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Evaluating the Physicochemical and Biological Features of Green Cerium Oxide Nanoparticles Synthesized Using *Syzygium cumini* Seeds Extract.

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KEYWORDS:

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Oxidative stress;
Antioxidant;
Superoxide dismutase;
catalase

ABSTRACT:

Introduction: Cerium Oxide nanoparticles have been proven as an effective antioxidative agent as well as an antimicrobial agent experimentally. Green synthesization with *Syzygium cumini* seed extract enhance the potential of Cerium oxide nanoparticles, which we are targeting in our study.

Objectives: As the primary objective of synthesize and partially characterize the SC-CNP conjugate done in our previous paper. The main objective of this paper is to characterize and compare the properties of synthesized Cerium oxide nanoparticles and Syzygium cumini seed extract conjugates, and then evaluate their physicochemical properties.

Methods: We have used a green synthesis method for the successful fabrication of Cerium oxide nanoparticles and *Syzygium cumini* seed powder conjugate(SC-CNP). We have emphasized the characterization of SC-CNP in this paper, specifically SEM, XRD, and FTIR. Moreover, we have evaluated the physiochemical properties of SC-CNP conjugate through Antimicrobial assay, α-amylase assay and anti-cancerous activity through MTT assay.

Results. The morphology of the obtained nanocomposite was examined using Scanning Electron Microscopy, which shows a smooth regular surface with some agglomeration. The crystallinity of the conjugate was characterised by X-Ray Diffraction, confirming peaks at 111,200,211,311 proved the crystal nature of the conjugate. FTIR confirms the presence of characteristic functional groups through the signature peaks at 3430 cm^{-1}, 1630 cm^{-1}, and 1380 cm^{-1} in the SC-CNP conjugate. Antibacterial activity against Staphylococcus epidermidis through the broth dilution method shows that SC-CNP conjugate has a 1.5-fold increase in antibacterial activity than Bare CNP. SC-CNP conjugate shows 63% anti-amylase activity determines its potential as an anti-diabetic agent. The anti-cancerous activity through the MTT assay shows the potential of the Conjugate

Conclusions: All these findings showed that in SC-CNP conjugate, there is a synergistic effect of both the plant extract as well as Cerium oxide nanoparticles. These results show the potential of conjugate as an antimicrobial, antioxidative and anti-cancerous properties which needs to be further analyzed.

1. Introduction

In recent years, the synthesis of nanoparticle-plant extract conjugates has drawn a lot of attention to enhance the properties of nanoparticles, specifically their therapeutic properties and toxicity reduction. Upon the conjugation, these nanoparticles demonstrated a synergistic effect, improving both their biological

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efficacy and stability *Syzygium cumini,* also known as jamun in India, belonging to the Myrtaceae family, is a medicinal plant that exhibits diverse therapeutic properties and also plays a significant role in traditional medicinal areas, specifically Ayurveda and Unani medicine. S. cumini has been utilized for centuries to treat ailments such as dysentery, diabetes, and digestive disorders [1]. This plant is rich in bioactive compounds such as flavonoids, phenolics, and tannins, which contribute to various health benefits [2]. It has been shown that the properties of lower blood sugar levels are beneficial for diabetes management [3]. Flavonoids and phenolic compounds of *S. cumini* exhibit significant antioxidative properties, thus helping in scavenging free radicals and enhancing cellular antioxidant status [4]. It can also reduce inflammation and combat microbial infections [5] and also aids health by lowering cholesterol levels and protecting against cardiovascular diseases [6]. Various parts of the plant, such as fruit, roots, and seed extracts, show a variety of properties. One such important part is the seed extract, which is used for its medicinal value, as methanolic and ethanolic extracts. It shows potent antioxidant activity in superoxide scavenging, lipid peroxidation, comparable to ascorbic acid [7]. The seed contains a high amount of bioactive compounds, which also contribute to its antimicrobial efficacy; it even demonstrates strong antibacterial activity, with inhibition zones against Staphylococcus epidermidis, surpassing standard antibiotics like gentamicin [7]. The seed extracts have also been utilized to produce disinfectants effective against pathogens like Bacillus cereus and *Pseudomonas aeruginosa,* showing their practical applications in hygiene and sanitation [8].

It is experimentally proven that Cerium Oxide Nanoparticles(CNP) reduce oxidative stress both in vivo and in vitro [9]. CNPs show significant antioxidative and antimicrobial properties, making them a promising candidate for biomedical applications due to their unique contribution of dual oxidation state (Ce^{3+} & Ce^{4+}) to scavenge free radicals. The redox properties of CNPs allow them to switch oxidation states, effectively neutralizing reactive oxygen species(ROS) and reducing oxidative stress in cells [10]. This property of CNPs is most comparable to the scavenging activity of Ascorbic acid [11,12,]. Cerium oxide nanoparticles also show antibacterial activity against some pathogens like *Staphylococcus aureus* and *Escherichia coli*, mainly effective against antibiotic-resistant strains [13]. Their ability to inhibit biofilm formation further enhances their potential in infection control strategies [14].

Here in our previously published study, we successfully synthesized a nanocomposite of *Syzygium cumini* seed extract and Cerium Oxide nanoparticles, referred to as SC-CNP conjugate. We have tried to enhance the functional properties of Cerium oxide nanoparticles through the bio-conjugation with *Syzygium cumini* seed extract. The integration of SC seed extract with cerium oxide nanoparticles has previously shown promising results in terms of antioxidant and antimicrobial properties. Through a series of investigations, the present study aims to evaluate the cellular compatibility, anti-diabetic potential, and structural characterization through SEM, XRD, and FTIR.

2. Objectives

As per our previously published work, the primary objective of our research is to synthesize the SC-CNP conjugate from *Syzygium cumini* seed extract and Cerium oxide nanoparticles(CNPs) by the green synthesis method. Characterization of SC-CNP conjugate through UV-VIS spectroscopy for absorption peak, Dynamic Light Scattering (DLS) for hydrodynamic radius, antioxidant activity by using SOD and Hydrogen peroxide and Antibacterial activity through broth dilution method has been discussed. This study focuses on analysing the structural organisation of SC-CNP conjugate through XRD, SEM, and FTIR. This investigation also explored the biocompatibility of the conjugate through MTT assay, anti-diabetic potential through α-amylase degradation, and anti-bacterial activity against *Staphylococcus epidermis.* Through this, we are trying to determine the potential of SC-CNP conjugate in biomedical and pharmaceutical fields.

3. Material and Methods:

3.1 Material:

Cerium nitrate hexahydrate[$Ce(NO_3)_3.6H_2O$]-Hi-Media (Cat. No GRM1441), *Syzygium cumini* seed extract powder- SA herbal Bioactives LLP (Bixa Botanical-FDA approved), Ammonium solution (30%)- Loba Chemie (Cat. No L376452107), Ascorbic Acid- Loba Chemie, Hydrogen peroxide – Loba Chemie (Cat. No. PCT1511), Methionine – Hi-Media (Cat. No. PCT0315), LB Broth – Hi-Media (Cat. No.

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L24060), α-Amylase – Hi-Media (Cat. No. GRM638), Starch – Hi-Media (Cat. No. GRM425), Nutrient agar- Hi-Media (Cat. No-M001-500G), Nutrient broth- Hi-Media (Cat. No-M002-500G). Bacterial culture obtained from the lab. All chemicals and reagents used were of analytical grade and used without further purification

3.2 Synthesis of Cerium oxide nanoparticle using *Syzygium cumini seed extracts* and bare Cerium oxide nanoparticles.

Synthesis of Bare Cerium Oxide Nanoparticles

For the preparation of bare CNP, 2.5 g of cerium nitrate hexahydrate was dissolved in 100 mL of Milli-Q water and heated with continuous stirring for 30 minutes at high temperature. To this, 10 ml of 1N ammonium hydroxide (30%), which was prepared by the addition of 6.881 ml of 30% NH4OH, was added along with 100 ml of Milli-Q water. The reaction was maintained for 4 hours at high temperature. The resulting precipitate was collected by centrifugation at 8000 rpm for 10 minutes. The supernatant was discarded, and the pellet was resuspended in 250 µl of fresh Milli-Q water [15]. This washing step was repeated twice. Finally, the suspension was diluted to 50 mL with Milli-Q water, the pH was adjusted to 3, and the solution was stored in a dark, contamination-free environment for 48 hours.

Preparation of Cerium oxide nanoparticle using *Syzygium cumini seed extracts*

Syzygium cumini seed powder was utilized for the synthesis of Cerium oxide nanoparticles conjugate. Initially, a crude extract of the seed powder was prepared by using Soxhlet extraction with methanol as the solvent. Separately, a 0.1 M aqueous solution of Cerium nitrate hexahydrate was prepared with continuous stirring at 550 rpm for 60 minutes. After this, 40 ml of the aqueous plant extract was added to the solution, and the mixture was continued to be stirred for an additional 120 min. The resulting mixture, which is homogenous, was then evaporated at approximately 80°C to obtain a semi-solid mass, which was calcinated at 400°C for 40 minutes using a muffle Furnace.

3.3 XRD, FTIR, and SEM Characterizations of synthesized Cerium oxide nanoparticles.

The crystalline nature of the SC-CNP conjugate was studied through the XRD technique, and the obtained planes were used to define its crystalline configuration. For the functional group confirmation on the surface of the conjugate nanomaterial, FTIR was carried out using an Agilent FTIR instrument. Dried samples of bare CNP, S cumini powder, and SC-CNP conjugate were analysed at the range of 4000-400 cm^{-1}. Characteristic peaks give better clarity for the conjugation of nanoparticles (Lori et al.,2020). SEM was performed to assess the surface morphology of the samples. In this, the nanoparticles were air dried on carbon-coated stubs and visualized under a scanning electron microscope at accelerating voltages of 10-20 kV.

Antimicrobial activity

Minimum inhibitory concentration(MIC) was determined using the broth dilution method in test tubes. A fresh culture of *S. epidermis* was prepared and standardised according to the required cell density of 1×10^6 CFU. A stock solution of CNPs, SC powder, and SC-CNP conjugate was prepared, which was diluted further in sterile growth media (ranging concentrations from 5mg/ml to 50 mg/ml). Each test tube received 100 µL of bacterial cells and 100µL of nanoparticles-conjugate solution. These tubes undergo 24 hours of incubation at 37°C [16]. After incubation, bacterial growth was assessed by measuring absorbance at 600 nm. The lowest concentration showing no visible turbidity was recorded as MIC. To determine MBC,10ul aliquots from MIC and higher concentration wells were plated on MH agar and incubated for 24 hours. The lowest concentration showing no bacterial colonies was considered the MBC.

3.4 α-amylase inhibition analysis of SC-CNP

The α-amylase inhibition assay was conducted using a modified DNS method. Alpha-amylase was diluted to a final concentration of 1 U/mL in 5 mL of 5 mM phosphate buffer (pH 6.8) for the alpha-amylase inhibition assay. Starch was solubilized by heating in 5 mM phosphate-buffered saline (pH 6.8) until a clear

(d)

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solution was obtained. A chromogenic non-pre-incubation method, based on the Sigma-Aldrich protocol, was employed. The assay was performed by incubating 40 µL aliquots of either bare CNP, seed extract, or SC-CNP., with 400 µL of starch solution and 150 µL of distilled water in screw-cap plastic tubes. Following a 40-minute incubation at room temperature, 25 µL of the reaction mixture was transferred to a separate test tube and mixed with 15 µL of DNS color reagent. After heating for 90 minutes, the absorbance was measured at 540 nm using a Nanodrop spectrophotometer [17].

3.5. Cellular biocompatibility assay

Cancerous cell line was used for the cellular biocompatibility assay, which is an MTT-based assay for SC-CNP conjugate. Initially, cells were seeded at 1×10^6 cells/well in 96-well plates and incubated in a 5% CO_2 incubator for 48 hours at 37°C. After the incubation period, all of these wells were exposed to SC-CNP conjugate at 5mg/ml. After treatment, 20 µL MTT (5 mg/mL) was added, incubated for 4 hours. After 4 hours, 100 µL of DMSO was introduced into each well to dissolve the formazon crystals. After that, absorbance was measured at 570 nm, and cell viability percentage was calculated. Results were expressed as percentage viability relative to the untreated control.

3.6. Statistical Analysis: The data was analysed by using SPSS. The experiments were performed in triplicates & the Mean ± S.D (Standard deviation) was calculated and represented

4. Results

4.1 Synthesis and characterization of SC-CNP conjugate

As previously published data, crude *Syzygium cumini* and Cerium oxide nanoparticles(SC-CNP) conjugate were successfully synthesized through the green chemistry method. It is confirmed through the UV VIS peak at 320nm, which shows the oxidation state of the Cerium ion. The hydrodynamic radius of 110nm for bare CNP and 105 nm for SC-CNP confirmed the conjugation of both materials. The confirmation of surface morphology was characterised through Scanning Electron Microscopy(SEM). These SEM images revealed that SC-CNP nanoparticles were roughly spherical to irregular in shape with a smooth, continuous surface. There was some agglomeration also present (Figure 1). X-ray diffraction analysis was also studied for the confirmation of the crystalline nature of the SC-CNP conjugate. XRD patterns displayed distinct Bragg peaks at 2θ values corresponding to cerium oxide crystalline structure, which shows confirmatory peaks at 47.5°,56.2°,66.0°, 98.3°,115.5°, and 123.1°, represents to 220. 311,400, 331, and 421 crystal planes (Figure 2). This confirms the nanoscale formation as well as successful bioconjugation. FTIR spectra confirmed the presence of characteristic functional groups in SC-CNP conjugates. This indicated the signature peaks of both bare CNPs and *Syzygium cumini* seed extract, which are observed around 3430 cm^{-1},1630 cm^{-1}, and 1380 cm^{-1}, showing the formation of cerium oxide nanoparticles and their conjugation with plant-derived compounds (Figure 3) [18].

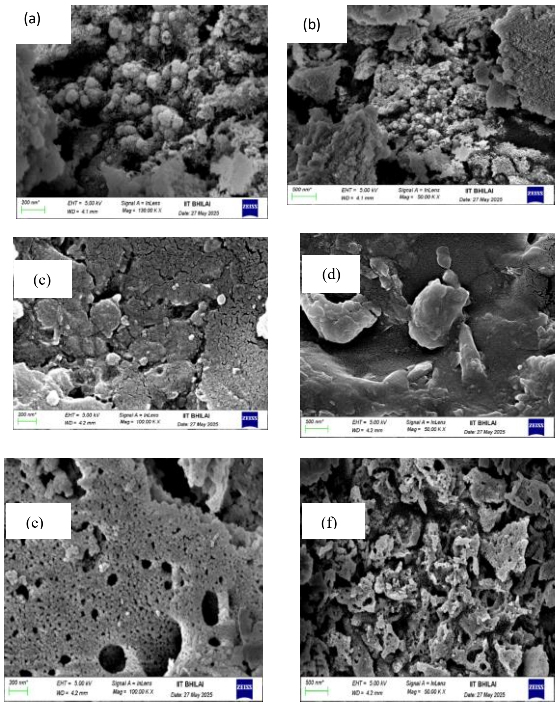

Figure 1. *SEM image showing surface morphology of bare CeO₂ nanoparticles (CNP)(a,b), Syzygium cumini extract (c,d), and SC-CNP conjugate (e,f).Bare CNPs appear as agglomerated, irregular particles, while SC-CNPs exhibit a more porous and dispersed structure due to phytochemical capping*.

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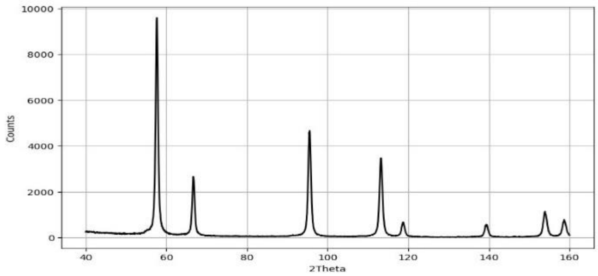

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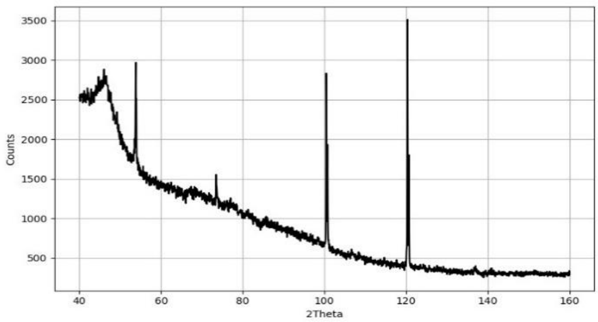

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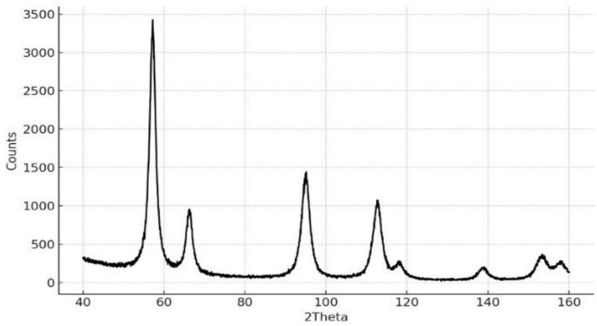

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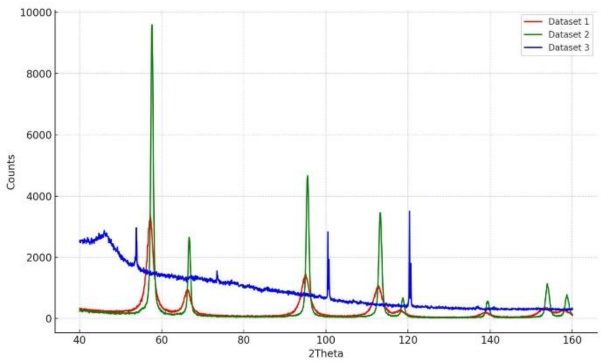
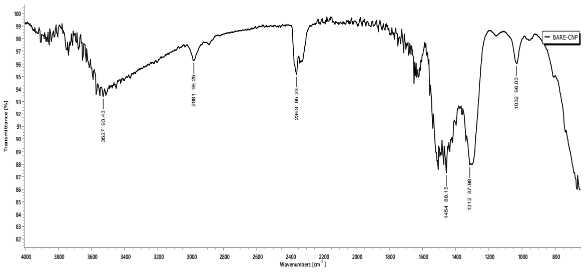


(d)

Figure 2. *XRD of (a) pure CeO_2 nanoparticles, (b) Syzygium cumini seed powder, (c) SC-CNP conjugates, and (d) Comparison of all three. The seed extract displays a broad amorphous pattern, while pure CeO_2 shows sharp peaks corresponding to the fluorite cubic phase. SC-CNPs retain characteristic CeO_2 peaks with reduced intensity and slight broadening, indicating successful phytochemical conjugation.*



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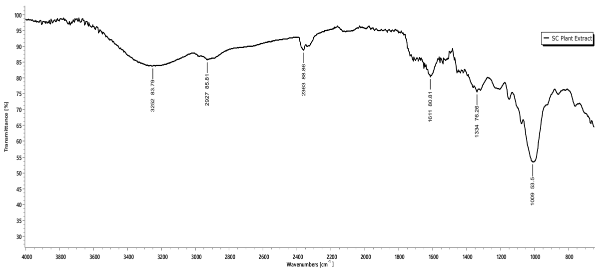

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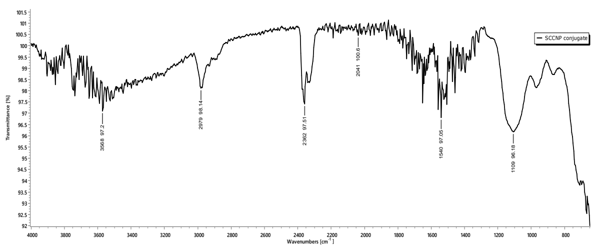

(c)

Figure 3. *FTIR spectra of (A) Bare Cerium oxide nanoparticles, (B) Syzygium cumini seed extract, and (C) SC-CNP conjugate. The observed characteristic peaks of both CNP and Plant extract correspond to various functional groups, including C-H (2979cm^{-1}) –OH (3568 cm^{-1}), C-N (1540 cm$^{-1)}$, C=O, and band observed below 1000, around around 500–800 cm^{-1}, confirm the presence of Ce–O vibrations, Ce–O(1109 cm^{-1}) vibrations, confirming the successful synthesis of conjugate*

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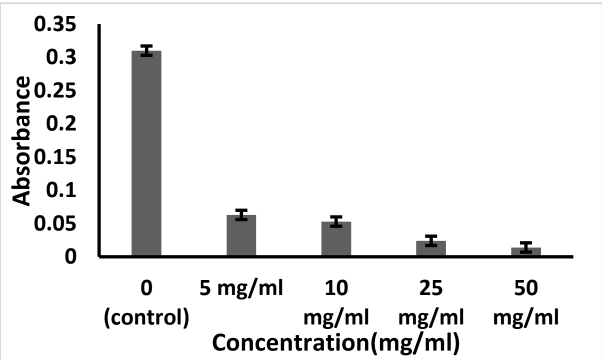
4.2 Antimicrobial Assay

Minimum Inhibitory Concentration (MIC) assay was carried out by using 1×10^6 CFU. MICs were determined against *Staphylococcus epidermidis* using the broth dilution method, which showed that there is an enhancement by the synergistic effect of conjugation, as the antimicrobial potential is less than bare CNP and Syzygium powder. The complete inhibition shows in a 25 mg/ml and 50mg/ml concentration. So, 25mg/ml can be considered as the Minimal Inhibitory concentration of SC-CNP conjugate. The percentage inhibition is nearly 86.8%, which shows the potential of antibacterial activity. The highest concentration inhibition confirms the dose-dependent antibacterial efficacy of the SC-CNP conjugate (Figure 4).



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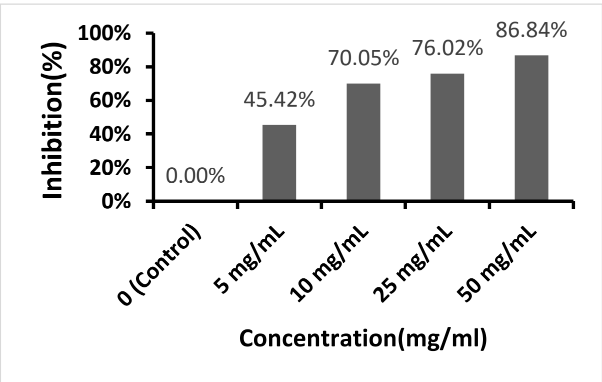


(b)

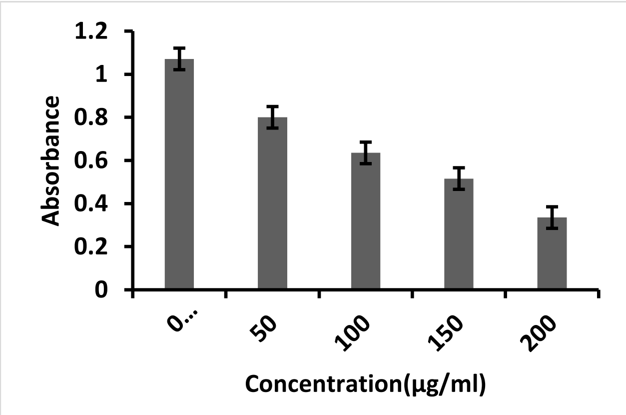
Figure 4. *Experiments are done in triplicate and data interpreted in the form of mean± SD (a) Absorbance vs concentration graph of (b)Percentage inhibition of bacterial growth by SC-CNP conjugates at various concentrations after 24 hours.*

4.3 α-amylase inhibition assay

The α-amylase inhibition activity exhibited a dose-dependent increase for SC-CNP conjugates, bare CNP, and *Syzygium cumini* seed extract. The α-Amylase inhibition assay was performed to demonstrate the anti-diabetic potential of the SC-CNPC conjugate. The crude plant extract exhibited α-amylase inhibition of up to 63%, consistent with the reported anti-diabetic properties of *Syzygium cumini*. In contrast, bare CNP demonstrated an inhibitory activity of up to 43%. Notably, the SC-CNP conjugate displayed a significantly enhanced α-amylase inhibitory activity of up to 86.8%, likely attributable to synergistic effects (Fig. 7). Dose-dependent experiments revealed a direct correlation between SC-CNP conjugate concentration and α-amylase inhibitory activity. Specifically, increasing the SC-CNP conjugate concentration resulted in a corresponding increase in α-amylase inhibition (Fig. 7c, d). Hence, it may be noticed that by optimizing the conjugation chemistry, effectiveness may be increased to a larger proportion. α-amylase, secreted by pancreatic cells, facilitates the breakdown of complex carbohydrates into simpler sugars such as glucose [19]. These findings suggest that optimization of the conjugation chemistry can enhance efficacy. Consequently, inhibiting α-amylase activity can reduce free glucose levels in the blood, as demonstrated in the biochemical assay used to assess inhibition activity.

4.4 Cellular biocompatibility and anti-cancerous activity of SC-CNP

The cytotoxic potential of SC-CNP was determined by using the MTT assay on cancerous cell lines. The study involved treating cells with SC-CNP solutions at varying concentrations, such as 5µg/ml, 10µg/ml, 25µg/ml, and 50µg/ml, and measuring the absorbance at 570nm with background correction at 670 nm, in which the highest concentration shows maximum inhibition. Following the treatment, an MTT assay was performed to examine the biocompatibility effects. The results of this investigation indicated that the synthesized SC-CNP exhibits cellular biocompatibility. Specifically, the cellular viability of cancerous cells treated with SC-CNP at a concentration of 50 µg/ml was approximately 87%, suggesting the potential of anticancerous activity. The results of the biocompatibility research conducted at various doses were evaluated. An anti-inflammatory assay was conducted using U937 cells, derived from human monocytes. These cells were cultured and maintained in RPMI medium containing 10% FBS and 100 U/ml penicillin-streptomycin antibiotics. The activity was measured by quantifying the reduction in TNF-α and IL-6 expression levels. Synthesized SC-CNP conjugate exhibited anti-inflammatory effects, as evidenced by the downregulation of IL-6 (Interleukin-6) and TNF-α expression by 89% and 81% of control values, respectively (Figure 5).



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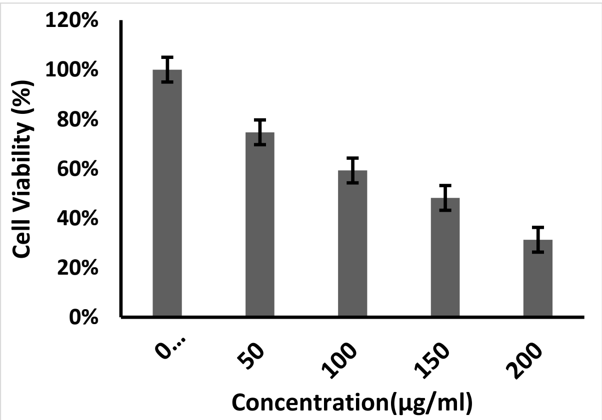

(b)

Figure 5. *Experiments are done in triplicate, and data are interpreted in the form of mean± SD. This figure(a,b) represents the percentage of cell viability(MCF7 cancerous cell line) through MTT assay upon treatment with various concentrations 50,100,150, and 200 µg/ml of SC-CNP conjugate. The viability decreases in a dose-dependent manner, with the highest reduction observed at 200 µg/ml*

5. Discussion

As we have seen in past years, a conjugate of a plant and nanoparticles represents a significant advancement in agricultural and medicinal applications, due to their unique properties for the enhancement of plant-derived compounds. These conjugates can improve the delivery and effectiveness of active ingredients, reduce toxicity, and promote plant growth [20]. There are many methods for the synthesis of conjugates, in which the green synthesis approach is the best method for the synthesis of nanoparticle conjugates. This method not only produces stable, less toxic nanoparticles but also combines their bioactivity with nanomaterial attributes. [21]. Combining nanoparticles with chemotherapeutic agents, such as a nano-drug, can enhance drug efficiency and provide a synergistic effect in treating diseases like cancer. Strategies like pre-incubation with polymer scaffolds can improve the stability and homogeneity of plant-based nanoparticle conjugates and facilitating better conjugation and preventing agglomeration during the delivery of hydrophobic ligands [22]. The confirmation of a proper bio-conjugation is done by basically UV-VIS spectrum, as per previously published data of our work. Furthermore, the surface morphology was studied through Scanning Electron Microscopy (SEM), demonstrating that there is smoothness as well as a slight agglomeration present on the surface of the conjugate as compared to the bare CNP. These images can be seen at a resolution of 1mm. For the confirmation of crystallinity, XRD is used, which shows the signature peak of conjugate at crystal planes at 220, 311, 222, 400, 420. This shows that SC-CNP conjugate has a less crystalline structure, with reduced peak intensity and slight broadening than the Bare CNP peak, which is nearly 98% crystalline in nature. This is due to nanoparticle capping and reduction in crystallinity is mainly due to partial amorphization caused by phytochemical capping and due to the presence of organic moieties. This is due to the agglomeration of seed extract (Ghanbary &Jafernejad,2017). FTIR spectra further supported this confirmation. The seed extract showed a prominent O-H (3286 cm^{-1}), C-H (2921cm^{-1}), C=C (1614 cm^{-1}), C-N (1384cm^{-1}), and (1046 cm^{-1}) stretching bands, which confirms the presence of polyphenols, flavonoids, and other bioactive compounds. As CNPs showed a characteristic Ce-O (<800 cm^{-1}) stretching bond, the SC-CNPs exhibited both

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phytochemical and nanoparticles peaks, which are O-H(3283cm^{-1}), C-H (2916 cm^{-1}), C=C (1602 cm^{-1}), C-N (1383 cm^{-1}), and Ce-O (500-800 cm^{-1}). This was confirmed by conjugation and functionalization. SC-CNP demonstrated potent antibacterial activity by disrupting bacterial membranes and generating Reactive Oxygen species (ROS).SC-CNP shows excellent radical scavanging activity as reported through the catalase assay and SOD assay this is due to the redox cycling ability of Cerium oxide between Ce3+ and Ce4+ which mimics the enzymatic activity of catalase and Superoxide dismutase. The polyphenolic compounds of *S. cumini,* known to donate hydrogen ions to neutralize reactive oxygen species, also contribute to the antioxidant activity of the conjugate. The enhancement in antibacterial effect is attributed to the synergistic effect between cerium oxide nanoparticles and phytoconstituents like flavonoids and tannins of *Syzygium cumini* seed powder. SC-CNP shows antibacterial activity against both Gram-positive (*S. epidermidis*) and Gram-negative (*E. coli*) bacteria, which increases up to 1.5-fold higher than bare CNP [23]. Moreover, SC-CNP conjugate shows more activity towards *E. coli* than *S. epidermidis* bacteria. This could be enhancing penetration and interaction due to the bioactive coating of *S. cumini* seed extract. This conjugate can form a chelate with essential metal ions for the formation of a biomembrane and interfere with microbial enzymes by polyphenolic compounds. This could lead to the disruption of the biofilm of the bacterial membrane. So both of the compounds show combined antimicrobial action [24]. Additionally, SC-CNP conjugates can enhance the inhibition of alpha amylase activity, which serves as the foundation of the antidiabetic activity of materials. Alpha amylase enzyme is secreted by the pancreas for the degradation of complex carbohydrates into smaller units like glucose. These assays of the SC-CNP conjugate demonstrated a concentration-dependent reduction in enzyme activity, suggesting its potential application in controlling hyperglycemia [25]. These inhibitory effects are due to the presence of bioactive phytochemicals like flavonoids, tannins, and phenolic acids present in *Syzygium cumini* seed extract. These are well known for their ability to bind at the active site of alpha-amylase and delay the starch hydrolysis. The conjugation of Cerium oxide nanoparticles enhances from 63% to 80%. These findings align with earlier reports highlighting the inhibitory role of plant-based nanoconjugates against carbohydrate-hydrolyzing enzymes [26]. The observed inhibition activity not only supports SC-CNP's potential anti-diabetic properties but also suggests its dual therapeutic role as both an antioxidant and metabolic regulator. Cytotoxicity was assessed through the MTT assay suggests there is a reduction in cell viability at specific concentrations specially 50 µg/ml shows the reduction in viability of cancerous cell line highlights the effective disruption of mitochondrial activity, suggesting some apoptosis and may be through necrosis by the nanoparticles [27].

5. Conclusion

This study has effectively shown the successful synthesis and multifaceted therapeutic potential of novel bio-nanocomposites(SC-CNP) through the green synthesis method. This conjugate was successfully synthesized from the conjugation of *Syzygium cumini* seed extract and Cerium oxide nanoparticles. Comprehensive characterization via SEM, XRD, and FTIR confirmed the successful synthesis of this structurally different crystalline nanocomposite [28]. This SC-CNP conjugate effectively integrates the bioactive compounds of the *Syzygium cumini* seed extract with the unique redox features of cerium oxide nanoparticles. The resulting SC-CNP conjugate showed a remarkable synergistic enhancement of its biological activities compared to seed extract and CNPs. One of its important findings is its anti-diabetic effects as indicated by a high inhibition of 86.8% on the 500 ppm extract. This 86.8% was significantly high as compared to both plant extract and nanoparticles. This demonstrates its possible role as a potent glycemic agent. Furthermore, the conjugate showed significant anti-cancerous activity through MTT assays. Finally, the antimicrobial assays also confirmed an enhanced bactericidal effect against *Staphylococcus epidermidis*. In conclusion, this investigation showed that the SC-CNP nanocomposite represents a promising, multifunctional platform for biomedical applications. Through the appropriate synergy of the therapeutic properties of *Syzygium cumini* with the functional advantages of cerium oxide nanoparticles, this investigation paves the way for the development of safe and effective therapies for managing diabetes, inflammation, and microbial infections. So, there is a need to develop advanced nanomaterials with the effectiveness of plant extracts.

Competing Interests: The authors declare that they have no known competing `financial interests or personal relationships that could have appeared to influence the work reported in this paper

Authors Contributions: Bhunesh Sharma contributed to Writing of original draft, Investigation, Methodology, Validation, Visualization of the data and manuscript. Iram Jahan contributed to writing of initial draft, Investigation, Methodology, Validation, Visualization of the data and manuscript. Sushant Singh and Padmalaya Das jointly contributed to the Conceptualization, Supervision, Review & Editing of this submitted manuscript.

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