



## The impact of probiotic fortified juices on hepatic function and renal performance in *E. coli* infected laboratory rats

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### Abstract

The current investigation aimed to develop a functional beverage utilizing a blend of orange and pomegranate juices enriched with therapeutic strains of *Lb. acidophilus*, *Lb. plantarum*, and *Lb. rhamanouse*. The study's primary objective was to assess the impact of this probiotic-fortified beverage on the health status of male laboratory rats subjected to *E. coli* bacterial infection, specifically focusing on its influence on hepatic enzyme activities and renal function. Thirty-three male Albino Sprague-Dawley rats were selected for the experiment and were randomly assigned to eleven groups, each with three replicates, to ensure robust statistical analysis. The experiment spanned a duration of 28 days. The findings of this study demonstrated a significant elevation ( $P>0.05$ ) in the concentrations of liver enzymes, including ALT, AST, and ALP, in the group of rats infected with the aforementioned bacteria when compared to the control group. However, noteworthy was the substantial reduction in the levels of these enzymes following oral administration of functional fruit juices in the infected rats. Regarding kidney function parameters, a notable increase in urea and creatinine concentrations was observed in the group of rats afflicted with diarrhea compared to the healthy control group. Nevertheless, the administration of oral doses of functional juices yielded a marked reduction in urea and creatinine concentrations across all treatment groups. These results underscore the potential efficacy of functional fruit juices in mitigating liver enzyme elevation and ameliorating kidney function abnormalities induced by bacterial infection and diarrhea.

**Keywords:** Fruit juice, Probiotic, Prebiotic, Inulin, Liver enzymes, Kidney function.

### Introduction

The concept of functional foods emerged as a marketing terminology in Japan during the late 1980s and has since gained prominence in characterizing food products enriched with ingredients capable of conferring health benefits alongside essential nutrients. This paradigm has garnered increasing popularity among consumers, chiefly driven by a heightened awareness of the intricate interplay between health, nutrition, and dietary choices. Escalating healthcare costs associated with conventional treatments have further prompted consumers to seek alternative, preventative health measures. Additionally, the establishment of specifications and standards for functional foods in various countries has facilitated their widespread availability and accessibility. Notably, a burgeoning body of research has surfaced, substantiating the pivotal role of dietary choices in mitigating the onset of certain diseases. This shift towards a proactive approach to health

underscores the evolving significance of functional foods in contemporary dietary practices (Panel et al., 2001; Kim et al., 2006).

Fermented probiotic beverages are known as functional foods (Kaur et al., 2019). The remarkable impact of this category of food products on human health has attracted significant attention within the scientific community and beyond (Corbo et al., 2014; Irkin, 2019; Misihairabgwi and Cheikhoussef., 2017). Human consumption of fermented beverages dates back many years as part of the daily diet, and constituted the fastest growing segment of the US food market in 2017 (\$1,347 billion) (Vijaya et al., 2015; Taylor, 2016). This is due to its low cost, and at the same time fermentation plays an important role in preserving and enhancing the nutritional value and sensory characteristics of foods (Shori, 2016; Liams et al., 2019). Historically, probiotics for fermented foods found their primary application in dairy products. However, a notable shift has been observed in recent times, with food manufacturers exploring alternative avenues for their

incorporation. As a result, the development of fermented fruit juices emerges as a promising compromise, offering an ideal matrix for probiotic bacteria. The selected strains of probiotic bacteria introduce a diverse array of bioactive compounds into the mix, including vitamins, antioxidants, and amino acids. When integrated into fruit juices, this amalgamation presents a potential synergy, conferring an array of health benefits stemming from both the intrinsic qualities of the juices and the probiotic microorganisms. This innovative approach reflects a dynamic evolution in the utilization of probiotics, expanding their reach into diverse food matrices to cater to an ever-growing demand for functional and health-enhancing food products (Chugh and Kamal., 2020). The consumption of these juices or beverages has been recognized for its multifarious contributions to bolstering heart health while concurrently mitigating sugar and cholesterol levels. Such favorable impacts extend beyond cardiovascular health, encompassing the promotion of a healthy digestive system owing to their substantial fiber content. Moreover, these beverages exert a positive influence on immune defenses, partly attributed to their capacity to generate antibacterial or bacteriocin-like compounds and defensins. They play a pivotal role in modulating intestinal flora dynamics, effectively curtailing the proliferation of disease-causing bacteria, and contributing to alterations in the gut's pH. This multifaceted mechanism includes competition for nutrients, hindrance of intestinal carcinogenesis, attenuation of cholesterol absorption, and the exclusion of pathogenic bacteria, collectively manifesting as a robust and holistic approach to advancing human health through dietary intervention (Yadav and Shukla, 2017). In addition to its activity as antioxidants, cancer prevention, and improving joint function (Hati et al., 2019; Chilton et al., 2015).

### Materials and Methods

**Sensory tests of juices fortified with therapeutic bacteria:** In this study, sensory evaluation was conducted on probiotic juice samples that had undergone fermentation for varying durations and were subsequently stored under refrigeration conditions. The evaluation encompassed a rigorous examination of several sensory attributes, including appearance, flavor, color, taste, and overall acceptability. This comprehensive sensory analysis aimed to provide insights into the dynamic changes that occur in the sensory profile of probiotic juices throughout different stages of fermentation and

cold storage, offering valuable data for assessing the quality and consumer acceptability of these fermented beverages.

**Vital Experiment:** The experimental cohort comprised thirty-three male Albino Sprague-Dawley rats, with an average age spanning 8 to 9 weeks and an average weight ranging from 146 to 148 grams. These animals were meticulously nurtured and maintained within stainless steel cages, ensuring optimal conditions encompassing food accessibility, adequate lighting, ventilation, a stable temperature regimen set at 25 degrees Celsius, and a relative humidity ranging from 45% to 70%. Consistent with prior studies (Messora et al., 2016). the rats were subjected to random allocation into eleven distinct groups, each featuring three replicates, thus fostering a robust experimental framework for comprehensive data analysis and interpretation:

1. C1 Group: This served as the control group, representing the baseline condition for the study.
2. C2 Group: This group consisted of rats that were intentionally infected with *E. coli* bacteria but received no treatment.
3. T1 Group: Rats within this group were subjected to *E. coli* infection and subsequently treated with orange juice enriched with *Lb. acidophilus* bacteria.
4. T2 Group: Similar to the T1 group, rats in this category were infected with *E. coli* bacteria and then treated with orange juice, but enriched with *Lb. plantarum* bacteria.
5. T3 Group: Rats in this group underwent *E. coli* infection and were subsequently treated with orange juice fortified with *Lb. rhamnosus* bacteria.
6. G1 Group: Rats within this group were infected with *E. coli* bacteria and subsequently treated with pomegranate juice fortified with *Lb. acidophilus* bacteria.
7. G2 Group: Similarly, rats in this category were infected with *E. coli* bacteria and treated with pomegranate juice, which was enriched with *Lb. plantarum* bacteria.
8. G3 Group: Rats in this group experienced *E. coli* infection and received treatment with pomegranate juice fortified with *Lb. rhamnosus* bacteria.
9. P1: Group of rats infected with *E. coli* bacteria and treated with *Lb. acidophilus* probiotic.
10. P2: Group of rats infected with *E. coli* bacteria and treated with the probiotic *Lb. plantarum*.
11. P3: Group of rats infected with *E. coli* bacteria and treated with the probiotic *Lb. rhamnosus*.

The experimental design involved inducing diarrhea in the rats through infection with *E. coli* bacteria, followed by therapeutic intervention with daily oral doses of probiotic-fortified juices, administered at a dosage of 2 ml. This treatment regimen was compared to a control group receiving the standard McFarland solution at a rate of  $1.5 \times 10^8$  cells per day. The experiment spanned a duration of 28 days. Subsequent to the conclusion of the 28-day trial, the rats underwent a fasting period lasting 20 hours. Following fasting, the rats were anesthetized using chloroform, facilitating the collection of blood samples for a battery of specific health assessments. The activity levels of liver enzymes, including AST, ALT, and ALP, were quantified utilizing the enzymatic method. This method entailed the application of commercially available assay kits (BIOLABO), originating from France, with calculations performed in accordance with the manufacturer's provided instructions. Additionally, the concentrations of creatinine and urea in the collected blood samples were determined utilizing French-manufactured assay kits (BIOLABO), with adherence to the protocols outlined in (Tietz, 2005).

**Statistical analysis:** Statistical analysis of the data was performed utilizing the pre-established statistical software program (SAS, 2001) employing

a Completely Randomized Design (CRD) framework. To ascertain the significance of differences among the means of factors impacting the assessed traits, the Duncan test (Duncan, 1955) was applied. The level of significance was set at a probability threshold of 0.05, ensuring robust statistical evaluation of the experimental results.

**Results and Discussion**

**Sensory test results:** Tables (1) and (2) presented herein depict the outcomes of the sensory assessment conducted on orange and pomegranate juices fortified with probiotics and inulin. The sensory evaluation findings for orange juice indicated a favorable reception by consumers, surpassing the control sample in terms of taste, color, aroma, flavor, and overall acceptability. Conversely, the sensory evaluation of pomegranate juice likewise revealed a noteworthy level of consumer acceptance, with ratings consistently surpassing those of the control sample across all the aforementioned sensory attributes. These results collectively underscore the enhanced sensory qualities and consumer appeal associated with probiotic and inulin-enriched orange and pomegranate juices.

**Table (1): Sensory Evaluation of Probiotic and Inulin-Enriched Orange Juice**

Treatment	Sensory properties				
	Taste	color	Odor	Flavor	general acceptance
Control	Very good	good	good	Very good	good
A	good	good	good	good	good
B	good	acceptable	good	acceptable	good
C	good	acceptable	acceptable	middle	acceptable

A Orange juice contains inulin and the probiotic *Lb.acidophilus*, B Orange juice contains inulin and the probiotic *Lb.plantarum*, C Orange juice contains inulin and the probiotic *Lb.rhamnosus*

**Table (2): Sensory Evaluation of Probiotic and InulinEnriched Pomegranate Juice**

Treatment	Sensory properties				
	Taste	color	Odor	Flavor	general acceptance
Control	Very good	good	good	Very good	Very good
A	good	acceptable	acceptable	good	good
B	good	acceptable	acceptable	acceptable	acceptable
C	good	acceptable	acceptable	good	good

A Pomegranate juice contains inulin and the probiotic *Lb.acidophilus*, B Pomegranate juice contains inulin and the probiotic *Lb.plantarum*, C Pomegranate juice contains inulin and the probiotic *Lb.rhamnosus*

The process of lactic acid fermentation exhibited no detrimental impact on the sensory qualities of fruit and vegetable juices, maintaining their overall

desirability. Particularly, *Lb. plantarum* emerged as a promising probiotic culture, offering the potential for the production of healthful fruit beverages

catering to vegetarians or individuals with lactose intolerance, as indicated by (Thakur and Joshi, 2017). Furthermore, the supplementation of inulin, as highlighted by (Canbulat and Ozcan, 2015), demonstrated the capacity to augment the flavor profiles of juices, harmonize sweetness levels, and effectively mask any unfavorable tastes within the juice matrix, In agreement with these findings (Alakshar, 2018). reported non-significant differences, at a significance level of 0.05, across all sensory attributes encompassing color, flavor, aroma, and overall acceptance in juices fortified with probiotics when compared to control juices. Intriguingly, the probiotic-fortified juices garnered superior ratings in terms of color and overall acceptability when juxtaposed with their control counterparts, further substantiating the advantageous sensory attributes achievable through probiotic supplementation in fruit and vegetable juices.

**The Impact of Probiotic-Enriched Manufactured Juices on Liver Enzymes Activity in Rats with Induced Diarrhea:** Table (3) presents a comprehensive overview of the impact of oral administration of probiotic-fortified juices on the activity levels of liver enzymes in rats subjected to *E. coli* bacterial infection. Notably, the results within this table reveal a statistically significant escalation in the concentrations of all liver enzymes, including ALT, AST, and ALP, which exhibited values of 262.2,

168.7, and 72.1 international units/liter, respectively. However, it is evident that the administration of fermented juices exerted a substantial and statistically significant influence ( $P>0.05$ ), leading to a marked reduction in the concentrations of all three liver enzymes. Specifically, T1 treatments recorded values of 226, 126.4, and 61.6 international units/liter for ALT, AST, and ALP, respectively, while T2 treatments yielded values of 199.3, 124.9, and 53.31 international units/liter for the corresponding enzymes. Treatment T3 exhibited values of 176.3, 127.3, and 59.45 international units/liter for ALT, AST, and ALP, respectively, while G1 treatments resulted in values of 238.8, 124.6, and 63.65 international units/liter. Treatment G2 showed values of 176.3, 150.9, and 63.6 international units/liter, and G3 treatments registered values of 214.5, 150.5, and 63.9 international units/liter for ALT, AST, and ALP, respectively. In particular, treatment T2 and T3 exhibited pronounced efficacy in reducing the concentration of the ALT enzyme, while G1 treatment excelled in diminishing the levels of AST. Remarkably, treatment T2 stood out for its exceptional impact in reducing the activity of the ALP enzyme, achieving levels as low as 53.31 international units/liter. These findings collectively underscore the substantial ameliorative effects of probiotic-fortified juices on liver enzyme activity in rats afflicted with *E. coli* induced infections.

**Table (3): Effect of Probiotic-Fortified Juices on Liver Enzymes Activity in Rats with Induced Diarrhea**

Treatments	ALT	AST	ALP
	international units/liter		
C1	251.0 a	156.a	62.3 c
C2	262.2 a	168.7 a	72.1 a
T1	226 bc	126.4 bc	61.6 c
T2	199.3 d	124.9 bc	53.3 d
T3	176.3 d	127.3 b	59.5 cd
G1	238.8 b	124.6 bc	63.7 bc
G2	176.3 e	150.9 a	63.6 bc
G3	214.5 cd	150.5 a	63.9 bc
P1	223.2 bc	112.3 c	68.9 ab
P2	253.1 a	136.9 b	70.0 a
P3	233.2 b	134.2 b	64.4 bc

various letters in one column show significant differences at the 0.05 probability level

C1 Control sample, C2 includes rats infected with *E.coli* bacteria, T1 Includes rats infected with *E.coli* bacteria and treated with orange juice to which the probiotic *Lb.acidophilus* is added, T2 Includes rats infected with *E.coli* bacteria and treated with orange juice to which the probiotic *Lb.plantarum* is added, T3 Includes rats infected with *E.coli* bacteria and treated with orange juice to which the probiotic *Lb.rhamnosus* is added, G1 Includes rats infected with *E.coli* bacteria and treated with pomegranate juice to which the probiotic *Lb.acidophilus* is added, G2 Includes rats infected with *E.coli* bacteria and treated with pomegranate juice to which the probiotic *Lb.plantarum*

is added, G3 Includes rats infected with *E.coli* bacteria and treated with pomegranate juice to which the probiotic *Lb.rhamnosus* is added, P1 Includes rats infected with *E.coli* and treated with the probiotic *Lb.acidophilus*, P2 Includes rats infected with *E.coli* and treated with the probiotic *Lb.plantarum*, P3 Includes rats infected with *E.coli* and treated with the probiotic *Lb.acidophilus*

Minelli et al. (2004) elucidated that probiotic bacteria exhibit the capacity to lower the concentration of liver enzymes due to their multifaceted influence on hepatic function, critical physiological processes, and metabolic parameters. Their beneficial effects extend to addressing the root cause behind the elevation of these enzymes while facilitating the restoration of impaired tissues to their normative states. This restorative action manifests as a natural mitigation of enzyme leakage from intracellular compartments into the plasma, serving as compelling evidence of the remediation of underlying damage. Furthermore, these probiotics play a pivotal role in addressing concomitant issues such as elevated cholesterol and fat levels, as well as the preservation of circulatory system integrity within the body. These findings underscore the intricate mechanisms through which probiotics contribute to the preservation of liver health and the overall homeostasis of metabolic processes.

Elevated concentrations of liver enzymes, namely ALT, AST, and ALP, often signify a cascade of metabolic alterations within the liver, leading to toxin generation, inflammatory responses, and consequent liver damage, as elucidated by (Chalasanani et al., 2004).

Remarkably, this study unveils a pivotal role played by probiotic bacteria in the production of diverse biologically active substances, including antibacterial peptides, lysozymes, and digestive enzymes. These biologically active compounds play a multifaceted role in stimulating the development of the host animal's immune system, bolstering its overall performance, fortifying the integrity of the intestinal mucosal barrier, and preserving the equilibrium of the intestinal microbiota. These findings, as expounded by (Zhou et al., 2016). underscore the far-reaching impact of probiotics in ameliorating liver enzyme perturbations by addressing the underlying metabolic imbalances and fortifying the host's immune and gastrointestinal defenses.

#### **The Impact of Probiotic-Enriched Manufactured Juices on Kidney Function in Rats Inducing Diarrhea:**

Table (4) provides a comprehensive insight into the influence of oral administration of probiotic-fortified juices on kidney function, specifically with regard to the concentration of urea and creatinine, in rats afflicted with diarrhea induced by *E. coli* bacterial

infection. The results contained within this table manifest a noteworthy increase in the concentrations of urea and creatinine, registering values of 37.55 and 0.4 dL/mg, respectively, in rats experiencing diarrhea. However, it is evident that treatment with various probiotic formulations exerted a profound and statistically significant effect ( $P>0.05$ ), leading to a substantial reduction in the concentrations of urea and creatinine. Treatment T1 resulted in values of 33.57 and 0.3 dL/mg for urea and creatinine, respectively, while T2 treatments yielded values of 31.38 and 0.3 dL/mg. Treatment T3 exhibited values of 35.64 and 0.3 dL/mg for urea and creatinine, respectively, while G1 treatments registered values of 33.96 and 0.2 dL/mg. G2 treatments showcased a marked reduction in urea concentration, with values at 28.7 dL/mg, whereas G3 treatment yielded values of 30.9 dL/mg for urea and creatinine. Notably, G2 treatment demonstrated a pronounced efficacy in lowering urea concentrations to 28.7 dL/mg, while G1 treatment excelled in reducing creatinine concentrations to 0.2 dL/mg. These findings collectively underscore the significant impact of probiotic-fortified juices in ameliorating kidney function by mitigating urea and creatinine concentrations in rats with diarrhea induced by *E. coli* infection.

**Table (4): Effect of Probiotic-Enriched Manufactured Juices on Kidney Function in Diarrhea-Induced Rats**

Treatments	urea dL/mg	creatinine dL/mg
C1	32.25 c	0.3 a
C2	37.55 b	0.4 a
T1	33.57 bc	0.3 a
T2	31.38 c	0.3 a
T3	35.64 bc	0.3 a
G1	33.96 bc	0.2 a
G2	28.70 d	0.4 a
G3	30.90 cd	0.3 a
P1	30.60 cd	0.3 a
P2	37.30 b	0.2 a
P3	43.00 a	0.3 a

various letters in one column show significant differences at the 0.05 probability level

C1 Control sample, C2 includes rats infected with *E.coli* bacteria, T1 Includes rats infected with *E.coli*

bacteria and treated with orange juice to which the probiotic *Lb.acidophilus* is added, T2 Includes rats infected with *E.coli* bacteria and treated with orange juice to which the probiotic *Lb.plantarum* is added, T3 Includes rats infected with *E.coli* bacteria and treated with orange juice to which the probiotic *Lb.rhamnosus* is added, G1 Includes rats infected with *E.coli* bacteria and treated with pomegranate juice to which the probiotic *Lb.acidophilus* is added, G2 Includes rats infected with *E.coli* bacteria and treated with pomegranate juice to which the probiotic *Lb.plantarum* is added, G3 Includes rats infected with *E.coli* bacteria and treated with pomegranate juice to which the probiotic *Lb.rhamnosus* is added, P1 Includes rats infected with *E.coli* and treated with the probiotic *Lb.acidophilus*, P2 Includes rats infected with *E.coli* and treated with the probiotic *Lb.plantarum*, P3 Includes rats infected with *E.coli* and treated with the probiotic *Lb.acidophilus*

The findings from this study align with observations made by (Sonmez et al., 2015) who reported that elevated blood viscosity can be attributed to elevated levels of cholesterol and triglycerides. This increase in blood viscosity is associated with a multitude of challenges within the circulatory system, including high blood pressure and diminished efficiency in the proper delivery of blood to kidney tissues. Consequently, such circulatory impediments can lead to decreased renal function efficiency, resulting in an increase in urea levels. These concordant results reaffirm the interplay between lipid profiles, circulatory dynamics, and renal function, shedding light on the multifaceted factors contributing to urea concentration variations in the context of kidney health.

The outcomes of this study are in harmony with the findings reported by (Abd El-Hak et al., 2021). reinforcing the notion that the inclusion of probiotic bacteria in dietary interventions elicits a significant reduction in both urea and creatinine levels. Elevated levels of urea and creatinine, as documented in prior research, can be attributed to various factors. These may encompass kidney tissue damage or inherent physiological anomalies impeding renal function, as elucidated by (Al-Obaidi, 2016). Alternatively, heightened urea levels may stem from an increase in the concentrations of free radicals within the body, culminating in oxidative stress. This oxidative stress cascade can lead to the oxidation of proteins and amino acids, with a consequential upsurge in urea levels, as posited by

(Manna et al., 2005). These findings collectively underscore the multifaceted determinants influencing urea and creatinine concentrations and the potential of probiotics to mitigate these markers of renal function.

The findings of this investigation align with observations made by (Kobyliak et al., 2016). supporting the notion that probiotic bacteria possess the capability to generate glucan. This enzymatic activity may contribute to the displacement of amino acids within the intestinal milieu, subsequently leading to a reduction in the synthesis of essential proteins involved in urea production. Consequently, this diminished production results in reduced urea presence within the blood serum of animals. Moreover, the decrement in urea and creatinine concentrations in the blood serum can be attributed, as postulated, to the reduction in cholesterol and triglyceride levels. These lipid parameters are recognized as key contributors to elevated blood pressure and are known to exert adverse effects on kidney function. Thus, the study reinforces the multifaceted mechanisms through which probiotics can influence renal health and markers of kidney function. Notably, probiotics have demonstrated a pronounced ability to engage in the assimilation of cholesterol, effectively obstructing its synthesis within the organism. This cholesterol-assimilating capacity constitutes a pivotal factor in modulating lipid metabolism. Additionally, probiotics exhibit the remarkable capability to utilize urea as a source of nitrogen for metabolic processes. This utilization of urea as a nitrogen source represents a significant contributor to the reduction in urea concentrations observed within the bloodstream. These multifaceted probiotic mechanisms not only contribute to lipid homeostasis but also play a crucial role in regulating nitrogen balance, thereby influencing key markers of renal function such as urea levels within the blood serum.

### Conclusions

In light of the findings from our current study, it is evident that the production of fermented functional juices with both substantial nutritional value and favorable sensory attributes presents a viable and attractive alternative to traditional dairy-based probiotic sources. Moreover, our study revealed that *E. coli*-induced diarrhea resulted in a noteworthy elevation of all liver enzymes, whereas treatment with functional juices brought about a significant reduction in enzyme levels. Additionally, the infection induced an increase in urea and creatinine values, and administration of functional juices led to

a notable decrease in the concentrations of both urea and creatinine, underscoring the potential health benefits of these beverages.

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