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Impact of soaking duration on chitosan yield and functional properties from shrimp shell

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ABSTRACT

This study investigates the effect of varying soaking times on the production of chitosan from shrimp shells. A sample of fresh shrimp shells was obtained from a market in Malacca, Malaysia, and pre-treated by washing, drying, and pulverizing into a homogeneous powder. The synthesis process involved three primary steps: demineralization, deproteinization, and deacetylation. Each step was executed under different conditions for four samples (S1-S4) to examine the impact of soaking duration on chitosan yield and properties. Demineralization was achieved using 1 M HCl, while deproteinization involved treatment with 1 M NaOH, both with varying soaking times. Deacetylation was conducted with 12.5 M NaOH at different temperatures and durations. The resultant chitosan was characterized using Fourier Transform Infrared (FTIR) spectroscopy, X-ray diffraction (XRD), and UV-Vis spectroscopy. The FTIR spectra confirmed the presence of characteristic chitosan functional groups, with higher degrees of deacetylation (DD%) corresponding to increased soaking times. XRD analysis indicated an amorphous structure for all samples, with S4 displaying the lowest crystallinity at the highest DD%. UV-Vis analysis confirmed that all samples were soluble in 1% acetic acid, suggesting good purity. The findings demonstrate that while soaking times affect the DD% and crystallinity of chitosan, all samples remained soluble and suitable for further applications. This work demonstrates that while soaking times affect the DD% and crystallinity of chitosan, all samples remained soluble and suitable for further applications. This study provides insights into optimizing chitosan production with variations in soaking time conditions.

Keywords: Chitin, Chitosan, Soaking Time

INTRODUCTION

Chitin and chitosan are both non-toxic, biocompatible, and biodegradable biopolymers. Additionally, they act as antimicrobial and hydrating agents. They are the second-most abundant natural polysaccharides on the planet after cellulose and are derived from the exoskeletons of marine crustaceans such as crabs [1], lobsters [2], shrimp [3], and squid pens [4]. Different sources of crustacean shell waste result in different chitin content. For example, black tiger shrimp (Penaeus monodon) waste has the highest chitin content [5]. Chitosan is a chitin derivative. In contrast to chitin, chitosan is soluble in a wide variety of solvents, particularly acidic aqueous solvents, which enables it to act as a cationic polyelectrolyte. In recent years, chitosan has surpassed chitin as the preferred material due to its greater tractability during the solution process. Chitosan's applications have been discussed previously [6] and include cosmetics, water engineering, paper manufacturing, textile manufacturing, food processing, agriculture, photography, and biomedical applications.

There are many literature studies on the preparation of chitin and chitosan from marine sources. However, two common methods used are the chemical method [6] and the biological method [7,8]. The chemical method involves three different steps: demineralization, deproteinization and deacetylation. The demineralization step is used to remove the calcium carbonate ($CaCO_3$) in the shell by agitation using different hydrochloric acid (HCl) concentrations. Traditionally, the process of deproteinization involved using aqueous solutions of sodium hydroxide (NaOH) or potassium hydroxide (KOH). The effectiveness of the deproteinization process depends on the temperature, concentration and ratio of its solution/solvent[5]. Essentially, in the deproteinization process an alkaline solution is used to hydrolyze the covalent bonds between the chitin and protein. The end product of this step will produce chitin [9]. Deacetylation reactions have also been observed as an adverse reaction during the demineralization process with high acid concentrations. According to [9], to overcome this problem, mild acid was preferred for use in the demineralization process. During demineralization, the conditions in terms of pH, time, and temperature will affect the molecular weight [10]. A high degree of acetylation was obtained by [10] using 0.25 M HCl at room temperature within 15 min.

The objective of this study was to investigate the effect of varying soaking times on the synthesis and characterization of chitosan derived from shrimp shells. By modifying the soaking times during the deproteinization and deacetylation stages, the study aims to understand how these changes influence key properties such as the degree of deacetylation (DD%), crystallinity, and solubility of the resulting chitosan. The study also employs techniques such as FTIR and XRD to analyze the functional groups

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and structural characteristics of chitosan under different processing conditions. This investigation will provide insights into optimizing chitosan production for various industrial and biomedical applications.

MERHOD

Pre-treated Sample

The 1.5 kg sample of fresh shrimp shells was taken from a market in Malacca, Malaysia. The first step of synthesizing the chitosan from the shrimp shells started with washing the crustaceans with flowing tap water to remove the soil and extraneous matter. The cleaning process is essential to clean the raw shrimp shell material before proceeding to the next step. The pre-treatment steps improved the quality of chitin and chitosan in terms of minimizing chemical usage and preventing bad odors from the samples [11]. The cleaned shrimp shell sample was dried in a hot air oven at 90 °C until a constant weight was achieved. Next, the dried shrimp shell was blended until it was a homogenous-sized powder using a kitchen blender. In this paper, the characterization of chitosan sample processing was divided into three different types of processes which are demineralization, deproteinization and deacetylation. Table 1 shows the details of the three stages used for the four different samples.

Table 1. Summary of demineralization, deproteinization, and deacetylation processes for shrimp shell samples S1, S2, S3, and S4, detailing the specific conditions for each step.

Process	Details
Demineralization	**S1:** 10 g shrimp shell + 80 ml 1 M HCl, Stir 5h, RT, 250 rpm, Soak 16h, Ethanol 20 min, Oven 70°C, 8h
	S2: Same as S1, Soak 17h
	S3: Same as S1, Soak 17h
	S4: Same as S1, Soak 17h
Deproteinization	**S1:** Sample + 1 M NaOH (1:10 g/ml), Stir 3h, 80°C, 250 rpm, No soak, Ethanol 10 min, Oven 70°C, 7-8h
	S2: Same as S1, Stir 1h, Soak 22h, Repeat twice
	S3: Same as S2, Soak 48h
	S4: Stir 1h, 60-70°C, Soak 5 days, Oven 80°C, 10h
Deacetylation	**S1:** Sample + 12.5 M NaOH (1:30 g/ml), Stir 2.5h, 115-120°C, No soak, Oven 70°C, 6h
	S2: Stir 1h, 100-120°C, Soak 24h, Repeat twice
	S3: Same as S1, Soak 2 days, Oven 80°C, 10h
	S4: Stir 2.5h, 70-80°C, Soak 5 days, Oven 80°C, 10h

Demineralization Process

After the pre-treatment of the sample, the process continued with the demineralization process by adding 1 M HCl to the dried sample powder with a 1:10 solid-to-solvent ratio, w/v. The stirring process proceeded at room temperature under agitation at 250 rpm for a few hours. Next, the demineralized shells were filtered using pump filtration and washed with distilled water until they reached neutral pH. It was important to achieve a neutralized sample before the next process proceeded. To further remove impurities from the samples, samples were bleached by immersing in ethanol for a few minutes and then drying in an oven at 70 °C until a constant weight was reached. Figure 1 shows the process of filtration of shrimp shell after HCL was added into the samples.

Fig. 1. Process of filtration of shrimp shell in demineralization process.

Deproteinization

The deprotienization process was undertaken by mixing the dried demineralized powder with 1 M of NaOH solution at a solid/liquid ratio of 1:10 w/v. The reaction was carried out under agitation at different temperatures and soaking times for each of the samples. After the process was completed, the solids were filtrated and washed with distilled water until neutral pH was achieved. Then the samples were immersed in ethanol for further bleaching, and the resulting chitin was dried in an oven at 70 °C. Figure 2 shows the results from deproteinization of shrimp shell.

Deacetylation

Deacetylation continued the processing by treating the chitin with a strong alkaline solution of 12.5 M NaOH at a solid/liquid ratio of 1:15 (g/mL). The process was achieved by using different temperatures and soaking times as shown in the Table 1. The resulting chitosan was filtrated, washed with distilled water until neutral pH was reached and dried in an oven at 70 °C. This resulted in the production of chitosan flakes. The deacetylation treatment produced chitosan which is a soluble polymer in acid aqueous medium. Figure 3 shows the chitosan flakes produced after going through the deacetylation process.

Fig. 2. Results from deproteinization of shrimp shell.

Fig. 3. Chitosan powder prepared from shrimp shell.

RESULTS

Solubility

Chitosan is known to be completely soluble in concentrated acids and partially soluble in dilute acid solutions. Many studies presented the solubility of chitosan in acetic acid at 1-2% [12]. For solubility studies, 3 mg of each of the chitosan samples were dissolved in 3 ml of 1% acetic acid and stirred using a magnetic stirrer until a homogenous solution was obtained as shown in Figure 4. From the observations, all of the samples were completely dissolved in acetic acid. Due to the obvious protonation of amino groups, chitosan is soluble in aqueous acids, but it is insoluble in water and most organic solvents, thus limiting its applications[13]. Chitosan's enhanced solubility is attributed to its structure, which differs significantly from that of chitin. Through deacetylation, chitosan's acetyl groups are partially removed, exposing amine groups ($–NH_2$) that increase hydrophilicity and enable dissolution in dilute acidic conditions. Based on the studies from [14], if the solvent/chitosan ratio was increased, the solubilization time also increased.

Fig.4. Solubility of chitosan (S1-S4) in 1% acetic acid.

FTIR Characterization

The Fourier transform infrared (FTIR) spectra of S1 to S4 in the 400–4000 cm^{-1} range are shown in Figure 5. FTIR studies were conducted for the different methods (temperatures and soaking times) used for the four samples. The absorption peaks at wavenumber 2872.17 cm^{-1} were due to the presence of methylene and methyl groups in the chitosan structure [15]. From the observations of the samples S1-S4, S2 produced a small peak compared with the other samples. From the results observed, all of the samples, S1-S4, produced an absorption at wavenumber 1644.49 cm^{-1} which indicates the C=O stretching vibration. This result is the same absorption as in [15]. Wavenumber 1590.72 cm^{-1} was indicated for all samples, representing the vibration absorption NH_2 groups. Meanwhile, the broad peak at wavenumber 3261 indicated the presence of three different stretching groups, as explained in [16,17]. Samples 3 and 4 showed higher intense peaks which appeared at 1149 cm^{-1} and 1031 cm^{-1}, possibly caused by characteristic peaks of C-N stretching vibration and is evidence of the amine group presence. The peaks were also similar to the peak found in [18]. The decrease in the intensity of the 1650 cm^{-1} (approximately) band corresponds to the carboxyl group and reflects a deacetylation process [19].

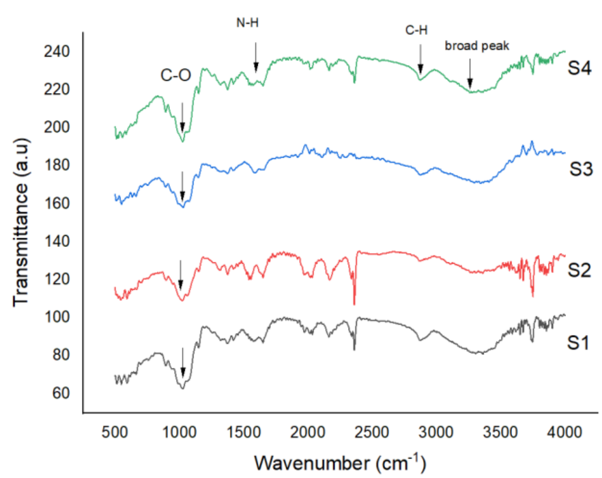

Fig.5. Infrared spectra of chitosan of S1-S4.

The DD is one of the chitosan characterization approaches that is often discussed in the literature. The most precise technique to measure DD is nuclear magnetic resonance (NMR) spectroscopy [20]. However, this technique requires higher costs compared with other techniques. So the research from [20] presented various calculation techniques based on UV-Vis and infrared spectroscopy. There is a range of bands of wavelength that have been chosen to measure the DD [20,21]. In this paper, further examination of chitosan DD used infrared spectroscopy. The DD was determined according to the calculation from [3]. The A1320 and A1420 were the peak areas of 1320 cm^{-1} and 1420 cm^{-1}, respectively. The peak at 1320 cm^{-1} is the amide group's distinctive band. DD can be calculated using the formula in Equation 1 as follows [3].

$$\% DA = \frac{\left(\frac{A1320}{A1420}\right) - 0.3822}{0.03133} \quad \textbf{Eq. 1.}$$

%DDA = 100 - %DA
Where, DDA = degree of deacetylation (%),
DA= degree of acetylation (%)

Table 2 represents DD% values of S1 to S4. From the results, S1 has the lowest DD% compared with the others. DD% in this paper was also found to be similar to [22]. During the deproteinization and deacetylation processes, S1 was not involved in any soaking treatment with chemicals after the stirring process. The highest DD% was obtained from S4. The results showed an increase in DD% when using longer soaking times during the deproteinization and deacetylation processes and higher temperatures produced a higher DD% (80.4818) compared to lower soaking times [7,11]. According to [3], DD% was increased when the deacetylation process was repeated twice with the aid of heating elements. In addition, all the samples that were soaked in HCl solution showed the total bacterial count of treated samples to be decreased [11].

There were three ranges of DD% that were discussed in [23] whereby the range of 55-70% of DD was classified as a low deacetylated degree of chitosan, which was entirely insoluble in water. A deacetylation degree of 70-85% was classified as the middle deacetylation degree of chitosan. In this paper, the chitosan was in the area of ~80% which may be partly dissolved in water. Finally, the range of 85-95% accomplished a good solubility in water and it is known as very high DD of chitosan, which is difficult to achieve. As DD rises, the chitosan backbone gains more amino groups, increasing the hydrophilicity of the chitosan films, and thus S1 (Sample1) increases correspondingly [13], because the higher the DD, the more amino groups there are in the molecule. The protonation of the -NH_2 functional group is vital for chitosan's biological effects and water solubility to show up [8].

Table 2. Calculation of DD% for different types of samples.

Sample / Peak Area	A1320	A1420	DD%
S1	88.1958	88.1508	80.264
S2	89.8743	90.2305	80.406
S3	92.0779	92.6352	80.472
S4	84.9688	85.5073	80.481

XRD Characterization

The crystalline structures of chitosan were determined by powder X-ray diffraction (XRD). The patterns indicate a crystallized structure at 2θ = 20°, which is the most intense peak height for the chitosan sample. This peak occurred in polymorphic forms in shrimp and crab shells [24], from the XRD result as shown in Figure 6. S1 and S3 produced higher intensity at 020 compared with other samples. It is shown that with decreasing DD values, the intensity at 020 is higher [13,24]. A small peak was observed near 2θ = 30° for S1, which was discussed as the formation of calcite and calcium phosphate family interferences [25]. The broad peak observed at both 020 and 110 was similar to [26].

From the results observed, the intensity at 020 reflections decreased when the DD was increased and moved the second peak at 110 reflections, and is also decreased when higher DD% was produced (S4: 80.48 %). This linear relationship between CrI020 and DD suggested that XRD determines the DD of macromolecular chitin and chitosan [24]. From the samples soaked in HCl had lower DD values than unsoaked samples. This might be caused by the long-term degradation of chitin and chitosan during the soaking step in the HCl solution. Trung et al. also observed low degradation of chitin and chitosan caused by the longer soaking time [11]. These samples are classified as chitosan based on an 80% degree of deacetylation (DDA). Chitosan is derived from chitin through deacetylation, where some of the acetyl groups are removed to expose amine groups (–NH_2) on the polymer chain. This alteration increases the hydrophilicity of chitosan. Chitosan has a more flexible structure compared to chitin due to the presence of these free amine groups, which can interact with water molecules, enabling it to dissolve in acidic solutions (e.g., dilute acetic acid).

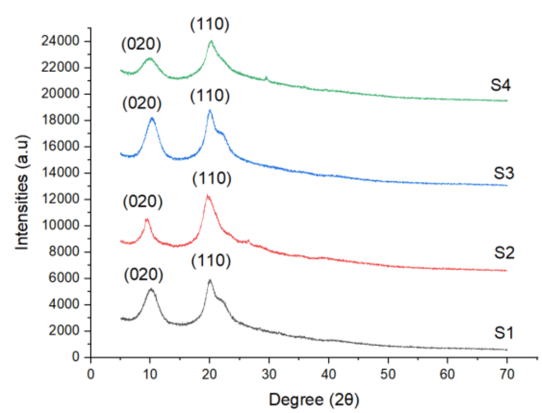

Fig.6. XRD patterns of chitosan films with various degrees of crystallinity.

UV-Vis Characterization

In the UV-Vis spectroscopy process, electromagnetic radiation within the wavelength range of 200–1100 nm is absorbed and electrons are then excited to higher energy states. The fabrication into chitosan film was started by dissolving the samples (S1-S4) in 1% acetic acid at room temperature under constant stirring. Then the chitosan solutions were obtained by spin coating the film onto a 2x2 cm glass slide at the same speed. Figure 7 shows the characteristic chitosan absorption below 300 nm, revealing the presence of chitosan. There was no discernible difference between the four samples (S1-S4), and the spectra showed very weak absorptions at wavelengths of more than 300 nm.

The wavelength versus absorption curve was plotted, and the optical band gap energy value was determined using Tauch plot methods. Tauch plotting is a technique for determining the optical band gap by examining the linear relationship graph. The relation between photon energy (hv) and absorption coefficient (α) was determined by [27]as in Equation 2 below:

$$(\alpha hv)\frac{1}{n} = k(hv - Eg) \qquad \textbf{Eq.2}$$

Where hv is the photon energy, h is Plank's constant, Eg is the optical band gap, k is constant and n is the transition state, i.e., direct or indirect transitions. A direct transition occurs when a photon excites an electron directly from the valence band to the conduction band if the momentum of electrons and holes in both bands is identical (conduction and valence). For direct transition, n = 1/2 is substituted in Equation 2. Figure 8 shows the determination of the optical gap series for all thin-film chitosan samples obtained by the straight-line intersection. The calculated values of bandgap were 4.06 eV for Sample 1, 4.04 eV for Sample 2, 4.02 eV for Sample 3, and 4.06 eV for Sample 4. The results attained were higher than the 2 eV which was reported from [28,29]. This could be due to the different thicknesses and sample preparations of chitosan concentration.

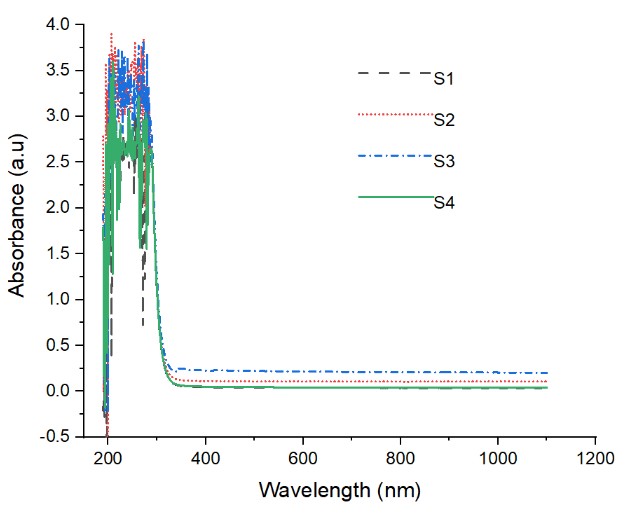

Fig.7. UV-Vis absorption spectra for different samples of chitosan (S1-S4).

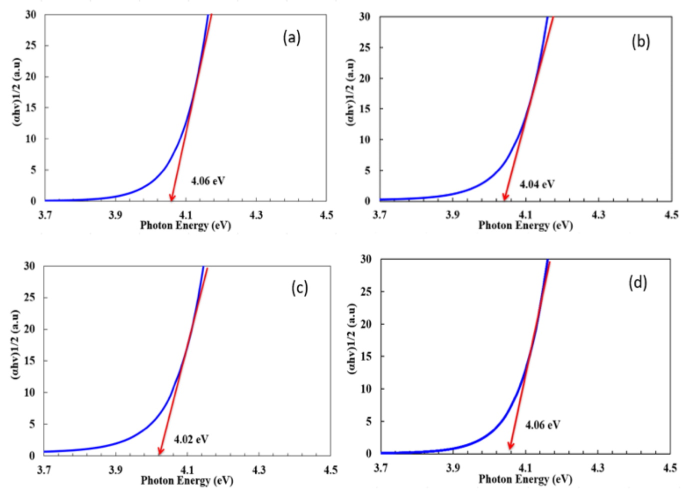

Fig.8. The determination of the optical gap energies of chitosan sample (a) S1, (b) S2, (c) S3, (d) S4

CONCLUSION

The extracted chitosan from shrimp shells was characterized by FTIR, XRD, and UV-Vis techniques. Four methods were used to synthesize chitosan, involving variations in soaking times and temperatures. The FTIR results showed varying degrees of deacetylation (DD%) across the samples, with an observed increase in DD% as the soaking time during demineralization, deproteinization, and deacetylation processes was extended. Sample 4 exhibited the highest DD% along with a less crystalline structure, as determined by XRD analysis. All chitosan samples were fully soluble in acetic acid, indicating high purity. The XRD patterns indicated an amorphous structure for all samples, suggesting that the chitosan can act as a polymer, with sharper peaks signifying greater crystallinity. The crystallinity of the chitosan appeared to decrease with increasing DD%, with Sample 4 (80.48% DDA) displaying the lowest crystallinity.

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Device application of GO: Ag nanoparticles produced by bacterial synthesis method

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ABSTRACT
In recent years, the bacterial synthesis method for nanoparticle production has gained significant attention in research due to its advantages over physical and chemical techniques. In this study, silver-doped graphene oxide (GO) nanoparticles were simultaneously reduced in composite form in a bacterial culture medium. The bacterial synthesis method simultaneously reduced the silver (Ag)-doped graphene oxide (GO: Ag) nanoparticles. The size and shape of the reduced GO:Ag nanoparticles were determined using advanced spectroscopic imaging techniques. Transmission electron microscopy (TEM) images of GO: Ag nanoparticles have reported their approximate dimensions to be around 30-70 nm. Thin films were created by spreading GO:Ag nanoparticles onto glass and p-Si surfaces and drying them at 350 °C. The optical, structural, and electronic properties of these thin films were investigated. The energy band gap value of the film was estimated as 0.75 eV employing the double-beam UV-Vis spectrophotometer technique to reveal its optical properties. The given value suggests the generation of an electron-rich thin film with a narrow energy band gap. X-ray diffraction (XRD) and Raman techniques were used to explore the structural properties of a GO:Ag semiconductor thin film. The Raman technique yielded peak values for the GO:Ag structure, specifically in the D and G band energy values, at 1348 and 1568 cm^{-1}. Rectifying contacts with a diameter of 1 micrometer were made using Ag metal on this film structure. The current-voltage characteristics of the Ag/GO: Ag/p-Si/Ag structure made after these contacts were investigated.

Keywords: Graphene oxide, Ag, Nanoparticles, Bacterial Synthesis, Current-Voltage

INTRODUCTION

Recent advancements in gas sensor applications have involved the creation of nanoparticles by physical, chemical, and biological methods. Biological procedures are desirable due to their simplicity, ecological sustainability, less toxic emissions, and lower costs compared to alternative manufacturing methods [1,2]. Moreover, employing microbes or bacteria for the production of nanoparticles with specific size, shape, and composition is a considerable benefit. The bacterial synthesis technique readily produces thin films on chosen substrates owing to its user-friendliness, cost-efficiency, energy-free characteristics, absence of costly components such as vacuum apparatus, and environmental safety [3]. The electrical, textile, energy, computer, medical food, optical, and aerospace sectors produce metal nanomaterials (including magnesium, gold, graphene, selenium, copper, zinc, silver, iron, titanium, and cadmium) for diverse uses. Certain bacterial synthesis mechanisms exhibit an exceptional capacity to withstand elevated chemical concentrations [4,5]. The synthesis must be scalable, straightforward, and economical, while also incorporating principles of "green" biological synthesis. The film deposition method should avoid energy-intensive procedures. Execute all processes with low thermal exposure and without the emission of hazardous gases.

This work is the inaugural publication of ecologically benign and readily available microbial biosynthesised complex GO: Ag nanoparticles. We examined the dimensions and architecture of GO:Ag nanoparticles via TEM. We similarly used approaches to directly generate high- quality GO:Ag compound thin films, grounded in the homogeneous nucleation and growth mechanism. Gold nanoparticles were sintered as a nano-thin layer on glass and p-Si substrates following their creation as compound nanoparticles via a bacterial manufacturing technique. The optical and structural characteristics of the synthesized GO:Ag thin films were examined. The Ag/GO: Ag/p-Si/Ag and device structures employed in this investigation were constructed on p-type silicon wafers with a (100) surface orientation and glass substrates. Several electronic properties of Ag/GO, Ag/p-Si/Ag, and the device structure were determined using I-V measurements.

METHOD

Fabrication and electrical characterization of the Ag/GO: Ag/p-Si/Ag device structure

The initial step in acquiring the Ag/GO: Ag/p-Si/Ag device structure was the chemical cleaning of a p-Si crystal wafer orientated in the (100) direction. The literature offers a detailed description of the chemical cleaning process [6]. In a vacuum chamber at a pressure of 1×10^{-5} Torr, we established an

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ohmic contact by thermally evaporating Ag onto the substrate's backside. The p-Si/Ag structure underwent annealing at about 550 °C for 3 minutes in a flowing dry nitrogen atmosphere to attain a low resistance back ohmic contact. The precursor with GO:Ag nanoparticles was applied to the polished surface of the p-Si/Ag structure, yielding low-resistance ohmic contact. This was accomplished by depositing roughly 5 cc at a substrate temperature of 350 °C. As a result, a GO:Ag thin film was fabricated.
The Ag metal, functioning as a rectifier contact with a diameter of roughly 1 mm on the pole of this film, was produced using a shadow mask in a vacuum chamber maintained at a pressure of 1×10^{-5} Torr. This procedure resulted in the creation of the Ag/GO: Ag/p-Si/Ag device architecture. The current-voltage (I-V) measurements of this structure were obtained using the Keithley 2400 source meter equipment.

RESULTS

Figure 1 illustrates the optical absorption spectra of a GO: Ag thin film deposited on a glass substrate as a function of wavelength in the range of 300 to 1000 nm. To figure out the numerical band gap energy of the GO:Ag thin film sample, the absorption coefficient as a function of photon wavelength is required. The below mathematical formula defines the transmission of light through a medium:

$$I = I_0 e^{-\alpha d} \quad \textbf{Eq. 1.}$$

In this context, I, I_0, and d indicate the transmitted light intensity, incident light intensity, and the thickness of the thin film sample, respectively.
The outcome of graphing $(\alpha h\nu)^2$ against hν is displayed in Fig. 1, where a curve is depicted in the inset. The band gap energy value of the GO: Ag thin film was determined to be 0.75 eV through the application of the extrapolation method to the linear section of the curve.

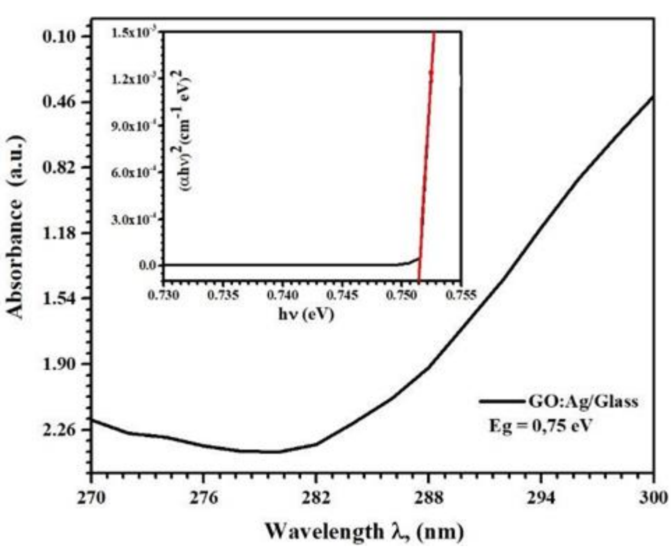

Fig. 1. The optical pilot of GO:Ag thin film on the glass substrate; Absorption vs. wavelength and band gap energy.

The XRD pattern of the GO:Ag thin film deposited on the glass substrate is illustrated in Fig. 2. The five XRD peaks positioned at 2Ɵ angles, as presented in Table 1, are clearly identified and match closely with the JCPDS 00-021-1016 pattern associated with a hexagonal phase of GO thin film. The analysis reveals that the GO:Ag thin film exhibits a polycrystalline nature, while the Ag thin film is characterized by a cubic crystal structure with a nano-crystalline nature.

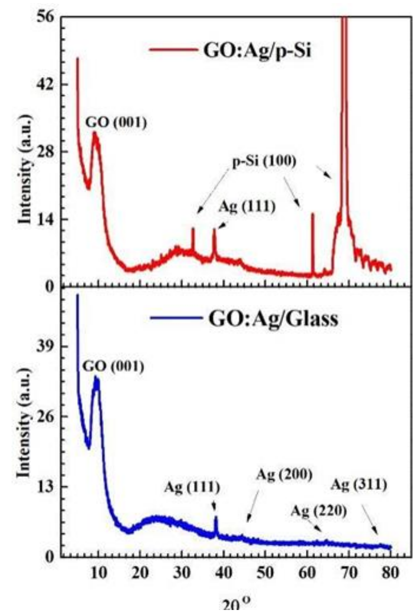

Fig. 2. XRD pilots of GO:Ag thin films on glass (blue line) and p-Si substrates (red line).

The newly formed graphite regions resulting from Ag doping in GO exhibit an increase in quantity, although they remain relatively minor, as illustrated in Fig 3. The spectra indicate the presence of the D (defect) and G (graphite) bands, along with a hexagonal structure. The characteristic Raman spectroscopy peaks of the GO crystal structure are observed at 1580 cm^{-1} and 1600 cm^{-1}. The incorporation of Ag in GO resulted in a minor shift in peak energy values when compared to the literature [5]. These results align consistently with the existing literature [5,6]. The intensity of the G peak (IG) observed in this study exceeds that of the D peak (ID). The operation performed on the sample maintains its regular structure.

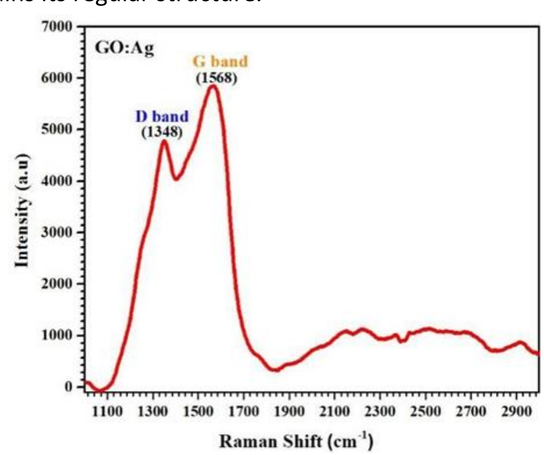

Fig. 3. Micro Raman shift result of GO: Ag thin film.

Table 1. The structural parameters of GO:Ag thin film evaluated on glass substrate

(hkl)	FWHM	FWHM (rad)	Intensity (a.u.)	2 (observed)	d-values (n.)	Crystal size (D) (nm)	Crystal
(001)GO	2,71682	0,047417	32,45833	9,92847	8,901	2,935	Hexagonal
(111)Ag	0,55367	0,009663	7,4375	38,19067	2,354	15,183	Cubic
(200)Ag	0,41185	0,007188	3,53125	44,38114	2,039	20,832	Cubic
(220)Ag	0,51917	0,009061	3,01042	64,60547	1,441	18,103	Cubic
(311)Ag	0,57497	0,010035	2,19792	77,60219	1,229	17,729	Cubic

Figures 4 (a) and (b) illustrate TEM micrographs of Ag and GO, exhibiting Ag nanoparticles at an average size of 200 nm. Silver nanoparticles are spherically distributed and significantly more apparent in Fig. 4 (a). In Fig. 4 (b), remarkable spherical particles are evenly dispersed throughout the GO structure within the typical sheet structures. The identified nanoparticles at the nanoscale measure between 30 nm and 70 nm. Comparison of the TEM micrographs of Ag and GO:Ag nanoparticles at 200 nm revealed that the aggregation of Ag nanoparticles in a cubic configuration resulted in the formation of nano-sized, regular spherical nanoparticles. Nonetheless, inside the two-dimensional characteristic sheet-like structure of GO, uniformly distributed Ag spherical nanoparticles were identified for GO:Ag.

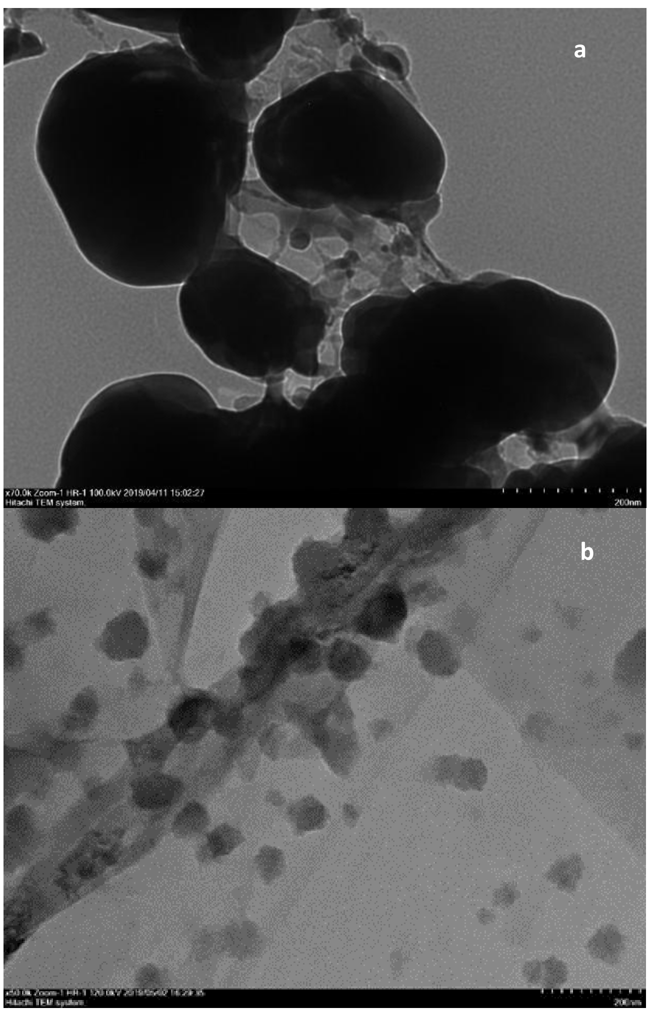

Fig.4. TEM image of Ag (a) and GO: Ag (b) nanoparticles at 200 nm.

Figure 5 shows the dark and room temperature semi-logarithmic I-V characteristic plots of the produced diodes. The rectifying activity of the Ag/GO:Ag/p-Si/Ag diode structure was easy within the bias voltage range that was examined.

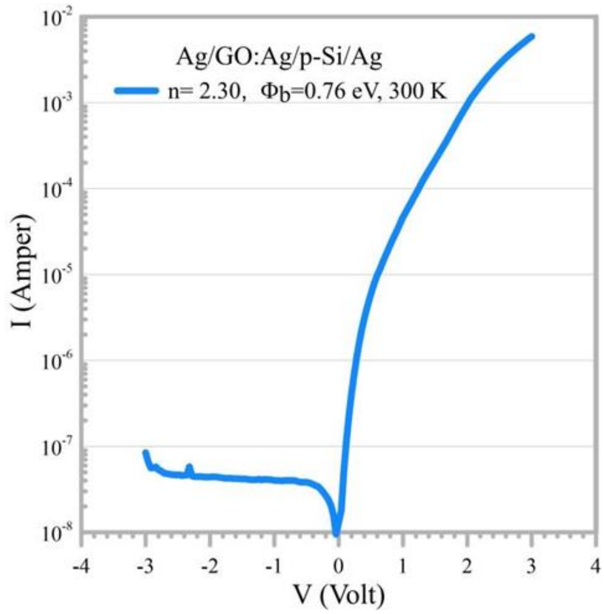

Fig.5. Semi-logarithmic I-V characteristic plots of the produced Ag/GO:Ag/p-Si/Ag at room temperature.

Diode parameters such as saturation current (I0), unbiased barrier height, and ideality factor (n) were derived from the forward bias region of the I-V characteristic plots to analyse the current transport mechanisms and performance of the produced diodes, based on various theoretical current conduction mechanisms proposed by the thermionic emission model [7]. The predominant current behaviour could be described through the thermionic emission model as:

$$I = I_0 \left[exp\left(\frac{eV}{nkT}\right) - 1\right] \qquad \textbf{Eq. 2.}$$

$$I_0 = A\ A^*\ T^2\ exp\ \left(-\frac{q\Phi_b}{kT}\right) \qquad \textbf{Eq. 3.}$$

$$n = \frac{q}{kT}\frac{dV}{d(ln\,I)} \qquad \textbf{Eq. 4.}$$

Equations 2, 3, and 4 were used to find the n and I_0 values for the Ag/GO: Ag/p- Si/Ag diode structure. They were 2.30 eV, 0.76 eV, and 1.27 x 10^{-8} Ampere, respectively. The n and I_0 values of the fabricated device were obtained by extrapolating the semi-logarithmic I-V graph (represented in Fig. 5) at low voltage values approaching the forward bias current, utilizing the slope equation.

CONCLUSION

This study presents the simultaneous reduction of GO: Ag nanoparticles within a single container using the bacterial synthesis method, indicating an innovative addition to the existing literature. Details regarding the approximate size and shape were obtained through the process of TEM analyses on GO: Ag nanoparticles. The nanoparticles were deposited and subsequently dried to create a film on glass and p-Si (100) by setting the substrate temperature to 350 °C. The dried nanoparticles underwent sintering, resulting in the formation of a thin film. The thin films underwent structural and optical characterization. The Ag/GO structure was established by directly applying Ag metal contacts onto these thin films, resulting in an Ag/p-Si/Ag configuration. The fundamental electrical parameters of this structure were analyzed under ambient conditions in the absence of light. This device structure demonstrates its effectiveness as a rectifier contact and shows potential applicability in photo-diodes for gas sensors.

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Emerging nanotechnologies in the field of highways and transportation engineering

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ABSTRACT

The developing uses of nanotechnology in the domain of transportation engineering and highway construction are investigated in this work. The goal is to characterize the present situation of nanotechnology in transportation engineering together with its advantages and drawbacks. Using a descriptive research design and depending on a thorough review of current material from scholarly publications, research reports, and conference proceedings, the study The data's themes and patterns are found by means of thematic analysis and grouped to create categories. Themes found in the literature review and the research goals direct the study. According to the findings of the research, nanotechnology could transform the transportation sector in several different respects. Infrastructure's lifetime and durability have been demonstrated to be improved by nanomaterials including graphene, nanoclay, and nano cellulose; fuel economy has been raised as well as safety and visibility enhancement. Furthermore, promising for development of new kinds of lighting and signaling systems for use in infrastructure and vehicles are quantum dots. Adoption of nanotechnology in transportation engineering does, however, also bring certain difficulties. Among the main issues that have to be resolved are possible environmental effects, safety issues, and manufacturing and implementation costs. To guarantee the responsible and safe use of nanotechnologies in transportation engineering, these difficulties will call for major research and development activities, stakeholder cooperation, and regulatory control. This work offers a thorough summary of the developing uses of nanotechnology in transportation engineering, so stressing both its possible advantages and difficulties. The results of this study can guide legislators, scholars, and professionals in the transportation sector on the possibilities of nanotechnology to raise the efficiency, sustainability, and safety of transportation systems.

Keywords: Nanotechnology, Transportation engineering, Infrastructure, Nanomaterials, Sensors, Sustainability, Durability, Environmental impact

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INTRODUCTION

Background on nanotechnology

Nanotechnology is a swiftly developing discipline concerned with the design, production, and application of nanoscale materials [1]. It involves manipulating matter at the atomic, molecular, and supramolecular levels to produce novel materials with improved properties and functionality [2]. Nano refers to materials whose dimensions are less than 100 nanometers. Nanotechnology development has the potential to revolutionize numerous industries, including transportation engineering [3].

In transportation engineering, nanotechnology offers innovative solutions to enhance the performance, safety, and sustainability of infrastructure and vehicles. For example, the integration of nanomaterials can lead to the development of ultra-lightweight and high-strength materials for vehicle components, improving fuel efficiency and overall performance [4]. Additionally, nanotechnology can be utilized to create advanced coatings with self-cleaning and anti-corrosive properties, extending the lifespan of transportation infrastructure such as bridges and roads [5]. Furthermore, nanosensors embedded in transportation systems can provide real-time monitoring and diagnostics, enhancing safety and maintenance capabilities [6]. The ongoing research and application of nanotechnology in this field are expected to drive significant advancements and transform how transportation systems are designed and managed.

Importance of nanotechnology in transportation engineering

The field of nanotechnology is expanding rapidly and is centered around the study, creation, and use of materials on the nanoscale [1]. It entails atomic, molecular, and supramolecular level manipulation of matter to generate new materials with enhanced characteristics and use [2]. Materials whose dimensions fall less than 100 nanometers are referred to as nano-scale. Among many sectors, including transportation engineering [3], nanotechnology development could completely transform many others.

Transportation engineering includes vehicle design and manufacture as well as the design, building, and maintenance of infrastructure including bridges, roads, and airports [4]. Transportation engineering systems' sustainability, safety, and efficacy may all be improved by nanotechnology. By means of better strength and resistance to environmental factors, nanomaterials can be used to raise the sturdiness and endurance of infrastructure components, including concrete and asphalt [4]. By means of self-cleaning surfaces and anti-corrosive layers, advanced coatings and treatments derived from nanotechnology can improve safety and visibility, for example.

By means of more effective catalytic converters and lightweight materials, nanotechnology can also help to lower vehicle emissions and enhance fuel economy [4]. Thanks to nanoscale technology, the development of new sensors and monitoring systems helps to enable real-time monitoring and diagnostics of infrastructure and vehicles, so promoting more proactive maintenance and improved safety [5]. Apart from enhancing performance, including nanotechnology into transportation engineering seeks to solve sustainability and environmental issues.

PURPOSE OF THE RESEARCH

The aim of this study is to investigate newly developed nanotechnologies in the domain of transportation engineering and highways. The study specifically seeks to find possible uses for nanotechnology in transportation engineering, including vehicle and infrastructure integration. It will examine both possible limitations and challenges as well as the advantages of applying nanotechnology in this field, including improvements in material strength, efficiency, and safety, alongside possible constraints. The study will look at present levels of nanotechnology research in transportation engineering, evaluating continuous advances and ideas. It will also assess how well nanotechnology improves vehicle safety, efficiency, and durability of transportation infrastructure. At last, the study will offer suggestions for next projects and development, stressing areas where additional study and technological innovation might have a major influence on the discipline.

LITERATURE REVIEW

The applications of nanotechnology in highway and transportation engineering are rapidly expanding, offering novel solutions for enhancing the performance of vehicles and buildings as well as infrastructure. The use of nanomaterials in infrastructure building and maintenance presents one of the most exciting uses. Pavement, bridges, and other structural components can have much improved durability and strength by means of nanomaterials including carbon nanotubes and silica. These materials help to improve resistance to environmental stresses including chemical attacks and high temperatures, so extending the lifetime of infrastructure and lowering the demand for regular repairs [6]. Moreover, nanotechnology helps to create sophisticated self-healing materials. These materials include nanoscale agents that, without human intervention, can independently heal small damages including surface wear and cracks. By guaranteeing quick resolution of structural problems, this ability not only lowers maintenance costs and time but also improves the safety and dependability of the transportation infrastructure [7,8]. Beyond only structural enhancements, nanotechnology can help create novel coatings and treatments. Enhanced anti-corrosion and anti-fogging qualities of nanostructured coatings, for example, would improve the lifetime and performance of road signs, markings, and vehicle surfaces. By means of nanotechnology in these domains, clear vision and optimal road conditions are preserved, so improving general safety for users [6].

Moreover, the inclusion of nanosensors into buildings and transportation enables real-time observation and diagnosis. Early wear, structural flaws, or environmental changes can be detected by these sensors, so allowing proactive maintenance and quick interventions [7]. Using these developments will help transportation engineering reach higher dependability and efficiency, so changing the design, construction, and maintenance of transportation systems.

Nanotechnology applications in highway and transportation engineering

In the field of transportation engineering, nanotechnology has a number of important applications, one of which is in transportation vehicle design and manufacturing. Vehicle weight is being lowered using nanomaterials, so improving fuel economy and lowering environmental impact. Advanced nanocomposites and nanostructured materials, for instance, can replace more weighty conventional materials, so enabling lighter vehicle designs that improve performance and fuel economy. Furthermore, enabled by nanotechnology are highly reflective materials that enhance vehicle visibility, particularly in low-light conditions, and materials resistant to scratches and other types of damage, so extending the aesthetic and functional lifetime of the vehicle [9].

Advanced sensors and monitoring systems for both vehicles and the transportation infrastructure are also being developed using nanotechnology. Along with vehicle systems, these nanoscale sensors offer real-time data on the state and performance of important infrastructure components including tunnels, bridges and roads. Real-time monitoring of these components helps to enable proactive maintenance and repair, so lowering the possibility of unanticipated problems and improving safety. Implementing these monitoring systems helps transportation networks to reach better dependability and efficiency [10,11].

Table 1 lists many uses for nanotechnology in transportation and highway building. It emphasizes how nanotechnology supports the creation of new materials and sensors for real-time monitoring, so improving fuel efficiency, safety via better vision, and infrastructure durability. Reflecting the transforming potential of nanotechnology in this sector, these developments together help to create more sustainable and efficient transportation systems.

The several uses of nanotechnology in highway and transportation engineering present great possibilities for enhancing the sustainability, durability, efficiency, and safety of vehicles and infrastructure. New and creative ideas can be developed to solve problems confronting the transportation sector as nanotechnology develops.

Table 1. Applications of nanotechnology in highway and transportation engineering

Category	Description	Additional Information	References
Infrastructure Construction and Maintenance	Nanotechnology offers various applications in highway and transportation engineering, particularly in the construction and maintenance of infrastructure.	Nanomaterials are utilized to enhance the durability and strength of pavement, bridges, and other structures. Additionally, they contribute to reducing the cost and time of maintenance and repair through the development of self-healing materials capable of repairing themselves when damaged.	6–8
Vehicle Design and Manufacture	Nanotechnology plays a significant role in revolutionizing vehicle design and manufacture in transportation engineering.	Nanomaterials are employed to reduce vehicle weight, thereby enhancing fuel efficiency and environmental friendliness. Moreover, they aid in improving vehicle safety and visibility by creating highly reflective and damage-resistant materials.	6,9
Sensors and Monitoring Systems	Nanotechnology advancements extend to the development of sensors and monitoring systems for transportation infrastructure and vehicles.	These sensors offer real-time insights into infrastructure and vehicle conditions and performance, enabling proactive maintenance and repair actions.	6,10,11

Benefits and challenges of using nanotechnology in transportation engineering

A number of recent studies have shown that there are several substantial advantages to using nanotechnology in transportation engineering. Thanks to the increased strength and resilience offered by nanomaterials, infrastructure like pavements and bridges have a longer lifespan and are more durable [11]. Vehicle visibility and safety are both improved by nanotechnology. Improved low-light visibility and vehicle protection are two benefits of nanotechnology-based advanced materials, such as self-healing surfaces and highly reflective coatings [12].

Vehicles' fuel efficiency and emissions are both enhanced by nanotechnology. Vehicles can run cleaner and more efficiently thanks to nanotechnology-enabled lighter materials and improved catalytic converters [13]. Nanotechnology also allows for proactive repair and maintenance via high-tech sensors and monitoring systems. Timely interventions are made possible by these technologies' real-time data on infrastructure and vehicle conditions, which in turn reduces the risk of unexpected failures [11]. Finally, by extending the lifespan of components and minimizing the need for frequent interventions, the use of self-healing materials and durable nanomaterials leads to reduced costs and time for maintenance and repairs [12].

Table 2 lists some of the advantages of using nanotechnology in transportation engineering. These include longer life for infrastructure materials, better fuel efficiency and fewer emissions from vehicles, better road visibility and safety, and the possibility of creating new materials and sensors for continuous monitoring.

Table 2: Benefits of using nanotechnology in transportation engineering

Category	Description	References
Benefits of Nanotechnology	The utilization of nanotechnology in transportation engineering presents numerous potential benefits.	11–13
Improved Durability and Lifespan	Nanotechnology contributes to enhancing the durability and lifespan of infrastructure.	11–13
Enhanced Safety and Visibility	Nanotechnology advancements improve the safety and visibility of vehicles.	11–13
Reduced Emissions and Improved Fuel Efficiency	Nanotechnology aids in reducing emissions and enhancing fuel efficiency in vehicles.	11–13
Proactive Maintenance and Repair	Nanotechnology enables proactive maintenance and repair of infrastructure and vehicles.	11–13
Reduced Cost and Time of Maintenance and Repair	Nanotechnology contributes to reducing the cost and time required for maintenance and repair activities.	11–13

To completely realize the possibilities of nanotechnology in transportation engineering, several issues must be resolved, though. Recent research indicates that one of the main obstacles is the great cost related with nanomaterials and their manufacturing techniques [12]. Widespread acceptance may be greatly hampered by the cost of manufacturing and using these advanced materials. Further issues regarding the safety and long-term effects of nanomaterials depend on their possible environmental and health hazards connected to their use [13].

Furthermore, lacking is standardizing and control over the application of nanotechnology in transportation engineering. Lack of consistent policies can impede the advancement and implementation of nanotechnology among several projects and areas [12]. Ultimately, the design, manufacturing, and application of nanomaterials sometimes call for specific tools and knowledge, which can be a constraint for many companies and experts in the field [13]. Maximizing the advantages of nanotechnology and guaranteeing its safe and efficient integration into transportation architecture depend on addressing these obstacles. Dealing with these issues will need cooperation among engineers, scientists, and legislators to create and apply sensible plans for the responsible and safe application of nanotechnology in transportation engineering [14].

By enhancing the performance, safety, and sustainability of transportation infrastructure and vehicles, nanotechnology has the overall potential to transform the discipline of transportation engineering [15]. Realizing this potential, however, will need addressing the difficulties with the use of nanomaterials and creating sensible plans for their responsible and safe application.

Review of nanomaterials and their applications in highway and transportation engineering

Nanoparticles

Nanoparticles are particles with sizes ranging from 1 to 100 nanometers in at least one dimension. They can be made from a variety of materials, including metals, metal oxides, and polymers. Nanoparticles have unique properties that are different from those of larger particles of the same material, including increased surface area, reactivity, and optical and magnetic properties [16]. In transportation engineering, nanoparticles have a variety of potential applications. One of the most promising applications is the use of nanoparticles in the construction and maintenance of infrastructure. Nanoparticles can be incorporated into construction materials, such as concrete and asphalt, to enhance their properties [17]. For example, nanoparticles can increase the strength and durability of concrete, making it more resistant to wear and tear, and reduce the need for maintenance and repair. Furthermore, it can also enhance the thermal and mechanical properties in asphalt to increase the resistance against cracking and deformation processes [18].

Another potential application of nanoparticles in transportation engineering is in the development of new sensors and monitoring systems. Nanoparticles can be used as sensing elements in sensors that detect changes in temperature, pressure, and other parameters [19]. These sensors also have possible applications in monitoring the condition and performance of infrastructure and vehicles in real time to enable proactive maintenance and repair. Given the manifold benefits of nanoparticles, there are equal apprehensions related to their safety and environmental effects [20]. Nanoparticles are capable of breaching all the defenses of the human body, such as the skin and lungs, and then accumulate in tissues and organs. That, in turn, can lead to toxic effects that may appear as inflammation, oxidative stress, and cell damage. Besides, there are questions about the ecotoxicological impact of NPs regarding their possible accumulation in soil and water and further disruption of ecosystems [21].

Accordingly, there is a need to develop safe and responsible strategies in the application of nanoparticles in transportation engineering [22]. These can be achieved by minimizing the rate of nanoparticle exposure using personal protective equipment and engineering controls. It also involves designing less toxic and environmentally benign nanoparticles. The same can be achieved through standardization and regulation of their use in transportation engineering to ensure that they are safely and responsibly used [23,24]. Several transportation engineering applications of nanotechnology in their summary are shown in Table 3 to elaborate on the benefits that relate to durability, fuel efficiency, and safety, among many others, together with the challenges of environmental, cost, and regulatory effects.

Nanofibers

Nanofibers are fibers of diameters between 1 and 100 nanometers. They can be made out of a variety of materials such as polymers, metals, and ceramics. Nanofibers have special properties that make them useful for application in transportation and highway engineering [25,26].

One of the most promising applications of nanofibers in transport and highway engineering is their use in developing new materials for application in construction and repair [27]. The nanofibers are added to conventional construction materials such as concrete and asphalt to enhance properties. For instance, nanofibers can enhance strength and durability for concretes that are more resistant to crack and deformation [28]. They can also upgrade the thermal and mechanical properties of asphalt to make the material resistant to wear and tear [29]. Another application of nanofibers that may be undertaken in transportation and highway engineering involves the development of filtration and separation technology. Nanofibers have high surface area to volume ratios and can be made with pore sizes smaller than those achievable in traditional filter materials. This makes them attractive for use in filters and membranes for water treatment and air filtration [30].

Other potential uses of nanofibers relate to developing sensor and monitoring systems for transportation or highway infrastructure. Nanofibers can be functionalized with sensing material responsive to temperature, pressure, and other parameters. Thus, they easily apply as a sensing element to sensors capable of monitoring infrastructure and vehicle performance and conditions in real time [31].

Table 3: Nanotechnology in transportation engineering: Applications, benefits, and challenges

Category	Description	Benefits	Challenges	Examples of Applications	References
Nanoparticles	Nanoparticles are particles sized between 1 to 100 nanometers, composed of various materials such as metals, metal oxides, and polymers. They possess unique properties, including increased surface area, reactivity, and optical and magnetic characteristics.	Improved strength and durability of construction materials, Enhanced thermal and mechanical properties	High cost, Environmental and health hazards, Lack of standardization and regulation, Specialized equipment and expertise	Incorporation of nanoparticles in concrete and asphalt, Nanoparticle-based sensors for real-time monitoring	16–24
Benefits of Nanoparticles in Transportation Engineering	Nanoparticles offer several benefits in transportation engineering applications.	Incorporation of nanoparticles in concrete and asphalt, Incorporation of nanoparticles in asphalt		Nanoparticle-based sensors for temperature, pressure, and other parameters	22
Challenges of Nanoparticles in Transportation Engineering	Despite their benefits, nanoparticles face challenges in transportation engineering applications.	High cost, Environmental and health hazards, Lack of standardization and regulation, Specialized equipment and expertise			22–24

Among others, the fibers also promise a possible application in the development of light and high-strength material applications in vehicles. Adding nanofibers to the polymer composites can enhance its strength and rigidity while decreasing its overall weight. The consequences would be improved fuel efficiency and reduced greenhouse gas emission [32].

With all these potential benefits associated with the use of nanofibers, there are equal apprehensions over their safety and environmental impact. Nanofibers may successfully breach human barriers such as skin and lungs and accumulate in organs and tissues, leading to toxic effects such as inflammation, oxidative stress, and cellular damage [33]. There is a concern about the environmental impact of nanofibers regarding accumulation in soil and water, with combined effects on ecosystems.

These are some of the concerns which the development of safe and responsible strategies in the use of nanofibers in transportation and highway engineering should address. These include exposure minimization of nanofibers through protective equipment and engineering controls among other approaches, and the design of nanofibers that are less toxic and more environmentally friendly. Standardization and regulation of the use of nanofibers in transportation and highway engineering can also contribute to their safety and responsible usage [34].

In short, nanofibers have enormous applications in transportation and highway engineering, covering a wide range from development of new materials for construction and repair, filtration and separation technologies to sensors and monitoring systems Figure [35]. Table 4 summarizes different transportation and highway engineering applications using nanofibers. At the same time, considering the benefits they can bring about in increased mechanical properties and reduction of material use, this area is also facing challenges that environmental impact and scalability of production methods have posed.

The wide range of nanofiber benefits may not outweigh the potential safety and environmental issues associated with such fibers, and any use in transportation or highway engineering needs to be cautiously approached and developed into safe and responsible strategies aimed at minimizing exposures with their safe and sustainable use in mind [35].

Nanotubes

Carbon nanotechnology comes in a family of nanotubes with some amazing mechanical, electrical, and thermal properties. These properties make carbon nanotubes attractive in a wide range of applications in transportation and highway engineering [36].

Probably one of the most promising applications of carbon nanotubes in transport and highway engineering involves the development of high-strength, lightweight materials for use in vehicles. Carbon nanotubes can be added to polymer composites to increase tensile strength and stiffness while reducing weight. This might yield a reduction in greenhouse gas emissions as a result of improved fuel economy. Another possible use is in the development of novel materials for tires and other parts of vehicles requiring high strength and durability [37,38].

Table 4. Applications and challenges of nanofibers in transportation and highway engineering

Category	Description	Benefits	Challenges	Examples of Applications	References
Nanofibers	Nanofibers are fibers with diameters typically ranging from 1 to 100 nanometers, crafted from various materials like polymers, metals, and ceramics.	Improved strength and durability of construction materials, Enhanced thermal and mechanical properties of asphalt, Real-time monitoring of infrastructure and vehicle condition	Concerns regarding safety and environmental impact, High cost, Lack of standardized testing and regulation, Requirement of specialized equipment and expertise	Incorporation into concrete and asphalt for enhanced properties, Development of filtration and separation technologies, Creation of sensors and monitoring systems for infrastructure and vehicles	25–31,33–35
Benefits of Nanofibers	Nanofibers offer advantages such as enhancing the strength and durability of construction materials, improving the thermal and mechanical properties of asphalt, and enabling real-time monitoring of infrastructure and vehicle condition.	Improved strength and durability of construction materials, Enhanced thermal and mechanical properties of asphalt, Real-time monitoring of infrastructure and vehicle condition		Incorporation into concrete and asphalt, Development of sensors for real-time monitoring	27–32
Challenges of Nanofibers	Challenges associated with nanofibers include concerns regarding their safety and environmental impact, high production costs, lack of standardized testing and regulation, and the need for specialized equipment and expertise.	Concerns regarding safety and environmental impact, High cost, Lack of standardized testing and regulation, Requirement of specialized equipment and expertise			33–35

Another potential application of carbon nanotubes in transportation and highway engineering is in the development of sensors and monitoring systems for infrastructure and vehicles. Carbon nanotubes can be functionalized with sensing materials that respond to changes in temperature, pressure, and other parameters. This allows them to be used as sensing elements in sensors that can monitor the condition and performance of infrastructure and vehicles in real-time. Carbon nanotubes can be used to develop new types of batteries and energy storage systems that could, one day, replace those in electric vehicles [39].

Carbon nanotubes can also be used in the development of new coatings and surface treatments for infrastructure and vehicles [40]. Carbon nanotube coatings can improve the corrosion resistance and wear resistance of infrastructure materials, such as steel and concrete. Carbon nanotube surface treatments can also improve the adhesion of coatings and paints to infrastructure materials, leading to longer-lasting and more durable finishes.

Aside from these, some other application areas include developing new kinds of concrete and asphalt that could be used in construction and repair. Carbon nanotubes can increase the strength and resilience of such materials, hence providing resistance against crack and deformation. Carbon nanotubes can increase such material properties like thermal and mechanical resistance to wearing and tearing [41].

Despite their many potential benefits, carbon nanotubes also raise several concerns about their safety and environmental impact. Carbon nanotubes are able to penetrate natural barriers such as skin and lungs and induce accumulation in tissues and organs, leading to toxic effects-as inflammation, oxidative stress, and cell damage. To this end, there is need for developing appropriate safe and responsible approaches to carbon nanotubes use in transportation and highway engineering. It involves reducing exposure to carbon nanotubes by the use of protective equipment and engineering controls, and the design of less toxic and greener carbon nanotubes. Standardization and regulation of the use of carbon nanotubes in transportation and highway engineering can also help ensure their safe and responsible use [42].

Table 5: A summary of the potential applications of carbon nanotubes in transportation and highway engineering: Benefits and concerns

Category	Description	Benefits	Challenges	Examples of Applications	References
Nanotubes	Carbon nanotubes possess unique mechanical, electrical, and thermal properties, making them appealing for various applications in transportation and highway engineering.	Development of high-strength and lightweight materials for vehicles, Real-time monitoring systems for infrastructure and vehicles, Coatings and surface treatments for infrastructure materials, Improvement of concrete and asphalt properties	Concerns regarding safety and environmental impact, High production costs, Lack of standardized testing and regulation, Specialized equipment and expertise required	Incorporation into polymer composites for lightweight materials, Development of sensors for real-time monitoring, Coatings to improve corrosion resistance, Enhancement of concrete and asphalt properties	27,36–42
Benefits of Nanotubes	Carbon nanotubes offer advantages such as the development of high-strength and lightweight materials for vehicles, enhancement of infrastructure materials' durability, and improvement of sensing and monitoring systems for real-time performance evaluation.	Development of high-strength and lightweight materials for vehicles, Real-time monitoring systems for infrastructure and vehicles, Coatings and surface treatments for infrastructure materials, Improvement of concrete and asphalt properties		Incorporation into polymer composites for lightweight materials, Development of sensors for real-time monitoring, Coatings to improve corrosion resistance, Enhancement of concrete and asphalt properties	27,36–42
Challenges of Nanotubes	Challenges associated with carbon nanotubes include safety and environmental concerns, high production costs, lack of standardized testing and regulation, and the need for specialized equipment and expertise.	Concerns regarding safety and environmental impact, High production costs, Lack of standardized testing and regulation, Specialized equipment and expertise required			27,36–42

In all, CNTs have possible applications in transportation and highway engineering, including: the manufacture of high-strength, lightweight materials for transportation vehicles; sensors and monitoring systems; the coating and surface treatment of infrastructure materials. However, their safety and impact on the environment need to be taken care of by developing safe and responsible strategies for their application [27]. Table 5 summarizes some of the many applications of carbon nanotubes to transportation and highway engineering - a strengthening of materials for better durability, yet with safety and environmental concerns that raise the flag for responsible use.

It is important to be in mind that despite the great potentials of carbon nanotubes in regard to transportation and highway engineering, considerable research and development are still required with regard to the issues of safety and its safe and responsible use. The applications of carbon nanotubes should be practiced in a manner whereby public health is considered and the safety of the environment is ensured.

Nanosensors

Nanosensors are specialized instruments designed to identify and quantify variations in physical, chemical, or biological characteristics at the nanoscale level [43]. Within the domains of transportation and highway engineering, these devices can be employed to assess the state and functionality of infrastructure and vehicles in real time, thereby supplying essential information to operators and maintenance teams. Nanosensors are capable of measuring a diverse array of parameters, such as temperature, pressure, strain, vibration, humidity, and concentrations of gases [44]. Nanosensors can be added to the material composition or attached to the surface of infrastructure and vehicles. In addition, they can be imbedded in coatings or paints that are applied on the surface of infrastructure to provide real-time monitoring capability. One of the key advantages that nanosensors have over other technologies is their ability to detect changes in conditions and performance at a very early stage, enabling operators to take remedial action before severe consequences occur. They could, for example, monitor for signs of corrosion, fatigue, or stress in infrastructure materials so maintenance staff can take steps to prevent failure [45].

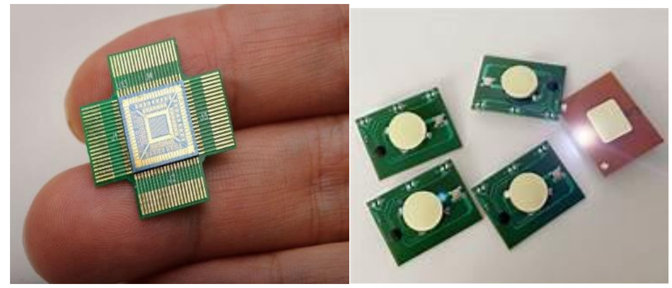

Fig. 1. A pictorial Representation of NanoSensors [1].

Table 6: A summary of applications of nanosensors in transportation and highway engineering

Parameter	Application	Potential Benefits	References
Temperature	Infrastructure and vehicles	Early detection of overheating, prevention of component failure	43
Pressure	Vehicles	Real-time monitoring of tire pressure, improved safety	44
Strain	Infrastructure	Early detection of fatigue or stress in materials, prevention of failure	45
Vibration	Infrastructure	Real-time monitoring of structural integrity, prevention of failure	46
Humidity	Infrastructure	Real-time monitoring of moisture levels, prevention of damage	47
Gas concentrations	Environment	Monitoring of air quality, detection of pollutants	48
Integration into materials	Infrastructure	Seamless monitoring without added bulk or weight	49
Surface attachment	Infrastructure and vehicles	Easy installation and removal, flexible placement	50
Coating or paint embedding	Infrastructure	Real-time monitoring without additional hardware or sensors	51

In other words, nanosensors are able to substantially contribute to improving the safety, productivity, and sustainability of transport systems and highway structures [47,48]. However, a number of concerns are still expressed regarding the potential environmental impact caused by these devices, in particular with regard to electronic waste management. Therefore, from this point of view, it is essential to work out safe and responsible ways of nanosensor manufacture and use in transport engineering.

Graphene

Aside from its excellent electrical and thermal properties, graphene also exhibits very remarkable strength and lightweight features. With these properties, it becomes an ideal material for different uses in transportation engineering, especially in the development of advanced batteries and energy storage systems for electric vehicles [49].

Graphene-based batteries have the potential to revolutionize the industry of electric vehicles by providing much higher energy density compared to conventional lithium-ion batteries. In addition, graphene-based batteries charge much faster than traditional ones, reducing the time taken for recharging the vehicle [50,51].

Graphene can be used to develop supercapacitors-energy storage devices that can retain and release massive amounts of energy instantaneously. This type of device offers great potential for the efficient performance of hybrid and electric vehicles because they can meet the high-powered surges required for accelerating and braking [52]. Other than energy storage, graphene can also be used to develop lightweight and strong materials in automobile applications. Graphene composites have the potential to enable the development of lightweight and strong structural components, which will reduce the overall vehicle weight and lead to improved performance and fuel economy [53].

Graphene also has the potential for application in sensors and monitoring systems for infrastructure and vehicle-based applications. For example, graphene-based sensors can detect temperature, pressure, and other parameter changes in real time with high sensitivity, providing, among others, the necessary feedback information for traffic and infrastructure maintenance management [54,55]. Table 7 summarizes the various applications of graphene in highway and transportation engineering with significant benefits in developing high-performance batteries and supercapacitors for energy storage,

constructing lightweight and strong materials for vehicles, and translating into sensors and monitoring systems for infrastructure and vehicles with improved safety, efficiency, and sustainability.
Overall, graphene has shown great promise as a material for use in transportation engineering, particularly in the development of high-performance batteries and energy storage devices for electric vehicles [56–58].

Nanoclay
A form of clay mineral, nanoclay has undergone modifications on a microscopic scale to enhance its characteristics. In transportation engineering, it can be applied to raise the durability and performance of asphalt concrete and other infrastructure materials [59].

In transportation engineering, one of the main uses for nanoclay is to enhance the mechanical qualities of asphalt concrete. Although asphalt concrete is a frequently used material in road and highway building, over time it can be prone to deformation and cracking [60]. Adding nanoclay to asphalt concrete increases its stiffness and deformation resistance, so enhancing its durability and capacity to resist heavy traffic loads.
Apart from its uses in asphalt concrete, nanoclay can also help to increase the lifetime of other infrastructure components including steel and concrete [61]. Concrete mixtures can include nanoclay to increase their strength and lower cracking, so enhancing their resistance to environmental elements including corrosion, weathering, and other stresses [3]. Nanoclay is reportedly used in the road depicted here in figure 2 below.

Table 7: A summary of graphene in highway and transportation engineering

Property/Application	Description	Example	References
Energy Storage	Graphene-based batteries have higher energy density and faster charging time compared to traditional lithium-ion batteries.	Development of high-performance batteries for electric vehicles.	49–51
Supercapacitors	Graphene can be used to develop energy storage devices that can store and release large amounts of energy quickly.	Improving the performance of hybrid and electric vehicles.	52
Lightweight Materials	Graphene composites can be used to develop lightweight and high-strength structural components, reducing the weight of vehicles and improving their performance and fuel efficiency.	Development of lightweight and strong vehicle components.	53
Sensors and Monitoring Systems	Graphene-based sensors can detect changes in temperature, pressure, and other parameters in real-time, providing valuable data for traffic management and infrastructure maintenance.	Infrastructure and vehicle monitoring systems.	54,55

Fig. 2. Pictorial Representation of Nanoclay and application in pavements [3].

Nanoclay has other uses in transportation engineering, such as creating coatings to protect infrastructure materials [62,63]. Coatings can include nanoclay to increase their adhesion to surfaces, boost their resistance to corrosion and abrasion, and offer more UV radiation protection [64]. Table 8 lists in highway and transportation engineering the advantages of nanoclay including better mechanical qualities, enhanced durability, more damage resistance, and longer lifespan of infrastructure materials.
Overall, nanoclay has the potential to greatly improve the performance and durability of infrastructure materials used in transportation engineering, reducing maintenance costs and increasing the lifespan of infrastructure assets.

Nanocellulose

Nanocellulose is a form of cellulose fiber that has undergone a process of microscopic degradation. With great strength and stiffness, among other mechanical qualities, it is a promising material for use in transportation engineering [65]. Among the main uses of nanocellulose in transportation engineering is the creation of robust and lightweight composites [66]. Combining nanocellulose with other materials—such as plastics and resins—allows one to produce composites with extraordinary mechanical qualities. By means of these composites, lightweight and fuel-efficient vehicles can be developed, so lowering their environmental impact and enhancing their performance.

Additionally able to enhance asphalt concrete's performance is nanocellulose. Nanocellulose can increase the stiffness and deformation resistance of asphalt concrete mixtures, so increasing their durability and capacity to resist high traffic loads [67]. Furthermore, bio-based asphalt binders—more ecologically friendly and sustainable than conventional petroleum-based binders—can be produced from nanocellulose [68–70]. Table 9 summarizes the uses of nanocellulose in highway and transportation engineering, stressing its part in creating lightweight and strong composites, enhancing asphalt concrete performance, and so improving sensors for real-time monitoring.

Another potential application of nanocellulose in transportation engineering is in the development of nanocellulose-based sensors. These sensors can be used to monitor the condition and performance of infrastructure and vehicles in real-time, providing valuable data for traffic management and infrastructure maintenance.

Table 8: Benefits of nanoclay in highway and transportation engineering

Properties of Nanoclay	Applications in Transportation Engineering	Examples of Applications	Potential Benefits	References
Improves mechanical properties	Improves stiffness and resistance to deformation of asphalt concrete.	Incorporation into asphalt concrete mixtures.	Enhanced durability and load-bearing capacity.	59,60
Enhances durability	Improves strength and reduces cracking in concrete mixtures.	Addition to concrete mixtures.	Increased lifespan and reduced maintenance costs.	61
Increases resistance to damage	Protects infrastructure materials, such as steel and concrete, from weathering and corrosion.	Coating application on infrastructure surfaces.	Enhanced longevity and reduced degradation.	3
Enhances adhesion	Improves coatings for infrastructure materials, providing greater protection against abrasion and UV radiation.	Integration into surface coatings.	Improved bonding and surface protection.	62–64

Table 9. Nanocellulose applications in highway and transportation engineering

Nanocellulose Properties	Application in Transportation Engineering	Examples of Applications	Benefits	References
Material	Development of lightweight and strong composites	Combination with plastics and resins to create lightweight vehicle components	- Reduces vehicle weight - Improves fuel efficiency - Enhances mechanical properties	65,66
Asphalt Concrete	Improves stiffness and resistance to deformation of asphalt concrete Creates bio-based asphalt binders	Addition to asphalt concrete mixtures Development of bio-based asphalt binders	- Enhances durability of asphalt concrete - Enables sustainable binder alternatives	67–70
Sensors	Development of nanocellulose-based sensors to monitor infrastructure and vehicle condition and performance in real-time	Integration into sensor systems for real-time monitoring	- Provides valuable data for traffic management - Enables proactive maintenance	70

Nanoceramics

Nanoceramics are a type of ceramic material that has been engineered at the nanoscale level, resulting in exceptional mechanical properties such as high strength, hardness, and toughness [71]. Particularly in the production of high-performance brake pads and other vehicle components, these features make nanoceramics a promising material for use in transportation engineering [72]. Development of brake pads more durable and wear-resistant than conventional brake pads is one of the main uses of nanoceramics in transportation engineering. Higher coefficient of friction brake pads made from nanoceramics will enable more effective braking and lower stopping distances by enabling more efficient braking and reduced stopping distances by means of which Furthermore more effective in extreme conditions such racing or heavy-duty trucking, nanoceramic brake pads can run at higher temperatures than conventional brake pads [30]. Other parts in vehicles, including bearings and engine components, can also be made more durable and performable using nanoceramics [73]. Longer lifespans and reduced maintenance costs follow from increased resistance to wear, corrosion, and other types of damage made possible by including nanoceramic materials into these parts [74]. Table 10 lists the several uses of nanoceramics in transportation engineering, stressing their use in developing high-performance brake pads, improving the durability and performance of vehicle components, and building lightweight and strong structural materials.

Another potential application of nanoceramics in transportation engineering is in the development of lightweight and strong structural materials for use in vehicles. Nanoceramic materials can be combined with other materials, such as polymers and metals [75,76], to create composites that have exceptional strength and stiffness, while also being lightweight and durable [77].

Table 10. Applications of nanoceramics in transportation engineering

Nanoceramics Properties	Application in Transportation Engineering	Examples of Applications	Advantages	References
Material with exceptional mechanical properties	Development of high-performance brake pads	Creation of brake pads with higher coefficient of friction and operating temperatures	- More efficient braking - Effective in extreme conditions	30,71,72
	Improvement of durability and performance of vehicle components	Incorporation into engine parts and bearings for increased resistance to wear and corrosion	- Longer lifespans - Lower maintenance costs	73,74
	Development of lightweight and strong structural materials	Combination with polymers and metals to create composites	- Exceptional strength and stiffness - Lightweight and durable	75–77

Quantum dots

Nanomaterials known as quantum dots have exceptional optical and electrical properties that make them useful in many fields, including transportation engineering [78]. Development of new lighting and signaling systems more efficient and effective than conventional lighting systems is one of the main uses of quantum dots in this field [79]. Development of premium LED lighting for use in infrastructure and vehicles could find one possible application for quantum dots. Better visibility and increased safety follow from quantum dot-based LEDs' more accurate color rendering and wider range of colors than conventional LEDs. Furthermore, more efficient they can be, which reduces energy consumption and extends lifespans [80]. Apart from illumination, quantum dots find application in signaling systems for infrastructure and vehicles. For low-light environments as well, quantum dots can be included into road marks and signage to increase visibility and reflectivity. Furthermore, they can help create more dependable and accurate traffic control and monitoring sensors [81]. The creation of displays and screens for use in vehicles represents still another possible use for quantum dots in transportation engineering. Better visibility and an interesting user experience follow from brighter and more vivid colors produced by quantum dot-based displays than by conventional ones [82]. Table 11 lists the uses of quantum dots in transportation engineering, including their use in high-quality LED lighting for vehicles and infrastructure, signaling systems for road safety, and displays for vehicles, so benefiting visibility, energy economy, and user experience.

Overall, quantum dots have the potential to greatly improve the efficiency, safety, and performance of lighting and signaling systems used in transportation engineering. However, more research is needed to fully understand the properties and behavior of quantum dots, and to develop safe and responsible methods for their use and disposal [83].

Analysis of the benefits and challenges of using nanotechnology in transportation engineering

Improved durability and lifespan of infrastructure

The application of nanotechnology in the field of transportation engineering has the potential to enhance the durability and lifespan of infrastructure materials like asphalt, concrete, and steel. This is one of the most significant advantages of this technology. Reversing these materials at the nanoscale using nanomaterials like carbon nanotubes and nanoclay helps to increase their resistance to wear, cracking, and other types of degradation. This can help to lower the demand for regular repairs and maintenance, so saving a great amount of money over time [84].

Table 11. Applications of quantum dots in transportation engineering

Quantum Dots Properties	Application in Transportation Engineering	Examples of Applications	Potential Benefits	References
Lighting	High-quality LED lighting for vehicles and infrastructure	Production of LEDs with wider color range and accurate color rendering	- Improved visibility and safety - Higher efficiency and longer lifespan	78–80
Signaling	Road markings and signage, traffic control and monitoring	Incorporation into signage for improved visibility and reflectivity	- Enhanced visibility in low-light conditions - More accurate and reliable sensors	81
Displays	Screens for use in vehicles	Development of displays with brighter and more vibrant colors	- Better visibility - More engaging user experience	82

Increased fuel efficiency and reduced emissions

Furthermore, helping to lower emissions and support sustainability is the ability of nanotechnology to increase vehicle fuel economy. For battery and energy storage systems, for instance, the use of nanomaterials such graphene and carbon nanotubes can boost their efficiency and lower their weight, so producing longer range and lower energy consumption. Furthermore, by encouraging more effective combustion, the use of nanocatalysts in exhaust systems can help to lower emissions [85].

Enhanced safety and visibility

Nanotechnology has the potential to improve road safety and visibility, which is an additional advantage in transportation engineering. More efficient lighting and signaling systems developed from nanomaterials including quantum dots and nanosensors will help to improve visibility and safety for drivers, pedestrians, and cyclists. Real-time monitoring of infrastructure and vehicle condition and performance made possible by nanosensors also enables proactive maintenance and repair [86].

Challenges of using nanotechnology in transportation engineering

Environmental impact

Concerns over nanoparticles' possible influence on the environment are a major barrier to their widespread application in transportation engineering. Nanoparticles and other nanomaterials can be hazardous to human and environmental health if not disposed of appropriately. Another potential environmental problem is the high energy and material costs associated with producing and using nanoparticles [87].

Cost

Another challenge associated with using nanotechnology in transportation engineering is the cost of developing and implementing new nanomaterials and technologies. Nanomaterials can be expensive to produce and may require specialized equipment and expertise, which can make them cost-prohibitive for some applications. Additionally, the long-term costs and benefits of using nanomaterials in transportation engineering are not yet well understood, which can make it difficult for policymakers and industry leaders to make informed decisions about their use [88].

Regulatory issues

Finally, the use of nanomaterials in transportation engineering is subject to various regulatory issues, including safety, environmental, and ethical concerns. There is currently a lack of clear guidance and regulations regarding the use of nanomaterials in transportation engineering, which can make it difficult for stakeholders to ensure that they are using these materials in a safe and responsible manner [89,90].

Research methodology

The research methodology is a critical element of any research project, as it outlines the procedures that will be implemented to achieve the research objectives. Here we will present the study plan that will be followed during the course of this investigation on the application of nanotechnologies to highways and transportation. This work aims to give a thorough overview of nanotechnology in transportation engineering together with its present state, uses, advantages, and drawbacks, so guiding a descriptive research design. We will systematically review pertinent materials including scholarly papers, research reports, and conference proceedings for the aim of gathering data for this project. Research of the scholarly literature will be done using academic databases including Google Scholar, Scopus, and Web of Science. Thematic analysis will be used on the gathered data for study. This entails classifying data based on trends and themes found in them. The research goals and themes found in the literature review will direct the investigation. Ethical Aspects: Primary data from human participants will not be gathered for this study. Ethical issues like informed permission and confidentiality thus have no relevance. Still, the study will follow ethical standards for using secondary data, including reference and citation of sources. Like any study depending just on secondary sources, this one could have problems with the availability and quality of its data. Furthermore, the scope of the study is limited to emergent nanotechnologies in transportation engineering, thus other facets of the discipline might not be fully addressed. With an eye toward a thorough knowledge of nanotechnology applications, benefits, and field challenges, Table 12 summarizes the research methodology used for investigating nanotechnologies in transportation engineering, which involves a descriptive research design, systematic literature evaluation, thematic analysis, and adherence to ethical guidelines [84-96].

Table 12. A summary of the research methodology for investigating nanotechnologies in transportation engineering.

Aspect	Description	References
	Benefits	
Improved Durability	Reinforcement of materials at the nanoscale reduces wear, cracking, and damage, resulting in less frequent repairs and maintenance, leading to cost savings over time.	84
Increased Fuel Efficiency	Nanomaterials enhance battery and energy storage systems, reducing weight and energy consumption, while nanocatalysts in exhaust systems promote efficient combustion, reducing emissions.	85
Enhanced Safety	Nanotechnology improves lighting and signaling systems, enhancing visibility and safety for drivers, pedestrians, and cyclists. Nanosensors monitor infrastructure and vehicle condition in real-time, enabling proactive maintenance.	86
	Challenges	
Environmental Impact	Concerns over nanoparticles' environmental effects and high energy/material costs of production.	87
Cost	Expensive production and specialized equipment/expertise make nanomaterials cost-prohibitive for some applications. Unclear long-term costs and benefits hinder decision-making.	88
Regulatory Issues	Lack of clear regulations regarding nanomaterial use poses safety, environmental, and ethical concerns, making it challenging to ensure safe and responsible use.	89,90
	Research Methodology	
Design	Descriptive research design focusing on a systematic literature review of scholarly papers, research reports, and conference proceedings.	91
Data Collection	Academic databases like Google Scholar, Scopus, and Web of Science used for systematic data collection.	92
Analysis	Thematic analysis categorizes data based on research objectives and themes identified in the literature review.	93
Ethical Considerations	Adherence to guidelines for secondary data usage, including citation and referencing, to ensure ethical research conduct.	94
	Limitations	
Data Quality	Potential issues with the quality and availability of secondary data may arise.	95
Scope	The study's scope is limited to emergent nanotechnologies in transportation engineering, potentially excluding other relevant aspects of the field.	96

Public perception and acceptance

Adoption of nanotechnology in transportation engineering also presents public acceptance and perception issue [28]. Though there are possible advantages, public knowledge usually lags far behind scientific developments. This discrepancy might cause opposition and mistrust of the application of nanomaterials in vehicles and infrastructure. Widespread acceptance and application of nanotechnology can be hampered by public worries on the unknown long-term health and environmental consequences of it [97]. Educating the public on the safety, advantages, and laws in place to control possible risks connected with nanotechnology depends on effective communication techniques [98].

Transparency and community involvement help to build public trust, so enabling a more favorable reception and support for uses of nanotechnology in transportation engineering [99]. Public participation projects including public forums, informational campaigns, and instructional seminars help to demystify nanotechnology and dispel typical misunderstandings. Clear, accurate, easily available knowledge on how nanotechnology operates, its advantages, and the safety precautions in place will help stakeholders encourage a more informed public debate [34,100].

Research Gap

Research in nanotechnology for transportation engineering exposes a number of important voids that demand filling. First of all, thorough field studies are needed to determine the long-term performance and durability of nanomaterials under real-world conditions so guaranteeing their effectiveness and safety outside of laboratories. Moreover, knowing how nanomaterials might affect transportation infrastructure calls for more thorough investigation considering both short- and long-term consequences. Furthermore, deserving of careful study are the social and financial effects of implementing nanotechnology-based transportation solutions on job markets and access across communities. Last but not least, investigating fresh nanotechnology-based solutions for unmet transportation needs including improved water resistance or corrosion prevention stays a crucial path forward in the field. Dealing with these gaps will help to create sustainable, safe, effective transportation system solutions.

Recommendations

The study advises government agencies and private businesses to support more research and development initiatives to investigate the great possibilities of nanotechnology in transportation engineering and hence higher investment. The safe and sustainable integration of nanotechnologies depends on cooperation among stakeholders, hence stressing the need of group efforts in addressing safety issues and building regulatory systems based on scientific evidence. Furthermore, environmental effects should be given great thought since initiatives meant to reduce negative effects should focus on them. These suggestions seek to direct practitioners, legislators, and researchers toward the responsible and efficient implementation of nanotechnologies in transportation engineering, so supporting sustainability, safety, ethics, and economy.

CONCLUSION

The incorporation of nanomaterials in transportation engineering possesses transformative potential, enhancing the durability, safety, and efficiency of transportation infrastructure. Researchers are diligently exploring innovative methods to improve pavement and road durability, increase visibility and safety protocols, reduce emissions, and enhance fuel efficiency. Utilizing nanomaterials in asphalt mixtures, concrete, road markings, lighting, tires, fuel additives, and lubricants can yield significant enhancements in infrastructure durability and environmental sustainability. However, issues related to the toxicity and environmental effects of nanomaterials, along with regulatory obstacles and financial factors, require coordinated efforts in research, regulation, and collaboration between transportation agencies and researchers. Confronting these challenges and further investigating nanotechnology's potential in the creation of novel materials and devices can promote a safer, more efficient, and sustainable transportation system.

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Overview of radiation shielding properties of tungsten oxide nanofibers

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ABSTRACT

Nanotechnology has garnered significant attention for providing innovative solutions across various fields, including fire safety, agriculture, corrosion protection, and environmental management. In the context of fire safety, nanostructured materials play a critical role, while in agriculture, nanoagrochemicals enhance crop protection and improve productivity. Similarly, nanoparticles used in corrosion protection significantly prolong the lifespan of materials. From an environmental perspective, these nanomaterials present eco-friendly and sustainable alternatives. Additionally, tungsten oxide (WO_3) has emerged as a key material in several industrial and technological applications, including diagnostic tools, protective equipment in healthcare, photocatalysis, electrochromic devices, energy storage, and radiation protection. The research also highlights the selective cytotoxicity of tungsten oxide-based composites, such as tungsten oxide-polyvinyl alcohol (PVA), tungsten oxide-polyvinylpyrrolidone (PVP), and tungsten oxide-thermoplastic polyurethane (TPU), particularly in targeting cancer cells, along with their radioactive properties. The process through which these materials are transformed into fibers what it is also discussed in detail.

Keywords: Nanotechnology, Tungsten oxide, Composite, Radioactivity properties

INTRODUCTION

Nanotechnology has become a rapidly developing technology field in recent years due to the development of innovative solutions in various fields such as materials science, agriculture, health and environmental management. Nanotechnology has played an important role in many sectors from fire safety to agriculture, from corrosion protection to environmental applications, and nanomaterials and nanostructures obtained with Nanotechnology have shown superior performance and efficiency compared to traditional methods. However, with the development of this technology, some difficulties such as intellectual property rights and human health have been encountered. Nanotechnology is used in the development of protective equipment and materials in the field of fire safety. Nanostructured materials that are specifically developed to reduce fire risks are produced and this equipment is integrated into the materials to reduce the risk of fire [1]. Nowadays, nanoagrochemicals in agriculture offer effective solutions to protect plants against diseases, weeds and pest species [2]. In addition, the positive effects of nanomaterials on plant germination and growth have been proven by scientific studies. These innovations are not only increase agricultural productivity, but also minimize environmental impacts and contribute to sustainable are agricultural practices. According to research, WO_3 nanoparticles are known to support plant growth by increasing seed germination. However, it was concluded that WO_3 nanoparticles doped with molybdenum (Mo) supported faster and healthier growth in plants. For example, in crops such as kodo millet, this material significantly increased seed germination rate and early growth success. At the same time, WO_3 exhibited antifungal properties against plant pathogens, increasing the productivity and durability of agricultural crops. For example, its photocatalytic bactericidal properties improve the environmental quality of agricultural areas by reducing ammonia concentration and pathogenic bacteria levels [3–9]. After agriculture, applications of nanotechnology in the field of corrosion protection have also gained significant popularity. Nanoparticles and nanocoatings increase the durability and safety of the material substrate and provide superior corrosion resistance. In addition, self-healing nanocomposites are being produced. These nanocomposites repair themselves regardless of damage, extend the life of the materials and minimize maintenance costs. Thus, they both support crop production and contribute to sustainable agricultural practices. The superior hydrophilic and oleophobic properties of WO_3 are of great importance in environmental technologies, especially in the field of water treatment. For example, WO_3 -coated stainless. steel mesh and other composite membranes separate oil-water mixtures with a separation efficiency of up to 98%. In addition, these membranes break down organic pollutants under UV light, providing self-cleaning, long-term performance and sustainability. Nanomaterials developed for wastewater management and reduction of gas emissions support environmental sustainability by adding value to industrial by-products [10].

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In addition, the photocatalytic activity of WO_3 plays a critical role in water treatment processes. Because its reactive oxygen species (ROS) production capacity has effectively eliminated microorganisms and pollutants, making access to clean water much easier [7,11–13]. In the field of energy storage, WO_3 offers high density and theoretical capacity. WO_3 is used as an electrode material for supercapacitors. By creating WO_3 nanostructures, we can improve its electrochemical performance and increase its energy density. For example, in symmetric supercapacitors, WO_3 has shown superior performance in terms of both energy density (34.45 Wh/kg) and power density (18.75 kW/kg). Moreover, thanks to its electrochromic properties, WO_3 has enabled the visualization of energy levels in energy storage devices through color change. This feature has provided a great advantage when used in integrated energy systems [14–20]. Nanotechnology also plays an important role in the healthcare sector. It has played a critical role in improving health security, especially during the COVID-19 pandemic. Nanoparticles are being investigated as effective carriers for vaccines, along with advanced diagnostic tools and protective equipment, and contribute to the improvement of delivery systems [21]. These innovations are of great importance for protecting and improving public health. However, despite the numerous advantages offered by this technology, it should be recognized that there are also potential risks to human health and the environment [2].

In the biomedical field, WO_3 nanoparticles show selective cytotoxicity against cancer cells while protecting healthy cells. This effect is associated with the pH sensitivity of WO_3 and its ability to generate reactive oxygen species (ROS). These properties allow WO_3 to induce apoptosis in cancer cells, making it a potential agent for targeted cancer therapies.

In human health, WO_3 attracts attention with its unique properties in cancer treatment. In fact, when WO_3 is modified with compounds such as polyglycerol and hyaluronic acid, it provides an increase in the drug carrying capacity specifically targeted to tumor cells. Therefore, WO_3 -based materials stand out as both effective and safe drug carriers [5,22–26]. For example, the ability to absorb near-infrared light makes WO_3 an ideal choice for photothermal therapy (PTT) and photodynamic therapy (PDT). In this process, WO_3, activated by laser light, destroys cancer cells through localized heat production, and this process is a highly effective method for tumor treatment. However, studies have proven that WO_3 nanoparticles have a direct cytotoxic effect on cancer cells. For example, experiments on human breast cancer cells (MCF-7) determined that 50% of the living cells were destroyed within a 24-hour period. Such success shows that WO_3 is one of the most promising materials of the future not only in cancer treatment but also in drug delivery systems. Moreover, the low cytotoxicity of WO_3 nanoparticles towards stem cells increases the safety and biocompatibility of this material [27–30]. As a result, nanotechnology offers revolutionary solutions in many sectors such as fire safety, agriculture, corrosion protection and healthcare. However, strengthening regulatory frameworks and ensuring public confidence are essential for the safe and effective implementation of this technology. This field, which is full of continuous growth and innovation, has seen extensive growth in the global market due to the versatile applications of tungsten oxide (WO_3) in sustainable and safe applications in various fields such as photocatalysis, electrochromic devices and energy storage systems. With its high stability, tunable band gap and unique electrochemical properties, WO_3 makes it a valuable component for many industries. Known for its high efficiency in photocatalytic processes such as pollutant degradation and CO_2 reduction, especially due to its band gap ranging from 2.5 to 2.7 eV, tungsten oxide offers innovative approaches to sustainable energy production through its integration with carbon-based composites [31]. This integration process enhances the optimization of photocatalytic efficiency and enables the development of promising solutions for environmentally friendly energy production. WO_3 finds wider application in WO_3 electrochromic devices, especially in smart windows and displays. Its superior electrochromic properties include high tinting efficiency and durability [32]. WO_3 is a versatile transition metal oxide that can be used in various high-tech applications such as optoelectronics, photocatalysis and sensors. The performance of this material depends on properties such as crystal structure, oxidation states and the presence of oxygen vacancies. WO_3 is an n-type semiconductor that usually exists in monoclinic and hexagonal phases, exhibiting high electrical conductivity and electron mobility. These properties make it suitable for use in gas sensors and electrochromic devices [33]. Oxygen vacancies in non-stoichiometric forms, such as WO_{3-x}, improve photocatalytic efficiency by increasing light absorption and affect the photochromic properties of the material [34]. Moreover, WO_3 thin films can be deposited by various techniques, such as thermal evaporation and chemical vapor deposition.

Their optical and electrical properties can be further improved by nanostructuring. However, there are still challenges to optimize the properties of this material, ensure its continuity in manufacturing processes, and increase stability under operational conditions.

This makes it difficult to fully realize its potential for advanced functional materials and smart devices. In recent years, developments in deposition techniques such as high-power pulsed magnetron sputtering have been optimized to improve the optical and electrochromic functions of WO_3 films [35]. These developments increase the market potential of WO_3, making it suitable for a wider range of applications [36]. The flexibility and efficiency of these devices make them suitable for a variety of applications and support innovative solutions in the field of energy storage. However, there are still several challenges in optimizing the performance and scalability of such capacitors for commercial use, requiring continuous research and development efforts [37].

The wide range of uses and unique properties of this material contribute to its increasing demand in the global market. With a wide range of applications ranging from photocatalytic processes to electrochromic devices and energy storage systems, this material is particularly in increasing demand in the global market.

GENERAL PROPERTIES OF TUNGSTEN OXIDE NANOFIBERS

The properties of WO_3 nanofibers vary depending on the synthesis methods and structural properties. For example, uniform nanofibers with a diameter range of 297–429 nm can be obtained by ultrasonic vapor deposition, while polycrystalline tungsten nanofibers with a diameter of 107 nm can be produced by needleless electrospinning technique [29]. These nanofibers are usually in monoclinic phase, which increases their surface area and light absorption capacity [38].

Black WO_{3-x} nanofibers improve their electrical conductivity and catalytic properties due to their low oxygen vacancies [38]. However, there are difficulties in large-scale production and consistent performance. Future studies should focus on optimization of synthesis processes and better understanding of the factors affecting the performance of nanofibers.

Properties of tungsten oxide and polyvinyl alcohol (PVA) nanofibers

WO_3 filled polyvinyl alcohol (PVA) composites have structural, optical and photocatalytic properties and therefore are of great interest in industries. WO_3 nanoparticles (Fig. 1) [39] are embedded into PVA nanofibers by electrospinning to obtain fibers with diameters ranging from 125 nm to 165 nm. These fibers can be obtained homogeneously by using surfactants (e.g., CTAB), thus affecting the morphology and diameter of the fibers. WO_3-PVA composites show high photocatalytic activity, especially for decolorization of methylene blue under UV (ultraviolet) light. Doping of WO_3 nanoparticles significantly enhances the photocatalytic property.

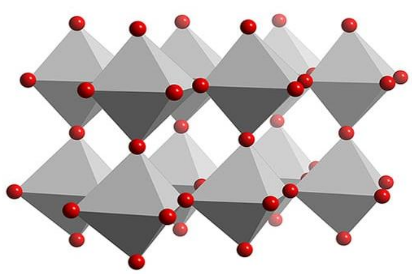


Fig. 1. 3D view of Tungsten Oxide [39]

Furthermore, WO_3 microfibers also exhibit effective photocatalytic activity in the degradation of Rhodamine B under UV light, enabling environmental remediation applications.

WO_3-PVA nanofibers are optically remarkable due to their high conductivity and low absorption properties. Nanoparticle content and electrospinning parameters affect the optical properties of these fibers, and these fibers exhibiting zero band gap energy are useful for various optical applications. Moreover, PVA deposited WO_3 thin films offer high electrochromic coloration efficiency and optical modulation, making them suitable for electrochromic devices.

The synthesis of PVA-doped WO_3 includes precipitation, coagulation and solvent casting methods. The process starts with dissolving the tungsten salt in water and mixing it with PVA. This mixture is then subjected to a heat treatment between 400-700°C. The average particle size of the obtained WO_3 is in the range of 20-50 nm. The specific surface area of the obtained product is between 10.5-21.5 m²/g. The structure obtained with this method consists of a semi-crystalline PVA matrix containing WO_3 nanoparticles.

Its chemical content is characterized by complexes formed through intermolecular hydrogen bonds between PVA and WO_3. These bonds increase the structural stability and functionality of the material. For characterization studies, the chemical and structural properties of the material are analyzed in detail using techniques such as FTIR, XRD, SEM and EDAX.

In conclusion, PVP and PVA doped WO_3 synthesis methods offer a powerful method to develop high-performance electrochemical materials. These methods provide a wide range of applications by providing both structural homogeneity and chemical stability [28,29].

Radiation protection features

WO_3-PVA composites (Fig. 2) [40] have also shown promising results in the field of radiation protection. Studies show that increasing the WO_3 concentration in PVA matrices significantly increases the gamma-ray attenuation coefficients. Nanocomposites provide superior protection compared to microcomposites due to the higher surface-to-volume ratio of WO_3 nanoparticles. Monte Carlo simulations have confirmed that nano-WO_3 outperforms micro-WO_3 fillers and that PVA/WO_3 composites provide effective protection against high-energy gamma photons [34]. These composites are lighter than traditional shielding materials and exhibit low conductivity, making them ideal for a variety of applications.

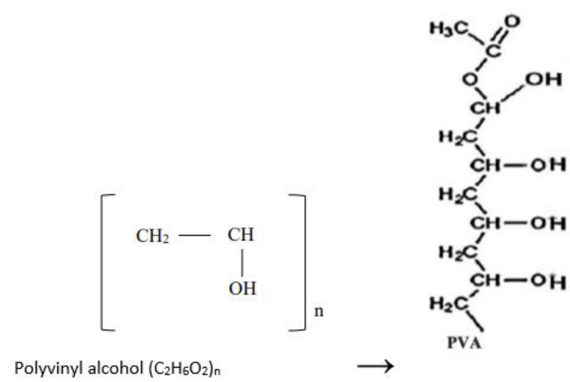


Fig. 2. Schematic view of tungsten oxide-PVA. [40]

Furthermore, WO_3-coated magnetic nanoparticles are promising for cancer treatment via neutron activation and magnetic hyperthermia (which uses the ability of magnetic nanoparticles to generate heat by vibration in an alternating magnetic field). These nanoparticles offer biocompatibility and hydrophilicity, increasing their usability in medical applications.

General properties of tungsten oxide - PVP nanofibers

Polyvinylpyrrolidone (PVP) stabilized WO_3 nanoparticles are characterized by their photochromic and photocatalytic performances. PVP enhances the stability of WO_3 while accelerating the formation of reduced tungsten species under UV irradiation, which improves their photochromic recycling ability. WO_3 nanoparticles can be effectively used in photocatalysis processes, which play an important role for environmental remediation applications.

WO_3 combined with polyvinylpyrrolidone (PVP) has also shown promising results in cancer treatment. These nanoparticles exhibit selective cytotoxic effects in cancer cells while showing minimal toxicity to healthy cells. This is due to the pH sensitivity and reactive oxygen species (ROS) generation ability of WO_3. WO_3 nanoparticles increase intracellular oxidative stress, leading to apoptosis in cancer cells.

The optical properties of WO_3 are further improved when combined with PVP. For example, PVP/WO_3 composites exhibit photochromic and photocatalytic properties as well as improved thermal stability and ionic conductivity, offering potential for use in areas such as energy storage and polymer solar cells [44].

The synthesis of PVP-doped WO_3 involves several steps based on the chemical composition and structural properties of the material. In this process, the use of dispersants such as polyvinylpyrrolidone (PVP) is important to improve the homogeneity and stability of WO3. The steps and characteristics of this method are as follows:

Dissolution and mixing

PVP is dissolved in deionized water and is usually obtained by combining with other polymers (P123). Then, hydrochloric acid (HCl) and sodium hydroxide (NaOH) are added to adjust the pH of the solution. This step ensures the stable preparation of the materials.

Precipitation

Substances such as sodium tungstate, used as a tungsten source, are added dropwise to the solution in a controlled manner. This process results in the formation of tungsten acid precipitates, which form the intermediate product required for the following steps.

Calcination

The resulting mixture is calcined at high temperatures (usually between 400-700°C) to form the desired WO_3 structure. This step improves the crystal structure and thermal stability of the material.

Doping

To improve the electrochemical properties of WO_3, it can be doped with metal ions such as zinc or yttrium. This process is an important step to improve the performance of tungsten oxide.

Use of polymeric binders

PVP plays a binding role in the WO_3 structure used as the electrode material. This improves the mechanical stability and electrochemical performance of the material.

Hydrothermal method

The hydrothermal method allows ultra-fine WO_3 particles of approximately 10 nm in size to be obtained. This nanometric size significantly improves the properties of the material such as conductivity and electrochemical activity.

Homogeneous composition and structural characterization

The balance between particle sizes and mole ratios during preparation ensures that the additives are evenly distributed within the homogeneous WO_3 matrix. This positively affects the performance of the material [41].

Tungsten oxide - PVP and radioactivity

The interactions of WO_3 nanoparticles with radioactivity have attracted interest, especially in radiation protection and therapeutic applications. WO_3 plays an important role in cancer treatment when used as a radiation dose enhancer. PVP-stabilized WO_3 nanowires have the potential to improve radiation therapy and photothermal therapies by providing heat and singlet oxygen production under NIR laser excitation. The VESPR appearance of WO_3 is as shown in the figure (Fig. 3) [42].

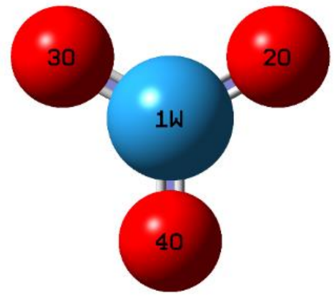


Fig. 3. VESPR view of WO_3 [42]

Tungsten oxide and TPU properties

WO_3 is a versatile and functional material with potential for use in various application areas [27]. When incorporated into polymer composites, WO_3 significantly improves the optical and mechanical properties of these materials.

For example, when WO_3 nanoparticles are used in thermoplastic polyurethane (TPU) matrices, the mechanical strength and thermal stability of the composites are also increased. Moreover, when WO_3 thin films are produced by magnetron sputtering, the optoelectronic properties can be optimized by adjusting the deposition parameters. Such thin films can be used in advanced technological applications such as transparent electronics.

Tungsten Oxide - TPU and radioactivity

Recent research has revealed the interactions of WO_3 with radioactivity and its potential in radiation shielding applications. Incorporation of WO_3 nanoparticles into polymer and cement matrices enhances the radioprotective properties of these materials [43]. The incorporation of WO_3 into glass and polyester composites leads to higher radiation attenuation capabilities, increasing their linear attenuation coefficients and effective atomic numbers [4]. Its morphological appearance is as shown in Figure 4 [44-45].

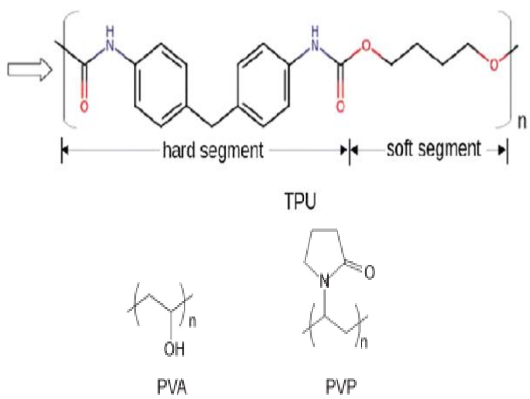


Fig. 4. Schematic view of tungsten oxide-TPU, tungsten oxide-PVA and tungsten oxide-PVP [44,45]

Combination with WO_3 PVP and PVA

The combination of WO_3 with PVP significantly increases its dispersibility in processing solvents and improves its photochromic properties, including bleaching rate. PVP acts as an effective organic ligand that optimizes the performance of tungsten oxide composites for practical applications (Figure 5.a.). The combination of WO_3 with PVP polymer stabilizes WO_3 nanoparticles and affects their structure [46]. Sodium cations significantly affect the photocatalytic behavior by promoting the formation of reduced tungsten species (W+5) upon UV irradiation and cause structural changes. It also increases the ionic mobility and reduces the optical energy gap [44]. It also highly improves the thermal stability and AC conductivity of the composite due to the interactions during complexation and charge transport. When WO_3 nanoparticles are combined with PVP polymer, the light-matter interaction is enhanced, the band gap is reduced and the localized defect states are increased. In this case, composite nanofibers improve the nonlinear absorption behavior. When WO_3 is combined with PVP polymer, tungsten undergoes thermal treatment. This treatment results in the removal of PVP and the growth of crystalline WO_3.

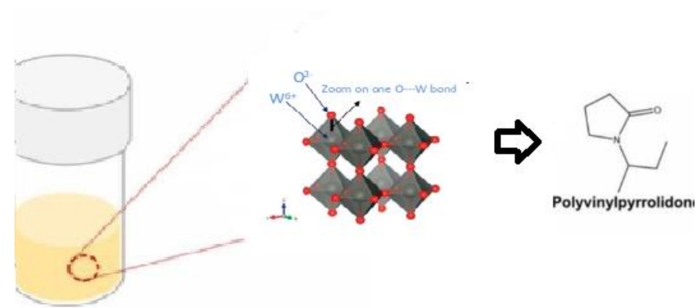
As a result of this treatment, the morphology of the nanofibers forms a rough surface and smaller diameter, improving the gas sensing properties [44].

When WO_3 is incorporated into the PVA polymer (Figure 5.b.). Interactions and complexes are formed with the OH groups of PVA. This results in structural repositioning. After this positioning, the crystallinity changes and complexes are formed, which lead to a changing structural order due to the decreased crystallinity and decreased intermolecular interactions between the PVA chains [47,48]. This causes changes in the microstructural properties and improves the mechanical properties of the composite. When WO_3 is incorporated into PVA, changes also occur in the structural, thermal and radiation protection properties of the composite [9,29]. The interaction improves dispersion, reduces crystallinity and increases mass attenuation coefficients, making the composites effective for protection against X and γ rays, resulting in more durable and improved materials. It is emphasized that the WO_{3-x}/Ag_2WO_4 photocatalyst increases photocatalytic disinfection and supports wound healing when loaded into the PVA hydrogel. When combined with PVA polymer, it facilitates better dispersion of nanoparticles and helps in obtaining thinner and straighter nanofibers during electrospinning [49]. When WO_3 is combined with PVA, flexible nanocomposites with rod-like morphology are formed.

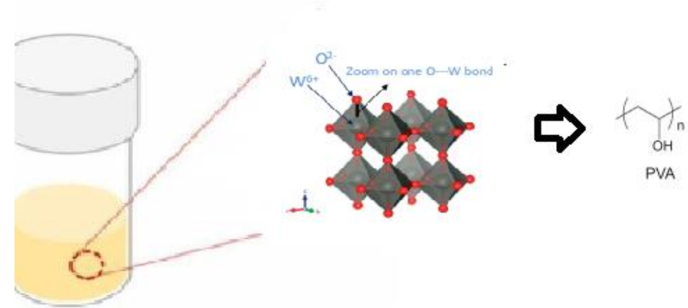
During synthesis, the formation of nano-sized particles is increased, resulting in an average size of 20-50 nm and minimal aggregation, which contributes to a high specific surface area of 10.5-21.5 m^2/g [28,36,46,50–54].

COMPARISON OF TUNGSTEN OXIDE (WO_3) AND POLYMER BASED COMPOSITES WITH ALTERNATIVE MATERIALS

In this study, alternative materials that offer similar structural, optical, photocatalytic and radiation protection properties to those offered by WO_3 and polymer-based composites were investigated. The suitability of these materials was evaluated.



a) Doping PVP



b) Doping PVA

Fig. 5. View of PVA and PVP. [18, 28]

Titanium dioxide (TiO_2)

TiO_2 is a material with high photocatalytic activity due to its wide band gap (3.2 eV) and high chemical stability. It has high optical transmittance and offers radiation shielding properties. TiO_2 is a suitable alternative to WO_3 in similar optical and photocatalytic applications and is generally less expensive [55].

Zinc oxide (ZnO)

ZnO has a wide band gap (3.37 eV) and high photocatalytic activity. It has high optical transmittance and is used in biomedical applications due to its antimicrobial properties. ZnO can be an alternative to WO_3 with its high photocatalytic efficiency and advantages in biomedical applications [44].

Cerium oxide (CeO_2)

With its unique redox properties, CeO_2 exhibits high photocatalytic activity and provides radiation protection. It is also valuable in biomedical applications due to its antioxidant properties. CeO_2 is a powerful material as a photocatalyst and radiation shield. It also stands out with its antioxidant properties in biomedical applications [41]. V_2O_5 has photocatalytic activity and offers electrochromic and energy storage properties. It is used as a cathode material in lithium-ion batteries. V_2O_5 offers photocatalytic and electrochromic properties similar to WO_3, and is also advantageous in energy storage applications.

Tritium (T)

As a result of atomistic simulations, the permeability of tritium was determined to be higher in WO_3 compared to W and WO_2, and it was observed that there was a negative discrimination on WO_3 surfaces in the high coverage area [56]. It was concluded that WO_3, which has radiation protection properties, increased WO_3 content in TeO_2-TiO_2-WO_3 glass systems increased the protection against gamma radiation and fast neutrons [57]. It was confirmed by scanning tunneling microscopy and X-ray photoelectron spectroscopy. WO_3 can form monodisperse cyclic trimers (WO_3) 3 on TiO_2 (110) surfaces. These different properties and applications make WO_3 play an important role in many areas ranging from medical diagnosis to radiation protection and surface science [55].

PRODUCTION OF TUNGSTEN OXIDE NANOFIBERS BY ELECTROSPINNING

To form a composite using PVA (Polyvinyl alcohol) and PVP (Polyvinylpyrrolidone) with WO_3, PVA and PVP are first dissolved separately in distilled water at certain concentrations. PVA solution is usually prepared by heating at 70-80°C, while PVP solution is dissolved at room temperature or by gentle heating. At the same time, WO_3 nanoparticles are dispersed in pure homogeneous water or alcohol with the help of an ultrasonic bath or magnetic stirrer. Then, PVA or PVP solutions are combined in the desired proportions and mixed until a homogeneous mixture is obtained. Then, WO_3 dispersion is slowly added and the mixture is further processed using an ultrasonic bath for uniform distribution of nanoparticles. Uniform distribution of WO_3 in the solution is important in order not to disrupt the morphology of the fibers. The viscosity of this prepared polymer/WO_3 solution is adjusted to the appropriate level for the electrospinning process. If the viscosity is too low, droplets may form and if it is too high, spraying becomes difficult, so the correct viscosity is a critical step. Fiber production from the prepared solution is done using an electrospinning device (Figure 6) [58].

The syringe containing the solution is connected to a metal needle to which a high voltage (usually 10-30 kV) is applied. The high voltage creates electrical forces on the surface of the solution, causing the solution to exit the needle in a fine spray and form fibers. As the solvent of the sprayed solution evaporates rapidly in the air, fine fibers form on the collector surface. The collector can usually be a flat surface covered with aluminum foil or a rotating cylinder. Finally, these fibers are dried at room temperature or by gentle heating, and if necessary, their mechanical properties are strengthened by heat treatment. The resulting WO_3/PVA/PVP composite fibers can be used in various areas such as sensors, optical devices and biomedical applications. The electrospinning method is frequently preferred in nanotechnology and advanced material applications because it provides advantages in obtaining high surface area and porous structures.

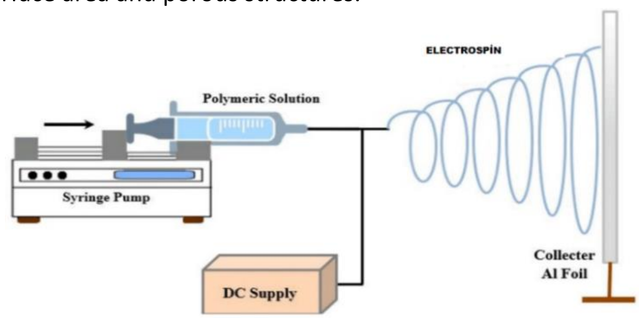


Fig. 6. Production stage of electrospinning [58]

CONCLUSION

WO_3 can act as a trap for radioactive isotopes. For example, studies on the permeability of WO_3 to tritium (T) suggest that this material has the potential to provide long-term stability and activity in radioactive environments. This supports the use of WO_3 in environments with radiation risks, such as nuclear power generation and space technology [55–57].

Furthermore, WO_3-doped thin-film transistors have been shown to exhibit high stability and excellent electrical performance even under high ionizing radiation. The presence of tungsten suppresses radiation-induced anomalous increases in conductivity and oxygen vacancy concentration, making 4% WO_3-doped devices reliable for use in radiation-prone environments such as nuclear energy and space technology, offering more effective and lightweight solutions than radiation shielding. Furthermore, WO_3 shows superiority in radiation attenuation parameters and optical and mechanical properties. When combined with polymers such as PVP or PVA, gamma radiation attenuation performance increases with increasing WO_3 content.

Tungsten oxide also acts as an effective radiation shield when incorporated into glass composites. Increasing the WO_3 content improves the optical properties and radiation attenuation capabilities of these glasses. WO_3 nanoparticles also serve as suitable dose enhancers for various radiation therapies, making them an important material in biomedical applications.

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Functionalized liposomes for colorectal cancer therapy

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ABSTRACT

Colorectal cancer (CRC) is one of the most common cancers. Many patients do not live for several years following their diagnosis, highlighting the urgent need for new treatment options, including new drug delivery methods. An effective strategy to increase the effectiveness of the treatment of this cancer is the use of a liposomal delivery system, which provides the possibility of providing hydrophobic and hydrophilic compounds with better biocompatibility and reduction of side effects by using several advantages, thus causing anti-cancer activity. Better tumor, drug accumulation is longer and they do not show any cytotoxic effect on normal cells. In this review, we will present nanoliposomes containing various compounds and ligands studied in CRC treatment. We will discuss on the benefits of liposomal administration in various forms, along with their effectiveness, specificity, and drug accumulation. Nanoliposome carriers have enormous potential to overcome the present constraints of cancer treatment, and the creation of this technology gives new possibilities in CRC treatment.

Keywords: Colorectal cancer, Liposomal delivery system, Cancer treatment

INTRODUCTION

One of the worldwide major health challenges is cancer, which causes high mortality in all ages. Cancer is a complex process caused by the uncontrolled growth of cells and the survival of mutated and deformed cells [1]. Colorectal cancer (CRC) is the third most frequent malignancy, with a significant global spread and fatality rate.

The survival rate in people whose disease is diagnosed in the early stages is more than 90%, while the same survival rate in people who are diagnosed after pathological diagnosis is less than 10% [2]. So, diagnosing the disease in different stages plays a significant role in the treatment and prevention process. Approximately 60% of patients with CRC needs surgery and chemotherapy as standard treatment, when the disease is diagnosed [3]. Lack of in time treatment, metastasis and progression of the disease largely lead to the death of patients with CRC [4].

One approach to treating colorectal cancer (CRC) is chemotherapy. However, its use is often limited by systemic side effects and a lack of tumor specificity. To address these challenges, alternative treatment strategies have been developed. These include integrating conventional chemotherapy with targeted molecular therapies and leveraging nanotechnology for enhanced therapeutic efficacy [5].

The design of drug carriers using nanotechnology has created a great change in the treatment of various diseases, especially cancer treatment [6]. This type of new drug delivery system has shown more effectiveness compared to conventional treatment methods [7]. Among the advantages that nano-based drug carriers have, the following can be mentioned: longer circulation time [8], increasing the half-life of drugs and sensitive proteins [9], increasing the effect of drugs [10], increasing the solubility of drugs, hydrophobic [11], facilitating controlled and targeted drug release in the desired areas and also reducing side effects [12].

Liposome is one of these nanocarriers, which is widely used to deliver drugs to the intended location [13]. Among the advantages of treatment methods based on liposome carriers, low toxicity, high biodegradability, controllable bio circulation, easy change in lipid composition and physical characteristics, accurate target identification, and very few side effects can be mentioned [14]. It is also possible to trap hydrophobic and hydrophilic drugs in the liposome, which has a hydrophilic center and a hydrophobic double layer membrane [15], in addition, the liposome has the ability to continuously release the substance that inside it [16].

So far, many results of the use of liposomes in the clinical phase have been published [17] and some of them have also obtained the necessary licenses [18]. Currently, in the United States, major clinical phase studies are being conducted to treat cancer, fungal infections, and Kaposi's sarcoma linked with acquired immunodeficiency syndrome [19].

Liposomal bupivacaine (Exparel®, developed by Pacira Pharmaceuticals, San Diego, CA) received approval from the U.S. FDA in 2011 for use as a local surgical site injection to manage postoperative pain following hemorrhoidectomy and bunionectomy [20]. Liposomes are utilized in cancer treatment

to enhance the delivery of chemotherapeutic agents, improve drug bioavailability, target tumor cells specifically, and minimize systemic toxicity, thereby increasing therapeutic efficacy [21].
Aroplatin- containing liposome, which treats metastatic colorectal cancer, passed the second phase of clinical trials [22], or Depocyt is a cytarabine-containing liposome with the ability to be injected into the spinal cord, which is FDA (Food and Drug Administration) is used to treat lymphomatous meningitis [23].
One of the characteristics of drug-carrying liposomes is that they can be targeted based on specific goals, so that they go to the desired location and release the drug in that area [24]. Various factors are used for target the liposome, for example, for targeting specific tumors, ligands for the desired cancer can be placed on the surface of the liposome [25]. These ligands must have a number of characteristics, including the ability to appear and exposure, affinity and specificity for the tumor in question [26]. Also, the liposomes improve tumor treatment by accumulating the drug at the target site, and prevent the toxic effect of the drug on normal tissues [27].
For these reasons, liposomes are used as a drug delivery system that increases the shelf life of the drug in vivo and in vitro [28]. Multi-drug treatment regimens are also used as a good strategy to reduce side effects and increase the therapeutic effect of drugs because they target several different pathways at the same time [29]. In this article, a review of the advances in drug delivery of targeted liposomes, which that used as carriers of multiple drugs to treat colon cancer, discussed. Furthermore, the primary challenges associated with the targeted release approach for colon cancer are delineated, and recommendations for the future are emphasized.

Targeted nanoliposomes for colorectal cancer treatment

The use of intelligent or targeted drug transport methods have provided good results in reducing adverse drug reactions by delivering the right amount of drug to a specific region. Accurate targeting of liposomal drug delivery systems reduces side effects in healthy tissues and has the potential to treat metastatic and recurrent cancer cells. Correct targeting of these systems offers several advantages, including; but not limited to: (i) selective internalization of therapeutic drugs by cancer cells, resulting in a lower risk of multidrug resistance (MDR) and fewer side effects in healthy tissues; (ii) the ability to pass the blood-brain barrier; and (iii) the ability to recognize, scan, and treat colon cancer cells that are metastatic, recurring, or linked to them [30].
Several clinical and preclinical studies have reported that the use of targeted nano-medicines to treat solid tumors is increasing [31]. Although targeted cancer therapy may seem simple, in fact, there is a significant challenge in this field due to the inherent complexities in the process of active targeting. For effective targeting, specific moieties must be placed on liposomes to achieve optimal affinity. Different reactive groups are used to modify the surface of liposomes depending on the intended purpose. In general, there are six methods for chemical functionalization: (a) cross-linking of imines with glutaraldehyde, (b and c) amide cross-linking of primary and free amine or carboxylic acid activated with p-nitrophenyl carbonyl, (d) using thiol and pyridyl dithiol groups with cross disulfide, (e) thiol maleimide click chemistry processes, and (f) hydrazone crosslinking of aldehyde and hydrazine groups [32].
The majority of research on medication targeting has relied on the use of certain ligands, including small molecules, peptides, monoclonal antibodies (mAbs), and aptamers. These ligands can directly bind to their receptors on or inside colon cancer or related cells. In addition, nanoliposomes can be directed to the vicinity of the tumor via a magnetic field or the acidic pH correlated with the tumor microenvironment or (TME) (Figure 1) [33].

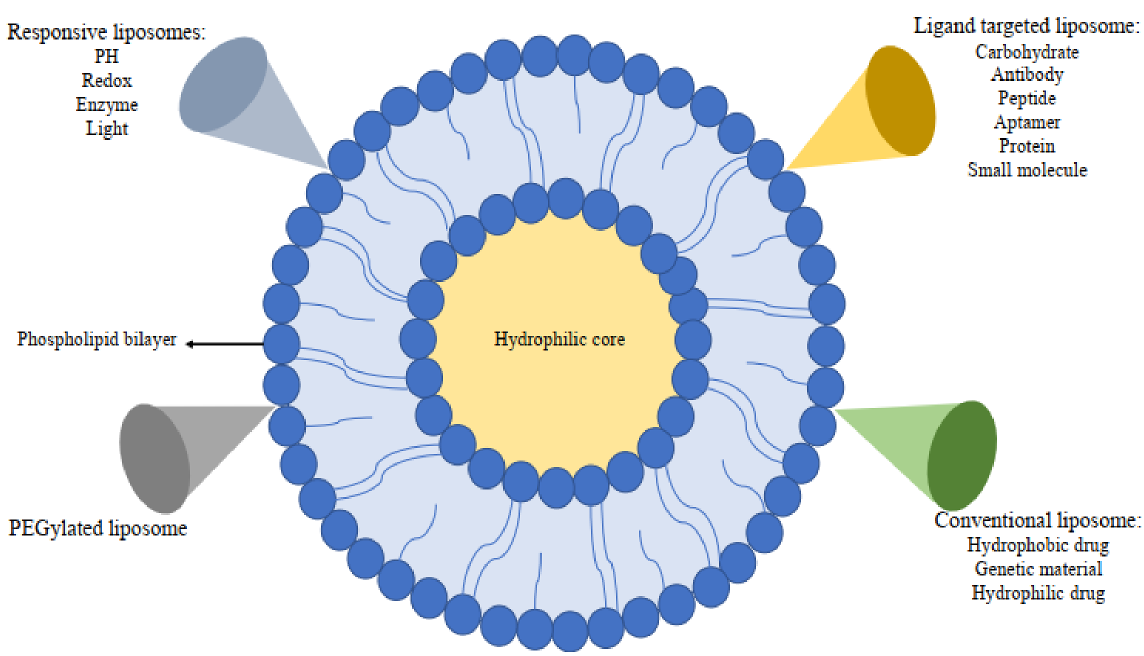

Fig. 1. Functionalized liposome delivery mechanisms for solid tumor therapy [33].

Types of drug-loaded nanoliposomes

According to recent studies, most of the new generation drugs that are used to treat diseases have the ability to provide accurate and targeted delivery systems [34]. According to the results published in Nature Nanotechnology, the use of drugs based on nanotechnology is increasing, of course, liposomes are the most common type of nanomaterials used as drug carriers due to their characteristics and advantages [35].

Sometimes, due to a series of limitations that some drugs may have individually in treatment, including neutralizing responses, overlapping pathways, cross-talk, etc., their combination with other drugs is used [36].

Nanoliposomes loaded with chemical drugs

Apigenin is a natural flavone that is being considered as a possible chemotherapeutic drug for the treatment of colon cancer [37]. For the effectiveness of this hydrophobic drug, a liposome carrier is used, which facilitates drug delivery [38]. The therapeutic effect of liposome containing apigenin is such that it stops the cell cycle in the G2/M phase [37]. 5-Fluorouracil (5-FU) is also a chemical that is used as an antitumor in the treatment of colon cancer [39]. The combination of 5-FU and apigenin via liposome carrier significantly increases the cytotoxic effect on CRC. Thus, it increases inhibition of angiogenesis, better reduction of cell proliferation and potential increase of apoptosis.

In general, it has been shown that the increase in the potential in vivo properties of this drug combination is due to the passive targeting activity of this carrier, and this drug can also be used in clinical cases [13].

In order to make 5-FU more effective and reduce its toxic effect, 5-FU is encapsulated in long-circulating liposomes (LCL-5-FU) and combined with liposomal prednisolone phosphate (LCL-PLP), which is a known anti-angiogenic compound against C26 colon cancer cells were investigated. Combined liposomal drug treatment in this case almost completely inhibits tumor growth, which is mostly related to the anti-inflammatory and anti-angiogenic effects of these compounds [40].

Considering the important role of folic acid in the body and the high expression of the folate receptor in some cancers, it is possible to use the high affinity of this receptor for folic acid in the colon tumor to direct anticancer drugs to the desired location [41]. Oxaliplatin is widely used to treat colon cancer. The anti-tumor effect of this substance is due to the inhibition of DNA replication and synthesis [42]. In a study the effect of liposomes conjugated with folic acid and containing Oxaliplatin enclosed with alginate beads and Eudragit-S-100, which is specifically degraded in the colon, was shown that this compound has the potential to target colon tumors [1].

High expression of indoleamine 2,3-dioxygenase 1 (IDO1) in tumor cells causes suppression of the immune system, which is also associated with poor prognosis in human colorectal cancer [43]. Therefore, the liposome containing Oxaliplatin (Oxa (IV)) and conjugated with alkylated phospholipid NLG-919 (aNLG) was used as an IDO1 inhibitor in the treatment of colon cancer. The aNLG/Oxa (IV)-Lip can cause the release of cytotoxic oxaliplatin into the cytosol and cause immunogenic cell death of cancer cells. The aNLG/Oxa (IV)-Lip in vivo showed that it has a longer circulation time and a strong antitumor effect, and also has a greater permeability in tumor CD8+ T cells [44].

Irinotecan hydrochloride (CPT-11) is a water-soluble drug that acts as an inhibitor of DNA topoisomerase I [45]. The combination of Oxaliplatin and CPT-11, with different functional mechanisms, causes the development of antitumor activity [46,47]. In addition, due to the presence of a hydrophilic core that can cause the encapsulation of hydrophilic drugs, liposome is used for the simultaneous transport of CPT-11 drug combination [48]. For this reason, in a study, Zhang et al put the combination of these two drugs into liposome and evaluated their effects in vitro and in vivo. The results of this study showed that liposome causes the accumulation of combined drugs in the tumor site compared to free drugs and has a greater anticancer effect [47].

One of the treatment methods and prevention of angiogenesis process (one of the basic processes of tumor growth and development) at the tumor site is the use of signaling pathway inhibitors, especially vascular endothelial growth factor 2 (VEGFR-2) [49–51].

Apatinib mesylate acts as a selective and strong inhibitor against VEGFR-2, which is also known as a strong antitumor by having anti-angiogenic activity, but due to its low bioavailability, poor solubility in water and low oral absorption, the use of this drug is limited [52]. Docetaxel (Taxotere®) is also used in the treatment of solid tumors due to its role in cell cycle disruption and apoptosis-like activity [53]. The combination of Apatinib and Docetaxel can act as a strong antitumor synergistic agent [54]. The simultaneous use of these two compounds in vitro inhibits cell proliferation and induces apoptosis of CT-26 cells, which indicates the anti-tumor and anti-angiogenesis activity of this medicinal compound [5].

By encapsulating doxorubicin in combination with fibrin gel and Apatinib in a self-synthesized Apatinib liposome (lipo-Apatinib), cellular uptake of doxorubicin increases in vitro. The combination of DOX-FG and Lipo-Apatinib significantly improves the antitumor effect in CRC. This drug combination successfully inhibits tumor proliferation and induces apoptosis [55].

PEG liposome containing Doxorubicin and curcumin enhances the antitumor effect on CT26 tumor cells. This anti-tumor effect depends on the inhibitory effect of this compound on most of the pre-tumor processes such as angiogenesis, inflammation, oxidative stress, invasion, resistance to apoptosis and downregulation of Th1/Th2 cells [56].

Nanoliposomes loaded with plant extracts

Although chemotherapy has been effective in improving the survival rate of patients with colorectal cancer, the continuous use of chemotherapy faces obstacles due to its resistance and adverse effects. So safe and natural alternative treatment methods are needed to reduce these long-term negativity consequences is necessary. Medicinal plants, which have inherent bioactive compounds, have shown significant apoptogenic and cytotoxic activity against a wide range of cancer types and thus are a useful alternative to conventional chemotherapy. According to studies, among these compounds, polyphenols such as curcumin, ellagic acid and gallic acid [57,58] have a preventive role against colon cancer.

Considering that the first anti-cancer drug was extracted from natural sources such as plant alkaloids, therefore, extensive attention was also paid to investigated the cytotoxicity of herbal drugs [57]. Favorable medicinal properties and extensive therapeutic indicators make the use of herbal medicines as anti-cancer agents [58]. Plants have various anticancer mechanisms, for example, they can suppress cancer proliferation, inhibit tumor cell growth, induce apoptosis, and inhibit angiogenesis. This variety of action mechanisms causes the treatment of different types of cancers such as breast, head and neck, etc. [59,60].

Plants usually contain secondary metabolites that have a wide range of different biological and medicinal activities, including antimicrobial, anti-inflammatory, antioxidant, cardioprotective, hypoglycemic, and anticancer properties [61–63].

Gallic acid (3,4,5-trihydroxybenzoic acid) (GA) and Quercetin (Qu) are phenolic compounds that have antioxidant, anti-inflammatory, analgesic, neuroprotective, anticancer and antidiabetic properties [64]. The possible antitumor effect of these two compounds seems to be inhibition of cell proliferation, induction of apoptosis, and protection of human cells against oxidative damage without negative effects on normal cells [65]. Nanoliposomes containing GA, Qu and the mixture of these two compounds together against breast, colorectal and lung cancer cells have shown that in vitro. The mixture of the two compounds as well as Qu does not cause any increase in cytotoxicity after loading into nanoliposomes, while which is a minor effect caused by GA after loading. Based on these observations, it can be concluded that nanoliposomes can increase or decrease the cytotoxic activity of bioactive agents, which depends on the physical and chemical properties of the loaded drug and the type of targeted cancer cells [66].

The extract of *Hypericum perforatum L.* (HP) as well as curcumin (CUR), which is obtained from the rhizome of turmeric (*Curcuma longa L.*), have several properties, including anti-inflammatory properties, antioxidant activities, anticancer, antiproliferative, cytotoxic, and they induce apoptosis, and for this reason, they are widely used in traditional medicine and even in food consumption [67,68]. HP and CUR have anticancer properties by activating apoptosis signal pathways, including caspase activation and cell cycle arrest, inhibition of metastasis and angiogenesis, suppression of proliferation, and modulation of cell signaling pathways [69,70]. In addition, based on the results of various studies, CUR may have a positive effect as an inhibitory agent against gastrointestinal cancers, including CRC [71]. In vitro, nanoliposomes containing both CUR/HP compounds have shown significant cytotoxic and pro-apoptotic activity against SW1116 and SW48 colon cancer cell lines. Based on this, the HP/CUR-Lip complex can be used as an effective method to achieve the synergistic effect of HP and CUR, and further induce apoptosis in the treatment of colorectal cancer [72].

Crocin is an unusual water-soluble carotenoid responsible for the crimson color of saffron. In a study of the effect of nanoliposome containing crocin on C26 colon carcinoma cells, considering the required dose (100 mg/kg), it showed that this nanoliposome composition has a high index and therapeutic effect for the treatment of colon cancer [73]. Crocin is an active medicinal compound that has the potential to inhibit tumorigenesis in all types of malignant cells in laboratory conditions [74]. For example, according to previous research, it has been determined that saffron is an inducer of tumor cell apoptosis and inhibits the proliferation of hepatocellular (HepG2) and cervical (HeLa) cancer cells [75].

Ginger contains many active compounds that cause its anti-inflammatory, antioxidant and anti-cancer effects [76]. The anticancer effect of ginger is caused by the induction of cancer cell death, stopping the cell cycle, inhibiting metastasis, and preventing angiogenesis [77]. The anti-tumor activity of ginger on gastrointestinal cancers occurs through the modulation of signaling molecules, inflammatory cytokines, caspase molecules and proteins involved in the regulation of cell growth [76]. It has been shown that pegylated nanoliposomes containing ginger at a dose of 100 mg/kg increase the expression of genes involved in the immune system, such as Bax and IFN-γ, in mouse models with colon cancer compared to ginger extract, also, the number of tumor-infiltrating lymphocytes (TILs) and CTLs (cytotoxic T cell lymphocyte) cell count in tumor tissue have been shown increases in this case. So, in this way, this compound can be used as an anti-colon cancer drug [78].

Nasturtium officinale, a perennial aquatic weed containing various bioactive components including phenolics and flavonoids, is considered as an important medicinal plant [79]. Flavonoid compounds increase the expression of p53, Bax and caspase-3 genes and cause anti-cancer effects [80]. Phenol-rich fractions (PRF) containing nanoliposomes from Nasturtium officinale at a concentration of 100 mg TPC/kg BW/day cause further improvement of gene expression in mouse models. The higher health promoting activity of nanoliposome-encapsulated PRF could be due to its increased intestinal absorption, bioavailability, bioavailability and bioactivity. In conclusion, nanoliposome-encapsulated PRF can be used as a promising anticancer agent against colorectal cancer [81].

Antibody-targeted nanoliposomes

Recently, as a result of the rising prevalence of colorectal cancer, targeted treatments are widely used to treat this disease [82]. Meanwhile, monoclonal antibodies such as cetuximab (CTX) and panitumumab target and deactivate specific signaling pathways that plays a key role in the development and progression of this cancer through Epidermal Growth Factor Receptor (EGFR) [83]. Long-term use of non-steroidal anti-inflammatory drugs (NSAIDs) reduces the risk of various types of cancer [84].

Celecoxib (CLX) can selectively inhibit cyclooxygenase-2 (COX-2) activity [85]. COX-2 enzyme has a very high expression in various tumors, including colon cancer [86]. COX-2 (or prostaglandin endoperoxidase synthase 2) is regulated in response to inflammatory factors, growth, and tumor stimuli [87]. EGFR has a very high expression in a wide range of solid tumors [88]. CTX is a chimeric monoclonal antibody that acts selectively against EGFR [89]. Targeting both EGFR and COX-2 can increase their synergistic effect together. EGFR-targeted immunoliposomes loaded with CLX have a significant toxic effect on cancer cells, especially cells that overexpress EGFR [90].

Oxaliplatin (L-OH), a platinum derivative, is currently used in combination with CTX to treat CRC with high EGFR expression. By encapsulating L-OH in liposomes and improving its pharmacokinetic properties, selective accumulation and targeted delivery of the drug to the tumor site can be achieved [91]. The effect of L-OH liposomes containing complete fragments of CTX or CTX-Fab on the expression of different levels of EGFR in four CRC cell lines showed that the use of CTX-Fab provides targeted L-OH liposomes that provide greater drug delivery and efficacy. It has anti-tumor properties compared to liposomes containing CTX and non-targeted liposomes [92].

Integrinβ6 (ITGβ6) is a protein that is highly expressed in the epithelium of malignant colon cancer cells, but is not normally found in the epithelium of normal cells, so it is related to the progression, metastasis and chemotherapy resistance of colon cancer [93]. The effect of PEGylated immunoliposomes containing 5-FU and also targeted with monoclonal antibody E7P6 which recognizes the extracellular domain of ITGβ6 showed, that immunoliposomes targeted for ITGβ6 have high intracellular uptake, and the growth of HT-29 and SW480b6 cell lines (colon cancer cell lines) almost to more than 90%. Additionally, cell apoptosis was increased approximately 1.5-fold by targeted immunoliposomes loaded with 5-FU. Therefore, targeted immunoliposomes against ITGβ6 are very efficient for targeted drug delivery in colon cancer and can be considered as a new and promising strategy for clinical treatment [94].

Frizzled proteins (FZDs) are cell surface receptors that are highly expressed in CRC cells [95]. Several studies have proven that FZDs plays an important role in various functions of cancer cells, including increasing their proliferation, migration, invasion, angiogenesis, and chemical resistance [96–100]. Among these FZD proteins, FZD10 is used as one of the promising receptors for the development of targeted CRC therapy due to the fact that it is expressed only in cancer cells and not in adjacent normal cells [101]. Scavo et al evaluated the anticancer effect of immunoliposomes loaded with 5-FU, conjugated with an antibody against FZD10 (anti-FZD10/5-FU/LPs), on two different CRC cell lines. The results of their work showed that the cytotoxic activity of 5-FU in the case of anti-FZD10/5-FU/LPs increases even at its lowest concentration [102].

MCC-465 is an immunoliposome-encapsulated doxorubicin. Pegylated liposome of doxorubicin (PLD) and non-targeted MCC-465 have no significant antitumor activity against colon cancer cell lines, however, when conjugated with monoclonal antibody, GAH, show better antitumor effects against colon cancer cell lines [103].

Aptamer functionalized nanoliposomes

Aptamers are single-stranded oligonucleotides that are identified through the systematic evolution of ligands by exponential enrichment (SELEX) process, and thus selectively bind to target molecules [104]. Preparation of aptamers is a very simple process [105]. They cause not immunogenicity in the human body and can be gradually decomposed and eliminated by nucleases, thus causing minimal toxicity [106].

Recently, among other methods of applying liposomes and targeted drug delivery systems, aptamers are widely used as effective targeting ligands [107].

Liposomes containing 5-FU and targeting with anti-nucleolin aptamer (AS1411) as ligand and coated with alginate/chitosan PEC have been investigated as a promising method for the treatment of colon cancer. Based on MTT cytotoxicity results on HT-29 cells, liposomes conjugated with aptamer significantly increased cell death compared to liposomes without aptamer and free drug. These nanoliposomal carriers are suitable for drug delivery to the target tissue and have a positive effect on the colon cancer treatment process [108].

Anti-nucleolin aptamer AS1411 (Apt-Lip-GEF) is widely used to target liposomes [109,110]. Nanoliposomes carrying gefitinib (GEF) targeted with anti-nucleolin aptamer AS1411 (Apt-Lip-) showed higher antiproliferative activity in CT26 tumor cells than HEK293 cells, and it was also observed in the colorectal tumor model that this compound was effectively compared to the form the release of GEF reduces the tumor cells growth [111].

Nanoparticles based on cationic liposome loaded with MiR-139-5P and surface modified with anti-epithelial cell adhesion molecule (EPCAM) aptamer are used for targeted treatment of CRC. These targeted nanoparticles inhibit the growth of HCT8 cells in vitro and suppress the colorectal tumor model. Therefore, this MANPs carrier can be used as an effective and suitable carrier to deliver the desired therapeutic miRNA to the CRC tumor site [112]. MiR-139-5P inhibits CRC invasion and migration by targeting Notch1 and being downregulated [113].

The results of investigating nanoliposome containing DOX and functionalized with anti-EpCAM aptamer on C26 colon cancer cell line have shown that the performance of this nanoliposome in cancer treatment is promising and also needs further investigation [114].

Magneto liposomes (MLPs)

Depending on the desired goals and specific conditions, researchers have developed new liposomes for smart therapy in the human body that respond to environmental stimuli such as temperature [115], pH [116], light [117], magnetic field [118,119], etc. they answer These specific environmental stimuli are used as the driving force for drug release based on the interaction between stimuli and liposomes [120]. Among these stimuli, magnetic stimulation has become one of the most potential strategies as release and targeting stimuli [121].

MLPs have many advantages in cancer treatment and diagnosis, including the delivery of antitumor drugs, hyperthermia therapy, diagnosis using imaging techniques, and even cell migration [122].

The MTT assay of magnetic liposomes loaded with DOX showed that these drug carriers have no cytotoxicity to L-929 cells, so this combination has excellent biocompatibility and causes a higher percentage of cell death on CT-26 and has a better effect compared to hyperthermia or chemotherapy alone. Therefore, the synergistic effects between chemotherapy and hyperthermia increase the ability to kill cancer cells [123].

Magnetic nanocarriers containing DOX and targeted with atherosclerotic plaque-specific peptide-1 (AP-1) efficiently bind to colon cancer cells (CT26-IL4Rα) and thereby induce tumor-targeted selection. This combination has great potential for use in the treatment of colon cancer [124].

Apart from the many advantages that MLPs have, biocompatibility and high performance after entering the cell are essential for their successful application [125]. By examining MLPs based on maghemite nanoparticles (γ-Fe_2O_3) on tumor and non-tumor colon cell lines, it was determined that these MLPs, based on their physical, chemical and biological properties, can be used effectively treat colon cancer [122]. Also, by examining the cytotoxicity of MLPs loaded with 5-FU in colon fibroblast cell lines CCD-18 and human colon cancer T-84, the absence of cytotoxicity was reported in these cells. If 5-FU is placed in the matrix of nanoparticles, more amounts of the drug can be loaded and its release will be more stable. Therefore, it was found that MLPs have important properties, including magnetically targeted delivery, hyperthermia inducibility, high 5-FU loading capacity, and hyperthermia-induced wide drug release, which indicate their potential for combination therapy against colon cancer [126].

pH-responsive liposomes

pH-sensitive liposomes are a type of liposomes that are stable at physiological pH (pH 7.4), but undergo changes in acidic conditions (such as tumor environment) and can release their contents [119]. According to the results obtained from the various reports, these are more efficient in delivering anticancer drugs than conventional or long-circulating liposomes due to their fusion properties [127].

Irinotecan (IRN) is a synthetic derivative of camptothecin that acts as a topoisomerase I inhibitor. IRN is used to treat colon cancer, which also causes serious side effects, such as diarrhea and myelocyte suppression [128]. The results of the investigation of a pH-sensitive folate coating liposome containing IRN in the treatment of colon tumors in a mouse model, showed a pH-dependent method with a long-term and sustained release system, and a high capacity of intracellular drug delivery. Extensive necrosis occurred in the tumor tissue in the areas containing IRN, and better antitumor activity was shown. Thus, this type of colorectal cancer carrier can potentially be an effective alternative to conventional treatment [129].

Release results of liposomal nanoparticles containing pH-sensitive 5-FU (pHLNps-5-FU) showed that this compound has the highest release rate of 5-FU at pH 3.8, almost twice that of pH 7.4. As a result, pHLNp3-5-FU can be a potential candidate for the treatment of colorectal cancer [130].

One of the effective methods for colon tumor treatment is liposomes coated with pH-sensitive polymer and containing biologically active compounds. For example, liposomes loaded with Betulinic acid and coated with pH-sensitive polymer Eudragit S100 (pH-BA-LP) have been shown that significantly inhibit tumor proliferation and cell migration in colorectal cancer. pH-BA-LP increases NK cells and CD3+ cells in tumor tissues, and it was also found that it can exert an antitumor effect by enhancing autoimmunity [131].

The main obstacles related to the targeted release method for colon cancer

Active targeting techniques minimize off-target effects and enable the targeted delivery of therapeutic medicines to CRC cells [132].

Despite the new strategies based on the use of nanoliposomes in the targeted treatment of CRC at different clinical levels, there are still some challenges, such as improving the localization, biodistribution, biocompatibility and efficiency of these nanopharmaceutical systems in vivo, for the accurate diagnosis and treatment of cancer, as well. are left Among the new nanotechnology platforms, liposome-based therapies have emerged as one of the most promising nanotools for the treatment of various tumors, including colorectal cancer [133].

Another important challenge in targeted drug delivery is tumor heterogeneity in different stages of the disease, which can also limit the effectiveness of treatment results. This tumor heterogeneity causes variations in the molecular profile and uneven expression of target receptors in various parts of the colorectal tissue, including the proximal colon, distal colon, and rectum [134].

There are several challenges related to the design of nanocarriers. These challenges include the following two groups: 1) the laboratory procedure used to manufacture nanocarriers, which has a big impact on their physicochemical characteristics as size, shape, type of surface coating, and drug loading capability. 2) difficulties with nanocarriers' in vivo behavior, such as biodistribution, toxicity, anticancer agent release, targeted medication delivery from receptor binding sites, and the makeup of the tumor microenvironment [132].

Another problem is to adjust the surface charge of nanocarriers and their toxicity potential, so the toxicity of nanocarriers is a serious factor that should be given special attention before using them in drug delivery and clinical applications [135].

CONCLUSION

Functionalized liposomes represent a promising advancement in colorectal cancer therapy, offering enhanced drug delivery, tumor specificity, and reduced systemic toxicity. By leveraging surface modifications, targeted ligands, and encapsulation strategies, these nanocarriers improve therapeutic efficacy while minimizing adverse effects, paving the way for more effective and personalized treatment approaches. Further research and clinical validation are essential to optimize their application and realize their full potential in colorectal cancer management. In future studies, it is possible to further investigate the challenges and obstacles in the development of drug delivery based on nanoliposomes technology in the treatment of colon cancer.

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