Advances in Bioresearch
Adv. Biores., Vol 15 (4) July 2024: 488-495

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.15.4.488495

Advances in Bioresearch

ORIGINAL ARTICLE

Effects of Probiotic Microbe: *Lactobacillus acidophillus* on The Hepatotoxicity Induced by CuoNPs in Swiss Albino Mice

Hansa Chalavariya[1], Neelu Kanwar Rajawat*
[1*]Department of Zoology, IIS (Deemed to be University), Jaipur – 302020, Rajasthan, India. Email: hansachaudhary014@gmail.com
* Corresponding author's Email: neelukanwar.rajawat@iisuniv.ac.in

ABSTRACT
Copper oxide nanoparticles (CuONPs) exhibit antibiotic, antimicrobial, and antifungal properties. They are utilised in conductive inks and pastes as a cost-effective alternative to pricey metals in display electronics and transmissive conductive thin film technologies. CuONPs induce neurobehavioral dysfunction, genotoxicity that varies with the dose, changes in haematological parameters, nephrotoxicity, and liver damage. The primary mechanism underlying the toxicity of most nanoparticles (NPs) is the activation of oxidative stress through the creation of reactive oxygen species (ROS). The bacteria Lactobacillus acidophilus (L. acidophilus), a significant probiotic found in the human intestinal tract, was first discovered in the human gastrointestinal tract and has been extensively researched since its identification in 1900. Lactobacillus acidophilus has been discovered to have significant contributions to various facets of human health. Its acidic nature and bile salt resistance make it highly suitable for use in functional, consumable probiotic formulations, offering wide-ranging application potential. In this study, Swiss albino mice were categorised into four distinct groups: group 1 was given distilled water (vehicle), group 2 was given only probiotic group 3 received CuONPs (80mg/kg body weight), and group 4 was given CuONPs + probiotic. Hepatotoxicity was evaluated by measuring serum parameters including ALT, ALP, and total protein and Oxidative stress was also assessed by certain antioxidant enzymes. CuONP was found to dramatically increase ALT and ALP levels, while decreasing total protein levels. The CuONPs had a significant impact on the oxidative stress as indicated by increased LPO and decreased GPx, SOD, and CAT activity. However, the administration of probiotic Lactobacillus acidophilus, in combination with CuONPS, resulted in the restoration of normal liver serum parameters and an increase in antioxidant enzymes. This indicates that the probiotic has protective effects against CuONPs induced hepatotoxicity.
Keywords*: Nanotoxicology, Nanoparticles, Copper oxide nanoparticles, Antioxidant, Probiotic.*

Received 24.03.2024 Revised 01.05.2024 Accepted 16.07.2024

How to cite this article:
Hansa C, Neelu K R. Effects of Probiotic Microbe: *Lactobacillus acidophillus* on The Hepatotoxicity Induced by CuoNPs in Swiss Albino Mice. Adv. Biores. Vol 15 [4] July 2024. 488-495

INTRODUCTION

Metal nanoparticles (NPs) are widely utilised and play a significant role in the fields including nanotechnologies as well as nanoscience. Nanoparticles (NPs) are utilised throughout various industries, including the medical, scientific, and pharmacological sectors, for applications related to nanotechnology. Nanoparticles are utilised well in medication delivery techniques, enzyme research, surface protective coatings, biological sensors, and diagnosis [1]. Moreover, metallic nanoparticles are employed in medical settings to address metabolic problems, as well as in other industries and common consumer goods, including sunblock, perfume, and skincare. They are widely utilised in the textile sector, food processing, antibiotic synthesis, and electrical components [2]. Due to their growing use, these substances are discharged into the environment, leading to direct exposure to humans [3]. Although nanotechnology offers numerous benefits, its widespread use presents significant health hazards for humans. They infiltrate the body through multiple means. Upon entering the human body, nanoparticles (NPs) disrupt the regular biological processes and result in harm to the kidneys, liver, lungs, and nerves [4]. The liver is located within the upper right quadrant in the abdomen and serves as the crucial organ responsible for detoxifying and the removal of waste products from the circulation. Due to its role as the main organ responsible for detoxification, the liver is highly susceptible to significant damage, even under normal

circumstances [5]. Nanoparticles (NPs) have an impact on several organs, such as the spleen, kidneys, brain, heart, and lungs. Nevertheless, the liver is particularly susceptible to the impact of NPs due to its role in the detoxification of excretory chemical [6].
Copper oxide nanoparticles can also function as a valuable catalyst for combustion in rocket propellants. Copper oxide nanoparticles (CuONPs) have emerged as a prominent category of nanomaterials that pose potential risks to organisms and the environment in several applications, including industrial, chemical, electrical, and medical fields [7]. CuONPs have become significant nanomaterials in various applications and their potential harm to living organisms and the environment has led to increased human exposure due to their wide range of uses [8,9]. "The induction of toxicity by copper oxide nanoparticles (CuO NPs) is primarily attributed to oxidative stress and the production of reactive oxygen species" [10].
Probiotics are live microbial supplements that can be ingested by the host. They exert beneficial impacts on their host by enhancing the microbial equilibrium in the gastrointestinal tract and by regulating the host's immune system [11-13]. Lactic acid bacteria (LAB), a type of bacterium, have been found to regulate hypertension, alter lipid levels as well as hyperglycemia, and to inhibit oxidative damage [14]. Introducing probiotic bacteria, such as LAB strains, into the gastrointestinal system can effectively remove or reduce the harmful effects caused by heavy metals or toxic fungus [15]. The presence of bacterial compounds such as the mannan oligosaccharides or peptidoglycans in the cell wall of these organisms allows the cells to attach to these toxins [16-19]. Certain strains of probiotic bacteria and yeasts, such as *L. rhamnosus, L. plantarum,* and *Saccharomyces cerevisiae*, have the ability to bind to different heavy metals like lead, cadmium, copper, and mercury [8, 2, 20, 21].
Several strains of Lactobacillus have a lengthy track record of being employed in the production of food. The reason behind that is due to Lactobacillus is a bacterium that produces lactic acid and is classified as "generally recognised as safe". Presently, there is a burgeoning interest in utilising it as a nutritional supplement for both people and animals [13]. Bacteria of the genus can be detected in the oral cavity, intestinal tract, and vagina [22, 23, 16]. Lactobacillus spp. has the potential to enhance gastrointestinal health, alleviate allergies, and mitigate liver disease through multiple methods, including the production of metabolites that directly hinder harmful microorganisms, modulation of the immune system, and alteration of the gut microbiota [24-26]. The presence of microbes in the gut has been observed to have an impact on liver disease. The reason for this is that the vein system of portal circulation establishes the connection between the gut and the liver, and there is a strong anatomical and functional relationship between the GI tract and the liver [27].The therapeutic benefits of several probiotics have been validated in both non-alcoholic and alcoholic liver disorders.

MATERIAL AND METHODS

Chemical structure and characterization of Copper Oxide Nanoparticles (CuONPs)

Copper oxide nanoparticles (less than 50 nm in size) were acquired from Sigma Aldrich. The CuONP powder was disseminated in distilled water and then aggressively stirred and sonicated to form a stock solution. Prior to each use, the stock solution underwent sonication for approximately 20 seconds to ensure proper particle suspension. The probiotic *Lactobacillus acidophilus* was purchased from Inlife and administered in accordance with the recommended dosage shown on the probiotic packaging.

Experiment Animal

Swiss albino male mice weighing between 25 and 30 gms were used. The animals are currently residing in an animal facility at an IIS (deemed to be University), Jaipur that has been officially authorised with CPCSEA (Registration No: 1689/PO/Re/S/13/CPCSEA).The subjects were maintained within a natural light-dark phase and provided with unrestricted availability of food and water. The animals were accommodated in the animal facility for a period of fifteen days before the start of the research, in order to facilitate their acclimation to the environment. Each group contained a minimum of 6 animals during the autopsy.

Agents and their dosage

A fraction of 1/5 of the lethal dose (dosage was employed).

- The dosage of copper oxide nanoparticles (CuONPs) is 80 milligrams per kilogramme of body weight.
- The concentration of *Lactobacillus acidophilus* (a type of probiotic) is 6.4 milligrams per kilogramme of body weight.
- Route of administration: The drug was administered orally.

Experimental groups

Four groups were established, with six animals per each group, and doses were administered via oral gavage. The dosage period lasted for duration of 30 days.

- GROUP 1: The control group is administered with distilled water.

- GROUP 2: *Lactobacillus acidophilus* (a type of beneficial bacteria known as a probiotic)
- GROUP 3: CuONPs (Copper oxide nanoparticles)
- GROUP4: consists of Copper Oxide Nanoparticles (CuONPs) combined with *Lactobacillus acidophilus*, which is a type of probiotic.

Preparation of the sample

At the conclusion of each treatment period, the animals were euthanized by cervical dislocation. The liver was then extracted with caution on a glass plate that had been chilled on ice. The liver was subsequently utilised to assess parameters related to oxidative stress. A cardiac blood sample was collected to analyse biochemical parameters employing serum.

Parameters related to oxidative stress

The activity of glutathione peroxidase (GPx) ; The activity of lipid peroxidation (LPO), Catalase and super oxide dismutase (SOD) activity was measured using a Kit Methods.

Biochemical measurements

The Accurex autozyme kit was utilised for the quantification of Alanine transaminase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), and total protein (TP).

Data evaluation

The data were generated using the statistical programme SPSS (version 21.0) employing a one-way analysis of variance (ANOVA).

RESULTS

In the present study CuONPs and a probiotic called *Lactobacillus acidophillus* changed the amounts of a liver biomarker in their serum. The first table shows that CuONPs caused liver damage, as shown by higher levels of ALT and ALP in the serum, while serum total protein levels were lower ($P < 0.01$) in comparison with the control amounts. The group that received copper oxide nanoparticles along with the probiotic *Lactobacillus acidophilus* had significantly higher serum total protein levels ($P < 0.01$) and lower serum ALT and ALP levels in comparison with the group that received 80 mg/kg of CuONPs, which caused hepatotoxicity (table no.1).

GROUPS	PARAMETRES		
	ALT (U/L protein)	ALP (U/L protein)	Total protein (g /dl protein)
Control	37.30 ± 1.077	65.11± 1.74 [c]	7.45 ± 0.05 [d]
PROBIOTIC *(Lactobacillus acidophilus)*	35.56 ± 0.61	64.30 ± 1.44 [c]	5.78 ± 0.28 [d]
CuONPs (80mg/kg)	162.99 ± 4.54	91.48 ± 0.965 [c]	3.20 ± 5.45 [d]
PROBIOTIC+ CuONPs (80mg/kg)	101.40 ± 2.77	85.24 ± .707 [c]	5.10 ± 2.77 [d]

Table1. The impact of a probiotic called *Lactobacillus acidophilus* with copper oxide nanoparticles on the amounts of alanine transaminase (ALT), alkaline phosphatase, and total protein on mice were exposed to copper oxide nanoparticles (CuONPs). The values are given as mean ± SEM (n=6). P value <0.01 value is significant. (c) Significantly distinct from the control group. (d) Significantly distinct from the group of male Swiss albino mice that were given copper oxide nanoparticles.

The analysis showed a significant increase ($p<0.01$) in the amount of malondialdehyde (MDA), which is a sign of lipid peroxidation (LPO), within the tissue of the liver of male mice that were given CuONPs compared to the control group (Fig1). A significant drop was seen in the amount of MDA in liver tissue in the group that was given 80 mg/kg of CuONPs with 6.4 mg/kg of *Lactobacillus acidophilus* probiotic, compared to the group that only received 80 mg / kg of CuONPs (the fig1).

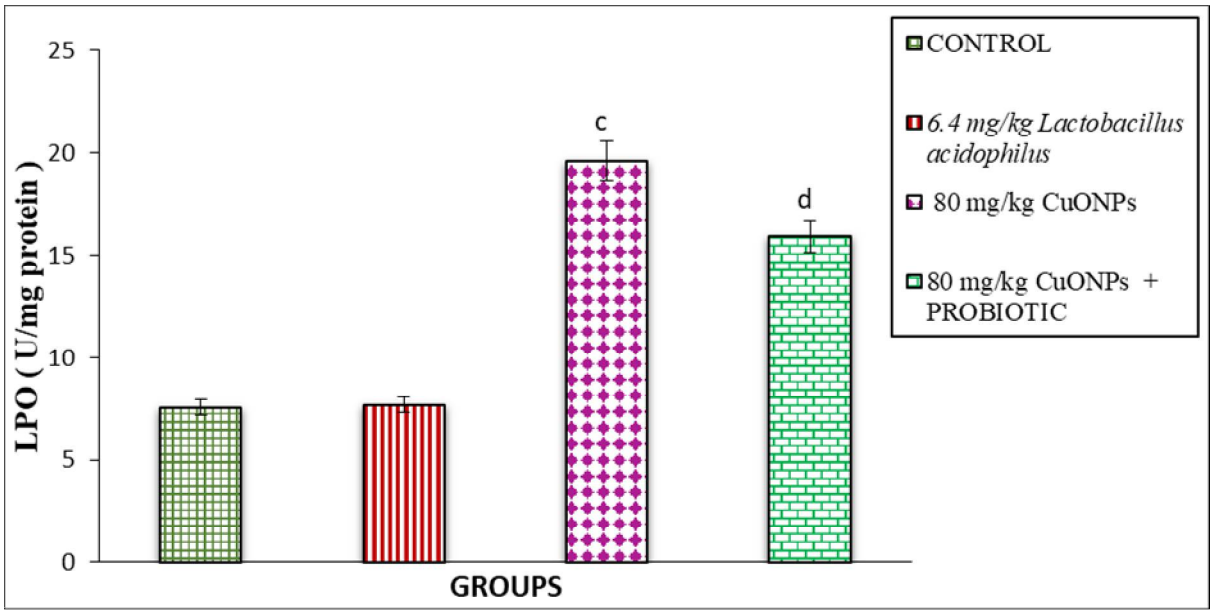

Figure 1:- shows how the probiotic *Lactobacillus acidophilus* changed the MDA levels of male mice. The results are shown as the mean ± the standard deviation. [c] Significant distinction when compared to a control group ($p < 0.01$). [d] significant distinction related to the groups that received 80 mg/kg of CuONPs.

There was a significant drop ($p<0.01$) in the amount of glutathione peroxidase within the tissue from the liver of mice that were given 80 mg / kg of CuONPs compared to the control group. When compared to the group that only received 80 mg/kg of CuONPs, the group that received 80 mg/kg of CuONPs along with 6.4 mg/kg of *Lactobacillus acidophilus* probiotic showed a significant rise in glutathione peroxidase (Figure2).

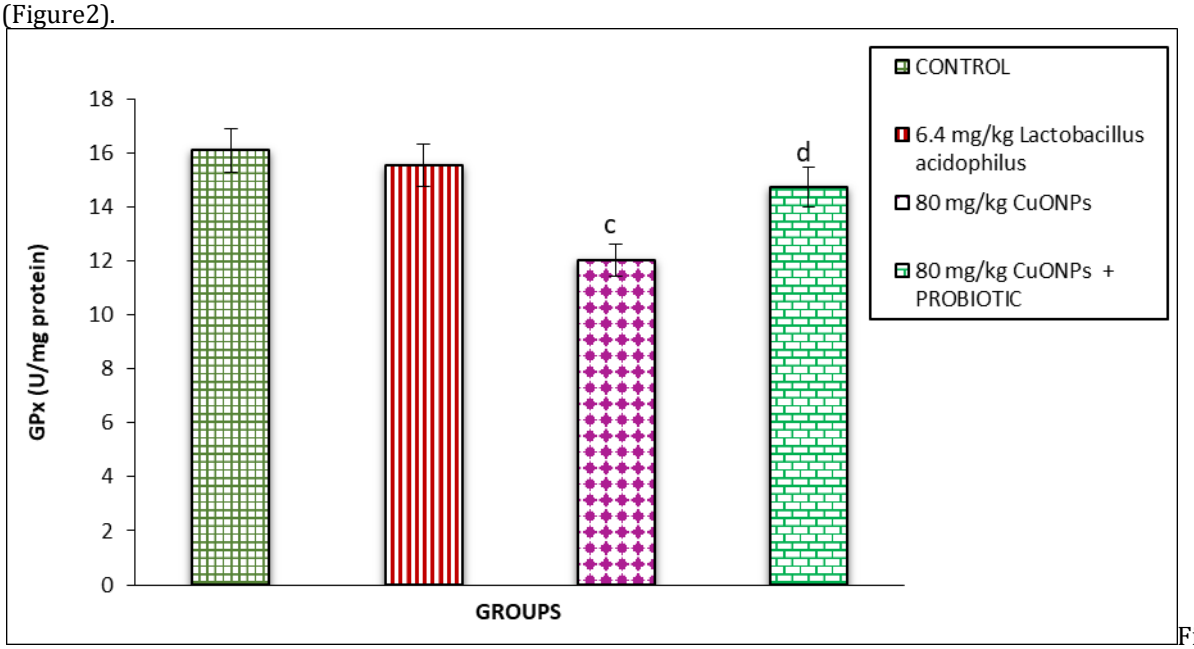

Figure 2:- shows how the probiotic *Lactobacillus acidophilus* changed the levels of glutathione peroxidase in male mice. The data are shown as the mean ± the standard deviation. There was an [c] significant difference to the control group ($p < 0.01$). There was a [d] significant difference between the CuONPs groups ± probiotic *Lactobacillus acidophilus* and the 80 mg/kg dose group.

The study discovered that liver tissue from mice given 80 mg/kg CuONPs had significant lower levels of superoxide dismutase than liver tissue from the control group. SOD activity rose up significantly in the group that received 80 mg/kg of CuONPs ± 6.4 mg / kg of *Lactobacillus acidophilus* probiotic, compared to the group that only received 80 mg / kg of CuONPs (Figure3).

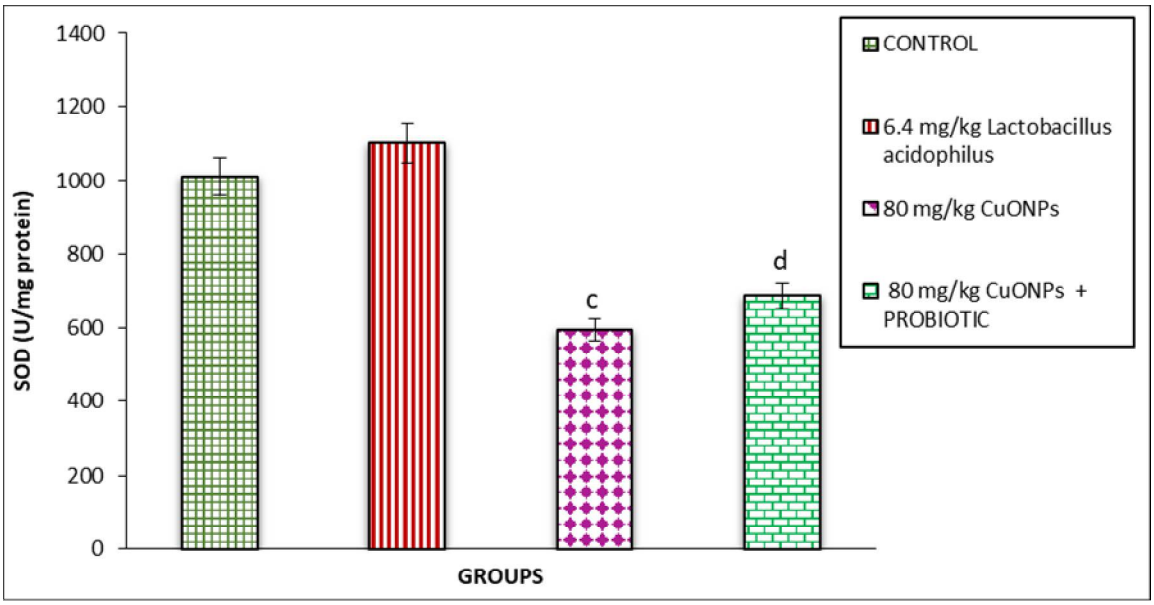

Figure 3:- The manner in which the probiotic *Lactobacillus acidophilus* changed the levels of superoxide dismutase in male mice. Numbers are shown as mean ± standard variation. [c] Difference that is statistically significant compared to the control group ($p < 0.01$); [d] Difference that is statistically significant compared to who received 80 mg/kg of CuONPs.

In the study, liver tissue from male mice that were given 80 mg per kg of CuONPs had significantly lower levels of catalase than liver tissue from the control group. The treated group's catalase activity rose up significantly after getting 80 mg/kg of CuONPs ± 6.4 mg/kg of *Lactobacillus acidophilus* probiotic, compared to 80 mg/kg of CuONPs (Figure 4).

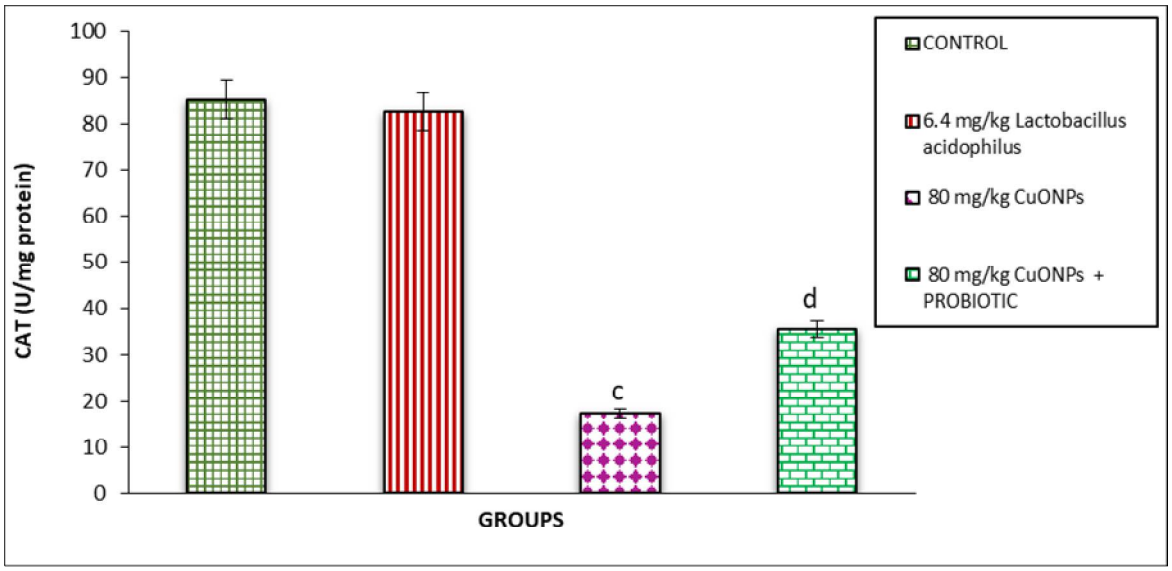

Figure 4:- The manner in which the probiotic *Lactobacillus acidophilus* changed the catalase levels of male mice. Numbers are shown as mean ± standard variation. [c] Difference that is statistically significant compared to the control group ($p < 0.01$); [d] Difference that is statistically significant compared to the groups that received 80 mg per kg of CuONPs.

DISCUSSION

Nanotechnology is growing very quickly, and nanomaterials (NPs) are thought to have a huge number of possible uses because of the special ways they behave [27]. The nanoparticles of metal (MNPs) have gotten a lot of attention in the business world because they are different from other NPs in a number of ways, such as their small size, different electronic, magnetic, optical, and mechanical qualities, as well as the shape of the particles, makes them more interesting. These tiny particles are mostly nanoparticles of metal and metal oxide nanoparticles. MNPs are used in a wide range of goods and fields, such as

electronics, cosmetics, paints, food additives, and biologic and medical systems [28] and [29]. Since MNPs are used in so many things, they will eventually get towards the environment or come into close contact with people. Because of this, the possible harms they could cause to people and the world have gotten even more attention [30]. There are several ways for MNPs to get into the body, such as through the skin, the lungs, or the digestive tract. They can then move through through the circulatory or lymphatic system and end up in different tissues [31]. Prior research on metal nanoparticles and metal oxide nanoparticles, such as nano-Nickle, nano-silver, nano-Copper, nano-zinc oxide, and nano-Titinium oxide, has demonstrated that these particles can enter the lungs and gastrointestinal tract via inhalation and ingestion, respectively. They can then move into the bloodstream and accumulate in specific organs, such as the liver and mononuclear phagocytic system [32]. The liver, as a secondary site of exposure, plays a crucial role in accumulating MNPs at far higher levels than other organs [33].

The groups that were administered a dose of CuONPs (80 mg / kg of body weight) exhibited a notable elevation in the levels of ALT, AST, and ALP activity in comparison to the control group. The enzymes' activity is typically employed to assess liver function. ALT is an enzyme involved in protein metabolism, while AST is a mitochondrial enzyme that contributes towards the metabolism for the amino acid alanine. Typically, ALT and AST are found inside liver cells, while ALP is situated at the cell membrane. Upon liver injury, these enzymes are released into the bloodstream. The level of hepatic cell death is elevated in cases of shock or medication toxicity [34]. The observed rise in enzyme activity results in the release and impairment of the functional integrity of the plasma membranes of the liver [35] and Mohammadyari [36] along with colleagues also observed comparable findings, noting a substantial rise in hepatic enzyme activity in Wistar rats undergoing an in-vivo toxicity evaluation of CuONPs. Rats exposed to CuONPs exhibited a notable reduction in the levels of SOD, GPx, GSH, and CAT activity in comparison to the control group. The findings of our study align with the previous research conducted by Sandhu and collaborators [37]. They also reported a decrease in GSH and CAT levels, along with an increase in ROS concentrations. This indicates that oxidative stress may be the initial mechanism via which CuONPs cause toxicity in rats after accumulation of O^{2-}, hydrogen peroxide (or their byproducts). Depletion of CAT activity leads to an inability to tolerate oxygen and triggers several negative responses, including oxidation of proteins and DNA, as well as cell death [38]. The data strongly indicate that CuONPs might directly or indirectly increase the production of free radicals by reducing antioxidant defence mechanisms, resulting in a decrease in the functioning of systemic antioxidants [39]. The CuONPs group had significantly greater AST, ALT and ALP values and lower TP, ALB,GBL ,BLB values than the control group ($P<0.01$) but when be administered probiotic (*Lactobacillus acidophilus*) with 80 mg/kg of CuONPs group had significantly lower AST, ALT and ALP values and greater TP, ALB, GBL ,BLB values than the 80 mg/kg of CuONPs group ($P < 0.01$). SGOT and SGPT activity were lower in the probiotics and conventional medication treated groups compared to controls, but ALB and TP levels were not statistically different in rats given 0.05 and 0.1 ml *L. acidophillus*. This finding was consistent with data from other research on the role of probiotics on liver enzyme activity by Cesaro C, *et al* [42] and Kirpich IA, *et al* [40]. The pervious facts indicate the toxicity caused by EDS, in which drug induced liver injury and nephrotoxicity was followed by an increase within fat, hepatic, and renal functional indicators (AST,ALT, ALP, urea, GGT, and protein creatinine) and lipid peroxidation, as well as a decrease in catalase and superoxide dismutase activities. This toxicity also caused programmed cell death. By mouth treatment of BJ0021 orally to pregnant mice dramatically reduced EDS produce toxic effects reported by Lin MY, *et al.,* [41].

The CuONPs group had significantly greater LPO values and lower GPx, SOD and CAT values than the control group (P 0.01) but when be administered probiotic (Lactobacillus acidophilus) with 80 mg/kg of CuONPs group had significantly lower LPO values and greater GPx, SOD and CAT values than the 80 mg/kg of CuONPs group ($P< 0.01$). The efficacy the prebiotics, synbiotics as well as probiotics preventing carbon tetrachloride induced hepatic damage within rats. Probiotic species *L. plantarum, L. pentosaceus, Lactobacillus acidophilus, and L. lactis* were employed in this research, as well as prebiotic species, oligofructan, and enulose alone or in mixture (symbiotic). Also, those probiotics aid for maintain a stable amount for liver enzymes, resulting in hepatoprotective effect. However, this CCl4 elevated LPO and lowered oxidative enzymes such as catalase, GPx and glutathione, which increases oxidative stress at the level of the cell and eventually causes liver rotted. However, even after administering probiotics, the levels of the antioxidants and LPO be left constant in these animals. Probiotics can decrease antioxidative stress caused by reactive oxygen species following CCl4 exposure [37].

ACKNOWLEDGEMENT
The infrastructural financial support under CURIE programme from the WISE- KIRAN division of Department of Science and Technology, New Delhi, India to IIS (deemed to be University), Jaipur, India (File No. DST/CURIE-02/2023/IISU) is gratefully acknowledged.

COMPETING INTEREST
The author declare that they have no known competing financial interest or personal relationships that could have appeared to influence the work reported in this paper.

CONCULSION
CuONPs in the liver caused several adverse effects including changes in liver enzyme activities and generation of ROS that causes changes in antioxidants levels of liver. Based on our results, we propose that probiotic that is *Lactobacillus acidophilus* could provide a cushion for protective benefit against CuONP induced hepatotoxicity without harmful side effects through its potent antioxidant properties.

REFRENCES
1. Brohi RD *et al,* Wang L, Talpur HS, et al. (2017). Toxicity of Nanoparticles on the Reproductive System in Animal Models:A Review. Front. Pharmacol. 8 https://doi.org/10.3389/fphar.2017.00606.
2. Jaleh B, Nasrollahzadeh M, Nasri A, Eslamipanah M, Moradi A, Nezafat Z. (2021). Biopolymer-derived (nano) catalysts for hydrogen evolution via hydrolysis of hydrides and electrochemical and photocatalytic techniques: A review. Int. J. Biol. Macromol. 182:1056-1090. https://doi.org/10.1016/j.ijbiomac.2021. 04.087.
3. Ajdary M, Keyhanfar F, Moosavi MA, Shabani R, Mehdizadeh M, Varma RS. (2021). Potential toxicity of nanoparticles on the reproductive system animal models: A review. J. Reprod. Immunol. 148:103384. https://doi.org/10.1016/j.jri.2021. 103384.
4. Ishii S, Bell J, Marshall F. (2007). Phytotoxic risk assessment of ambient air pollution on agricultural crops in Selangor State, Malaysia. Environ. Pollut. 150:267-279. https://doi.org/10.1016/ j.envpol.2007.01.012.
5. Addolorato G, Abenavoli L, Dallio M, et al. (2020). Alcohol associated liver disease. A clinical practice guideline by the Italian Association for the Study of the Liver (AISF). Dig. Liver. Dis. 52:374-391. https://doi.org/ 10.1016/j.dld.2019.12.008.
6. Cornu R, Béduneau A, Martin H. (2020). Influence of nanoparticles on liver tissue and hepatic functions: A review. Toxicology.430:152344. https://doi.org/10.1016/j.tox.2019.152344..
7. Tang Y, He R, Zhao J, Nie G, Xu L, Xing B. (2016). Oxidative stress-induced toxicity of CuO nanoparticles and related toxicogenomic responses in Arabidopsis thaliana. Environmental Pollution.212:605-614
8. Karlsson HL, Gustafsson J, Cronholm P, Möller L. (2009). Size-dependent toxicity of metal oxide particles—a comparison between nano-and micrometer size. Toxicology Letters. 188(2):112-118.
9. Dai Y, Wang Z, Zhao J, Xu L, Xu L, Yu X, WeiY,Xing B. (2018). Interaction of CuO nanoparticles with plant cells: Internalization, oxidative stress, electron transport chain disruption, and toxicogenomic responses. Environmental Science: Nano. 5(10):2269-2281.
10. Borowska S, Brzóska MM. (2015). Metals in cosmetics: Implications for human health. Journal of Applied Toxicology. 35(6):551-572.
11. Arani NM, Emam-Djomeh Z, Asemi Z, Tavakolipour H, Chaleshtori RS, Alizadeh S-A. (2019). Physiochemical and microbial properties of honey containing heat-resistant ***Bacillus coagulans*** T11. *Food Measure*. 13:1917–23. doi: 10.1007/s11694-019-00110-x.
12. Chaleshtori RS, Jadi Z, Arani NM, Arian A. (2021). Survey of physiochemical and microbial properties of functional beverage of date juice and ***Salix aegyptiaca*** L. distillate contained ***Bacillus coagulans***. *J Appl Microbiol Food Ind*. 6:41–53.
13. Davoodvandi A, Fallahi F, Tamtaji OR, Tajiknia V, Banikazemi Z, Fathizadeh H, et al. (2021). An update on the effects of probiotics on gastrointestinal cancers. *Front Pharmacol*. 12:680400. doi: 10.3389/fphar.2021.680400.
14. Davoodvandi A, Marzban H, Goleij P, Sahebkar A, Morshedi K, Rezaei S, et al. (2021). Effects of therapeutic probiotics on modulation of microRNAs. *Cell Commun Signal*. 19:4. doi: 10.1186/s12964-020-00668-w.
15. Arani NM, Emam-Djomeh Z, Tavakolipour H, Sharafati-Chaleshtori R, Soleimani A, Asemi Z. (2019). The effects of probiotic honey consumption on metabolic status in patients with diabetic nephropathy: a randomized, double-blind, controlled trial. *Probiotics Antimicrob Proteins*. 11:1195–201. doi: 10.1007/s12602-018-9468-x.
16. Zhu YT, Lai JH, Liao XD, Liu SL. (2018). Screening of lactic acid bacteria strains for their ability to bind phthalate monoesters ***in vitro*** and the binding characteristics. *Food Control*. 90:364–71. doi: 10.1016/j. foodcont. 2018.02.013.
17. Lili Z, Hongfei Z, Shoukat S, Xiaochen Z, Bolin Z. (2017). Screening lactic acid bacteria strains with ability to bind di-n-butyl phthalate via Turbiscan technique. *Antonie Van Leeuwenhoek*. 110:759–69. doi: 10.1007/s10482-017-0846-2.
18. Yang Y, Pei J. (2020). Isolation and characterization of an Enterococcus strain from Chinese sauerkraut with potential for lead removal. *Eur Food Res Technol*.246:2055–64. doi: 10.1007/s00217-020-03555-3.

19. Alcántara C, Crespo A, Solís C, Devesa V, Vélez D, Monedero V, et al.(2020). Lipoteichoic acid depletion in Lactobacillus impacts cell morphology and stress response but does not abolish mercury surface binding. *Benef Microbes*. (2020) 11:791–802. doi: 10.3920/BM2019.0184.
20. Do Nascimento JM, de Oliveira JD, Rizzo ACL, Leite SGF. (2019). Biosorption cu (II) by the yeast ***Saccharomyces cerevisiae***. *Biotechnol Rep*. 21:e00315. doi: 10.1016/j.btre.2019.e00315.
21. Huang H, Jia Q, Jing W, Dahms H-U, Wang L. (2020). Screening strains for microbial biosorption technology of cadmium. *Chemosphere*. 251:126428. doi: 10.1016/j.chemosphere.2020.126428.
22. Hammes P. (1992). The genera lactobacillus and carnobacterium. *Prokyatyotes.*1535–1594.
23. Sookkhee S., Chulasiri M., Prachyabrued W. (2001). Lactic acid bacteria from healthy oral cavity of Thai volunteers: Inhibition of oral pathogens. *J. Appl. Microbiol.* 90:172–179. doi: 10.1046/j.1365-2672.2001.01229.x.
24. Buck L.M., Gilliland S. (1994). Comparisons of freshly isolated strains of *Lactobacillus acidophilus* of human intestinal origin for ability to assimilate cholesterol during growth. *J. Dairy Sci.* 77:2925–2933. doi: 10.3168/jds.S0022-0302(94)77233-7.
25. Kaewnopparat S., Dangmanee N., Kaewnopparat N., Srichana T., Chulasiri M., Settharaksa S. (2013). In vitro probiotic properties of Lactobacillus fermentum SK5 isolated from vagina of a healthy woman. *Anaerobe.* 22:6–13. doi: 10.1016/j.anaerobe.2013.04.009.
26. Hojsak I., Snovak N., Abdović S., Szajewska H., Mišak Z., Kolaček S. (2010). Lactobacillus GG in the prevention of gastrointestinal and respiratory tract infections in children who attend day care centers: A randomized, double-blind, placebo-controlled trial. *Clin. Nutr.* 29:312–316. doi: 10.1016/j.clnu.2009.09.008.
27. Joo H.-M., Hyun Y.-J., Myoung K.-S., Ahn Y.-T., Lee J.-H., Huh C.-S., Han M.J., Kim D.-H.(2011). *Lactobacillus johnsonii* HY7042 ameliorates Gardnerella vaginalis-induced vaginosis by killing *Gardnerella vaginalis* and inhibiting NF-κB activation. *Int. Immunopharmacol.* ;11:1758–1765. doi: 10.1016/j.intimp.2011.07.002.
28. Yonekura S., Okamoto Y., Okawa T., Hisamitsu M., Chazono H., Kobayashi K., Sakurai D., Horiguchi S., Hanazawa T. (2009). Effects of daily intake of *Lactobacillus paracasei* strain KW3110 on Japanese cedar pollinosis. *Allergy Asthma Proc.*;30:397–405. doi: 10.2500/aap.2009.30.3256.
29. Parada J, Rubilar O, Fernández-Baldo MA, et al. (2018). The nanotechnology among US: are metal and metal oxides nanoparticles a nano or mega risk for soil microbial communities? Crit Rev Biotechnol. 39 (2):157–172. doi:10.1080/07388551.2018.1523865 3. Andra S, Balu SK, Jeevanandham J. (2019). Phytosynthesized metal oxide nanoparticles for pharmaceutical applications. Naunyn Schmiedebergs Arch Pharmacol. 392(7):755–771. doi:10.1007/s00210-019-01666-7
30. Amde M, Liu JF, Tan ZQ, Bekana D. (2017). Transformation and bioavailability of metal oxide nanoparticles in aquatic and terrestrial environments. A review. Environ Pollut. 230:250–267. doi:10.1016/j.envpol. 2017.06.064.
31. Yah CS, Iyuke SE, Simate GS. (2012). A review of nanoparticles toxicity and their routes of exposures. Iran J Pharm Res. 8(1):299–314.
32. Gustafson HH, Holt-Casper D, Grainger DW, Ghandehari H. (2015). Nanoparticle uptake: the phagocyte problem. Nano Today. 10 (4):487–510. doi:10.1016/j.nantod.2015.06.006
33. Almeida JPM, Chen AL, Foster A, Drezek R. (2011). *In vivo* biodistribution of nanoparticles. Nanomedicine. ;6(5):815–835. doi:10.2217/nnm. 11.79.
34. Sally A, Tice RP, Dean Parry RP. (2001). Medications that need hepatic monitoring. Hosp Pharm; 36:456–464..
35. Liu HT, Ma LL, Zhao JF, Liu J, Yan JY, Ruan J, Hong FS. (2010). Toxicity of nanoanatase TiO2 to mice: Liver injury, oxidative stress. Toxicol Environ Chem; 92:175–186..
36. Mohammadyari A, Razavipour ST, Mohammadbeigi M, Negahdary M, Ajdary M. (2014). Explore in vivo toxicity assessment of copper oxide nanoparticles in Wistar rats. J Biol Today? World; 3:124–128
37. Sandhu NS, Chopra D, Kaur S. (2010). Amelioration of paracetamol induced hepatotoxicity by a protein isolated from the leaves of the herb *Cajanus acutifoliuslinn*. Int J Pharm Pharm Sci; 2:75–80.
38. Bruck R, Aeed H, Shirin H, Matas Z, Zaidel L, Avni Y, Halphem Z. (1999). The hydroxyl radical scavenger's dimethyl sulfoxide and dimethylthioures protect rats against thioacetamide induced fulminant hepatic failure. J Hepatol ; 31:27–38.
39. Anreddy RN, Yellu NR, Devarakonda KR. Oxidative biomarkers to assess the nanoparticles induced oxidative stress. Methods Mol Biol 2013; 1028:205–219.
40. Kirpich IA, Solovieva NV, Leikhter SN, Shidakova NA, Lebedeva OV, Sidorov PI, et al. (2008). Probiotics restore bowel flora and improve liver enzymes in human alcohol induced liver injury: a pilot study. Alcohol. 2008;42(8):675-82. doi: 10.1016/j. alcohol. 2008.08.006.
41. Lin MY, Chang FY. (2000). Antioxidative effect of intestinal bacteria Bifidobacterium longum ATCC 15708 and *Lactobacillus acidophilus* ATCC 4356. Digest D Sci. 45:1617–1622.
42. Cesaro C, Tiso A, Del Prete A, Cariello R, Tuccillo C, Cotticelli G, et al. (2011). Gut microbiota and probiotics in chronic liver diseases. Dig Liver Dis. 43(6):431-38.