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RESEARCH PAPER

Synthesis as Well as Characterization of New PEG-Coated Nanoparticles for Biomedical Application

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ABSTRACT

In the domains of nanotechnology and nanoscience, green chemistry plays crucial roles in the production of various nanomaterials. Mong the best often utilized polymers that are synthetic for surface modification of nanoparticles that are magnetite (MNPs) to offer a fresh way to create excellent colloidal stability is polyethylene glycol (PEG). Polyethylene glycol which can be used to coat Fe_2O_3 nanoparticles to synthesized nanoscale remedies. Numerous samples have been made for this purpose by employing the casting process to add Fe_2O_3 nanoparticles to polyethylene glycol at varying weight percentages. The physicochemical properties of the produced nanosolutions were examined using FTIR and SEM techniques. Scanning Electron Microscopy is utilized to portray both morphology and structure (SEM). Because of its usage in medicinal applications, Fe_2O_3 nanoparticles have been proven to exhibit high antifungal activity. Fe_2O_3 nanoparticles that have been produced can have their size and shape altered to modify their antifungal activity. The produced polyethylene glycol-coated (Fe_2O_3) nanoparticle's antifungal properties were further tested on a range of fungus species. The synthesized polymer has remarkable antifungal properties.

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INTRODUCTION

Since the structure and characteristics of nanoparticles, in particular, vary considerably from those of molecules, atoms, as well as materials that are bulk, nanotechnology and specifically nanomaterials have drawn a lot of attention [1]. Because of their unique chemical and physical characteristics, which offer a wide range of possible applications, metal nanoparticle production has received a lot of attention in the literature [2,3]. The synthesis and processing of resources need the use of "non-toxic solvents, biodegradable materials", as well as inexpensive green chemicals due to the green reaction approach employed in these procedures. "The stabilizer, reaction medium, and green reducing agent are the three key ingredients in the synthesis and stabilization of metallic nanoparticles" [4].

Iron oxide nanoparticles have gained significant attention in various industries in recent years. This is primarily due to their exceptional properties, including superparamagnetism, size, surface, and

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biocompatibility [5]. These unique characteristics have made them an appealing platform for numerous biomedical and bioengineering applications. Among these uses include medication delivery [9], cancer therapy [7], hyperthermia [8], cell separation and detection [6], and the use of dissimilarity agents in " magnetic resonance imaging" (MRI) [10]. It is interesting to look at the magnetic properties of iron oxide nanoparticles because of their special qualities and huge potential in bio-applications. However, "iron oxide nanoparticles" own a number of disadvantages, such as a propensity to agglomerate because of van der Waals forces as well as potent dipole-dipole interactions. [11]. Therefore, it is significant to improve their stability by mixing them with an appropriate coating, such polyethylene glycol (PEG), "dextran, polyvinyl alcohol (PVA), chitosan, polyvinylpyrrolidone (PVP), polylactic-co-glycolic acid (PLGA), etc." [12-16].

The present investigation has opted for "polyethylene glycol (PEG)" as a prospective synthetic polymer for modifying the external of MNPs [17]. PEG is a hydrophilic, biocompatible, nonantigenic, as well as protein-resistant polymer that exhibits a high solubility in aqueous environments. The solubility of PEG in water is attributed to its hydration with associated water molecules, a characteristic which becomes more pronounced as the "molecular weight of the polymer" increases. [18].

Polyethylene glycol, a biocompatible polymer, was employed in this research to coat iron oxide nanoparticles (Fe3O4 NPs) with the aim of developing a promising antifungal polymer. It is worth noting that polyethylene glycol is recognized for its water solubility, hydrophilicity, non-antigenicity, and biocompatibility [19].

MATERIAL AND METHODS

Polyethylene glycol (MERCK), F_2O_3 nanoparticles (MERCK). ciprofloxacin and amphotericin –B drugs (BDH).

Instruments

The FTIR TENSOR 27 spectroscope from BRUKER in Germany was utilized for the measurement, which took place at the "College of Engineering" in the "University of AL Qadisiyah". The shape of the nanoparticles' fracture surface and the distribution of the nanoparticles are resolute utilizing scanning electron microscopy (SEM). The in-strument was a "FEI Nova Nano SEM 230" from Eindhoven, the Netherlands, and it was utilized at IRAN on the "Electron Microscopy Unit at the" setting.

Synthesis of polymer-coated nanoparticles (Fe_2O_3)

A quick and inexpensive hydrothermal synthesis technique was used to create polymer-coated nanoparticles (NPs) under ambient air conditions. The synthesis techniques have been previously published with changes. The polymer coated nanoparticles were made by mixing 25 mL of ultrahigh quality water and 3.6 g of polymer (carboxymethylcellulose) at 80 °C for 10 minutes. The solution was swirled at 80°C. Fe_2O_3 Nano-particles (1.0 gm) were added to the solution and agitated for another 10 minutes at 80 °C. Sonication was used to redistribute the suspension in water. For the experiment on oil removal, NPs solutions were kept.

Antifungal activities

The antifungal effectiveness of "the synthesized polymers" is evaluated through the utilization of the poisoned food technique on a growth medium known as potato dextrose agar (PDA). For the purpose of this investigation, pure cultures of pathogenic fungi, more specifically "Alternaria solani, Fusarium oxeyspurum, Aspergillus niger, as well as Mucor", were employed. In this experimental procedure, sterile petri dishes were full with 20 ml of the "potato dextrose agar" medium, along with 1.0 ml of the synthesized polymers at a "concentration" of 1.0 mg/ml. Following this, circular cups with a diameter of 6 mm were carefully extracted from the center of each plate, and mycelia discs from a 7-day-old culture were then inoculated into these cups. Furthermore, a control group was established using the PDA medium without the addition of the synthesized polymers. The degree of inhibition in fungal growth was determined by comparing it to a standard drug, as outlined in literature [20].

RESULTS AND DISCUSSION

FTIR Spectra of P.E.G-Fe_2O_3

Fig. 1 displays the FTIR spectra of P.E.G- Fe_2O_3 (Polyetheleneglycol- Fe_2O_3). In all samples, the spectra reveal absorption bands at 577 cm^{-1} as well as 477 cm^{-1}, which agree toward the Fe-O stretching vibration of Fe_2O_3. The Polyethylene glycol demonstrates absorptions similar to "those of a primary alcohol". Therefore, these absorptions

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consist of stretching as well as "bending vibrations" that are limited to C-C stretch, C-O stretch, CH stretch (methylene absorptions), as well as "the C-H bending". The OH stretching vibration, indicating a hydrogen bonded nature, is observed in the area 3478 cm^{-1}. PEG contains a methylene

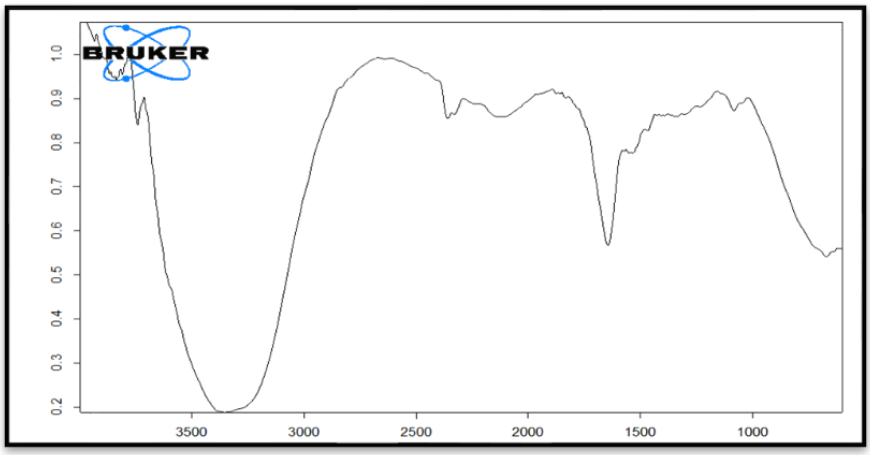

Fig. 1. FTIR Spectrum of P.E.G-Fe_2O_3

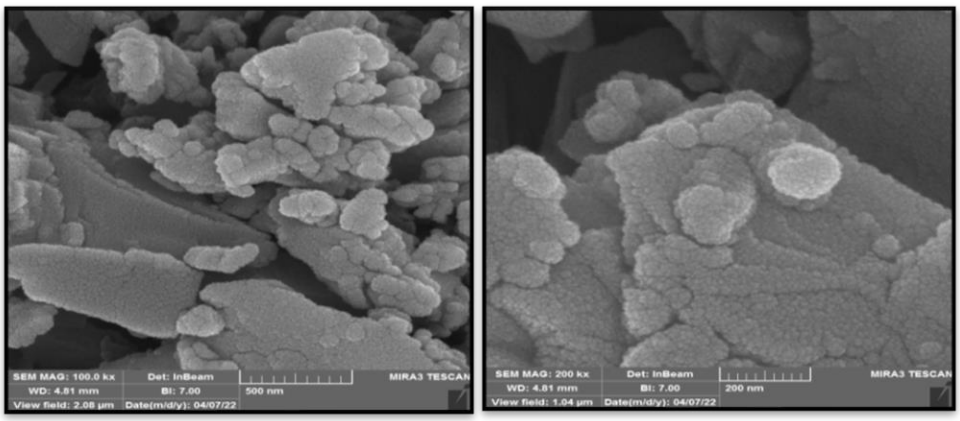

Fig. 2. SEM Image of PEG-coated Fe_2O_3 nanoparticles at of 500 and 200 nm.

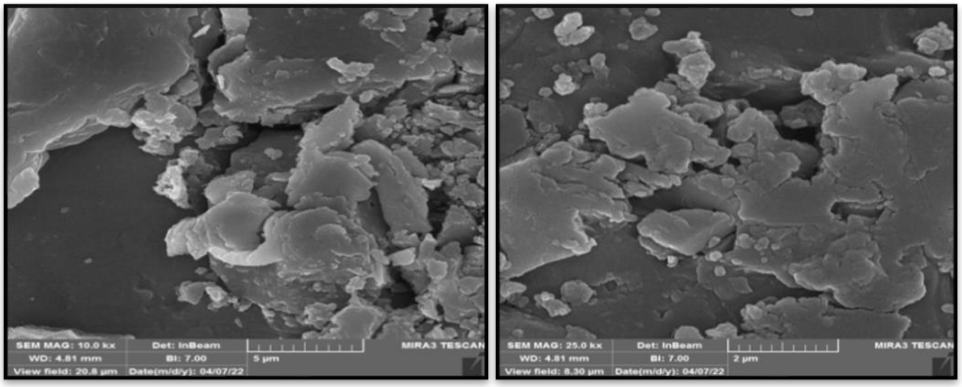

Fig. 3. SEM Image of PEG-coated Fe_2O_3 nanoparticles at 5 and 2nm

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group that exhibits stretching mode "vibrations at approximately 2803 cm^{-1}". "The absorption at 1474 cm^{-1}" is attributed to the required vibration of -CH_2. Additionally, similar to primary alcohols, strong bands about 1362 cm^{-1} as well as 1287 cm^{-1} are witnessed to the C-O stretching vibration [21-23].

SEM of Polyethylene Glycol-Coated Fe_2O_3 Nanoparticles

Fig. 2 displays the SEM image of the Fe_2O_3 nanoparticles coated with polyethylene glycol (PEG). The incorporation of Fe_2O_3 with PEG resulted in the formation of large aggregated nanostructures, with diameters measuring approximately 500 nm. These nanostructures primarily consist of smaller nanoparticles, with diameters of around 200 nm, rather than forming a mesoporous structure. This phenomenon can be attributed to the relatively small size of the individual nanoparticles, which caused them to aggregate around the polar terminals of the surfactant. As a result, well-defined tubular arrays, typically observed in mesoporous structures, were not formed.

The PEG-coated Fe_2O_3 SEM image also revealed a consistent polymer coating with a thin layer surrounding the clustered nanoparticles. The examination provides insights into the shape and dimensions of the Fe_2O_3 nanoparticles at two

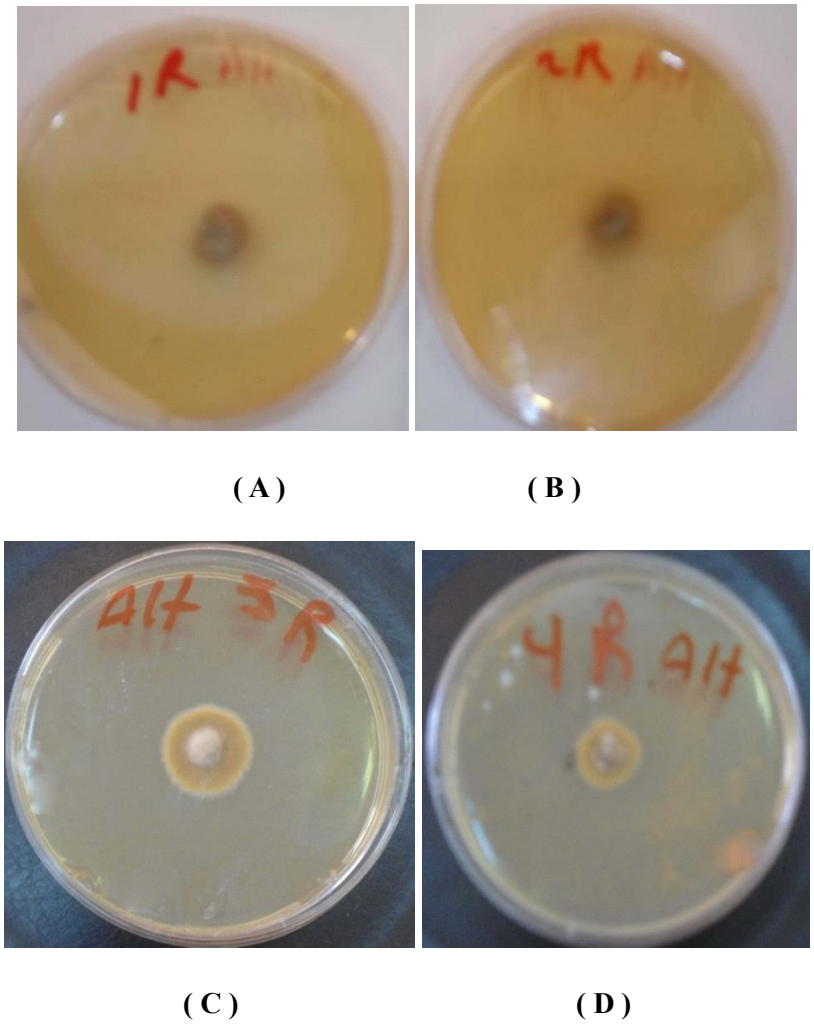

Fig. 4. "Statistical representation for biological activity of prepared polymers on *Alternaria Solani* " (A) Influence of P.E-Coated Fe_2O_3 (1.0 µg/ml) (B) Effect of P.E-Coated Fe_2O_3 (1.4 µg/ml) (C) Effect of P.E-Coated Fe_2O_3 (1.2 µg/ml) (D) Effect of P.E-Coated Fe_2O_3 (1.6 µg/ml).

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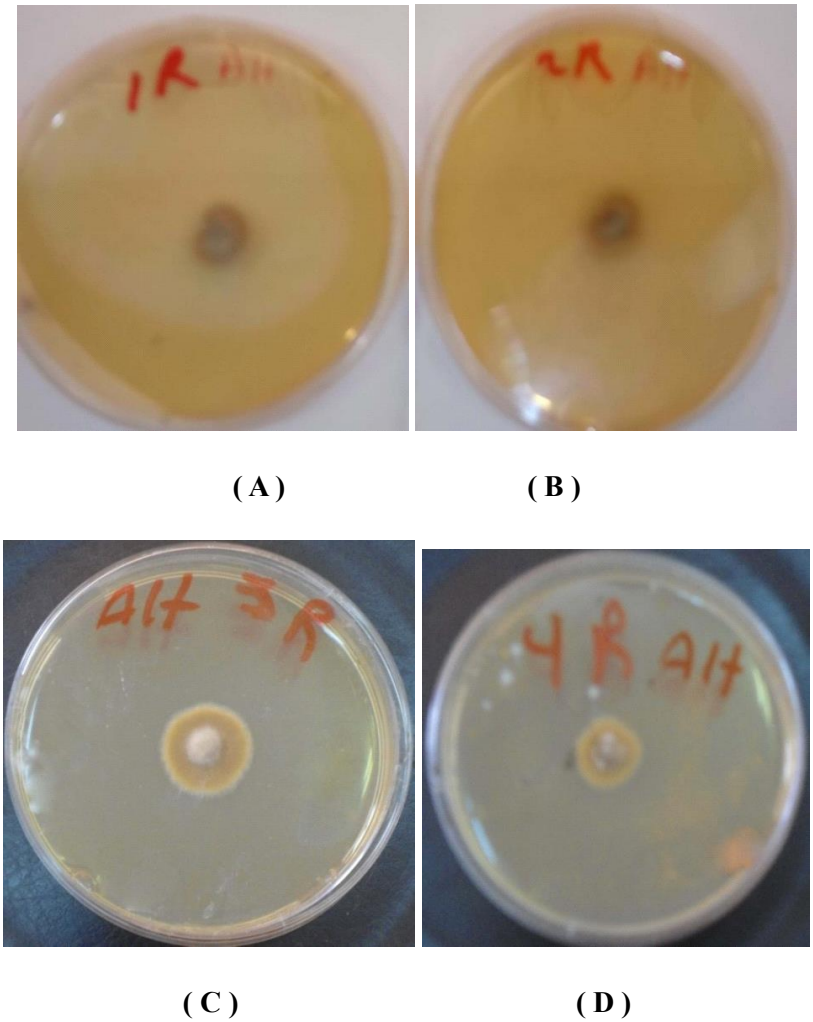

Fig. 5. "Statistical representation for biological activity of prepared polymers on *Fusarium Oxeyspurum*" (A) Effect of P.E-Coated Fe_2O_3 (1.6 µg/ml), (B) Effect of P.E-Coated Fe_2O_3 (1.4 µg/ml), (C) Effect of P.E-Coated Fe_2O_3 (1.2 µg/ml), (D) Influence of P.E-Coated Fe_2O_3 (1.0 µg/ml)

Table 1. "Biological activity data (zone of inhibition in mm) of P.E-Coated Fe_2O_3 against fungal pathogens".

polymers	"Zone of Inhibition"			
	Alternaria Solani	*"Fusarium Osey Sporum"*	**"***Mucor"*	*"Aspergillus niger"*
P.E-Coated Fe_2O_3 (1.0 µg/ml)	22	16	16	30
P.E-Coated Fe_2O_3 (1.2 µg/ml)	21	15	14	**25**
P.E-Coated Fe_2O_3 (1.4µg/ml)	16	14	**13**	15
P.E-Coated Fe_2O_3 (1.6µg/ml)	15	13	**10**	0
Standard	12	6	6	9

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different magnifications, 5 and 2 nm, as depicted in Fig. 3. These visuals effectively illustrate the composition and layered structure of the nanosolution.

Effects of Antimicrobials on Growth of Organism

"Antimicrobials" are materials capable of either eradicating or impeding the proliferation of "microbial cells" . Certain antimicrobials, like penicillin, were resultant from microorganisms and find application in therapeutics for the conduct of illnesses produced by "microbial pathogens" . Such agents exhibit choosy activity, meaning they disrupt specific metabolic factors or processes in the pathogen while having minimal to no impact on the host. The selectivity is mainly attributed to the absence of the major factor or process in the host cell [24].

Factors effected on antimicrobial activity based on synthetic polymers

Several research teams have successfully shown the capability to imitate the activity that is biochemical of polymers that are antimicrobial. This achievement has been attained through precise adjustments in the hydrophobicity of the molecule, as well as the intricacies of membrane supplement as well as charge density. The biological characteristics of synthetic polymeric mimics are influenced by various factors, and currently, it remains impossible to accurately anticipate the specific properties of these molecules solely based on their chemical structure. The understanding of the impact of design elements like charge as well as hydrophobicity onto the features of a polymer series has been demonstrated. However, it is noteworthy that the knowledge about the

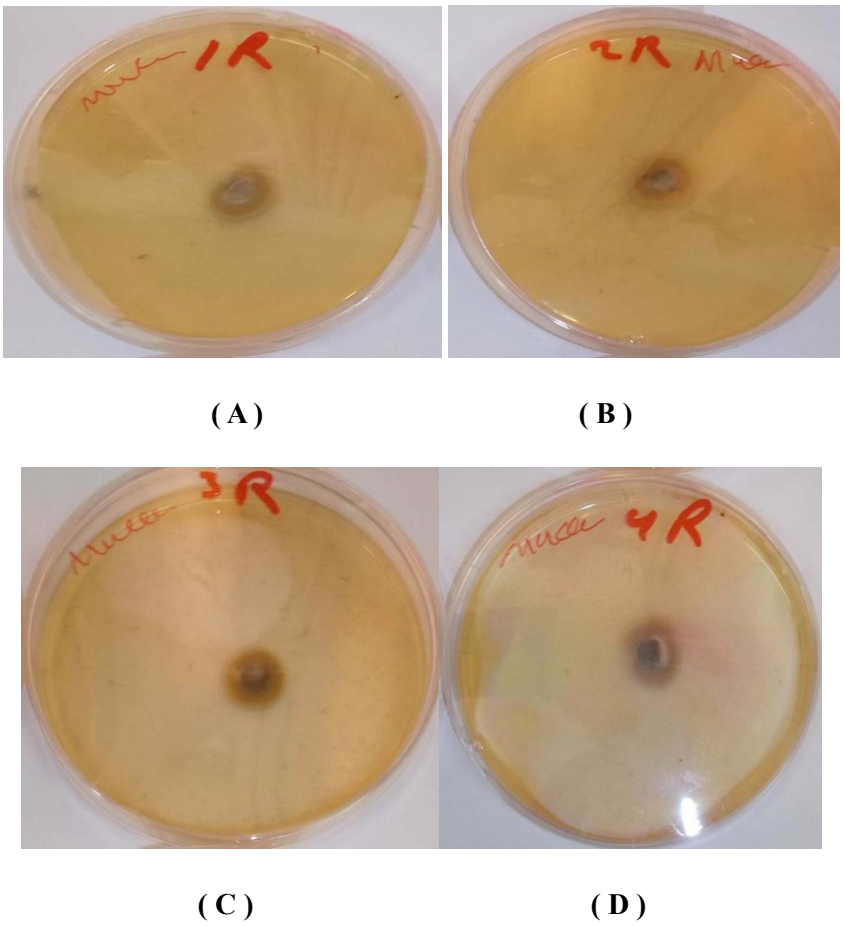

Fig. 6. "Statistical representation for biological activity of prepared polymers on Mucor fungi" (A) Effect of P.E-Coated Fe_2O_3 (1.2 µg/ml), (B) Effect of P.E-Coated Fe_2O_3 (1.6 µg/ml), (C) Effect of P.E-Coated Fe_2O_3 (1.0 µg/ml), (D) Effect of P.E-Coated Fe_2O_3 (1.4 µg/ml).

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interaction of polymeric with membranes is The knowledge of the interfaces between minor "antibacterial molecules" and membranes as well as cells is somewhat restricted in comparison to the comprehensive understanding of mechanistic intricacies. [26].

Antifungal activities

A fungus is an organism resembling a plant, lacking the pigment chlorophyll and therefore devoid of color. Infections caused by fungi that impact the human body can take on the form of either "yeast-like or mold-like"organisms, as well as are commonly known as " mycotic or fungal infections" .

There are numerous fungi that can lead to plant diseases, however, out of the thousands of types of yeast as well as molds, only around 100 can cause diseases in animals or humans. It is worth noting that only candida and dermatophytes are typically conveyed out of one person to one more [27,28].

Mycotic infection can manifest in either of two distinct forms: 1. Supercactial mycotic infections. 2. Deep (systemic) mycotic infections.

Shallow fungal infections refer to those that occur on the surface of the body, while deep fungal infections occur within the body, like in the lungs. Treating profound fungal infections can be challenging and may require prolonged use of antifungal drugs, which can be either fungicidal or fungistatic. Antifungal medications are employed for the purpose of addressing both surface-level and profound fungal infections, with the particular applications delineated in alternative references. Amphotericin B is widely regarded as the most

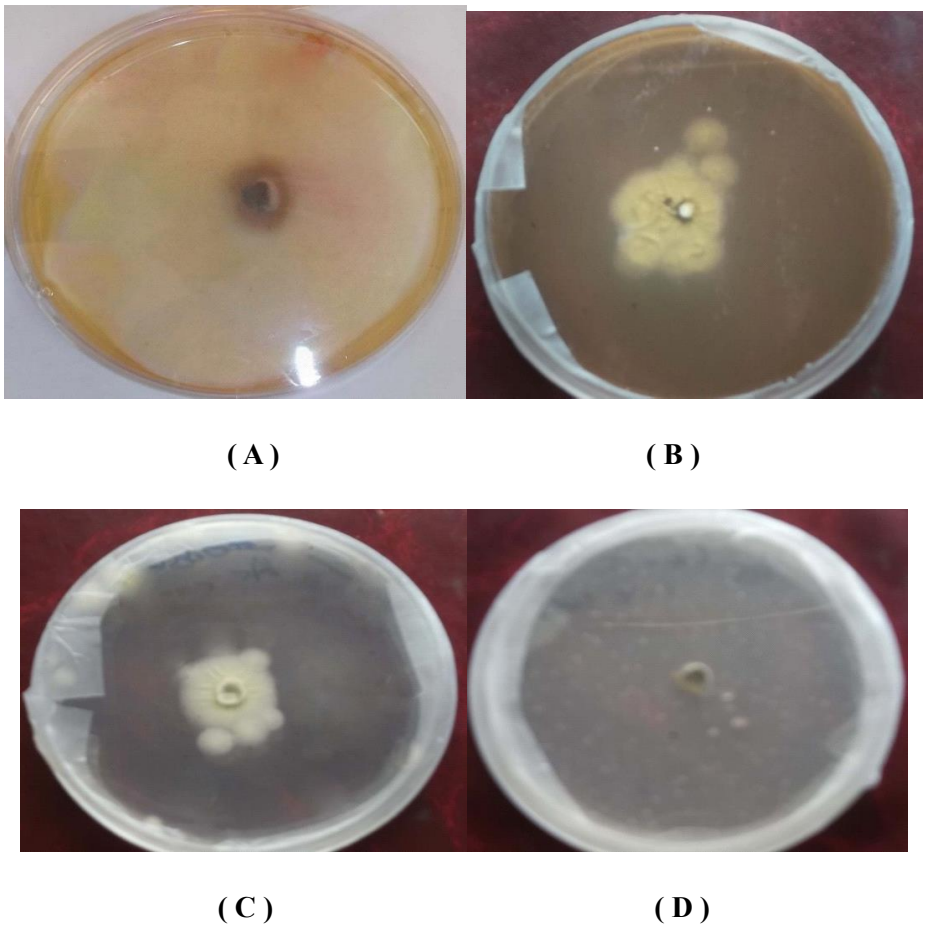

Fig. 7. "Statistical exemplification for biological activity of prepared polymers on Aspergillus niger Fungi" (A) Influence of P.E-Coated Fe_2O_3 (1.0 µg/ml), (B) Effect of P.E-Coated Fe_2O_3 (1.2 µg/ml), (C) Effect of P.E-Coated Fe_2O_3 (1.6 µg/ml), (D) Effect of P.E-Coated Fe_2O_3 (1.4 µg/ml).

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efficacious pharmaceutical agent in the treatment of the majority of systemic fungal infections. In cases where the fungal infection affects the skin or mucous membranes, alternative treatment options include the use of topical or vaginal preparations.

The investigation of the antifungal characteristics of the synthesized polymers involved the use of pure "cultures of pathogenic fungi", specifically "Alternaria solani, Fusarium oxeyspurum, Aspergillus niger, as well as Mucor". The antifungal activity of these fungi was evaluated by utilizing the "poisoned food technique on a potato dextrose agar (PDA) medium". After incubating the microorganism "cultures for 7 days at 37 ºC, the inhibition zones were measured" in millimeters (Table 1).

The result demonstrates that the P.E-Coated Fe_2O_3 give good sensitivity vary from (15 mm) to (22 mm) and to be greater at (15 mm) in concertation at (1.6µg/ml) (Fig. 4).

Despite that Fusarium oxeyspurum displays little activity against at (1.0 µg/ml), but it gives greater against at (13 mm) in concentration at (1.6 µg/ml) (Fig. 5).

The antifungal activity of the Mucor fungi was assessed, and it was found that the highest result was obtained against P.E-Coated Fe_2O_3 (1.6µg/ml), with a pathogen kill zone of 10 mm on solidification media. On the other hand, the lowest effect was observed with P.E-Coated Fe_2O_3 (1.0µg/ml), resulting in a pathogen kill zone of 16 mm (Fig. 6).

Upon conducting a test on Aspergillus niger Fungi, it was found that the P.E-Coated Fe_2O_3 (1.6µg/ml) had the greatest impact, resulting in zero mm growth in pathogens. However, the P.E-Coated Fe_2O_3 (1.0µg/ml) had the lowest effect on fungi, with a result of only 30 mm (Fig. 7).

Polymer P.E coated Fe_2O_3 NPS with different concentrations (1.0,1.2,1.4, and 1.6 µg/ml) showed inhibition activities against all tested fungal. The highest inhibition zone of NPs observed in fungi was (0 mm) with concentration (1.6 µg/ml) polymer P.E-coated Fe_2O_3, while the lower inhibition zone was (30mm) in with concentration (1.0 µg/ml) in polymer P.E-coated Fe_2O_3 NPs. It was very similar to other reports where the NPs could inhibit the growth of fungi at high concentration.

CONCLUSION

A chemical process was utilized to prepare P.E-coated Fe_2O_3 nanosolution, as discussed in this article. The nanopolymer solutions were analyzed using SEM techniques, which revealed that they were of nanoscale size. The Fe_2O_3 cores were coated thru a tinny layer of polyethylene glycol. The chemical structure of P.E in the nanosolution was determined through FT-IR spectra. SEM images demonstrated that the Fe_2O_3 NPs were spherical in form, with average diameters of 5 and 2 nm for different stirring timesIt could be argued that the connection between particles and fungi is effective thru the surface region of the particles available for interaction. Furthermore, research has shown that lesser particles own a larger superficial region compared to greater ones, resulting in a greater fungal effect during interaction. When the P.E-coated It underwent testing against fungal pathogens including "Alternaria solani, Fusarium oxeyspurum, Aspergillus niger, and Mucor " exhibited excellent activity. This activity was compared to that of the standard antifungal drug, Amphotericin-B.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

REFERENCES

1. Murphy CJ. Sustainability as an emerging design criterion in nanoparticle synthesis and applications. J Mater Chem. 2008;18(19):2173.
2. Aihara N, Torigoe K, Esumi K. Preparation and Characterization of Gold and Silver Nanoparticles in Layered Laponite Suspensions. Langmuir. 1998;14(17):4945-4949.
3. Lin XZ, Teng X, Yang H. Direct Synthesis of Narrowly Dispersed Silver Nanoparticles Using a Single-Source Precursor. Langmuir. 2003;19(24):10081-10085.
4. Sharma VK, Yngard RA, Lin Y. Silver nanoparticles: Green synthesis and their antimicrobial activities. Advances in Colloid and Interface Science. 2009;145(1-2):83-96.
5. Lu AH, Salabas EL, Schüth F. Magnetic Nanoparticles: Synthesis, Protection, Functionalization, and Application. Angew Chem Int Ed. 2007;46(8):1222-1244.
6. Yang C, Rait A, Pirollo KF, Dagata JA, Farkas N, Chang EH. Nanoimmunoliposome delivery of superparamagnetic iron oxide markedly enhances targeting and uptake in human cancer cells in vitro and in vivo. Nanomedicine : nanotechnology, biology, and medicine. 2008;4(4):318-329.
7. Ling Y, Wei K, Luo Y, Gao X, Zhong S. Dual docetaxel/superparamagnetic iron oxide loaded nanoparticles for both targeting magnetic resonance imaging and cancer therapy. Biomaterials. 2011;32(29):7139-7150.
8. Zhang Z-Q, Song S-C. Thermosensitive/superparamagnetic iron oxide nanoparticle-loaded nanocapsule hydrogels for multiple cancer hyperthermia. Biomaterials. 2016;106:13-23.
9. Saikia C, Das MK, Ramteke A, Maji TK. Effect of crosslinker

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on drug delivery properties of curcumin loaded starch coated iron oxide nanoparticles. Int J Biol Macromol. 2016;93:1121-1132.
10. Mashhadi Malekzadeh A, Ramazani A, Tabatabaei Rezaei SJ, Niknejad H. Design and construction of multifunctional hyperbranched polymers coated magnetite nanoparticles for both targeting magnetic resonance imaging and cancer therapy. Journal of Colloid and Interface Science. 2017;490:64-73.
11. Theerdhala S, Bahadur D, Vitta S, Perkas N, Zhong Z, Gedanken A. Sonochemical stabilization of ultrafine colloidal biocompatible magnetite nanoparticles using amino acid, l-arginine, for possible bio applications. Ultrason Sonochem. 2010;17(4):730-737.
12. Ngaboni Okassa L, Marchais H, Douziech-Eyrolles L, Cohen-Jonathan S, Soucé M, Dubois P, et al. Development and characterization of sub-micron poly(d,l-lactide-co-glycolide) particles loaded with magnetite/maghemite nanoparticles. Int J Pharm. 2005;302(1-2):187-196.
13. Jarrett BR, Frendo M, Vogan J, Louie AY. Size-controlled synthesis of dextran sulfate coated iron oxide nanoparticles for magnetic resonance imaging. Nanotechnology. 2007;18(3):035603.
14. Li L, Chen D, Zhang Y, Deng Z, Ren X, Meng X, et al. Magnetic and fluorescent multifunctional chitosan nanoparticles as a smart drug delivery system. Nanotechnology. 2007;18(40):405102.
15. Mahmoudi M, Simchi A, Imani M, Milani AS, Stroeve P. Optimal Design and Characterization of Superparamagnetic Iron Oxide Nanoparticles Coated with Polyvinyl Alcohol for Targeted Delivery and Imaging. The Journal of Physical Chemistry B. 2008;112(46):14470-14481.
16. Masoudi A, Madaah Hosseini HR, Shokrgozar MA, Ahmadi R, Oghabian MA. The effect of poly(ethylene glycol) coating on colloidal stability of superparamagnetic iron oxide nanoparticles as potential MRI contrast agent. Int J Pharm. 2012;433(1-2):129-141.
17. Ramimoghadam D, Bagheri S, Hamid SBA. In-situ precipitation of ultra-stable nano-magnetite slurry. J Magn Magn Mater. 2015;379:74-79.
18. Huang L, Nishinari K. Interaction between poly(ethylene glycol) and water as studied by differential scanning calorimetry. J Polym Sci, Part B: Polym Phys. 2001;39(5):496-506.
19. Mahmoudi M, Simchi A, Milani AS, Stroeve P. Cell toxicity of superparamagnetic iron oxide nanoparticles. Journal of Colloid and Interface Science. 2009;336(2):510-518.
20. Joshi A, Kanthaliya B, Arora J. Current Scenario of Potential Renewable Energy Sources for Sustainable Development in India. THE JOURNAL OF PLANT SCIENCE RESEARCH. 2019;35(2):205-214.
21. An introduction to organic chemistry. 7th ed. By Alexander Lowy, Benjamin Harrow, and Percy M. Apfelbaum. John Wiley & Sons, Inc., New York, 1951. xiv + 480 pp. Illustrated. 14.5 × 22 cm. Price $5. Journal of the American Pharmaceutical Association (Scientific ed). 1951;40(10):533.
22. Vyvyan JR, Pavia DL, Lampman GM, Kriz GS. Preparing Students for Research: Synthesis of Substituted Chalcones as a Comprehensive Guided-Inquiry Experience. J Chem Educ. 2002;79(9):1119.
23. Erratum. Relict Species: Springer Berlin Heidelberg; 2009. p. 451-451.
24. Saif MJ, Anwar J, Munawar MA. A Novel Application of Quaternary Ammonium Compounds as Antibacterial Hybrid Coating on Glass Surfaces. Langmuir. 2008;25(1):377-379.
25. Mahmoud YAG, Aly MM. Anti-Candida and mode of action of two newly synthesized polymers: a modified poly (methylmethacrylate-co-vinylbenzoylchloride) and a modified linear poly (chloroethylvinylether-co-vinylbenzoylchloride) with special reference to Candida albicans and Candida tropicalis. Mycopathologia. 2004;157(2):145-153.
26. Juergensen L, Busnarda J, Caux PY, Kent RA. Fate, behavior, and aquatic toxicity of the fungicide DDAC in the Canadian environment. Environ Toxicol. 2000;15(3):174-200.
27. Hume EBH, Baveja J, Muir B, Schubert TL, Kumar N, Kjelleberg S, et al. The control of Staphylococcus epidermidis biofilm formation and in vivo infection rates by covalently bound furanones. Biomaterials. 2004;25(20):5023-5030.
28. Acharya V, Ratna Prabha C, Narayanamurthy C. Synthesis of metal incorporated low molecular weight polyurethanes from novel aromatic diols, their characterization and bactericidal properties. Biomaterials. 2004;25(19):4555-4562.

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