Research Article

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Multisystem Evaluation of the Physiological Effects of the Grape seed

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Abstract Grape seed extraction has many beneficial effects on the cardiovascular system and blood pressure and has also been proven to have anti-obesity effects and/or improve fatty acid oxidation and insulin responses. The objective of this study is to evaluate the effectiveness of grape seed extract on some physiological parameters in multiple systems. To this end, male mice were injected intraperitoneally with (100 mg/kg B.W) for 7 days. Serum was collected to detect the concentration of ALT and TSB (liver functions). Urea and creatinine (a kidney function) concentration was measured. Testosterone, LH, and FSH (male reproductive function) concentration were evaluated. Our results revealed a significant reduction in ALT concentration in the grape seed extraction group compared with the control group. Total serum bilirubin was non-detectable in both the grape seed extraction group as well as the control group. Urea and creatinine concentrations appeared to have no significant change between both grape seed extraction and the control group. Testosterone, LH, and FSH hormone levels were significantly raised in the grape seed extraction group compared with the control group. Prolactin hormone results revealed no change in both the grape seed extraction group and the control group. Our study showed up that grape seed extract can improve male reproductive hormones without any toxic effect on the liver or kidney.

Keywords: Grape seed, Testosterone, Male rat.

Introduction: Grape seed proanthocyanidins (PACs) have shown a variety of pharmacological and therapeutic health effects against cancer, diabetes, obesity, and other illnesses associated with oxidative stress and inflammatory processes, including cardiovascular disease (1). It has been demonstrated that grape seed proanthocyanidins are more potent free radical scavengers than vitamins C, E, and -carotene.(2).

Grape seed supplementation has been demonstrated to prevent oxidative damage by significantly reducing malondialdehyde (MDA) levels and increasing the activities of glutathione reduced (GSH), superoxide dismutase (SOD), and total antioxidant capacity (T-AOC) (3).Early studies in animal models revealed that grape seeds have anti-inflammatory properties, primarily via preventing the production of pro-inflammatory cytokines (4). Grape products were found to enhance the quality of rat sperm and show sperm protection from oxidative stress *in vitro*. (5) A recent study using grape seed extraction indicated that medium doses decreased TNF- and IL-1 activity in plasma and skeletal muscle and improved strenuous exercise, in a rat model of exhaustive exercise-induced weariness (6). These results imply that grape seed has antioxidant and anti-inflammatory properties that mitigate kidney injury in type 2 diabetic rats (7).In light of the aforementioned findings, this research was carried out to examine the toxic effects of grape seeds on the liver and renal functions as well as to detect the effects of grape seeds on reproductive hormones in adult male rats.

Material and method: In the present study50 mature male mice were divided equally and randomly into Two groups each group of 25 mice; group control was served as a control group; group grape seed animals of this group were administrated intraperitoneal (100 mg/kg /B.W.), this schedule of administration was repeated daily for 7 consecutive days Blood collection was directly from the preorbital vein from the eye collection was at the end of the study, each blood sample tubes without heparin to estimate and calculate biochemical and hormone parameters as a follow:

1-Biochemical parameters include: Blood samples were taken on the final day of the research and immediately stored in the refrigerator at 4 C until they were centrifuged for 10 minutes at 3000 rpm to separate the serum. Before analysis, serum

was collected and kept at 20 C. Alanine aminotransferase (8) was detected according to the colorimetric method demonstrated by (9) total bilirubin was determined by the Diazo method (10); Creatinine concentration was detected according to Jaff's reaction and Urea concentration by Berthlot reaction (11).

2. Hormone concentrations include:

Using kits from Beijing North Institute of Biological Technology to determine hormone levels, follicle-stimulating hormone (FSH), luteotropic hormone (LH), and testosterone (T) were evaluated using the radioimmunoassay (RIA) method (12).

Statistical analysis: GraphPad Prism 8.0 software was used for statistical analysis, and multiple t-test comparisons with the Holm-Sidak correction method were applied (13). Each experimental group was composed of 25 mice. P <0 .05 was considered to be statistically significant. Different alphabetic letters indicate a statically differed from another group.

Results and discussion:

1-The effect of grape seed extraction on adult mice serum ALT, and Bilirubin concentrations.

The results of liver function tests in this study showed a significant ($P<0.05$) decrease in serum ALT concentration in the grape seed group in comparison with the control group. Total serum bilirubin concentration was not detectable in either grape seed or control groups. Liver enzyme alteration may be the accompanying biochemical picture in a patient with symptoms or indications suggestive of liver diseases, such as ALT, bilirubin, and AST (14). Our findings concur with another researcher who discovered that grape seed reduced ALT levels (15). According to the findings of another scientist treatment of mice with grape seed did not affect their total serum bilirubin levels (16). Therefore, our data showed that there was no increase in liver enzymes, which may be because grape seed did not have a harmful effect on hepatocytes. The results of another researcher's discovery that there are no adverse effects on bilirubin concentration go hand in hand with the effects of grape seed consumption (17). Typha domingensis pers also decreased ALT levels because it has alkaloids, phenols, flavonoids, tannins, and saponins (18).

2- **The effect of grape seed on adult mice serum creatinine and urea**

concentrations: Renal function biomarkers results showed insignificant differences between the grape seed group and the control group. Another scientist also, found that grape seed treatment ameliorates renal failure of chronic kidney disease patients via decreasing proteinuria and has no significant effect on plasma uric acid and urea (19). Another researcher stated that grape seed treatment has no effect on creatinine and urea concentration in both control and different concentration of grape seed groups (7).

3-The effect of grape seed on serum LH, FSH, prolactin, and testosterone hormones level in adult mice. Levels of LH, FSH, and testosterone hormones were improved significantly ($p<0.05$) in the grape seed group in comparison with the control group. While prolactin concentration had no significant change between both the grape seed and control groups. By decreasing nitric oxide synthase activity, the grape seed reduced nitric oxide (NO) invasion of the testis (20).

Additionally, grape seed has been shown to reduce the death of germ cells brought on by the contortion or twist of the testicles (20). According to studies, grape seeds contain significant levels of flavonoid anthocyanin oligomers. This substance boosts intracellular vitamin C levels and removes free radicals from the body (21, 22). The scientist found that Coco's extraction can also affect positively sperm concentration (23).

By reducing oxidative stress and testicular apoptosis, grape seed therapy can mitigate the harmful effects of a high-fat diet on the testicles. These studies offer crucial insights into the use of grape seed in treating high-fat diet-induced testicular dysfunction.

grape seed may be a viable and innovative therapeutic medication for male reproductive dysfunction brought on by obesity (24). According to the results of our investigation, grape seed extract can boost male reproductive hormones without having a negative impact on the liver or kidneys.

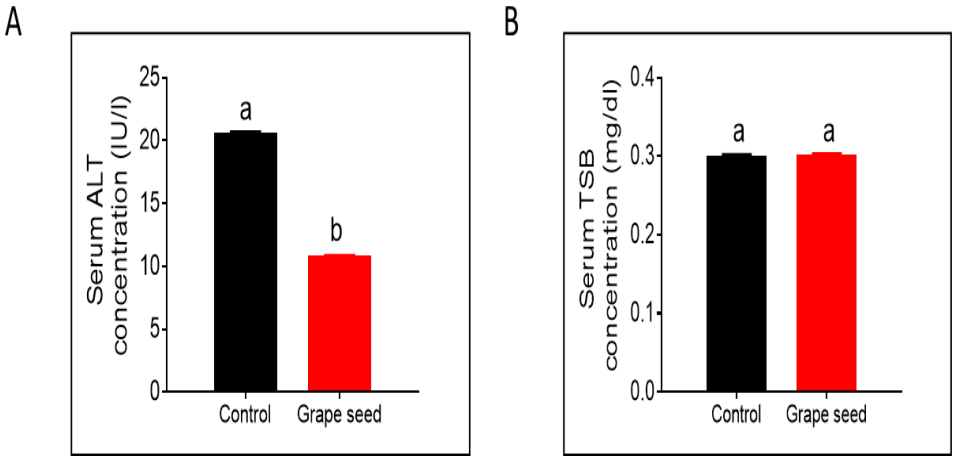

Figure 1: Grape seed effects on liver function in mice. Grape seed was administered intraperitoneal injection for 7 days interval. A: Serum Alanine aminotransferase (20). B: Total serum bilirubin (TSB) concentration. Vertical bars show data from 10 mice with Mean+/-SEM. Statistical significances are depicted as b $P<0.05$ between the groups

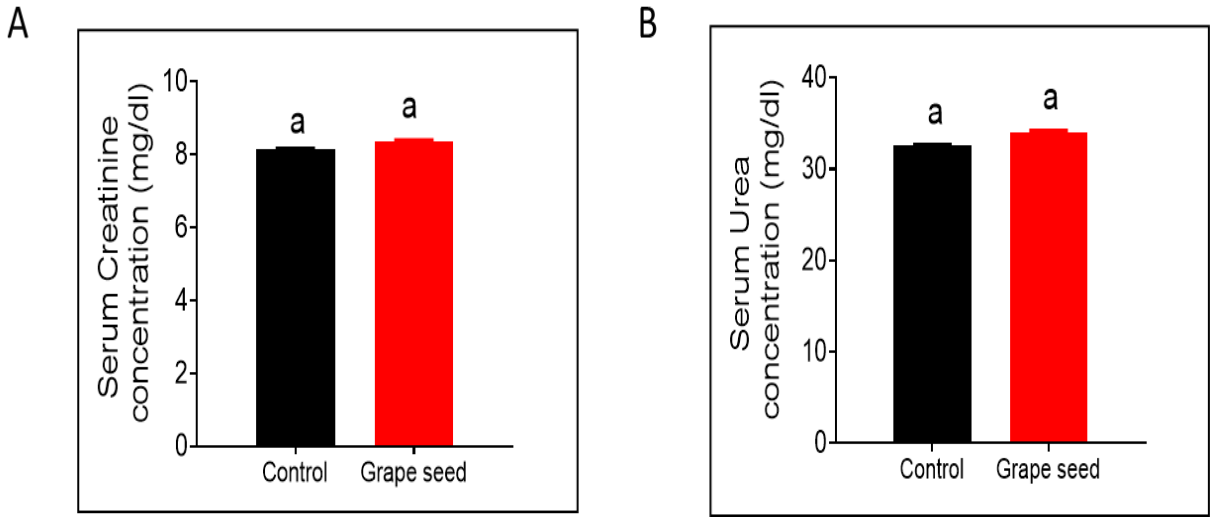

Figure 2: Grape seed effects on kidney function in mice. Grape seed was administrated intraperitoneal injection for 7 days interval. A: Serum creatinine concentration. B: Serum urea concentration. Vertical bars show data from 10 mice with Mean+/-SE-M. Statistical significances are depicted as b P<0.05 between the groups.

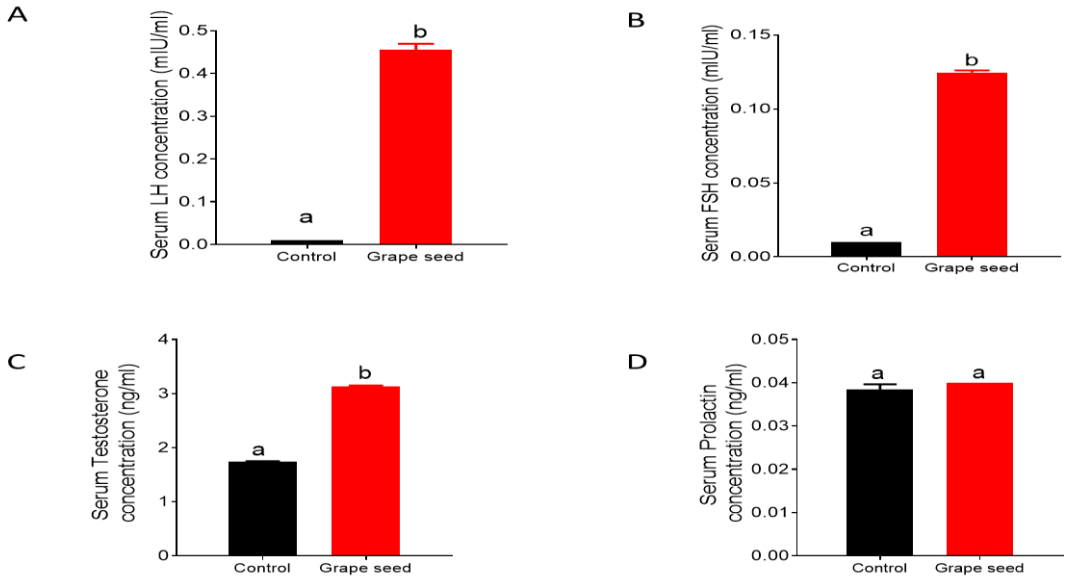

Figure 3: Grape seed effects on male reproductive hormones function in mice. Grape seed was administered intraperitoneal injection for 7 days interval. A: Serum levels of the luteotropic hormone (LH) B: Serum levels of follicle-stimulating hormone (FSH). C: Serum levels of testosterone (T). D: Serum levels of prolactin. Vertical bars show data from 10 mice with Mean+/-SEM. Statistical significance is depicted as b P<0.05 between the groups.

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تقييم للتأثيرات الفسيولوجية لبذور العنب في اجهزة متعددة

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الخلاصة

مستخلص بذور العنب له العديد من الآثار المفيدة على الجهاز القلبي الوعائي وضغط الدم ، كما ثبت أن له تأثيرات مضادة للسمنة و / أو يحسن أكسدة الأحماض الدهنية واستجابات الأنسولين. الهدف من هذه الدراسة هو تقييم فاعلية مستخلص بذور العنب في بعض المتغيرات الفسيولوجية في اجهزة متعددة. ولهذه الغاية تم حقن ذكور الفئران داخل التجويف البريتوني بجرعة (100 مجم / كجم من وزن الجسم) لمدة 7 أيام في حين تركت مجموعة اخرى بدون اي تدخل علاجي كمجموعة

سيطرة. تم جمع المصل للكشف عن تركيز ALT و TSB (وظائف الكبد). تم قياس تركيز اليوريا والكرياتينين (وظائف الكلى) و تم تقييم تركيز التستوستيرون ، LH ، و FSH (الوظيفة الإنجابية للذكور) عند انتهاء التجربة. أظهرت نتائجنا انخفاضًا معنويًا في تركيز ALT في مجموعة استخلاص بذور العنب مقارنة بمجموعة السيطرة، وكان مستوى البيليروبين الكلي في الدم غير متغير في كل من مجموعة استخلاص بذور العنب ومجموعة التحكم. لم تظهر تراكيز اليوريا والكرياتينين أي تغير معنوي بين مستخلص بذور العنب ومجموعة السيطرة. في حين سجل ارتفاع معنوي في مستويات هرمون التستوستيرون ، LH ، و FSH بشكل ملحوظ في مجموعة استخلاص بذور العنب مقارنة مع مجموعة السيطرة. أظهرت نتائج هرمون البرولاكتين عدم وجود تغيير في كل من مجموعة استخلاص بذور العنب ومجموعة السيطرة. من النتائج اعلاه يمكن ان نستنتج أن مستخلص بذور العنب يمكن أن يحسن هرمونات التكاثر الذكرية دون أي تأثير سام على الكبد أو الكلى.

الكلمات المفتاحية: بذور العنب، الشحمون الخصوي، ذكر الجرذان.