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Original article

Influence of Cinnamon Supplementation on Liver Enzymes in Male Rabbits

Amani Salem[1], Marwa Abdullah[2], Fayrouz Khaled[3]*, Marwa Mohammd[3]

[1]*Department of Biomedical Science, Faculty of Pharmacy, Omar Al-Mokhtar University, El -Beida-Libya*
[2]*Higher Institute of Medical Sciences and Technologies, El -Beida-Libya*
[3]*Department of Chemistry, Faculty of Science, Omar Al-Mokhtar University, El -Beida-Libya*

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Corresponding Email. *fayrouzalzobair@yahoo.com*

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ABSTRACT

The liver, a vital organ in the body, plays a central role in managing the metabolism of both internal and external substances. It is crucial for drug processing and detoxification; however, it is vulnerable to damage from foreign chemicals, alcohol intake, poor nutrition, environmental pollutants, illnesses, and various medications. Besides being commonly used as a spice, the inner bark of cinnamon (Cinnamomum zeylanicum L.) has gained popularity for its applications in disease prevention and treatment. Current evidence has indicated potential health benefits associated with cinnamon intake; however, its effects on liver function remain unclear. Therefore, this systematic review and meta-analysis aimed to investigate the effects of cinnamon supplementation on liver enzymes in male rabbits. Relevant studies were identified through a comprehensive search of PubMed/Medline, Scopus, Web of Science, Cochrane Library, and Embase databases up to September 2023. Ten male New Zealand White rabbits were randomly divided into two groups: (1) a control group, and (2) a group treated with cinnamon at a dose of 200 mg/kg body weight. Blood samples and liver homogenates were used to assess liver function markers in both serum and liver tissue. The results showed that cinnamon treatment led to a significant ($P<0.05$) reduction in the activity of blood plasma and liver enzymes "LDH", "AST", and "ALT", while "ALP" and "AcP" levels significantly ($P<0.05$) increased compared to the control group. Further high-quality studies are necessary, especially in populations with abnormal liver enzyme levels, to more definitively establish the clinical efficacy of cinnamon on liver function.

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INTRODUCTION

Cinnamon bark is one of the most important and commonly used spices globally, valued not only in cooking but also in traditional and modern medicine. The cinnamon genus is widespread, with over 250 identified species found around the world [1]. Because of its scent, which may be added to a wide range of foods, fragrances, and pharmaceutical items, cinnamon is mostly employed in the aroma and essence sectors [2]. Cinnamaldehyde and trans-cinnamaldehyde (Cin), the two most significant components of cinnamon, are found in the essential oil and contribute to both the aroma and the different biological activity associated with cinnamon [3].

Antioxidants protect the body from oxidative damage caused by free radicals, and cinnamon is rich in powerful antioxidants, particularly polyphenols. In a study comparing the antioxidant capacity of 26 spices, cinnamon stood out as the top performer, even surpassing well-known "superfoods" like oregano and garlic. As noted by [4], cinnamon's strong antioxidant properties make it a potential natural food preservative. The medical benefits of cinnamon, which is made from the bark of the Cinnamomum plant, have been extensively researched. These benefits include anti-inflammatory and antioxidant actions. Bioactive substances that help shield cellular processes from oxidative damage, such as cinnamon aldehyde, cinnamic acid, and other polyphenols, are primarily responsible for these qualities. Cinnamon's proven ability to lower oxidative stress, a major contributor to liver damage, has sparked interest in it as a possible therapeutic agent for liver health.

As a crucial indication of liver function, antioxidant properties and liver enzyme modulation, recent research has started to look precisely at how supplements of cinnamon affect liver enzyme activity [5]. Hepatic damage is largely caused by inflammation in the liver, which frequently coexists with oxidative stress. By blocking pro-inflammatory cytokines and enzymes like NF-kB and COX-2, the active ingredients in cinnamon, particularly cinnamon aldehyde, have anti-inflammatory properties. Supplementing with cinnamon has been demonstrated to lower inflammatory indicators in animal models, such as rabbits, and this is correlated with stable liver enzyme levels. This implies that cinnamon offers a two-pronged strategy for maintaining liver function since its anti-inflammatory properties enhance its antioxidant properties [6]. The primary objective of this study is to evaluate the effects of cinnamon supplementation on liver enzyme activity in male rabbits. This research aims to determine whether cinnamon, known for its antioxidant and anti-inflammatory properties, can positively influence liver function, as indicated by changes in key liver enzymes such as alanine aminotransferase (ALT) and aspartate aminotransferase (AST). Additionally, the research will investigate the optimal dosage range for cinnamon supplementation to maximize benefits while minimizing any potential risks associated with its use. This study examined the impact of cinnamon on the biochemical parameters of male rabbits.

METHODS

Study setting

The cinnamon used in the study was obtained from the public herbal market in Al-Bayda city. Six-month-old adult male New Zealand White rabbits were selected for the experiment. Each rabbit was housed individually and weighed weekly over a period of 12 weeks. The ten rabbits were randomly divided into two groups of five each: Group I served as the control group with no treatment for 12 consecutive weeks, while Group II received a daily oral dose of cinnamon at 400 mg/kg body weight over the same period [7].

Experiment

Blood enzyme activity and biochemical parameters Samples of blood were promptly put on ice. Samples were centrifuged at 860 xg for 20 minutes to produce plasma, which was then kept at -20°C until it was needed for analysis. The plasma glucose concentrations in stored plasma samples were measured based on a validated analytical technique as described in a previous study [8]. This method utilized enzymatic reactions coupled with spectrophotometric detection to ensure accurate quantification of glucose levels in the plasma. The activity of plasma aspartate transaminase (AST; EC 2.6.1.1) and alanine transaminase (ALT; EC 2.6.1.2) was determined using a colorimetric assay outlined in prior research [9]. This assay relies on the catalytic actions of AST and ALT on their respective substrates, resulting in the formation of measurable products that indicate enzyme activity.

The alkaline phosphatase (ALP; EC 3.1.3.1) activity in plasma was assessed using a specific biochemical methodology documented in earlier studies [10]. The approach involved the enzymatic hydrolysis of a phosphate-containing substrate under alkaline conditions, producing a detectable chromogenic product.

The activity of acid phosphatase (AcP; EC 3.1.3.2) in plasma was evaluated through a standardized technique reported in the literature [11]. This procedure measured the enzymatic hydrolysis of a phosphate substrate in an acidic medium, leading to the production of quantifiable end-products.

The lactate dehydrogenase (LDH; EC 1.1.1.27) activity was measured using a well-established statistical and biochemical analysis [12]. This method employs a spectrophotometric assessment of the conversion of lactate to pyruvate, which is coupled to a secondary reaction for improved sensitivity and reliability.

Statistical analysis

Where applicable, statistical analyses were conducted using Minitab software (version 17) and GraphPad Prism 8. The significance of differences among groups was evaluated using ANOVA analysis, followed by Tukey's multiple

comparison test for post hoc analysis. The normality of data distribution was confirmed prior to analysis, with statistical significance set at a threshold of $P < 0.05$ to ensure rigorous interpretation of results.

RESULTS

The results presented in tables 1 and 2, alongside Figures 2–11, illustrate the influence of cinnamon supplementation on various plasma biochemical parameters and testicular enzyme activities in male rabbits. The study focuses on liver-associated enzymes—lactate dehydrogenase (LDH), aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP), and acid phosphatase (AcP)—to assess the impact of cinnamon on liver function and overall metabolic enzyme activity. A significant reduction in LDH, AST, and ALT levels in both plasma and testes was observed, suggesting a protective effect of cinnamon against potential hepatocellular damage and oxidative stress. Plasma Biochemistry (Table 1 and Figures 1-5).

Table 1 shows a statistically significant decrease in plasma LDH, AST, and ALT levels in the cinnamon-treated group compared to the control ($p < 0.05$), indicated by the differing superscripts. Specifically, LDH levels dropped from 730 ± 21.0 U/L in the control group to 644 ± 20.2 U/L in the cinnamon group. Similarly, AST and ALT also showed a reduction, with AST decreasing from 43.3 ± 1.03 U/L to 40.2 ± 0.74 U/L and ALT from 45.4 ± 0.71 U/L to 41.5 ± 1.08 U/L. This reduction in enzyme levels may indicate that cinnamon has a hepatoprotective effect, possibly due to its antioxidant properties, which help prevent oxidative stress-induced liver damage. On the other hand, plasma ALP and AcP levels showed an opposite trend, with ALP and AcP levels rising significantly in the cinnamon group. ALP increased from 145.2 ± 3.74 U/L to 162.8 ± 6.08 U/L, while AcP rose from 19.26 ± 0.22 U/L to 21.52 ± 0.43 U/L. This increase could be associated with an adaptive response or enhanced enzyme synthesis as part of a metabolic regulatory process in response to cinnamon's bioactive compounds.

In the testicular homogenates, the results in table 2 indicate that cinnamon supplementation led to substantial reductions in LDH, AST, and ALT levels, similar to the plasma findings (Table 2 and Figures 6-10). Testicular LDH decreased from 548.3 ± 4.03 IU/gT in the control to 280.1 ± 4.2 IU/gT in the cinnamon group, while AST and ALT were reduced from 66.6 ± 0.99 IU/gT and 48.8 ± 1.66 IU/gT to 46.3 ± 1.82 IU/gT and 25.3 ± 1.66 IU/gT, respectively. The sharp decrease in these enzymes may suggest that cinnamon's antioxidant properties extend to the testes, reducing cellular damage or stress in testicular tissue. Conversely, ALP and AcP activities in the testes increased significantly in the cinnamon group, with ALP rising from 92.3 ± 1.66 IU/gT to 109.3 ± 3.63 IU/gT and AcP from 53.6 ± 1.53 IU/gT to 71.3 ± 0.72 IU/gT. The increase in ALP and AcP might indicate enhanced testicular metabolic activity, potentially stimulated by cinnamon's bioactive compounds. This elevation in enzyme levels may also relate to tissue-specific responses that differ between liver and testes, reflecting complex interactions influenced by cinnamon supplementation. The overall data suggest that cinnamon supplementation has a protective effect on liver function, as shown by the reduced levels of liver enzymes LDH, AST, and ALT, indicating potentially decreased hepatic stress. The increase in ALP and AcP across both plasma and testes could suggest tissue-specific metabolic activation or a regulatory response, possibly associated with cinnamon's stimulatory effects on cellular metabolism. Further studies are needed to clarify these findings and explore the mechanisms by which cinnamon influences both liver and testicular tissues, particularly regarding enzyme modulation and its broader implications for metabolic health.

Table 1. The average plasma in male rabbits given cinnamon

Animal Groups	Lactate dehydrogenase	Aspartate transaminase	Alanine transaminase	Alkaline phosphatase	Acid phosphatase
Control "Mean±SE"	730 ± 21.0^{b}	43.3 ± 1.03^{b}	45.4 ± 0.71^{ab}	145.2 ± 3.74^{b}	19.26 ± 0.22^{b}
Cinnamon "Mean±SE"	644 ± 20.2^{c}	40.2 ± 0.74^{c}	41.5 ± 1.08^{c}	162.8 ± 6.08^{a}	21.52 ± 0.43^{a}

Five rabbits' mean ± SE is used to express the data. At $p<0.05$, the means with distinct superscripts (a, b, c, or d) within each row differed substantially. A substantial difference is not there ($p>0.05$) when means superscripts with the same letters are present".

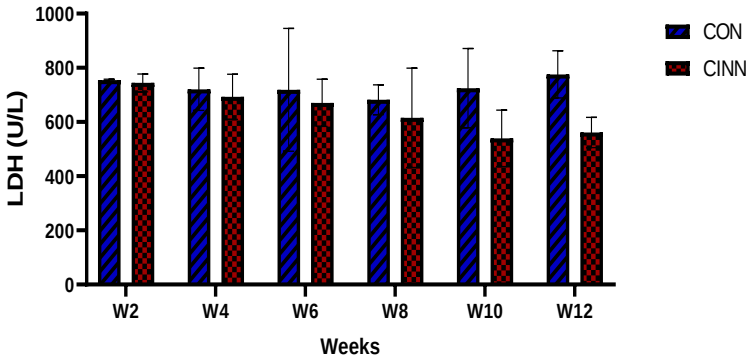

Figure 1. Alterations in lactaaate dehydrogenase "LDH" when male rabbits are given cinnamon.

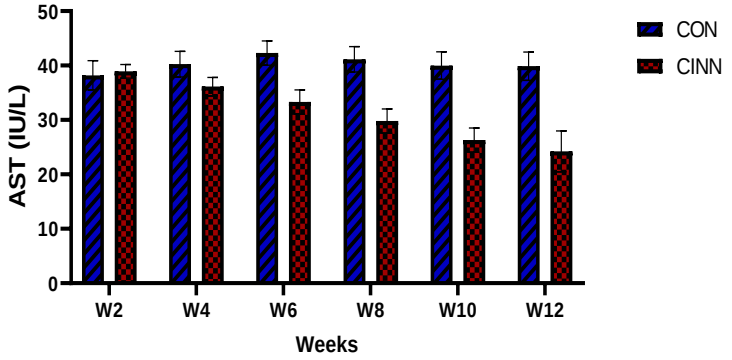

Figure 2. Alterations in aspartate transaminase "AST" when male rabbits are given cinnamon.

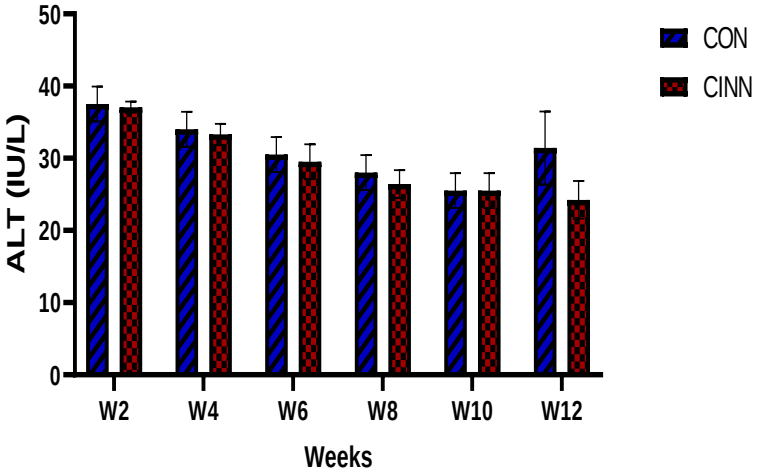

Figure 3. Alterations in alanine transaminase "ALT" when male rabbits are given cinnamon.

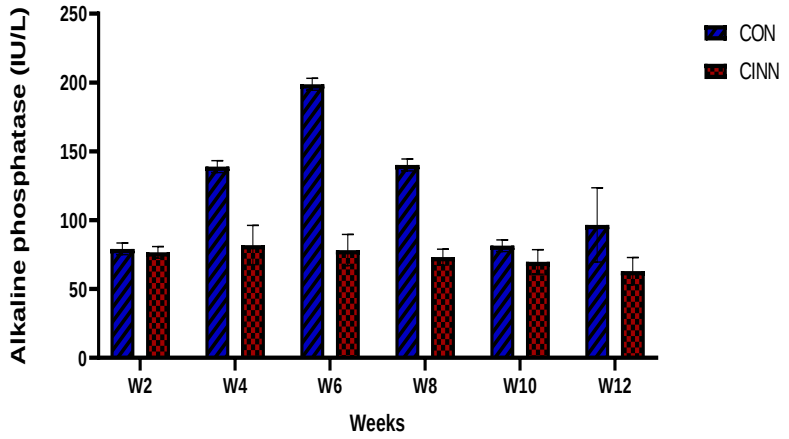

Figure 4. "Alterations in alkaline phosphatase "ALP" when male rabbits are given cinnamon".

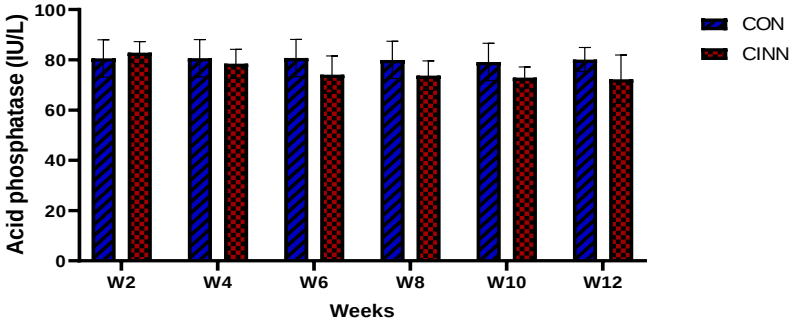

Figure 5. Alterations in acid phosphatase "AcP" when male rabbits are given cinnamon.

Table 2. The average testicular homogenates in male rabbits given cinnamon

Animal Groups	Lactate dehydrogenase	Aspartate transaminase	Alanine transaminase	Alkaline phosphatase	Acid phosphatase
Control "Mean±SE"	548.3±4.03^{b}	66.6±0.99^{b}	48.8±1.66^{c}	92.3±1.66^{b}	53.6±1.53^{b}
Cinnamon "Mean±SE"	280.1±4.2^{c}	46.3±1.82^{c}	25.3±1.66^{d}	109.3±3.63^{a}	71.3±0.72^{a}

Five rabbits' mean ± SE is used to express the data. At $p<0.05$, the means with distinct superscripts (a, b, c, or d) within each row differed substantially. A substantial difference is not there ($p>0.05$) when means superscripts with the same letters are present.

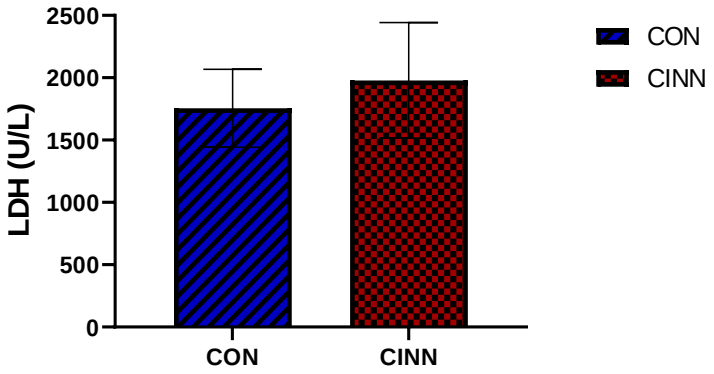

Figure 6. Alterations in lactate dehydrogenase "LDH" when male rabbits are given cinnamon.

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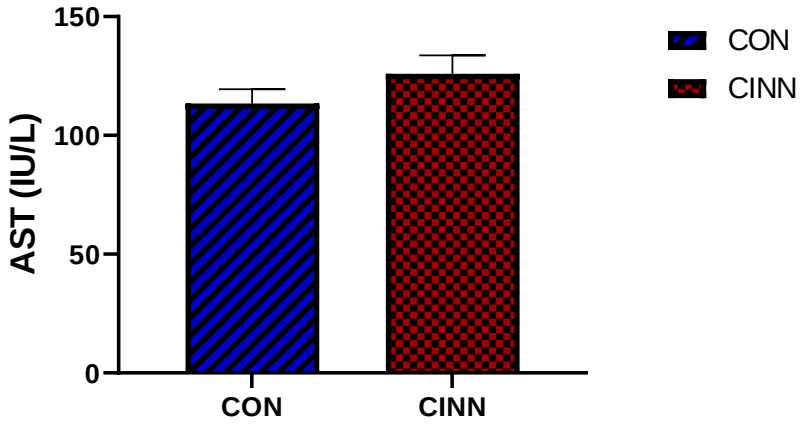

Figure 7. Alterations in aspartate transaminase "AST" when male rabbits are given cinnamon.

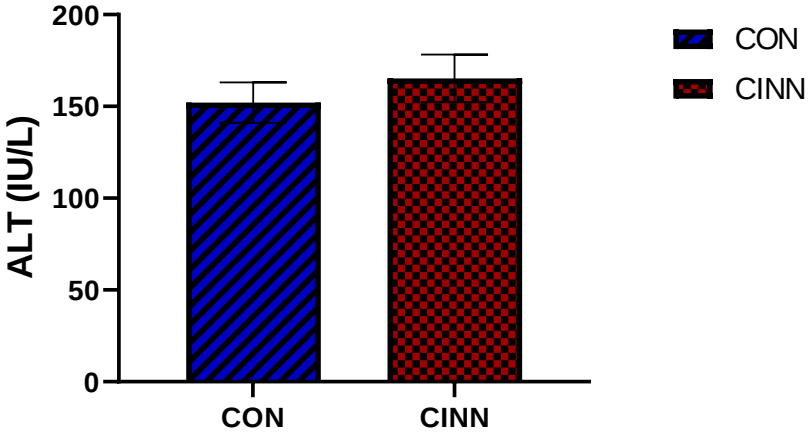

Figure 8. Alterations in alanine transaminase "ALT" when male rabbits are given cinnamon.

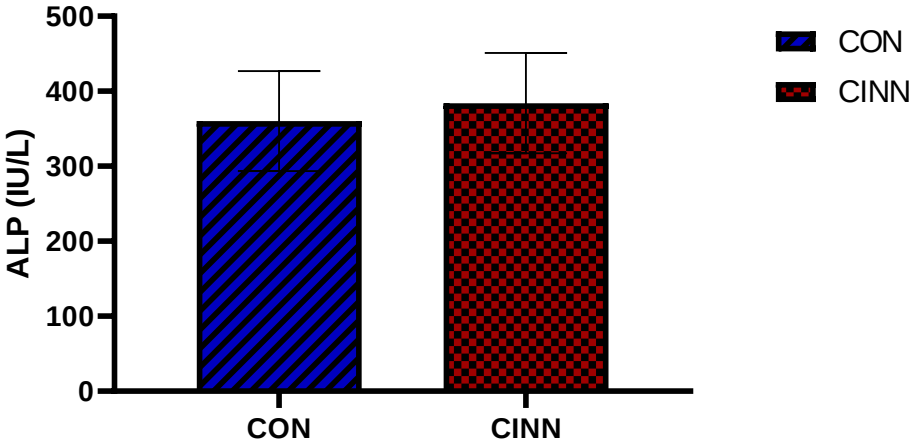

Figure 9. Alterations in alkaline phosphatase "ALP" when male rabbits are given cinnamon.

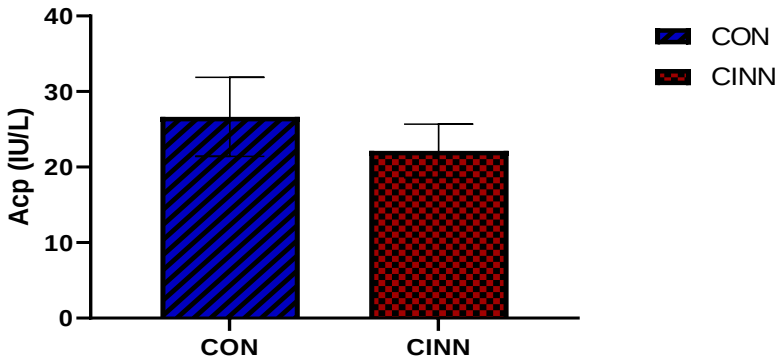

Figure 10. Acid phosphatase "Acp" alterations in male rabbits treated with cinnamon.

DISCUSSION

This study demonstrates that cinnamon supplementation can influence liver enzyme activities in male rabbits, suggesting potential hepatoprotective effects. Liver enzymes, such as LDH, AST, and ALT, are essential markers of hepatic function and cellular integrity. The observed reduction in LDH, AST, and ALT levels in the cinnamon-supplemented group indicates that cinnamon may mitigate liver stress. This effect is likely due to cinnamon's antioxidant components, including cinnamaldehyde and polyphenols, which combat oxidative damage and help prevent hepatocellular injury.

A previous study [13] reported similar protective effects, highlighting the role of antioxidant-rich plant extracts in reducing oxidative stress and maintaining cellular integrity in hepatic tissues. The anti-inflammatory properties of cinnamon also appear to contribute to its effects on liver enzyme activity. Inflammatory processes in the liver often result in elevated enzyme levels, a common response in cases of liver injury.

Compounds found in cinnamon, particularly cinnamic acid and cinnamaldehyde, have demonstrated the ability to inhibit pro-inflammatory cytokines, thereby reducing inflammation and preserving liver function. The observed reduction in AST and ALT levels in this study aligns with findings by a related investigation [14], which documented decreased liver enzyme activity following the administration of natural anti-inflammatory agents. These findings further support the notion that cinnamon reduces hepatic inflammation and cellular damage.

The increase in ALP and AcP activities in cinnamon-supplemented rabbits may indicate enhanced metabolic activity or an adaptive response to cinnamon's bioactive compounds. While ALP elevation is not typically associated directly with liver injury, it can reflect changes in biliary function or metabolic adaptations. This observation is consistent with previous research [15], which demonstrated that certain plant extracts could simultaneously lower markers of liver stress while increasing phosphatase levels, suggesting a metabolic shift in response to phytochemical intake. One important consideration in this study is the dosage of cinnamon used. Excessive amounts of cinnamon can lead to adverse effects, such as coumarin-induced hepatotoxicity.

Research emphasizes that moderate doses, such as those employed in this study, are effective in harnessing cinnamon's beneficial effects while minimizing toxicity risks. As noted in earlier work [16-19] on medicinal plant dosages, there is often a dose-dependent effect, where low to moderate levels of antioxidants or anti-inflammatory agents provide protection, but high doses may induce cellular toxicity. Overall, this study suggests that cinnamon supplementation may play a protective role in liver health through its antioxidant and anti-inflammatory properties. The changes in liver enzyme levels observed in this study align with the existing body of literature regarding the hepatoprotective effects of natural plant compounds. Future research should focus on refining the optimal dosage and elucidating the molecular mechanisms underlying cinnamon's therapeutic effects to maximize its potential benefits for liver health.

CONCLUSION

Overall, the antioxidant and anti-inflammatory qualities of cinnamon have a protective impact on male rabbits' liver function. Cinnamon may help preserve liver function under stress, according to the regulation of liver enzymes, especially AST and ALT. To guarantee effectiveness and safety, more study is needed to ascertain the ideal dosage and long-term consequences of supplementing rabbits with cinnamon. The promise of cinnamon as a natural supplement for liver health is highlighted by this study, but it also emphasizes how crucial dose control is.

Conflict of interest. Nil

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تأثير مكملات القرفة على إنزيمات الكبد لدى الأرانب الذكور

أماني محمد سالم[1] ,مروة جمعة عبدالله[3]، فيروز الزبير خالد[3] ,مروة سالم محمد

[1]قسم العلوم الطبية, الحيوية كلية الصيدلة, جامعة عمر المختار, البيضاء, ليبيا
[2]المعهد العالي للعلوم الطبية والتكنولوجيا , البيضاء, ليبيا
[3]قسم الكيمياء, كلية العلوم, جامعة عمر المختار, البيضاء, ليبيا

المستخلص

يلعب الكبد، وهو عضو حيوي في الجسم، دورًا محوريًا في إدارة عملية التمثيل الغذائي للمواد الداخلية والخارجية. وهو أمر بالغ الأهمية لمعالجة الأدوية وإزالة السموم؛ ومع ذلك، فهو عرضة للتلف الناتج عن المواد الكيميائية الغريبة، وتناول الكحول، وسوء التغذية، والملوثات البيئية، والأمراض، والأدوية المختلفة. بالإضافة إلى استخدامه بشكل شائع كتوابل، اكتسب اللحاء الداخلي للقرفة شعبية لتطبيقاته في الوقاية من الأمراض وعلاجها. أشارت الأدلة الحالية إلى فوائد صحية محتملة مرتبطة بتناول القرفة؛ ومع ذلك، لا تزال آثارها على وظائف الكبد غير واضحة. لذلك، تهدف هذه المراجعة المنهجية والتحليل التلوي إلى التحقيق في آثار مكملات القرفة على إنزيمات الكبد لدى الأرانب الذكور. تم تحديد الدراسات ذات الصلة من خلال بحث شامل في عدة قواعد بيانات حتى سبتمبر 2023. تم تقسيم عشرة أرانب بيضاء من نيوزيلندا بشكل عشوائي إلى مجموعتين: (1) مجموعة تحكم، و(2) مجموعة عولجت بالقرفة بجرعة 200 ملغ. ملجم/كجم من وزن الجسم. تم استخدام عينات الدم ومتجانسات الكبد لتقييم علامات وظائف الكبد في كل من المصل وأنسجة الكبد. أظهرت النتائج أن علاج القرفة أدى إلى انخفاض كبير ($P<0.05$) في نشاط بلازما الدم وإنزيمات الكبد "LDH" و"AST" و"ALT"، بينما ارتفعت مستويات "ALP" و"AcP" بشكل كبير ($P<0.05$) مقارنة بمجموعة التحكم. هناك حاجة إلى مزيد من الدراسات عالية الجودة، وخاصة في السكان الذين يعانون من مستويات غير طبيعية من إنزيمات الكبد، لتحديد الفعالية السريرية للقرفة على وظائف الكبد بشكل أكثر دقة".

الكلمات المفتاحية. القرفة، انزيمات الكبد، ارانب.