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Effects of oral administration *of Curcuma longa* rhizome (turmeric) powder on some reproductive hormones, reproduction related serum biochemical parameters and uterine histomorphology of female rabbits

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Abstract

This study evaluated the effects of oral administration *of Curcuma longa* rhizome (turmeric) powder on some reproductive hormones, reproduction related serum biochemical parameters and uterus of female rabbits. Sixteen mature rabbit does were used for the experiment. They were randomly assigned to four groups (A – D) of four does each. Groups A, B and C does received 250, 500 and 1000 mg/kg body weight of turmeric powder mixed with 1 ml of distilled water. Group D (control) received 1 ml of distilled water as a placebo. All treatments were given per os, once daily for 45 days. Blood samples for the assay of the female reproductive hormones were collected on days 15 and 45 of treatment, while that for the assay of other reproduction related serum biochemical metabolites was only on day 45 of treatment. The uteri were collected on day 45 from three females in each group for histological evaluation. All laboratory evaluations followed standard procedures. Results showed that on both days 15 and 45, the mean serum levels of follicle stimulating hormone (FSH) of rabbits in Groups B and C were significantly higher ($p < 0.05$) than those of rabbits in Groups A and D. The serum triglyceride levels of Groups B and C does were significantly higher ($p < 0.05$) than those of Groups A and D. The serum total protein levels of Group B does were significantly ($p < 0.05$) lower than that of Group D does, while the serum MDA of group B was significantly ($p < 0.05$) lower than those of Groups A and C. The serum phosphorus levels of Group A does were significantly ($p < 0.05$) lower than those of all other groups. Uterine sections from rabbits in all groups showed no lesions. It was concluded that *Curcuma longa* powder, as used in the study, especially at higher doses (500 mg/kg and 1000 mg/kg), led to significantly higher serum levels of FSH and did not lead to any deleterious effects on serum levels of oestradiol, other reproduction related biochemical metabolites, and the uterine histomorphology of the rabbit does.

Keywords: *Curcuma longa* rhizome; Turmeric; Female rabbits; Reproductive hormones; Serum biochemistry; Uterus.

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Introduction

The rabbit (*Oryctolagus cunniculus*) has been identified as one of the animals that can be successfully reared at the family level (FAO, 1996), due to its favourable biological characteristics, such as being a monogastric with a short gestation interval and high prolificacy (Beaumont *et al*., 2002). Rabbits are also well-known in the fields of medicine and biotechnology (Chantry-Darmon *et al*., 2003), making them versatile animal species for both research and human use. Rabbits require inexpensive feed, simple housing, and do not compete with humans for cereals as much as chickens or pigs (Petrescu *et al*., 2013). In comparison to beef, pork, chicken or lambs, rabbit meat has lower cholesterol, fewer calories, and a lower fat percentage (Aduku and Olukosi, 1990). According to Janieri (1987), the low cholesterol value makes it a potentially life-saving animal protein source for people with high blood pressure.

Inadequate supply of animal protein from traditional livestock (cattle, sheep, goats, pigs, and chicken) sources is reported to be causing a decline in animal protein consumption in many developing countries around the world, and approximately 854 million people, or 12.6% of the global population, are severely malnourished FAO (2006). There is thus need to improve the reproductive performance of rabbits in order to increase their ability to provide the much-needed animal protein.

Previously, drugs and synthetic hormones were used to boost fertility and treat reproductive diseases in farm animals. There is however a global campaign for organic livestock production to prevent the harmful effects of drug residues and hormones derivable from edible animal tissues on humans.

Turmeric, a spice derived from the rhizome of *Curcuma longa Linn* (Zingiberaceae), is widely used for colouring, flavouring, and medicinal purposes (Ammon and Wahl, 1991). *Curcuma longa* rhizomes contain volatile oils, which are primarily made up of monoterpenes and curcuminoids, as well as minerals, carotene, and vitamin C (Leung and Foster, 1996). Curcumin, the active principle in turmeric, is widely used as a colouring agent in foods, drugs, and cosmetics and has been reported to have a variety of effects (Anto *et al*., 1996). Indians has long utilised turmeric for a variety of medical applications (Akram *et al*., 2010). According to reports, *C. longa* extract has the following benefits: anti-diabetic (Kowluru and Kanwar, 2007), neuroprotective (Shukla *et al*., 2003; Aggarwal and Harikumar, 2009), gonadoprotective (Ilbey *et al*., 2009), hepatoprotective (Khazdair *et al*., 2016), and renal protective (Aggarwal and Harikumar, 2009).

The primary and biologically active ingredient in *C. longa* (curcumin) was identified as being responsible for the variedly reported therapeutic effects of *C. longa* (Sharma and Singh, 2010). Curcumin has been shown to have a variety of other pharmacological effects, including anti-inflammatory (Jurenka, 2009), anti-oxidant, and anti-cancer (Aggarwal and Harikumar, 2009). It has been reported that the anti-cancer properties of curcumin is based on its ability to scavenge free radicals, raise glutathione levels, and aid in the liver's detoxification of mutagens and carcinogens (Kunchandy and Rao, 1990; Akram *et al*. 2010).The United States Food and Drug Administration (FDA) has approved curcumin as safe for human consumption (Chainani-Wu, 2003), and its pharmacological safety has been demonstrated (Ammon and Wahl, 1991).

With regards to reproduction, El-Sayed (2008) investigated the effects of curcumin on in vitro uterine contractility of non-pregnant rats. In the rat uterus, curcumin demonstrated possible tocolytic effects, potentially via antagonising receptor-dependent process (oxytocin-induced contraction); it was speculated that this effect may be advantageous for women experiencing

dysmenorrhea or going through early labour (El-Sayed, 2008). According to findings from a different study, curcumin relaxed the smooth muscles of the rat uterus through both receptor-dependent and independent mechanisms (Itthipanichpong *et al*., 2003). Liduan and colleagues (Liduan *et al*., 2004) also looked into the growth inhibitory effect of curcumin on human ovarian cancer: following treatment with varying doses of curcumin, the growth of cancerous masses was significantly inhibited in the ovary. Some cancer cells presented characteristic morphological changes of apoptosis. Estradiol has been established as a risk factor for cervical cancer and has been shown to play a synergistic role with viral oncoproteins. One study conducted showed that curcumin counteracts the proliferative effects of estradiol and induces apoptosis in cervical cancer cells through inhibition of the pathways which were improved by estradiol (Singh and Singh, 2011).

There is paucity of information on the effect of turmeric on female reproduction in animals, particularly in rabbits. Although a lot of work has been done to verify the medicinal properties of this plant, to the best of our knowledge, very little has been reported concerning its effect on rabbit reproduction. The present study evaluated the effects of oral administration *of Curcuma longa* rhizome (turmeric) supplement on some reproductive hormones, reproduction related serum biochemical parameters and histomorphology of the uterus of female rabbits.

Materials and Methods

Study location: The study was conducted at the Animal House of the Department of Veterinary Obstetrics and Reproductive Diseases, Faculty of Veterinary Medicine, University of Nigeria, Nsukka. The location of the study is in the Northern Guinea Savannah Zone of Nigeria, at an elevation of 646 metres above sea level, between latitudes 11˚3 N and 12˚N and between longitudes 7˚42 E and 8˚E. The region receives 1100 mm of rain on average annually, or 816 mm of rain per month, from May to October. During the wet season, the average daily temperature is 25˚C with a mean relative humidity of 72%. November through April is considered the dry season, with average daily temperatures between 18 and 36˚C and relative humidity between 20 and 30°C (Ezeh and Ugwu, 2010).

Turmeric used for the study: The turmeric (Tiger® brand) used for this study was procured from Tiger Foods Limited, Obosi, Anambra, Nigeria. The turmeric powder was reconstituted in distilled water into different concentrations of 250, 500 and 1000 mg/kg as needed.

Experimental animals: Sixteen sexually mature Chinchilla rabbit does, of seven months of age, weighing between 950 to 1000 g, were used for the experiment. They were acclimatized for two weeks prior to commencement of the experiment.

Experimental design: Following acclimatization, the does were assigned to four groups (A – D) of four each. Groups A, B and C does received 250, 500 and 1000 mg/kg body weight of turmeric powder, respectively. For each doe, the powder was weighed out and mixed with 1 ml of distilled water and administered per os daily. Group D (control) received 1 ml of distilled water as a placebo. The treatment lasted for 45 days. Blood sample collection for the assay of the female reproductive hormones was done on days 15 and 45 of treatment, while that for the assay of other reproduction related serum biochemical parameters was done on day 45 only. At the end of the experimental period (Day 45), the does were humanely sacrificed, and their uteri were collected and processed for histological evaluation.

Blood sample collection for the hormonal assay and other biochemical evaluations: Blood samples were collected from the jugular

vein of the does into plain sample bottles and allowed to clot for 45 minutes. The clotted blood was subsequently centrifuged at 3,000 revolutions per minute for 10 minutes. The supernatant was carefully aspirated and used for hormonal and other biochemical assays.

Hormonal assay procedures: The serum levels of follicle stimulating hormone (FSH) were assayed by the quantitative sandwich ELISA technique (Beastall *et al*., 1987). Serum estradiol levels were determined using the competitive enzyme-linked immunosorbent assay (ELISA) technique (Gronowski, 2008).

Other serum biochemical assays: Serum levels of total protein were determined by the direct Biuret method (Johnson, 2008). The serum total cholesterol levels was determined by the enzymatic colorimetric method, while the serum triglyceride levels was determined by glycerol-phosphate oxidase method (Rifai *et al*., 2008). Determination of serum calcium levels was done following the ortho-cresolphthalein direct method (Endres and Rude, 2008). Serum levels of inorganic phosphorus were determined by the Fiske-SubbaRow method (Fiske and SubbaRow, 1925). Serum malondialdehyde was assayed following the modified thiobarbituric acid method (Draper and Hadley, 1990).

Statistical analysis: Data generated from the study were subjected to one-way analysis of variance (ANOVA) and variant means were separated post-hoc using the least significant difference (LSD) test. The statistical analysis was done using the IBM Statistical Package for Social Sciences (SPSS) software, version 16.0 for Windows. Probability values less than 0.05 were considered significant. Summary of the results of the analysis were presented as means ± standard deviation in tables and bar charts.

Results

On both days 15 and 45, the mean FSH levels of rabbits in Groups B and C were significantly higher ($p < 0.05$) than those of rabbits in groups A and D (Figure 1). However, for the serum estradiol levels there were no significant ($p < 0.05$) variations among the groups on days 15 and 45 (Figure 2).

There were no significant ($p > 0.05$) variations among the groups in their serum total cholesterol levels (Table 1), but the serum triglyceride levels of groups B and C rabbit does were significantly higher ($p < 0.05$) than those of groups A and D (Table 1). The serum total protein levels of group B does was significantly ($p < 0.05$) lower than that of group D, while the serum MDA of group B was significantly ($p < 0.05$) lower than those of groups A and C (Table 1). The serum calcium levels of the groups did not significantly ($p > 0.05$) vary, but the serum phosphorus levels of group A was significantly ($p < 0.05$) lower than those of all other groups (Table 1).

Histological examination of the uterus showed no significant histomorphological changes in the uterus of the treated groups when compared with the untreated control (Figure 3). Uterine sections from rabbits in all groups showed normal rabbit uterine histo-architecture, consisting of normal endometrium and myometrium (Figure 3).

Discussion

The evaluation of the hormonal profiles of female animals and humans may help clinicians to understand potential reproductive efficiency or deficiency. Simoni and Nieschlag, (1995) remarked that follicle stimulating hormone (FSH) is essential for gonadal development and maturation at puberty as well as gamete production during the fertile phase of life. In another study (Modupe, 2015), it was reported that FSH stimulated growth and maturation of ovarian follicles by

acting directly on the receptors located on the granulosa cells. Findings in the present study showed significantly higher levels of mean serum FSH concentration in groups B and C does that were given higher (500 and 1000mg/kg) doses of *Curcuma longa* powder, in comparison to other groups. The significantly positive effect on serum FSH concentration of the does after dietary supplementation with higher doses of *Curcuma longa* in this study may possibly be attributed to findings in previous studies by Sak *et al,* (2013) and Kunnumakkara *et al.* (2016) which suggested that curcumin can reduce ovarian cell death and cause ovarian follicle atresia (the breakdown of the ovarian follicles, which consist of an oocyte surrounded by granulosa cells and internal and external theca cells) through its anti-oxidatve properties in both ovarian and non-ovarian tissues. The possible implication of the finding in the present study of significantly higher serum FSH levels in does given 500 and 1000 mg/kg turmeric powder is that there may be a potential increase in viability and fecundity (the number of live-born and weaned pups), as well as in production and growth of ovarian follicles (Sirotkin *et al,* 2018) in groups fed higher doses of *Curcuma longa* compared to group A and control does. This present finding as regards serum FSH levels of does given turmeric powder is contrary to earlier reports by Thakur *et al.* (2009) which showed significantly dose-dependent lower serum FSH concentration in does given oral doses of ethanolic extract of *Curcuma longa.* Meanwhile, the serum FSH level of does in Group A given 250 mg/kg turmeric powder (lower dose) did not significantly differ, compared to the control group, throughout the period of treatment. This result of does given the lower dose may be attributed to inability of lower dose of *Curcuma longa* components to significantly induce enhanced FSH biosynthesis in the does.

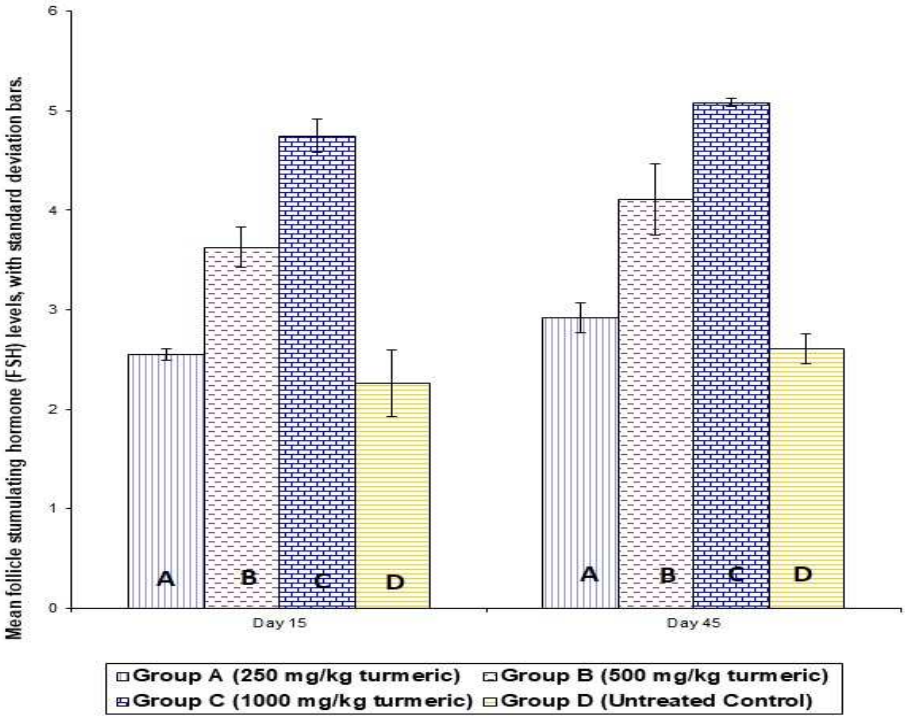

Figure 1. Serum levels of follicle stimulating hormone (FSH) in does given varied doses of *Curcuma longa* (turmeric) powder for 45 days.

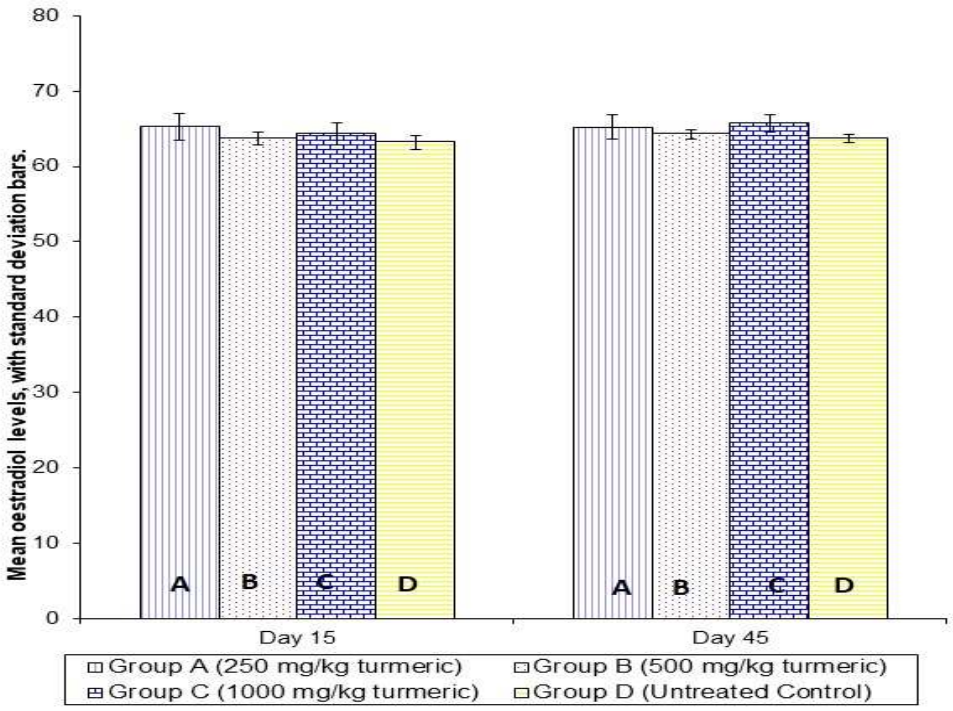

Figure 2. Serum oestradiol levels of female rabbit groups given varied doses of *Curcuma longa* (turmeric) powder for 45 days.

Table 1. Reproduction related serum biochemical parameters of female rabbits given varied doses *Curcuma longa* (turmeric) powder for 45 days.

Parameters	Means of serum biochemical parameter ± standard error			
	Group A (250 mg/kg turmeric)	**Group B (500 mg/kg turmeric)**	**Group C (1000 mg/kg turmeric)**	**Group D (Untreated Control)**
Total Cholesterol (mg/dl)	56.40 ± 0.29^{a}	56.68 ± 0.20^{a}	56.64 ± 0.27^{a}	56.50 ± 0.12^{a}
Triglycerides (mg/dl)	27.81 ± 1.61^{a}	31.74 ± 0.63^{b}	32.16 ± 0.87^{b}	25.28 ± 0.81^{a}
Total Protein (g/dl)	5.60 ± 0.10^{ab}	5.28 ± 0.23^{a}	5.58 ± 0.12^{ab}	6.17 ± 0.39^{b}
MDA (nmol/ml)	5.08 ± 0.15^{b}	3.58 ± 0.51^{a}	4.60 ± 0.16^{b}	4.42 ± 0.60^{ab}
Calcium (mg/dl)	7.34 ± 0.04^{a}	7.41 ± 0.03^{a}	7.38 ± 0.18^{a}	7.47 ± 0.24^{a}
Phosphorus (mg/dl)	6.88 ± 0.70^{b}	8.12 ± 0.71^{a}	8.12 ± 0.41^{a}	8.45 ± 0.70^{a}

$^{a, b, c}$ Means with different alphabetical superscripts in a row indicate significant ($p < 0.05$) difference.

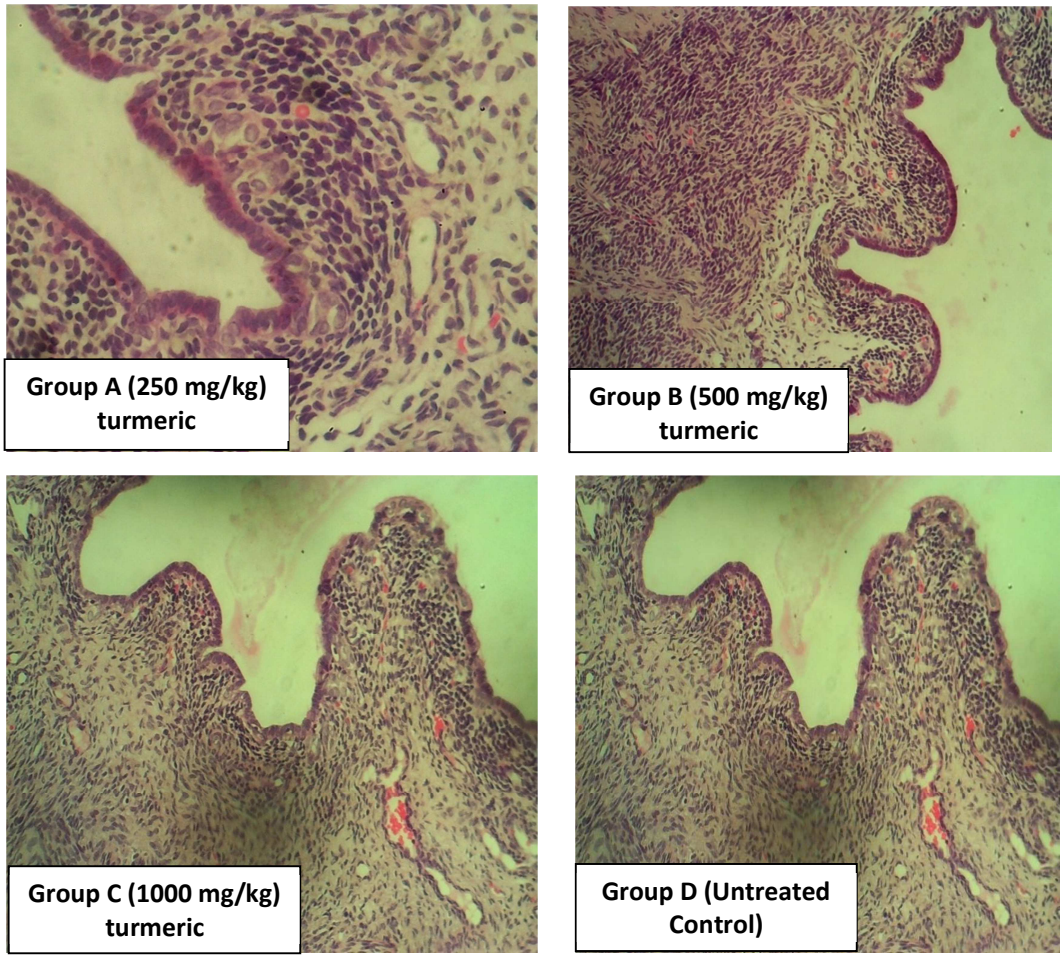

Figure 3. Photomicrograph of the uteri of rabbit does treated with varied doses of turmeric for 45 days, (H & E × 100).

Oestradiol is a steroid hormone, which together with other hormones, is responsible for the control of ovulation cycle, mating behavior and preparation of the reproductive tract for pregnancy in mammals. In synergy with FSH, it is reported that oestradiol stimulates granulosa cell proliferation during follicular development (Levin and Hammes, 2011). Findings in the present study indicated no significant variations among all the groups in their serum oestradiol levels. It could be posited that in the present study, supplementation with *Curcuma longa* in the diets of does exerted no deleterious impact on oestradiol biosynthesis in the treated does.

An understanding of the interplay between reproduction related serum biochemical parameters of females can help in understanding their fertility potentials. Cholesterol and total protein have been reported to be among key nutrients affecting fertility and cyclicity in farm animals (Park *et al.,* 2010). Cholesterol is reported to be essential for building and maintaining key parts of cells (such as cell membranes) and making of several important female reproductive hormones. It had also been reported in a previous study (Arosh *et al.,* 1998) that low levels of plasma protein resulted in deficiency of amino acids required for biosynthesis of gonodatropins and gonadal

hormones, and might cause reproductive hormonal disturbances in animals leading to inactive ovaries. The results of the present study showed no significant difference between the groups in the serum total cholesterol levels. This is in agreement with the findings of Majeed *et al.* (2019) who reported no significant variations in total cholesterol, serum total protein and triglyceride levels in adult female rats after treating them with graded doses of tretrahydrocurcumin in comparison to untreated controls.

Serum triglyceride levels of does in groups given higher doses of *Curcuma longa* powder for 45 days in the present study was significantly higher than that of the control and group A does given 250 mg/kg. This finding is contrary to the results obtained by Majeed *et al.* (2019) who reported no significant variation in serum triglyceride (TG) concentrations in adult female rats after oral administration of graded doses tretrahydrocurcumin in comparison to untreated controls. In some earlier reports, serum total cholesterol and triglyceride levels were reported to positively correlate with obesity (Ahmad *et al.,* 2004; William e*t al.,* 2004). In turn, dysfunction of female gonads has been linked to obesity which results to complications in fertility, including delayed conception, increased rate of miscarriage and reduced outcome in assisted conception treatments (Silvestris *et al.,* 2018).

In this present study, there were no significant effects of the supplementation with turmeric powder on the serum calcium and phosphorus levels of the does. These present findings are in agreement with reports by Majeed *et al.* (2019), which showed no significant variation in serum calcium and phosphorus concentrations in female rats orally given various doses of tetrahydrocurcumin for 90 days compared to untreated control rats. Serum mineral profiles of mammals had been used in some studies to predict reproductive strength. It was opined (Samad *et al.,* 1987) that serum calcium and phosphorus imbalance may result in infertility in mammals. Levels of calcium were found to be significantly higher in normal cyclic buffalos than in non-cyclic and repeated breeders, while supplementation with calcium and phosphorus of deficient dairy cows was reported to improve reproductive performance (Samad *et al.,* 1987).

Biochemical assay of malondialdehyde can be used as a marker of oxidative stress and potential tool in predicting assisted reproductive outcome (Oral *et al.,* 2006). In female mammals, oxidative stress is found to be associated with poor reproductive health status, which can affect ovarian steroidogenesis, oocyte maturation, ovulation as well as luteal maintenance during pregnancy (El-Ratel *et al.,* 2017). Pregnancy rates were found to be decreased in females with high serum malondialdehyde levels (Oral *et al.,* 2006). The result of this study showed a dose-dependent outcome with low MDA levels in the group treated with 500 mg/kg and 1000 mg/kg while the MDA levels in the group treated with 250 mg/kg was high. It is probable that at a higher dose (500 mg/kg and 1000 mg/kg), *C. longa* exhibits significant anti-oxidative effects.

Histological examination of uteri of the rabbit does given varied doses of turmeric powder supplement showed no obvious lesions. The absence of obvious lesions in the does treated with turmeric powder in this study suggests that *Curcuma longa* has no deleterious effect on the morphology of the uterus of the does.

Conclusion: The administration of *Curcuma longa* powder as used in this study, especially at higher doses (500 mg/kg and 1000 mg/kg) led to significantly higher serum levels of FSH and did not lead to any deleterious effects on serum levels of oestradiol and other reproduction related biochemical metabolites and also on the histomorphology of the uterus of the rabbit does.

Conflict of interest

The authors declare no conflict of interest.

References

Aduku AO and Olukosi JO (1990). Rabbit Management in the Tropics: Production, Processing, Utilization, Marketing, Economics, Practical training, Research and Future Prospects, Living Book Services, G.U. Publications, Abuja, Nigeria.

Aggarwal BB and Harikumar KB (2009). Potential therapeutic effects of curcumin, the anti-inflammatory agent, against neurodegenerative, cardiovascular, pulmonary, metabolic, autoimmune and neoplastic diseases. *International Journal of Biochemistry and Cellular Biology,* 41: 40 – 59.

Ahmad I, Lodhi LA, Qureshi ZI and Younnis M (2004). Studies on blood glucose, total proteins, urea and cholesterol levels in cyclic, non-cyclic and endometritic crossbred cows. *Pakistan Veterinary Journal*, 24: 92 – 94.

Akram M, Uddin S, Ahmed A, Usmanghani K, Hannan A, Mohiuddin E and Asif M (2010). *Curcuma longa* and curcumin: a review article. *Romanian Journal of Biology – Plant Biology,* 55: 65–70.

Ammon HPT and Wahl MA (1991). Pharmacology of *Curcuma longa*. *PlantaMedica*, 57: 1 – 7.

Anto RJ, George J, Babu KVD, Rajasekharan KN and Kuttan R (1996). Anti-mutagenic and anti-carcinogenic activity of natural and synthetic curcuminoids. *Mutation Research* 370: 127 – 131.

Arosh A, Kathiresan D, Devanathan TG, Rajasundaram RC and Rajasekaran J (1998). Blood biochemical profile in animal cyclical and anoestrous cows. *Indian Journal of Animal Sciences,* 68: 1154 – 1156.

Beastall GH, Ferguson KM, O'Reilly DS, Seth J and Sheridan B (1987). Assays of follicle stimulating hormone and luteinizing hormone: guidelines for the provision of a clinical biochemistry service. *Annals of Clinical Biochemistry, 24*: 246 – 262.

Beaumont CO, Roussot N, Marissal Avry P, Prunet and Roubertoux P (2002). Génétiqueet adaptation des animaux d'élevage. *INRA Production Animal*, 15(5): 343 – 348.

Chantry-Darmon C, Rogel-Gaillard C, Bertaud M, Urien C, Perrocheau M, Chardon P and Hayes H (2003). 133 new gene localizations on the rabbit cytogenetic map. *Genome Research*, 103: 192 – 201.

Chainani-Wu N (2003). Safety and anti-inflammatory activity of curcumin: a component of turmeric (*Curcuma longa*). *Journal of Alternative and Complementary Medicine,* 9: 161–168.

Draper HH and Hadley M (1990).Malondialdehyde determination as an index of lipid peroxidation. *Methods in Enzymology*, 186: 421 – 431.

El-Ratel IT, Abdel-Khalek AE, El-Harairy MA, Fouda SF and El-Bnawy LY (2017). Impact of green tea extract on reproductive performance, haematology, lipid metabolism and histogenesis of liver and kidney of rabbit does. *Asian Journal of Animal Veterinary Advances*, 12(2): 51 – 60.

El-Sayed ESM (2008). The Uterine relaxant effect of curcumin in rats; An *in vitro* study. *Journal of Basic and Applied Science* 4(1): 45 – 48.

Endres DB and Rude RK (2008). Measurement of calcium. In: Burtis CA, Ashwood ER and Bruns DE (Eds.), Tietz Fundamentals of Clinical Chemistry. 6th ed. Saunders Elsevier, Missouri, pp. 715 – 717.

Ezeh CC and Ugwu GZ (2010). Geoelectrical sounding for estimating groundwater potential in Nsukka LGA Enugu state,

Nigeria. *International Journal of Physiological Sciences*, 5: 415 – 420.

FAO (Food and Agriculture Organization) (1996). For all poor world summits, FAO Rome, pp.64.

FAO (Food and Agricultural Organization) (2006). Food aid's intended and unintended consequences, by C.B. Barrett. ESA Working Paper 06-05. Rome.

Fiske CH and SubbaRow Y (1925). The colorimetric determination of phosphorus. *Journal of Biological Chemistry*, 66: 375 – 400.

Gronowski AM (2008). Measurement of oestrogens in blood. In C Burtis, E Ashwood and D.Bruns, *Tietz Fundamentals of Clinical Chemistry* (6 ed.), Saunders Elsevier, Missouri, p. 793.

Ilbey YO, Ozbek E, Cekmen M, Simsek A, Otunctemur A and Somay A (2009). Protective effect of curcumin in cisplatin induced oxidative injury in rat testis: mitogen-activated protein kinase and nuclear factor-kappa B signaling pathways. *Human Reproduction,* 24: 1717 – 1725.

Itthipanichpong C, Ruangrungsi N, Kemsri W and Sawasdipanich A (2003). Antispasmodic effects of curcuminoids on isolated guinea-pig ileum and rat uterus. *Journal of the Medical Association of Thailand*, 86(2): 299 – 309.

Janieri A (1987). Nutritional quality of rabbit meat. (In Italian). *Rivdi Coniglicoltura,* 24(1): 27.

Johnson AM (2008). Amino acids and proteins. In: Burtis CA, Ashwood ER and Bruns DE (Eds.), Tietz Fundamentals of Clinical Chemistry. 6th ed. Saunders Elsevier, Missouri, pp. 206 – 316.

Jurenka JS (2009). Anti-inflammatory properties of curcumin, a major constituent of *Curcuma longa*: a review of preclinical and clinical research. *Alternative Medicine Review,* 14: 141 – 153.

Khazdair MR, Mohebbati R, Karimi S, Abbasnezhad A andHaghshenas M (2016). The protective effects of *Curcuma longa* extract on oxidative stress markers in the liver induced by Adriamycin in rat. *Physiological Pharmacology* 20, 31 – 37.

Kowluru RA and Kanwar M (2007). Effects of curcumin on retinal oxidative stress and inflammation in diabetes. *Nutritional Metabolism*, 4: 8.

Kunchandy E and Rao MNA (1990). Oxygen radical scavenging activity of curcumin. *International Journal of Pharmcology,* 58: 237 – 240.

Kunnumakkara AB, Bordoloi D, Padmavathi G, MonishaJ, Roy NK, Prasad S and Aggarwal BB. (2016). Curcumin, the golden nutraceutical: multi targeting for multiple chronic diseases. *British Journal of Pharmacology,* 174: 1325 – 1348.

Leung AY and Foster S (1996). Encyclopedia of common natural ingredients used in food and cosmetics. 2nd ed., Merk and Sons Inc., New York, USA, pp. 499 – 501.

Levin ER and Hammes SR (2011).*Estrogens and Progestins.* 12th edition, McGraw Hill, New York, USA, pp. 1163 – 1194.

Liduan Z, Qiangsong T and Cuihuan W (2004). Growth-inhibitory effects of curcumin on ovary cancer cells and its mechanisms. *Journal of Huazhong University of Science and Technology,* 24(1): 558.

Majeed M, Natarajan S, Pandey A, Sarang B and Mundkur L (2019). Subchronic and reproductive/developmental toxicity studies of tetrahydrocurcumin in rats, *Toxicological Research*, 35: 65 – 74.

Modupe EM (2015). Effects of oral administration of a decoction on serum levels of luteinizing hormone, follicle stimulating hormone, progesterone and estradiol in female Dutch-white rabbits. *Research Journal of Medicinal Plants,* 9(3); 141 – 145.

Oral O, Kutlu T, Aksoy E, Ficicioglu C, Uslu H and Tugrul S (2006). The effects of oxidative stress on outcomes of assisted reproductive techniques. *Journal of Assisted Reproduction and Genetics,* 23(2): 81 – 85.

Park MS, Yang YX, Shinde PL, Choi JY, Jo JK, Kim JS, Lohakare JD, Yang BK, Lee JK, Kwon IK. and Chae BJ (2010). Effect of dietary glucose inclusion on reproductive performance, milk compositions and blood profiles in lactating sows. *Journal of Animal Physiology and Animal Nutrition*, 94: 677 – 684.

Petrescu DC, Oroian IG, Mihaiescu T, Paulette L, Varban D and Patrutoiu TC (2013). Rabbit statistics overview: production, trade, market evolution. *Rabbit Genetics*, 3(1):15 – 22.

Rifai N, Warnick GR and Remaley AT (2008) Analysis of lipids, lipoproteins and apolipoproteins. In: Burtis CA, Ashwood ER and Bruns DE (Eds.), Tietz Fundamentals of Clinical Chemistry. 6th ed. Saunders Elsevier, Missouri, pp. 422 – 427.

Sak ME, Soydinc HE, Sak S, Evsen MS, Alabalik U, Akdemir F and Gul T (2013). The protective effect of curcumin on ischemia reperfusion injury in rat ovary. *International Journal of Surgery*, 11, 967–970.

Samad HA, Ali CS, Rehman A and Ahmad N (1987). Clinical incidence of reproductive disorders in buffalo. *Pakistan Veterinary Journal*, 7(1): 16 – 19.

Sharma P and Singh R (2010). Protective role of curcumin on lindane induced reproductive toxicity in male Wistar rats. *Bulletin of Environmental and Contamination Toxicology,* 84: 378–384.

Shukla PK, Khann VK, Khan MY and Srimal RC (2003). Protective effect of curcumin against lead neurotoxicity in rat. *Human Experimental Toxicology,* 22: 653–658.

Silvestris E, De Pergola G and Loverro G (2018). Obesity and disruptor of the female fertility. *Reproductive Biology and Endocrinology*, 16: 22.

Simoni M and Nieschlag E (1995). FSH in therapy: physiological basis, new preparations and clinical use. *Reproductive Medicine Review*, 4; 163 – 177.

Singh NK and Singh DP (2001). Ethnobotanical survey of Balrampur. *Flora-Fauna*, 7(2): 59 – 66.

Sirotkin AV, Kadasi A,Stochmalova A, Balazi A, Földesiová M, Makovicky P, Makovicky P, Chrenek P and Harrath AH (2018). Effect of turmeric on the viability, ovarian folliculogenesis, fecundity, ovarian hormones and response to luteinizing hormone of rabbits. *The Animal Consortium*, 12(6): 1242 – 1249.

Thakur S, Bawara B, Dubey A, Nandini D, Chauhan N and Saraf D (2009). Effect of *Carum carvi* and *Curcuma longa* on hormonal and reproductive parameter of female rats, *International Journal of Phytomedicine*, 1: 31 – 38.

William AB, Alan BC, Robinson SM, Moinudinn A, Shultz JM, Nakaoke R and Morley JE (2004). Triglycerides induce leptin resistance at the blood-brain barriers. *Diabetes*, 53(5): 1253 – 1260.