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The melatonin as follicle antioxidant

Hira Sajjad[1], Iqra Bano[2], Imran Samo[3], Muhammad Ali Chandio[4], Miqdad Ali Talpur[5] and Saba Samo[6]*

[1]Key Laboratory of Agricultural Animal Genetics, Breeding, and Reproduction, Education Ministry of China, Huazhong Agricultural University, Wuhan, Hubei 430070, People's Republic of China.
[2]Faculty of Bio- Sciences, Shaheed Benazir Bhutto University of Veterinary & Animal Sciences Sakrand, Pakistan,
[3,4,5,6] Faculty of Animal Husbandry and Veterinary Sciences, Department of Poultry Husbandry. Sindh Agriculture University Tandojam Sindh, Pakistan

Abstract: The Melatonin is a hormone released during darkness via Conarium gland, it controls a variety of significant activities connected to diurnal rhythms beside reproduction. Some researchers have suggested that this hormone maintain the function of ovaries by the maintenance of release of gonadotropin hormone from the hypophysis through its detailed receptors. The detection of melatonin as a hunter of reactive oxygen species has significantly increased need of getting proper knowledge about its mechanisms of action to regulate the reproductive physiology. Sophisticated ratios of melatonin are detected in mammalian follicular liquid linked to the serum, beside this there is rising indication of the possessions of this hormone on ovarian job particularly oocyte ripening and embryo progress. Countless experts have focused on the actions of melatonin upon growing oocyte, embryo development and as antioxidant agent to diminish the oxidative stress persuaded by reactive oxygen species. The existing review we summarize current implications and new discoveries connected to the described helpful belongings of melatonin on reproductive system and its role to defend against oxidative stress, particularly inside ovaries, during the process of oocyte development and embryogenesis.

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***Author for correspondence:** iqrashafi05@yahoo.com

INTRODUCTION

The free radicals also named as reactive oxygen species (ROS) are continuously produced within cells either due to the oxidative reactions or due to various other peripheral factors. Although physiological ratios of oxygen are essential for cells to survive, generally the ROS including the hydroxyl radical (·OH) and superoxide radical (O_2-) as well as the hydrogen peroxide (H_2O_2) are produced from oxygen molecules. Usually within the cells, the ROS can normalize function of cell by supervising the manufacture and initiation of materials that possess living events and by triggering main cell-signalling paths[1]. However, excess synthesis of ROS interrelates through some biomolecules like protein, lipids besides some nucleic acids ensuing in damage of physical structures specially outer covering of cells. Beside this it also affects the integrity of cell and some functional variations in amino acids, along with impairment of nucleic acid forms. Hence rise in the construction of ROS have negative belongings on cell job and donates meaningfully to numerous illnesses, counting those that negotiate the process of reproduction and fecundity[2]. The ovary is consisting of various follicles inside it, within these follicles ROS are synthesised predominantly during the mechanism of oogenesis. According to some previous studies the normal ratios of ROS are very essential for release of ovum from the follicles. Though, an extreme quantity of ROS leads to a condition known as oxidative stress (OS) beside this it may also hurt the developing oocyte. The Amassing figures have revealed that excess concentration of ROS boost up the aging of oocyte and decline its quality. Conversely, antioxidant protective schemes are naturally existing within ovaries including various antioxidants like the superoxide dismutase (SOD) and glutathione (GSH) enzymes respectively. Hence in order to protect growing ovum inside follicles there must be an equilibrium among ratios of ROS and antioxidants[3].

Melatonin and its functions

The pineal is a small endocrine gland present in brain of all vertebrate animals. It is also known as Conarium or the Epiphysis Cerebri. Structurally it looks like a pine cone so it was named pineal. It is located within epithalamus region, between two hemispheres placed at the junction where two halves of thalamus combine. It produces a hormone named as Melatonin. The Melatonin is comprising of serotonin derivatives which controls sleep wake cycle in animals[4] it performs variety of other functions including the control of neuroendocrine[5], circadian rhythms[6], cardiovascular[7], reproductive[8] and oncostatic actions[9]. Some investigation have publicized that it also performs a major role in metabolism of fats[10], parturition and maintenance of gestation period[11], in addition to regulation of function of corpus luteum (CL)[12]. Many reviewers have confirmed that melatonin is an influential searcher of ROS. In disparity to other recognized radical hunters, melatonin is a universal and

multifunctional antioxidant agent. The increased lipophilicity as well as hydrophilicity characteristics of melatonin allows its quick transmission into various parts of body. Beside this it can very easily pass from cell sheaths. Fascinatingly, the high stages of melatonin were detected in human follicular fluid[13].Thus, the intention of current paper is to review current progresses in the ground of melatonin survey, with an attention to learn that by what means melatonin directly guards oocyte from OS inside the ovarian follicle.

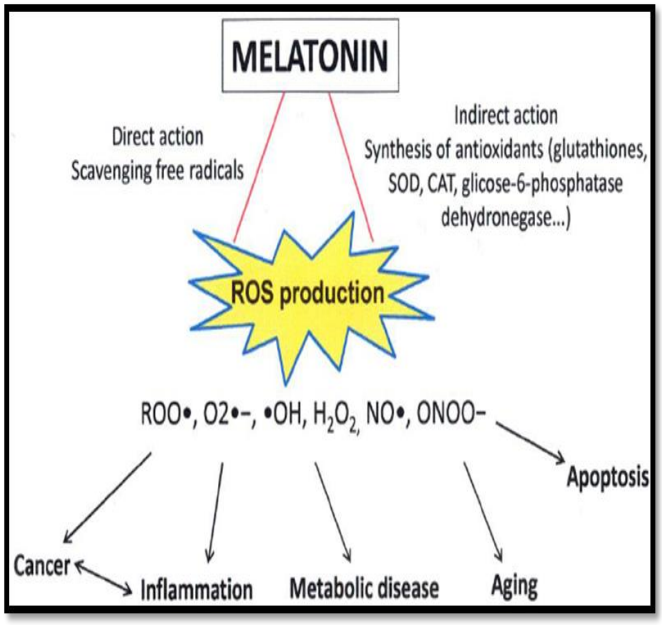

Figure1: various effects of melatonin on internal physiology of body[35]

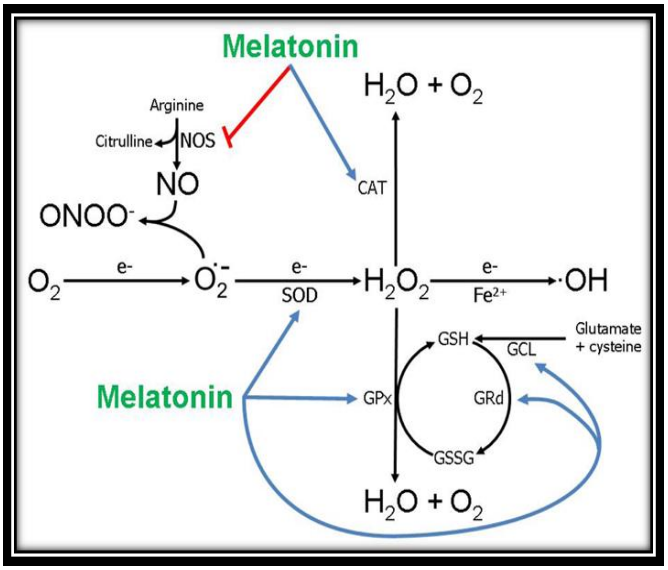

Figure2: Melatonin as an antioxidant agent[36].

Generation of ROS within ovarian follicles

The ROS are designed throughout the follicular breakage and might be elaborated in the releasing of ovum. The Luteinizing hormone (LH) rush persuades a termination of the cellar casing among the granulosa and theca interna sheets and an extension of the theca vessels into the non-vascular cell coating to formula a thick web of capillaries. The macrophages beside neutrophils are well-recognized to exist in in follicles[14]. The Incredible quantities of ROS are generated inside the follicle from both macrophages as well as neutrophils but then likewise through the endothelial compartments of the vessels. Nearby created ROS have an important impact on follicle breakage, they also act as subsequent messengers controlling the expression of DNA segment that rule courses of oocyte ripening[15].Though, additional ROS are also answerable for OS they can harm particles and assemblies of oocyte and granulosa compartments inside the follicle. Therefore, the ROS should be endlessly neutralized to retain just the minor quantity required to sustain the ordinary cell responsibilities. The follicular machineries, cumulus in addition the follicular liquid, might defend the oocytes from the destructive belongings of ROS[16].

Antioxidants within Ovarian follicles

An agent which prevents creation of OS is known as antioxidant. There are various types of antioxidant including both enzymatic as well as non-enzymatic antioxidant residing in different parts of body. The ovarian follicles are naturally gifted with some internal antioxidant enzymes as well as some non-enzymatic antioxidants which are employed to combat or decrease ROS. The Letdown or shortage of these mechanisms could lead gathering of ROS and the progress the OS condition which causes oocyte impairment[17]. Moreover, ROS may be overproduced due to numerous circumstances, like radiation, inflammation, infections, chemotherapy and superovulation in sterility therapy. It is verified that some antioxidant enzymes, like (SOD), glutathione peroxidase (GPx) in addition catalase, and some non-enzymatic antioxidants, like the vitamin C, uric acid, albumin and vitamin E, are existing inside the follicles[17]. Reduction in antioxidant levels, like GPx, in the follicular liquids leads to infertility[2]. Additional report established that a elevated ratios of SOD in follicular liquefied resourcefully condensed the DNA impairment produced by OS in swinish

oocytes besides cumulus cells, ensuing in fruitful fertilization and expansion to the blastocyst phase later in vitro impregnation. Yet, these capabilities were intermittent via the SOD inhibitor[18]. Once the rats were provided the antioxidant enhancements of vitamins E and C and the reduced fraction of apoptotic oocytes were experiential in contrast with the control group[19].Thus the equilibrium among ROS and antioxidants inside the follicle is serious for oocytes maturation.

Melatonin as ROS rummager

Though the melatonin employs belongings over its receptors, and can act as an influential ROS hunter. According to literature during 1993, the melatonin was exposed to behave as a shortest ROS scavenger after it was exposed to purify the extremely responsive hydroxyl radical[20].Meanwhile at that moment, numerous studies have now proved the capability of melatonin to decrease OS[21].In these reviews, the melatonin was initiated to chase free radicals produced from both oxygen as well as nitrogen[22]. Counting the superoxide radical, hydroxyl radical, singlet oxygen, hydrogen peroxide and nitric oxide (NO·) besides some peroxynitrite anion[23]. Three important agents are elaborated in ROS impairment to cells include the hydrogen peroxide, superoxide radical and hydroxyl radical. The hydrogen peroxide and superoxide radicals are supposed to generate fewer impairment than hydroxyl radical. Though, in the existence of unrestricted iron, precisely ferrous iron, hydrogen peroxide is rehabilitated to hydroxyl radical. The hydroxyl radical is the powerful unrestricted radicals and is recognized to harvest impairment to all casings of cells and DNA. Melatonin can effortlessly pass from cell sheaths since of its possessions of both lipophilicity as well as hydrophilicity, and recent investigations have confirmed that elevated level of melatonin occurs not both in cytoplasm as well as within the nucleus. Moreover, the antioxidant possessions of melatonin as a cell guardian have been widely confirmed[24].

Melatonin and reproduction

Melatonin is involved in regulation of reproductive activity and blastocyst implantation in several different mammalian species, counting ruminants, ferrets, equines, hamsters and rodents. Additionally, the maternal transfer of melatonin in mammals indicates that the daily photoperiod obtained by the mother during pregnancy or lactation is shifted to the foetus via the placenta or the milk [25]. Some studies have proved that this hormone has the stipulations to be considered an anti-estrogen drug, by interfering with estrogen receptors. Furthermore, it is also involved in the synthesis of estrogen by inhibiting the aromatase enzyme which generally controls its interconversion from its androgenic precursors, altering the whole blastocyst implantation process and growth of the follicle [26]. Experimentally, the melatonin averts the progress and advancement of impulsive or chemically persuaded mammary tumours in rats. Based on some previous researches it has been suggested that this hormone also prevents the propagation and inappropriateness of cells at the time of blastocyst imbedding procedure. The additional revisions with female rodents and hamsters stated that elimination of the pineal gland principals to a reduction in melatonin heights with resultant early vaginal opening, the ovarian enlargement, amplified cornification of vaginal cells besides prolonged anovulation, effects that can be overturned subsequently intake of melatonin[27].

Moreover, the melatonin also grounds variations in the emission of both Follicle stimulating hormone (FSH) and luteinizing hormone (LH) hormones which are very much essential hormones for regulation of reproductive effeciancy[8]. Based on a study when expecting sheep were sustained in adequate light for about 138 days of gestation, there was a reduction in melatonin ratios and augmented metabolic action in the gonads. Additionally, pinealectomy accompanying by means of melatonin dealing in gravid ewes altered the daily outline of foetal breathing patterns, signifying that photoperiodic data delivers the foetus through circadian differences over parental melatonin [29]. Various revisions have recommended that melatonin takes part in maintenance of the ovarian physiology, assumed that high amount of melatonin have been noticed within the follicular fluid[30]. In addition, the occurrence of melatonin receptors within the follicular compartments of rodents have[31] revealed conceivable melatonin construction within the ovary. Beside this many researchers have proved that the role of this hormone as an antioxidant agent could be related by means of follicular progress and oocyte superiority, interfering in procedures like the oocyte ripening and releasing of ovum[32].An investigation has showed that one of the hormonal influences supposed to control

follicular progress is melatonin, due to occurrence of its receptors (MT1 and MT2) inside the follicles sustenance the supposition of its part in regulation of ovarian physiology. Though, there are still deficient revisions concerning the impacts of melatonin upon the follicle growth and minute data about its action in the early, pre-antral stage[33].

Effects of Melatonin on oocyte value

Following fertilization, the Ooplasm converts into the cytoplasm of embryo the contribution of spermatozoa in this method is negligible. Thus, it is suggested that the initial phases of embryogenesis are controlled totally by maternal information existing in the oocyte. Thus, the value of oocytes is a crucial feature in determining the superiority of the primary phases of embryo growth. The oocyte ripening starts with the recommencement of meiosis, then oocytes are detained at the stage named as prophase through the primary meiotic division. Just few completely-grown oocytes continue meiosis against to LH rush. The oocytes then move towards the initial meiotic division and are detained at the metaphase stage of the next meiotic division till the occurrence of fertilization. Throughout this elongated phase of meiotic ripening, the oocyte gathers particles of some lipids, mRNA, peptides and some sugars and progress OS. The OS within the oocyte must be diminished to produce good quality embryo. As they encourage the lipid peroxidation of sheaths and cause damage of DNA beside this they are expected to lead disturbance in cell division, its metabolite transportation, and the mitochondrial function[34].

CONCLUSIONS

The detection of melatonin as hunter of ROS has significantly extended the consideration of its numerous functional roles. The current discoveries concerning the latent task of melatonin in physiology of reproductive system is correspondingly increasing. It has been thought that the melatonin is related to the maintenance of periodic generative procedures in photoperiod dependent breeding animals. Though, freshly countless investigators have started to explore the action of melatonin as an antioxidant agent. In this paper, we focused upon the intra-follicular functions of melatonin inside the ovary. The Melatonin, synthesized via pineal gland, is engaged with the follicular liquid by the blood. The ROS formed inside the ovary, particularly throughout the time of ovum discharge, are scavenged by means of melatonin, and condensed the OS, which has a greater impact in oocyte ripening and embryo progress.

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