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Research Article

Curcumin Phytosome as an Anti- inflammatory and Hypolipidemic in Nano-Silicon Treated Female Rats

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Abstract | The oral toxicity of silicon dioxide nanoparticles (SiO_2NPs) effect the immune system and lipid profile, Curcumin Phytosome nanoparticles (CPNPs) possess several biological activities including anti-inflammatory, and hypolipidemic effects. We determined dyslipidemia and inflammatory state induced by exposure to silicon dioxide nanoparticles (SiO_2NPs) in female rats could be ameliorated by the administration of Curcumin Phytosome nanoparticles (CPNPs). Curcumin Phytosome NPs' impact on dyslipidemia and inflammatory state in SiO_2NPa-exposed female rats was investigated. Approximately 32 female rats were divided into four groups as follows: T1: was administered oral 200 mg/kg of SiO_2NPs, T2: received oral SiO_2NPs and 100mg/kg of curcumin phytosome, and T3: was administered oral 100 mg/kg of curcumin phytosome. Blood samples were collected from anesthetized rats through cardiac puncture by terminating the experiment. The samples were analyzed for total cholesterol (TC), triacylglycerols (TAG), high-density lipoprotein (HDL)-c, low-density lipoprotein (LDL)-c, very low-density lipoprotein (VLDL)-c concentrations, tumor necrosis factor-alpha (TNF-), and interleukin 10 (IL-10) concentrations. The results revealed the development of signs of incitement such as increased TC and reduced IL-10, decreased HDL-C, and increased TC, TAG, VLDL-C, and LDL-C, along with an increase in inflammatory markers. CPNPs reduced dyslipidemia and inflammation in female rats. We implied the protective impact of CPNPs, which may be seen in the anti-inflammatory and hypolipidemic, against the deleterious effects of silica.

Keywords | Curcumin Phytosome, Interleukin 10, Lipid profile, Silica nanoparticle, Tumor necrosis factor-alpha

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INTRODUCTION

Due to its extensive use in the food and consumer goods industries, silica dioxide (SiO2) is manufactured on a large scale (Peters et al., 2020). Food additives containing silica dioxide (Younes et al., 2017). Silica The pharmaceutical sector makes extensive use of nanoparticles for a variety of different functions, such as adsorbents, anti-caking agents, emulsifiers, thermal stabilizers, and improving the flow ability of solid formulations (Jonat et al., 2004). Nanosilica has been proposed as a solvent for the upgrading of Iraqi heavy crude oil by Shakir et al. (2022). Nanoilica's antibacterial properties have been documented (AL-Azawi et al., 2019). Noodles, soups, rubs, and coffee creamers are among the most common food items that include SiO2 NPs (Kesteren et al., 2015). Intentional or unintentional exposure to SiO_2NPs can occur through inhalation, oral ingestion, transdermal penetration, or parenteral injection, as demonstrated by some *in vivo* studies (Yazdimamaghani et al., 2018). Nanoparticles of amorphous silicon dioxide (SiO2) have become increasingly popular in recent years for a variety of applications, including coatings, paints, ad-

hesives, composites, cosmetics, culinary additives, medication delivery, and diagnostics (Rastogi et al., 2019). Turmeric, or curcumin, is a polyphenolic substance isolated from the rhizomes of the plant Curcuma longa. Antioxidant, anti-inflammatory, immunomodulatory, anti-dyslipidemic, and antithrombotic effects have all been linked to curcumin, a bioactive molecule that has garnered attention in recent years. (Baqer, 2020; Khdair et al., 2021; Momtazi-Borojeni et al., 2018; Cicero et al., 2017; Keihanian et al., 2018). and curcumin (Husch et al., 2013) have benefited from the use of phytosomes in formulations to increase bioavailability, as have drug delivery techniques that aim to boost therapeutic efficacy while minimizing unwanted effects and toxicities. Lepidium sativum phytosome extract as an antidiarrheal for *E. coli*-induced diarrhea in mice (Jaafar et al., 2020).

In rats, SiO_2 can harm the T-cell immune system (Gmoshinski et al., 2020), but it does not influence the severity of anaphylaxis. There may be harmful consequences on the liver, kidneys, and brain from being exposed to SiO_2NPs of 6, 20, and 50 nm diameters. Phytochemicals like propolis (Ghazi and AL-Bayati, 2020; Jaafar et al., 2020). According to Almansour et al. (2018), the immunological response to damage brought on by ROS renewal is thought to be the infiltration of inflammatory cells. The toxicity of SiO2 nanoparticles increased the production of free radicals, which led to the oxidation of mitochondrial DNA, proteins, and lipids (Powers et al., 2006). Rats treated with SiO_2NPs had high levels of lipid peroxides in their livers, indicating that there had been significant oxidative stress, which is directly associated with a decline in the activity of antioxidant enzymes (Parveen et al., 2012).

Curcumin's efficacy in the treatment of atherosclerosis, as well as its anti-inflammtory and lipid-lowering special effects, have been the subject of several studies (Soetikno et al., 2013; EL-Gizawy et al., 2020; Bateni et al., 2021). As an immunomodulatory substance, curcumin has the power to stop inflammation and the progression of tissue damage. By raising the expression of CD80 and CD86 on dendritic cells(DCs), decreasing the manufacture of reactive-oxygen-species(ROS) in macrophages, altering T cell proliferation, and increasing the expression of CD80 and CD86 on DCs, curcumin may affect the immune system (Bose et al., 2015). By increasing the activity of lipoprotein lipase and through processes that change the expression of genes for lipids and cholesterol, curcumin has also been shown to lower plasma cholesterol and triglycerides. (Jimenez-Osorio et al., 2016).

We aimed to combine the active element of a plant extract (*curcumin phytosmoe*) and investigate its ameliorative role in the removal of the destructive impact of SiO_2NPs in female rats.

Experimental animals and management

The institutional approval number for the study (P.G 900 Data 27-4-3023). CPNPs got the material in capsule form from a company(Now Foods, USA) SiO2NPs got the material in powder from a company (US Nano, USA) in rodents. Thirty-two (32) mature female rats weighing (175 g) and (at four months) of age were taken from the animal house at AL-Nahrain University's Biotechnology Research Centre. The animals were housed in well ventilated well-ventilated cages with dimensions 40 × 60cm and reared under controlled conditions of 12-hour light and 12-hour dark at 23˚C±2. Animals were fed standard laboratory food pellets consisting from (Milk 20.0, Wheat particles 17.0, Wheat powder 17.0, Barley particles 20.0, Corn particles 25.0, and Food salt 1.00) and drinking tap water. The animals were allowed to acclimatize in the animal house and randomly divided into four groups. Rats were given a gavage of sterile distilled water as a placebo.

Treatments

Rats were administered 200 mg/kg of SiO_2 nanoparticles orally. T2 was given a combination of curcumin phytosome (100mg/kg) and SiO_2-Nanoparticles (200 mg/kg) orally (Sun et al., 2020), and T3 was given 100 mg/kg of curcumin phytosome orally (Sun et al., 2020). All animals were given an intramuscular injection of a mixture of 90mg/kg/B.W. Ketamine and 40mg/kg/B.W. xylazine post-trial following an overnight fast (Lei et al., 2001). Eight samples were collected for each group, so the total number of samples was 32 blood samples, centrifuged for 15 min at 3000 rpm, and sera were stored in firmly stoppered tubes at 20˚C until biochemical and anti-inflammatory analysis. Sera levels of TNF- by using (MyBioSource, USA) and IL-10 by using (MyBioSource, USA) were measured.

Determination of Serum Total Cholesterol(TC) Concentration (mg/dl) According to Tietz, (1999), the blood TC concentration was measured enzymatically using the total cholesterol (TC) kit. Determination of Serum Triglyceride(TAG) Concentration (mg/dl) According to Tietz (1999), a triglyceride (TAG) kit was used to measure the serum TC concentration using the Fossati and Principe technique in conjunction with the Trinder reaction. Determination of Serum HDL-C Concentration (mg/dl) According to Tietz (1999), an enzyme-based method was employed to measure the blood HDL-C concentration using the HDL-C kit. Calculation of Serum VLDL-C concentration (mg/dl): The amount of VLDL-c was calculated by multiplying the triglyceride readings (in mg/dl) by 5. (Friedewald et al.,1972). VLDL-c conc.(mg/dl) = triglycerides conc / 5. Calculation of Serum LDL-C Concentration: LDL-c conc.(mg/dl) = Total cholesterol-HDL-VLDL (Friedewald et al.,1972). All kits of lipid profile from (Biolabo, France) and use a Spectrophotom-

eter device.

Statistical Analysis

The findings were analyzed statistically using SPSS Version 24's one-way analysis of variance (ANOVA), with a P value of less than 0.05 being considered statistically significant. Least-significant-difference (LSD) tests were employed to identify statistically significant differences across groups (Zar,1984).

RESULTS

Lipid Profile

Figures (1)–(5) showed the mean values of the serum lipid profile. The concentrations of serum total cholesterol, triglyceride, VLDL-c, and LDL-c are significantly (P<0.05) higher in the (T1) group, while the concentration of HDL-c decreases significantly (P<0.05) in comparison to the treated groups. Correction of lipid profile values with a reduction in mean value when compared to the value in the T1 group after oral administration of curcumin phytosomes in the T3 group or (T2 groups). HDL-c concentrations, on the other hand, rose significantly (P<0.05) in the same groups.

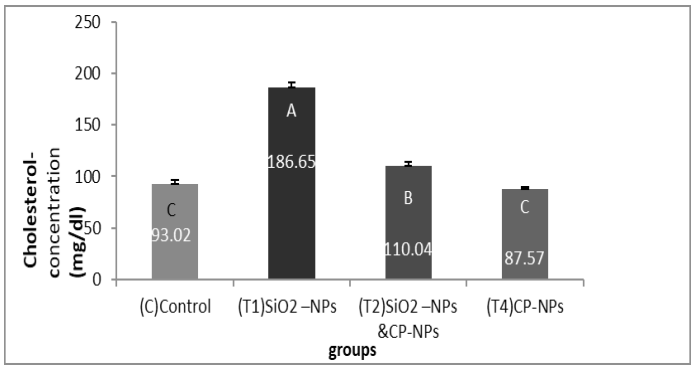

Figure 1: Effect of curcumin phytosome on serum total cholesterol concentration (mg/dl) in Silica nanoparticles (SiO2 NPs) treated rats

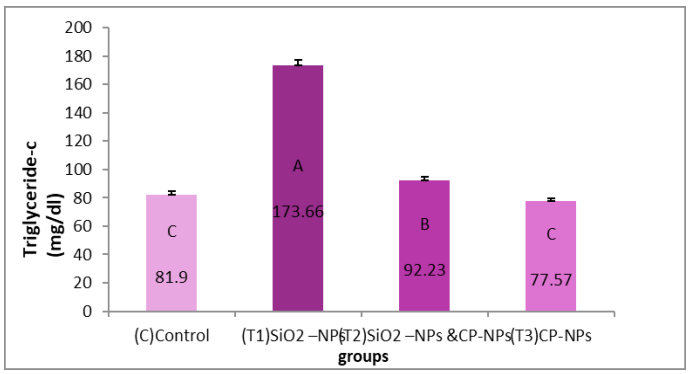

Figure 2: Effect of curcumin phytosome on serum Triacylglyceride (TAG) concentration (mg/dl) in Silica nanoparticles (SiO2 NPs) treated rats

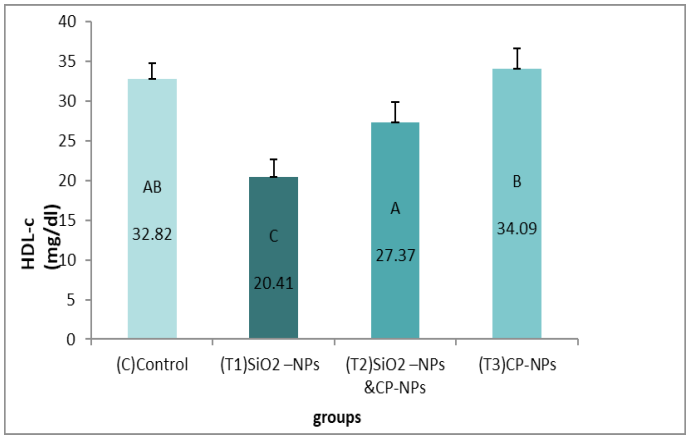

Figure 3: Effect of curcumin phytosome on serum high-density lipoprotein-cholesterol(HDL-c) concentration (mg/dl) in Silica nanoparticles (SiO2 NPs) treated rats

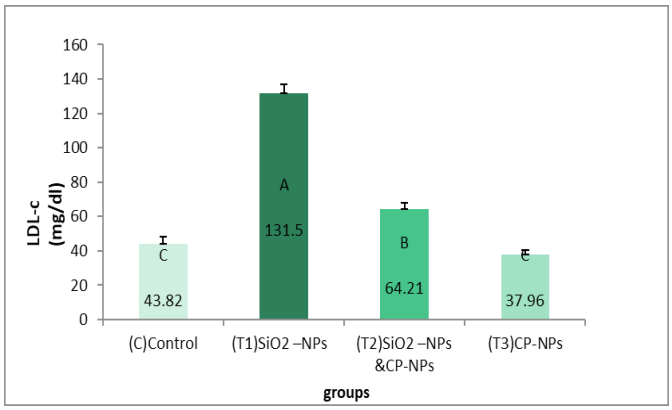

Figure 4: Effect of curcumin phytosome on Serum low-density lipoprotein-cholesterol (LDL-c) concentration (mg/dl) in Silica nanoparticles (SiO2 NPs) treated rats

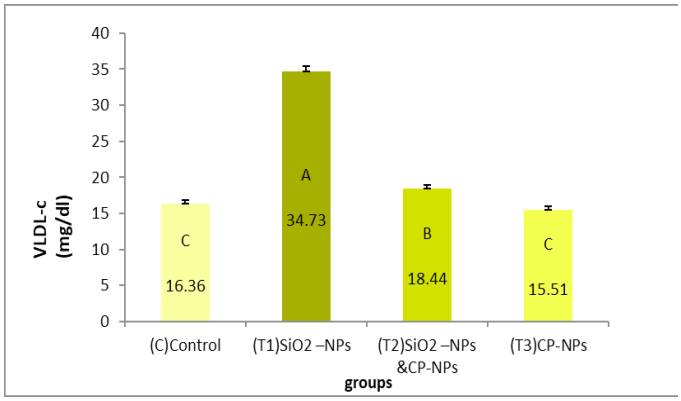

Figure 5: Effect of curcumin phytosome on Serum Very-low-density lipoprotein-cholesterol (VLDL-c) concentration (mg/dl) in Silica nanoparticles (SiO2 NPs) treated rats

Serum Tumor Necrosis Factor- Alpha(TNF-A) And Interlukin-10(IL-10) Serum Concentration.

Histograms (6 and 7) showed the average levels of serum TNF- and IL-10 across the various experimental groups. Serum TNF-alpha and IL-10 concentrations were found

to be significantly (P<0.05) different between the T1 group and the other treatments. When comparing T1 to T2 and T3, the concentrations of TNF- and IL-10 were found to be significantly (P<0.05) lower in the T3 and T2 groups, respectively. The CPNPs-treated group showed the greatest drop in this parameter (Figures 6 and 7).

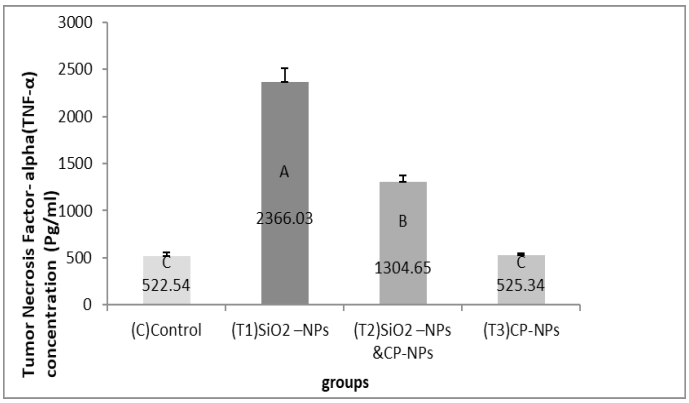

Figure 6: Effect of curcumin phytosome on Serum Tumor Necrosis Factor- alpha (TNF-α) concentration (Pg/ml) in Silica nanoparticles (SiO2 NPs) treated rats

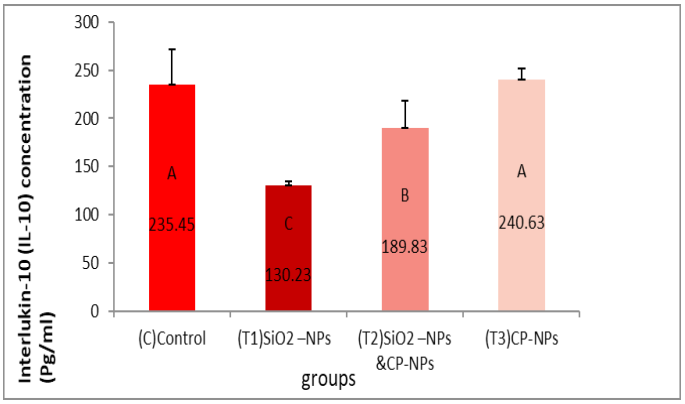

Figure 7: Effect of curcumin phytosome on Serum Interleukin -10 (IL-10) concentration (Pg/ml) in Silica nanoparticles (SiO2 NPs) treated rats

DISCUSSION

Here, we see that the pro-inflammatory effect documented by Parveen et al. (2017) is confirmed by an increase in TNF-alpha and a decrease in serum IL-10 concentrations in T1. Interleukin-1 beta (IL-1), tumor necrosis factor-alpha (TNF-alpha), nuclear factor kappa B (NfKB), cyclooxygenase-2 (COX-2) (El-Demerdash et al., 2021), and IL-6 (Mendoza et al., 2014) were all upregulated following SiO_2NPs treatment. Therefore, inflammation may account for a great deal of the toxicity of SiO_2NPs. SiO_2NPs may have induced inflammatory cytokine production by modulating the expression of genes linked to the increased endoplasmic reticulum (ER) stress and reactive oxygen species (ROS) formation. For example, cytokines like TNF- and IL-6 may phosphorylate IRS1 and the MAPK pathway (Massaro et al., 2016; Hu et al., 2019). Many proinflammatory cytokines are reduced by nano-curcumin, as shown by various studies (Abdolahi et al. 2017, Zhang et al. 2019, Trivedi et al. 2017, Wang et al. 2017). The current study's findings corroborate those of the aforementioned studies. Researchers El-Gizawy et al. (2020) found that CUR NPs suppress TNF- gene expression and inactivate nuclear transcription factor kappa B, two mechanisms that diminish TNF- levels. Pro-inflammatory cytokines including interleukin-1(IL-1), interleukin-6(IL-6), and nuclear factor kappa light chain enhancer of stimulated B-cells(NF_B) are suppressed by CURC, as reported by many authors (Zhong et al., 2016; Derosa et al., 2016; Ghosh et al., 2015). Nano-curcumin may slow the progression of mRNA production of inflammatory cytokines, as shown by Valizadeh et al. (2020). Mollazadeh et al. (2019) and Abo-Zaid et al. (2020) found similar results, demonstrating that curcumin boosted IL-10 secretion. Abo-Zaid et al. (2020) also found that curcumin inhibited hepatic inflammation and boosted IL-10 production, suggesting that it might shield the liver from the aging effects of CCl4.

This study discovered a positive correlation between the usage of CP-NPs and HDL cholesterol levels and a negative correlation between CP-NP use and dyslipidemia, whether CP-NPs were used alone or in conjunction with SiO2 NPs. The discovery of SiO2 nanoparticles was followed, according to several studies, by hyperlipidemia. *In-vivo* studies have shown that SiO2 nanoparticles cause hyperlipidemia and interfere with hepatic lipid metabolism (Sun et al., 2011). 2018 (Duan et al., 2018) Carnitine palmitoyltransferase 1A (CPT1A) protein levels were reduced by silica nanoparticles (SiNPs), which led to an increase in fatty acid synthesis and a reduction in fatty acid beta-oxidation. One of the most important reasons for the development of fatty liver illnesses and atherosclerosis is a lipid metabolism issue, which may be brought on by an imbalance between lipogenesis and lipid utilization (Gong et al., 2017). To get over the drawbacks of the current delivery techniques, phytosome technology has been shown to enhance curcumin absorption and bioavailability (Vaishnavi et al., 2021). Similar justifications to those provided here were provided in a large number of earlier experimental studies of CP's hypolipidemic effect. Curcumin therapy in diabetic patients (Hodaei et al., 2019) and nano-micelle curcumin (Bateni et al., 2021) both significantly decreased plasma TG. giving obese people with non-alcoholic fatty liver disease 80 mg of nano curcumin. After three months of therapy, patients with nonalcoholic fatty liver disease (NAFLD) had significantly higher HDL-C levels and reduced TG, TC, and LDL-C levels (Jazayeri-Tehrani et al., 2019). The blood glucose (sGlu), alpha-fetoprotein (AFP), protein kinase C (PKC), and lipid profiles of diabetic rats

are all returned to their normal states by Nano-CUR as compared to controls (El-Desoky et al., 2022). The levels of HDL and total cholesterol are also markedly raised. Triglycerides and low-density lipoprotein improvements are comparable to one another (Chien et al., 2021). Numerous hypotheses have been made on the potential mechanisms by which curcumin alters the lipid profile of the serum. Downregulation of 3-hydroxy-3-methylglutaryl-CoA (HMG-CoA) reductase, sterol regulatory element-binding protein-1/2 (SREBP-1/2), and fatty acid synthase is a key mechanism for inhibiting de novo lipid biosynthesis (Panahi et al., 2014; Saberi- Karimian et al., 2018; Sahebkar et al., 2015). By boosting CYP7A1 gene expression and inducing lipid catabolism, curcumin also encourages biliary lipid excretion (Panahi et al., 2014). It is also possible to increase the activation of the PPAR- (Peroxisome proliferator-activated receptor gamma) (Mohammadpour et al., 2016; Jamilian et al., 2020). In hepatocytes, curcumin lowers cholesterol and triglyceride synthesis while increasing LDL receptor expression. The breakdown of cholesterol is promoted, and bile acids are excreted in the stool (Chien et al., 2021). Antioxidant plant components have been shown to decrease nanoparticle toxicity and boost bioavailability (Ali and Khudair, 2019; Sood and Khudair, 2018). As a result, the inflammatory and dyslipidemic effects of SiO_2NPs are diminished by the combination of curcumin phytosomes with SiO_2NPs.

CONCLUSION

The current study documented the ameliorative role of CP NPs against the damaging effect of the SiO2 NPs. Better results were obtained in the T3 group that received CP alone, where CP NPs can be considered as an antioxidant factor.

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CONFLICT OF INTEREST

The authors have declared no conflict of interest.

NOVELTY STATEMENT

This work has highlighted the role of anti-inflammatory and hypolipidemic effects of curcumin phytosome in SiO2 NPs -treated female rats.

AUTHORS' CONTRIBUTIONS

The authors of the current experiment contributed equally.

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