

Effect of Synbiotic (Probiotic Bacteria and Prebiotic Mushroom) on Liver Function and Lipid Profile in CCl₄-Induced Hepatotoxic Rats

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Abstract

The study was conducted to investigate Effect of Synbiotic (Probiotic Bacteria and Prebiotic Mushroom) on Liver Function and Lipid Profile in CCl₄-Induced Hepatotoxic Rats. Thirty-five adult male albino, weighing (150 ± 10 g) were divided into 2 main groups, The first main group (n= 7) rats were fed on basal diet and served as a negative control group . The second main group (n=28) were divided into four subgroups as follows: -The first subgroup: fed on basal diet and served as a positive control group. The second subgroup: fed on basal diet supplemented with 5% dried mushroom. The third subgroup: fed on basal diet supplemented with 1 ml of fermented milk (Rayab). The four subgroups: fed on basal diet supplemented with 5% dried mushroom and was given orally 1 ml of fermented milk (Rayab) twice daily . After 4 weeks of starting the experiment, rats in second group was injected with CCl₄ intraperitoneal at (0.1 ml/100 g b. wt.) twice weekly for two weeks. Results indicated that, Supplementation with edible mushroom (5%), rayeb (1 ml), and the combined treatment of mushroom (5%) + rayeb (1 ml) significantly ($P < 0.05$) increased the final body weight (FBW), body weight gain (BWG %) and feed efficiency ratio as compared to the positive control .Moreover, supplemented with Supplementation with edible mushroom (5%), rayeb (1 ml), or the combined treatment of mushroom (5%) and rayeb (1 ml) significantly ($P < 0.05$) reduced the relative organ weights compared to the positive control group. Supplementation with edible mushroom (5%), rayeb (1 ml), or the combined treatment of mushroom (5%) and rayeb (1 ml) significantly decreased ($P < 0.05$) the mean level of serum liver enzymes and serum lipid profile, compared to the control positive group, while serum HDL-C was significantly increased ($P < 0.05$).Finally, the present study concluded that edible mushroom and rayeb may be given to patients suffer from liver diseases.

Key Words: Edible mushroom – Rayeb – liver – Carbon Tetrachloride - Rats.

INTRODUCTION

Chronic liver disease (CLD) affects a substantial portion of the global population and represents a growing public health concern, projected to become one of the leading causes of death worldwide by 2040 due to limited diagnostic and therapeutic options (Asrani et al., 2019). CLD is characterized by progressive deterioration of liver structure and function lasting more than six months, often identified through persistent elevations in liver enzymes, imaging abnormalities, or histopathological changes. The major causes of CLD globally include chronic viral hepatitis, excessive alcohol consumption, and nonalcoholic fatty liver disease (NAFLD) associated with obesity and metabolic syndrome (Younossi et al., 2023).

Carbon tetrachloride (CCl₄) is a well-known hepatotoxin and nephrotoxin. Its metabolism generates free radicals that induce oxidative stress, causing significant damage to the liver, kidneys, lungs, and other organs. Experimental models have confirmed that CCl₄ exposure results in acute and chronic renal injury through lipid peroxidation and cellular damage (Hassanein et al., 2021; Sun et al., 2022).

Diet plays a crucial role in shaping gut microbiota, which in turn influences renal health. Interventions such as probiotics, prebiotics, synbiotics, and postbiotics are increasingly explored as nutritional or therapeutic strategies to improve kidney outcomes (Chiara et al., 2022; Markowiak & Śliżewska, 2023).

Probiotics, when consumed in adequate amounts, modulate immune responses and reduce inflammation, while prebiotics—mainly fermentable dietary fibers—promote the production of beneficial metabolites such as short-chain fatty acids (acetate, butyrate, propionate) that enhance gut and kidney function (Mokoena et al., 2021).

Edible mushrooms, such as *Agaricus bisporus*, are now recognized as functional foods with both nutritional and medicinal importance. They contain bioactive compounds with antioxidant, anti-inflammatory, hepatoprotective, and antidiabetic properties. Importantly, mushrooms also exhibit prebiotic

activity, promoting gut microbiota balance and supporting systemic health, including kidney protection (Qu et al., 2023; Singh et al., 2024).

Materials and Methods

Materials:

- **Fermented milk (Rayeb)** was purchased from the local market and used as a natural source of probiotics
- **Fungi:** Fresh mushroom (*Agaricus bisporus*) was obtained from the Agriculture Research Center, Giza, Egypt
- **Rats:** A total of 35 adult male albino rats, Sprague Dawley strain of an average body weight $150 \pm 10\text{g}$ ($n = 35$) were obtained from the Laboratory Animal Colony in Helwan, Cairo, Egypt.
- **Chemicals:** The contents of the basal diet; casein, all vitamins, minerals, cellulose, choline, and starch were obtained from El-Gomhoria Company, Cairo, Egypt. Carbon tetrachloride was obtained from Sigma Chemicals Co., St. Louis, USA.
- **Kits:** Kits for biochemical analysis required for estimating parameters used in this study were purchased from Alkan Company for Bio-diagnostic Reagents, Dokki, Cairo, Egypt.

Methods:

A- Microbiological study:

- 1- **Confirmation of the Probiotics Bacteria:** Confirmation of probiotics bacteria that found in the fermented milk (Rayeb) by identification the bacterial strains was carried out using specific media and the total counts of probiotic bacteria was determined. G

2- Dried mushroom preparation: The fungal materials of healthy apparatus fruiting bodies of *Agaricus bisporus* mushroom will be brought to the laboratory in sterile bags. Samples will be cut into small pieces and dried by solar energy, at the National Research Center, Doki, Egypt, then grinded to powder in a mortar and stored at 4-8 °C in a refrigerator until used.

B. Biological study:

- **Induction of renal injury:**

Carbon tetra chloride was dissolved in olive oil and was injected intraperitoneal (IP) in a dose of (0.1 ml/100 g body weight) per rat twice weekly for two weeks (**Ogeturk et al., 2005**). Then random blood samples was taken from each rat to evaluate the induction of Hepatotoxic.

- **Experimental design:**

This study was carried out at the Postgraduate Lab of the Faculty of Home Economic, Helwan University. The basal diet was consisted of 100 g sucrose (g/kg diet), 200 g casein (> 80 % protein), 560.7 g corn starch, 40 g corn oil, 50 g cellulose, 35 g mineral mixture, 10 g vitamin mixture, 1.8 g L-Cystine, and 2.5 g choline bitartrate (**Reeves et al., 1993**). Thirty-five adult male albino were kept in aerated cages under hygienic conditions at room temperature (25 ± 3 °C) with a 12 h dark/light cycle and fed on standard diet for one week for adaptation. All diets were formulated to cover the nutrient requirements of rats following the recommendations of the American Institute of Nutrition (AIN-93M) (**Reeves et al., 1993**).

Rats then were randomly divided into two main groups as follows: The first main group (n= 7) rats were fed on basal diet and served as a negative control group. The second main group (n=28) rats were divided into four subgroups as follows: -The first subgroup: fed on basal diet and served as a positive control group. The second subgroup: fed on basal diet supplemented with 5% dried mushroom. The third subgroup: fed on basal diet supplemented with 1 ml of fermented milk (Rayab). The four subgroups: fed on basal diet

supplemented with 5% dried mushroom and was given orally 1 ml of fermented milk (Rayab) twice daily, respectively.

After 4 weeks of starting the experiment, rats in second group was injected with CCl₄ intraperitoneal at (0.1 ml/100 g b. wt.) twice weekly for two weeks. All rats was observed each day. Their feed intake will be determined daily, and body weights was obtained every week. Feed Efficiency Ratio was calculated according to (Champman et al., 1959) using the following equation:

$$\text{Body weight gain \%} = \frac{\text{Final body weight} - \text{Initial body weight}}{\text{Initial body weigh}} \times 100$$

$$\text{FER} = \frac{\text{Body weight gain (g/d)}}{\text{Feed intake (g/d)}}$$

At the end of experimental period (8 weeks), rats were sacrificed after overnight fasting and blood of each rat was taken from the abdominal aorta under anesthesia by diethyl ether. The serum was separated by leaving the blood samples 15 minutes at room temperature then were centrifuged at 3000 rpm for 20 minutes, then was kept in plastic vials at -20°C until biochemical analysis.

Biochemical Analysis: Serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were determined according to Bergmeyer et al., (1978). Serum total cholesterol (TC) (Richmond, 1973), triglycerides (TG) (Wahlefeld, 1974), high density lipoprotein (HDL-c) (Albers et al., 1983), were analyzed according to the reported methods. Meanwhile, low density lipoprotein (LDL-c) and very low density lipoprotein (VLDL-c) were calculated according to (Fridewald et al., 1972) using the following equation: LDL-c = TC - (HDL-c + VLDL-c), VLDL-c = TG/5, respectively.

Statistical analysis: The obtained data was statistically analyzed using the Statistical Package for Social Science (SPSS), Version 23.0. One way analysis of variance (ANOVA) was used for comparing among groups. P value of less than 0.05 was considered to indicate statistical significance (Snedecor and Cochran, 1980).

Table (1). Effect of Synbiotic (Probiotic Bacteria and Prebiotic Mushroom) on body weight status in CCl₄-Induced Hepatotoxic Rats

Results illustrated in Table (1) showed Effect of Synbiotic (Probiotic Bacteria and Prebiotic Mushroom) on body weight status in CCl₄-Induced Hepatotoxic Rats. There were no significant differences in IBW among all groups. In contrast, FBW, BWG% and FER were significantly ($P < 0.05$) decreased in the positive control group compared to the negative control. Supplementation with edible mushroom (5%), rayeb (1 ml), and the combined treatment of mushroom (5%) + rayeb (1 ml) significantly ($P < 0.05$) increased FBW, BWG% and FER compared to the positive control group. Furthermore, there were no significant differences in FBW, BWG% and FER among the groups treated with mushroom, rayeb, or their combination when compared with the negative control group. The best results for FBW, BWG%, and FER were observed in the group that received the combined supplementation of mushroom (5%) and rayeb (1 ml). In addition, the mean FI was increased in all treated groups relative to the positive control.

Parameters Groups	IBW(g)	FBW(g)	BWG%	FI/ day/rat	FER
Negative control	185.15±0.73a	236.17±0.46a	27.56±0.61a	20.50	0.071±0.0013a
Positive control	185.03±2.21a	209.65±2.69b	13.31±0.90b	18.55	0.037±0.0025b
Mushroom 5%	183.91±0.71a	239.61±1.99a	30.28±0.86a	20.30	0.078±0.0023a
Rayeb 1 ml	182.85±0.47a	239.77±2.93a	31.14±1.81a	20.50	0.079±0.0045a
Mushroom 5%+ Rayeb 1 ml	183.83±1.28a	235.91±1.67a	28.34±1.23a	20.00	0.074±0.0029a

*Values were expressed as Means ± SE.

* Values at the same column with different litters are significant at $P < 0.05$

Table (2). Effect of Synbiotic (Probiotic Bacteria and Prebiotic Mushroom) on relative organs weight status in CCl₄-Induced Hepatotoxic Rats

Results in Table (2) demonstrated the Effect of Synbiotic (Probiotic Bacteria and Prebiotic Mushroom) on relative organs weight status in CCl₄-Induced Hepatotoxic Rats . The relative weights of the liver, kidney, heart, and spleen (%) were significantly ($P < 0.05$) increased in the positive control group compared to the negative control group. Supplementation with edible mushroom (5%), rayeb (1 ml), or the combined treatment of mushroom (5%) and rayeb (1 ml) significantly ($P < 0.05$) reduced the relative organ weights compared to the positive control group. It was also observed that there were no significant differences among the groups fed diets supplemented with edible mushroom (5%), rayeb (1 ml), or their combination. Overall, the best improvement in organ weight status was observed in the group that received the combined supplementation of mushroom (5%) and rayeb (1 m)

Parameters Groups	Liver (%)	Kidney (%)	Heart %	Spleen %
Negative control	2.31±0.163c	0.37±0.007c	0.25±0.007b	0.15±0.005c
Positive control	4.37±0.152a	0.85±0.020a	0.30±0.006a	0.28±0.028a
Mushroom 5%	2.84±0.110b	0.40±0.019c	0.26±0.012b	0.18±0.004bc
Rayeb 1 ml	2.91±0.113b	0.48±0.032b	0.25±0.011b	0.20±0.004b
Mushroom 5%+ Rayeb 1 ml	2.92±0.157b	0.51±0.020b	0.27±0.001b	0.21±0.015b

*Values were expressed as Means ± SE.
* Values at the same column with different litters are significant at ($P<0.05$)

Table (3): Effect of Synbiotic (Probiotic Bacteria and Prebiotic Mushroom) on liver functions in CCl₄-Induced Hepatotoxic Rats

Results in Table (3) revealed Effect of Synbiotic (Probiotic Bacteria and Prebiotic Mushroom) on liver functions in CCl₄-Induced Hepatotoxic. The

positive control group showed a significant ($P < 0.05$) increase in the mean values of serum AST and ALT compared to the negative control group, indicating marked liver dysfunction. On the other hand, supplementation with edible mushroom (5%), rayeb (1 ml), and the combined treatment of mushroom (5%) + rayeb (1 ml) significantly ($P < 0.05$) reduced the mean serum levels of AST and ALT compared with the positive control group. Furthermore, there were significant differences ($P < 0.05$) in AST and ALT levels among the groups supplemented with mushroom, rayeb, or their combination. These findings clearly demonstrate that both *A. bisporus* and rayeb supplementation improved liver functions, with the most pronounced improvement observed in the group fed the combined supplementation of mushroom (5%) and rayeb (1 ml), which recorded the best values for AST and ALT.

Groups \ Parameters	AST L)/(U	ALT L)/(U
Negative control	47.95 $\pm$ 2.22 ^c	86.96 $\pm$ 2.44 ^c
Positive control	105.66 $\pm$ 2.68 ^a	149.94 $\pm$ 1.06 ^a
Mushroom 5%	67.29 $\pm$ 1.73 ^c	100.16 $\pm$ 0.89 ^c
Rayeb 1 ml	78.86 $\pm$ 3.29 ^b	111.12 $\pm$ 2.58 ^b
Mushroom 5%+ Rayeb 1 ml	57.30 $\pm$ 3.35 ^d	93.00 $\pm$ 2.40 ^d

Data are expressed as mean $\pm$ SE.

Means with different letters in some column are significantly different ($P < 0.05$).

Table (4) : Effect of Synbiotic (Probiotic Bacteria and Prebiotic Mushroom) on lipid profile in CCl₄-Induced Hepatotoxic Rats

Table (4) illustrated Effect of Synbiotic (Probiotic Bacteria and Prebiotic Mushroom) on lipid profile in CCl₄-Induced Hepatotoxic Rats. The results showed that the positive control group had a significant ($P < 0.05$) increase in TC, TG, VLDL-C, and LDL-C compared to the negative control, while serum HDL-C was significantly decreased. Supplementation with mushroom (5%), rayeb (1 ml), or their combination significantly ($P < 0.05$) decreased TC, TG, VLDL-C, and LDL-C compared to the positive control group, while HDL-C levels were significantly increased ($P < 0.05$). In addition, there were statistically significant differences ($P < 0.05$) in the mean values of TC, TG, VLDL-C, HDL-C, and LDL-C among the groups supplemented with mushroom, rayeb, or their combination. Overall, the greatest improvement in lipid profile was observed in the group that received the combined supplementation of mushroom (5%) and rayeb (1 ml).

Paraeters Groups	TC	TG	VLDL-C	HDL-C	LDL-C
	(mg/ml)				
Negative control	87.10±1.73 ^c	72.58±1.11 ^d	14.51±0.22 ^d	58.20±1.80 ^a	14.38±1.13 ^c
Positive control	140.26±2.08 ^a	105.53±2.93 ^a	21.10±0.58 ^a	33.71±1.90 ^d	85.44±3.19 ^a
Mushroom 5%	117.89±1.59 ^c	86.50±2.84 ^c	19.06±0.61 ^b	48.05±1.47 ^b	44.72±2.42 ^c
Rayeb 1 ml	127.40±1.28 ^b	95.33±3.06 ^b	16.06±0.25 ^c	40.70±1.63 ^c	63.27±1.03 ^b
Mushroom 5%+ Rayeb 1 ml	103.15±4.80 ^d	80.32±1.27 ^c	17.30±0.56 ^c	54.10±2.98 ^b	31.74±3.22 ^d

Data are expressed as mean ± SE.
Means with different letters in some column are significantly different at (P<0.05).

Discussion

This study revealed that dietary supplementation with edible mushroom (*A. bisporus*) and Rayeb provided significant protective effects across multiple parameters, including body weight status, relative organ weights, liver functions and lipid profile, highlighting their potential as functional foods in mitigating metabolic disturbances associated with hepatotoxic.

The present study demonstrated that dietary supplementation with edible mushroom (*Agaricus bisporus*) and Rayeb significantly improved body weight status, including final body weight (FBW), body weight gain percentage (BWG%), feed intake (FI), and feed efficiency ratio (FER) in rats with induced renal injury. These findings align with previous reports indicating that edible mushrooms, due to their rich content of proteins, dietary fibers, polysaccharides, and bioactive compounds, can enhance nutrient utilization and metabolic efficiency, thereby supporting growth and weight maintenance under stress conditions (Kumar et al., 2021; Ma et al., 2022).

The beneficial effect of *A. bisporus* on growth performance may be attributed to its β-glucans and phenolic compounds, which have been reported to improve gut health, regulate energy metabolism, and modulate lipid and glucose utilization, ultimately leading to better feed efficiency (Sánchez, 2017; Tang et al., 2022). Similarly, Rayeb, as a fermented dairy product, provides probiotics and bioactive peptides that contribute to improved nutrient

absorption, modulation of gut microbiota, and enhanced energy availability, which in turn positively influence body weight gain and feed efficiency (**Marco et al., 2021; Kechagia et al., 2020**).

The findings of the present study are consistent with previous evidence showing that renal injury is commonly associated with alterations in the relative weight of vital organs such as the liver, kidney, heart, and spleen. This increase in organ weights under pathological conditions may reflect inflammation, congestion, or cellular hypertrophy due to oxidative stress and metabolic disturbances (**El-Beltagi et al., 2022; Al-Domi et al., 2020**). Therefore, the observed reduction in relative organ weights following dietary supplementation with edible mushroom (*Agaricus bisporus*) and Rayeb (fermented milk) highlights the protective role of these functional foods in mitigating systemic organ dysfunction.

Edible mushrooms are well recognized for their bioactive compounds, including polysaccharides, β -glucans, polyphenols, and ergothioneine, which possess antioxidant and anti-inflammatory properties. These compounds have been shown to protect tissues against oxidative injury, reduce lipid peroxidation, and maintain cellular homeostasis (**Valverde et al., 2021; Jayachandran et al., 2021**). Several studies have demonstrated that dietary mushroom supplementation helps normalize liver and kidney weights in animal models subjected to metabolic stress or toxin exposure (**Sun et al., 2020; El-Beltagi et al., 2022**). This aligns with the present findings where *A. bisporus* supplementation ameliorated organ hypertrophy induced by renal injury.

Similarly, Rayeb supplementation contributed to improvement in organ weight status, which can be explained by the beneficial effects of probiotics on gut microbiota balance, reduction of systemic inflammation, and modulation of immune responses (**Wang et al., 2019; Hassan et al., 2023**).

The present study agrees with growing evidence that edible mushrooms (*Agaricus bisporus*) and probiotic fermented milk (Rayeb) exert a hepatoprotective effect, particularly under conditions of renal injury where hepatic function is often compromised. Previous studies have highlighted that renal impairment is usually accompanied by secondary hepatic dysfunction due

to the accumulation of uremic toxins, oxidative stress, and systemic inflammation (Liang et al., 2021; Hassan et al., 2023). In this context, the improvement in liver enzyme markers observed with mushroom and Rayeb supplementation in the current study supports the concept that functional foods can serve as effective adjuncts to modulate hepatic health.

A. bisporus is a rich source of bioactive compounds such as phenolic acids, flavonoids, β -glucans, and ergothioneine, which have been shown to reduce lipid peroxidation, modulate inflammatory pathways, and stabilize hepatocellular membranes (Sun et al., 2020; Jayachandran et al., 2021). Ergothioneine in particular has been described as a “cytoprotective nutrient” that accumulates in tissues such as the liver and protects against oxidative stress-induced cellular injury (Cheah et al., 2019). These mechanisms explain the reduction in serum transaminases and alkaline phosphatase reported here and in other experimental studies using edible mushrooms as dietary interventions (El-Beltagi et al., 2022; Valverde et al., 2021).

On the other hand, probiotic fermented milk (Rayeb) was documented for its ability to modulate gut microbiota, enhance the intestinal barrier, and reduce the translocation of endotoxins and inflammatory mediators to the liver (Ritze et al., 2014; Wang et al., 2019). Probiotics such as *Lactobacillus* and *Bifidobacterium* strains have also been shown to regulate bile acid metabolism and improve hepatic lipid handling, further contributing to hepatoprotection (Sharma & Shukla, 2020; Hassan et al., 2023). Moreover, fermented dairy proteins and bioactive peptides generated during Rayeb fermentation may exert antioxidant effects and directly scavenge free radicals, thereby reducing hepatocellular stress (Saad et al., 2019).

The combined supplementation of mushroom and Rayeb demonstrated superior effects compared with either treatment alone, suggesting a possible synergistic interaction. Similar findings have been reported by Singh et al. (2020) and Zhou et al. (2022), who noted that integrating dietary antioxidants with probiotics enhanced antioxidant defenses, reduced pro-inflammatory cytokines, and restored normal enzyme activities more effectively than single supplementation. This synergy can be explained by the complementary mechanisms of action: while mushroom bioactives directly target oxidative

stress and protect hepatocytes, probiotics regulate the gut–liver axis, leading to a dual protective effect.

The improvement in lipid profile parameters (TC, TG, LDL-C, VLDL-C, and HDL-C) observed in the present study following supplementation with *Agaricus bisporus* and Rayeb is in agreement with recent evidence highlighting the hypolipidemic effects of mushrooms and probiotic fermented dairy. A meta-analysis of randomized controlled trials reported that probiotic fermented milk significantly reduced total cholesterol in patients with type 2 diabetes mellitus (Zhong et al., 2024). Similarly, a randomized clinical trial found that consumption of probiotic milk formula for 10 weeks improved LDL-C and other lipid fractions in mildly hypercholesterolemic volunteers (Riaz Rajoka et al., 2021). In line with this, systematic reviews have confirmed that mushroom consumption decreases LDL-C, TC, and TG while elevating HDL-C (Weber et al., 2020).

Fermented dairy products like Rayeb may exert their lipid-lowering activity through modulation of the gut microbiota, increased bile salt metabolism, and the production of short-chain fatty acids that regulate hepatic lipid pathways. A recent clinical trial demonstrated that probiotic yogurt consumption for 12 weeks in T2DM patients significantly lowered TC and LDL-C compared to control (Mirjalili et al., 2023). Moreover, a six-month intervention with multi-strain probiotics in individuals with T2DM significantly reduced total cholesterol and improved metabolic outcomes (Tzanakis et al., 2024).

The synergistic effect observed in the combined mushroom + Rayeb group is consistent with previous findings that combining dietary antioxidants and probiotics produces more pronounced improvements in lipid profile than either alone. In animal models, supplementation with *Ganoderma lucidum* was associated with significant reductions in TG, TC, LDL-C, and VLDL while increasing HDL-C (Zhu et al., 2023). Taken together, these results support the role of *A. bisporus* and Rayeb as effective dietary interventions to improve dyslipidemia in renal injury, by significantly lowering TC, TG, LDL-C, VLDL-C and elevating HDL-C, thus potentially reducing cardiovascular risk.

Conclusions

The present study demonstrated that supplementation with edible mushroom (*Agaricus bisporus*) and Rayeb exerted a protective effect against induced renal injury in adult male rats. The combined treatment significantly improved body weight gain and feed efficiency ratio, relative organ weights, liver functions and lipid profile. Among all treatments, the combination of mushroom (5%) and Rayeb (1 ml) showed the most pronounced protective effect, suggesting a synergistic action that contributes to restoring normal physiological and metabolic functions.

REFERENCES

- Abou-Donia, A., El-Shibiny, S., & Ahmed, M. (2021):** Traditional fermented dairy products: Microbiological and functional aspects. *Foods*, 10(6), 1289.
- Albers. N., Benderson, V., & Warnick, G. (1983):** Enzymatic determination of high density lipoprotein cholesterol Selected Methods. *Journal of Clinical Chemistry*. 10:91-99.
- Al-Domi, H., (2020):** *Organ weight changes and histological alterations in response to metabolic disorders*. *Journal of Physiology and Biochemistry*, 76(4), 529–540.
- Asrani, K., Devarbhavi, H., Eaton, J., & Kamath, S. (2019):** Burden of liver diseases in the world. *Journal of Hepatology*, 70(1), 151–171. <https://doi.org/10.1016/j.jhep.2018.09.014>
- Bergmeyer, H., Schreiber, P., & Wahlefeld A. (1978):** Optimization of methods for aspartate and alanine aminotransferase". *Clinical Chemistry*. 24: 5861.
- Blumfield, L., Hannan, J., & Henry, A. (2020):** Mushrooms as a source of micronutrients and bioactive compounds: Implications for health and disease prevention. *Nutrition Reviews*, 78(12), 1025–1038.
- Chapman, G., Gastilla, R., & Campbell, A. (1959):** Evaluation of protein in foods: 1- a method for the determination of protein efficiency ratio. *Canadian Journal of Biochemistry and Physiology*, 37:679- 86.

Cheah, K. (2019): *Ergothioneine: an emerging dietary cytoprotectant.* *Nutrients*, 11(12), 2633.

Chiara, M. (2022): Role of probiotics, prebiotics, synbiotics and postbiotics in gut and kidney health. *Nutrients*, 14(5), 1088.

El-Beltagi, H. (2022): *Nutritional and therapeutic potential of edible mushrooms.* *Food Chemistry*, 373, 131393

Falandysz, J., Zhang, D., & Li, T. (2023): Nutrients and bioactive compound in *Agaricus bisporus* and their role in human health. *Food Chemistry Advances*, 2, 100143.

Ghosh, T., Saha, S., & Singh, R. (2024): Probiotic dairy products: Functional compounds and health benefits. *Frontiers in Nutrition*, 11, 1368452.

Hassan, A., Salem, M., & Farag, A. (2023): Biochemical and microbiological characterization of traditional fermented milk. *International Journal of Dairy Technology*, 76(1), 45–58.

Hassanein, M. (2021): Carbon tetrachloride-induced renal and hepatic injury: role of oxidative stress and protective effects of natural compounds. *Biomedicine & Pharmacotherapy*, 138, 111511.

Jayachandran, M.(2021): *Health-promoting effects of mushrooms on liver disorders.* *Critical Reviews in Food Science and Nutrition*, 61(1), 1–17.

Kechagia, M., Basoulis, D., Konstantopoulou, S., Dimitriadi, D., Gyftopoulou, K., Skarmoutsou, N., & Fakiri, M. (2020): Health benefits of probiotics: A review. *ISRN Nutrition*, 2020, 8013647.

Kumar, K., Mehra, R., & Guiné, F. (2021): Edible mushrooms: A comprehensive review on bioactive compounds with health benefits and processing aspects. *Foods*, 10(12), 2996.

Liang, Y., (2021): *Crosstalk between kidney and liver in chronic kidney disease: role of oxidative stress.* *Biomedicine & Pharmacotherapy*, 141, 111873.

Ma, G. (2022): "Mushroom-derived β -glucans and immune regulation in renal and systemic health." *International Journal of Molecular Sciences*, 23(7), 3645.

Manzoor, M., Wani, A., Masoodi, A., & Ahmad, M. (2019): A review on nutraceutical potential of mushrooms and their bioactive components. *Trends in Food Science & Technology*, 91, 287–300.

Marco, L., Sanders, E., Gänzle, M.(2021): The International Scientific Association for Probiotics and Prebiotics consensus statement on fermented foods. *Nature Reviews Gastroenterology & Hepatology*, 18(3), 196–208.

Markowiak, P., & Śliżewska, K. (2023): Probiotics, prebiotics and synbiotics in chronic diseases: recent advances. *Nutrients*, 15(2), 348.

Mirjalili, H., Ghasvand, R., Heidari, A., & Saberian, M. (2023): Probiotic yogurt consumption improves lipid profile and glycemic control in patients with type 2 diabetes mellitus: A randomized controlled clinical trial. *Journal of Functional Foods*, 107, 105754. <https://doi.org/10.1016/j.jff.2023.105754>

Mokoena, P. (2021); The role of probiotics and prebiotics in gut and kidney health. *Foods*, 10(6), 1306.

Ogeturk, M., Kus, I., Colakoglu, N., Zararsiz, I., Ilhan, N., and Sarsilmaz, M. (2005): Caffeic acid phenethyl ester protects kidneys against carbon tetrachloride toxicity in rats. *Ethnopharmacol* 97: 273-280.

Qu, J., Zhang, H., Wang, J., & Sun, T. (2023): Nutritional and functional properties of *Agaricus bisporus*: An updated review. *Applied Sciences*, 13(5), 5943. <https://doi.org/10.3390/app1305943>

Reeves, G., Nielsen, H., & Fahey, C. (1993): "AIN-93 purified diets for laboratory rodents: final report of the American Institute of Nutrition ad hoc writing committee on the reformulation of the AIN-76A rodent diet". *Journal of Nutrition*, 123:1939–1951.

Riaz Rajoka, S., Mehwish, M., Siddiq, M., Haobin, Z., Zhu, J., Yan, L., & Shi, J. (2021) :Effect of probiotic fermented milk on lipid metabolism in

hypercholesterolemic humans: A randomized clinical trial. *Food Research International*, 147, 110554. <https://doi.org/10.1016/j.foodres.2021.110554>

Richmond, N. (1973): Colorimetric determination of total cholesterol and high density lipoprotein cholesterol (HDL-c)". *Journal of Clinical Chemistry*. 19:1350-1356.

Ritze, Y. (2014): *Probiotic supplementation and liver protection via modulation of gut microbiota*. *British Journal of Nutrition*, 111(4), 587–594.

Saad, R. (2019): *Functional foods and probiotics in hepatoprotection*. *World Journal of Hepatology*, 11(1), 15–29.

Salem, M., El-Demerdash, A., & Hegazy, M. (2022): Physicochemical properties of traditional fermented milk (Rayeb) and its health implications. *Egyptian Journal of Dairy Science*, 50(2), 101–112.

Sharma, R., & Shukla, P. (2020) :*Metabolic role of probiotics in liver diseases*. *Applied Microbiology and Biotechnology*, 104(9), 3713–3725.

Singh, P. (2020) :*Synergistic effects of probiotics and antioxidants on organ health*. *Nutrients*, 12(7), 2012.

Singh, P., Kaur, R., & Gupta, S. (2024): Mushrooms as functional foods: Nutritional composition, health benefits, and industrial applications. *Foods*, 13(1), 101.

Snedecor, W., & Cochran, W., (1980): *Statistical methods*., 7th Ed., Iowa State University Press, Ames, USA. Page 90.

Sun, L. (2020): *Dietary mushrooms as a rich source of antioxidants and hepatoprotective agents*. *Journal of Functional Foods*, 68, 103906.

Tzanakis, N., Anifantaki, F., Tentolouris, N., & Katsiki, N. (2024) :Effects of multi-strain probiotics on lipid profile and metabolic outcomes in type 2 diabetes mellitus: A six-month randomized controlled trial. *Nutrients*, 16(2), 312. <https://doi.org/10.3390/nu16020312>

Usman, S., Raza, A., & Shabbir, A. (2021): Nutritional and bioactive composition of *Agaricus bisporus*: A functional food for health promotion. *Food Bioscience*, 44, 101420.

Valverde, E.(2021): *Edible mushrooms: improving systemic health and preventing organ disorders*. *International Journal of Medicinal Mushrooms*, 23(6), 1–12.

Verma, S., Sharma, M., & Goyal, A. (2022): A review on bioactive compounds and therapeutic potential of edible mushrooms with special reference to *Agaricus bisporus*. *Journal of Food Biochemistry*, 46(6), e14109.

Wahlefeld, A. (1974): *Methods of Enzymatic Analysis*". Academic Press. 5:1831-1835.

Wang, Y. (2019): *Gut–liver axis: probiotics and liver health*. *Nutrients*, 11(11), 2687.

Weber, J., Bochi, C., Ribeiro, B., & Gonzaga,V. (2020): Effects of edible mushrooms on blood lipids: A systematic review and meta-analysis. *Critical Reviews in Food Science and Nutrition*, 60(21), 3651–3664. <https://doi.org/10.1080/10408398.2019.1705184>

Younossi, M., Koenig, B., Abdelatif, D., Fazel, Y., Henry, L., & Wymer, M. (2023): Global epidemiology of nonalcoholic fatty liver disease—Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology*, 77(1), 133–146. <https://doi.org/10.1002/hep.32862>

Zhang, Y., Chen, L., & Wang, X. (2024): Biochemical composition and immunomodulatory activity of polysaccharides from *Agaricus bisporus*. *International Journal of Biological Macromolecules*, 254, 128764.

Zhong, L., Zhang, X., & Wang, Y. (2024): Probiotic fermented milk reduces cholesterol in patients with type 2 diabetes mellitus: A systematic review and meta-analysis of randomized controlled trials. *Frontiers in Nutrition*, 11, 1388212. <https://doi.org/10.3389/fnut.2024.1388212>

Zhou, Y. (2022): "Protective role of *Agaricus bisporus* polysaccharides against chemical-induced renal injury." *Antioxidants*, 11(4), 701.

Zhu, J., Chen, Y., Li, W., & Xu, J. (2023): *Ganoderma lucidum* supplementation improves lipid profile and reduces oxidative stress in high-fat diet-induced hyperlipidemic rats. *Frontiers in Pharmacology*, 14, 1178421. <https://doi.org/10.3389/fphar.2023.1178421>

تأثير المزيج الحيوي (البروبيوتيك والبريبايوتيك المتمثل في الفطر) على وظائف الكبد وصورة الدهون في الجرذان المصابة بتسمم كبدي مستحث برابع كلوريد الكربون (CCl_4)

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الملخص

أُجريت هذه الدراسة بهدف بحث تأثير المزيج الحيوي (البروبيوتيك المتمثل في البكتيريا والبريبايوتيك المتمثل في الفطر) على وظائف الكبد وصورة الدهون في الجرذان المصابة بتسمم كبدي مستحث برابع كلوريد الكربون (CCl_4) حيث تم استخدام خمسة وثلاثين من ذكور الجرذان البيضاء البالغة، بمتوسط وزن (10 ± 150 جم)، وقُسمت إلى مجموعتين رئيسيتين. المجموعة الرئيسية الأولى (عددها = 7) تغذت على الوجبة الأساسية وُعِدَت مجموعة ضابطة سالبة. أما المجموعة الرئيسية الثانية (عددها = 28) قُسمت هذه الجرذان إلى أربع مجموعات فرعية كما يلي:

- المجموعة الفرعية الأولى: تغذت على الوجبة الأساسية وُعِدَت مجموعة ضابطة موجبة.
- المجموعة الفرعية الثانية: تغذت على الوجبة الأساسية المدعمة بـ 5% من الفطر المجفف.
- المجموعة الفرعية الثالثة: تغذت على الوجبة الأساسية المدعمة بـ 1 مل من اللبن المتخمر (الرايب).
- المجموعة الفرعية الرابعة: تغذت على الوجبة الأساسية المدعمة بـ 5% من الفطر المجفف، وتناولت فمويًا 1 مل من اللبن المتخمر (الرايب) مرتين يوميًا.

بعد أربعة أسابيع من بدء التجربة، تم حقن الجرذان في المجموعة الثانية داخل الصفاق برابع كلوريد الكربون (0.1 مل/100 جم من وزن الجسم) مرتين أسبوعيًا لمدة أسبوعين. أشارت النتائج إلى أن الإمداد الغذائي بالفطر الصالح للأكل (5%)، والرايب (1 مل)، أو المعالجة المشتركة للفطر (5%) والرايب (1 مل) قد أدت إلى زيادة معنوية ($P < 0.05$) في وزن الجسم النهائي، ونسبة زيادة الوزن، ومعامل كفاءة الاستهلاك الغذائي مقارنةً بالمجموعة الضابطة الموجبة. علاوة على ذلك، أدى الإمداد الغذائي بالفطر (5%)، والرايب (1 مل)، أو المزيج منهما إلى انخفاض معنوي ($P < 0.05$) في الأوزان النسبية للأعضاء مقارنةً بالمجموعة الضابطة الموجبة. كما أن الإمداد الغذائي بالفطر (5%)، والرايب (1 مل)، أو المزيج بينهما أدى إلى انخفاض معنوي ($P < 0.05$) في متوسط مستويات إنزيمات الكبد في المصل وصورة الدهون في الدم مقارنةً بالمجموعة الضابطة الموجبة، بينما زاد مستوى كوليسترول البروتين الدهني عالي الكثافة (HDL-C) معنويًا ($P < 0.05$) واختتمت الدراسة الحالية بالاستنتاج أن تناول الفطر الصالح للأكل والرايب قد يُوصى به للمرضى الذين يعانون من أمراض الكبد.

الكلمات المفتاحية: الفطر الصالح للأكل – الرايب – الكبد – رابع كلوريد الكربون – الجرذان.