


## ORIGINAL ARTICLE

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# Effects of estradiol on in vitro maturation of buffalo and goat oocytes

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## Abstract

**Purpose:** The effects of estradiol on oocyte development seem to be varied among species. The present study investigated the effects of 17 $\beta$ -estradiol on in vitro maturation of buffalo and goat oocytes.

**Methods:** Cumulus oocyte complexes (COCs) were aspirated from large antral follicles of slaughtered buffalo and goat ovaries. COCs were cultured in TCM-199 medium supplemented with 0, 0.5, 1, and 1.5  $\mu$ g/mL of 17 $\beta$ -estradiol for in vitro maturation. Then, oocytes were used for the examination of state of nuclear maturation and cumulus expansion.

**Results:** In both species, oocytes treated with 17 $\beta$ -estradiol showed higher cumulus expansion rate than control (0  $\mu$ g/mL treated). In buffalo, the percentage of oocytes matured to the metaphase II (MII) stage increased in the concentration-dependent manner of 17 $\beta$ -estradiol. Similarly, estradiol positively influenced nuclear maturation of goat oocytes in vitro.

**Conclusions:** Estradiol has promoting effects on normal progress of in vitro oocyte meiosis in buffalos and goats.

## KEYWORDS

17 $\beta$ -estradiol, buffalo, goat, in vitro maturation, oocyte

## 1 | INTRODUCTION

Assisted reproductive technologies (ARTs) can be applied to improve reproductive efficiencies in livestock species. In addition, ARTs have significant roles in the preservation of endangered species.<sup>1</sup> ARTs including artificial insemination (AI), cryopreservation, intra-cytoplasmic sperm injection (ICSI), multiple ovulation and embryo transfer (MOET), and in vitro embryo production (IVEP)

have been used for improvement of domestic animals. In buffaloes, the response to superovulation treatment is poor, and ultimately, MOET is hardly applicable. However, oocytes recovered from slaughtered animals are used for IVEP. In vitro maturation (IVM) is the initial step of IVEP technology. IVM of oocytes involves collection of cumulus oocyte complexes (COCs) from antral follicles and culturing them until they reach to the metaphase II (MII) stage.<sup>2</sup>

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The success in IVM of oocytes depends on many factors including the size of follicles and oocytes,<sup>3</sup> the maturation environment,<sup>4,5</sup> and the culture media used.<sup>6-8</sup> Steroids influence oocyte maturation in vitro.<sup>9</sup> Estradiol is a major female steroid hormone, produced from cholesterol. To improve the nuclear and cytoplasmic maturation of oocytes as well as the expansion of the cumulus cells, gonadotrophin hormones and estradiol are usually used in IVM of buffalo<sup>10</sup> and caprine<sup>11</sup> oocytes. Although the estradiol is supplemented occasionally in IVM, its role in IVM of oocytes remains contentious. Estradiol has been shown to increase IVM of bovine oocytes<sup>12,13</sup> but Gliedt and colleagues have reported that estradiol negatively regulates cumulus expansion and in vitro embryo production in bovine.<sup>14</sup> It has also been reported that estradiol reduces the maturation of mouse oocytes<sup>15,16</sup> and that in vitro maturation of pig oocytes has been inhibited by estradiol.<sup>17</sup> A high concentration of estradiol (100 µg/mL) has also inhibited oocyte maturation in boer goats.<sup>18</sup> High concentration of estradiol inhibits spindle formation and polar body extrusion in bovine oocytes.<sup>19</sup> The effects of estrogen on oocyte maturation, ovulation, and embryo development seem to be species-dependent.<sup>20</sup> Its role is still unclear in some mammalian species.

Black Bengal goats are important genetic resource, available in Bangladesh and India. They are dwarf in size and popular for delicious meat with high marbling, high prolificacy, disease resistance, and adaptability in high temperature and humidity. Similarly, buffalo is economically an important species in livestock agriculture in Asia. They are popular for their high butter fat content in their milk, high feed conversion efficiency, and high disease resistance. In Bangladesh, buffaloes are non-descriptive and river type. A few reports are available on in vitro development of oocytes in Black Bengal goats and indigenous river buffaloes in Bangladesh.

The aim of this study was to examine the effects of estradiol on in vitro maturation of oocytes from river buffaloes and Black Bengal goats.

## 2 | MATERIALS AND METHODS

### 2.1 | Chemicals

Unless otherwise mentioned, all chemicals were purchased from Sigma-Aldrich (St. Louis).

### 2.2 | Collection and processing of ovaries

Ovaries were collected from indigenous river buffaloes and Black Bengal goats at local slaughter house and kept in a thermo flask containing 0.9% physiological saline for transportation to the laboratory. The ovaries were washed in Dulbecco's phosphate buffer saline (DPBS) solution supplemented with gentamycin (50 µg/mL) once and following three times in DPBS. After trimming surrounding tissues, ovaries were washed again with saline solution.

### 2.3 | Collection of COCs

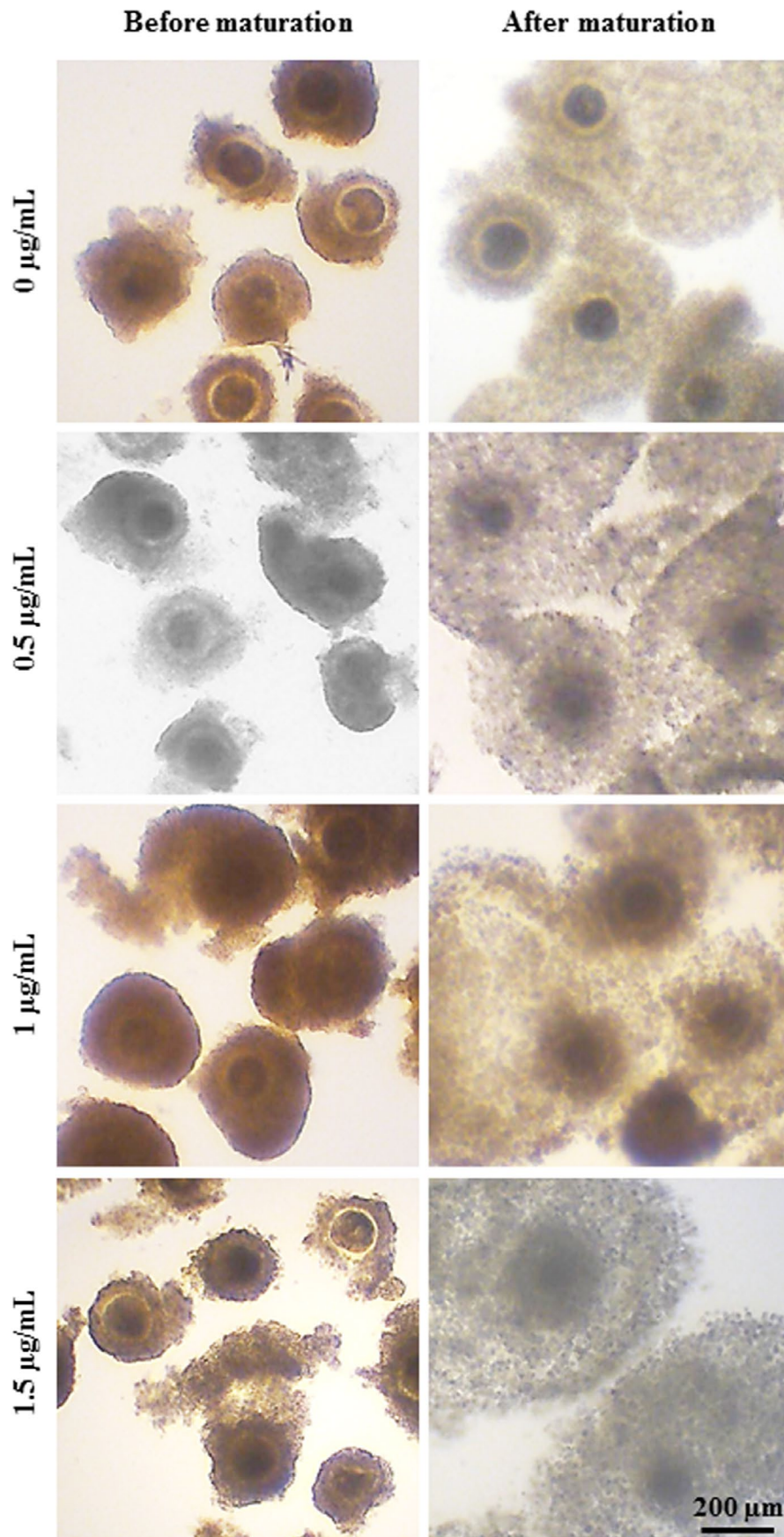
The collection and in vitro maturation of cumulus oocyte complexes (COCs) were done according to Totey et al<sup>21</sup> with some modifications. Briefly, COCs were aspirated from visible large antral follicles having diameter of 4-6 mm using a syringe (10 mL; Henke Sass Wolf) and needle (18 G; Henke Sass Wolf). COCs with oocyte of 120-125 µm in diameter (excluding the zona pellucida) were selected with the help of a stereomicroscope. Diameters of oocytes were measured using an ocular micrometer attached to an inverted microscope (Labomed, Inc). COCs containing healthy oocytes were selected based on their morphological appearance (uniformly granulated cytoplasm surrounded by multilayered compact cumulus cells) for further experimentation.

### 2.4 | In vitro maturation of COCs

The maturation medium was prepared with TCM-199 supplemented with 0.1 mg/mL sodium pyruvate, 0.08 mg/mL gentamycin sulfate, 5% (v/v) fetal bovine serum (FBS), and 100 ng/mL follicle-stimulating hormone (FSH).<sup>22</sup> In order to investigate the effects of 17β-estradiol, maturation medium was also supplemented with 0, 0.5, 1.0, or 1.5 µg/mL of 17β-estradiol. COCs were placed in 50 µL maturation droplets of maturation medium under paraffin oil. Each droplet was placed in a separate culture dish (No. 430165, 35 mm cell culture dish, Corning Incorporated). They were cultured for 24 hours at 38.5°C temperature with 5% CO<sub>2</sub> in humidified air.

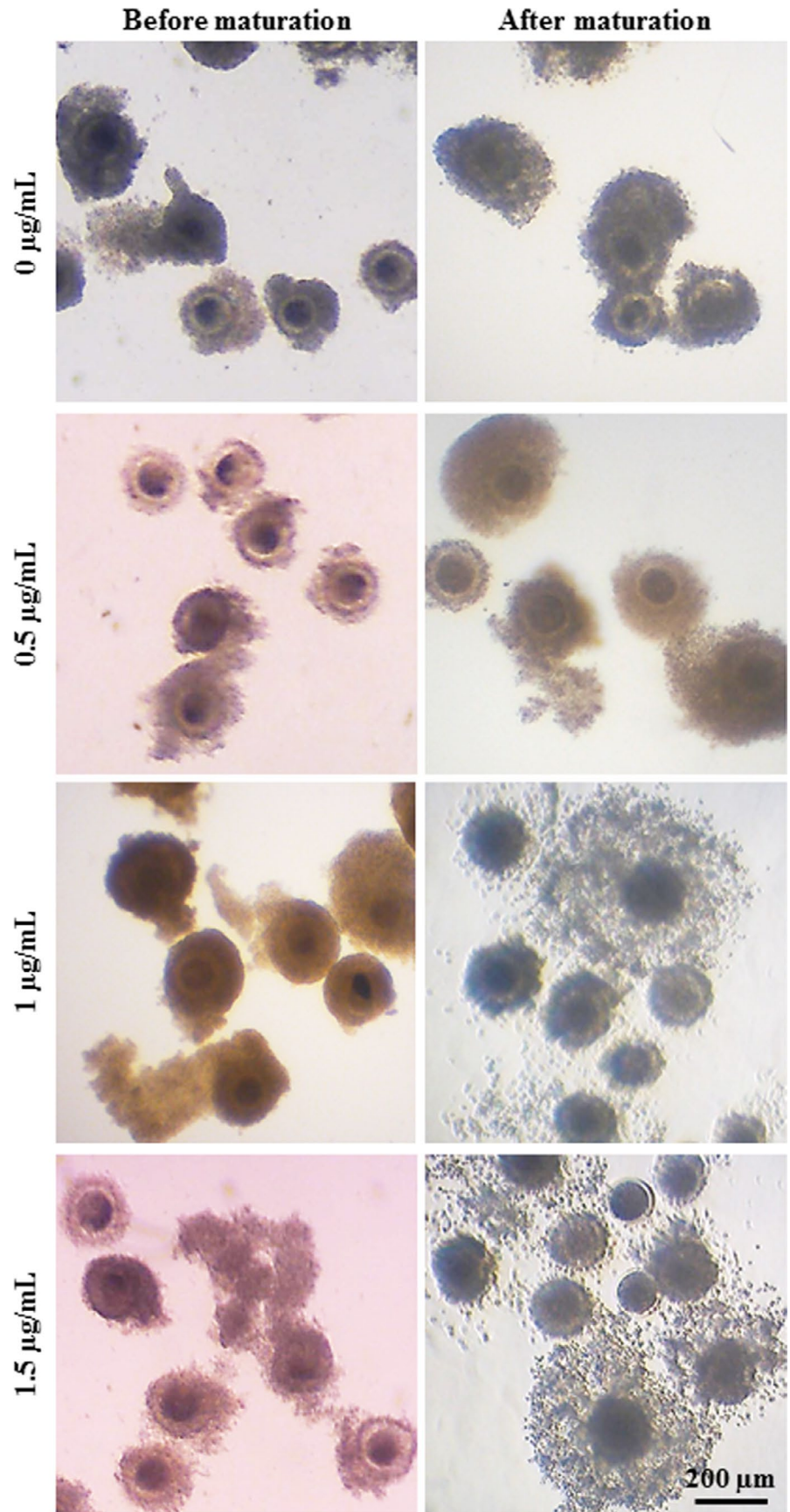
### 2.5 | Assessment of cumulus expansion and meiotic stage of oocytes

After in vitro maturation, the assessment of cumulus expansion was carried out as described by Maruska et al<sup>23</sup> with some modifications. Briefly, COCs with one or two layers expanded, one-half of the cumulus expanded, all layers expanded other than last layers of corona radiata, or all layers expanded, including corona radiata, were classified as expanded COCs. All of the COCs other than expanded COCs such as COCs without cumulus expansion (no observable sign of cumulus expansion) were classified as non-expanded COCs. Cumulus cells surrounding the oocytes were mechanically removed with the help of 0.1% (w/v) hyaluronidase and using a small-bore pipette. Denudate oocytes were fixed in aceto-ethanol (acetic acid:ethanol = 1:3) for 48 hours and stained with 1% (w/v) aceto-orcin to examine the stage of oocyte maturation. The stained oocytes were classified on the basis of morphology of the chromatin and nuclear envelope.<sup>24-27</sup> Oocytes after resumption of meiosis, the stages were classified into early diakinesis (ED), late diakinesis (LD), metaphase I (MI) and metaphase II (MII). Oocytes showing cytoplasmic or nuclear abnormalities were considered degenerated oocytes.



**FIGURE 1** Buffalo cumulus oocyte complexes (COCs) before and after in vitro maturation. The in vitro maturation medium was supplemented with 0, 0.5, 1, and 1.5  $\mu\text{g/mL}$  of 17 $\beta$ -estradiol. Scale bar represents 200  $\mu\text{m}$  [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

**FIGURE 2** Goat cumulus oocyte complexes (COCs) before and after in vitro maturation. The in vitro maturation medium was supplemented with 0, 0.5, 1, and 1.5  $\mu\text{g/mL}$  of  $17\beta$ -estradiol. Scale bar represents 200  $\mu\text{m}$  [Colour figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]



## 2.6 | Data presentation and statistical analysis

All data from cumulus expansion and meiotic stage assessment experiments were subjected to one-way ANOVA followed by Tukey's HSD test (IBM SPSS Statistics 22). Differences at  $P < .05$  were considered statistically significant.

## 3 | RESULTS

### 3.1 | Effect of $17\beta$ -estradiol on cumulus expansion during in vitro maturation of COCs

The typical morphologies of COCs before and after in vitro maturation in the medium supplemented with 0, 0.5, 1, and 1.5  $\mu\text{g/mL}$  of  $17\beta$ -estradiol in buffaloes and goats are shown in Figures 1 and 2, respectively. Assessment of oocyte maturation by visualization of cumulus expansion of COCs revealed a significant difference in expansion rate due to estradiol supplementation in both buffaloes and goats. In buffaloes, supplementation of in vitro maturation medium with  $17\beta$ -estradiol (0.5, 1.0 and 1.5  $\mu\text{g/mL}$ ) significantly increased cumulus expansion rate (93%, 100%, and 100%, respectively) compared to control (Figure 3A). In goats, supplementation of medium with 1  $\mu\text{g/mL}$   $17\beta$ -estradiol significantly increased cumulus expansion rate (100%) compared to 0, 0.5, and 1.5  $\mu\text{g/mL}$  groups (73%, 80%, and 70%, respectively) (Figure 3B).

### 3.2 | Effect of $17\beta$ -estradiol on nuclear maturation of buffalo and goat oocytes

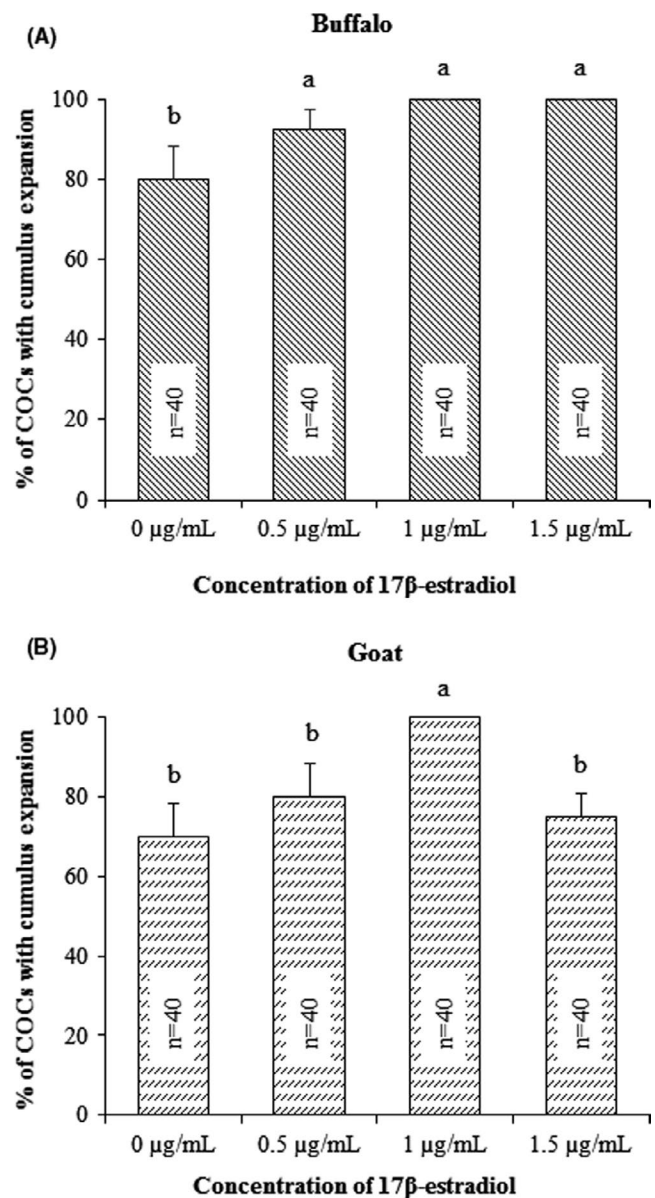
The representative images of nuclear morphology of buffalo and goat oocytes after maturation are shown in Figure 4. After resumption of meiosis, few proportion of buffalo oocytes were at early diakinesis in 0.5  $\mu\text{g/mL}$  (10%) and 1  $\mu\text{g/mL}$  (5%) of  $17\beta$ -estradiol supplemented groups (Figure 5A). The proportions of buffalo oocytes at late diakinesis increased with increment of  $17\beta$ -estradiol concentration. The percentages of MII oocytes increased in concentration-dependent manner with  $17\beta$ -estradiol treatments.

In goat, the proportion of MII stage oocytes (83%) was higher in 1  $\mu\text{g/mL}$  of  $17\beta$ -estradiol than 0  $\mu\text{g/mL}$  (53%) and 1.5  $\mu\text{g/mL}$  (55%) of  $17\beta$ -estradiol groups (Figure 5B). In addition, supplementation of medium with 1  $\mu\text{g/mL}$  of  $17\beta$ -estradiol significantly reduced degenerated oocytes compared to the other treatments.

## 4 | DISCUSSION

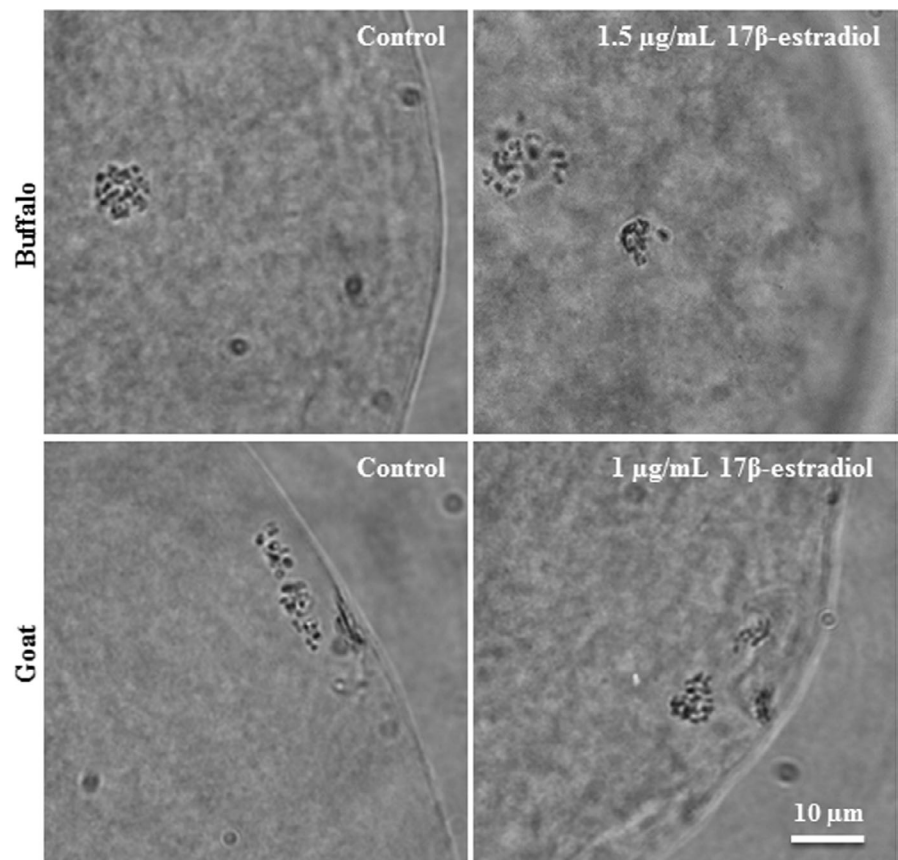
The rates of in vitro maturation of mammalian oocytes including mice, cattle, and sheep are low compared with oocytes matured in vivo.<sup>28-30</sup> This might be due to poor nuclear maturation caused by inadequate culture conditions.<sup>31-34</sup> Several factors are included

in culture media to improve the success rate of in vitro maturation. Here, we found that estradiol increased the percentage of MII oocytes. It is thought that estradiol supports nuclear maturation of oocytes during in vitro maturation. It has been reported that estradiol increases nuclear maturation of human oocytes.<sup>35</sup> Steroid hormones act via two distinct mechanisms. The classical or genomic theory describes a model where intracellular nuclear receptors and transcriptional modulation of the genes are involved. Several reports have revealed the evidence against the classical mode of estradiol. The non-genomic model of steroid action has been identified recently and many researchers have explained its characteristics.<sup>36-38</sup> The non-genomic steroid action does not involve transcriptional



**FIGURE 3** Effect of  $17\beta$ -estradiol on cumulus expansion of buffalo and goat COCs during in vitro maturation. Bar diagrams indicate the percentages of COCs with cumulus expansion after in vitro maturation of buffalo (A) and goat (B) oocytes. The numbers of complexes (n) used in each group are shown in each graph bar. Bars with different superscripts (a, b) differ significantly ( $P < .05$ )

**FIGURE 4** Nuclear morphologies of buffalo and goat oocytes after in vitro maturation. COCs were cultured in medium supplemented with 0, 0.5, 1, and 1.5  $\mu\text{g/mL}$  of 17 $\beta$ -estradiol during in vitro maturation. After maturation, oocytes were denuded mechanically, fixed with aceto-ethanol, stained with aceto-orcein, and examined for nuclear maturation. Scale bar represents 10  $\mu\text{m}$

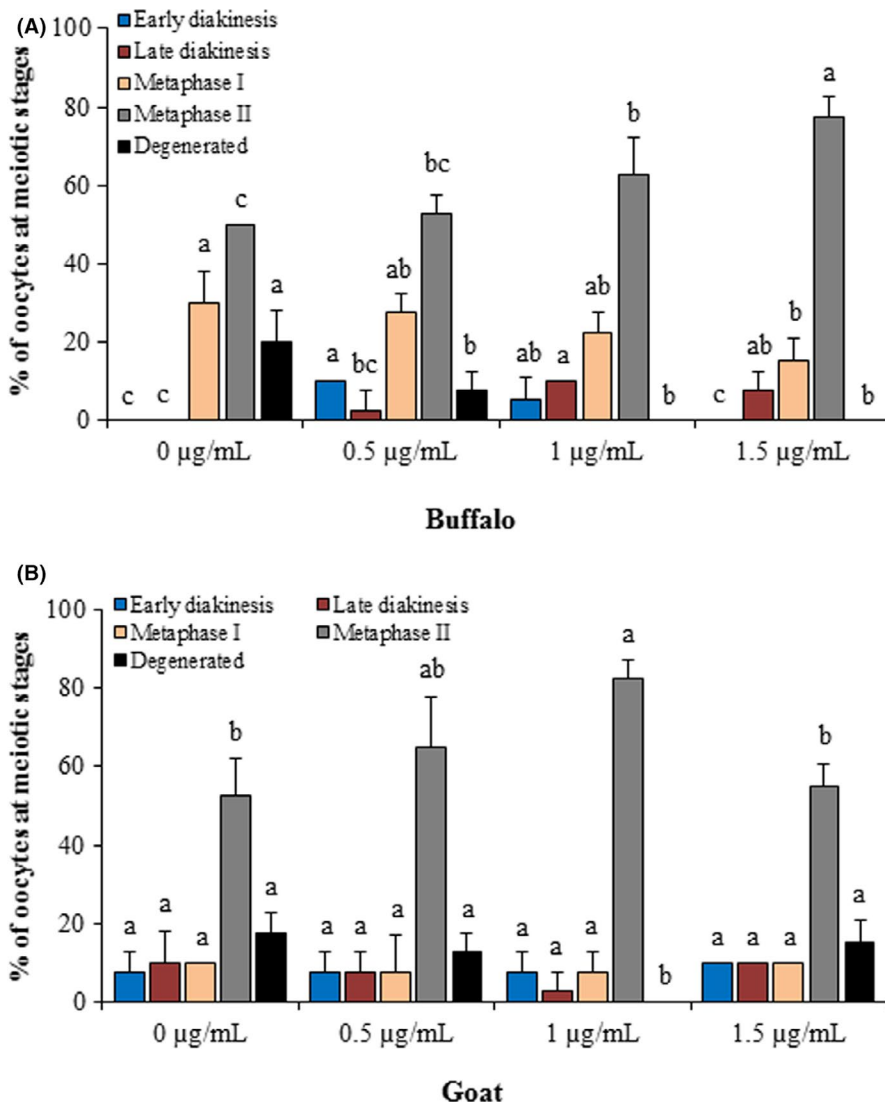


activation. Estradiol works on the cell surface and improves the potential of oocytes for development.<sup>35</sup>

For oocyte maturation, a bidirectional communication between oocytes and cumulus cells is essential.<sup>39</sup> The morphology and metabolic activity of cumulus cells are changed during meiotic maturation of mammalian oocytes. Thus, cumulus cells influence maturation and developmental competence of oocytes.<sup>40-45</sup> Moreover, the cumulus cells synthesize the extracellular matrix. This phenomenon is known as cumulus expansion. The component in the expanded cumulus is hyaluronic acid (HA),<sup>46</sup> and the amount of HA synthesis is correlated with the degree of expansion.<sup>47</sup> The presence of oocytes is essential for FSH-induced cumulus expansion.<sup>48,49</sup> It is also known that estradiol and oocyte-derived paracrine factors including growth differentiation factor 9 (GDF9) and bone morphogenetic protein 15 (BMP15) promote the development and expansion of cumulus cells.<sup>50</sup> Estradiol improves nuclear and cytoplasmic maturation as well as cumulus expansion in several species including bovine,<sup>51</sup> equine,<sup>52</sup> porcine,<sup>53</sup> and caprine.<sup>11</sup> Although estrogen supports the reproductive cycle in females, the necessity for estrogen in regulating specific events, including oocyte maturation, is species-dependent.<sup>20</sup> In the present study, supplementation of medium with 17 $\beta$ -estradiol increased cumulus expansion rate in oocytes from

both river buffaloes and Black Bengal goat oocytes. Thus, it is thought that 17 $\beta$ -estradiol coordinates with oocyte-derived factors in the culture medium, which in turn promotes cumulus expansion.

The concentration of estradiol for in vitro maturation of oocytes varies among different mammalian species. Concentration of 1  $\mu\text{g/mL}$  is commonly used for oocyte maturation medium in the caprine,<sup>54-56</sup> ovine,<sup>57-59</sup> and bovine.<sup>60</sup> This concentration mimics the presence of estradiol ( $1.1 \pm 0.06 \mu\text{g/mL}$ ) in preovulatory follicle in vivo.<sup>61</sup> Higher concentrations (10 and 100  $\mu\text{g/mL}$ ) of estradiol prevented in vitro maturation of oocytes in boer goats.<sup>18</sup> However, a clear comparison of effective concentrations of estradiol between different species has not been studied in the same culture condition. The present study compared the efficacy of estradiol on in vitro maturation of oocytes from Black Bengal goats and river buffaloes. Here, higher numbers of buffalo oocytes treated with 1.5  $\mu\text{g/mL}$  of estradiol reached the MII stage than other groups. In goat, the number of oocytes at the MII stage significantly increased in 1  $\mu\text{g/mL}$  estradiol but decreased with 1.5  $\mu\text{g/mL}$  of estradiol, which further indicated that high concentration of estradiol inhibited meiotic maturation of goat oocytes. Previously, it was reported that a proportion of estradiol was absorbed by paraffin oil covering the microdrops of culture medium.<sup>62</sup> In the present study, each droplet was placed in a separate culture dish and, thus, estradiol could not move



**FIGURE 5** Effects of 17 $\beta$ -estradiol on nuclear maturation of buffalo and goat oocytes. Vertical axis shows the percentages of oocytes at meiotic stages. The concentrations of 17 $\beta$ -estradiol are shown in horizontal axis in buffalo (A) and goat (B) species, respectively. Bars with different color indicate different meiotic stages. Bars with different superscripts (a-c) differ significantly ( $P < .05$ ) in the same species [Colour figure can be viewed at [wileyonlinelibrary.com](https://onlinelibrary.wiley.com)]

from one droplet to another. It was considered that estradiol was equally absorbed from each droplet without affecting the estradiol concentration.

In conclusion, estradiol enhances nuclear maturation of oocytes in both buffaloes and goats.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

## HUMAN/ANIMAL RIGHTS

This article does not contain any studies with human and animal subjects performed by the any of the authors.

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## REFERENCES

- Herrick JR. Assisted reproductive technologies for endangered species conservation: developing sophisticated protocols with limited access to animals with unique reproductive mechanisms. *Biol Reprod.* 2019;100:1158-1170.
- Gilchrist RB, Thompson JG. Oocyte maturation: emerging concepts and technologies to improve developmental potential *in vitro*. *Theriogenology.* 2007;67:6-15.
- Fair T, Hyttel P, Greve T. Bovine oocyte diameter in relation to maturational competence and transcriptional activity. *Mol Reprod Dev.* 1995;42(4):437-442.
- Park JI, Hong JY, Yong HY, Hwang WS, Lim JM, Lee ES. High oxygen tension during *in vitro* oocyte maturation improves *in vitro* development of porcine oocytes after fertilization. *Anim Reprod Sci.* 2005;87:133-141.
- Wrenzycki C, Stinshoff H. Maturation environment and impact on subsequent developmental competence of bovine oocytes. *Reprod Domest Anim.* 2013;48(1):38-43.

6. Wang WH, Abeydeera LR, Cantley TC, Day BN. Effects of oocyte maturation media on development of pig embryos produced by *in vitro* fertilization. *J Reprod Fertil*. 1997;111:101-108.
7. Eppig JJ, Hosoe M, O'Brien MJ, Pendola FM, Requena A, Watanabe S. Conditions that affect acquisition of developmental competence by mouse oocytes *in vitro*: FSH, insulin, glucose and ascorbic acid. *Mol Cell Endocrinol*. 2000;163(1-2):109-116.
8. Bevers MM, Izadyar F. Role of growth hormone and growth hormone receptor in oocyte maturation. *Mol Cell Endocrinol*. 2002;197(1-2):173-178.
9. Ainsworth L, Tsang BK, Downey BR, Marcus GJ, Armstrong DT. Interrelationship between follicular fluid steroid levels, gonadotrophic stimuli and oocyte maturation during preovulatory development of porcine follicles. *Biol Reprod*. 1980;23:621-627.
10. Abdoon ASS, Kandil OM, Otoi T, Suzuki T. Influence of oocyte quality, culture media and gonadotropins on cleavage rate and development of *in vitro* fertilized buffalo embryos. *Anim Reprod Sci*. 2001;65:215-223.
11. Pawshe CH, Palanisamy A, Taneja M, Jain SK, Totey SM. Comparison of various maturation treatments on *in vitro* maturation of goat oocytes and their early development and cell numbers. *Theriogenology*. 1996;46:971-982.
12. Fukui Y, Fukushima Y, Terawaki Y, Ono H. Effect of gonadotropins, steroids and culture media on bovine oocyte maturation and fertilization *in vitro*. *Theriogenology*. 1982;18:161-175.
13. Younis AI, Brackett BG, Fayrer-Hosken RA. Influence of serum and hormones on bovine oocyte maturation and fertilization *in vitro*. *Gamete Res*. 1989;23:189-201.
14. Gliedt DW, Rosenkrans CF, Rorie RW, Munyon AL, Pierson JN, Miller GF. Effects of media, serum, oviductal cells and hormones during maturation on bovine embryo development *in vitro*. *J Dairy Sci*. 1996;79:536-542.
15. Smith DM, Tenney DY. Effects of steroids on mouse oocyte maturation *in vitro*. *J Reprod Fertil*. 1980;60:331-338.
16. Eppig JJ, Koide SL. Effects of progesterone and oestradiol-17 $\beta$  on the spontaneous meiotic maturation of mouse oocytes. *J Reprod Fertil*. 1978;53:99-101.
17. Richter JD, McGaughey RW. Specificity of inhibition by steroids of porcine oocyte maturation *in vitro*. *J Exp Zool*. 1979;209:81-90.
18. Lv L, Yue W, Liu W, et al. Effect of oocyte selection, estradiol and antioxidant treatment on *in vitro* maturation of oocytes collected from prepubertal boer goats. *Ital J Anim Sci*. 2010;9:50-54.
19. Beker-van Woudenberg AR, van Tol HT, Roelen BA, Colenbrander B, Bevers MM. Estradiol and its membrane-impermeable conjugate (estradiol-bovine serum albumin) during *in vitro* maturation of bovine oocytes: effects on nuclear and cytoplasmic maturation, cytoskeleton, and embryo quality. *Biol Reprod*. 2004;70(5):1465-1474.
20. Moudgal NR, Shetty G, Selvaraj N, Bhatnagar AS. Use of a specific aromatase inhibitor for determining whether there is a role for oestrogen in follicle/oocyte maturation, ovulation and preimplantation embryo development. *J Reprod Fertil Suppl*. 1996;50:69-81.
21. Totey SM, Pawshe CH, Singh GP. *In vitro* maturation and fertilization of buffalo oocytes (*Bubalus bubalis*) effects of media, hormones and sera. *Theriogenology*. 1993;39:1153-1171.
22. Islam MN, Alam MH, Khatun A, et al. Effects of stem cell factor on *in vitro* growth of buffalo oocytes. *Theriogenology*. 2019;142:114-119.
23. Maruska DV, Lorraine Leibfried M, First NL. Role of calcium and the calcium-calmodulin complex in resumption of meiosis, cumulus expansion, viability and hyaluronidase sensitivity of bovine cumulus-oocyte complexes. *Biol Reprod*. 1984;31(1):1-6.
24. Motlík J, Koefoed-Johnsen HH, Fulka J. Breakdown of the germinal vesicle in bovine oocytes cultivated *in vitro*. *J Exp Zool*. 1978;205:377-383.
25. Hirao Y, Tsuji Y, Miyano T, et al. Association between p34<sup>cdc2</sup> levels and meiotic arrest in pig oocytes during early growth. *Zygote*. 1995;3:325-332.
26. Makita M, Miyano T. Steroid hormones promote bovine oocyte growth and connection with granulosa cells. *Theriogenology*. 2014;82:605-612.
27. Alam MH, Lee J, Miyano T. Inhibition of PDE3A sustains meiotic arrest and gap junction of bovine growing oocytes in *in vitro* growth culture. *Theriogenology*. 2018;118:110-118.
28. Schroeder AC, Eppig JJ. The developmental capacity of mouse oocytes that matured spontaneously *in vitro* is normal. *Dev Biol*. 1984;102(2):493-497.
29. Sirard MA, Parrish JJ, Ware CB, Leibfried-Rutledge ML, First NL. The culture of bovine oocytes to obtain developmentally competent embryos. *Biol Reprod*. 1988;39(3):546-552.
30. Galli C, Moor RM. Somatic cells and the G2 to M-phase transition in sheep oocytes. *Reprod Nutr Dev*. 1991;31(2):127-134.
31. Eppig JJ, Schultz RM, O'Brien M, Chesnel F. Relationship between the developmental programs controlling nuclear and cytoplasmic maturation of mouse oocytes. *Dev Biol*. 1994;164:1-9.
32. Eppig JJ. Coordination of nuclear and cytoplasmic oocyte maturation in eutherian mammals. *Reprod Fertil Dev*. 1996;8:485-489.
33. Krisher RL, Bavister BD. Responses of oocytes and embryos to the culture environment. *Theriogenology*. 1998;49:103-114.
34. Schramm RD, Bavister BD. A macaque model for studying mechanisms controlling oocyte development and maturation in primates. *Hum Reprod*. 1999;14:2544-2555.
35. Tesarik J, Mendoza C. Nongenomic effects of 17 $\beta$ -estradiol on maturing human oocytes; relation to oocytes developmental potential. *J Clin Endocrinol Metab*. 1995;80:1438-1443.
36. Christ M, Haseroth K, Falkenstein E, Wehling M. Nongenomic steroid actions: fact or fantasy? *Vitam Horm*. 1999;57:325-373.
37. Haseroth K, Gerdes D, Berger S, et al. Rapid nongenomic effects of aldosterone in mineralocorticoid-receptor-knockout mice. *Biochem Biophys Res Commun*. 1999;266:257-261.
38. Gerdes D, Christ M, Haseroth K, Notzon A, Falkenstein E, Wehling M. Nongenomic actions of steroids-from the laboratory to clinical implications. *J Pediatr Endocrinol Metab*. 2000;13:853-878.
39. Matzuk MM, Burns KH, Viveiros MM, Eppig JJ. Intercellular communication in the mammalian ovary: oocytes carry the conversation. *Science*. 2002;296(5576):2178-2180.
40. Sutovsky P, Fléchon JE, Pavlok A. Microfilaments, microtubules and intermediate filaments fulfil differential roles during gonadotropin-induced expansion of bovine cumulus oophorus. *Reprod Nutr Dev*. 1994;34(5):415-425.
41. Procházka R, Srsen V, Nagyová E, Miyano T, Flechon JE. Developmental regulation of effect of epidermal growth factor on porcine oocyte-cumulus cell complexes: nuclear maturation, expansion, and F-actin remodeling. *Mol Reprod Dev*. 2000;56(1):63-73.
42. Qian Y, Shi WQ, Ding JT, Sha JH, Fan BQ. Predictive value of the area of expanded cumulus mass on development of porcine oocytes matured and fertilized *in vitro*. *J Reprod Dev*. 2003;49:167-174.
43. Karja NWK. Nuclear maturation of porcine oocytes *in vitro*: effect of the cumulus-oocyte complexes quality. *Indo J Biotech*. 2008;13:1078-1084.
44. Ju S, Rui R. Effects of cumulus cells on *in vitro* maturation of oocytes and development of cloned embryos in the pig. *Reprod Domest Anim*. 2012;47:521-529.
45. Auclair S, Uzbekov R, Elis S, et al. Absence of cumulus cells *in vitro* maturation affects lipid metabolism in bovine oocytes. *Am J Physiol Endocrinol Metab*. 2013;304:599-613.
46. Salustri A, Yanagishita M, Hascall VC. Synthesis and accumulation of hyaluronic acid and proteoglycans in the mouse cumulus cell-complex during follicle-stimulating hormone-induced mucification. *J Biol Chem*. 1989;264(23):13840-13847.
47. Chen L, Wert SE, Hendrix EM, Russell PT, Cannon M, Larsen WJ. Hyaluronic acid synthesis and gap junction endocytosis are

- necessary for normal expansion of cumulus mass. *Mol Reprod Dev.* 1990;26:236-247.
48. Buccione R, Vanderhyden BC, Caron PJ, Eppig JJ. FSH-induced expansion of the mouse cumulus oophorus *in vitro* is dependent upon a specific factor(s) secreted by the oocyte. *Dev Biol.* 1990;138(1):16-25.
  49. Vanderhyden BC, Caron PJ, Buccione R, Eppig JJ. Developmental pattern of the secretion of cumulus expansion-enabling factor by mouse oocytes and the role of oocytes in promoting granulosa cell differentiation. *Dev Biol.* 1990;140(2):307-317.
  50. Sugiura K, Su YQ, Li Q, Wigglesworth K, Matzuk MM, Eppig JJ. Estrogen promotes the development of mouse cumulus cells in coordination with oocyte-derived GDF9 and BMP15. *Mol Endocrinol.* 2010;24(12):2303-2314.
  51. Sirotkin AV. Involvement of steroid hormones in bovine oocytes maturation *in vitro*. *J Steroid Biochem Mol Biol.* 1992;41(3-8):855-858.
  52. Carneiro G, Lorenzo P, Pimentel C, et al. Influence of insulin-like growth factor-I and its interaction with gonadotropins, estradiol, and fetal calf serum on *in vitro* maturation and parthenogenic development in equine oocytes. *Biol Reprod.* 2001;65:899-905.
  53. Kubo N, Cayo-Colca IS, Miyano T. Effect of estradiol-17 $\beta$  during *in vitro* growth culture on the growth, maturation, cumulus expansion and development of porcine oocytes from early antral follicles. *Anim Sci J.* 2015;86(3):251-259.
  54. Mogas T, Palomo MJ, Izquierdo MD, Paramio MT. Developmental capacity of *in vitro* matured and fertilized oocytes from prepubertal and adult goats. *Theriogenology.* 1997;47:1189-1203.
  55. Katska-Ksiazkiewicz L, Rynska B, Gajda B, Smorag Z. Effect of donor stimulation, frozen semen and heparin treatment on the efficiency of *in vitro* embryo production in goats. *Theriogenology.* 2004;62(3-4):576-586.
  56. Hammami S, Morato R, Romaguera R, et al. Developmental competence and embryo quality of small oocytes from pre-pubertal goats cultured in IVM medium supplemented with low level of hormones, insulin-transferrin-selenium and ascorbic acid. *Reprod Domest Anim.* 2013;48:339-344.
  57. Leoni GG, Rosati I, Succu S, et al. A low oxygen atmosphere during IVF accelerates the kinetic of formation of *in vitro* produced ovine blastocysts. *Reprod Domest Anim.* 2007;42:299-304.
  58. Catala MG, Izquierdo D, Rodriguez-Prado M, Hammami S, Paramio MT. Effect of oocyte quality on blastocyst development after *in vitro* fertilization (IVF) and intracytoplasmic sperm injection (ICSI) in a sheep model. *Fertil Steril.* 2012;97:1004-1008.
  59. Wang Z, Lin P, Yu S. Effects of ghrelin on developmental competence and gene expression of *in vitro* fertilized ovine embryos. *Theriogenology.* 2013;79:695-701.
  60. Beker ARCL, Colenbrander B, Beveres MM. Effect of 17 $\beta$ -estradiol on the *in vitro* maturation of bovine oocytes. *Theriogenology.* 2002;58:1663-1673.
  61. Fortune JE, Hansel W. Concentrations of steroids and gonadotropins in follicular fluid from normal heifers and heifers primed for superovulation. *Biol Reprod.* 1985;32(5):1069-1079.
  62. Miller KF, Pursel VG. Absorption of compounds in medium by the oil covering microdrop cultures. *Gamete Res.* 1987;17(1):57-61.

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