



## Stress Oxidative and Effect of Herbal Antioxidant in Animal Reproduction: Future and Perspective

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### Abstract

*This investigation examines empirical knowledge about the effect of stress oxidative and the advantageous and harmful role of produced antioxidants on animal reproduction in both sexes. An antioxidant treatment is impressive in barricade stress oxidative. Although many improvements have been made regarding use of antioxidants to reduce oxidative stress, there are still debatable issues. Since many studies on the use of plant extracts containing antioxidants showed inappropriate results in a variety of identical animal species, the plant-produced antioxidants may have beneficial or harmful effects on reproduction of animals, including spermatogenesis sperm and ovary tumors, ovulation cycles, fetal growth, and pregnancy. Accordingly, achieving accurate results requires more studies.*

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### Introduction

Free radicals include reactive oxygen species (ROS), reactive nitrogen species (RNS) and proxy sodium [1]. The

three types of ROS are superoxide (O<sub>2</sub>), hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) and hydroxyl (OH), Although nitric oxide (NO) is an

important part of the nitrogen species. In the reproductive system, the physiological concentration of free radicals is vital. Free radicals can contribute to ROS such as damage to sperm or ovarian, endometriosis degeneration, preeclampsia, intrauterine abortion, growth retardation and infertility under normal physiological conditions [2]. To remove excess free radicals, organisms have a wide range of enzymatic condition antioxidants such as superoxide dismutase (SOD), catalase, and glutathione peroxidase (GPx) and non-enzymatic antioxidants including glutathione, uric acid, and coenzyme Q [3]. However, pathophysiological state, endogenous antioxidants may not be sufficient and do not counteract [4]. Excess free radicals are, therefore, always present [5]. With this, the demand for antioxidants outside the body increases. A study has reported that external antioxidants are also bilateral [6]. Antioxidants are generally safe in normal and physiological amounts, while being harmful above normal levels [7]. Many natural plants, their seeds, leaves or roots have antioxidants. Extracts rich in polyphenols, flavonoids, carotenes, gallic acid, tannins and essential oils are known to be suitable antioxidants [8]. In this study, these aspects, the bilateral effects, and possible mechanisms of plant antioxidants in animal reproduction were investigated.

### Oxygen oxidative stress in reproduction of male animals

Normal surface of ROS have a necessary role in cellular responses [9]. In the male reproductive system, moderate concentrations of ROS cause sperm motility through ATP production [10], it is while increased ROS levels cause lipid peroxidation and death of spermatozoa [11,12]. The high rate of cell division combined with the high rate of mitochondrial oxygen consumption causes the production of free radicals [13]. Hence, free radical imbalance causes oxidative stress and damage to it [14]. Free radicals and damage to fats, proteins, aminoacids and sugars in sperm and testis lead to penurious semen quality [15]. Decreased semen quality leads to failure of more than 80% of fertility and abortion, and infertility in domestic animals [16].

In addition to normal conditions and in the process of spermatogenesis, ROSs are also produced in vitro [17]. In livestock sperm freezing methods, sperm are reveal to freezing stress and oxygen, This increases the chance of damaging the cells [18]. In addition to peroxidation, many other factors, such as extreme temperatures, chemicals agent, drugs, and other toxins, cause the production of ROS in the reproductive system [19-22]. After many studies, it was found that increased activity of ROS decreases catalase activity and increases cyclophosphamide in rats [23-24]. Harmful effects of heat on the reproductive system of rats, bulls and chickens have also been confirmed [25].

### Oxygen oxidative stress in the reproduction of female animals

Free radicals are produced in different ways in matter [26]. In the reproductive system in culture medium, ROS may be produced directly from ovum, embryos, or the environment [27]. In addition to ROS production, RNS is also involved in embryo transfer processes [28]. Free radicals play a dual role in reproduction [29-30]; for example, higher environment temperatures and different toxins are components causing oxidative stress. Ovum or embryo responses to heat shock include changes in membrane properties, chromatin deformation, and defects in the embryonic stages. A close communication between blood lead concentration and uterine damage had been reportage and shown that in pathogenesis, lead and cadmium cause oxidative stress and defects in animal reproduction [31-35].

Free radicals in the reproductive system of animals cause preeclampsia, molar hydratidiform, birth defects, infertility and abortion. Studies have shown that domestic animals such as those exposed to H<sub>2</sub>O<sub>2</sub> and the destructive factors of oxidative stress show reduced ovulation maturity [36-37].

### Animal reproduction and external antioxidants

The presence of external antioxidants in the body can have a great impact on the balance between oxidation agent and antioxidants [38]. Antioxidant activity strongly depends on its concentration. In most cases, the physiological dose of

antioxidants plays a beneficial role; however, their excessive consumption shows harmful effects [39] (Table 1).

Although natural antioxidants that presence in food, such as vitamin C and E, are conserved the ovarian, they may harm the developing fetus [40]. Consumption of antioxidant vitamins such as vitamin E, however, significantly improves bovine blastocyst formation [41].

Recent studies have proven the pattern herbals as an antioxidant in animals, and the results of many studies have led to the use of these types of antioxidants in the treatment of infertility [42]. The most effective plant antioxidants are phenolic compounds such as flavonoids, hydrolyzed tannins, phenolics and tropensine pepper [43].

**Table 1.** The role of antioxidant on oxidative stress in different study

Authors	Method	Result
Uppangala et al.2020	Reduced ovarian response to controlled ovarian stimulation is associated with increased oxidative stress in the follicular environment	Patients with low Serum estradiol had elevated oxidative stress in their follicular environment and poor quality embryos implicating the risk of oxidative stress in patients with poor ovarian response.
Eva Tvrdá et al.2016	This study was performed to investigate the effect of curcumin and changes caused by reactive oxygen species (ROS) on sperm motility.	The CUR treatment led to a preservation of spermatozoa motion, mitochondrial activity and antioxidant characteristics with effective for sustaining spermatozoa viability.
Parisa Darabi et al.2019	This study investigated the effect of flavonoid apigenin on the levels of antioxidant and anti-inflammatory factors in ovarian tissue of PCOS rats.	The total antioxidant capacity and superoxide dismutase activity significantly increased in treated groups compared to the PCOS control group.
Hayashi et al.2020	Novel ovarian endometriosis model causes infertility via iron-mediated oxidative stress in mice	Iron accumulation was significantly increased in the ovarian endometriosis group
Zhu et al.2019	Negative effects of ROS generated during linear sperm motility on gene expression and ATP generation in boar sperm mitochondria	sperm linear motility, ATP levels and mitochondrial activity were decreased with increasing ROS levels in sperm during 6 h of incubation with the low-glucose medium
Fang et al.2014	Inhibition of ROS production through mitochondria-targeted antioxidant and mitochondrial uncoupling increases post-thaw sperm viability in yellow catfish	Their findings indicate that ROS inhibition through mitochondrial-targeted antioxidant or mild mitochondrial uncoupling is beneficial for sperm cryopreservation in yellow catfish.
Ferramosca et al.2013	Oxidative stress negatively affects human sperm mitochondrial respiration	Oxidative stress has a negative correlation with DNA fragmentation and progressive motility of spermatozoa

## Antioxidants derived from natural plants in the reproduction of male animals

Many factors, including spermatogenesis, sperm function, sperm quality, and fertility, must be considered to assess the reproductive status of male animals.

Spermatogenesis depends on hormonal regulatory processes inside and outside the testicle. Sperm parameters including sperm count, viability, motility and morphology are important factors in sperm evaluation. Semen function of an infertile person is a major public health problem. It has also involved animals due to feeding system [44-45].

Oxidative stress inhibits sperm production and reduces sperm quality, while it can even lead to infertility. A relative increase in ROS causes damage to spermatozoon DNA and cell apoptosis, thus leading to low fertility rates [46]. Proper use of the environment and nutrition derived from plant antioxidants for enhance the reproductive circumstances of the animals. A number of plant flavonoids contain antioxidants, androgenic and anti-infertility activities [47]. These compounds are widely used for animal reproductive diseases [48]. Furthermore herbal vegetable, extracts of antioxidant fruits with vegetables show beneficial effects on the animal reproductive system. Some plants, though containing antioxidants, also have harmful effects; therefore, they cause defects and failures in the fertility of male animals. This is related to the dose of these antioxidant compounds [49-50].

Furthermore in vitro sperms freezing are a necessary method that has special benefits for the livestock industry. Sperm cryopreservation is performed regularly for artificial insemination in the calf breeding industry [51]. High production of ROS in these methods creates oxidative stress, which in turn reduces the quality of reproductive cells. This is main barrier to prosperous sperm freezing. Studies have shown that the fertility rate and value of ovum fecundate together freeze and then thawed sperm are approximately 20% lower than fresh and normal sperm [52-53].

The aqueous extract of a Chinese plant called scara, used as an antioxidant, improved the biochemical parameters of bovine sperm in the freezing process [54]. Rosemary is a perennial plant that with its antioxidant properties and bioactive substances plays an important role in improving sperm quality. Ingredients in this plant include triterpenes, flavonoids and polyphenols [55].

## Antioxidants derived from natural plants in the reproduction of female animals

To assess the reproductive condition of female reproductive of animals, several agent are propounded including ovarian and ovulatory function cycle, embryonic growth, pregnancy and fetal growth [56]. Histological, physiological, morphological and biochemical changes occur in these cycles in the ovary. Interactions between oxidants and antioxidants lead to ovarian and cyclic dysfunction. Various physiological conditions such as hormonal changes and immune system responses are involved in controlling ovarian function [57-58]. Mammalian ova are formed inside the ovarian follicles, so the health status of the ovaries affects the nutrient levels in the ova. Intra-follicular conditions may also affect ovum maturity, fertility, and fetal growth. One of the topics discussed in animal infertility is endometritis, which is a common disease in cattle. Unfortunately, endometritis is always overlooked in animals. It can cause ovum dysfunction and infertility. As a result, disorders of the ovaries and uterus lead to pregnancy failure and fetal growth. The use of plant antioxidants in the treatment of endometritis has been very effective [59]. Oxidative stress is a main reason of irregular cycles, polycystic ovary syndrome and endometritis, infertility, pregnancy failure and fetal growth. As a result, increasing the level of antioxidants in the reproductive system can improve the ability of ovum growth, pregnancy and fetal growth [60].

In addition, significant livestock losses occur each year as a result of poisonous plants containing antioxidant compounds that cause fetal death, miscarriage, and fetal malformations. High doses of plant toxins pass easily through the placenta and can affect the developing fetus if taken at a specific time of pregnancy (61).

## Dual action of plant antioxidants

Four reasons can explain the effects of antioxidants on animal reproduction:: 1) its dose-dependent method [62]; 2) its combination with other substances [63]; 3) similar antioxidant substances that have low drug action and have been tested against plant and animal species [64]; 4) the different chemical structure of antioxidants [65].

## Future trends

A equivalence among oxidation and antioxidants is essential for the protection and stability of the reproductive system in animals. Many studies have been done on the use of antioxidant effects, but the results still need further investigation. Most importantly, the information obtained, including cellular and molecular mechanisms, has not yet been fully displayed. In the following, we can say that two very important cases can be considered. One of these discussions is the use of appropriate doses of plant extracts in the treatment discussion. For research experiments, identification of biologically active and optimal species and the effective Herbal extracts according to their dosage and harmful compounds of the extract are required. Therefore, the derivation method distinctive and standardized can be recognizing.

Another issue related to this issue is that information about the effects of antioxidants on the reproductive system of cattle, sheep and goats is very limited and most studies have been reported in mice, rats and humans. Also, the experiments did not report any details of the results and therefore many accurate results were not fully proven. However, one of the main reasons is that plant extracts are very expensive and scarce and are not cost-effective for in vivo experiments in domestic animals.

## Conclusion

This study investigated the importance of oxidative stress and the role of antioxidants in the reproductive system of male and female. Reactive oxygen species is dually involved in animal reproduction. Antioxidant therapies, including vitamins E, C, and glutathione, have been evidence in multitude animal researches; however, many studies have been conducted on the side effects of synthetic antioxidants in the reproduction of animals, plants and their extracts. This is why the present study attempted to provide evidence of oxidative stress in the entire reproductive period of male and female animals, such as spermatogenesis, sperm efficiency, sperm storage, estrous cycle, ovarian tumor, ovulation, endometrium, embryonic development and pregnancy. Based on limited known results, arbitrary parallel results could not be applied tested for a variety of animals. In addition, the extracts obtained are usually not from the plant

itself, and most of the information is from the seeds, leaves and roots of the plants, which in turn does not provide accurate information to researchers. This is while these results are obtained using different experiments in vivo and in vitro in different plant and animal species. Accordingly, the exact results and the exact mechanism of plant-produced antioxidants in animal reproduction system could be obtained by this method.

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## Authors' contributions

All authors contributed equally.

## Conflict of interest

All authors claim that there is no competing interest.

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## Ethics statement

Not applicable.

## Data availability

Not applicable.

## Abbreviations:

ROS: Reactive Oxygen Species, RNS: Reactive Nitrogen Species, SOD: Superoxide Dismutase, GPx: Glutathione Peroxidase and NO: Nitric Oxide

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