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IMPACT OF *Pleurotus tuber-regium*(Rumph. ex Fr.)EXTRACT LOADED SILVER NANOPARTICLES ON LIPID PROFILE OF MAMMALIAN MODEL,WISTAR ALBINO RATS(*Rattus norvegicus*)

SUKUMAR DANDAPAT[1]*, MANOJ KUMAR[2], ROHIT SRIVASTAVA[1] AND MANORANJAN PRASAD SINHA[1]
[1] University Department of Zoology, Ranchi University, Ranchi-834 008, Jharkhand, INDIA
[2] Department of Zoology, St. Xavier's College, Ranchi-834 001, Jharkhand, INDIA
e-mail: dr.sukumar2018@gmail.com

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***Corresponding author**

ABSTRACT
The effect of silver nanoparticles (SNPs) loaded with *Pleurotus tuber-regium* extract on the lipid profile of Wistar albino rats as mammalian model has been assessed and compared with that of crude extract.The SNPs loaded with *P. tuber-regium* extract showed significant ($p < 0.05$) increase in HDL (High Density Lipoprotein) cholesterol (52.74 ± 1.12 mg dL^{-1}) in rats treated with 400 mg kg^{-1} dose (group 3) of nanoparticles in comparison to 200 mg kg^{-1} dose (group 2) and control group (group 1). However, a significant decrease ($p < 0.05$) in total cholesterol (65.24 ± 0.70 mg dL^{-1}), LDL cholesterol (29.82 ± 0.29 mg dL^{-1}) and triglyceride (63.91 ± 0.99 mg dL^{-1}) in rats of Group-3 was observed compare to the Group-2 and control group of rats. The results of SNPs treatment, when compared to the crude extract treatment for the similar parameters, have shown significantly ($p < 0.05$) better performance. The medicinal properties of SNPs exhibited better efficacy than the crude extract. On the basis of the observations, it can be concluded that crude extract of *Pleurotus tuber-regium* as well as silver nanoparticles loaded with extract of *Pleurotus tuber-regium* be used in formulation and delivery of drug for hypercholesterolemia.

INTRODUCTION

Among life-supporting biomolecules, lipids are vital ones responsible for a number of physiological functions, but when at higher concentration they produce cardiovascular disorders. According to the World Health Organization (2015), cardio vascular diseases are one of the major reasons of mortality (Tang, 2016). Recent researches and technologies are focused on developing low-cost medicines with little or no side effects in this context.

Contemporary researches are concentrating on development of medicineutilizing the compounds obtained from chlorophyllous and non-chlorophyllous plants with medicinal potentiality, either in crude or modified form. The transport and effectiveness of therapeutic agents are frequently constrained due to their site- or target-specific actions. Many synthetic and natural drugs need modest tweaks, such as changing the drug's chemical structure or adding it to a carrier system, to guarantee proper action and distribution (Dandapt *et al.,* 2014a).Such desired results are obtained through nanobiotechnology applications. Nanotechnology in medicine and pharmacology refers to materials with dimensions of less than 100 nanometers with unique qualities such as ultra-small size, huge surface to volume ratio, high reactivity, and unique interactions with structural components (Dandapt *et al.,* 2014b).

Pleurotus tuber-regium is a species of mushroom. Mushrooms in general have been used as a dietary supplement and as therapeutic agent since long. During the last few decades, mushrooms including the species under study have been consumed as nutritional foods and therapeutic supplements (Patel *et al.*, 2012). *Pleurotus tuber-regium* (*P. tuber-regium*) belongs to Pleurotaceae family and has also been used to cure infections, renal and hepatic disorders, diabetes, along with other health problems (Sharma *et al.*, 2019).

Presently nanoparticles of various metals using different plants are synthesized with different goals (Pawar *et al.,* 2023; Sheikh *et al.,* 2023., Padhiary *et al.*,2023).

A number of pharmacological assessments of *P. tuber-regium* extract have been conducted; however its application in synthesis of nanoparticles and the study of the impact of SNPs on the lipid profile in a mammalian model (Wistar albino rats) has not yet been investigated. Hence the present paper deals with effect and efficacy of synthesised SNPs on lipid profile of mammalian model in comparison to crude extract of *Pleurotus tuber-regium*.

MATERIALS AND METHODS

Synthesis of SNPs

The nanoparticles were synthesized and characterized following standard methods described elsewhere (Kumar *et al.,* 2022; Dandapat *et al.,* 2022; Kumar *et al.,* 2023)

Animals

Wistar albino rats (*Rattus norvegicus*) weighing 175 to 200 g BW (Body weight) were procured from the National Institute of Nutrition, Hyderabad, India. The rats were kept in hygienic laboratory condition, with a day and night cycle of 12 hours under atmospheric temperature of 25 ± 2 °C and humidity of $50 \pm 15\%$. Rats were given a commercial pallet food

manufactured by Sadguru Shri Shri Industries Pvt. Ltd., Pune, India and free access to water . The experiments were carried out in accordance with ethical committee resolution (Ranchi University, Animal Ethical Committee, Proceeding no. 46, page no. 137of Department of Zoology).

Acute toxicity test

According to OECD (Organization for Economic Cooperation and Development) test guideline 425, an acute toxicity experiment of *P. tuber-regium* extract loaded SNPs on rats was performed using the staircase method (Saleem *et al.*, 2017).

Experimental design

The effect of extract-loaded SNPs on lipid profiles of Wistar albino rats was investigated using a low dosage (LD) and a high dosage (HD) of SNPs. Total of fifteen healthy animals were distributed evenly among three treatment groups (Groups 1, 2, and 3).Two doses (high dose: 400 mg $kg^{-1}$and low dose: 200 mg kg^{-1}) of SNPs (average 71.36 nm diameter with –11.2 mV zeta potential) were administered according to the body weight of the animals (Oghenesuvwe *et al.*, 2014).

Group 1

Rats of this group served as control and were not administered SNPs but received 1mL distilled water orally for 7 days.

Group 2

Rats of this group were orally administered 200 mg kg^{-1} body weight of *P. tuber-regium* extract loaded SNPs for 7 days and were considered as LD treatment group.

Group 3

Rats of this group were orally administered 400 mg kg^{-1} body weight of *P. tuber-regium* extract loaded SNPs for 7 days and were considered as HD treatment group.

Study of impact of SNPs on lipid profile

The effects of macrofungal extract-mediated SNPs on lipid profile were investigated using the cholesterol oxidase phenol 4-aminoantipyrine peroxidise technique to estimate total cholesterol (Rifai *et al.*, 1998).Immunological precipitation technique was used to calculate high density lipoprotein cholesterol (Nauck *et al.*, 2000). Friedewald equation was used to calculate low density lipoprotein cholesterol (LDL-C) from the combined findings of total cholesterol, HDL cholesterol, and triglycerides (Bachorik and Ross, 1995), while the 3-phosphate-oxidase (GPO) technique was used to calculate serum triglycerides (Dandapat *et al.*, 2020). The cholesterol parameters were measured using a spectrophotometer and DiaSys international Pvt. Ltd.'s cholesterol diagnostic reagent kit (Holzheim, Germany).

Statistical analysis

The data were collected five times, and the findings were reported as a mean ± standard error of the mean. The t-test was used for statistical analysis, and $p < 0.05$ was regarded statistically significant. The programme WinSTAT was used to conduct all statistical studies (Dandapat *et al.*, 2019).

RESULTS AND DISCUSSION

Mushrooms with therapeutic characteristic have been utilised in the treatment of variety of illness. According to World Health Organization ethnomedicinal use of herbs and mushroom for treatment of illness should be assessed and investigated for health safety and harmful consequences (Vaghasiya *et al.*, 2011). Animals are a valuable resource in non-human research for scientific purposes, and previous studies have been found that mushrooms having medicinal properties and SNPs are toxic to animals (Massimiliano *et al.*, 2017). As a result, this study was carried out to investigate the acute toxicity of silver nanoparticles mediated by *P. tuber-regium* aqueous extract using the OECD's guideline no-425 (OECD, 2008). There was no death, on convulsion, on itching, on allergic reactions, no coma, and no salivation and other adverse activities produced as a result of toxicity till 14 days. Within 30 minutes of treatment of SNPs, animals showed minor deep breathing and sleepy effect. Short term stress was concern with deep breathing and sleeping in rats administrated with nanoparticles within 30 minutes of the treatment time period, which returned to normal after 30 minutes (Noble*et al.,* 2017).

The result of impact of SNPs loaded with *P. tuber-regium* extract on the lipid profile of rat is presented in Table-1. The result reveals that the nanoparticles both at low dose (200 mg kg^{-1}) and high dose (400 mg kg^{-1}) effectively reduced total cholesterol, LDL cholesterol and triglyceride level. However, as compared to the control group of rats, the low dosage and

Table 1: Impact of *P. tuber-regium* extract loaded SNPs on lipid profile of rat, n = 5 ± SEM, * = p < 0.05.

Treatment groups	Group-1 (Control)	Group-2 (Low dose/200 mg kg^{-1})	Group-3 (High dose/400 mg kg^{-1})
Parameters			
Total cholesterol (mg dL^{-1})	79.37 ± 0.66	69.49 ± 1.57*	65.24 ± 0.70*
HDL-C (mg dL^{-1})	46.35 ± 0.94	49.10 ± 0.87*	52.74 ± 1.12*
LDL-C (mg dL^{-1})	39.63 ± 0.69	32.76 ± 1.05*	29.82 ± 0.29*
Triglyceride (mg dL^{-1})	119.51 ± 1.39	69.65 ± 1.57*	63.91 ± 0.99*

Table 2: Change in different lipid parameters in terms of percentage as result of administration of different doses of SNPs in Wistar albino rats

Parameters	**Percentage change % change in group 2 as compared to group 1**	**%change in group 3 as compared to group 1**	**% change in group 3 as compared to group 2**
Total cholesterol (mg dL^{-1})	-12.45	-17.8	-6.12
HDL-C (mg dL^{-1})	5.93	13.79	7.41
LDL-C (mg dL^{-1})	-17.34	-24.75	-8.97
Triglyceride (mg dL^{-1})	-41.72	-46.52	-8.24

high dose SNPs treated group showed a substantial increase in HDL cholesterol.

In terms of percentage change in total cholesterol, HDL-C, LDL-C, and triglyceride (Table-2) maximum decrease was observed in triglyceride by 46.52% in Group -3 in comparison to Group-1.Similarly minimum decrease was noticed in total cholesterol (6.12%) in Group-3 in comparison to Group-2. Maximum increase on the other hand was observed in HDL-C (13.79%) in Group-3 with respect to Group-1.

The hypolipidemic activity of *P. tuber-regium* extract loaded SNPs on lipid profile of rat was also compared with the activity of *P. tuber-regium* crude extract on lipid profile of rat (Dandapat *et al*., 2020). The current study showed significantly higher($p < 0.05$) hypolipidemic activity when compared with the results of previous published work. Both the low dose (200 mg/kg body weight) and high dose (400 mg/kg body weight) treated groups of rats , exhibited significant decrease ($p < 0.05$) in total cholesterol levels 75.52 ± 0.39 mg/dL and 72.25 ± 1.11 mg/dL respectively as compared to the total cholesterol levels of control group (79.37 ± 0.66 mg/dL). There was a significant increase in HDL cholesterol levels in both low dose group (55.23 ± 0.87 mg/dL) and high dose group (61.23 ± 1.36 mg/dL) as compared to the control group (46.35 ± 0.93 mg/dL). The LDL cholesterol was 26.37 ± 1.21 mg/dL and (34.58 ± 1.69 mg/dL) in case of low dose group and high dose group respectively, which are significantly ($p < 0.05$) as compared to LDL cholesterol level of control group (39.80 ± 1.49 mg/dL). A significant decrease ($p < 0.05$) was observed in serum triglyceride levels in low dose group (69.42 ± 0.72 mg/dL) and high dose group (81.31 ± 1.25 mg/dL) as compared to the serum triglyceride level of control group (119.50 ± 1.39mg/dL).

Active components such as polysaccharides, mevinolin, and essential fatty acid, dietry fibres, key minerals, and certain vitamins with hypocholesterolaemic properties have been reported in mushroom belonging to the genus *Pleurotus* (Khan and Tania, 2012). Earlier Singh (2017) reported that *Pleurotus citrinopileatus*(a mushroom) shows hypolipidemic effect.

In terms of the percentage change if different parameters (Table-2) maximum decrease was noticed in triglyceride which was treated with high dose (46.52%). As shown in the table -2, minimum decrease was observed as an effect of low dose treatment in total cholesterol content. HDL-C was found to increase by 13.79% under influence of high dose.

Similarly species of mushroom namely *Pleurotus ostreatus, Pleurotus sajor-caju* and *Pleurotus florida*have been reported to reduced plasma total cholesterol level by 37 percent, 21 percent, and 16 percent respectively. Similarly the extract of these three mushroom reduced LDL/HDL ratio by 64 percent, 45 percent, and 41 percent, and declined the triglyceride level by 45 percent, 24 percent, and 14 percent, respectively (Alam *et al*., 2009). Rats treated with *P.florida* extract and powder had higher lipid excretion in their faeces and had lower LDL, VLDL, serum triglyceride, total cholesterol. However, there was a significant increase in HDL cholesterol (Fombang *et al*., 2016).

In a study, it was shown that when rats were fed AuNPs, their HDL cholesterol level rise significantly, and HDL cholesterol has the ability to move LDL cholesterol and triglyceride away from the arteries and back to liver. HDL has the ability to transport from atheroma of artery to the liver for discharge or re-utilize (Graham *et al*., 2007).When compared to control group in the present study there was a substantial rise in HDL cholesterol and decline in total cholesterol, LDL and triglyceride (Table-1). A significant drop in cholesterol might be attributed to cholesterol excretion or appropriate biocomburtion of cholesterol in the body.

As *P. tuber-regium* extract loaded SNPs showed no acute toxicity and significantly reduced total cholesterol, LDL-C and triglyceride and the SNPs increasing significantly HDL-C hencethese *P. tuber-regium* extract loaded SNPs show potential be used as a hypolipidemic medication.

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