



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

Maziar Malekzadeh Kebria^{1,2}, Iman Zangiabadi³, Taha Ghantabpour⁴, Mahdi heydari^{4*}

¹Cellular and Molecular Research Centre, Iran University of Medical Sciences, Tehran, Iran

²Department of Tissue Engineering and Regenerative Medicine, Faculty of Advanced Technologies in Medicine, Iran University of Medical Sciences, Tehran, Iran

³Department of Anatomical Sciences School of Medicine kerman University of Medical Sciences, Kerman, Iran

⁴Department of Anatomical Sciences, School of Medicine, Iran University of Medical Sciences, Tehran, Iran

Article Info

*Correspondence to:

Mahdi heydari
mahdiheydari438@yahoo.com

Article History:

Received: 18 March 2022

Accepted: 22 April 2022

ePublished: 18 April 2022

Keywords: Reactive Oxygen Species, Herbal, Antioxidant, Reproductive

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.

How to cite this paper

Malekzadeh Kebria M, Zangiabadi I, Ghantabpour T, Heydari M. Stress Oxidative and Effect of Herbal Antioxidant in Animal

Reproduction: Future and Perspective. *Plant Biotechnol Persa* 2021; 3(2): 82-89.

Introduction

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

three types of ROS are superoxide (O₂), hydrogen peroxide (H₂O₂) 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 H2O2 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.

Acknowledgments

Special thanks to Cellular and Molecular research centre, Iran University of medical Science, Tehran, Iran.

Authors' contributions

All authors contributed equally.

Conflict of interest

All authors claim that there is no competing interest.

Funding

There was no founding.

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

References

1. Heikinheimo O, Gibbons WE. The molecular mechanisms of oocyte maturation and early embryonic development are unveiling new insights into reproductive medicine. *Mol Hum Reprod* 1998;4(8):745-56

2. Bevers M, Izadyar F. Role of growth hormone and growth hormone receptor in oocyte maturation. *Mol Cell Endocrinol* 2002; 197(1):173-8.
3. Andersen CY, Byskov AG. Progesterone and 17 α -OH-progesterone in concentrations similar to that of preovulatory follicular fluid is without effect on resumption of meiosis in mouse cumulus enclosed oocytes cultured in the presence of hypoxanthine. *Steroids* 2002; 67(12):941-5.
4. Xia P, Tekpetey FR, Armstrong DT. Effect of IGFI on pig oocyte maturation, fertilization, and early embryonic development in vitro, and on granulosa and cumulus cell biosynthetic activity. *Mol Reprod Develop* 1994; 38(4):373-9.
5. Tsafiriri A, Cao X, Ashkenazi H, Motola S, Popliker M, Pomerantz S. Resumption of oocyte meiosis in mammals: on models, meiosis activating sterols, steroids and EGF-like factors. *Mol Cell Endocrinol* 2005; 234(1):37-45.
6. Khazaei M, Aghaz F. Reactive oxygen species generation and use of antioxidants during In vitro Maturation of oocytes. *Int J Fertil Steril* 2017;112: 33-35
7. Zavareh S, Talebi A, Hasanzadeh H. Amending in vitro culture condition to overcome oxidative stress in assisted reproduction techniques (ART). *J Paramed Sci* 2015; 3: 6-2
8. Hussein MR. Apoptosis in the ovary: molecular mechanisms. *Hum Reprod* 2005; 11(2):162-78.
9. Abedelahi A, Salehnia M, Allameh A, Davoodi D. Sodium selenite improves the in vitro follicular development by reducing the reactive oxygen species level and increasing the total antioxidant capacity and glutathione peroxide activity. *Hum Reprod* 2010; 25(4):977-85.
10. Baker T. A quantitative and cytological study of germ cells in human ovaries. *J Biol Med Sci* 1963; 158-972.
11. Chian R-C, Nargund G, Huang JY. Development of in vitro maturation for human oocytes. *Springer* 2017.123.146-154
12. Ginther O, Bergfelt D, Kulick L, Kot K. Selection of the dominant follicle in cattle: role of estradiol. *Reprod Biol* 2000; 63(2).
13. Bomsel-Helmreich O, Gougeon A, Thebault A, Saltarelli D, Milgrom E, Frydman R. Healthy and atretic human follicles in the preovulatory phase: differences in evolution of follicular morphology and steroid content of follicular fluid. *Int J Clin Endocrinol Metab.* 1979.77(4).
14. Freeman B. The active migration of germ cells in the embryos of mice and men is a myth. *Anim Reprod* 2003; 125(5): 635-43.
15. Morriss-Kay G. Langman's Medical Embryology. *J Anat* 1991; 175:273.
16. Gougeon A. Regulation of ovarian follicular development in primates: facts and hypotheses. *Endocrine Rev* 1996; 17(2):121-55.
17. La Marca A, Broekmans F, Volpe A, Fauser B, Macklon N. Anti-müllerian hormone (AMH), what do we still need to know? *Hum Reprod* 2009; 24(9):2264-75.
18. Gougeon A. Ovarian follicular growth in humans. ovarian ageing and population of growing follicles. *Maturitas* 1998; 30(2):137-42.
19. Knight PG, Glister C. TGF- β superfamily members and ovarian follicle development. *Hum Reprod* 2006; 132(2):191-206.
20. Oktem O, Urman B. Understanding follicle growth in vivo. *Hum Reprod* 2010; 25(12):2944-54.
21. Gougeon A. Dynamics of follicular growth in the human: a model from preliminary results. *Hum Reprod* 1986; 1(2):81-7.
22. Kimura S, Matsumoto T, Matsuyama R, Shiina H, Sato T, Takeyama K-i. Androgen receptor function in folliculogenesis and its clinical implication in premature ovarian failure. *Trends Endocrinol Metab* 2007; 18(2).
23. Fauser BC, van Heusden AM. Manipulation of human ovarian function: physiological concepts and clinical consequences. *Endocrine Rev* 1997; 18(1):71-106.
24. Hsueh AJ, Adashi E, Jones PB, Welsh Jr TH. Hormonal regulation of the differentiation of

- cultured ovarian granulosa cells. *Endocrine Rev* 1984; 5(1):76-127.
25. Baird D, Bäckström T, McNeilly A, Smith S, Wathen C. Effect of enucleation of the corpus luteum at different stages of the luteal phase of the human menstrual cycle on subsequent follicular development. *J Reprod Fertil* 1984; 70(2):615-24.
 26. Peng X-R, Hsueh AJ, Lapolt PS, Bjersing L, Ny T. Localization of luteinizing hormone receptor messenger ribonucleic acid expression in ovarian cell types during follicle development and ovulation. *Endocrinol* 1991; 129(6):3200-7.
 27. Gordo AC, He CL, Smith S, Fissore RA. Mitogen activated protein kinase plays a significant role in metaphase II arrest, spindle morphology, and maintenance of maturation promoting factor activity in bovine oocytes. *Mol Reprod Develop* 2001;59(1):106-14.
 28. Trounson A, Anderiesz C, Jones G. Maturation of human oocytes in vitro and their developmental competence. *Hum Reprod* 2001; 121(1):51-75.
 29. Lincoln AJ, Wickramasinghe D, Stein P, Schultz RM, Palko ME, Maria P. Cdc25b phosphatase is required for resumption of meiosis during oocyte maturation. *Nat Genet* 2002; 30(4):446-9.
 30. Fissore RA, He CL, Vande Woude GF. Potential role of mitogen-activated protein kinase during meiosis resumption in bovine oocytes. *Biol Reprod* 1996; 55(6):1261-70.
 31. Dedieu T, Gall L, Crozet N, Sevellec C, Ruffini S. Mitogen activated protein kinase activity during goat oocyte maturation and the acquisition of meiotic competence. *Mol Reprod Develop* 1996; 45(3):351-8.
 32. Gavin A-C, Cavadore J-C, Schorderet-Slatkine S. Histone H1 kinase activity, germinal vesicle breakdown and M phase entry in mouse oocytes. *J Cell Sci* 1994;234:98.
 33. Colledge W, Carlton M, Udy G, Evans M. Disruption of c-mos causes parthenogenetic development of unfertilized mouse eggs. *Nature* 1994;370(6484):65
 34. Richards JS, Ireland JJ, Rao MC, Bernath GA, midgley JR AR, Reichert LE. Ovarian follicular development in the rat: hormone receptor regulation by estradiol, follicle stimulating hormone and luteinizing hormone. *Endocrinol* 1976; 99(6):1562-70.
 35. Conti M, Andersen CB, Richard FJ, Shitsukawa K, Tsafiriri A. Role of cyclic nucleotide phosphodiesterases in resumption of meiosis. *Mol Cell Endocrinol* 1998; 145(1):9-14.
 36. Van den Hurk R, Zhao J. Formation of mammalian oocytes and their growth, differentiation and maturation within ovarian follicles. *Theriogenol* 2005; 63(6):1717-51.
 37. Carabatsos MJ, Sellitto C, Goodenough DA, Albertini DF. Oocyte-granulosa cell heterologous gap junctions are required for the coordination of nuclear and cytoplasmic meiotic competence. *Develop Biol* 2000; 226(2):167-79.
 38. Homa ST. Calcium and meiotic maturation of the mammalian oocyte. *Mol Reproduction Develop* 1995; 40(1):122-34.
 39. Conti M, Andersen CB, Richard F, Mehats C, Chun S-Y, Horner K, et al. Role of cyclic nucleotide signaling in oocyte maturation. *Mol Cellular Endocrinol* 2002; 187(1):153-9.
 40. Meyer T, Hanson PI, Stryer L, Schulman H. Calmodulin trapping by calcium-calmodulin-dependent protein kinase. *J Med Sci* 1992;256(5060):1199-202.
 41. Szollosi D, Calarco P, Donahue R. Absence of centrioles in the first and second meiotic spindles of mouse oocytes. *J Cell Sci* 1972; 11(2):521-41.
 42. Wassarman PM, Josefowicz WJ. Oocyte development in the mouse: an ultrastructural comparison of oocytes isolated at various stages of growth and meiotic competence. *J Morphol* 1978; 156(2):209-35.
 43. Mehlmann LM, Terasaki M, Jaffe LA, Kline D. Reorganization of the endoplasmic reticulum during meiotic maturation of the mouse oocyte. *Developmental biology*. 1995;170(2):607-15
 44. Gosden R, Krapez J, Briggs D. Growth and development of the mammalian oocyte. *Bioessays* 1997; 19(10):875-82.

45. Coticchio G, Dal Canto M, Fadini R, Mignini Renzini M, Guglielmo MC, Miglietta S. Ultrastructure of human oocytes after in vitro maturation. *Mol Hum Reprod* 2015; 22(2):110-8.
46. Reyes M. Mitochondrial distribution and meiotic progression in canine oocytes during in vivo and in vitro maturation. *J Theriogenol* 2011; 75(2):346-53.
47. Pincus G, Enzmann E. The comparative behavior of mammalian eggs in vivo and in vitro. The activation of tubal eggs of the rabbit. *J Ecol Genet and Physiol* 1936; 73(2): 1.
48. Edwards R. Maturation in vitro of mouse, sheep, cow, pig, rhesus monkey and human ovarian oocytes. *Nature* 1965; 208(5008):349-51.
49. Miyara F, Migne C, Dumont Hassan M, Meur AL, Cohen Bacrie P, Aubriot F. Chromatin configuration and transcriptional control in human and mouse oocytes. *Mol Reprod Develop* 2003; 64(4):458-70.
50. Chian R-C, Nargund G, Huang JY. Development of In vitro maturation for human oocytes: Natural and Mild Approaches to Clinical Infertility Treatment: Springer 2017.33.1.
51. Mizuno S, Fukuda A. In vitro maturation of oocytes for IVF. *Principles of IVF. Lab Practice: Optimizing Performance and Outcomes* 2017:125.
52. Cha KY, Koo JJ, Ko JJ, Choi DH, Han SY, Yoon TK. Pregnancy after in vitro fertilization of human follicular oocytes collected from nonstimulated cycles, their culture in vitro and their transfer in a donor oocyte program. *Fertil and Steril* 1991; 55(1):109-13.
53. Braw-Tal R, Yossefi S. Studies in vivo and in vitro on the initiation of follicle growth in the bovine ovary. *J Reprod and Fertil* 1997; 109(1):165-71.
54. Dröge W. Free radicals in the physiological control of cell function. *Physiol Rev* 2002; 82(1):47-95.
55. Sorg O. Oxidative stress: a theoretical model or a biological reality *Comptes rendus biologies.Mol Hum Reprod* 2004; 327(7):649-62.
56. Valko M, Leibfritz D, Moncol J, Cronin MT, Mazur M, Telser J. Free radicals and antioxidants in normal physiological functions and human disease. *Int J Biochem Cell Biol* 2007; 39(1):44-84.
57. Kohen R, Nyska A. Invited review: Oxidation of biological systems: oxidative stress phenomena, antioxidants, redox reactions, and methods for their quantification. *Toxicol Pathol.* 2002.
58. Murphy MP. How mitochondria produce reactive oxygen species. *J Biochem* 2009; 417(1):1-13.
59. Schrader M, Fahimi HD. Mammalian peroxisomes and reactive oxygen species. *Histochem Cell Biol* 2004; 122(4):383-93.
60. Santos CX, Tanaka LY, Wosniak Jr J, Laurindo FR. Mechanisms and implications of reactive oxygen species generation during the unfolded protein response: roles of endoplasmic reticulum oxidoreductases, mitochondrial electron transport, and NADPH oxidase. *Antioxid Redox Signal* 2009; 11(10):2409-27.
61. Roberts RA, Smith RA, Safe S, Szabo C, Tjalkens RB, Robertson FM. Toxicological and pathophysiological roles of reactive oxygen and nitrogen species. *J Toxicol* 2010; 276(2):85-94.
62. Yin H, Xu L, Porter NA. Free radical lipid peroxidation: mechanisms and analysis. *Chemical Rev* 2011; 111(10):5944-72.
63. Stadtman ER. Protein oxidation and aging. *Free Radic Res* 2006; 40(12):1250-8.
64. Miki H, Funato Y. Regulation of intracellular signalling through cysteine oxidation by reactive oxygen species. *Biochem Mol Biol J* 2012; 151(3):255-61.
65. Dizdaroglu M, Jaruga P. Mechanisms of free radical-induced damage to DNA. *Free Radic Res* 2012; 46(4):382-419.
66. Kebria MM, Salehnia M, Zavareh S, Moazzeni SS. The effect of sodium selenite on apoptotic gene expression and development of in vitro cultured mouse oocytes in comparison with in vivo obtained oocytes. In *Veterinary Research Forum* 2020 (Vol. 11, No. 4, p. 377). Faculty of Veterinary Medicine, Urmia University, Urmia, Iran.