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Ameliorative and Preventive Effects of *Boswellia dalzielii* Leaf-Mediated Magnetite (Fe_3O_4) Nanoparticles on Lipid Profile of Diethylnitrosamine-Induced Carcinogenesis in Wistar Rats

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ABSTRACT
Hepatocarcinogenesis is a global health burden often characterized by profound alterations in lipid metabolism and oxidative stress. This study investigated the ameliorative and preventive effects of synthesized magnetite (Fe_3O_4) nanoparticles from *Boswellia dalzielii* leaf diethylnitrosamine (DEN)-induced carcinogenesis in Wistar rats. The leaf sample was collected from Minda village of Lau Local Government Area, Taraba State, dried at room temperature, pulverized and sieved. Aqueous extract of the leaf sample was used to synthesize Fe_3O_4 nanoparticle using green method. The synthesized nanoparticle was administered to the groups of the animals in both ameliorative and preventive treatments at concentration of :100 ppm, 300 ppm, 500 ppm and 800 ppm after induction with 200 mg/kg body weight DEN. The animals were sacrificed at the end of four weeks and the blood analysed for lipid biochemical parameters such as total cholesterol (TCHOL), high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides (TGL) and malondialdehyde (MDA). However, treatment with *Boswellia dalzielii*-mediated magnetite nanoparticles significantly ($p < 0.05$) improved these parameters, reducing elevated cholesterol; 97.99±19.34, 53.69±13.42, 72.48±19.80, 96.64±71.12 and triglyceride; 58.37±15.43, 42.56±3.73, 25.12±5.73, 48.66±2.44 for ameliorative treatments, while cholesterol; 164.96±16.76, 142.28±104.23, 126.17±123.88, 178.52±75.43, and triglyceride; 18.57±12.71, 21.16±8.28, 31.86±1.95, 33.02±6.02 for preventive treatments. There was increasing HDL concentrations with different treatments; 9.02±5.33, 10.16±7.00, 13.37±4.02, 11.81±2.68 for ameliorative and 10.36±1.55, 14.51±5.27, 13.06±1.06, 14.40±26.42 for preventive. Furthermore, a marked reduction in MDA levels (from 9.37 ± 2.05 mg/dL in the control to 4.04 ± 0.18 mg/dL in treated groups) indicated decreased lipid peroxidation and enhanced antioxidant status. The study demonstrated the potential of this plant-based nanotherapeutics possessing significant protective and therapeutic effects against carcinogenesis-associated lipid metabolic disturbances, likely due to the synergistic action of the plant's phytochemicals and the nanoparticles' delivery capabilities.

Keywords: Magnetite nanoparticles, *Boswellia dalzielii,* lipids, carcinogenesis, diethylnitrosamine.

INTRODUCTION
Cancer remains one of the leading causes of morbidity and mortality worldwide, with liver related malignancies contributing significantly to the global cancer burden (Tan *et al.*, 2025). Hepatocarcinogenesis is frequently associated with profound alterations in lipid metabolism, oxidative stress imbalance, and chronic inflammatory processes that collectively disrupt normal cellular homeostasis (Khan *et al.*, 2021). Experimental models employing chemical carcinogens have been widely

utilized to elucidate the biochemical and molecular mechanisms underlying cancer development and progression (Dou *et al.*, 2025). Among such carcinogens, diethylnitrosamine has gained extensive research relevance due to its potent hepatotoxic and carcinogenic properties, which closely mimic human liver carcinogenesis (Raza *et al.*, 2026). Emerging therapeutic strategies increasingly emphasize the use of bioactive natural products and nanotechnology-based delivery systems to mitigate carcinogen induced metabolic derangements (Ahmad *et al.*, 2022). In this context, *Boswellia dalzielii*, a medicinal plant with established anti-inflammatory and antioxidant properties (Raza *et al.*, 2015, Dogara *et al.*, 2023, Elango *et al.*, 2023, Aboulthana *et al.*, 2025), coupled with magnetite nanoparticles as targeted delivery vehicles, represents a novel approach in cancer related lipid metabolism modulation. Investigating the combined effect of *Boswellia dalzielii* loaded magnetite nanoparticles on lipid profile alterations in diethylnitrosamine induced carcinogenesis is therefore of substantial scientific and biomedical relevance (Akhtar *et al.*, 2015, Elsharkawy *et al.*, 2019, Khan *et al.*, 2021, Raza *et al.*, 2026).

Figure 1: *Boswellia dalzielii* (Hutch) plant showing the complete tree (a), leaves (b), stem (c), stem bark (d) growing in its natural habitat
Source/ Location: Picture taken at Minda village of Lau LGA, Taraba State.

Lipid metabolism plays a central role in cellular energy homeostasis, membrane integrity, and signaling pathways, all of which are critically altered during carcinogenesis. Dyslipidemia characterized by elevated total cholesterol, triglycerides, and low-density lipoproteins alongside reduced high density lipoproteins has been consistently reported in chemically induced liver cancer models. These lipid abnormalities not only reflect hepatic dysfunction but also actively contribute to tumor cell proliferation and survival through altered membrane synthesis and oncogenic signaling cascades (Raza *et al.*, 2026). Diethylnitrosamine, a nitrosamine compound commonly found in processed foods, tobacco smoke, and contaminated water sources, has been extensively employed to induce hepatocellular carcinoma in

laboratory animals due to its ability to generate reactive oxygen species and DNA adducts during hepatic metabolism (Khan *et al.*, 2021). The oxidative stress generated by diethylnitrosamine exposure further exacerbates lipid peroxidation, leading to profound disturbances in lipid profile and cellular integrity (He *et al.*, 2020; Liu *et al.*, 2021).

Medicinal plants have historically served as valuable sources of chemopreventive agents due to their rich phytochemical composition (Ahmad *et al.*, 2022). *Boswellia dalzielii*, a member of the Burseraceae family widely distributed in West Africa, has been traditionally used for the management of inflammatory disorders (Salehi *et al.*, 2020, Idu *et al.*, 2023), liver ailments, and metabolic diseases (Patra *et al.*, 2018; Hassan *et al.*, 2021, Raza *et al.*, 2026). Phytochemical investigations have revealed the presence of boswellic acids, flavonoids, and terpenoids, compounds known to exhibit antioxidant, hypolipidemic, and anticancer activities (Salehi *et al.*, 2020). Recent advances in nanotechnology have further enhanced the therapeutic potential of plant derived compounds by improving bioavailability, stability, and targeted delivery (Bakrim *et al.*, 2022, Anthony and Hamman, 2023). Magnetite nanoparticles, owing to their biocompatibility, magnetic responsiveness, and capacity for surface functionalization, have emerged as promising carriers for drug delivery in cancer therapy (He *et al.*, 2020, Barathi *et al.*, 2024, Ali *et al.*, 2025). Integrating *Boswellia dalzielii* extracts with magnetite nanoparticles may therefore provide synergistic benefits in modulating lipid metabolism and attenuating carcinogen induced hepatic damage (Abdel Aziz *et al.*, 2019).

This research highlights the critical need for a systematic investigation into the synergistic impact of *Boswellia dalzielii*-mediated magnetite nanoparticles on lipid metabolism and evaluate the effect of *Boswellia dalzielii* Leaf-mediated magnetite nanoparticles on the lipid profile of albino rats with diethylnitrosamine induced carcinogenesis, which could lead to the findings and development of safer, plant based nanotherapeutic strategies for cancer management and also expand existing knowledge on the pharmacological applications of *Boswellia dalzielii.*

MATERIALS AND METHODS

Plant Sample Collection

The plant sample, leaves of *Boswellia dalzielii* was collected from Minda village of Lau LGA, Taraba state, it was cleaned and air dried at room temperature for approximately 30 days between November and December, 2025. The sample was pulverized and sieved with locally manufactured sieve. The fine powder was stored in air-tight container until use.

Magnetite Nanoparticle Synthesis

To 250 mL aqueous extract of *Boswellia dalzielii*, 250mL of 0.2 M ferric chloride hexahydrate ($FeCl_3.6H_2O$) (MOLYCHEM, Product code: 14400, Batch Number: MCR-24624, India) and0.1 M ferrous sulfate heptahydrate ($FeSO_4.7H_2O$) (LOBA Chemie, Pvt Ltd, India) (ratio 2:1) was added and stirred with magnetic stirrer for 1h at room temperature. Further, 0.1 M sodium hydroxide (NaOH) (MOLYCHEM, Product code: 18500, Batch Number: MCR-19845, Mumbai, India) was added dropwise for the precipitation of NPs. Alkaline pH of 11- 12 was maintained. It was further stirred and decanted, and evaporated at 70 °C using water bath. The synthesized nanoparticle was then powdered using hand crusher (Eldeeb *et al.*, 2023).

Experimental Animals

A total of 11 groups, each consisting of five (5) animals was used. Group 1 to 3 servesd as control groups; normal, negative and positive controls respectively. Group 4 to 7

served as ameliorative treatment and group 8 to 11 served as preventive treatments. One time dose of 200 mg/kg body weight diethylnitrosamine (DEN) was induced in the ameliorative treatment and two weeks later, administration of nanoparticle with concentration; 100 ppm, 300 ppm, 500 ppm, and 800 ppm for two weeks. For the preventive treatments; 100 ppm, 300 ppm, 500 ppm, and 800 ppm nanoparticle was administered and 200 mg/kg DEN was administered after two weeks of treatments. The animals were sacrificed at the end of four weeks and their blood sample was collected for analysis. The lipid parameters where carried out using the method described by Suryawanshi *et al.*, (2006).

The data were analysed by the analysis of variance (ANOVA) using SPSS program (version 25 SPSS Inc., IL, Chicago, USA). The differences in parameters between the various animal groups were compared using the Bonferroni multiple comparison test (post-hoc test). The results were expressed as mean ± standard deviation (SD). P value less than 0.05 was considered as significant ($P< 0.05$). Results were presented in table, charts and graphs using Microsoft word and Excel.

RESULTS

Table 1: Ameliorative Effects of Magnetite Nanoparticle on Lipid Parameters of DEN-Induced Carcinogenesis in Wistar Rats

GROUP	TCHOL (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	MDA (mg/dL)	TGL (mg/dL)
GP1	87.28±28.07$^{a\,b}$	15.75±4.94^{a}	11.31±1.05^{a}	3.85±0.00^{a}	8.84±4.77^{a}
GP2	206.57±44.37^{c}	8.50±6.92^{a}	23.46±4.29^{a}	9.37±2.05^{d}	71.53±3.49^{f}
GP3	179.87±52.07$^{b\,c}$	14.51±5.27^{a}	15.54±7.59^{a}	4.04±0.18^{a}	44.42±2.38^{d}
GP4	97.99±19.34$^{a\,b}$	9.02±5.33^{a}	12.64±1.35^{a}	4.03±0.13^{a}	58.37±15.43^{e}
GP5	53.69±13.42^{a}	10.16±7.00^{a}	12.31±3.04^{a}	4.12±0.05^{a}	42.56±3.73^{d}
GP6	72.48±19.80^{a}	13.37±4.02^{a}	13.58±2.31^{a}	7.49±1.74^{c}	25.12±5.73$^{b\,c}$
GP7	96.64±71.12$^{a\,b}$	11.81±2.68^{a}	15.20±15.16^{a}	5.51±0.29^{b}	48.66±2.44^{d}

n=5; Results are in mean ± standard deviation; values with different superscripts down the columns are significantly different at $p < 0.05$. TCHOL: total cholesterol, TGL: triglyceride, HDL: high density lipoprotein, LDL: low density lipoprotein

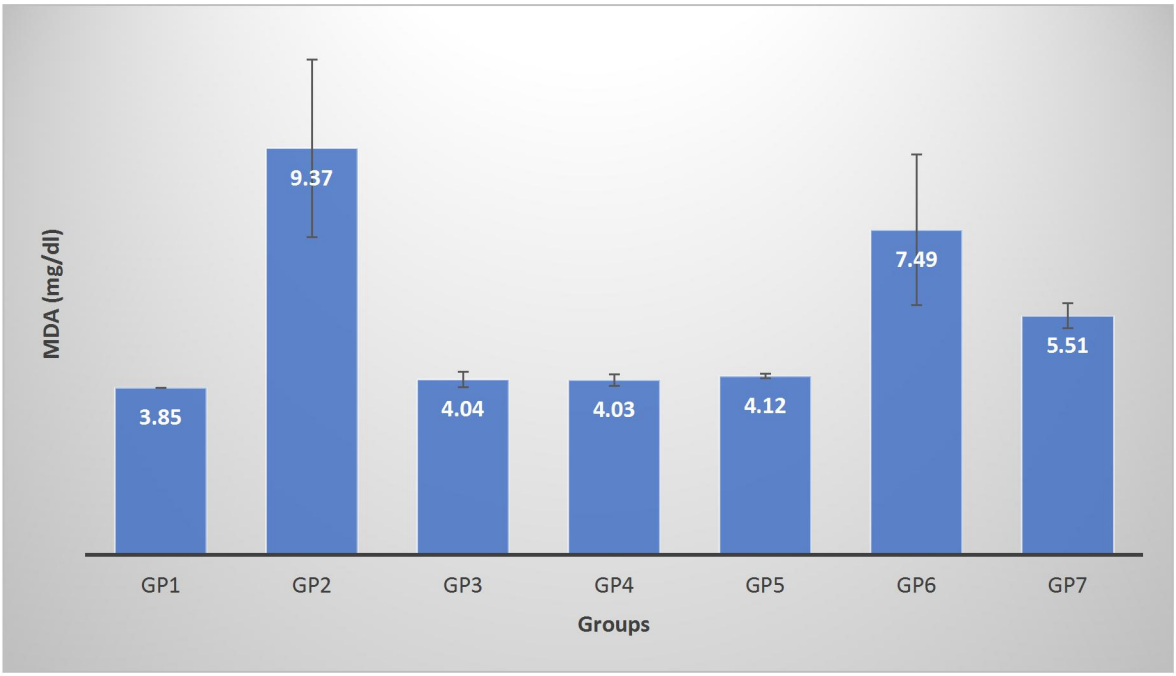

Figure 2: Ameliorative Effects of Magnetite Nanoparticle on MDA of DEN-Induced Carcinogenesis in Wistar Rats

Results are in mean ± standard deviation; values are significantly different at $p < 0.05$. MDA (Malondialdehyde), GP (Group)

Table 2: Preventive Effects of Magnetite Nanoparticle on Lipid Parameters of DEN-Induced Carcinogenesis in Wistar Rats

GROUP	TCHOL (mg/dL)	HDL (mg/dL)	LDL (mg/dL)	MDA (mg/dL)	TGL (mg/dL)
GP1	87.28±28.07$^{a\,b}$	15.75±4.94^{a}	11.31±1.05^{a}	3.85±0.00^{a}	8.84±4.77^{a}
GP2	206.57±44.37^{c}	8.50±6.92^{a}	23.46±4.29^{a}	9.37±2.05^{d}	71.53±3.49^{e}
GP3	179.87±52.07$^{b\,c}$	14.51±5.27^{a}	15.54±7.59^{a}	4.04±0.18^{a}	44.42±2.38^{d}
GP4	164.96±16.76$^{b\,c}$	10.36±1.55^{a}	12.39±4.30^{a}	5.53±0.03^{b}	18.57±12.71^{b}
GP5	142.28±104.2$^{a\,b\,c}$	14.51±5.27^{a}	10.52±7.29^{a}	7.21±0.54^{c}	21.16±8.28^{b}
GP6	126.17±123.88^{abc}	13.06±1.06^{a}	17.99±22.66^{a}	5.69±1.03^{b}	31.86±1.95^{c}
GP7	178.52±75.43$^{b\,c}$	14.40±26.42^{a}	16.56±5.05^{a}	4.04±0.12^{a}	33.02±6.02^{cd}

n=5; Results are in mean ± standard deviation; values with different superscripts down the columns are significantly different at $p < 0.05$. TCHOL: total cholesterol, TGL: triglyceride, HDL: high density lipoprotein, LDL: low density lipoprotein

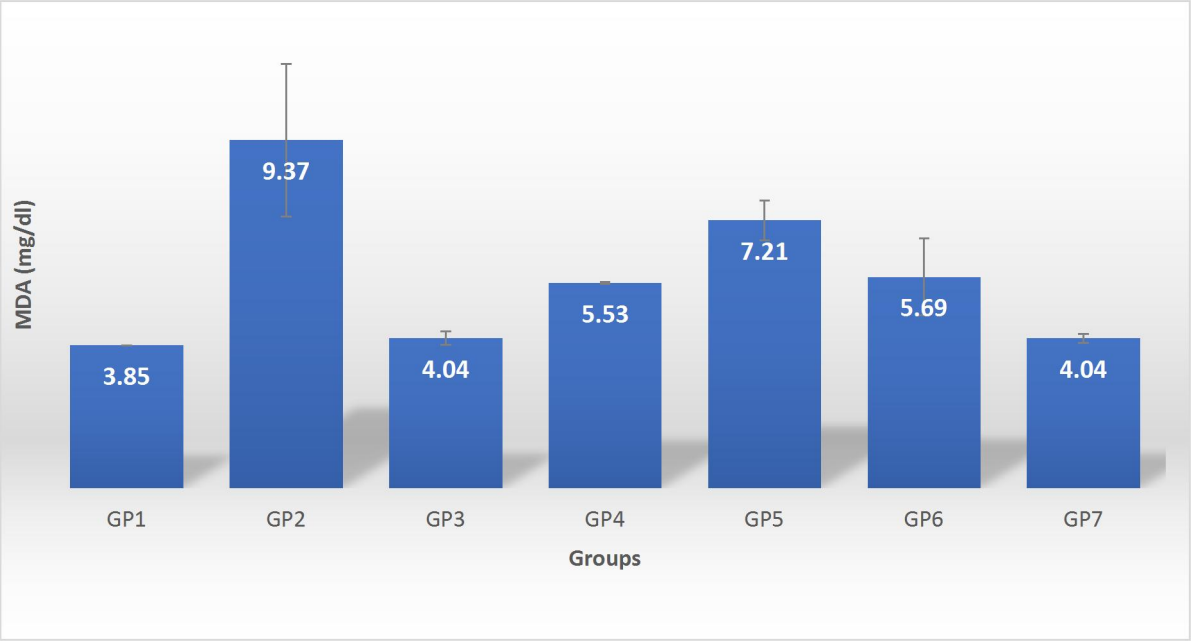

Figure 3: Preventive Effects of Magnetite Nanoparticle on MDA of DEN-Induced Carcinogenesis in Wistar Rats. n=5; Results are in mean ± standard deviation; values are significantly different at $p < 0.05$. MDA: Malondialdehyde, GP: Group

DISCUSSION

This study investigated the effect of *Boswellia dalzielii* leaf-mediated magnetite nanoparticles on the lipid profile of albino rats subjected to diethylnitrosamine (DEN)-induced carcinogenesis (Fathy *et al.*, 2017, Mansour *et al.*, 2019). The study was motivated by the increasing prevalence of cancer and the associated metabolic disturbances, particularly alterations in lipid metabolism that accompany carcinogenic processes. DEN is a well-established hepatocarcinogen widely used in experimental studies to induce hepatocellular carcinoma due to its ability to generate

reactive metabolites that cause oxidative stress, DNA damage, and lipid peroxidation (Wang *et al*., 2023, Dhanarasu, 2024). The research focused on evaluating whether plant-derived nanoparticles synthesized from *Boswellia dalzielii* could ameliorate or prevent lipid metabolic disturbances associated with DEN-induced carcinogenesis. *Boswellia dalzielii* is known to contain several bioactive phytochemicals such as boswellic acids, flavonoids, and phenolic compounds, which possess antioxidant, anti-inflammatory, and potential anticancer properties. Integrating these phytochemicals with magnetite nanoparticles was expected to enhance their bioavailability and therapeutic efficiency.

In this study, DEN exposure significantly disrupted lipid metabolism in group 2 (tables 1 and 2), resulting in elevated levels of total cholesterol (206.57±44.37), triglycerides (71.53±3.49), and LDL (23.46±4.29), along with reduced HDL (8.50±6.92) levels. This agrees with the findings of Mayengbam *et al.* (2021). These alterations are consistent with previous studies demonstrating that chemical carcinogens induce dyslipidemia through oxidative stress and hepatic dysfunction (Bhatnagar *et al*., 2022). Treatment with *Boswellia dalzielii*-mediated magnetite nanoparticles significantly improved the lipid profile by lowering the elevated cholesterol (97.99±19.34, 53.69±13.42, 72.48±19.80, 96.64±71.12) and triglyceride (58.37±15.43, 42.56±3.73, 25.12±5.73, 48.66±2.44) levels while increasing HDL (9.02±5.33, 10.16±7.00, 13.37±4.02, 11.81±2.68) concentrations. This was observed for both the ameliorative and preventive treatments. Additionally, the nanoparticles reduced MDA levels, indicating decreased lipid peroxidation and improved antioxidant status, which agrees with the studies of; Hamadjida, *et al*., (2023) and Allegra *et al*., (2024).

The role of lipids in advancement of cancer and its significance in a number of disorders is growing. With increasing awareness about the importance of lipids and its impact on the survival and quality of life, scientists are focusing more on its pathophysiology in various diseases. Lipids are important for monitoring prognosis of a disease, so it has become essential to work on such parameters to improve treatment outcome and survival period among cancer patients (Jee *et al*., 2016, Zehra and Loya, 2025). The result of the study in group 2 which showed significant increase in lipid parameters could be a clear indication of malignancy associated with the DEN exposure. However, various treatments with the magnetite nanoparticle which varies from: 100 ppm (GP4), 300 ppm (GP5), 500 ppm (GP6) and 800 ppm (GP7) in both the ameliorative and preventive treatments show some marked improvements, when compared to the negative control group (GP2) and positive control group (GP3) which was treated with known anticancer drug silymarin (100 mg/kg) body weight.

It has been shown that, proper immune responses of tumor cells depend on the control of lipid metabolism (Allegra *et al*., 2024). The significant increase, $p < 0.05$ in the HDL levels from the negative control group (GP2) of 8.50±6.92 to; 10.36±1.55 (100ppm), 14.51±5.27 (300 ppm), 13.06±1.06 (500 ppm), 14.40±26.42 (800 ppm) in table 2, when administered nanoparticles indicates a proper response in preventive treatments. This proper response is also observed in table 1 which is the ameliorative treatment. A role for high density lipoproteins (HDL) has been hypothesized. In fact, in addition to the reverse cholesterol transport, HDL exert pleiotropic roles such as anti-oxidant and anti-inflammatory properties (Diab *et al*., 2022). Previous clinical studies indicate a negative relationship between levels of HDL and breast cancer risk (Campos *et al*., 2023). This relates to the significant decrease in the LDL from the study as HDL level increases when compared to the negative control (group 2, table 1 and table 2).

Since the HDL is the lipoprotein that is most prevalent in most species, it is likely that this particle has significant roles. HDL may have anti-inflammatory, anti-oxidative, and anti-apoptotic effects in addition to regulating innate and adaptive immune responses (Pirro *et al*., 2018; Allegra *et al*., 2024). Low HDL levels may contribute to the development of cancer by disrupting some of these characteristics (Pirro *et al*., 2018), the HDL value in the present study, group 2, table 4.5 and 4.6 (8.50mg/dL) is lower as a result of carcinogenesis unlike the normal group (GP1), positive control mgroup (GP2) and the treatment groups. Other lipid parameters; TCHOL, LDL, TGL have significantly higher values which is as a result of carcinogenesis which agrees with the findings of Chen *et al*., (2024).

The Higher plasma levels of markers of lipid peroxidation and alterations of activities of enzymes which exert key roles in HDL properties are described in breast cancer patients. HDL functionality is affected by its apolipoprotein composition and activity of enzymes. The lower lecithin cholesterol acyltransferase (LCAT) activity suggests alterations of cholesterol metabolism (Gao *et al*., 2025). Moreover, the lower activities of enzymes involved in the antioxidant properties of HDL such as Paraoxonase-1 (PON1) and phospholipase A2 (PLA_2) suggests this key role of HDL could be impaired in breast cancer patients (Ganjali *et al*., 2019). Dysfunctional HDL exert a lower protective effect against lipid peroxidation and induce proliferation and migration of breast cancer cells (Mazzuferi *et al*., 2021).

Lowering LDL leads to more survival rate in cancer patients (Lee *et al*., 2022). In cancer, the role of dyslipidemia has been observed significantly important in many other diseases like Metabolic Syndrome, Hypertension, Chronic Obstructive Pulmonary Disease (COPD), and coronary artery disease (Markelić *et al*., 2021). The result of the preventive and ameliorative lipid parameters showed lowering of the values ($p < 0.05$) both for total cholesterol (TCHOL), low density lipoprotein (LDL), triglyceride (TGL) which agrees with the findings of Lee *et al*., (2022). The higher the dosage of the treatments, it shows the higher the efficiency of the treatments, comparing the values in the groups with a known anticancer drug silymarin.

Serum malondialdehyde (MDA), a biomarker of oxidative stress in various malignancies and to correlate its significance with clinicopathological parameters. Since MDA is highly cytotoxic and carcinogenic agent, it is frequently used as a biomarker of oxidative stress during major health problems such as cancer. An increase in lipid peroxidation level (MDA) has been demonstrated in various tumors. Increased lipid peroxidation is attributed to deficiency in antioxidant defenses. Serum antioxidant deficiency may be due to sequestration by tumor cells as well as scavenging of lipid peroxides. In the current study, figure 2 and figure 3 showed a significantly $p < 0.05$ increased level of MDA in both the ameliorative and preventive studies in the DEN-induced group.

CONCLUSION

This study's results indicated that diethylnitrosamine-induced carcinogenesis causes substantial changes in lipid metabolism, marked by elevated serum cholesterol, triglycerides, and LDL levels, coupled with reduced HDL concentrations. Lipid abnormalities are intricately linked to oxidative stress and lipid peroxidation processes implicated in cancer progression. The administration of *Boswellia dalzielii* leaf-mediated magnetite nanoparticles shown both preventative and therapeutic effects on these metabolic abnormalities. The treatments significantly enhanced lipid profile measures and diminished oxidative stress markers, indicating robust hypolipidemic and antioxidant effects. The therapeutic effects reported may be ascribed to the combined impact of bioactive phytochemicals in *Boswellia dalzielii* and the improved delivery efficacy of magnetite nanoparticles. Consequently, *Boswellia dalzielii* leaf-mediated magnetite nanoparticles may act as a potential

natural nanotherapeutic agent for alleviating lipid metabolic disorders linked to carcinogenesis.

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CONFLICTS OF INTEREST
The authors declare there is no conflicts of interest.

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