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Oral Presentations

O-29
Designing a new delivery system containing quercetin and edible oils to treat male infertility induced by nonalcoholic fatty liver in rats

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Background: Recent molecular and physiological studies have shown that adverse effects of nonalcoholic fatty liver diseases (NAFLD) extend far beyond the liver. NAFLD can impair male reproductive function by increasing reactive oxidative stress levels, reducing the expression of antioxidant genes and inducing damage in testes immune privilege. Antioxidant therapy and its effectiveness depend on whether the exogenous antioxidant will be readily absorbed to reach high enough that are required to decrease the pathological damages. Quercetin (Quer), as an antioxidant, is able to ameliorate oxidative stress but has low bioavailability in the body. Therefore designing new drug delivery systems are needed to reach the best effects.

Objective: We aimed to prepare a new delivery system containing edible oils for quercetin entrapment to slow release.

Materials and Methods: Bigels were prepared using cottonseed oil/cannabis oil/alginate/ferula gum. Sprague-Dawley rats were housed for 2 wk, then NAFLD was induced by 58% of dietary calorie as lard and 42 g/L fructose for 16 wk. The experimental protocol was approved by the ethical committee of Zanjan University of Medical Sciences, Zanjan, Iran. After confirming the NAFLD induction, animals were divided into five groups: Control, control NAFLD, received 2 mg/kg Quer loaded on bigels, free bigels, and free Quer for 45 days as daily gavage. Semen parameters (count, motility, and morphology), viability (Eosin-nigrosine staining) and serum testosterone levels were analyzed. In addition, histological sections of testicular tissues were investigated by Hematoxylin-Eosin staining method. In situ detection of apoptosis was performed using terminal deoxynucleotidyl-transferase dUTP nick end labeling (TUNEL) assay.

Results: The sperm count, sperm motility, normal morphology and testosterone level were significantly lower in the NAFLD group than those the controls. Moreover, higher head and tail abnormality percentages were seen in the sperm of these groups. Bigel-Quer significantly improved the serum testosterone level, sperm count, motility, and morphology compared with the NAFLD group. Spermatogenic cells in all stages of differentiation (spermatogonia, primary spermatocytes, early spermatids, late spermatids) are observed and preserved normally in the testicular tubules and lumen filled with mature sperms in the control group. Interestingly, atrophic changes in the testicular tubule architecture with swelling in spermatogonia cells, detachment from tubule membrane, reduced number of mature sperm, and reduced lumen thickness were seen in the NAFLD. In the Quer, bigel and bigel-Quer-treated groups, swelling and vacuolation rate of germ cells decreased. The testicular morphology, and tubule structure were significantly normalized, especially in the bigel-Quer-treated group. Serum testosterone levels significantly increased and reached the healthy control group in the bigel-Quer group. TUNEL-positive cells in testes increased significantly after NAFLD induction. Quantitative analysis showed a significant decrease in testicular TUNEL-positive cells following bigel-Quer treatment, but not in other groups.

Conclusion: The bigel showed synergistic effects with Quer for treating infertility in rats with NAFLD. Stability and bio-availability of Quer are important aspects that should be considered to justify its supplementation. Empowering antioxidant shield of NAFLD patients by Quer supplementation can improve various damage effects and clinical status of diseases.

Key words: *Quercetin, Non-alcoholic fatty liver, Semen parameters, Bigel.*

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