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Silver nanoparticles decorated natural products doped polyaniline hybrid materials for biomedical applications

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ABSTRACT

The use of silver nanoparticles (AgNPs) and other combinations of AgNPs with various biomaterials is being exploited by the scientific community to regulate bacterial growth. In the present study, one-pot synthesis of AgNPs functionalized natural products doped polyaniline hybrid materials (SNPs) has been successfully synthesized The signature of the functional groups, morphology, and elemental composition of the new SNPs were studied by Fourier transform infrared, scanning electron microscopy, energy-dispersive X-ray spectroscopy, and X-ray diffraction techniques. The synthesized SNPs were investigated for their antibacterial potency against *Escherichia* coli, *Klebsiella* pneumoniae, *Streptococcus* mutans, and *Enterococcus* faecalis *and* antifungal properties against *Aspergillus niger, Fusarium oxysporum, Epidermophyton floccosum, and Trichophyton rubrum*. Our results have demonstrated the antibacterial activities of new SNPs of gallic acid and myoinositol on S. mutans and E. faecalis with minimal inhibitory concentration and minimal bactericidal concentration values of 1.5 and 2 mg/mL, respectively. The SNP of phloroglucinol was effective against *E. floccosum* and *T. rubrum* at 5 mg/mL concentrations. This study indicates that SNPs exhibited significant antibacterial and antifungal activity against selected strains of bacteria and fungi when compared to AgNPs functionalized polyaniline hybrid materials (SPs) alone.

1. INTRODUCTION

Nanotechnology has evolved as a fascinating domain of research due to its potential applications in diverse areas of science and technology, such as material science, optical sensors, surface modification, catalysis, water purification, diagnostics, drug delivery systems, and nanoformulations of useful drugs [1]. Nanoparticles are often synthesized through different chemical, physical, and biochemical processes from organic and inorganic materials. Nanoparticles have a high surface-to-volume ratio, which gives them a significant advantage in a variety of applications [2-4].

Synthesis of functionalized nanomaterials and investigation of their applications for practical utility has been a leading domain of research during the past decade [5-8]. Natural products have been the source of drugs, and many of them have been successfully incorporated into nanomaterials to form functional nanocomposites [9,10]. Drug resistance of pathogenic bacteria is a global challenge in therapeutics due to the incredible adaptability of these microorganisms. This makes the research on antimicrobial drugs an evergreen domain and there is an ever-growing demand for new therapeutic agents with antimicrobial potential [11,12]. The fortification of silver nanoparticles (AgNPs) with antimicrobial phytochemical extracts has been proven as an agile process for the green synthesis of potential antimicrobial pro-drugs to combat drug-resistant microbial strains [4,13]. Quite a large number of independent studies have reported the green synthesis of AgNPs by employing several plant extracts [14-18] for different applications. It has been well documented that AgNPs exhibit antimicrobial and fungistatic efficacy [19,20]. Interestingly, few researchers have also reported the antimicrobial efficacy of AgNPs fortified with components of lower terrestrial plants like ferns [4,21]. Apart from this, many of the nanocomposites of silver in combination with natural products have been found to possess potential therapeutic applications. Anticancer, antidiabetic, anti-inflammatory, and antimicrobial activities are some of the few identified applications [4,13,22-24].

Due to its ease of synthesis, low cost, excellent electrical conductivity, optical property, and admirable stability, polyaniline (PANI) has gained significant attention in numerous emerging technologies, including energy conservation and storage, molecular electronics, and sensors [25-29]. PANI has been received by researchers as a preferred choice of material to incorporate a wide variety of functional groups

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and subunits, to investigate antimicrobial activities, cytotoxicity, biocompatibility, antioxidant activity, drug delivery, tissue engineering, wound healing, and biosensor applications [30]. The present study aims to synthesize silver nanoparticles functionalized natural products doped PANI (SNPs) (as depicted in Scheme 1) and to evaluate the efficiency of the natural products as dopants in combination with PANI and AgNPs against selected microbial pathogens.

2. MATERIALS AND METHODS

2.1. Preparation of AgNPs Functionalized Natural Products Doped PANI (SNPs)

The chemicals used in the present study have been purchased from standard commercial sources. Aniline, silver nitrate, paraphenylenediamine, oxalic acid, adipic acid, and myoinositol were sourced from S.D. Fine Chemicals, ellagic acid and phloroglucinol from Sigma-Aldrich, and gallic acid from Spectrochem. SNPs were synthesized by dissolving 1 g of aniline as monomer and 0.1 equivalent of paraphenylenediamine as an initiator in 100 mL of distilled water containing 0.3 equivalent of natural products. To the above reaction mixture, three equivalents of $AgNO_3$ dissolved in 50 mL of distilled water were added drop by drop with constant stirring. After complete addition, the reaction mixture was stirred for additional 24 h at room temperature. The product obtained was filtered, washed with water followed by methanol, and vacuum dried at 60°C for 12 h.

2.2. Characterization of SNPs

The analysis of SNPs was performed by Fourier transform infrared (FTIR), X-ray diffraction (XRD), scanning electron microscopy (SEM), and energy-dispersive X-ray spectroscopy (EDX).

2.2.1. FTIR spectroscopy

The active functional groups existing in SNPs synthesized were scrutinized by employing an FT/IR-6000 modeled FTIR spectrometer. To obtain the data, the resolution was maintained at 4 cm^{-1} and the wavenumber range was set between 4000 and 400 cm^{-1}. To perform this analysis, the samples were combined with KBr to get pellets from which transmittance was observed. This analysis would provide information relating to functional groups present in as synthesized SNPs.

2.2.2. XRD

XRD was performed by ARL™ Equinox 100 modeled XRD utilizing monochromatic X-rays of Cu Kα radiation operating at 30 mA and 40 kV with 2θ ranging from10° to 70°. The average crystallite size of prepared nanoparticles was analyzed by Scherrer's formula utilizing full width at half maximum (FWHM) of the highest peak.

2.2.3. SEM and EDX

The surface morphology of prepared SNPs was determined by SEM, using Thermo Scientific Quattro ESEM with an accelerating voltage of 1 kV or 5 kV. Each sample was placed on a stub adhered with carbon tape and sputtered with gold to capture images. SEM was equipped with EDX, which was employed to examine the qualitative chemical composition of SNPs synthesized in this study.

2.3. Evaluation of the Antibacterial Activity of SNPs

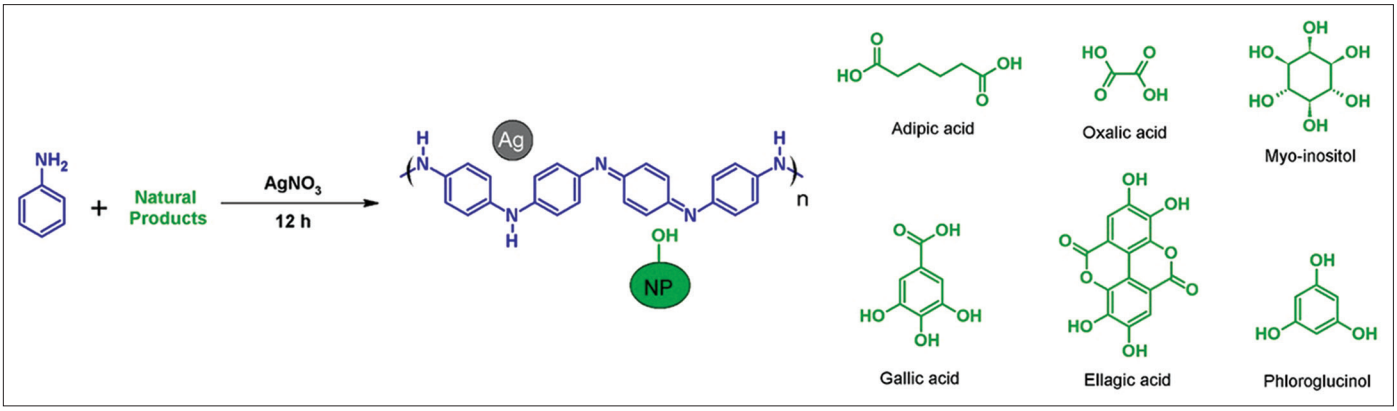
2.3.1. Bacterial strains

Four different strains of bacteria were used in the study which are *Escherichia coli* MG 1586, *Klebsiella pneumoniae* MTCC 4030 (both clinically important strains), *Enterococcus faecalis* ATCC 29212, and *Streptococcus mutans* MTCC-890 (two common oral pathogens). These bacterial strains were originally procured from MTCC, Chandigarh, and maintained at the laboratory of Dextrose Technologies Pvt. Ltd., Bengaluru. *E. coli* and *K. pneumoniae* were cultured on Luria-Bertani agar/broth at 37°C. *E. faecalis* and *S. mutans* were cultured in brain heart infusion broth at 37°C. All the media used for culturing bacteria were procured from HiMedia Laboratories.

2.3.2. Well diffusion assay

The well diffusion method was used to assess the antibacterial activity of SNPs. About 150 µl pre-cultured test organisms were dispersed onto agar plates and 6 mm diameter wells in specified agar media were punched. SNPs with various concentrations (1, 2.5, 5, and 10 mg/mL) were placed on each agar plate inoculated with bacterial strains. The zone of inhibition was measured after 24 h of incubation at 37°C. Effective concentrations of the samples showing good activity were determined in terms of minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) by the broth dilution method.

The newly synthesized SNPs have been tested for their bacteriostatic activity by well diffusion assay on four species of bacteria, namely, *E. coli*, *K. pneumoniae*, *S. mutans*, and *E. faecalis* at concentrations of 1, 2.5, 5, and 10 mg/mL in triplicates. Amoxicillin at a concentration of 30 µg/mL was used as positive control and DMSO as a negative control. The concentrations of SNPs for the experimental trials have been chosen according to Iftikhar *et al.* [16]. By determining MIC and MBC, the



Scheme 1. Synthesis of silver nanoparticles functionalized natural products doped PANI.

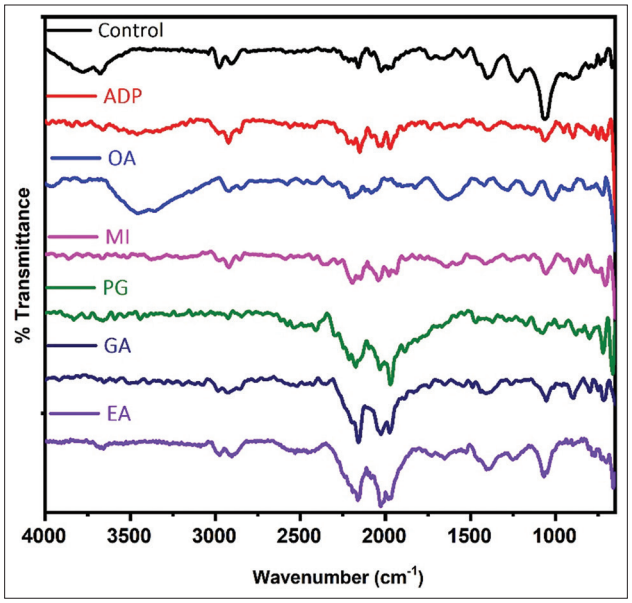


Figure 1: FTIR spectra of SNPs (a) control – SPs, (b) adipic acid [ADP], (c) oxalic acid [OA], (d) myoinositol [MI], (e) phloroglucinol [PG], (f) gallic acid [GA], and (g) ellagic acid [EA].

reproducibility of the results of the zone of inhibition has been confirmed using the broth dilution method.

2.3.3. Analysis of bacterial cells treated with SNPs

The effect of SNPs on bacteria was evaluated by incubating bacterial cells in overnight cultures with different concentrations of the SNPs and imaging the treated cells. The procedure was carried out inside a biosafety cabinet until mounting of the sample. The bacterial cells were fixed using 1% paraformaldehyde and 2% glutaraldehyde (1:1) for an hour. The bacterial suspension of 100 µL was released into 5 mL of medium and filtered using a filter with a pore size of 0.08 µm. If the filter gets clogged, the suspension was diluted further and the filter was washed with diluted ethanol. Later, the filter was removed and allowed to dry at room temperature and then cut into pieces to mount on the carbon tape, which was fixed on the stub. The stub was removed from the biosafety cabinet and placed for sputtering to capture the SEM images.

2.4. Evaluation of the Antifungal Activity of SNPs

2.4.1. Fungal strains

The fungal species used in the present study include common species *Aspergillus niger* locally isolated from the soil and identified based on macroscopical and microscopical characters [31,32] and *Fusarium*

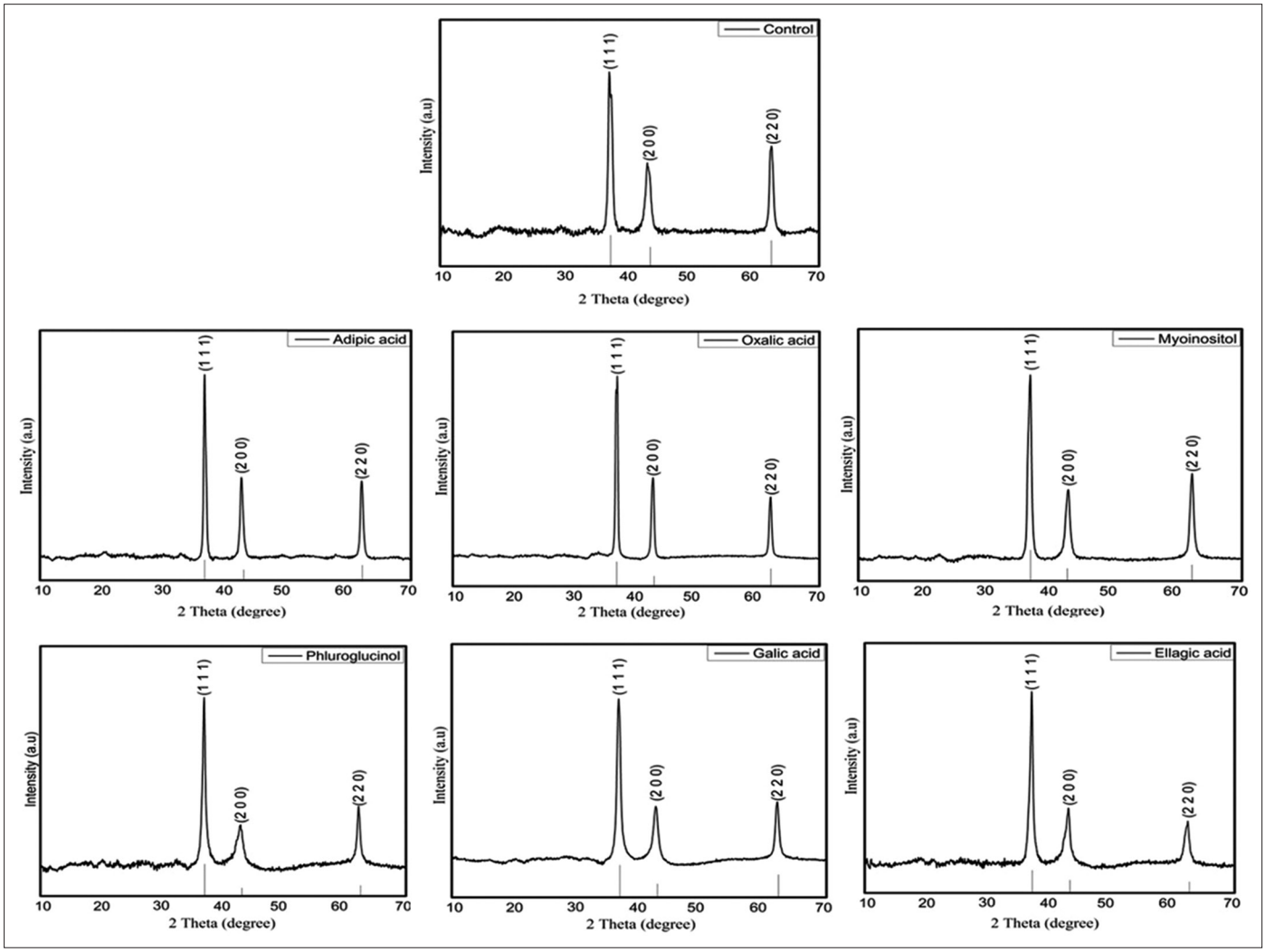


Figure 2: XRD images of synthesized SNPs.

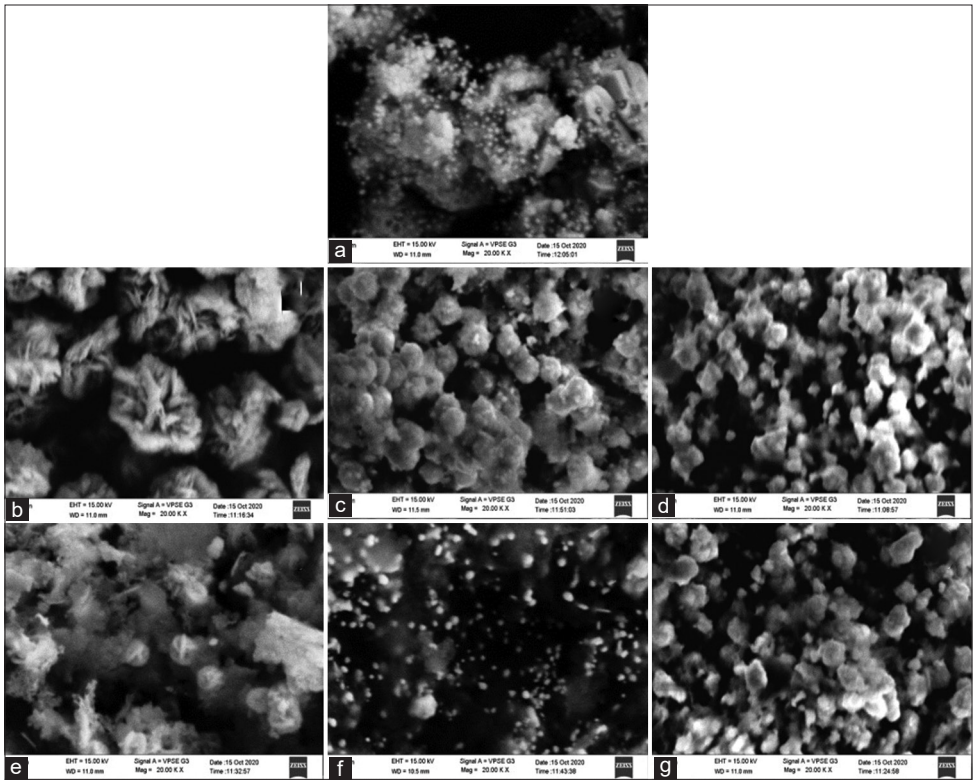


Figure 3: SEM images of SNPs synthesized using (a) control – SPs, (b) adipic acid, (c) ellagic acid, (d) gallic acid, (e) oxalic acid, (f) myoinositol, and (g) phloroglucinol.

oxysporum MTCC 3327 sourced from MTCC. Dermal pathogenic fungi, *Epidermophyton floccosum* MTCC 7880, and *Trichophyton rubrum* MTCC 3272 also were procured from MTCC, Chandigarh, and maintained at Dextrose Technologies laboratory.

2.4.2. Well diffusion assay

Evaluation of the antifungal activity of the SNPs was performed by well diffusion assay. About 150 µL of pre-cultured test organisms were spread onto the agar plates and wells of 6 mm in diameter were punched in specific agar media. Based on previously documented literature, various concentrations of SNPs such as 1, 2.5, 5, and 10 mg/mL were loaded into the wells [16]. Fungal plates were incubated at room temperature for 48–96 h, after which zones of inhibition were measured and tabulated.

3. RESULTS AND DISCUSSION

3.1. Characterization of SNPs

3.1.1. FTIR spectra

The FTIR spectra of AgNPs functionalized polyaniline nanocomposites (SPs) and SNPs are presented in Figure 1. The spectra of SPs indicate the presence of C-H vibration peaks at 2977 and 2896 cm^{-1}. The C-H bending in SPs can be observed at 1398 and 1060 cm^{-1}. SPs exhibited a C=N bond vibration peak at 1662 cm^{-1}, C-N bond vibration at 1230 cm^{-1}, and C=C bond vibration peaks at 1540 cm^{-1} [33]. Similar peaks are observed in all SNPs. In addition, ellagic acid doped SNP exhibited phenolic OH group at 3660 cm^{-1} and C=O stretching at 1719 cm^{-1} [34]. Adipic acid, gallic acid, and oxalic acid doped SNPs exhibited a broad peak at around 3400 cm^{-1} corresponding to carboxylic acid. Phloroglucinol and myoinositol doped SNPs showed the presence of −OH groups at 3447 cm^{-1} and 3362 cm^{-1}, respectively.

3.1.2. XRD analysis

The diffraction pattern was observed in the XRD spectrum of the SNPs, indicating their crystalline nature. The fingerprint diffraction patterns of SNPs are illustrated in Figure 2, which shows three major peaks at 2θ = 37.51°, 43.12°, and 63.47° corresponding to the planes (111), (200), and (220), thereby indicating the face-centered cubic patterns of SNPs [35]. Using Scherrer's formula, the average crystallite size of the SNPs obtained from FWHM of the more intense peak corresponding to the (111) plane located at 37.51º was determined to be ~40 nm.

3.1.3. SEM and EDX analysis

The SEM images of SNPs are illustrated in Figure 3 and their respective EDX in Figure 4. The SEM images were captured with X 20,000. The surface morphology of SNPs certainly reveals the uniform and good dispersion of nanoparticles. The agglomeration of nanoparticles might have occurred because of the electrostatic interaction of SNPs. The images captured here resemble that of [36], where the morphology was spherical in appearance with aggregation as found in our analysis.

The qualitative and quantitative profile of elements present in the synthesized SNPs was confirmed by analysis of EDX. The spectral analysis has indicated intense signals relating to the Ag element, which further affirms the incorporation of the natural products into the AgNPs during the synthesis of the SNPs. The EDX profile of Ag at 3 keV is indicated by a strong peak, confirming it as the major elemental component of the SNPs. In addition to Ag, elements such as C and O were observed in SNPs, which can be attributed to carbon and oxygen present in the PANI and dopants.

To study the effect of SNPs on bacterial cells, overnight grown bacterial cells were treated with different concentrations of the

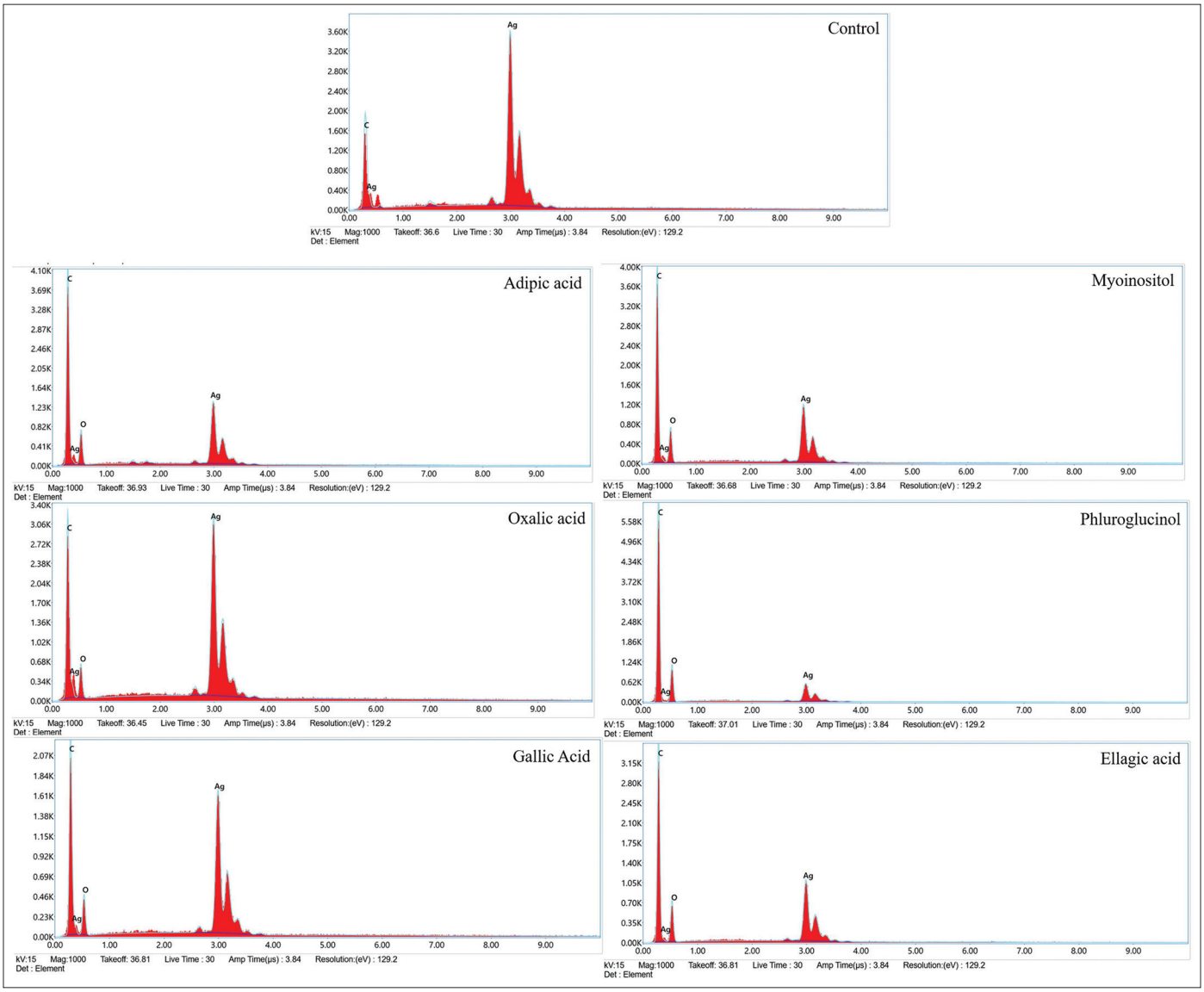


Figure 4: EDX images of synthesized SNPs.

SNPs and a change in surface morphology was observed using SEM analysis. Figure 5 illustrates the images of *E. coli* cells treated with SNPs doped with adipic acid and gallic acid. Loss of integrity of the cells is indicated by the uneven shapes of cells, indicating the development of cracks or ruptures on the cell wall in SNPs treated cells when compared to control. The disruption of cells was observed among SNPs treated cells of *E. faecalis* and *S. mutans*. The same is depicted in Figure 5.

3.2. Evaluation of the Antimicrobial Activity of SNPs

Bacterial infections are a significant cause of morbidity and mortality in humans [37]. In traditional medicine, crude drugs formulated from extracts of plants in combination with other natural products are used for treating bacterial infections, which impart dual benefits, inhibiting bacterial proliferation along with enhancing general immunity of the body [38]. Therefore, traditional medicines provide long-term protection against a broad spectrum of infections [39]. Contrary to this approach, modern medicine relies on isolated active compounds, synthesized or produced on a large scale, to address the issue of meeting the higher demand. This trend has led to the phenomenon of antibiotic resistance among pathogenic [40]. Recently, nanoparticles conjugated with active drug molecules have emerged as novel tools for developing antibacterial formulations [41]. A combination of natural products with green synthesized nanoparticles would be an ideal choice for drug development. This idea has prompted us to synthesize SNPs, which have both AgNPs and the natural antimicrobial qualities of organic dopants.

The microbial growth inhibition induced by SNPs has been demonstrated in selected bacterial and fungal strains. Easy methods of synthesis and enhanced efficacy demonstrated by the nanoparticles in damaging microorganisms have made them acceptable for antimicrobial applications. The reason for such an enhanced effect is the release of cations from nanoparticles while entering the cell, which causes a transformation in their normal functioning and hence kills the bacterium. Gram-negative bacteria, which possess a thin peptidoglycan layer in their cell walls when compared to Gram-positive bacteria, allow better penetration of nanoparticles and hence exhibit a larger zone of inhibition [42] in well/disk diffusion assays and the same observation was found in our present study as well.

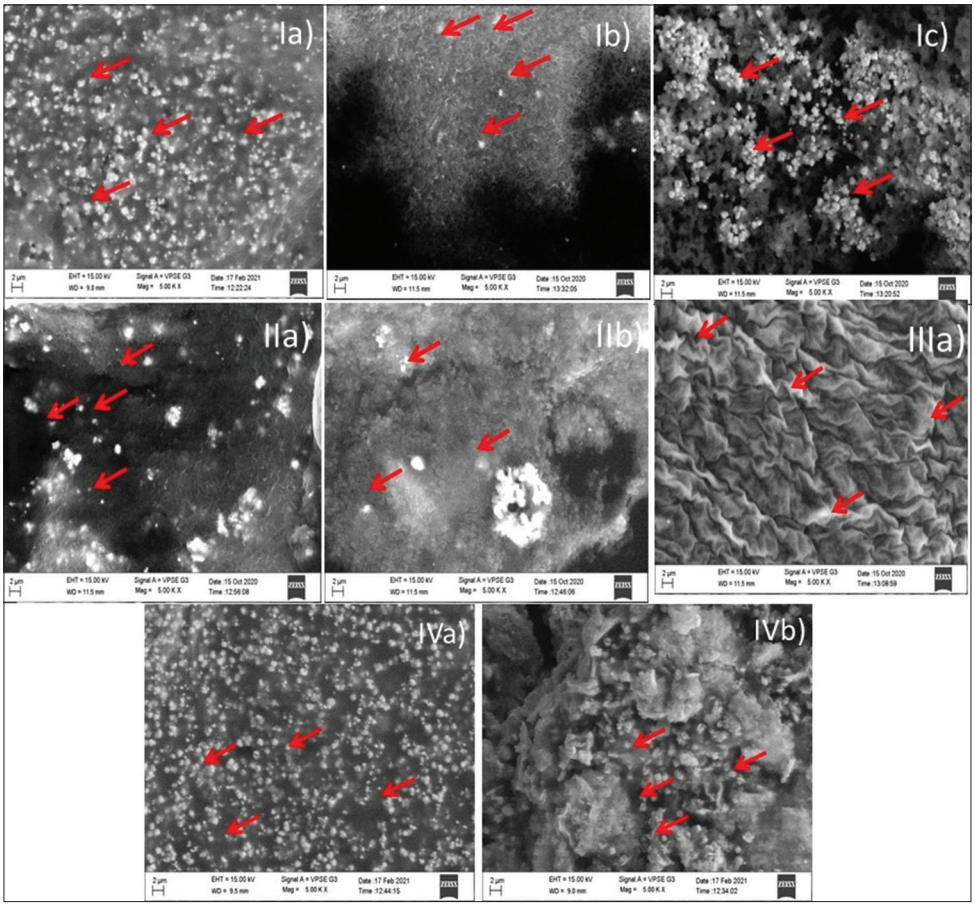


Figure 5: SEM images of I) *E. coli* treated with SNPs (a) control – SPs, (b) adipic acid and (c) gallic acid; II) *E. faecalis* treated with SNPs (a) gallic acid and (b) myoinositol; III) *S. mutans* treated with SNP a) oxalic acid; and IV) *E. faecalis* treated with SNPs (a) gallic acid and (b) myoinositol.

3.2.1. Bacteriostatic activity of SNPs on E. coli and K. pneumoniae

The concentration-dependent bacteriostatic efficiency of SNPs on different strains of bacteria is depicted in Table 1. The zone of inhibition and MBC of the top three SNPs on *E. coli is* provided in supplementary information [Figures S1-S3]. It can be understood from the data that all SNPs except phloroglucinol showed bacteriostatic activity against *E. coli*. It is evident from the data that myoinositol doped SNP-treated *K. pneumoniae* showed growth inhibition, implying superior activity in comparison to other SNPs. Multivariate ANOVA of the MBC values of ellagic acid-doped SNP against *E. coli* has yielded 15.0137 as F statistic and 0.001959 as *P*-value for intercept and 9.7051 as F value and 0.007256 as *P*-value for MIC, indicating the null hypothesis to be true. In the case of oxalic acid-doped SNP, the *P*-value for the intercept is 0.05064, indicating that it is false and so it must be rejected whereas, the MIC did not affect the *P*-value (0.30005). Adipic acid-doped SNP showed a true null hypothesis [Table 2]. Multivariate ANOVA of the MIC and MBC results of the treatment of myoinositol-doped SNP on *K. pneumoniae* indicated 36.238 as F-statistic and 9.766 10^{-5} as *P*-value for intercept, while 11.557 as F-statistic and 0.00437 as *P*-value for MIC, which affirms the true null hypothesis [Table 2]. Ellagic acid-doped SNP results displayed a true null hypothesis in both intercept and MIC, which signifies that they were effective in controlling the growth of *K. pneumoniae*. Furthermore, to be specific, the two SNPs, that is, ellagic acid and myoinositol-doped SNP, revealed the same activity. The SNPs doped with gallic acid, adipic acid, and phloroglucinol did not show any inhibition of growth in the case of *K. pneumoniae*. The reason behind such interactions could be ascribed to the phytochemical properties possessed by individual SNPs that account for their ability to hinder the growth of bacteria.

3.3. Evaluation of the Antimicrobial Efficacy of SNPs on Dental/Oral Pathogens

3.3.1. Bacteriostatic activity of SNPs on S. mutans

Subsequently, we have evaluated the antibacterial effect on Gram-positive dental pathogens like *S. mutans*. The bacteriostatic effect along with standard deviation on *S. mutans* due to the treatment with SNPs, SPs, and control is presented in Table 1, and it can be observed that all the SNPs have demonstrated good antibacterial activity. The MIC and MBC values of SNPs in *S. mutans* are illustrated in Table 2. All the samples tested on *S. mutans* have emerged as equally potent bacteriostatic candidates. Multivariate ANOVA of the data of myoinositol-doped SNP yielded a high F-static of 114.778 and a *P*-value of 1.653. This shows that the hypothesis was true and the null hypothesis was rejected. Gallic acid-doped SNP showed no effect on hypothesis testing, and phloroglucinol-doped SNP showed significant true hypothesis testing. The zone of inhibition and MBC test results for myoinositol doped SNP on *S. mutans* are presented in Figure 6.

3.3.2. Bacteriostatic activity of SNPs on E. faecalis

E. faecalis is another dental pathogen on which the efficacy of SNPs has been tested. The bacteriostatic efficacy of the SNPs on this pathogen is presented in Table 1. We performed the multivariate ANOVA for the results of MIC and MBC tests on this pathogen for different SNPs using Roy's method and the results are presented in

Table 2. Myoinositol-doped SNP has yielded 13.182 under F-static and 0.006372 as *P* value defined for intercept, while MIC showed 11.636 for F-static and 0.008612 for *P*-value. This indicates that the null hypothesis was tested and found to be true. The parallel evaluation was also obtained for adipic acid and gallic acid doped SNPs. The images of MIC and MBC treatment of gallic acid-doped SNP are presented in Figure 7.

The above results indicate that SNPs showed better antimicrobial activity than SPs and can also perform on par with the commercially available antibiotics. Nanoparticles are known to possess the tendency to react with sulfur and phosphorus predominantly present in the outer membrane of bacteria, leading to the formation of pores in the bacterial cell wall. The interaction of nanoparticles to the bacterial membrane leads to the outflow of intracellular substances which causes shrinkage and finally lysis of the cell [43]. Different mechanisms are being proposed for the mode of action of nanoparticles on bacterial cells, such as cell wall and membrane damage, intracellular penetration and damage, and oxidative stress [44]. Our attempt to control the antibiotic-resistant bacterial phenotype was found to be successful as discussed in Section 3.1.3. SNPs have been shown to break the bacterial cell wall [Figure 5], indicating that they could be used as pro-drug antibiotic candidates.

Table 1: Bacteriostatic efficacy of SPs and SNPs on *E. coli*, *K. pneumoniae*, *S. mutans*, and *E. faecalis*.

Bacterial strains	SNPs	Zone of inhibition (in mm)*				SD
		1 mg/mL	2.5 mg/mL	5 mg/mL	10 mg/mL	
E. coli	Gallic acid	0	0	5.6	9	4.4
	Adipic acid	0	5.3	6	9.3	3.9
	Ellagic acid	5.6	6.3	11.7	12.3	3.5
	Oxalic acid	0	5.6	7.6	7.6	3.6
	Myoinositol	0	0	7.3	8	4.4
	SPs	0	10	10	13	3.2
K. pneumoniae	Ellagic acid	0	0	0	9.6	4.8
	Oxalic acid	0	0	0	8	4
	Myoinositol	0	0	4.6	13.6	6.4
	SPs	0	0	0	0	0.0
S. mutans	Gallic acid	0	9	9.6	11.3	5.08
	Ellagic acid	0	0	8.6	13.6	6.73
	Oxalic acid	0	0	5.6	14	6.62
	Phloroglucinol	0	4.3	8	8.6	3.97
	Myoinositol	0	9.6	11.6	16	6.75
	SPs	0	6	11	10	4.6
E. faecalis	Gallic acid	0	0	10.6	9.6	5.85
	Adipic acid	0	0	8.3	12.3	6.17
	Ellagic acid	0	0	0	7.6	3.80
	Oxalic acid	0	0	0	12.3	6.150
	Myoinositol	4.3	5.3	7.6	11.3	3.11
	SPs	0	0	0	6	3.0
	−ve control (DMSO)	0	0	0	0	0.0
	+ve control amoxicillin 30 µg/ml	18	NT	NT	NT	0.0

*Average of three replicates. NT: Not tested, *E. coli*: *Escherichia coli*, *K. pneumoniae*: *Klebsiella pneumoniae*, *S. mutans*: *Streptococcus mutans*, *E. faecalis*: *Enterococcus faecalis*

Table 2: MIC and MBC of SNPs on bacteria.

S. No.	SNPs	*E. coli*		*K. pneumoniae*		*S. mutans*		*E. faecalis*	
		MIC	MBC	MIC	MBC	MIC	MBC	MIC	MBC
1.	Gallic acid	>5	>5	NA	NA	1.5	2	1.5	2
2.	Adipic acid	2.5	3	NA	NA	NA	NA	NA	NA
3.	Ellagic acid	1	1.5	>5	>5	>5	>5	>5	>5
4.	Oxalic acid	2.5	3	NA	NA	>5	>5	>5	>5
5.	Phloroglucinol	>5	>5	NA	NA	5	>5	5	>5
6.	Myoinositol	>5	>5	>5	>5	1.5	2	1.5	2
7.	SPs	1.5	2	NA	NA	5	>5	>5	>5

All values are in mg/mL. NA: No activity, *E. coli*: *Escherichia coli*, *K. pneumoniae*: *Klebsiella pneumoniae*, *S. mutans*: *Streptococcus mutans*, *E. faecalis*: *Enterococcus faecalis*, MIC: Minimal inhibitory concentration, MBC: Minimal bactericidal concentration

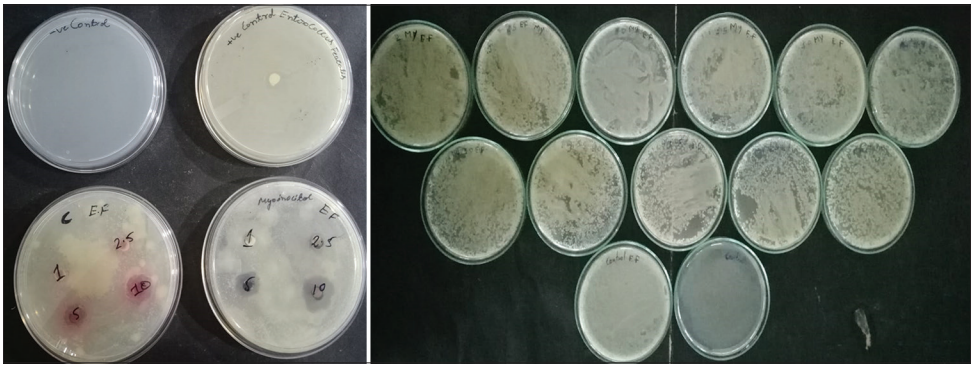


Figure 6: Zone of inhibition and MBC of myoinositol SNP by *Streptococcus mutans*.

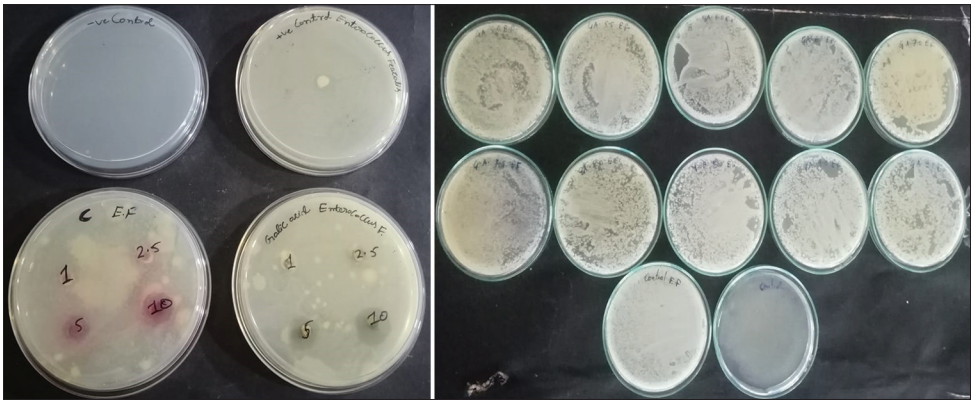


Figure 7: Zone of inhibition and MBC of gallic acid by *Enterococcus faecalis*.

Table 3: The fungistatic activity of SNPs in terms of zone of inhibition.

S. No.	SNPs	Target fungal species			
		A. niger	*F. oxysporum*	*E. floccosum*	*T. rubrum*
1.	Gallic acid	-	-	-	-
2.	Adipic acid	-	-	-	-
3.	Ellagic acid	-	-	10 mg/mL (12 mm)	-
4.	Oxalic acid	5 mg/mL (7.33 mm)	10 mg/mL (20 mm)		-
5.	Phloroglucinol	-	-	5 mg/mL (11 mm)	5 mg/mL (9.67 mm)
6.	Myoinositol	-	-	-	-
7.	SPs	-	-	-	-

A. niger: *Aspergillus niger*, *F. oxysporum*: *Fusarium oxysporum*, *E. floccosum*: *Epidermophyton floccosum*, *T. rubrum*: *Trichophyton rubrum*

3.4. Antifungal Activity of SNPs

Fungi are found all over the world, and their pathogenic varieties are highly resistant which makes them tough to combat. Therefore, it is important to study the fungistatic activity of the SNPs, as well. *A. niger* is known to cause critical diseases such as aspergillosis and otomycosis, *F. oxysporum* can cause mycotoxicosis and skin-related infections, while *E. floccosum* is recognized for triggering septicity such as tinea pedis, tinea cruris, tinea corporis, and onychomycosis, and *T. rubrum* is noted for athlete's foot, infections such as jock itch and ringworm. We have evaluated the effect of our SNPs against predominant pathogenic fungi *A. niger*, *F. oxysporum*, *E. floccosum*, and *T. rubrum*. The fungal virulence factor, encrypting gene rearrangements, and other similar observed behaviors are attributed to the adaptation to any stress environment [45]. It was observed from Table 3 that oxalic acid- and phloroglucinol-doped SNP exhibited better antifungal effects compared to the other SNPs. The gallic acid-, adipic acid-, and myoinositol-doped SNPs have hardly exhibited any mycostatic activity. These data are supported by Figures S4-S7 signifying the zone of inhibition exhibited by SNPs and control against individual fungal strains. Oxalic acid-doped SNP was effective against *A. niger* and *F. oxysporum* with 7.33 mm of inhibition at 5 mg/mL and 20 mm at 10 mg/mL, respectively. Ellagic acid-doped SNP inhibited the growth of *E. floccosum* by 12 mm at a 10 mg/mL concentration. When the fungal strains were dosed with 5 mg/mL of phloroglucinol-doped SNP, the growth inhibition of 11 mm and 9.67 mm was observed in *E. floccosum* and *T. rubrum* organisms, justifying their fungistatic activity.

Organic acids can be efficiently used as antifungal agents due to their properties relating to bioactivity, polarity, and high solubility in many solvents including water [46]. There is evidence for the fact that commercial antifungals have limited utilization and also related medicinal values because of side effects and slow recovery [47], and hence, there is

an urgent need to design and develop nanoparticles with better antifungal activities. Therefore, we opted to incorporate selected natural products with AgNPs and PANI to enhance their antifungal activity, which has been proved in our study through the significant difference in the antifungal activities of SNPs with those of the control samples [Table 3]. Similar observation on enhanced antifungal activity of nanomaterial reported earlier by Xia *et al.* [48]. Our study has demonstrated interesting results by inhibiting human and animal pathogenic fungi, indicating their potential as alternatives to commercial antifungal products.

4. CONCLUSION

Our investigation is directed toward the synthesis of the natural products as dopants in combination with redox-active PANI and AgNPs and to evaluate antimicrobial and antifungal activities against selected microbial pathogens. Based on the outcomes of the bioassays, myoinositol- and gallic acid-doped SNPs have been found effective against dental pathogens compared to SPs. Ellagic acid-doped SNP was effective against *E. coli*. In addition, the antifungal activities of the SNPs have also been assessed by *in vitro* bioassays against four fungal species, including dermal pathogens. It was evident from our study that, when compared to SPs, the SNPs exhibited better antifungal activity. Oxalic acid-doped SNP showed good inhibition against the growth of common fungi *A. niger* and *F. oxysporum*. The effective arrest of dermal pathogens *E. floccosum* and *T. rubrum* was observed on SNP-doped phloroglucinol. Our investigation into the antimicrobial properties of AgNPs in combination with natural products and redox-active polyaniline hybrid materials has yielded encouraging results when compared with AgNPs-polyaniline nanocomposite without dopants, indicating their scope in therapeutic domains. These findings can provide a profound impact on combating the antibiotic-resistant strains of pathogenic bacteria. More focused and in-depth investigations in these areas are warranted to reap the full benefits of this finding.

5. AUTHORS' CONTRIBUTIONS

All authors made substantial contributions to conception and design, acquisition of data, or analysis and interpretation of data; took part in drafting the article or revising it critically for important intellectual content; agreed to submit to the current journal; gave final approval of the version to be published; and agreed to be accountable for all aspects of the work. All the authors are eligible to be an author as per the International Committee of Medical Journal Editors (ICMJE) requirements/guidelines.

6. FUNDING

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7. CONFLICTS OF INTEREST

There are no financial or other conflicts of interest reported by the authors in this study.

8. ETHICAL APPROVALS

This research does not include any animal or human subjects.

9. DATA AVAILABILITY

All data generated and analyzed are included within this research article and its supplement data.

10. PUBLISHER'S NOTE

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SUPPLEMENTARY INFORMATION

Silver nanoparticles decorated natural products doped polyaniline hybrid materials for biomedical applications

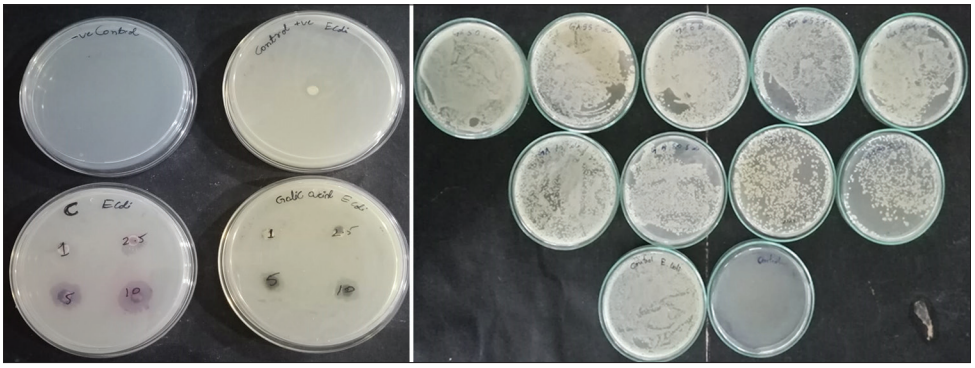

Figure S1: Zone of inhibition and MBC of gallic acid SNP by *Escherichia coli.*

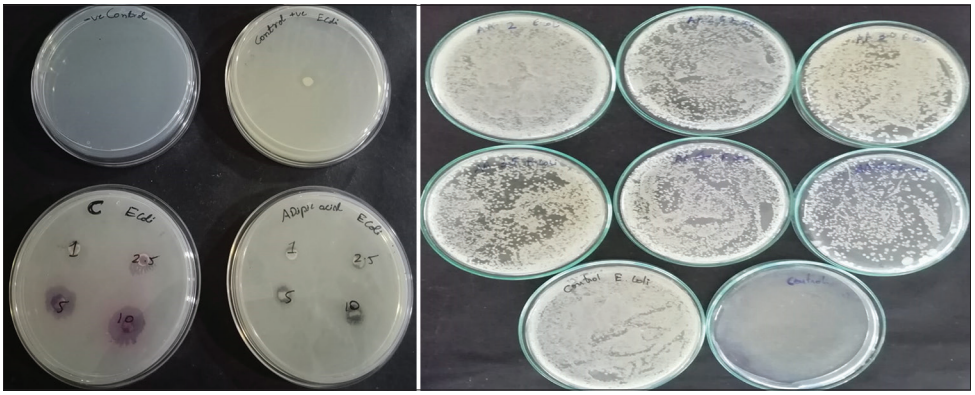

Figure S2: Zone of inhibition and MBC of adipic acid SNP by *Escherichia coli.*

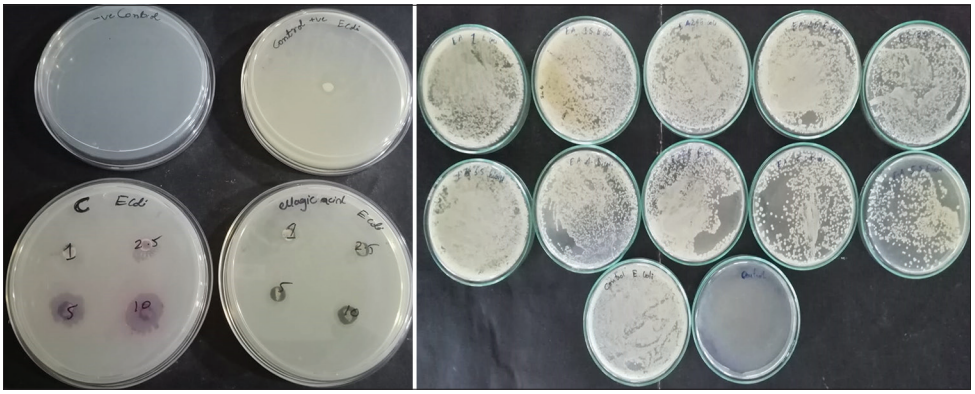

Figure S3: Zone of inhibition and MBC of ellagic acid SNP by *Escherichia coli.*

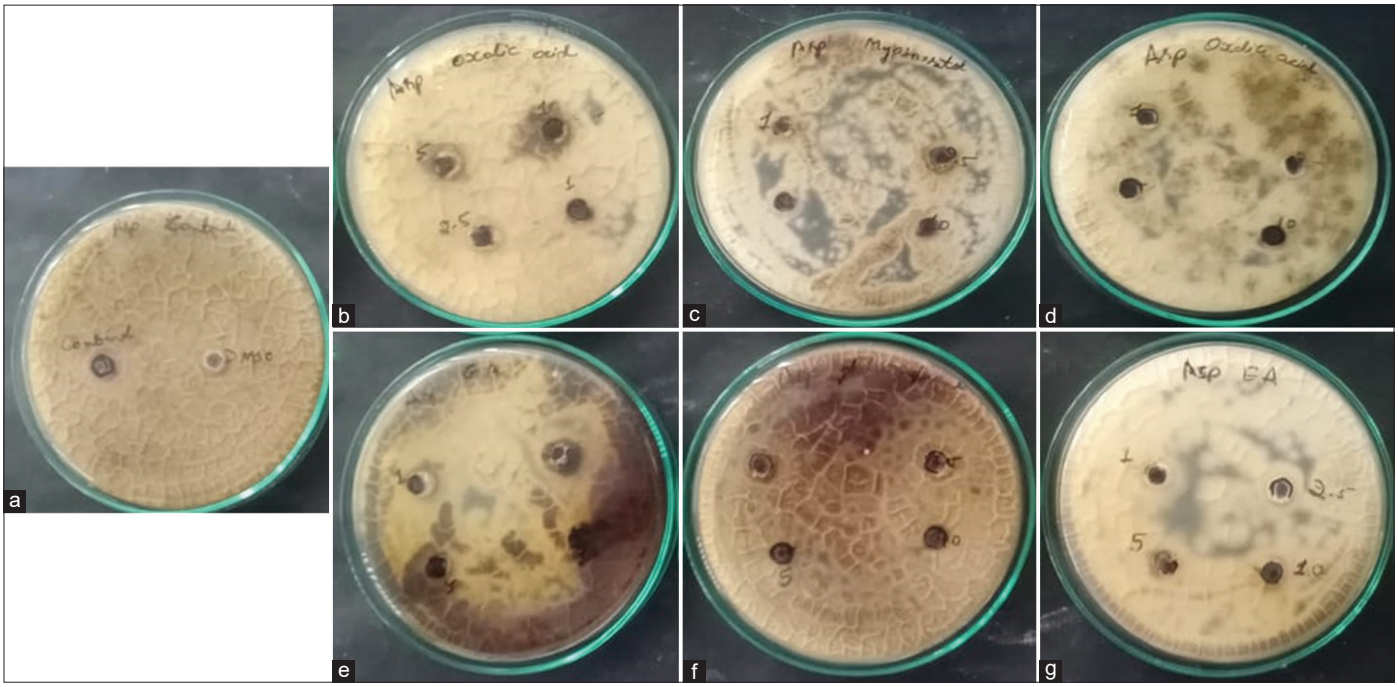

Figure S4: Zone of inhibition of SNPs on *Aspergillus niger* (a) control – SPs, (b) oxalic acid, (c) myoinositol, (d) adipic acid, (e) gallic acid, (f) phloroglucinol, and (g) ellagic acid.

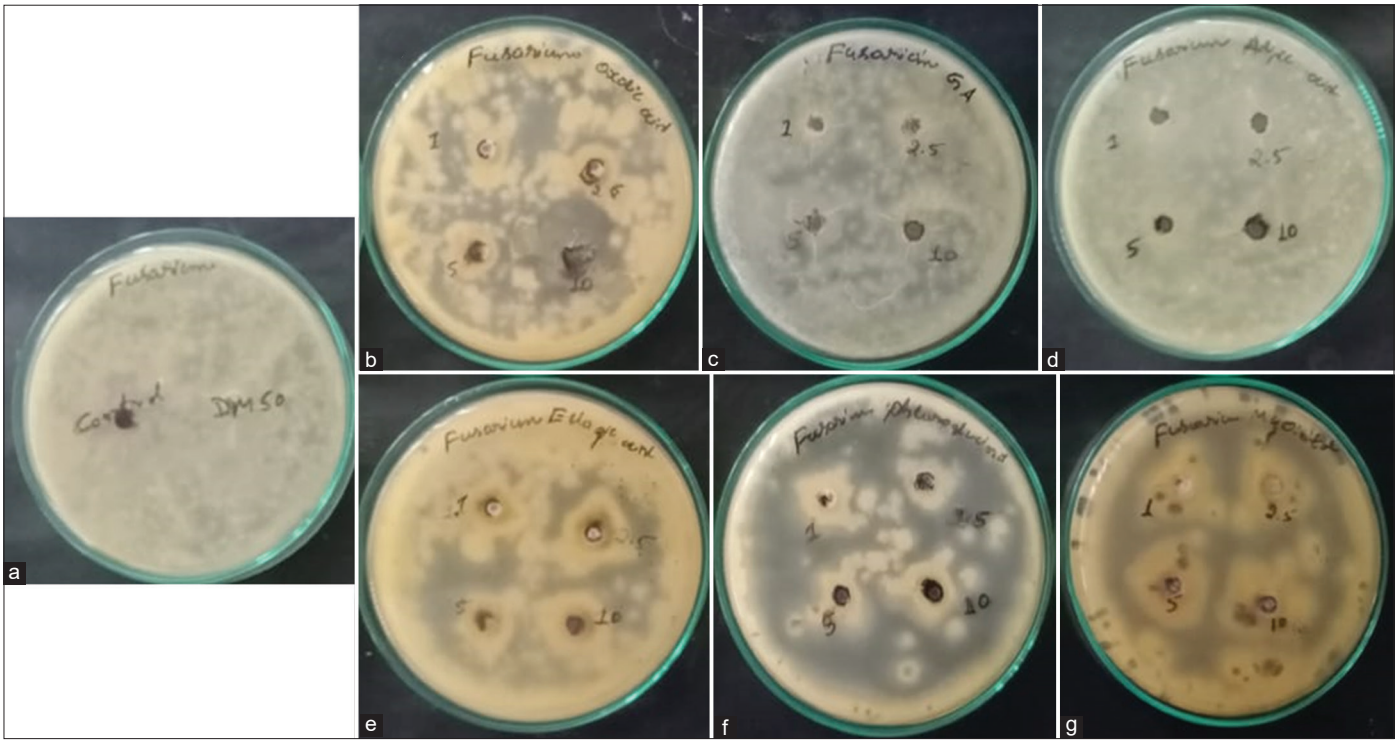

Figure S5: Zone of inhibition of SNPs on *Fusarium oxysporum* (a) control – SPs, (b) oxalic acid, (c) gallic acid, (d) adipic acid, (e) ellagic acid, (f) phloroglucinol, and (g) myoinositol.

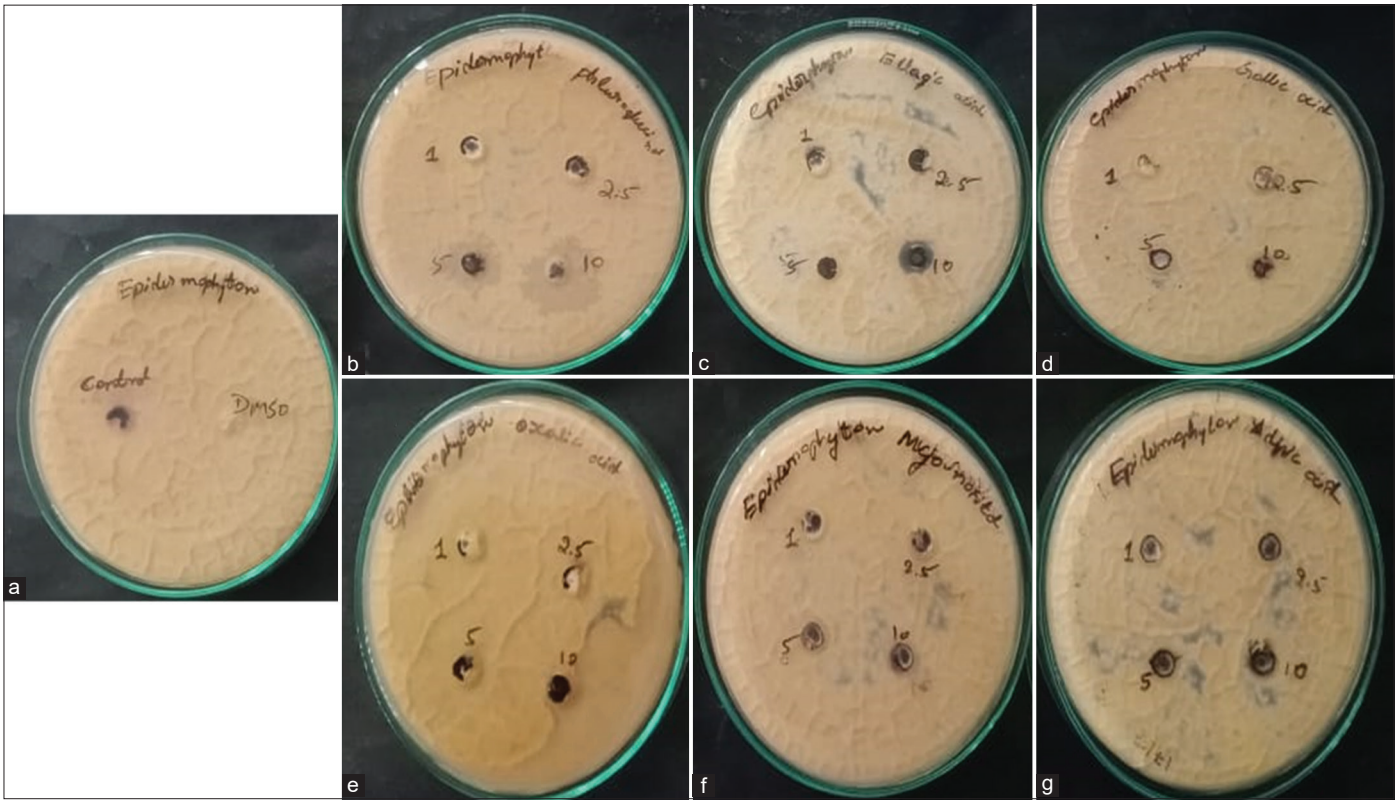

Figure S6: Zone of inhibition of SNPs on *Epidermophyton floccosum* (a) control – SPs, (b) phloroglucinol, (c) ellagic acid, (d) gallic acid, (e) oxalic acid, (f) myoinositol, and (g) adipic acid.

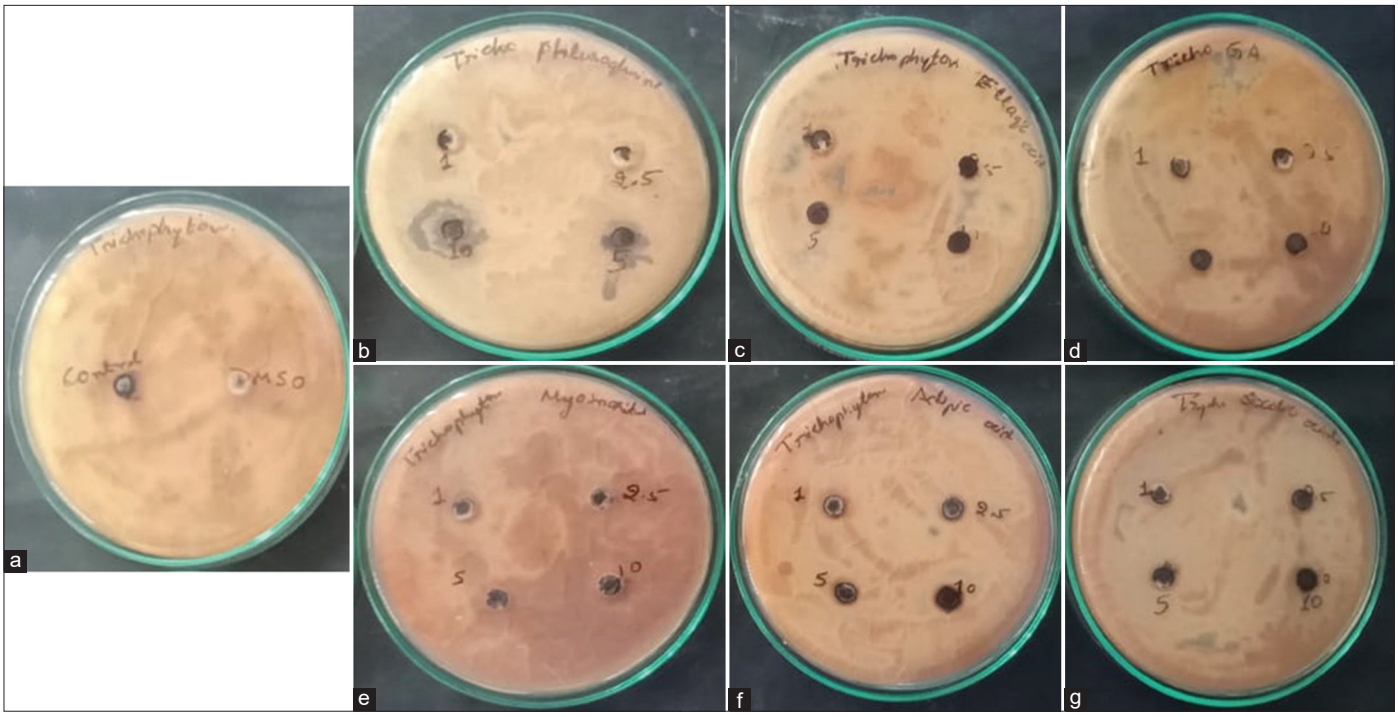

Figure S7: Zone of inhibition of SNPs on *Trichophyton rubrum* (a) control – SPs, (b) phloroglucinol, (c) ellagic acid, (d) gallic acid, (e) myoinositol, (f) sadipic acid, and (g) oxalic acid.