RESEARCH ARTICLE

Effects of Hydrolytic and Oxidizing Agents on the Properties of Low Density Polyethylene/Halloysite Nanocomposites for Biomedical Applications

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ABSTRACT

Low density polyethylene (LDPE) nanocomposites reinforced with natural halloysite nanotubes (HNTs) were synthesized and evaluated as a prospective material for biomedical applications via in vitro biostability studies in this work. A twin-screw extruder machine was used to fabricate the examined LDPE and LDPE/HNTs nanocomposites (NCs), followed by in vitro treatment of the prepared NCs via immersion in oxidizing & hydrolytic chemicals for four weeks at 37°C. The materials' in vitro mechanical characteristics were evaluated under these harsh conditions. The analysis showed that the LDPE with 3 wt% HNTs exhibited the best nanofiller dispersion characteristics. This NC also presented smoother surface degradation characteristics compared to the plain LDPE and other LDPE NCs. Furthermore, as compared to plain LDPE, the LDPE NCs showed enhanced mechanical capabilities, and these qualities were less impacted by the in vitro conditions. The introduction of 3 wt% HNTs into the LDPE gave the best in vitro mechanical characteristics. Furthermore, the existence of a better-scattered nanotube structure was thought to offer a more sinuous pathway for the propagation of H_2O and the oxidants, thereby reducing their penetration across the matrix chains. Hence, the kinetics of disintegration inside the LDPE molecular chains were slower, resulting in improved biostability.

Keywords: Biomedical applications, Halloysite nanotubes (HNTs), Low-density polyethene (LDPE), Nanocomposites, Nanofiller dispersion characteristics.

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INTRODUCTION

Now that disease and health issues are a major concern among the general public, there has been a growing demand for high-quality clinical research in the biomedical sector. This is driven by the restricted number of currently existing materials suitable for medical use, particularly durable materials needed for prolonged and heavy-use applications. This has been the case due to the demanding requirements of such materials, such as characteristics, biostability, availability, and design limits.[1] Hence, the art of synthesizing novel nanocomposites (NCs) for biomedical applications has been considered a trending research area. The most significant material property for biological usage is the ability of the material to tolerate repeated sterilization processes using high temperatures, gamma irradiation, electron beams, hydrolytic and oxidative agents.[2] A material for biomedical application must also have great chemical resistance, color stability, hardness, and clarity.[1,2]

Polymer NCs that contain nanoclays have received more attention in recent years owing to their abundance in nature, low cost, non-toxicity, and increased availability in a variety of sizes, forms, and characteristics[3] Nanoclay-containing NCs have been mostly developed for automotive, industrial, and packaging applications[4] while their biomedical applications, on the other hand, have received less attention. The study by Xie *et al.* (2020) focused on the functionalization of raw halloysite nanotubes (RHNTs) with (3-aminopropyl) triethoxysilane (APTS) using ethylene glycol diglycidyl ether (EGDE) as the cross-linker; the study evaluated the potential characteristics of modified halloysite nanotubes reinforced with chitosan ffor biomedical usage. From the results, the chitosan reinforced HNTs-NH_2 improved the material's physical

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qualities, such as thermal stability, water resistance, rate of water vapor transmission, as well as mechanical characteristics, making them viable candidates for use in biomedical cases.[5]

HNTs is one of the environmentally benign 1D natural nanofillers; they are biocompatible, eco-sustainable, and non-toxic.[6] HNTs also have good adsorption and mechanical capabilities and great heat stability due to their large aspect ratio, huge surface area, and unique hollow nanotubular structure.[7,8] They are frequently utilized as fillers to improve polymers. The fabrication of sodium alginate (SA)/HNTs composite hydrogels was reported by Huang *et al.*[9] for use in bone tissue engineering. The study noted improved compressive mechanical strength of the resulting material and the subsequent cell attachment and proliferation capabilities upon the addition of HNTs to the SA/HNTs composite hydrogels compared to the addition of only sodium alginate. Liu *et al.*[10] reported the development of novel chitosan/HNTs NC scaffolds by combining solution-mixing and freeze-drying processes. When comparing the thermal and mechanical parameters of the resulting NC scaffolds to those of the pure chitosan scaffold, the study observed better compressive strength, thermal stability, and compressive modulus of the NC scaffolds. As a result, NCs made with HNTs as inorganic fillers showed significant promise in a variety of applications.[11] Among the factors that affect the characteristics of HNTs are the size impact, hydrogen bond formation of their surface OH- and surface electron effect; these promote the agglomeration of HNTs and complicates the process of dispersing in the polymer matrix.[12] This problem has had a significant impact on HNTs application; as a result, HNTs are frequently modified before usage.

LDPE is an engineering polymer (thermoplastic) widely used in a variety of industries, particularly in the biomedical and medical fields where they are used to make artificial heart valves, catheter tubing, stents, blood bags, and other medical devices.[13] The comparably cheap cost of manufacture, ease of processing, good durability, non-toxicity, and low cost of finished LDPE products are all important factors in the selection of LDPE for various applications. The lightweight, impermeability, and chemical inertness[14] of LDPE NCs make them suitable for use in making catheter tubing[13] and other packaging materials like sterile blister packs and coil hoops for medicinal packing. Their flexibility implies that they can tolerate extended periods of flexing.[15] However, the type of nanofiller used, which cause a loss in hardness and scratch and/or wear resistance, remains a major impediment to the use of LDPE nanoparticles in medicine.[14,16]

Hence, it is necessary to investigate the structure and properties of LDPE NCs reinforced with HNTs nanoclay under different conditions (ambient and in vitro) to check their potential in a range of medical devices; this will aid in the development of a novel brand of biomedical materials. Given that LDPE NCs will be in contact with physiological fluid, it is important to evaluate their mechanical performance under specified settings. For "screening" novel potential materials for medical devices, *in-vitro* studies in liquid media that closely imitate physiological temperature and chemical conditions are required. As a result, this work presents preliminary findings on the NCs' in vitro mechanical properties after exposure to a biologically relevant oxidizing agent.

EXPERIMENTAL

Materials

The main material of this study is Low Density Polyethylene (LDPE). The density of LDPE was approximately 0.92 g/cm^3. It was purchased from Titan Chemicals, Malaysia. Halloysites Nanotubes (HNTs) used to reinforce LDPE was purchased from Sigma-Aldrich chemicals company. Hydrogen peroxide was utilized as an oxidizing agent in this study; it was provided by Qrec (Asia) Sdn. Bhd. as H_2O_2, 30–32% solution (Qrec®). Sigma-Aldrich supplied the utilized phosphate-buffered saline (PBS) tablets used to make the hydrolytic agent.

Preparation of LDPE/HNTs Nanocomposites Films

The sample preparation was done by melting LDPE with various HNT ratios (0, 1, 3, and 5%) using a Twin-screw extruder (Model: Lab Tech Co. LZ80). The resulting pellets of NCs were further compressed in a GOTECH Co. GT-7014-H30C compression molding machine to thick sheets of 1 mm. The samples were further reduced in size before the characterization process.

Transmission Electron Microscopy (TEM)

The samples were electron micrographed at 200 kV using a Philips CM200 TEM or at 100 kV using a Philips CM100 TEM (for DG only). DG was made up of commercially prepared clay fractions that were employed without modification. Halloysite was initially precipitated in an aqueous solution by agitating 20 mg of samples in ethanol (3 mL) for 2 minutes, followed by 2 minutes of sonication. Then, the suspended particles were dropped into a glass vial and dried for 24 hours in air on a 400-mesh carbon-coated copper grid.[17]

Scanning Electron Microscopy (SEM)

The neat LDPE and LDPE/HNTs NCs films was examined using SEM (Leo 1530 FESEM Zeiss) before and after immersion in hydrogen peroxide for 4 weeks at 37^{o}C to check for surface degradation. Before the microscopy, the samples were coated with thin platinum layer to prevent electrostatic charging.

Ambient and *In-vitro* Tensile Tests

To evaluate the influence of oxidative agents on the tensile characteristics of LDPE/HNTs films, the mechanical properties were measured pre and post-immersion in PBS and H_2O_2 (Table 1). The sample films were tested using the ASTM D882-02 standard's strip tensile test method. Film was cut into 10.0 x 2.0 cm strips and mounted on a mechanical (tensile test) rig (LRX Tensile Testing) in-between the manual grips; then, the strip was stretched to rupture at a displacement rate of 10 mm/min at a 50 mm initial grip to grip distance. The testing of the films was done at a higher strain rate of 42 mm/min.

Table 1: TS characteristics of neat LDPE and LDPE/HNTs nanocomposites, before and after 28 days exposure to H_2O_2 at 37°C)

Mechanical properties	*H_2O_2 exposure*	*Neat LDPE*	*1% HNTs*	*3% HNTs*	*5% HNTs*
TS (MPa)	Before	14.52	15.45	16.72	15.21
	After	13.12	14.17	15.55	13.48
EAB (%)	Before	67.15	71.23	74.82	70.16
	After	60.38	67.09	72.12	65.15
Toughness (MPa)	Before	51.59	53.76	56.34	52.62
	After	35.95	38.05	44.83	40.64

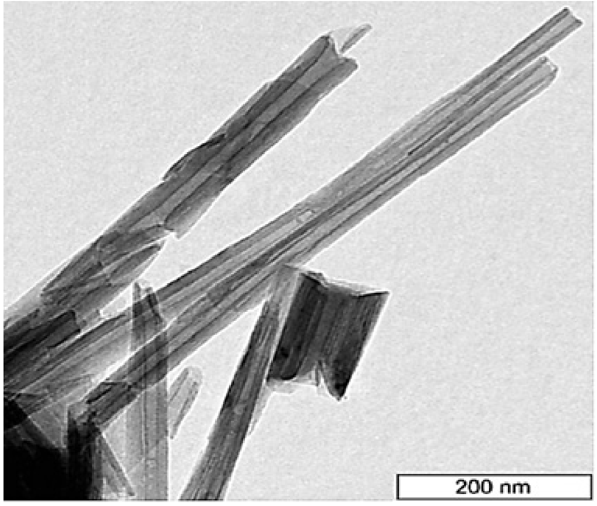

Figure 1: TEM micrograph of halloysite sample.

Water Permeability Test

The hydrolytic features of the examined materials were investigated and related to their in vitro biostability in PBS utilizing a water permeability test. The samples were cut into rectangular shapes (Length=Width=30 mm) and dried around 60 min to eliminate moisture; the weight of the sample was measured to ascertain their original mass before being placed in PBS in a beaker at 37°C (mimics the normal human body temperature). After the period of immersion, the samples were measured again weekly and the percentage mass increase after each week of immersion was used to calculate the hydration properties of the materials; the calculation was done thus:

The rise of weight (%) = (final weight - Initial weight) × 100/Initial weight

RESULTS AND DISCUSSION

Transmission Electron Microscopy (TEM)

The individual particles were scanned on a high magnification TEM and the obtained micrographs revealed the morphological properties of halloysite as summarized in Table 2; an average of 100 particles per sample was examined, creating about 40 TEM micrographs per sample. Figure 1 shows a representative example of this process. The tubular halloysite particles had an outside and inside diameter of 20–200 nm and 5–70 nm, respectively, while the length was 50–5000 nm. The sample had a large proportion of blocky, platy, and sub-spherical particles and very short tubes. The sample particles showed cylindrical, open-ended tubular particles with an electron-transparent center lumen.

Table 2: Mass percentage increase of EVA and EVA NCs pre and post in-vitro exposure to PBS at 37°C.

Sample	*Rise of weight upon 28 days exposure (%)*
Neat LDPE	0.15
LDPE + 1% HNTs	0.10
LDPE + 3% HNTs	0.07
LDPE + 5% HNTs	0.11

In this work, the tubular halloysites included the above-mentioned range and PATCH halloysite, which has tubes up to 5 meters long. The fibrous halloysite found in PATCH clay could be near to the optimum fibrous form; it exhibited the "highest lumen volume also. For the PATCH tubes, they are long and of a regular thin diameter. According to Norrish (1995), they are not so flexible, and their thin walls could fragment further during dispersion; they may also collapse, causing the sections to flatten out and lath-shaped under specific conditions.

SEM Analysis of the LDPE/HNTs Nanocomposites

All samples were characterized using SEM before and after 28 days of contact with an H_2O_2 solution. The acquired SEM images are seen in Figure 2 which indicate symptoms of surface degradation in the neat LDPE and LDPE/HNTs NCs. The featureless and smooth surface of the pristine EVA sample was first achieved, but after exposure to H_2O_2, the surface became rough with cracks and pits. Oxidative treatment for 4 weeks improved the smoothness of the LDPE NCs containing 1 and 3 wt% HNTs owing to improved surface degradation features compared to the neat EVA. The LDPE NCs with 1 wt% HNTs reported the smoothest surface. It is possible that this material also has the best nanofiller dispersion properties. However, the well scattered HNTs can be argued to be the reason for the lower degree of degradation in this NC. Previous studies has shown that a well-dispersed nano-filler might generate a more convoluted path for oxidants to enter the polymer chain, decreasing breakdown rates.[18,19] However, because of nanofillers' weaker and poorer dispersion attributes, there was an increase in the degradation kinetics as the nano-filler content increased. Owing to its more severe deterioration, the LDPE

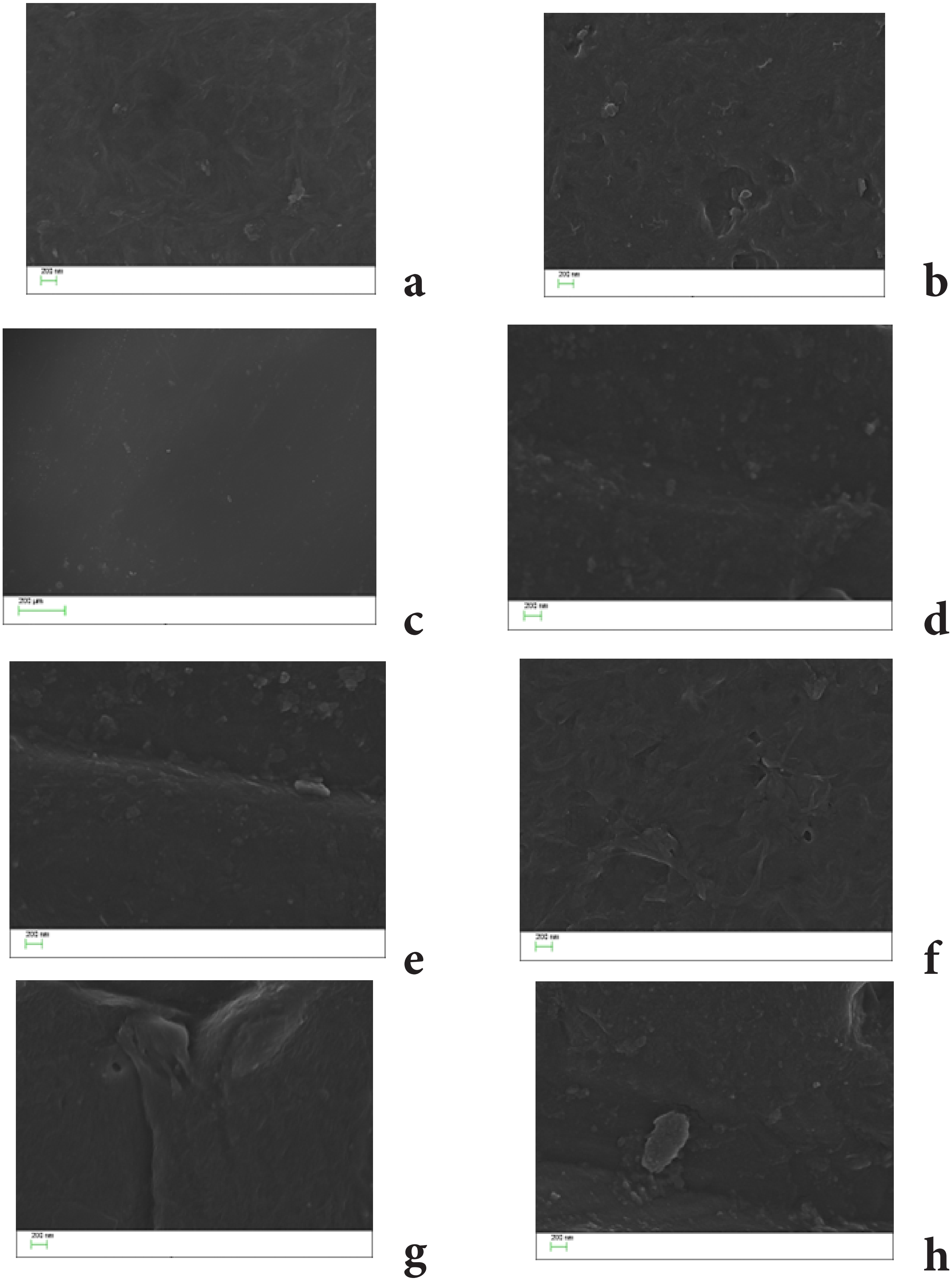

Figure 2: SEM images of neat LDPE and LDPE nanocomposites, before (A, C, E, G) and after (B, D, F, H) being exposed to oxidative agent at 37°C for 28 days, for the HNTs loading (0, 1, 3 and 5%), respectively.

NC with 5 wt% HNTs has the rougher surface morphology, with bigger pits and fissures.

Mechanical Properties Before and After Exposure to Oxidative Agent

Table 2 summarizes the tensile strength of pure LDPE and LDPE NCs (pre and post-exposure to oxidative agent). The inclusion of 1, 3 and 5 wt% HNTs into the LDPE improved the TS and EAB. The incorporation of 3 wt% HNTs gave the maximum tensile strength, toughness, and elongation at break, with improvements of 15.4, 10.1, and 25.5%, respectively. However, these qualities were negatively affected upon increasing the nanofiller content from 3 to 5%, probably due to the inferior HNT dispersion characteristics should be noted that the tensile properties of NCs can be affected by the dispersion, orientation, content of the nanofiller, as well as the filler–polymer interaction.[20,21]

The achieved reinforcement by the dispersed halloysite nanotubes is responsible for the increased tensile strength of the polymer NC. Because of the increased contact surface area and polymer-nanotubes interactions, better dispersed HNTs may improve tensile strength.[22] The energy dissipation and load transfer in a high-stress area may be enabled by the well-bonded interface. Our findings reveal that adding 3 wt% HNTs to LDPE improved tensile strength the most and that this was also the loading that gave the optimum nanofiller dispersion. The plasticizing effect of HNTs, which affects LDPE polymer chains conformation at the nanotubes–matrix interface, could explain the increase in LDPE toughness when HNTs were added. These effects enable the material to attain greater elongation at break by promoting relaxation at local stress zones.[23]

Based on our findings, the integration of nanofillers has a stronger impact on the stress-strain behavior of LDPE upon exposure to H_2O_2 at 37°C. When compared to neat LDPE, the tensile properties of the NCs were better in terms of improved tensile strength and elongation at break. Surprisingly, the nanocomposites containing 3 wt% HNTs not only have the greatest TS characteristics but retain the highest TS after being exposed to hydrogen peroxide.[24] Table 1 shows that after 4 weeks of exposure to hydrogen peroxide, there was only a 5.8% reduction in the toughness of the LDPE NCs with 3 wt% HNTs, whereas that of the plain LDPE was dramatically reduced (6.2%), showing that the oxidant molecules could have traveled a more circuitous path owing to the presence of the HNTs nanotube structure, thereby reducing their absorption into the LDPE chemical chains. The mechanical characteristics of the NCs were better preserved when less oxidant entered the polymer molecular chains.[25] Material strength is critical for biomedical use because it slows crack propagation and extends the life of the material. The outcome of the tensile tests showed that the LDPE NCs with 3 wt% HNTs remained the most biostable. However, the biostability was reduced upon increasing the nanofiller content to 5 wt% due to increased HNT clumping.

Water Permeability (Before and After Exposure to the Hydrolytic Agent)

The permeability of polymer NCs to liquid water is believed to be affected by factors such as the filler loading, degree of dispersion, disrupted molecular packing, defects at the polymer–filler interface, and high availability of polymer-free volume elements; this can increase the water transmission rate across the polymer.[26] This study conducted a water permeability test to evaluate the hydration properties of the LDPE and LDPE NCs, as well as the relationship between these qualities and mechanical properties. For the test, the samples were immersed in PBS at 37 °C before the analysis. Table 2 shows a summary of the findings. After 4 weeks of hydrolytic exposure, it was discovered that NCs containing 5% HNTs had the maximum water uptake because of the higher rate of mass increase (0.35%) compared to the neat LDPE. When 3% organo-MMT is added to LDPE, however, the water uptake was reduced. In comparison to the other materials, this NC had the smallest mass gain (0.07%). These findings are consistent with the observed mechanical characteristics where sample with 3 wt% HNTs had the best nanofiller dispersion in the LDPE matrix. The well dispersed water molecules may have a more circuitous path of diffusion, limiting their entry into the LDPE polymer chains.

CONCLUSION

The configuration of the HNT nanotubes, and their aggregation behavior in the LDPE matrix may be affected by the HNTs loading. The dispersed HNTs (added in different wt %) showed greater aggregations that are still visible within the LDPE matrix. After 3% loading, the extent of HNTs dispersion reduced with increases in the nanofiller loading. Among the NCs, the LDPE NC with 3 wt% HNTs had the most nanofiller dispersion. After 28 days of oxidative exposure, the SEM images revealed symptoms of surface degradation in the pure LDPE and its NCs. After 4 weeks of exposure to hydrogen peroxide, LDPE NCs with 3 wt% HNTs showed smoother surface degradation features than the neat LDPE and other NCs possibly due to the material's morphology, which reveals more evenly distributed HNTs throughout the LDPE matrix. Tensile characteristics of neat LDPE and LDPE NCs were investigated (pre and post-exposure to hydrogen peroxide). The NCs with 3 wt% HNTs had the best mechanical qualities and was less affected by oxidative exposure than the other materials, including the permeability features of the NCs. The well-distributed HNTs were believed to have produced a more tortuous path for the diffusion of the oxidants and water molecules which prevents more severe breakdown in the molecular chains of LDPE. Also, the addition of 3 wt% HNTs to hydrated LDPE (which had been subjected to PBS at 37°C) increased its tensile strength.

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