Green synthesis of *Ficus benghalensis* mediated copper nanoparticle and its antioxidant activity.

Devika. B[1], S. Rajeshkumar[2*], D. Ezhilarasan[3], T Lakshmi[4]
[1,3,4] Department of pharmacology, Saveetha Dental College and hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai - 600077, Tamilnadu, India;
[2] Nanomedicine lab; Department of pharmacology, Saveetha Dental College and hospitals, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai - 600077, Tamilnadu, India;
Dr. S. Rajeshkumar - Email: ssrajeshkumar@hotmail.com, * corresponding author.

Abstract:

Ficus benghalensis, a large evergreen tree, belongs to the family Moraceae. It is commonly known as "Indian Banyan Tree". Antioxidants protect the body against oxidative stress by neutralizing free radicals and reactive oxygen species (ROS) for example, superoxide radicals, hydroxyl radicals, hydrogen peroxide radicals. This oxidative damage produces a lot of chronic human diseases like diabetes mellitus, cancer, atherosclerosis, arthritis, and neurodegenerative diseases. Nanoparticles (NPs) have shown notable advances owing to a wide range of applications in biomedicine, sensors, antimicrobial agents, catalysts, electronics, optical fibers, agricultural, biolabeling, and other areas. The aim of this study is to synthesize the *Ficus benghalensis* mediated copper nanoparticle and to see its antioxidant activity. The plant extract was prepared using the bark of *Ficus benghalensis* and mixed with copper nanoparticles. 0.507 g of anhydrous copper sulphate was added to 70 mL of distilled water and 30 mL of plant extract. It was kept in an orbital shaker for uniform dispersion. It was centrifuged and pellets were collected. The pellets obtained were used for antioxidant activity, DPPH assay. For DPPH assay, diverse concentrations of Ficus benghalensis bark extract interceded copper nanoparticles and 1 ml of 0.1 mM DPPH in methanol. It was incubated for 30 minutes. The reduction of DPPH free radicals was assessed dependent on the absorbance at 517 nm. The results were collected and statistically analyzed. The percentage of inhibition of DPPH free radicals was calculated. The values were 64.2% at 10 µL concentration, 63.1% at 20 µL, 55.5% at 30 µL, 46.2% at 40 µL (85.2%) and 46.7% at 50 µL. As the concentration increases the antioxidant activity of the nanoparticles increases. Percentage of Inhibition was highest at 50µL. The values for antioxidant properties of nanoparticles were found to be higher than the standard values at all concentrations except at 50 µL. This study was done to find a way for a greener approach of synthesizing the copper nanoparticles, thereby giving pharmacological evidence against the antioxidant activity. The copper nanoparticle synthesized using *Ficus benghalensis* has potent free radical scavenging activity, hence has antioxidant property and has a wide array of medical and dental applications.

Keywords: Green synthesis, Eco-friendly, antioxidant activity, *Ficus benghalensis,* in-vitro study, copper nanoparticle.

Background:

According to the WHO (World Health Organization), 70–80 % of the population in developing countries still relies on non-conventional medicine mainly from herbal sources in their primary healthcare. Pharmacological screening of plants, provides a basis for the development of new lead molecules, in allopathy [1]. The recent developments in phyto-chemistry and molecular biology have renewed and reinvigorated our interest in herbal medicines. Again, anecdotal claims of 'no side effects', easy access and cheap price have lured people from all walks of life to turn back to nature [2]. *Ficus benghalensis*, a large evergreen tree, belongs to the family *Moraceae*. It is commonly known as "Indian Banyan Tree". The genus *Ficus* includes around 750 species growing in most tropical and subtropical forests throughout the world. The genus is remarkable for the large variation in the habits of its species [3]. *Ficus benghalensis* has a wide range of uses. Some of those are, leaves are good for ulcers, aerial roots are useful in gonorrhea, seeds and fruits are used as coolant and tonic. The roots of *Ficus bengalensis* are given for obstinate vomiting and infusion of its bark is considered as a tonic and astringent and is also used in diarrhea, dysentery and diabetes [4]. Antioxidants protect the body against oxidative stress by neutralizing free radicals and reactive oxygen species (ROS) for example, superoxide radicals, hydroxyl radicals, hydrogen peroxide

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radicals. Flavonoids, flavonols and terpenoids are favorite choices among natural antioxidants [5]. It reduces the risk of chronic disease including cancer and heart disease. Some of the antioxidants are O_2, H_2O_2 and OH radical. This oxidative damage produces a lot of chronic human diseases like diabetes mellitus, cancer, atherosclerosis, arthritis, and neurodegenerative diseases [6]. Green chemistry is nothing but implementation, development and designing of chemical products and making it eco-friendly and biocompatible for the usage in medicine and food industry. It was found to be more suitable than other methods like electrochemical reduction, chemical reduction, heat evaporation, photochemical reduction, etc., as it was cost effective, simple, use of less temperature and toxic materials. Here, the plant extract acts as a capping and reducing agent in the synthesizing of copper nanoparticles because of the reducing properties in the leaf extract [7].

In a previous study, the extract was examined for its antioxidant activity by DPPH radical scavenging activity, hydroxyl radical scavenging activity, reducing capacity, hydrogen peroxide activity, total phenolic content using Folin-Ciocalteu's phenolic reagent. The results revealed the extreme scavenging activity of DPPH radical (96.07%) at 250 µg mL-1 concentration. It shows good results when compared with other compounds. This shows the scavenging activity of the extract. The green synthesis of nanoparticles has been improved in order to design new materials that are ecological, valuable, and stable [8]. Bark extracts have excellent properties as bio reductants [9]. In recent years, nanobiotechnology has attracted considerable research, which has had an impact on all life forms [10]. Nanoparticles (NPs) have shown notable advances owing to a wide range of applications in biomedicine, antimicrobial agents, catalysts, agricultural, biolabeling, etc. [11]. Due to their size, different shapes, and increased surface area, nanoparticles show very different properties. The interest in nanoparticles applicability in biomedical science, is increasing with every new research study in this field[12] . The copper nanoparticles (Cu NPs) have been a strong possession of applications in health-related actions [13]. In recent years, the implementation of the synthesis of Cu NPs is a challenge due to the complexity of metal nanoparticles instead of metal oxides [14]. In a previous study, Scanning electron microscopy results showed the distribution of nanoparticles and particle sizes are found to be in the range of 5-20 nm. X-ray diffraction spectrum characteristic diffraction peaks for copper nanoparticles were observed at 35.5 and 43.2° corresponding to lattice planes (1 1 1) and (2 0 2), respectively. X-ray photoelectron spectroscopy shows that two distinct peaks at binding energy resulted in the chemical states of copper [15]. In another study, The morphology and characterization of the synthesized copper nanoparticle were studied using UV-Visible spectroscopy at a wavelength of 350–380 nm. XRD studies were performed for analyzing the crystalline nature; SEM and TEM for evaluating the spherical shape within the size range of 60–90 nm and AFM was performed to check the surface roughness [16]. In a previous study, 0.861 g of the copper sulfate powder was added in 50 ml of distilled water and to this; the lodhra bark extract was being added. The solution was kept in a shaker and the readings were taken for the synthesis of copper nanoparticles [17].The use of plant extracts in the production assembly of metallic NPs is rapid, eco-friendly, non-pathogenic, and economical [18]. Our team has extensive knowledge and research experience that has translate into high quality publications [19] [20] [21] [22] [22,23] [24] [25] [26] [27] [28] [29] [30] [31] [32] [33] [34] [35]. The aim of this study is to synthesize the *Ficus benghalensis* mediated copper nanoparticle and to see its antioxidant activity.

Materials and method:

Plant Material and Extraction

The bark of *Ficus benghalensis* was obtained from the local market and was made to dry in a shady region to finalize the moisture content. After this, they were crushed to fine powder using a grinder. Then 50 mL of water was added to 0.5 g of Ficus benghalensis in a conical flask which was then labeled and set for heating (fig 1(A and B)). For this heating process, the heating mantle was set to a temperature of 50 to 60°C and the time taken for this process to complete was 6-8 minutes. The solution was then filtered using a filter paper and finally the plant extract was prepared (fig 2).

Synthesis of (CuNPs) Copper Nanoparticles

0.507 g of anhydrous copper sulphate and 70 mL of distilled water was added to 30 mL of plant extract that was already prepared before and found that the solution was light blue in color. The extract was then further clogged with foil paper. Using an orbital shaker, uniform dispersion was made to initiate the synthesis process and the color change of the solution was observed periodically [36] (fig 3 (A)). The product was then dried and heated in a furnace. The annealed product thus obtained was taken as the sample for this study.

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Characterization Nanoparticles of Synthesized

The copper nanoparticles synthesized were measured optically using double beam UV–vis spectroscopy . It refers to absorption spectroscopy in visible ranges and directly affects the color of the chemicals present. It is mostly used in analytical chemistry for quantitative determination of different ions, compounds and biological macromolecules at different wavelengths. The synthesized CuNPs were optically measured at different wavelengths ranging from 250 nm to 350 nm.

Antioxidant activity

DPPH assay was used to test the antioxidant activity of biogenic synthesized copper nanoparticles. Diverse concentrations (2-10 µg/ml) of *Ficus benghalensis* bark extract interceded copper nanoparticle was mixed with 1 ml of 0.1 mM DPPH in methanol and 450 µl of 50 mM Tris HCl buffer (pH 7.4) and incubated for 30 minutes (fig 4). Later, the reduction in the quantity of DPPH free radicals was assessed dependent on the absorbance at 517 nm. BHT (Butylated hydroxytoluene) was employed as control. The percentage of inhibition was determined from the following equation,

$$\% \text{ inhibition} = \frac{\text{Absorbance of control} - \text{Absorbance of test sample}}{\text{Absorbance of control}} \times 100$$

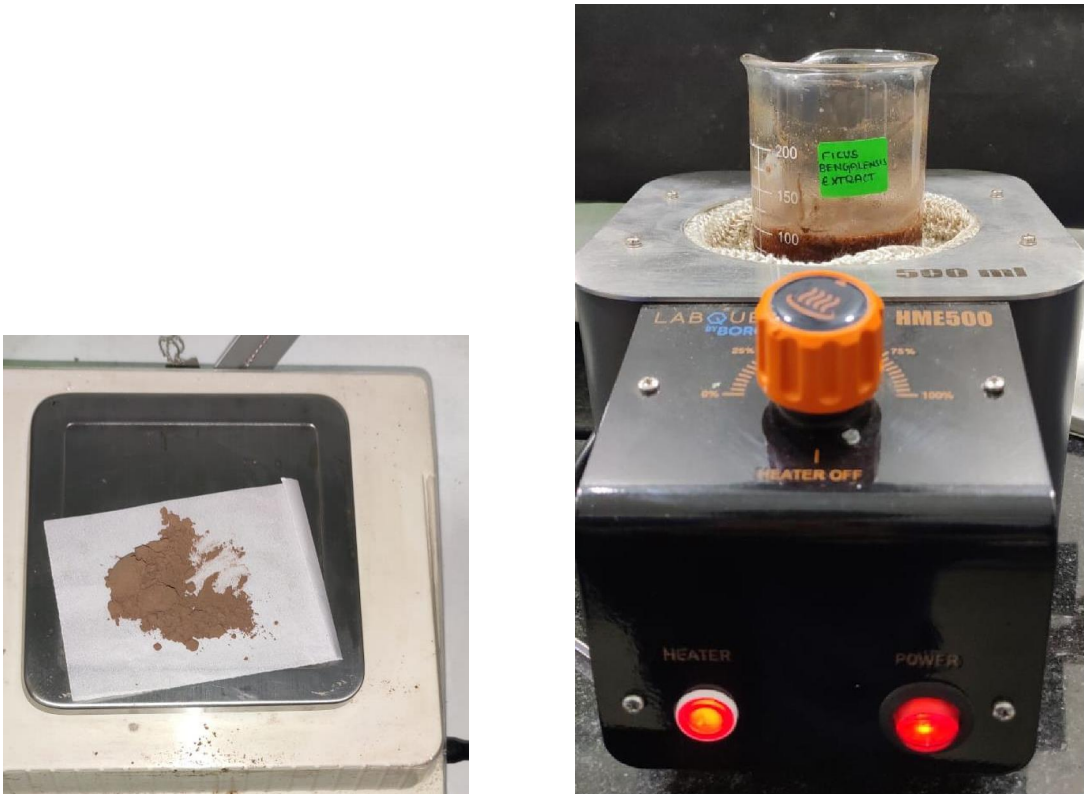

Fig 1: (A) weighing *Ficus benghalensis* bark powder in a weighing machine. (B) heating it along with water to make a solution.

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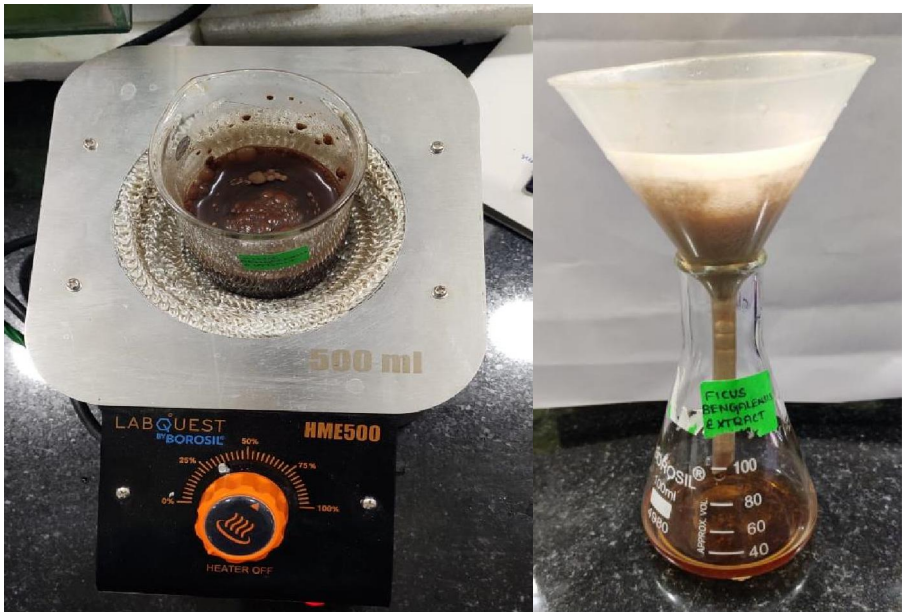

Fig 2: filtering the solution of *Ficus benghalensis* to get the extract.

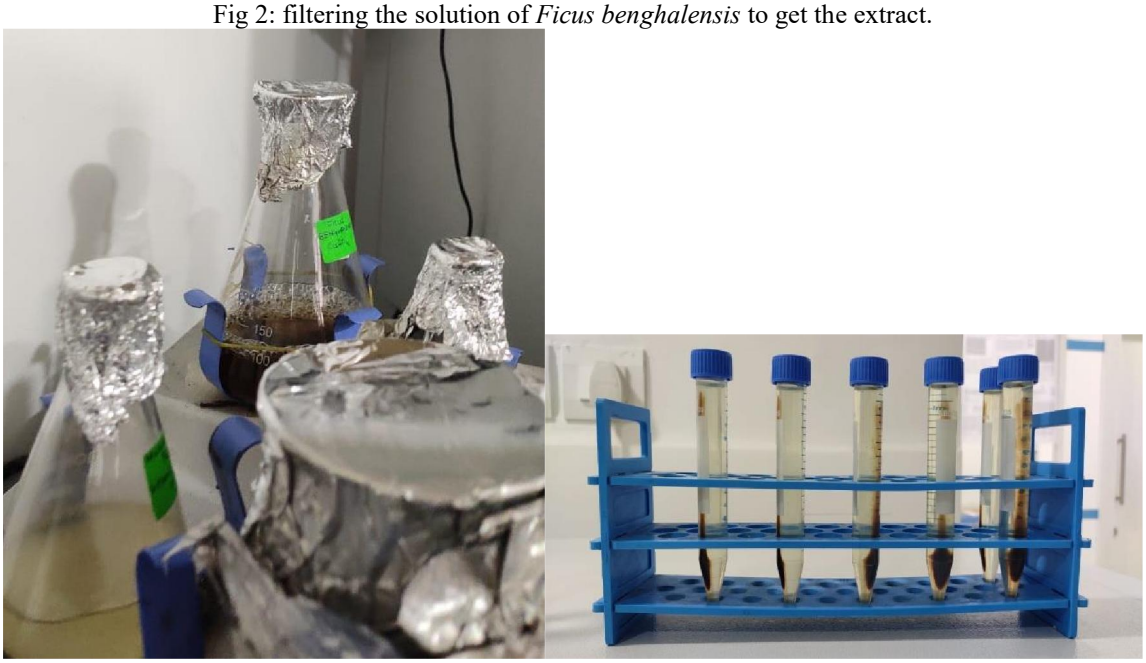

Fig 3: (A) placing the extract in a shaker. (B) after incubating, the pellets were collected

Results and discussion:

In the present study, *Ficus benghalensis* bark powder was weighed in a weighing machine. The weighed sample was heating it along with water to make a solution. Later, filtering the solution of *Ficus benghalensis* to get the extract. Extract was placed in a shaker. After incubating, the pellets were collected. Different concentrations of solution are added in a test tube for checking the antioxidant activity. The quality of antioxidant activity of copper nanoparticles synthesized using *Ficus benghalensis* (Fig 5). The values obtained during UV-vis absorption spectra analysis were tabulated in table 1. The percentage of inhibition of DPPH free radicals (antioxidant activity) was calculated using the formula mentioned above. The values were 64.2% at 10 µL concentration, 63.1% at 20 µL, 55.5% at 30 µL, 46.2% at 40 µL (85.2%) and 46.7% at 50 µL. As the concentration increases the antioxidant activity of the nanoparticles increases. Percentage of Inhibition was highest at 50µL.

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UV- vis absorption spectra analyses of copper nanoparticles synthesized using *Ficus benghalensis* recorded as function of time (Fig 6).

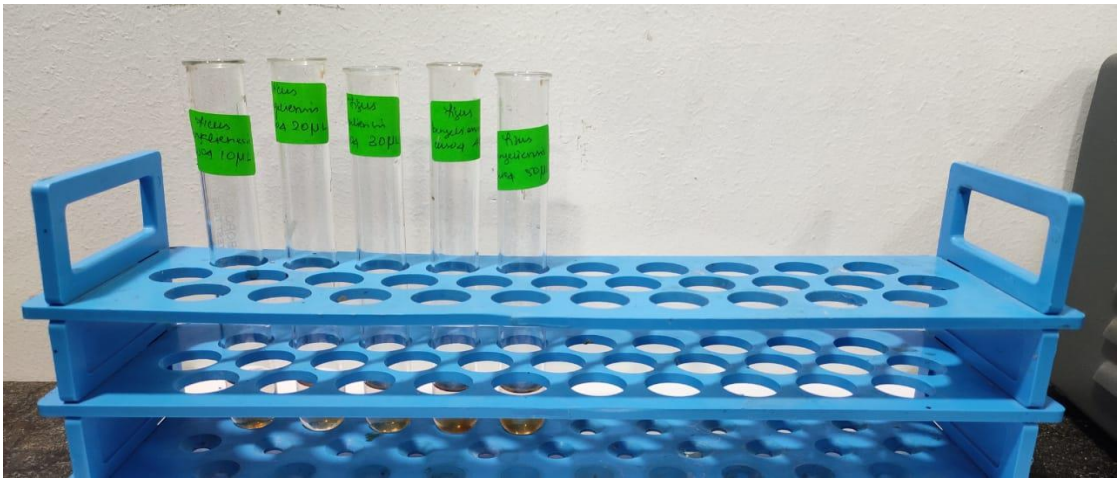

Fig 4: different concentrations of solution are added in a test tube for checking the antioxidant activity.

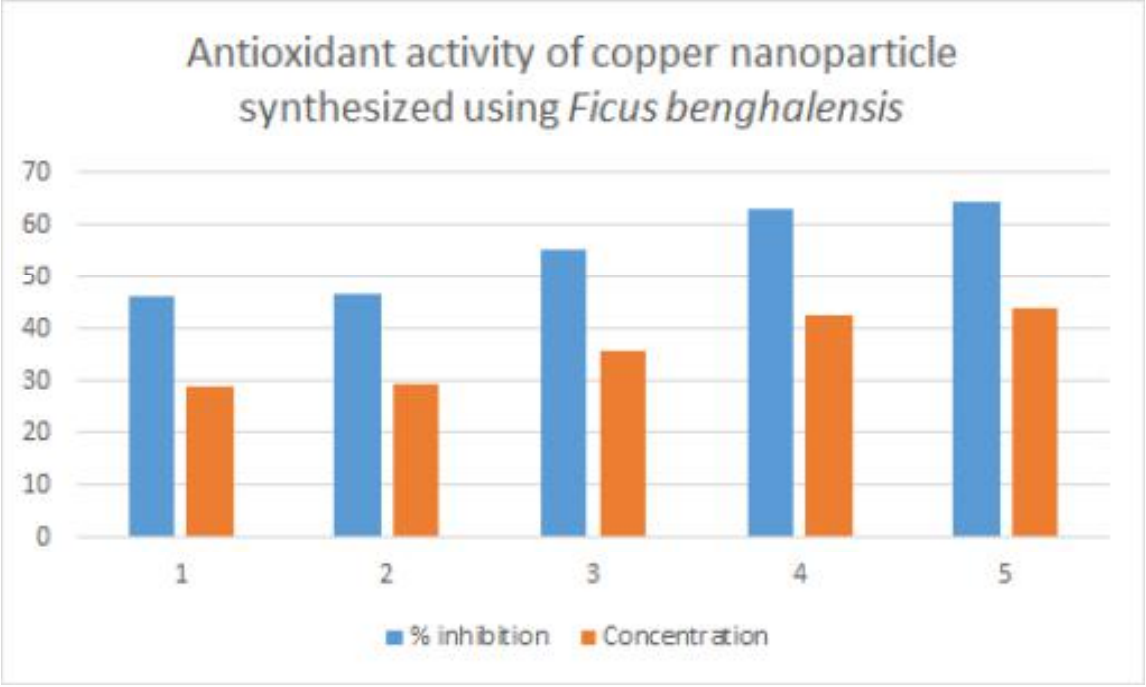

Fig 5: The quality of antioxidant activity of copper nanoparticles synthesized using *Ficus benghalensis.* X-axis shows the Concentration of nanopartilces and Y axis is the % of inhibition

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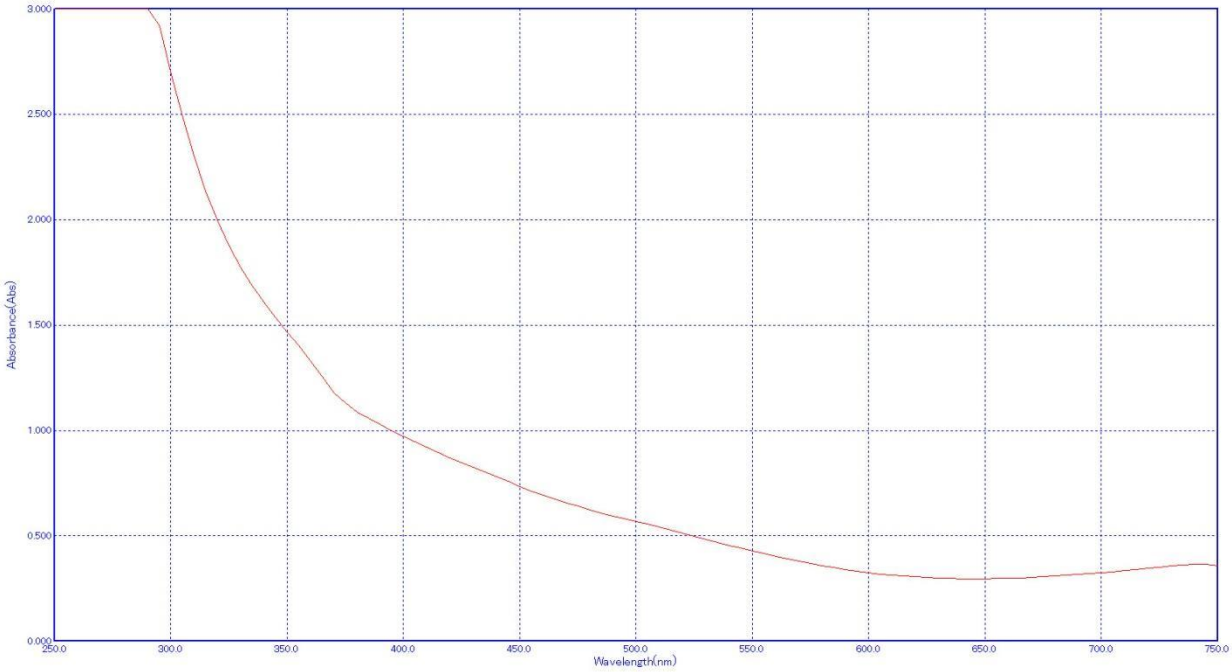

Fig 6: UV- vis absorption spectra analyses of copper nanoparticles synthesized using *Ficus benghalensis* recorded as function of time

There has been a rapid evolution of nanoparticle synthesis recently as compared to the early part of the century. Earlier, physio-chemical methods were involved in nanoparticle synthesis. Even though less time is utilized for synthesizing large quantities of nanoparticles using conventional physical and chemical methods, toxic chemicals are required as capping agents to maintain stability, thus leading to toxicity in the environment. Keeping this in consideration, green nanotechnology using plants is emerging as an eco-friendly alternative, as plant extract mediated biosynthesis of nanoparticles is cost-effective. We therefore undertook this study to evaluate the antioxidant property of copper nanoparticles reinforced with *Ficus benghalensis* extract.

In the present study, the values obtained during UV-vis absorption spectra analysis were tabulated in table 1. The percentage of inhibition of DPPH free radicals (antioxidant activity) was calculated using the formula mentioned above. The values were 64.2% at 10 µL concentration, 63.1% at 20 µL, 55.5% at 30 µL, 46.2% at 40 µL (85.2%) and 46.7% at 50 µL. As the concentration increases the antioxidant activity of the nanoparticles increases. Percentage of Inhibition was highest at 50µL. The values for antioxidant properties of nanoparticles were found to be higher than the standard values at all concentrations except at 50 µL. Oxide nanoparticles are not yet entirely understood, but the generation of hydroxyl radicals (OH•), superoxide anion, and perhydroxyl radicals from the surface of Copper nanoparticles are believed to be major components [37]. Due to their outstanding chemical and physical properties, large surface-to-volume ratio, constantly renewable surface, low cost, and nontoxic preparation, copper nanoparticles have been of great interest for applications in different fields. Copper nanoparticles show catalytic activity, antibacterial activity, cytotoxicity of anticancer activity, antioxidant activity, and antifungal activity in different applications [38]. Copper nanoparticles are used for degradation of different dyes such as methylene blue, degradation of atrazine, and reduction of 4-nitrophenol [39].

In a previous study, a wavelength of 565 nm was used (pH 6) and an incubation period of 30 mins. The formation of CuNPs was analysed by UV-Vis spectral analysis. The bands were red-like in color, indicating metallic copper. The characteristic absorption peak was at 565 nm [40]. In a preceding study, the calibration curve for the quantification of DPPH assay was linear over the range of standard concentrations of 500–2000 µg/ml with correlation coefficient of R^2 = 0.957 about the validity, accuracy, and precision of the method being also in the acceptable range. Methanolic fraction was more effective than the others [41]. In an earlier study, the copper oxide nanoparticles at the concentration of 50 µL have shown the highest radical scavenging activity (94.7%) [42]. In another study, the aqueous extract of *F. benghalensis* Linn. root had maximum scavenging of DPPH radical (96.07%) at 250 µg mL^{-1} concentration [43]. In a prior study, methanolic extract of *F. benghalensis* aerial roots had immune stimulatory activity with specific and nonspecific mechanisms, which may be due to the presence of a prominent amount of

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flavonoids, phenols, and tannins [44]. The antioxidant and immunomodulatory activities of *F. benghalensis* leaves fractions were evaluated, and this article indicated that the radical scavenging effects of fractions on DPPH were less than reference antioxidants [45]. The results of a previous study indicate that all the solvent tested have a noticeable effect on DPPH radical. Among the solvents tested, methanol extract of *F. bengalensis* bark exhibited more DPPH radical scavenging activity. At 800µg/mL concentration, methanol extract of *F. bengalensis* possessed 118.16% scavenging activity on DPPH. The concentration of methanol extract of *F. bengalensis* needed for 50% inhibition (IC 50) was found to be 43.81µg/mL; whereas 31.75µg/mL was needed for ascorbic acid [46]. Our team has extensive knowledge and research experience that has translate into high quality publications [47–51],[52],[53],[47],[54],[55],[56],[57][49,58,59],[60–64] . Further studies are needed to explore the potential phenolic and flavonoid compounds from *F. bengalensis* bark and *in vivo* studies are needed for better understanding their mechanism of action. To summarize, this study reports that *Ficus bengalensis* mediated copper nanoparticles is a potent antioxidant and it is one of the studies which has used bark of *F. bengalensis.*

Conclusion:

This study was done to find a way for a greener approach of synthesizing the copper nanoparticles, thereby giving pharmacological evidence against the antioxidant activity. In the future, plant bark has a wide potential for the synthesis of NPs in health care and commercial products. Implementing green synthesis methods with proven advantages has great potential. The results obtained using different characterization techniques showed prominent similarities such as antioxidant activity present in methanolic extracts of root of F. benghalensis, leaves of F. bengalensis, etc. The synthesized copper nanoparticles showed enhanced antioxidant property against DPPH (2,2-diphenyl-1-picrylhydrazyl) free radicals, which suggests possible bio-medical applications.

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Conflict of interest:

The authors declare that there was no conflict of interest

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