. These two hormones might have altered the threshold for osmotically induced arginine vasopressin (AVP), the primary hormone involved in the regulation of renal free water release and thirst onset [38]. This might have contributed to the decrement in water intakes observed in all the groups.

This reduction of FSH observed in group IV was not expected because group IV received distilled water. However, the blood samples might have been collected when the rats were in their luteal phases of menstral cycles. In the luteal phase, LH is dominant over FSH. In addition to this, the dominant follicle during its development secretes increasing levels of estradiol and inhibin B which act to reduce FSH secretion through a negative feedback mechanism [39]. At high dosage, the test drug could enhance FSH level thus having pro-fertility effect. The reduction observed in group V was as expected because group V received levonorgestrel, a standard anti-fertility drug [40]. The reduction in group VI might be due to the prolonged administration of the drug clomiphene. FSH might have risen to a level that triggered negative response that resulted to the decline in FSH level. Estradiol also exerts negative feedback on FSH secretion from the pituitary gland [41]. The test drug (Super7) had dose dependent increases in LH concentrations. Therefore, group III should have recorded an increase more than that obtained in groups I and II. This was not as expected and the reason could be due to the high dose coupled with prolonged administration. The LH might have been raised to a level that triggered negative response that resulted in the decline in LH level. LH release is stimulated by gonadotropin-releasing hormone (GnRH) and inhibited by estrogen in females and testosterone in males [42]. This was evident in group VI which received clomiphene – a standard pro-gonadotropin drug. LH is critical to luteinization of the ovarian follicles and post-ovulatory follicular function [43].

The test drug had dose dependent increases in MDA concentrations. This implied aggravation of lipid peroxidation – an oxidative process that modifies lipid and fatty acids in both sperm and oocyte membranes thereby increasing the likelihood of infertility [44]. Since the low dose of Super7 recorded a less MDA concentration when compared to the control group IV, it implied that appropriate down modification of the dosage and duration of treatment will unfold the lipid peroxidation lowering potential of the test drug [45]. The test drug had a good antioxidant property by increasing the concentration of super oxide dismuthase in a dose dependent manner. SODs form the front line of defense against reactive oxygen species (ROS) mediated injury [46].

Conclusions

This study showed that the test drug Super7 when used at the right dosage and for the right duration of treatment will have positive gonadotropin effects that will be comparable to those of a standard pro-fertility and positive gonadotropin drug Clomiphene. However, it has to be used during the luteal phase for a short duration and at a dose between 1,014.6 mg/kg body weight and 2,029.2 mg/kg body weight.

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