Effects of Lupeol on experimental ovary ischemia / reperfusion injury in rats

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Introduction

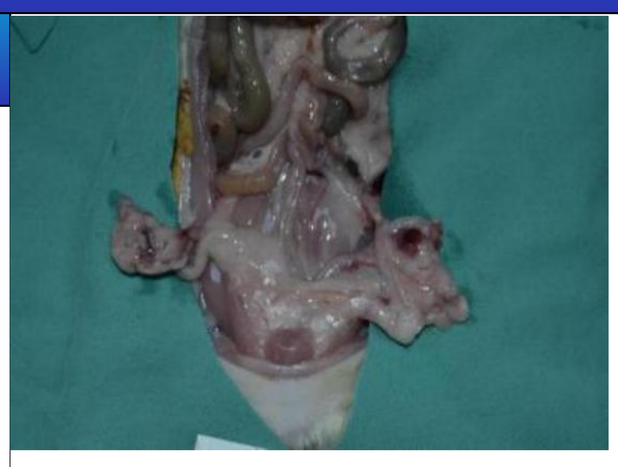
Ovarian ischemia reperfusion injury occurs following ovarian torsion. The pathological conditions that commonly lead to ovarian torsion include benign cystic teratoma, hemorrhagic/follicular cysts, paratubal cysts, hydrosalpinx, and cystadenomas. Only 0.5-1.8% of ovarian torsions are associated with ovarian malignancies. In ovarian torsion, venous and lymphatic circulation is compromised initially. If the process persists, arterial blood flow is also impaired, leading to rapid progression of the ovary to necrotic and gangrenous tissue. In this study, we aim to investigate the histopathological and biochemical effects of lupeol during ovary ischemia reperfusion injury in a rat model of experimental ovarian torsion.

Methods

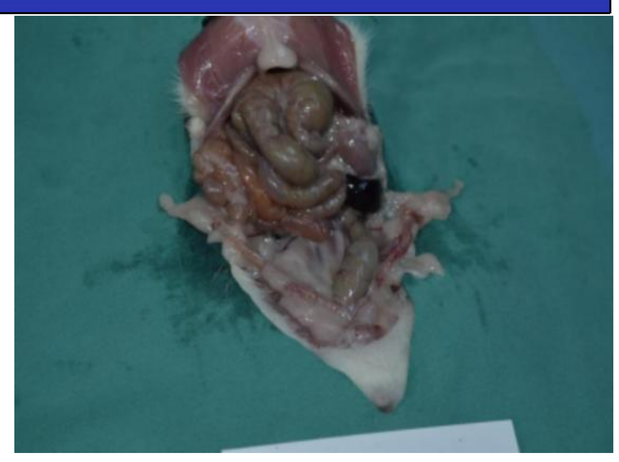
In the study, 24 Wistar Albino female rats were divided into 4 groups: Control, lupeol, ischemia and treatment. In the lupeol group, 100 mg/kg lupeol was given intraperitoneally. A bilateral ovarian torsion model was created by rotating ovaries 720 degrees clockwise and maintaining torsion for 3 hours. In the Torsion group, only torsion-detorsion was performed, whereas the Treatment group received intraperitoneal lupeol (100 mg/kg) 30 minutes before detorsion. A 24-hours reperfusion period was allowed before collecting tissue and serum samples for biochemical and histopathological evaluation. Biochemical analysis included measurements of TAS (Total Antioxidant Status), TOS (Total Oxidant Status), OSI (Oxidative Stress Index), Caspase-3, AMH (Anti-Müllerian Hormone); histopathological assessment evaluated as follicular degeneration, hemorrhage, vascular congestion, edema which was scored for each group.

Results

Statistical analysis was performed using SPSS Version 22.0. The Treatment group showed reduced follicular degeneration, hemorrhage, vascular congestion, and edema scores compared to the Ischemia group. Tissue TOS and serum OSI levels were lower in the Treatment group than in the Ischemia group. Serum TAS (mmol/L) was higher in the Treatment group (1.34 ± 0.05) than in the Ischemia group (1.17 ± 0.07). Caspase-3 levels decreased in the Treatment group compared to the Ischemia group. Tissue AMH levels significantly increased in the Treatment group versus the Ischemia group.



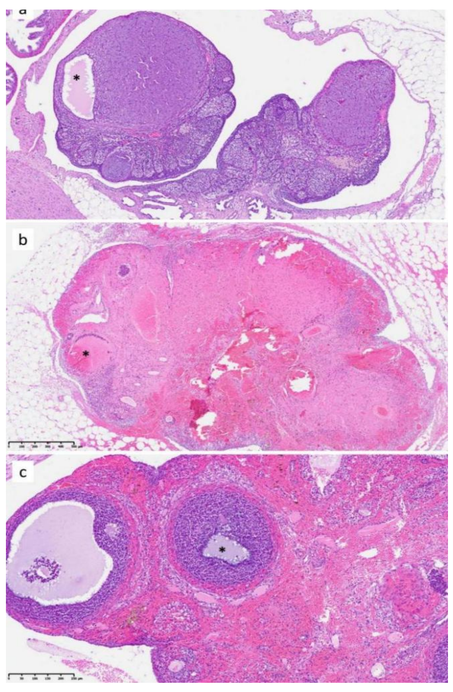
Picture 1. Appearance of adnexa in the ischemia group before sacrification



Picture 2. Appearance of adnexa in the treatment group before sacrification

Biochemical Parameters	Control	Lupeol	Ischemia	Treatment	p
Serum TAS (mmol/L)	1,42±0,14	1,53±0,13	1,17±0,07	1,34±0,05	<0,001
Tissue TAS (mmol/L)	0,16±0,07	0,21±0,07	0,08±0,04	0,14±0,04	0,019
Serum TOS (µmol/L)	2,17±0,56	2,14±0,59	4,09±1,93	2,55±0,73	0,02
Tissue TOS (µmol/L)	0,42±0,27	0,49±0,37	2,41±0,28	0,8±0,41	<0,001
Serum OSI	0,15±0,04	0,13±0,03	0,35±0,17	0,19±0,05	0,003
Tissue OSI	0,33±0,30	0,26±0,24	3,40±1,67	0,62±0,45	0,002
Serum Caspase-3 (ng/ml)	0,46±0,04	0,44±0,02	0,51±0,02	0,48±0,04	0,023
Tissue Caspase-3 (ng/ml)	0,56±0,08	0,53±0,07	0,58±0,04	0,56±0,07	0,72
Serum AMH (ng/ml)	2,70±0,11	2,58±0,22	2,72±0,12	2,72±0,06	0,290
Tissue AMH (ng/ml)	2,44±0,22	2,5±0,28	1,85±0,31	2,4±0,29	0,002

Pathological Changes	Control	Lupeol	Ischemia	Treatment	p
Follicular Degeneration	0	0,33±0,51	2,5±0,54	1,33±0,81	<0,001
Hemorrhage	0	0	1,83±0,75	0,66±0,81	<0,001
Vascular Congestion	0,33±0,81	0,5±0,83	2,66±0,51	1,33±0,81	<0,001
Edema	0,33±0,51	0,5±0,54	1,66±0,51	0,66±0,51	<0,001



Picture 3. Microscopic view of pathology examinations a. Ovarian parenchyma without pathology other than follicular degeneration (*) (Hematoxyl & eosin, x50). b. Ovarian parenchyma with areas of congestion and bleeding (Hematoxyl & eosin, x50). c. Ovarian parenchyma with follicular degeneration, bleeding, and congestion (Hematoxyl & eosin, x100).

Conclusion

This study is the first in the literature to demonstrate that lupeol exerts antioxidant, anti-apoptotic and protective effects in ovarian ischemia-reperfusion injury, while also enhancing ovarian reserve via increased AMH levels. Due to its plant-derived origin, absence of toxicity in the literature, accessibility, lupeol holdspromising clinical potential as a safe adjunctive therapy for ovarian torsion.

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References:

1.Cass DL. Ovarian torsion. Semin Pediatr Surg. 2005 May;14(2):86-92

2.Kelleher, Cassandra M. MD; Goldstein, Allan M. MD. Adnexal Masses in Children and Adolescents. Clinical Obstetrics and Gynecology 2015 Mar; 58(1):p 76-92

3.Kokoska ER, Keller MS, Weber TR. Acute ovarian torsion in children. Am J Surg 2000;180:462–465

4.Erel O. A new automated colorimetric method measuring total oxidant status.Clin. Biochem. 2005 Dec; 38(12):1103-1111

5.Erel O. A novel automated direct measurement method for total antioxidant capacity using a new generation, more stable ABTS radical cation. Clin. Biochem. 2004 Apr; 37(4):277-285

6. Kaya C, Kapisiz A, Eryilmaz S, Karabulut R, Turkyilmaz Z, Inan MA et al. Effects of Lupeol on Intestinal Anastomosis After Experimental Intestinal Ischemia-Reperfusion Injury in Rats. Drug Des Devel Ther. 2025 Jan 23;19:479-490

7. Kapisiz A, Kaya C, Eryilmaz S, Karabulut R, Turkyilmaz Z, Inan MA et al. Protective effects of lupeol in rats with renal ischemia-reperfusion injury. Exp Ther Med. 2024 Jun 7;28(2):313

8. Azzam A, Karabulut R, Kaya C, Eryılmaz S, Kapisiz A, Turkyilmaz Z et al. Effects of lupeol on experimental testicular ischemiareperfusion damage in rats. Ulus Travma Acil Cerrahi Derg. 2025 Feb;31(2):95-102