

(NO)

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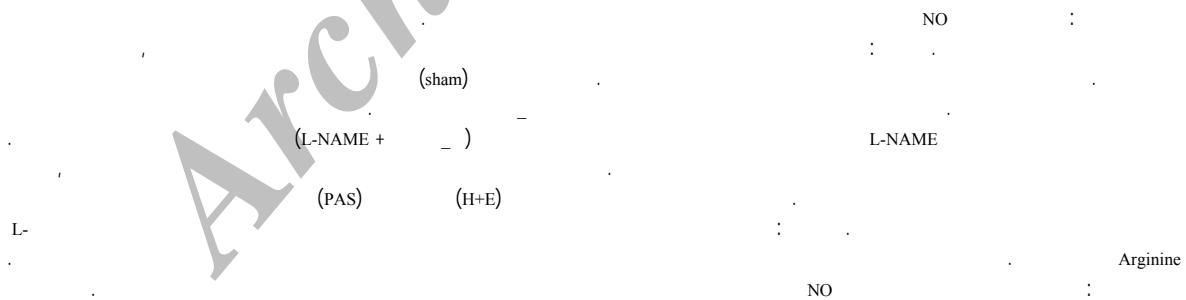
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Nitric oxide (NO) induced Histo-morphological changes in the rat ovaryHamzeiy H.^{1*}, Ghaderi A.², Eghbal M.A.³^{1,3} Research Center for Pharmaceutical Nanotechnology, Faculty of Pharmacy, Tabriz University of Medical Sciences,² Department of Zoology, Payamnoor University of Ardebil

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Objectives: Considering nitric oxide (NO) as one of important molecular regulators in genital organs, we examined its effects on histo-morphologic changes in the rat ovary. **Methods:** 40 rats were divided in 5 groups of 8 upon observing vaginal plaque that has been considered as day zero of pregnancy. Control group, normal saline, L-NAME, L-Arginine and L-NAME + L-Arginine groups. Except the control group the remaining groups received normal saline (2 ml / kg / ip), L-NAME (20mg / kg / ip), L-Arginine (200 mg / kg / ip) and a mixture of the same doses of L NAME + L- Arginine, respectively on the 3rd, 4th and 5th days of pregnancy. On the 18th day of pregnancy the rats were anesthetized by diethyl ether and then paralyzed by cutting the spinal cord. After laparotomy the ovaries were fixed in 10% formalin and after tissue sample preparation, general (H + E) and specific (PAS) staining was performed. The histo-morphological changes were observed by optical microscopy and the necessary photographs were taken. **Results:** Degenerative changes and dissemination were observed in most parts of ovaries of L- Arginine group as well as reduction in growth and weight of the rats. Ovarian volume and number of corpus Luteum were also reduced in this group. **Conclusion:** It seems that NO induces inhibition of cell growth in the pregnancy period and can interfere with normal functions of the ovary.

Key words: Nitric oxide, ovary, Corpus Luteum, Rat.



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Diagram illustrating the synthesis and inhibition of NO by L-NAME.

Chemical Reactions:

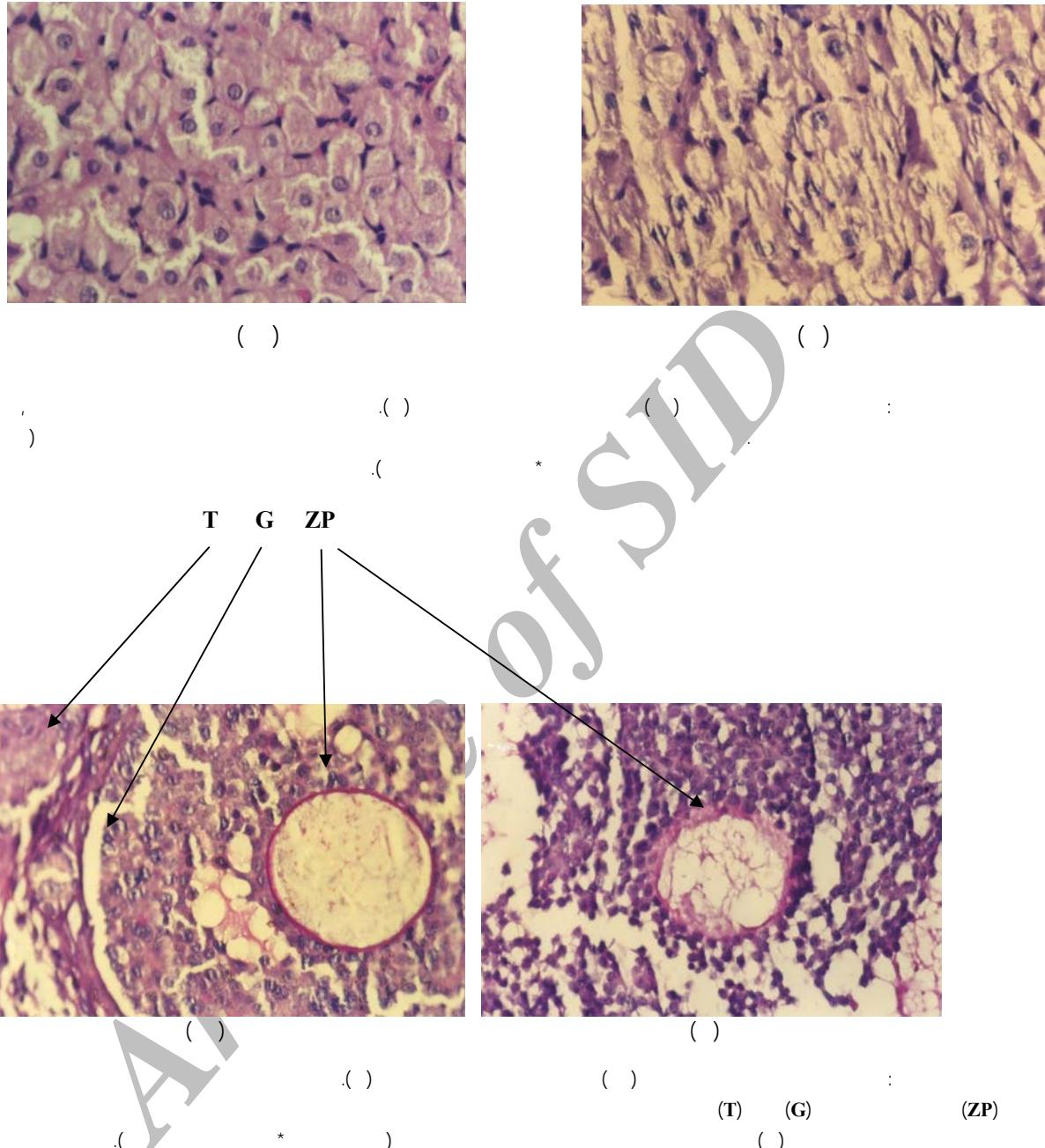
- L-arginine $\xrightarrow{\text{NOS}}$ L-citrulline + NO
- L-NAME inhibits NOS: $\text{L-NAME} + \text{NOS} \rightarrow \text{Inhibition}$

Statistical Analysis:

- (sham) vs (L-NAME +) $\text{P} < 0.05$
- (L-NAME +) vs (NAME) $\text{P} < 0.05$
- (L-NAME +) vs (ZP) $\text{P} < 0.05$
- (L-NAME +) vs (NAME) $\text{P} < 0.05$
- (L-NAME +) vs (sham) $\text{P} < 0.05$

Legend:

- (sham)
- (L-NAME +)
- (NAME)
- (ZP)
- (NO synthase)
- (inducible) iNOS
- (endothelial) eNOS
- (neuronal) nNOS
- NOS



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Tukey HSD

L-NAME L-Arginine

L-NAME + L-Arginine

L-

L-Arginine

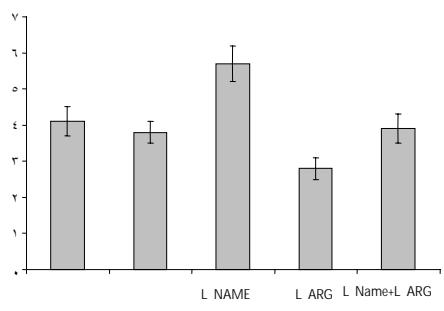
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NAME

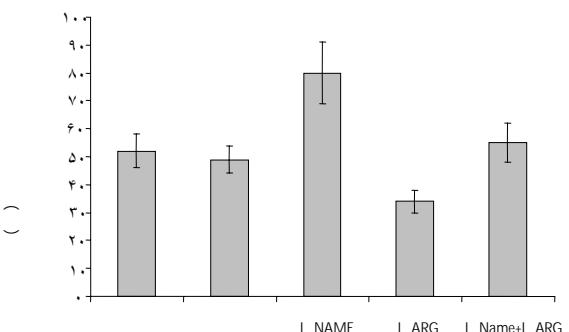
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Welch

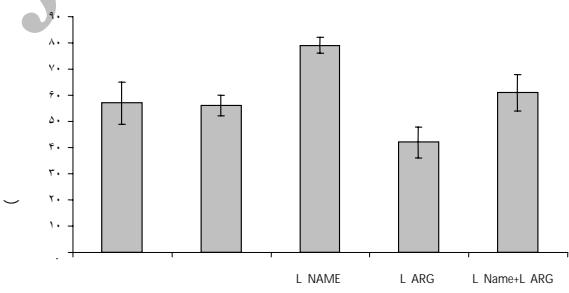
Brown-Forsythe



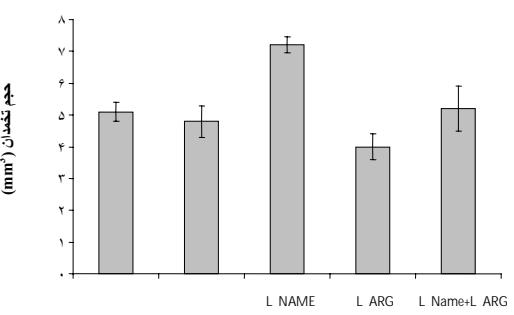
.(n=) mean±se



mean \pm se



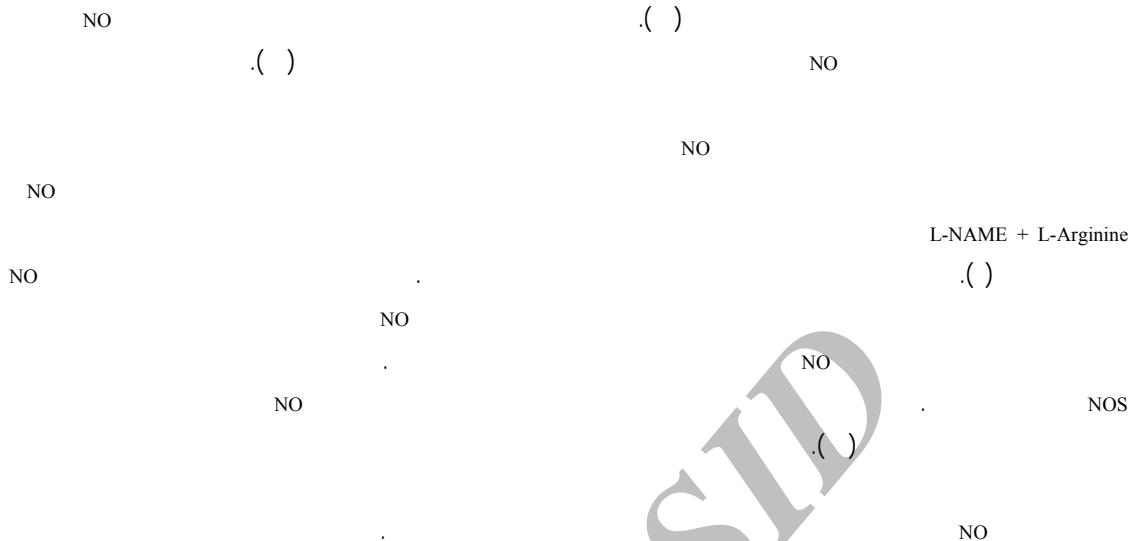
.(n=) mean±se



.(n=) mean±se

(reactive oxygen species)

L-Arginine



6- References

- 1- Bredt D.S., Snyder S.H. Nitric oxide, a novel neuronal messenger. *Neuron*, 1992, 8: 3-11.
- 2- Crane B.R., Arvai A.S., Gachhui R., Wu C., Ghosh D.K., Getzoff E.D., Stuehr D.J., Tainer J.A. The structure of nitric oxide synthase oxygenase domain and inhibitor complexes. *Science*, 1997, 279: 425-431.
- 3- Packard M.G., Whit N.M. Dissociation of hippocampus and caudate nucleus memory systems by post training intracerebral injection of dopamine agonists. *Behav. Neurosci.*, 1991, 105: 295-306.
- 4- Kenrokuro M., Zackrisson U., Brannstrom M. Nitric oxide regulates ovarian blood flow in the rat during the periovulatory period. *Hum. Reprod.*, 2002, 17 (10): 2509-2516
- 5- Motta A.B., Estevez A., Tognetti T., Gimeno M.A.F., Franchi A.M. Dual effects of nitric oxide in functional and regressing rat corpus luteum. *Mol. Hum. Reprod.*, 2001, 7 (1): 43- 47.
- 6- Voznesenskaia T.I., Blashkiv T.V. The effect of Nitric oxide synthase blockers, nitric oxide donors and anti-ovarian antibodies on murine oocytes. *Eksp. Klin. Farmakol.*, 2002, 65 (4): 30 – 2.
- 7- Rosselli M., Keller P.J., Dubey R.K. Role of Nitric oxide in the biology, physiology and pathophysiology of reproduction. *Hum. Reprod. Update*, 1998, 4 (1): 3-24.
- 8- Zackrisson U., Mikuni M., Wallin A., Delbro D., Hedin L., Brannstrom M. Cell-specific localization of nitric oxide synthases (NOS) in the rat ovary during follicular development, ovulation and luteal formation. *Hum. Reprod.*, 1996, 11: 2667-2673.
- 9- Purcell T.L., Given R., Chwalisz K., Garfield R.E. Nitric oxide synthase distribution during implantation in the mouse. *Mol. Hum. Reprod.*, 1999, 5: 467-475.
- 10- Battaglia C., Regnani G., Marsella T., Facchinetto F., Volpe A., Venturoli S., Flamigni C. Adjuvant L-arginine treatment in controlled ovarian hyperstimulation: a double-blind, randomized study. *Hum. Reprod.*, 2002, 17 (3): 659-65.
- 11- Head K., Miller A. Bad medicine, bad reportage, or both? *Alter. Med. Rev.*, 2005, 10 (4): 1-8.
- 12- Tamanini C., Basini G., Grasselli F., Tirelli M. Nitric oxide and the ovary. *J Anim Sci.*, 2002, 81 (E Suppl. 2): E1-E7.
- 13- Motta A.B., Estevez A., de Gimeno M.F. The involvement of nitric oxide in corpus luteum regression in the rat: feedback mechanism

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- between prostaglandin F_{2α} and of nitric oxide. Mol. Hum Reprod., 1999, 5: 1011-1016
- 15-Vega M., Urrutia L., Iniguez G., Gabler F., Devoto L., Jonson M.C. Nitric oxide induces apoptosis in the human luteum in Vitro. Mol. Hum. Reprod., 2000, 6 (8): 681-688.
- 16- Morley J.E., Kumar V.B., Mattamal M.B., Farr S., Morley P.M., Flood J.F. Inhibition of feeding by a nitric oxide synthase inhibitor: effects of aging. Eur. J. Pharmacol., 1996, 5; 311 (1): 15-9.
- 17- Faletti A.G., Mohn C., Farina M., Lomniczi A., Rettori V. Interaction among beta endorphin, nitric oxide and prostaglandins during ovulation in rat. Reproduction, 2003, 125 (4): 469-477.
- 18-Battaglia C., Ciotti P., Notarangelo L., Fratto R., Facchinetti F., de Aloysio D. Embryonic production of nitric oxide and its role in implantation: a pilot study. J. Assist. Reprod. Genet., 2003, 20 (11): 449-54.

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