Incorporating graphene oxide and Cu nanoparticles to alter PVA based nanofibers through adding curcumin with high antibacterial activities used in wound healing

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ABSTRACT

The main purpose of this study is the optimization and fabrication of bacterial cellulose-based on GO-Cu-Cur nanocomposite and PVA/GO-Cu-Cur as a wound dresser in order to accelerate the wound repairing process. First of all, graphene oxide, GO-Cu nanohybrid, and GO-Cu-Cur nanohybrid were synthesized, and by the were characterized. Then, the PVA/GO-Cu-Cur was synthesized by the electrospinning method, and by the FTIR was characterized. SEM analysis indicates that the diameter of the nanofibers is 328 nm. Mechanical characteristic of PVA/GO-Cu-Cur was investigated by the tensile resistance, and it reveals that the GO-Cu-Cur nanohybrid cause the improvement of mechanical characteristic. The bacterial cellulose/GO-Cu-Cur by the floating method was synthesized, and also, the biodegradable behavior of nanocomposite was optimized, and the sample shows a degradation percentage of 44% after 98 h. For investigation of the antibacterial effect of synthesized materials, the MIC and optical density (OD) were used. The results show that these materials have a great ability to inhibition of gram-negative and gram-positive bacteria growth. The toxicity, survival, and cell proliferation of the fibroblast cells by the MTT were investigated, and results show that the GO-Cu-Cur nanohybrid does not have a toxic effect. Therefore, the PVA/GO-Cu-Cur nanofiber is a promising wound dressing for inhibiting bacterial growth and promoting skin wound repair.

OBJECTIVES

- To survey the role and effect of copper and graphene oxide and curcumin nanoparticles on antimicrobial properties;
- To optimize and fabricate graphene-copper-curcumin Nano-composites and polyvinyl alcohol/graphene-copper-curcumin nanofibers as wound dressings to accelerate wound healing;
- To combine copper nanoparticles, graphene oxide, and curcumin and optimize the composite to provide an ideal dressing with antibacterial properties that reduces the course of treatment and infection control simultaneously and can eventually replace the present methods.

Materials & METHODS

Polyvinyl alcohol nanofibers were produced using the electrospinning method and their properties were modified with graphene oxide-copper-curcumin nanocomposite.

All substances, including bovine fetal serum, cell culture medium dimethyl sulfoxide (DMSO), streptomycin penicillin, and 3-2,5-diphenyl-tetrazolium bromide (MTT), were purchased from Sigma-Aldrich.

NIH 3T3 fibroblast cells were obtained from ATCC (Virginia, USA), cultured in a culture medium containing 1% penicillin/streptomycin and 10% fetal bovine serum.

The cells were then cultured in a wet incubator with 5% carbon dioxide for 24 h at a constant temperature of 37 ° C for further tests.

Hummers' method was used to synthesize graphene oxide.

An RGO-Cu solution with a concentration of 7 mg/L was prepared in situ. Then30 mg of Curcumin was added to the synthesized Nano-hybrid and stirred for 10 minutes to prepare GO/Cu/Cur Nano hybrid with a concentration of 7.5 mg/ml.

The electrospinning solution was prepared by stirring the PVA in deionized water.

The response surface method (RSM) applying central composite design (CCD) with two factors and three levels was employed to optimize the concentration effect of GO/Cu/Cur nanocomposite and volume ratio of GA to PVA-GO/Cu/Cur.

The antibacterial activities of GO, GO/Cu, and GO/Cu/Cur nanomaterial's against Gram-negative E. coli and Grampositive S. aureus bacteria were investigated by applying MIC and OD tests.

The simple tensile test was used to evaluate the mechanical properties of materials including ultimate stress, modulus of elasticity, and maximum elongation at the moment of failure.

Table 1. Experimental range and levels of independent factors

Independent factors	Levels		
	-1	0	1
Volume ratio of $\frac{GA}{GO/Cu/Cur}$	2	3.5	5
$[GO/Cu/Cur\,](mg.mL^{-1})$	14	21	28

RESULTS

Figure 1 shows the FTIR spectra according which the functional groups are determined as follows:

As shown in Figure 2, the surface of the PVA/GO-Cu-Cur nanofibers is spun perfectly smooth and without considerable willow. This uniform morphology indicates that the GO-Cu-Cur Nano hybrid is embedded in the fibers. Fiber diameters are measured at an average of 328 nm.

The results of the study of the minimum inhibitory concentration are shown in Table 2. As can be seen the antibacterial effect of graphene-copper Nano hybrids is significantly increased compared to graphene oxide, this increase is due to the antibacterial properties of copper.

Figure 3 shows the stress-elongation diagram of the polyvinyl alcohol /graphene-copper-curcumin sample. Initially the material shows elastic behavior which changes to plastic one after the peak point after which the fibers are separated from each other at the Break point. In similar studies, the values of tensile strength and young modulus for PVA nanofibers have been reported to be 3 and 9.85 MPa. However, by adding the desired composite to the fibers, these are increased to 4.5 and 68 MPa, respectively.

Figure 4 shows the test results in different dilutions of the composite compared to the control group after 24 hours. It can be seen that the dilution rate of 1 to 500 compared to the other groups increased survival, this amount was not a significant difference compared to the control group (P>0.05). As can be seen in the graph, after dilution 1 to 500 survival decreased compared to the control group (P <0.05). This decrease may be due to an increase in graphene oxide concentration. Liu et al. showed that graphene oxide at a concentration of 12.5 µg/ml reduces cell viability.

Table 2. Minimum inhibitor concentration in mg/ml

Bacteria	MIC graphene oxide	MIC Graphene-Copper Nano Hybrid	MIC Graphene-Copper-Curcumin Nano Hybrid	MIC tetracycline antibiotic
S.aureus	2.23	1.55	1.28	**0.9**
E.coli	1.56	1.23	0.92	**0.9**

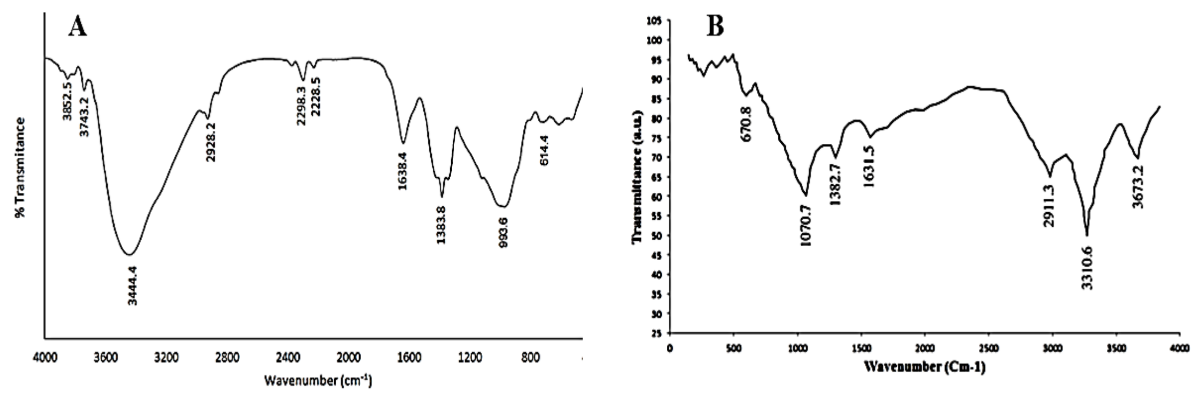

Figure 1. FTIR spectra of A) GO/Cu/Cur , B) PVA/GO/Cu/Cur

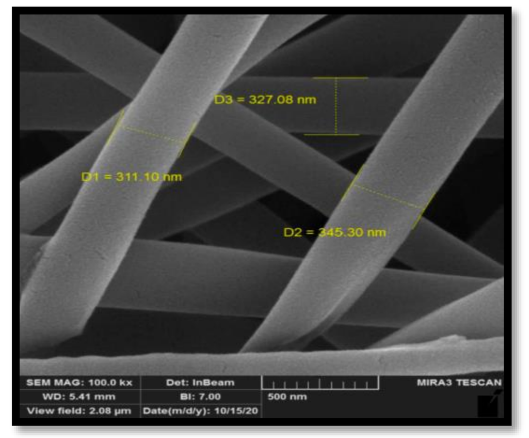

Figure 2. Scanning electron microscope (SEM) image of PVA/GO-Cu-Cur nanofibers

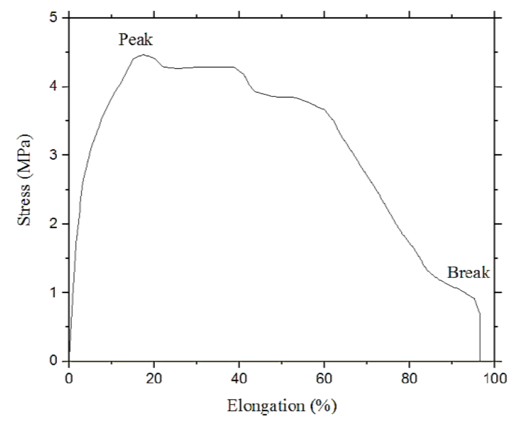

Figure 3. Stress-elongation of polyvinyl alcohol / graphene-copper-curcumin

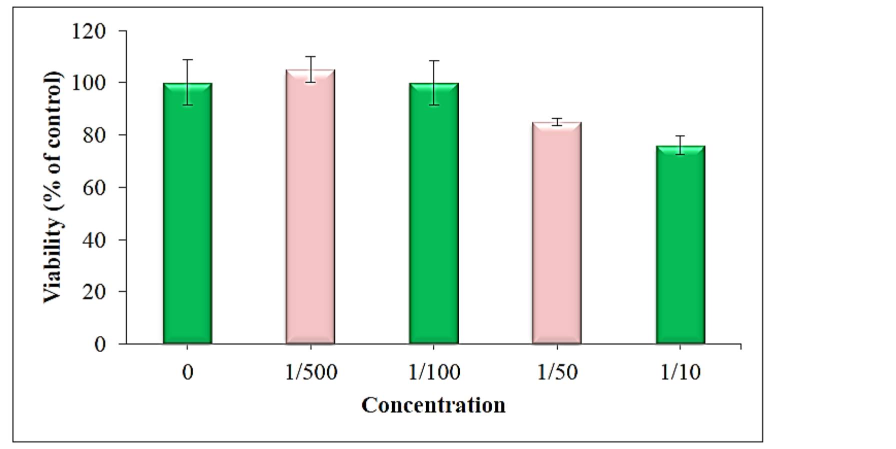

Figure 4. Results of cell survival and proliferation

CONCLUSIONS

Natural biopolymers have good biological properties such as reproduction, survival, restoration, and differentiation, etc., but inferior mechanical properties limits their applications. On the other hand, synthetic bio-polymers have good mechanical properties, but inferior biological properties. Adding natural biopolymers to synthetic biopolymers makes the most of the ability of both groups to have both biological and mechanical properties, each of which has many positive effects on wound healing. In this study, we were able to partially compensate for these shortcomings by identifying the properties of each material used along with their disadvantages. Loading of the synthesized composite in polyvinyl alcohol improved its mechanical properties and the efficient wound dressing can be produced by optimizing the concentration of the composite based on the swelling test. The wound dressing was able to show good performance in terms of mechanical properties. One of the most important factors in wound healing is that the wound site should remain moisturized. According to various analyzes performed on the composite as well as optimizing it based on water and moisture absorption, the wound dressing produced was able to provide a suitable amount of moisture at the wound site, which in turn facilitates the healing process. Its antibacterial properties, non-toxicity, and high ability to migrate cells were successfully proven and these results showed that we were able to improve the disadvantages of each of them and provide a more efficient wound dressing

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