

Comparison of cytocompatibility and anticancer properties of traditional and green chemistry-synthesized tellurium nanowires

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Background: Traditional physicochemical approaches for the synthesis of compounds, drugs, and nanostructures developed as potential solutions for antimicrobial resistance or against cancer treatment are, for the most part, facile and straightforward. Nevertheless, these approaches have several limitations, such as the use of toxic chemicals and production of toxic by-products with limited biocompatibility. Therefore, new methods are needed to address these limitations, and green chemistry offers a suitable and novel answer, with the safe and environmentally friendly design, manufacturing, and use of minimally toxic chemicals. Green chemistry approaches are especially useful for the generation of metallic nanoparticles or nanometric structures that can effectively and efficiently address health care concerns.

Objective: Here, tellurium (Te) nanowires were synthesized using a novel green chemistry approach, and their structures and cytocompatibility were evaluated.

Method: An easy and straightforward hydrothermal method was employed, and the Te nanowires were characterized using transmission electron microscopy, scanning electron microscopy, energy-dispersive X-ray spectroscopy, Fourier-transform infrared spectroscopy, X-ray powder diffraction, X-ray photoelectron spectroscopy, and optical microscopy for morphology, size, and chemistry. Cytotoxicity tests were performed with human dermal fibroblasts and human melanoma cells (to assess anticancer properties). The results showed that a treatment with Te nanowires at concentrations between 5 and 100 µg/mL improved the proliferation of healthy cells and decreased cancerous cell growth over a 5-day period. Most importantly, the green chemistry -synthesized Te nanowires outperformed those produced by traditional synthetic chemical methods.

Conclusion: This study suggests that green chemistry approaches for producing Te nanostructures may not only reduce adverse environmental effects resulting from traditional synthetic chemistry methods, but also be more effective in numerous health care applications.

Keywords: nanowires, tellurium, biocompatibility, anticancer, green chemistry

Introduction

In a world of constant duality where the population density increases as dramatically as natural resources disappear, there are some concerns that arise from the increased use of synthetic chemicals in society. Traditional chemistry has undoubtedly enhanced the quality of life, but at a price of threatening the environment and, in some cases, human health. Chemical processes, to a certain extent, are responsible for the contamination of all the known ecosystems all over the world.¹⁻³

This is especially true for nanotechnology or nanomaterials. Nanotechnology produces materials at a small scale that have novel properties much different from

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those of the bulk materials. In recent years, the increased implementation of nanotechnology has provided solutions for specific problems including antimicrobial resistance,⁴⁻⁶ cancer treatments,⁷⁻⁹ bioimaging,^{10,11} and drug delivery.¹²⁻¹⁴ The traditional physicochemical approaches for the synthesis of nanomaterials involve easy and straightforward protocols, using available techniques such as laser ablation^{15,16} or chemical vapor deposition.^{17,18} Nevertheless, there is a cost associated with these synthesis methods, such as the production of toxic by-products, the use of harsh chemicals, and lack of biocompatibility of the nanomaterials, if not pure.

Another worldwide concern is cancer, which is defined as the uncontrollable growth of cells and the abnormal behavior of cells.¹⁹⁻²¹ It is stated to be the second cause of death in the USA, with >1.7 million estimated cases each year.^{22,23} There are potential known cancer treatments such as chemotherapy,²⁴ radiotherapy,²⁵ and surgery;²⁶ nevertheless, they present a huge variety of side effects including fatigue, anemia, and death.^{27,28} Therefore, there is a need to find alternative treatments that avoid these limitations. Here, nanotechnology – with the synthesis of different nanostructures – can be considered a solution, as cancer cells do not have the mechanism to eliminate some metallic structures, unlike normal cells that have this ability, leading to selective cancer cell death while maintaining the viability of healthy cells.^{29,30}

Therefore, new methods are needed, and green chemistry offers a suitable and novel answer, with the safe and environmentally friendly design, manufacturing, and use of chemical products that do not produce toxic and harsh by-products.^{31,32}

Green chemistry is considered an alternative approach in that it combines materials coming from synthetic chemistry and nature to overcome issues from traditional synthesis. Green chemistry approaches are especially useful for the generation of metallic nanoparticles (NPs), which have nanometric structures that effectively and efficiently address concerns in both health care and industrial applications.³³⁻³⁵ Therefore, these approaches offer the chance to use living organisms (such as bacteria,³⁶ human cells,^{37,38} fungi,³⁹ or plants^{40,41}) as well as dietary and organic natural compounds (such as coffee,⁴² tea, or honey extracts⁴³) or biological waste materials produced from industrial alimentary plants,⁴⁴ to naturally synthesize NPs. These nanostructures exhibit antibacterial and/or anticancer properties and can be used as drug delivery carriers and in industrial applications. These approaches are cost-effective and environmentally friendly, using standard reaction parameters in redox-reduction or

hydrothermal techniques to generate specifically metallic nanostructures with a high throughput.

Several studies have implemented green nanotechnology for the synthesis of nanostructures to exhibit low cytotoxicity to human cells. For instance, garlic extract has been used to synthesize silver NPs with no cytotoxicity for fibroblasts,⁴⁵ and Mukherjee et al used gold NPs synthesized using plant leaves to show both biocompatibility and anticancer properties against breast cancer cells.⁴⁶ With such a promise shown in previous studies, there has been an increased interest in the generation of green NPs that also have anticancer properties. For example, copper oxide NPs made by Rehana et al⁴⁷ and silver NPs produced by Kelkawi et al⁴⁸ that were both synthesized using different plant extracts showed attractive anticancer properties.

There are also plenty of studies that compare the effect of the NP synthesis method (ie, green or traditional synthetic chemistry) on the anticancer, antimicrobial, and biocompatibility properties. These studies have shown continuously that NPs made using green approaches are nontoxic or less toxic than those produced by traditional synthetic processes. For example, nickel NPs made from root extracts were nontoxic to mammalian cells compared with the same ones made using conventional chemistry.⁴⁹

During the past years, as mentioned earlier, different methodologies have been studied to produce NPs. For instance, Liu et al prepared tellurium (Te) nanotubes with a controllable size and morphology by using a microwave approach and monosaccharides as reducing agents.⁵⁰ Another approach is via hydrothermal reactions, which use high pressure and temperature in addition to water and the organic compound to obtain metallic NPs.^{51,52} Different materials have been reported to work, such as platinum⁵³ or titanium oxide⁵⁴ NPs for the catalytic industry, and Te, a rare metalloid, is also considered a good candidate.^{55,56} Te nanowires (TeNWs) have been synthesized by employing hydrothermal reactions mainly for semiconductor and catalytic applications;^{57,58} however, their biomedical applications are largely unknown, as Te – even has similarities with oxygen, selenium, or sulfur – is not a trace element, and it has not been considered for biochemical interests. Nevertheless, some compounds of Te including tellurides (Te^{2-}) and tellurites (TeO_3^{2-}) are known to inhibit different proteins and enzymes and are capable of killing microorganisms such as bacteria and plasmodia. Besides, they can induce apoptosis in certain cancer cells.⁵⁹ As Sredni mentioned, two Te compounds – ammonium trichloro(dioxoethylene-O,O')tellurate (AS101) and octa-O-bis-(R,R)-tartarate ditellurane – have been reported as

anticancer agents by modulating the enzymatic activity and inhibiting tumor proliferation.⁶⁰

As a consequence, Te has been considered a good candidate for biological applications. There are only a few reports on their antibacterial properties against *Escherichia coli* and *Staphylococcus aureus* showing much promise, using TeNWs nanowires made from the fungus *Aspergillus welwitschiae*⁶¹ and a combination of Te and Au nanowires over a carbon surface using a chemical approach with hydrazine.⁶² Low cytotoxicity on mammalian epithelial cells was reported for the latter.

In this research, for the first time, TeNWs were synthesized using both traditional synthetic and green approaches, and their properties were compared. The two ways to synthesize such nanowires were as follows: 1) a clean (green) and cost-effective hydrothermal synthesis employing Te salt and starch and 2) a traditional approach using metallic salt and chemical synthetic reducing agents such as ammonia (NH₃) and hydrazine. Both methods were similar in subsequent reaction conditions. After purification, the nanostructures were characterized using transmission electron microscopy (TEM), scanning electron microscopy (SEM), energy-dispersive X-ray (EDX) spectroscopy, Fourier transform infrared spectroscopy (FT-IR), X-ray powder diffraction (XRD), X-ray photoelectron spectroscopy (XPS), and optical microscopy regarding morphology, size, and composition. Cytocompatibility and anticancer properties of the chemically synthesized TeNWs (CHEM-TeNWs) and green-synthesized TeNWs (GREEN-TeNWs) were compared. Cytotoxicity assays were performed over 5 days with both human dermal fibroblast (HDF) cells and human melanoma cancer cells. The results showed much promise for the further study of GREEN-TeNWs compared with CHEM-TeNWs for numerous medical applications.

Materials and methods

TeNW synthesis and purification

Following a variation of the protocol described by Hong et al,⁵⁵ in a typical process of integration, sodium tellurite (Na₂TeO₃; Sigma-Aldrich, St Louis, MO, USA) was mixed with 1 g of polyvinylpyrrolidone (PVP; Sigma-Aldrich) and dissolved in 30 mL of deionized water. Next, 1.5 mL of hydrazine hydrate (Sigma-Aldrich) and 3 mL of an NH₃ (Sigma-Aldrich) solution (25% w/w) were added. The solution was stirred at a room temperature, then transferred into a teflon-lined stainless steel reactor and placed into an oven at 180°C for 4 hours. After the reaction, the mixture was allowed to cool down at a room temperature.

For the green synthesis route, the procedure was followed as described by Lu et al.⁵⁶ with some modifications. Briefly, telluric acid (H₂TeO₄; Sigma-Aldrich) was mixed with 0.15 g of a starch (Sigma-Aldrich) solution in deionized water. Then, the mixture was transferred into a teflon-lined stainless steel reactor and placed into an oven at 160°C for 15 hours. The mixture was then allowed to cool down at a room temperature.

At a room temperature, the final products from both synthesis methods were purified using the same protocol. The nanowire solutions were centrifuged at 10,000 rpm for 20 minutes, and the pellet was subsequently washed twice with water and centrifuged again at the same rate and time. Finally, the precipitate was resuspended in 35 mL of deionized water. The resulting solution containing the nanowires was transferred into a 20-mL glass vial, which was then placed in a freezer at -80°C for 4 hours and lyophilized overnight. The final powder was weighed and resuspended in a suitable amount of deionized and autoclaved water to reach the final concentration needed for further experiments.

Instruments and characterization

A Heratherm™ General Protocol Oven (Thermo Fisher Scientific, Waltham, MA, USA) was used to produce the hydrothermal reaction in both chemical synthetic and green methodologies. An Eppendorf™ Model 5804-R Centrifuge was used for the centrifugation of the samples. A FreeZone Plus 2.5-L Cascade Console Freeze Dry System was used to purify the samples and to obtain the final TeNW structures.

TeNWs prepared by both chemical synthetic and green approaches were properly characterized using a JEM-1010 transmission electron microscope (JEOL USA Inc., Peabody, MA, USA). For sample preparation, purified nanostructures were air-dried on 300-mesh copper-coated carbon grids (Electron Microscopy Sciences, Hatfield, PA, USA). The samples were then imaged up to an 80,000× magnification with an accelerating voltage of 80.0 kV.

EDX spectroscopy analysis was performed using a dedicated EDX detector coupled with a Hitachi S-4800 scanning electron microscope. TeNW samples were affixed to 300-mesh copper-coated carbon grids and placed into an aluminum pin mount. An accelerating voltage of 10.0 kV was used to obtain an elemental spectrum for the NPs.

FT-IR spectra were recorded using a PerkinElmer Spectrum 400 FT-IR/FT-near infrared in attenuated total reflectance mode. For FT-IR spectroscopy measurements, 5 µg of the dried sample was used.

Powder XRD patterns were obtained using a Rigaku Miniflex 600 (Rigaku Co. Tokyo, Japan) operating at a voltage of 40 kV, a current of 15 mA, and a Cu-K α radiation of 1.542 Å. All XRD patterns were recorded at a room temperature with a step width of 0.05 (2) and a scan speed of 0.2°/min. The samples were used from the powder obtained after the purification process.

In the XPS, drops of both compounds dispersed in water were deposited on clean copper substrates for sample preparation. After water evaporation, the samples were loaded in a vacuum load lock chamber and then transferred to the XPS ultra-high vacuum chamber with a base pressure of 10⁻¹⁰ mbar. The XPS chamber is equipped with a hemispherical electron energy analyzer (SPECS Phoibos 100 spectrometer, Berlin, Germany) and an Mg-K α (1,253.6 eV) X-ray source. The angle between the hemispherical analyzer and the plane of the surface was kept at 60°. Wide scan spectra were recorded using an energy step of 0.5 eV and a pass energy of 40 eV, while specific core level spectra (Te 3d, O 1s, and C 1s) were recorded using an energy step of 0.1 eV and a pass energy of 20 eV. The absolute binding energies of the photoelectron spectra were determined by referencing to the Te 3d 5/2 metallic core level at 573 eV.⁶³ Data processing was performed with CasaXPS software (Casa software Ltd., Cheshire, UK). The contributions of the Mg-K α satellite lines were subtracted.

Optical microscopy analysis was done on a phase contrast mode using an Axio Observer Z1 Inverted Fluorescence Microscope (Carl Zeiss, Oberkochen, Germany). For sample preparation, cells were grown on a 6-well plate with the presence of different GREEN-TeNWs and CHEM-TeNWs for 1, 3, and 5 days. Images were taken at these time points.

In vitro cytotoxicity assays with TeNWs

Cytotoxicity assays were performed with primary HDF cells (human skin fibroblast/human skin cells, strain CCL-110; American Type Culture Collection® [ATCC®], Manassas, VA, USA) and human melanoma cells (Human Malignant Melanoma (A375), strain CRL-1619; ATCC®). The cells were cultured in DMEM (Thermo Fisher Scientific), supplemented with 10% FBS (ATCC® 30–2020™) and 1% penicillin/streptomycin (Thermo Fisher Scientific). MTS assays (CellTiter 96® Aqueous One Solution Cell Proliferation Assay; Promega, Madison, WI, USA) were carried out to assess cytotoxicity. The cells were seeded onto tissue-culture-treated 96-well plates (Thermo Fisher Scientific) at a final concentration of 5,000 cells per well in 100 µL of cell culture medium. An incubation period of 24 hours at 37°C in a humidified incubator with 5% carbon dioxide was employed.

The culture medium was then replaced with 100 µL of fresh cell culture medium containing concentrations from 5 to 100 µg/mL of either CHEM-TeNWs or GREEN-TeNWs.

The cells were cultured for three different periods of time to compare the effects of the nanostructures on the cells after days 1, 3, and 5 following exposure.

The cells were washed with PBS, and the original media were replaced with 100 µL of the MTS solution (prepared using a mixing ratio of 1:5 of MTS/medium). After the addition of the solution, the 96-well plate was incubated for 4 hours in the incubator to allow for a color change. Then, the absorbance was measured at 490 nm on an absorbance plate reader (SpectraMAX® M3; Molecular Devices, San Jose, CA) for cell viability after exposure to the TeNWs. Cell viability was calculated by dividing the average absorbance obtained for each sample by that of the control sample and then multiplied by 100. Controls containing cells and media, only media and nanowires in media, were also added in the 96-well plate to identify the healthy growth of cells without nanowires and to determine the absorbance of both the media and the nanowires.

Statistical analysis

All experiments were repeated in triplicate (N=3) to ensure the reliability of the results. Statistical significance was assessed using Student's *t*-tests, with *P*<0.05 being statistically significant. The results are displayed as mean ± SD.

Results and discussion

Synthesis of green biogenic TeNWs

The hydrothermal synthesis of TeNWs was successfully completed using both chemical and green synthesis protocols. Table 1 shows the comparison between the methods.

One of the most remarkable differences between the two synthesis methods is the relative cost and quantity of the reducing agents needed to reduce ionic Te to elemental Te. On one hand, CHEM-TeNWs were generated in an aqueous solution with the presence of two reducing agents (hydrazine and NH₃) and PVP as stabilizing and structure-directing agent. Liu et al⁶⁴ found that PVP has a steric effect

Table 1 Synthesis conditions of the protocols used to prepare TeNWs

Reaction features	CHEM-TeNWs	GREEN-TeNWs
Reducing agents	NH ₃ /N ₂ H ₄	Starch
Conditions	180°C/4 hours	160°C/15 hours

Abbreviations: CHEM-TeNWs, chemically synthesized TeNWs; GREEN-TeNWs, green-synthesized TeNWs; TeNWs, tellurium nanowires.

on the growth of Te along the [0001] direction. On the other hand, GREEN-TeNWs were generated under the action of starch as unique reducing and stabilizing agent, which makes the synthetic approach cheaper and more environmentally-friendly than the one followed for the production of CHEM-TeNWs.

In the chemical synthesis, using hydrazine and NH_3 raises a huge safety concern when performing this process, as both are flammable, extremely toxic, and hazardous. Hydrazine in particular produces explosive vapors/air mixtures at about 38°C . Besides, it is corrosive to metals and skin and a real threat to the environment. Face shields and full-face respirators are needed to work with this chemical. PVP is however a water-soluble polymer that contributes to the formation of the nanostructures, and it is US Food and Drug Administration-approved.

On the other hand, the green synthetic approach needs only starch that is clearly a safe, naturally occurring reducing and stabilizing agent. This polymeric carbohydrate consists of a large number of glucose units that can reduce the Te ions to their elemental form. Therefore, because no additional agent is needed, this method holds advantages over the chemical synthesis method in terms of both cost and safety. Another concern to note is the production of toxic by-products. While waste produced from CHEM-TeNWs synthesis should be considered hazardous, the generation of reaction-derived products from the green synthesis process developed should not be viewed as an environmental threat.

Regarding the time for the reactions, the chemical synthesis of TeNWs took 4 hours at 160°C , while the green process took 15 hours at 180°C . This extra time can be explained by the reducing power of starch, which is lower than when using hydrazine and NH_3 ; however, considering the hazards of the chemicals and by-products of the chemical synthesis approach, the green methodology still has plenty of advantages such as being more economical and easy and following a straightforward hydrothermal synthesis method. Nevertheless, the green synthetic approach employed can be made quicker since the time used for the growth of the nanowires can be reduced to a couple of hours. It was hypothesized that the density of wires would be less than that using 15 hours; however, this is a hypothesis that needs further development.

Moreover, in the control experiment, a colorless solution was obtained in comparison with the dark one of both GREEN-TeNWs and CHEM-TeNWs (Figure 1) after the reaction process.

The control experiment was also characterized with TEM, and no nanostructures were found; therefore, no nanowires were obtained without the use of starch. Consequently, the



Figure 1 Solutions of GREEN-TeNWs after the reaction. The colorless solution without starch (left) and dark solution containing starch (right).

Abbreviation: GREEN-TeNWs, green-synthesized tellurium nanowires.

role of starch is crucial to reduce the metal and obtain the nanostructures.

Characterization

Morphological characterization was completed for both of the synthesis approaches with size and coating characteristics reported in Table 2.

Specifically, CHEM-TeNWs (Figure 2A and B) had an average diameter of 30 nm with a length of several micrometers. The wires showed a low degree of aggregation. On the other hand, GREEN-TeNWs (Figure 2C and D) showed an average diameter of about 20 nm with a similar length. The peculiarity of these structures was due to their morphology. It seemed that nanowires started growing from a particular point, and they extended as far as they could. The main trunk was divided into several smaller sections at the end of the structure as ramifications, which produced branches that grew alongside one another.

SEM characterization was performed on the GREEN-TeNWs (Figure 3C and D). The wires started growing from a cluster and extended for several micrometers, with a star-shaped uniform structure that was difficult to observe when the clusters were close to one another.

Table 2 Data from transmission electron microscopy for size and coating

Structures	CHEM-TeNWs	GREEN-TeNWs
Length	Several microns	Several microns
Width	32 ± 11 nm	25 ± 8 nm
Coating	No	Yes

Abbreviations: CHEM-TeNWs, chemically synthesized TeNWs; GREEN-TeNWs, green-synthesized TeNWs; TeNWs, tellurium nanowires.

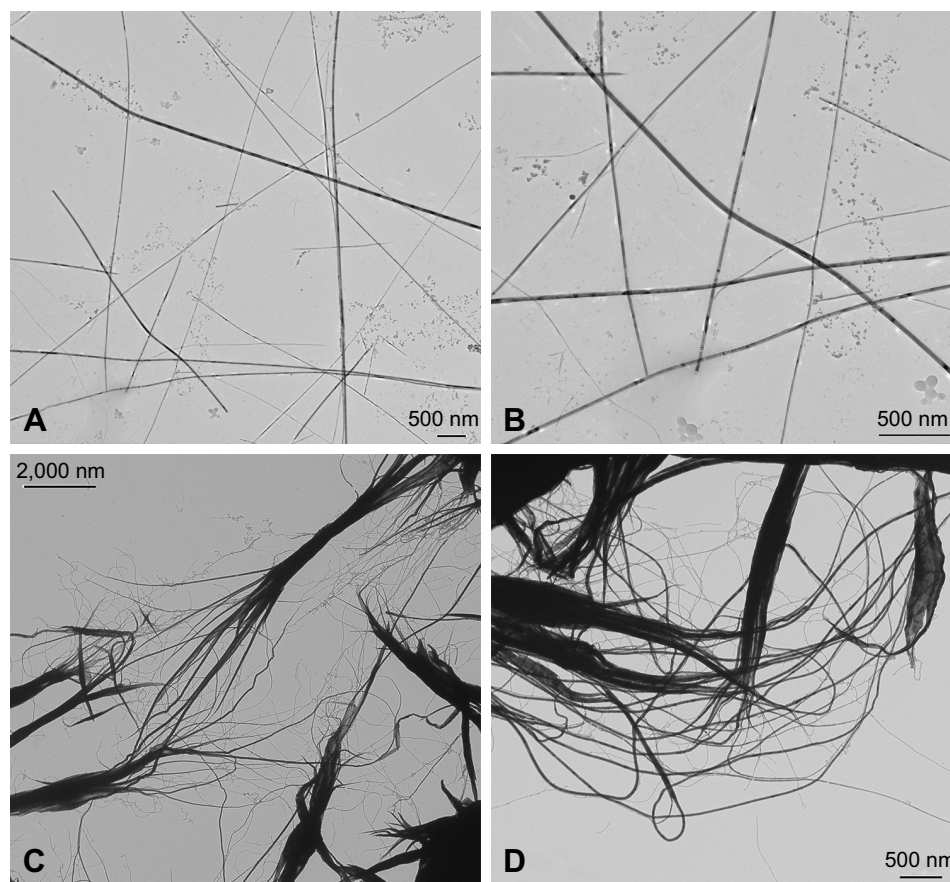


Figure 2 Transmission electron microscopy images of TeNWs. CHEM-TeNWs with a low degree of aggregation were found dispersed within the solution (**A**) and (**B**). GREEN-TeNWs (**C** and **D**) showed a higher degree of aggregation, and the presence of an organic coating was observed.

Abbreviations: CHEM-TeNWs, chemically synthesized TeNWs; GREEN-TeNWs, green-synthesized TeNWs; TeNWs, tellurium nanowires.

When CHEM-TeNWs were observed, the structures were found to grow on the top of each other generating a cluster that could affect cell viability (Figure 3A). Besides, different morphologies (Figure 3B) – crystals, nanowires (NWs) with variable widths and irregular structures – were found in solution which can lead to potential distinct performance regarding their biomedical applications.

It has been hypothesized that the differences between both structures came from the presence of starch. This polymer is known to have ramifications, and it has been elucidated that TeNW grow following the template of starch. Moreover, the uniformity of the GREEN-TeNWs morphology is thought to enhance their action in anticancer and biocompatibility properties in comparison with the chemically synthesized products.

EDX spectroscopy measurements were completed for both the chemically synthesized and green-synthesized nanostructures. For CHEM-TeNWs (Figure 4A), EDX spectroscopy analysis showed that the electron-dense nanowires had specific Te absorption peaks. For GREEN-TeNWs, the peaks for Te were higher due to the higher concentration of Te within

the sample (Figure 4B). When the analysis focused on the surrounding areas of the nanostructures, the carbon peak was significantly raised compared with the measurement of the Te metallic core. This, aside from the absence of a Te peak, indicated an organic composition of the coating (Figure 4C).

In Figure 5, we compare the FT-IR spectra of CHEM-TeNWs, GREEN-TeNWs, and potato starch. The CHEM-TeNWs and GREEN-TeNWs samples show absorption bands of Te oxide at around 765 and 585 cm^{-1} , which can be related to the symmetrical equatorial and asymmetrical axial stretching frequencies of the Te–O bond, respectively.^{65,66} The FT-IR spectrum of GREEN-TeNWs presents a vibrational band at around $3,300\text{ cm}^{-1}$ related to the O–H stretching mode of starch. The vibrational bands at the region of $1,300$ – $1,400\text{ cm}^{-1}$ are due to C–O–H bending and CH_2 twisting of the starch structure.⁶⁷

Figure 6 shows the XRD patterns for CHEM-TeNWs and GREEN-TeNWs. Practically, all the diffraction peaks in both experimental XRD patterns can be indexed to hexagonal Te structure (*h*-Te, space group P3121).⁶⁸ The lattice parameters calculated for both the samples are in good

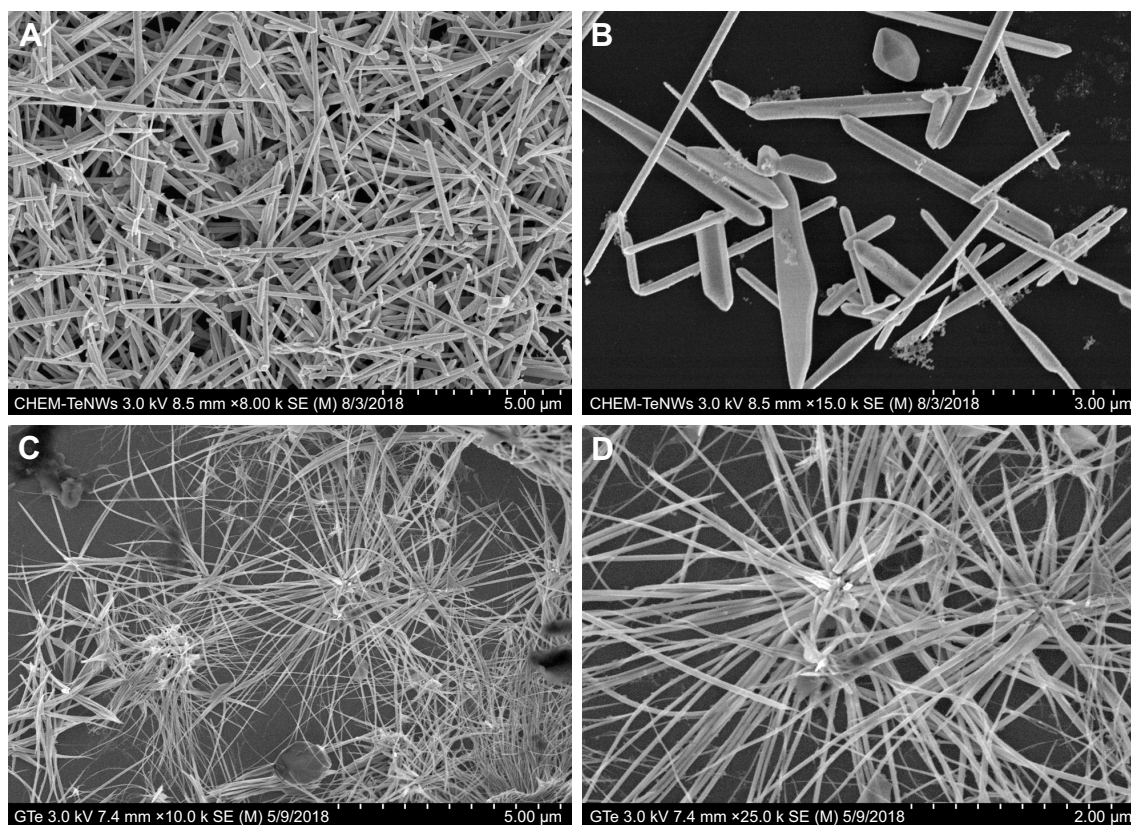


Figure 3 SEM images of CHEM-TeNWs (**A** and **B**) and GREEN-TeNWs (**C** and **D**). GREEN-TeNWs grew with a star-shaped structure, while CHEM-TeNWs had different morphologies.

Abbreviations: CHEM-TeNWs, chemically synthesized TeNWs; GREEN-TeNWs, green-synthesized TeNWs; SEM, scanning electron microscopy; TeNWs, tellurium nanowires.

agreement with the reported values for *h*-Te,⁶⁸ as shown in Table 3. In the case of the XRD pattern of GREEN-TeNWs the presence of foreign phases related to Te-based oxides compounds were also detected (Figure 6).

For CHEM-TeNWs, three different phases were identified corresponding to elemental Te, sodium tellurate hydrate, and an organic compound. This last one was present on a relatively little amount compared with the other ones; it has

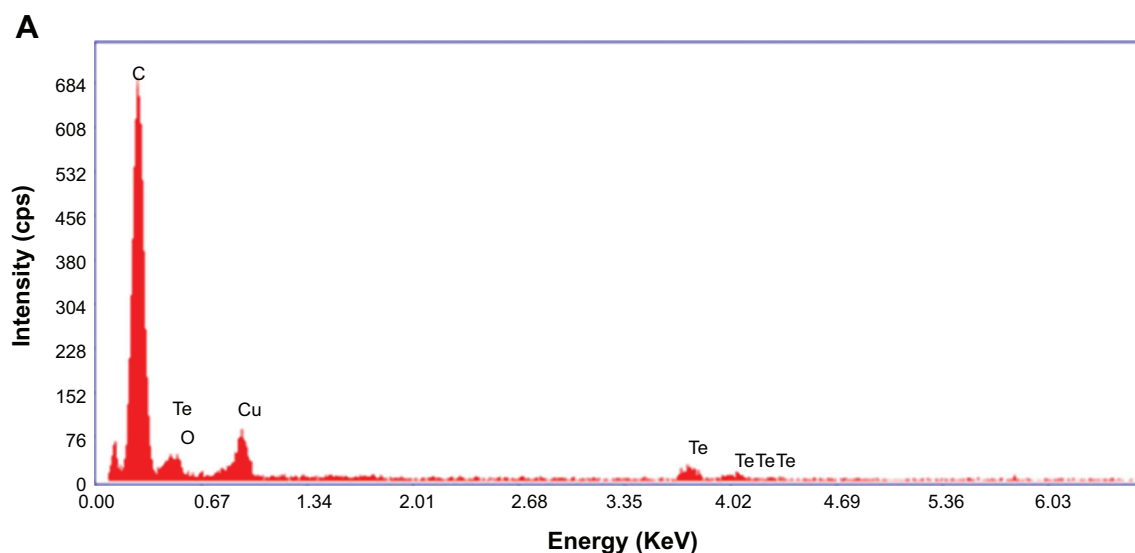


Figure 4 (Continued)

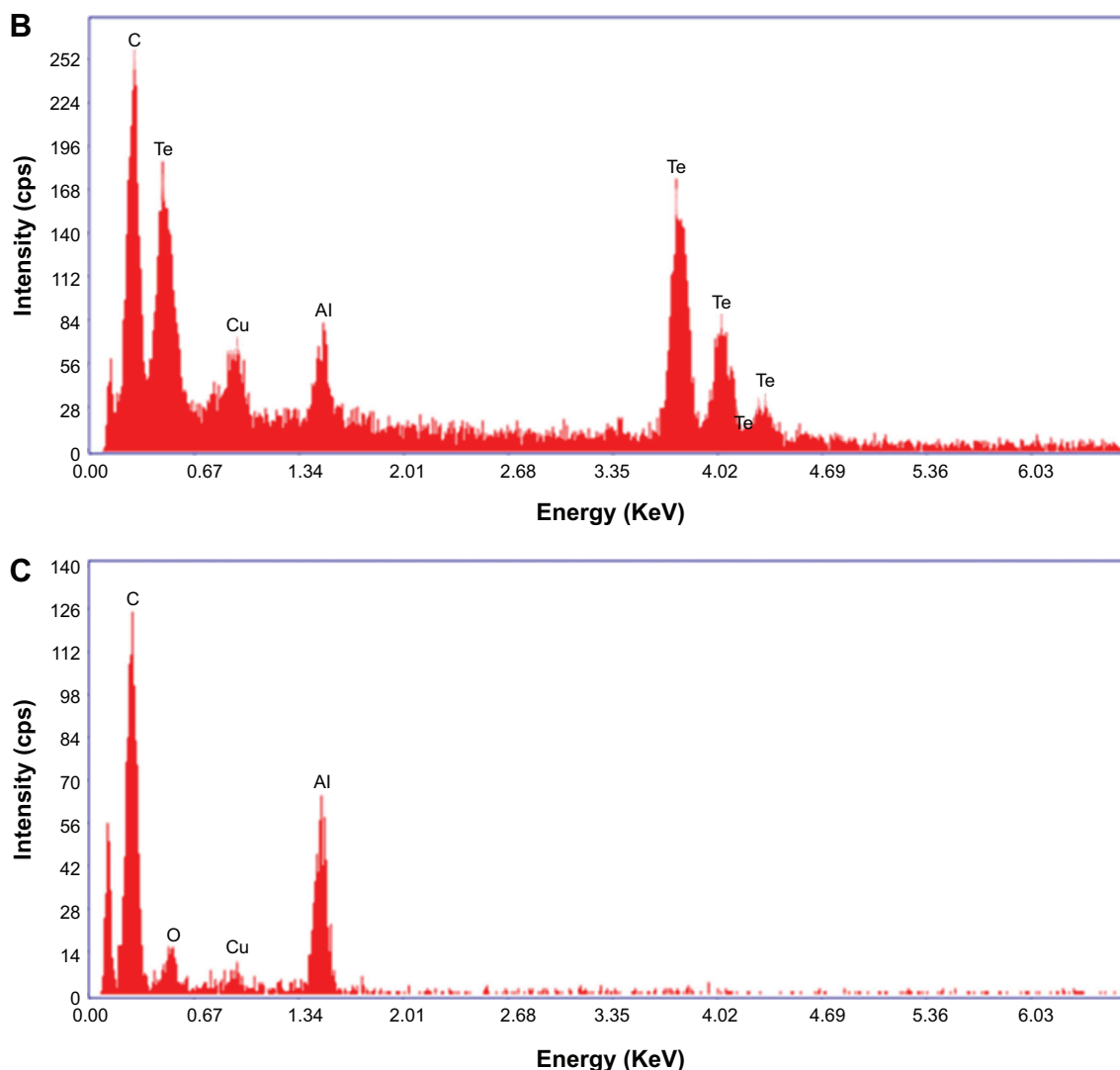


Figure 4 Energy-dispersive X-ray of TeNWs. CHEM-TeNWs were characterized (A) as well as GREEN-TeNWs in both the metallic core (B) and the surrounding coating (C). **Abbreviations:** CHEM-TeNWs, chemically synthesized TeNWs; GREEN-TeNWs, green-synthesized TeNWs; TeNWs, tellurium nanowires.

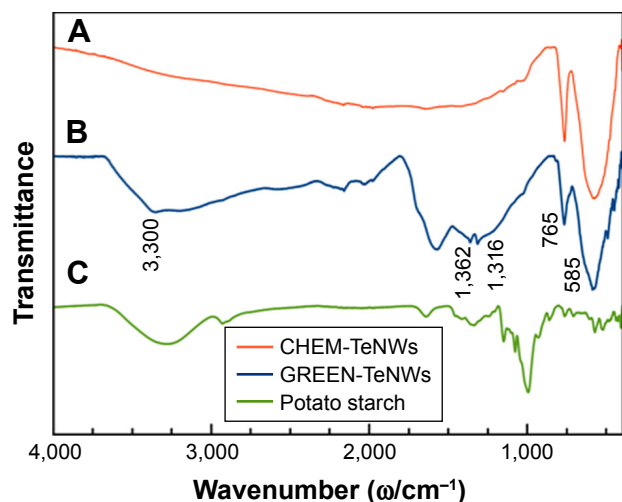


Figure 5 FT-IR spectra of (A) CHEM-TeNWs, (B) GREEN-TeNWs, and (C) potato starch.

Abbreviations: CHEM-TeNWs, chemically synthesized TeNWs; FT-IR spectra, Fourier-transform infrared spectra; GREEN-TeNWs, green-synthesized TeNWs; TeNWs, tellurium nanowires.

been hypothesized that its presence came from a hydrocarbon-based deposition of organic matter on the top of the sample either after the purification or after the preparation of the sample. On the other hand, GREEN-TeNWs present elemental Te, Te oxide, and organic compound phases. The presence of Te oxide has been related to the use of starch as a reducing agent as oxygen was integrated into the structure. It has been elucidated that the organic compound was associated with the use of starch. Additional information can be found in Supplementary Material (Figures S1–S4 and Tables S1–S4).

XPS was used to characterize the chemical composition and electronic states of both CHEM-TeNWs and GREEN-TeNWs.

Figure 7 displays the wide scans that have been normalized arbitrarily to the C 1s core level peak for comparison. The main features have been identified in the spectra.

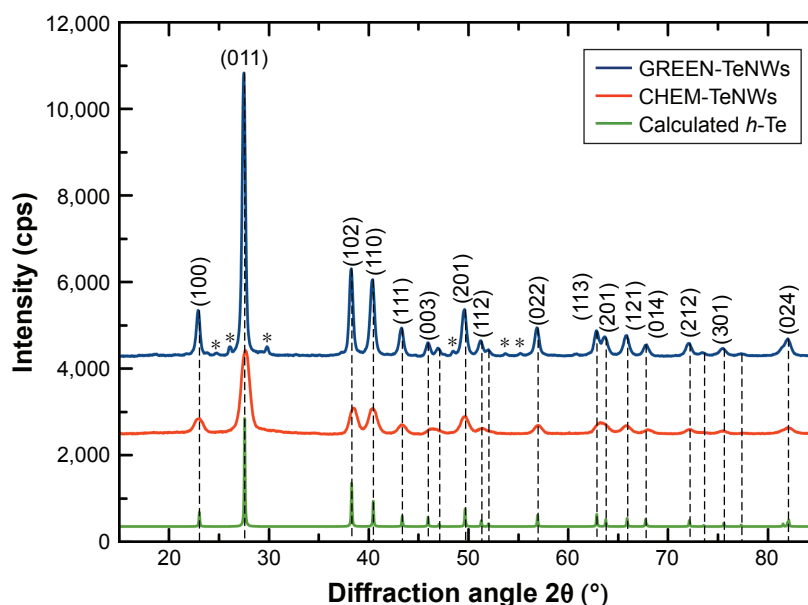


Figure 6 Comparison between the experimental XRD patterns for GREEN-TeNWs and CHEM-TeNWs and the calculated XRD patterns for bulk hexagonal Te (*h*-Te).⁶⁸ The diffraction peaks marked with (*) may be related to Te-based oxides.

Abbreviations: CHEM-TeNWs, chemically synthesized TeNWs; GREEN-TeNWs, green-synthesized TeNWs; TeNWs, tellurium nanowires; XRD, X-ray powder diffraction.

Clear differences can be observed between the two compounds. As the spectra are normalized to the C 1s core level peak, the higher intensity at the Te 3d core level for CHEM-TeNWs indicates that this compound has a higher content of Te than that in GREEN-TeNWs. In addition, the double structure for the Te 3d core level peaks (CHEM-TeNWs) is likely to indicate that this element is partially oxidized. Finally, it clearly appears that GREEN-TeNWs have no nitrogen (absence of N 1s core level peak) as compared to the CHEM-TeNWs; these differences can be explained due to the use of hydrazine and NH_3 as reductor agents in the chemical synthetic approach.

The chemical analysis performed at the Te 3d, O 1s, N 1s, and C 1s core level peaks revealed the composition given in Table 4.

Differences between the two compounds are better appreciated when comparing the Te 3d core levels as shown in Figure 8. The spectra have been normalized to the Te 3d_{5/2} oxide component (at a binding energy of 576 eV) and shifted vertically for comparison.

Table 3 Hexagonal lattice parameters calculated for GREEN-TeNWs and CHEM-TeNWs

Sample	<i>a</i> /Å	<i>c</i> /Å
CHEM-TeNWs	4.478	5.816
GREEN-TeNWs	4.484	5.915
<i>h</i> -Te ⁶⁸	4.456	5.921

Abbreviations: CHEM-TeNWs, chemically synthesized TeNWs; GREEN-TeNWs, green-synthesized TeNWs; *h*-Te, hexagonal Te; TeNWs, tellurium nanowires.

As can be observed, metallic and oxide components could clearly be identified. The metallic components are located at 573 eV (chosen as a reference in order to correct the charging effects) and 583.4 eV for the Te 3d_{5/2} and Te 3d_{3/2} peaks, respectively, whereas the oxide components are located at 576 eV and 586.6 eV for the Te 3d_{5/2} and Te 3d_{3/2} structures, respectively, which are in agreement with the previous results.^{63,69} It also clearly appears that GREEN-TeNWs have more of a Te oxide (79%) component than the CHEM-TeNWs (61% oxide) as seen previously on the XRD results.

The two compounds also present differences at the C 1s and O 1s core levels (Figure 9).

The C 1s core levels spectra (Figure 9, left) could be fitted with the following minimum number of components at 281.1 eV (13%), 283.7 eV (71%), and 286.6 eV (16%) for GREEN-TeNWs and 285.1 eV (57%) and 286.8 eV (43%) for CHEM-TeNWs. The peaks located at 286.6 eV and 286.8 eV can be ascribed to hydroxyl (C–O/C–OH) groups,^{70,71} meaning that CHEM-TeNWs have more hydroxyl groups than GREEN-TeNWs. At a lower binding energy, a peak located at 285.1 eV could be identified in CHEM-TeNWs. This peak corresponds to the presence of either C–C or C–H bonds in the sp³ tetrahedral configuration,⁷¹ and surprisingly, it was not observed in GREEN-TeNWs. Instead, two peaks at lower binding energies of 281.1 eV and 283.7 eV were identified on it. The peak at 283.7 eV could be ascribed to C–C bonds in the sp² configuration, while the less abundant component with an XPS peak at 281.1 eV could not be clearly

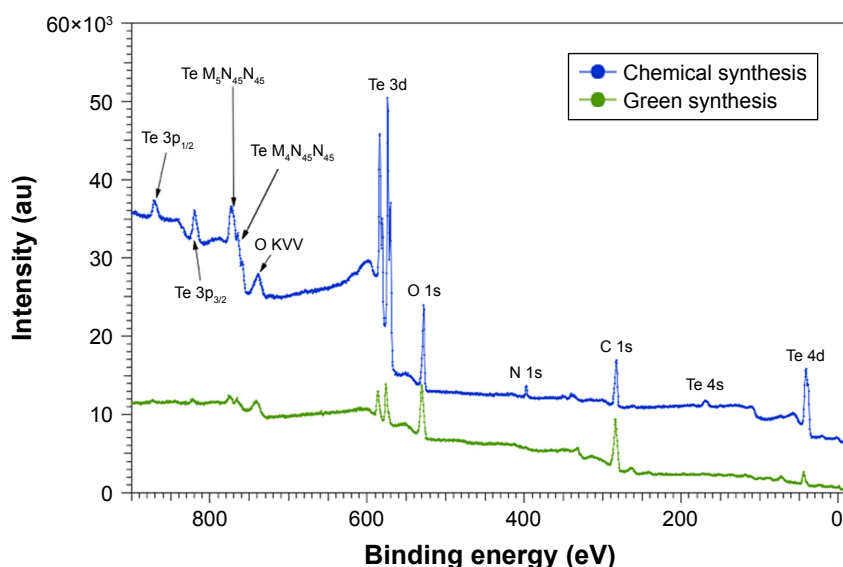


Figure 7 Wide scans recorded on both compounds synthesized through the green and chemical routes.

identified. It is inferred that this last component corresponds to C atoms weakly bonded. Thus, no evidence of the presence of carbonyl (C=O at 288.1 eV) or carboxyl (O–C=O at 289.0 eV) groups could be observed.⁷¹

In the case of the O 1s core level spectra (Figure 9, right), the spectrum corresponding to GREEN-TeNWs could be fitted with a single component at 530 eV, while CHEM-TeNWs have two components located at 530.6 eV (44%) and 531.3 eV (56%). These relatively weak binding energies suggest that the oxygen atoms are weakly bonded and do not correspond to O–C bonds that would appear at a binding energy of around 533 eV.⁷⁰ This in turn agrees with the absence of carbonyl and carboxyl groups in the C 1s spectra.

In vitro cytotoxicity of TeNWs

In vitro cytotoxicity assays were performed with HDF cells and melanoma cells (ATCC® CRL-1619). Data from the nanowire treatment were compared with a control that contained only cells and media. A comparison was made between HDF and melanoma cells with the aim of determining potential anticancer activity. The same experiments were performed using chemical and green-synthesized nanowires

to determine the effect of the natural coating present on GREEN-TeNWs on the proliferation of the cells.

For HDF experiments, nanowires at a concentration between 5 and 100 µg/mL were tested. For CHEM-TeNWs, the same proliferation trend was observed within the third and fifth day for concentrations up to 15 µg/mL compared with the control (Figure 10A). However, the number of cells was less than that for the control in all the cases. Larger concentrations showed degeneration of the cell proliferation. When GREEN-TeNWs were tested on the cells, a similar proliferation trend was observed for each of the concentrations (Figure 10B). An especially unusual behavior was shown at levels between 15 and 75 µg/mL, with a higher number of

Table 4 Chemical composition (in percentage atomic concentration) extracted from the Te 3d, O 1s, N 1s, and C 1s core level peaks

	Green route	Chemical route
Tellurium	2.6	17.1
Oxygen	67.8	31.5
Nitrogen	–	5.3
Carbon	29.6	46.1

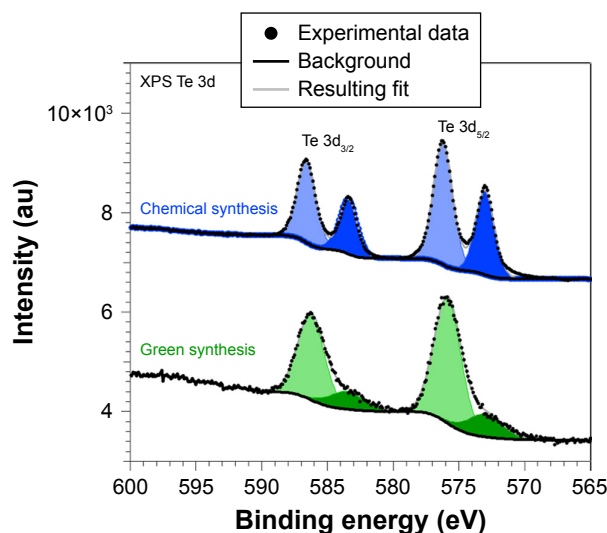


Figure 8 XPS spectra recorded at the Te 3d core levels for samples synthesized through the chemical and green routes.

Abbreviation: XPS, X-ray photoelectron spectroscopy.

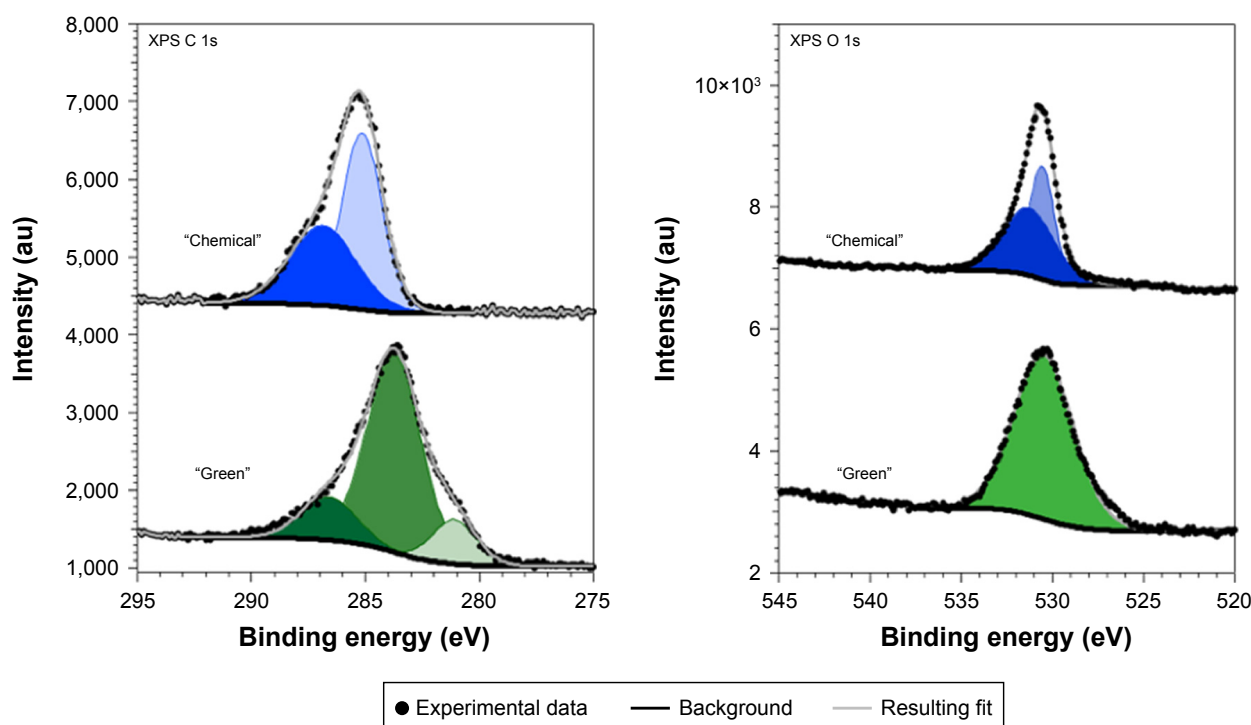


Figure 9 XPS spectra recorded at the C 1s (left) and O 1s (right) core levels for samples synthesized through the chemical and green routes.

Abbreviation: XPS, X-ray photoelectron spectroscopy.

cells growing within the third and the fifth day compared with the first 24 hours. When both nanostructures were compared, it can be concluded that the green-synthesized structures enhanced cell proliferation over a broader range of concentrations compared with the chemical synthetic ones.

The cytotoxic effect of Te nanostructures is the result of active physicochemical interactions of elemental Te with the functional groups of intracellular proteins and the bases and phosphate groups in DNA.⁶⁰ While cytotoxicity was apparent for the CHEM-TeNWs (Figure 10A), we hypothesized that the enhanced biocompatibility in GREEN-TeNWs (Figure 10B) is most likely due to the presence of a natural, organic coating that encompasses the Te core. The presence of a carbon layer as the natural coating introduces a biodegradable material that can enhance cell proliferation.

When melanoma cells were treated with CHEM-TeNWs, cell proliferation showed a similar trend as that of the control at concentrations up to 25 $\mu\text{g/mL}$ (Figure 10C). GREEN-TeNWs showed a similar behavior (Figure 10D). Nonetheless, levels between 10 and 100 $\mu\text{g/mL}$ showed a delay in the cell proliferation compared with the control over the tested time period. It has been hypothesized that TeNWs have the potential ability to slow down the signaling processes present in cancerous cells due to the effect of Te.^{72,73} Therefore, we propose that both synthesis methods produce nanostructures with anticancer

properties, but specifically this behavior was particularly enhanced in the case of the green synthetic structures.

In this report, the cytocompatibility and anticancer activity of Te nanostructures were observed with a potentially improved performance using GREEN-TeNWs. Thus, not only were the GREEN-TeNWs produced with significantly fewer toxic materials, but their properties toward enhancing healthy cell proliferation and decreasing cancer cell proliferation were also greater.

A comparison was done on the fifth day of the experiments between samples to show the tendency of both cell compatibilities with HDF cells (Figure 11A) and cytotoxic effects with melanoma cells (Figure 11B).

The low cytotoxicity for HDF cells can be appreciated especially at high concentrations of TeNWs, with a noticeable difference between CHEM-TeNWs – with higher cytotoxicity for HDF – and GREEN-TeNWs, which allow for a high cell proliferation. At low concentrations – between 5 and 15 $\mu\text{g/mL}$ – the difference in terms of biocompatibility was almost inappreciable. The biggest difference was observed at a concentration of 25 $\mu\text{g/mL}$. For experiments with cancerous cells, the opposite behavior occurred. GREEN-TeNWs did not allow for the proliferation of melanoma cells at concentrations ranging between 15 and 100 $\mu\text{g/mL}$. As with HDF cells, the bigger difference was observed for a concentration of

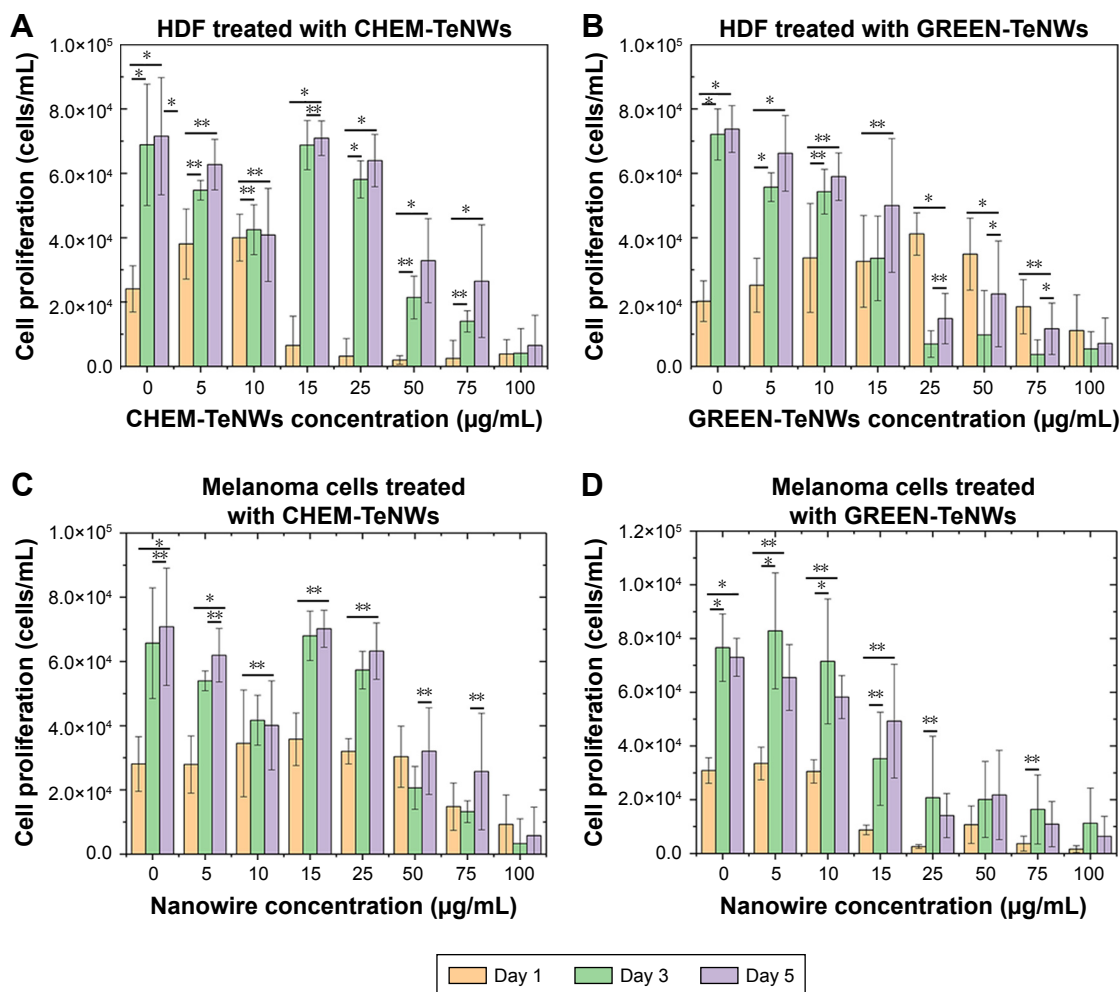


Figure 10 MTS assays on HDF (A, B) and melanoma (C, D) cells in the presence of CHEM-TenWs (A, C) and GREEN-TenWs (B, D) at concentrations ranging from 5 to 100 µg/mL. N=3. Data are presented as mean \pm SD; * P <0.01, ** P <0.005.

Abbreviations: CHEM-TenWs, chemically synthesized TenWs; GREEN-TenWs, green-synthesized TenWs; HDF, human dermal fibroblasts; TenWs, tellurium nanowires.

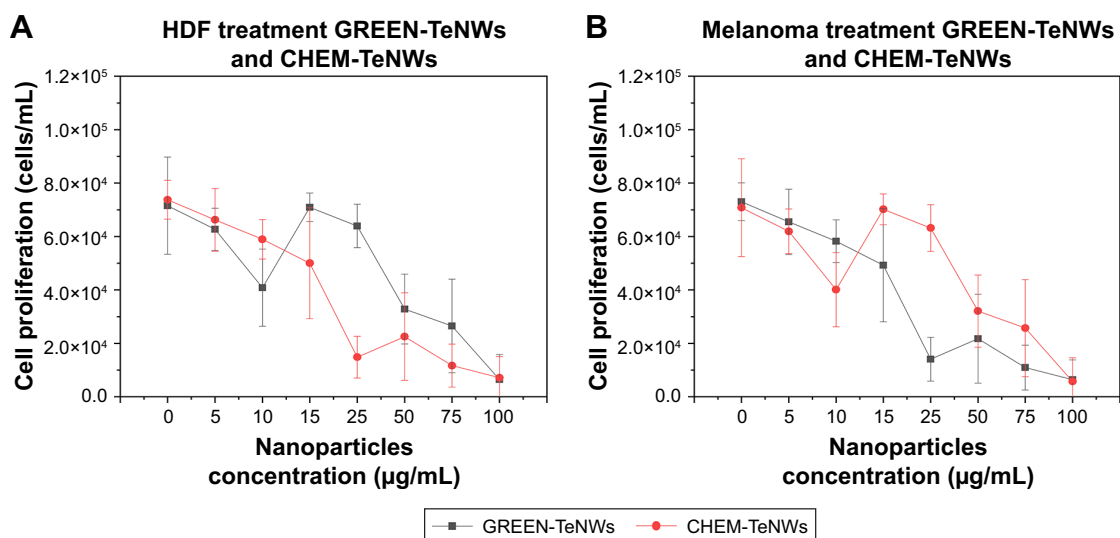


Figure 11 Comparison between CHEM-TenWs and GREEN-TenWs for HDF (A) and melanoma (B) cells at the fifth day of experiment. Data from MTS assays on HDF and melanoma cells in the presence of TenWs.

Abbreviations: CHEM-TenWs, chemically synthesized TenWs; GREEN-TenWs, green-synthesized TenWs; HDF, human dermal fibroblasts; TenWs, tellurium nanowires.

Table 5 IC₅₀ values for both CHEM-TeNWs and GREEN-TeNWs in experimental assays with HDF and melanoma cells after 5 days of experiments

Cell assay	CHEM-TeNWs	GREEN-TeNWs
HDF	60.22±15.25 µg/mL	70.05±10.58 µg/mL
Melanoma	63.14±6.078 µg/mL	16.46±1.96 µg/mL

Abbreviations: CHEM-TeNWs, chemically synthesized TeNWs; GREEN-TeNWs, green-synthesized TeNWs; HDF, human dermal fibroblasts; TeNWs, tellurium nanowires.

25 µg/mL. Therefore, it was possible to hypothesize that at a concentration of 25 µg/mL of GREEN-TeNWs, both the maximum biocompatibility for HDF and the maximum cytotoxic effect for melanoma cells were achieved in comparison with the same concentration of CHEM-TeNWs. As a general view, the behavior of GREEN-TeNWs after 5 days in terms of low and high cytotoxicity for HDF and melanoma cells, was enhanced in comparison with CHEM-TeNWs.

IC₅₀ values were calculated for all the experiments in Table 5, with the aim of showing the minimum inhibitory concentration

for both HDF and melanoma cells. This value was obtained after 5 days of experiments, measuring the potency of the nanowires to inhibit the normal biological functioning of the cells.

The interaction between the cells and the nanostructures was studied using SEM imaging of melanoma and HDF cells. Different concentrations – 100, 50, and 0 µg/mL – of TeNWs were tested in order to elucidate the mechanism of cell death on both cell types. SEM imaging allowed the observation of modifications in the membrane and shape of cells.

For HDF cells, NWs were found to be in contact with the cells; however, no interaction between them was observed at lower concentrations. GREEN-TeNWs surrounded the cells without producing any damage (Figure 12A and B) when compared to the control (Figure 12C). The membrane remained intact without any sign of swelling or blebbing. Thus, it has been hypothesized that the presence of starch encases the TeNWs and prevents their interaction with HDF cells.

Nevertheless, higher concentrations of 100 µg/mL NPs seem to produce necrosis on cells (Figure 12D). As shown in

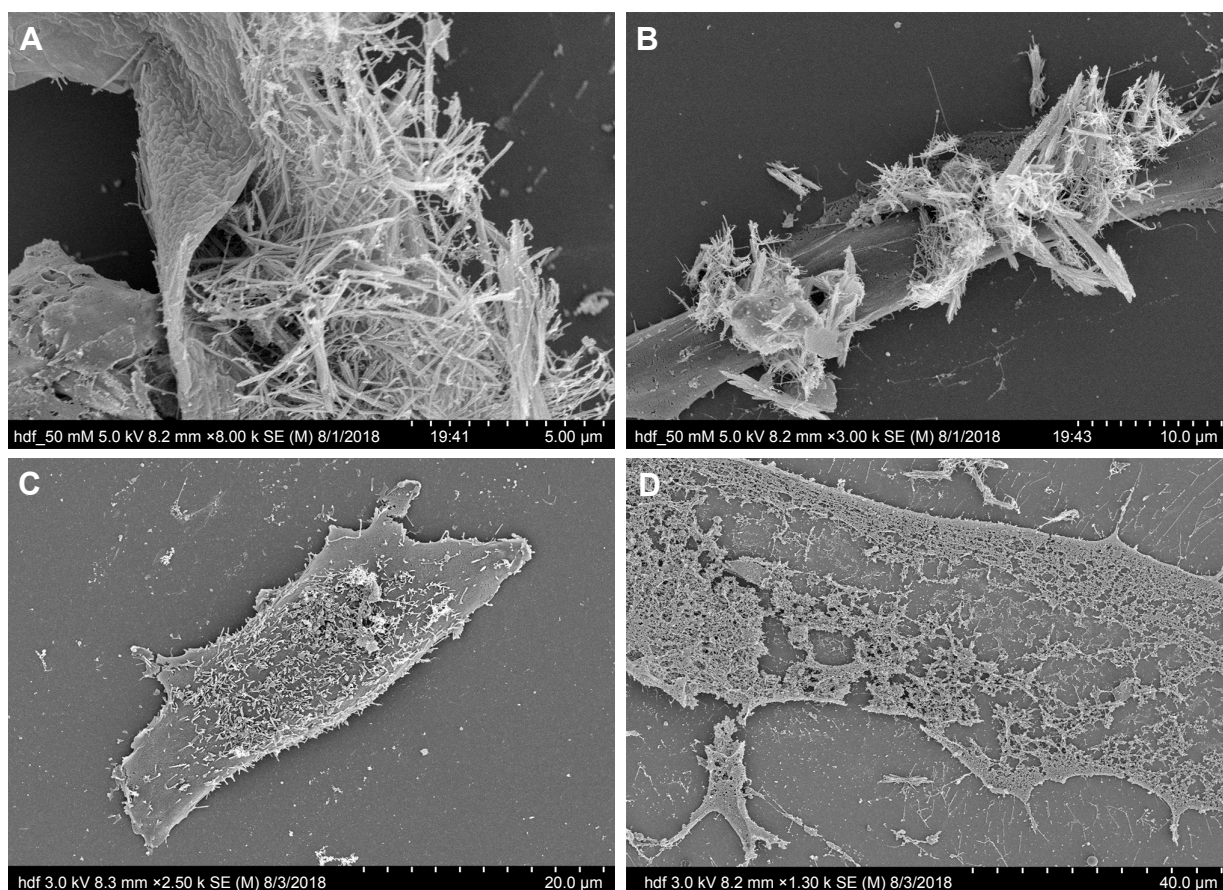


Figure 12 Interaction between HDF cells and GREEN-TeNWs. Interaction between 50 µg/mL (A, B), 0 µg/mL (C), and 100 µg/mL (D) of GREEN-TeNWs and HDF cells was analyzed.

Abbreviations: GREEN-TeNWs, green-synthesized TeNWs; HDF, human dermal fibroblasts; TeNWs, tellurium nanowires.

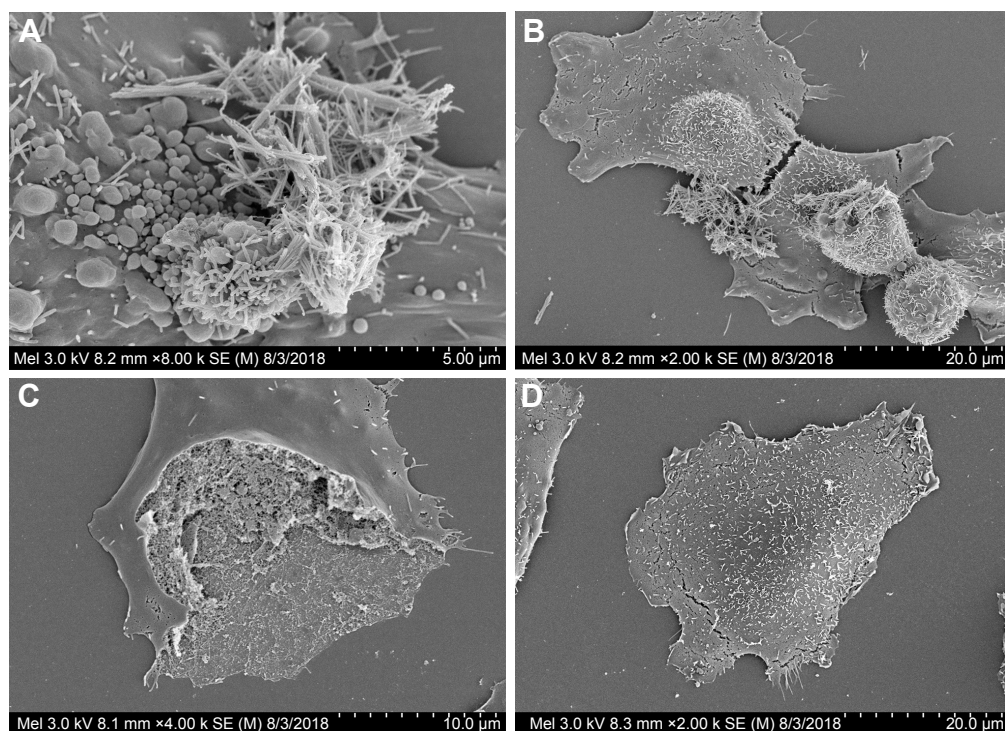


Figure 13 Interaction between melanoma cells and GREEN-TeNWs. Bubbling (**A**) and rupture (**B** and **C**) of the cell membrane were observed in comparison with the control (**D**).

Abbreviation: GREEN-TeNWs, green-synthesized tellurium nanowires.

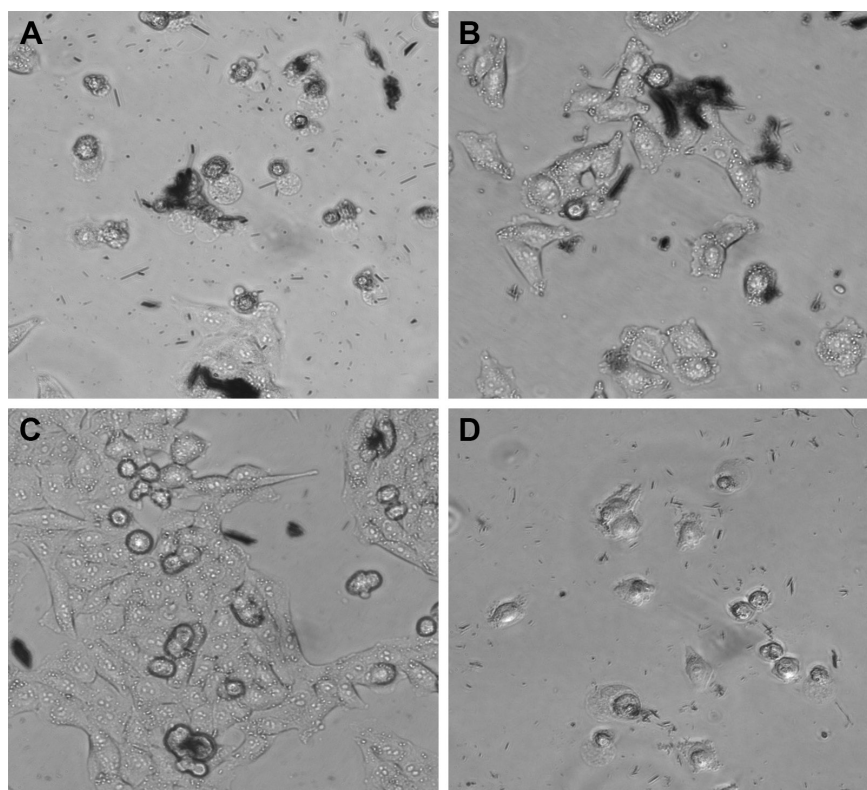


Figure 14 Optical microscopy characterization of HDF (**A**, **B**) and human melanoma (**C**, **D**) cells cultured in the presence of both CHEM-TeNWs and GREEN-TeNWs for 24 hours.

Abbreviations: CHEM-TeNWs, chemically synthesized TeNWs; GREEN-TeNWs, green-synthesized TeNWs; HDF, human dermal fibroblasts; TeNWs, tellurium nanowires.

the literature, swelling of the cell due to a hydration process and discontinuities on the membrane previous to its rupture are dictated as signs of necrosis.^{74,75} SEM captured the different stages of the rupture of the cytoplasmic membrane due to a swelling process (Figure 12D); hence, the mechanism of death was interpreted as necrosis.

In contrast, blebbing (Figure 13A) was observed on melanoma cells in comparison with the control (Figure 13D), indicating a process of apoptosis. These formations on the membrane are associated with a rearrangement in the cytoskeleton, which eventually ended in the rupture in fragments of the cell.^{76,77} It has been hypothesized that differently than HDF, NWs interact with melanoma cells by inducing chemical signaling, which leads to apoptosis, hence reducing cell proliferation by breaking cells apart (Figure 13B and C). It has been elucidated that different mechanisms of death are possible due to the use of different kinds of cells.

Optical microscopy showed preliminary results of how different cells behaved in the presence of both GREEN-TeNWs and CHEM-TeNWs. After 24 hours of treatment, 50 µg/mL CHEM-TeNWs (Figure 14A) showed a remarkable disturbance in the growth of HDF cells after 24 hours of treatment, with poor cell development, while the same concentration of GREEN-TeNWs (Figure 14B) allowed the development of the cells to a large extent. When melanoma human cells were tested with the same concentration of CHEM-TeNWs (Figure 14C), the cells showed better development than the ones cultured with GREEN-TeNWs (Figure 14D) for the same period.

Conclusion

Nanotechnology has taken an advantage of traditional chemical synthesis methods, both physical and chemical, to solve many of the biomedical and technological challenges that society faces today. Nevertheless, there is an environmental impact associated with such synthesis. Concerns such as the production of toxic by-products and harsh reaction conditions should be addressed. Therefore, new and alternative approaches are on the rise. One of the most promising comes from the use of green chemistry.

In this work, we successfully explored and compared two different synthesis approaches (a traditional chemical method and a green chemistry method) to elucidate the differences between the cytocompatibility and anticancer behavior of the respective NPs produced from each process. Experiments with healthy fibroblasts and cancerous melanoma cells were performed over a range of concentrations between 5 and 100 µg/mL and showed both an improvement

in the cell proliferation of HDF cells and a decrease in the proliferation of cancerous cells when GREEN-TeNWs were compared with CHEM-TeNWs. An enhancement of healthy fibroblast proliferation was observed for the green synthesis of TeNWs compared with the CHEM-TeNWs, which suggests that these should be explored for a wide range of medical applications. Therefore, we propose that the present green synthetic approach offers important improvements in terms of safety, economy, efficiency, and biocompatibility for numerous biomedical applications, overcoming the main drawbacks of traditional Te nanowire chemical approaches.

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Disclosure

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Supplementary materials

X-ray diffraction peak list of identified samples:

- 1) Green-synthesized tellurium nanowires
- 2) Chemically synthesized tellurium nanowires

Peak list:

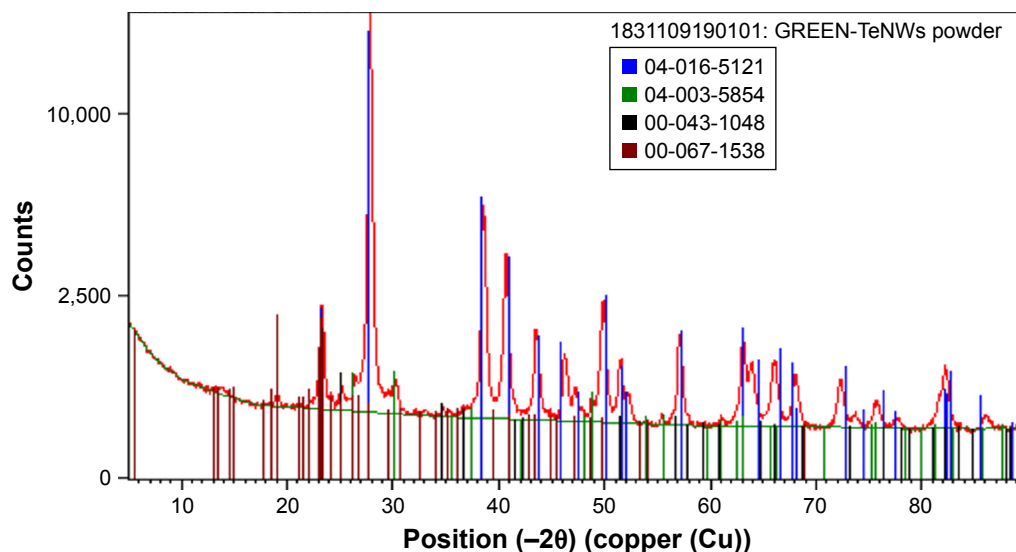


Figure S1 XRD pattern for GREEN-TeNWs.

Abbreviations: GREEN-TeNWs, green-synthesized tellurium nanowires; XRD, X-ray powder diffraction.

Table S1 Peak identification list for XRD pattern for GREEN-TeNWs

Position (°2θ)	Height (cts)	FWHM left (°2θ)	d-spacing (Å)	Rel. Int. (%)	Tip width (°2θ)	Matched by
13,1957	94,44	0,0768	6,70,966	0,59	0,0921	00-067-1538
13,8910	85,08	0,6140	6,37,530	0,53	0,7368	
19,1180	132,77	0,4605	4,64,242	0,83	0,5526	00-067-1538
21,0578	75,13	0,1919	4,21,896	0,47	0,2303	00-067-1538
23,2745	1901,95	0,3838	3,82,192	11,85	0,4605	04-016-5121, 00-067-1538
24,1109	164,10	0,1151	3,69,119	1,02	0,1382	00-067-1538
25,1056	299,79	0,3070	3,54,716	1,87	0,3684	00-043-1048, 00-067-1538
26,3655	453,76	0,2303	3,38,045	2,83	0,2763	04-003-5854, 00-067-1538
27,8158	16,047,72	0,3454	3,20,740	100,00	0,4145	04-016-5121, 00-067-1538
29,5937	288,81	0,1151	3,01864	1,80	0,1382	00-067-1538
30,1177	468,19	0,1535	2,96,730	2,92	0,1842	04-003-5854
30,4329	323,99	0,1535	2,93,728	2,02	0,1842	
32,0904	30,05	0,1535	2,78,925	0,19	0,1842	
32,9668	47,28	0,4605	2,71,708	0,29	0,5526	
34,7455	86,37	0,1535	2,58,195	0,54	0,1842	00-043-1048
35,3832	63,62	0,2303	2,53,687	0,40	0,2763	04-003-5854, 00-067-1538
36,5894	109,18	0,1151	2,45,596	0,68	0,1382	00-043-1048
38,5228	5267,40	0,3454	2,33,704	32,82	0,4145	04-016-5121
40,6315	3468,21	0,4221	2,22,048	21,61	0,5066	04-016-5121
43,5252	1440,62	0,3838	2,07933	8,98	0,4605	04-016-5121, 00-067-1538
44,8734	107,74	0,0768	2,01994	0,67	0,0921	00-043-1048, 00-067-1538
46,1746	863,30	0,3454	1,96,601	5,38	0,4145	

(Continued)

Table S1 (Continued)

Position (°2θ)	Height (cts)	FWHM left (°2θ)	d-spacing (Å)	Rel. Int. (%)	Tip width (°2θ)	Matched by
47,3322	352,20	0,2686	1,92,059	2,19	0,3224	04-016-5121, 00-067-1538
47,9396	144,27	0,1151	1,89,767	0,90	0,1382	04-003-5854
48,6845	205,85	0,1535	1,87,036	1,28	0,1842	04-003-5854, 00-067-1538
49,7893	2084,93	0,4221	1,83,142	12,99	0,5066	00-067-1538
51,5206	817,40	0,3838	1,77,387	5,09	0,4605	04-016-5121, 00-043-1048
52,2020	312,70	0,1535	1,75,231	1,95	0,1842	04-016-5121
54,0039	39,28	0,3070	1,69,802	0,24	0,3684	04-003-5854, 00-067-1538
55,4375	104,24	0,1535	1,65,746	0,65	0,1842	04-003-5854
57,1566	1365,80	0,4221	1,61,163	8,51	0,5066	04-016-5121
58,3000	27,99	0,1919	1,58,272	0,17	0,2303	
61,0927	81,73	0,3838	1,51,689	0,51	0,4605	04-003-5854, 00-043-1048
63,0172	1213,72	0,2686	1,47,512	7,56	0,3224	04-016-5121, 04-003-5854
63,7614	778,02	0,2340	1,45,848	4,85	0,2808	
63,9862	769,47	0,1535	1,45,510	4,79	0,1842	
65,9294	779,38	0,2340	1,41,567	4,86	0,2808	04-003-5854, 00-043-1048
66,1437	825,67	0,2303	1,41,277	5,15	0,2763	04-003-5854, 00-043-1048
68,0895	579,45	0,3454	1,37,707	3,61	0,4145	04-016-5121
72,2240	506,74	0,1919	1,30,808	3,16	0,2303	
73,7367	119,08	0,4605	1,28,494	0,74	0,5526	
75,8096	262,89	0,6140	1,25,488	1,64	0,7368	04-003-5854
77,5390	115,96	0,1151	1,23,116	0,72	0,1382	04-016-5121
81,5887	282,16	0,1535	1,17,998	1,76	0,1842	
82,1625	782,00	0,1872	1,17,222	4,87	0,2246	04-016-5121, 00-043-1048
82,3791	688,99	0,1535	1,17,065	4,29	0,1842	04-016-5121, 00-043-1048
85,9082	104,27	0,5373	1,13,138	0,65	0,6447	04-016-5121, 04-003-5854

Abbreviations: GREEN-TeNWs, green-synthesized tellurium nanowires; FWHM, full width at half maximum; XRD, X-ray powder diffraction; Rel. Int., relative intensity.

Table S2 List of identified patterns on XRD analysis of GREEN-TeNWs

Reference code	Score	Compound name	Displacement (°2θ)	Scale factor	Chemical formula
04-016-5121	44	Tellurium	0,000	0,840	Te
04-003-5854	36	Tellurium oxide	0,000	0,031	TeO ₂
00-043-1048	25	Tellurium oxide	0,000	0,028	TeO ₃
00-067-1538	30	Poly(ethylene glycol) 7500	0,000	0,093	((CH ₂) ₂ O) _n

Abbreviations: GREEN-TeNWs, green-synthesized tellurium nanowires; XRD, X-ray powder diffraction.

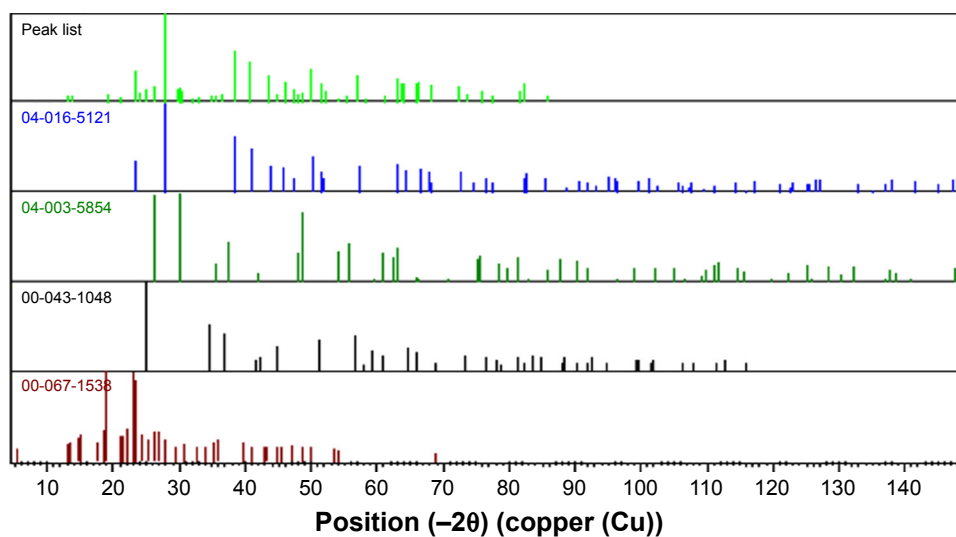


Figure S2 XRD pattern for GREEN-TeNWs.

Abbreviations: GREEN-TeNWs, green-synthesized tellurium nanowires; XRD, X-ray powder diffraction.

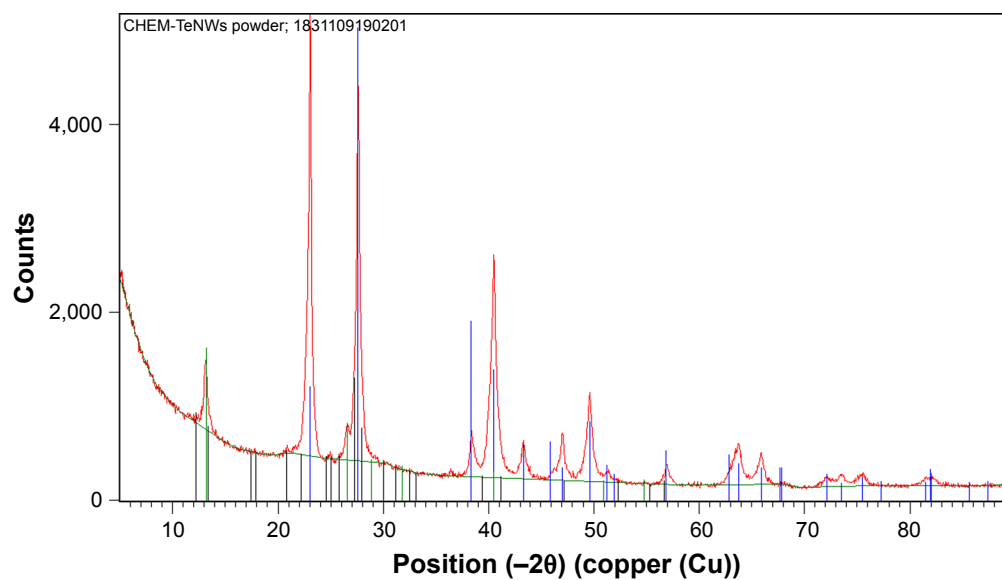


Figure S3 XRD pattern for GREEN-TeNWs.

Abbreviations: GREEN-TeNWs, green-synthesized tellurium nanowires; XRD, X-ray powder diffraction.

Table S3 Peak identification list for XRD pattern for CHEM-TeNWs

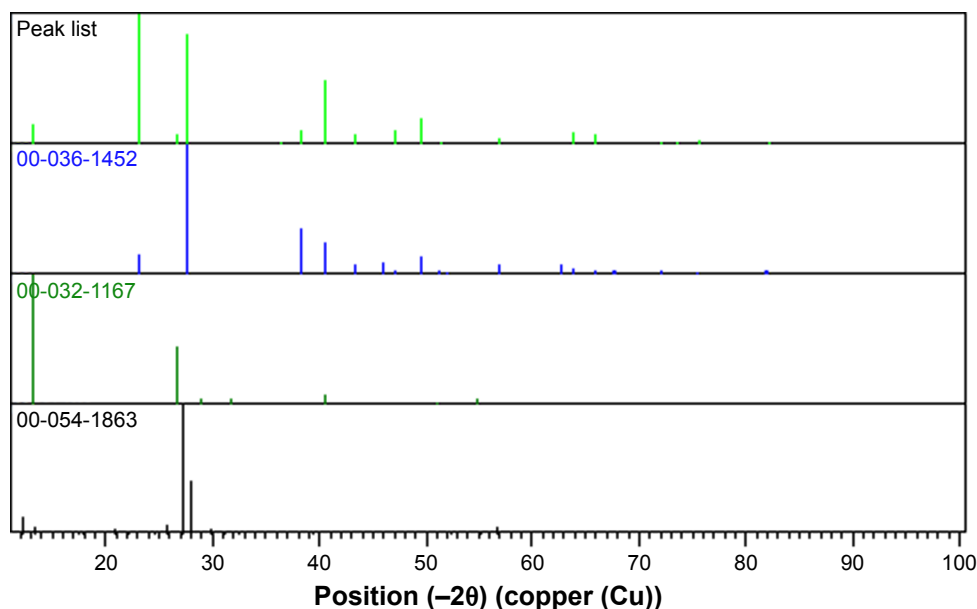
Position (°2θ)	Height (cts)	FWHM (°2θ)	d-spacing (Å)	Rel. Int. (%)	Tip width (°2θ)	Matched by
13,1969	741,73	0,2686	6,70,902	15,76	0,3224	00-032-1167; 00-054-1863
23,0429	4707,03	0,1535	3,85,981	100,00	0,1842	00-036-1452
26,6138	357,02	0,3454	3,34,947	7,58	0,4145	00-032-1167
27,5994	3979,25	0,1535	3,23,206	84,54	0,1842	00-036-1452
36,4139	50,56	0,2303	2,46,739	1,07	0,2763	
38,3353	482,31	0,1535	2,34,803	10,25	0,1842	00-036-1452
40,4878	2325,95	0,1919	2,22,803	49,41	0,2303	00-036-1452; 00-032-1167
43,3289	383,69	0,2303	2,08830	8,15	0,2763	00-036-1452
47,0262	505,58	0,2303	1,93,237	10,74	0,2763	00-036-1452; 00-054-1863
49,6237	941,80	0,1919	1,83,714	20,01	0,2303	00-036-1452
51,3913	116,05	0,3070	1,77,803	2,47	0,3684	00-036-1452
56,8808	221,45	0,2686	1,61,878	4,70	0,3224	00-036-1452; 00-054-1863
63,7370	438,99	0,2303	1,46,019	9,33	0,2763	00-036-1452
65,8686	324,54	0,2303	1,41,800	6,89	0,2763	00-036-1452
72,0718	98,14	0,3838	1,31,047	2,08	0,4605	00-036-1452
73,6438	114,88	0,5373	1,28,633	2,44	0,6447	00-036-1452
75,6068	136,85	0,3838	1,25,774	2,91	0,4605	00-036-1452
82,2074	76,41	1,6848	1,17,169	1,62	2,0218	00-036-1452

Abbreviations: CHEM-TeNWs, chemically synthesized tellurium nanowires; FWHM, full width at half maximum; XRD, X-ray powder diffraction; Rel. Int., relative intensity.

Table S4 List of identified patterns on XRD analysis of CHEM-TeNWs

Reference code	Score	Compound name	Displacement (°2θ)	Scale factor	Chemical formula
00-036-1452	64	Tellurium, syn	0,000	0,890	Te
00-032-1167	43	Sodium Tellurate Hydrate	0,000	0,170	Na ₂ Te ₄ O ₉ · 14,5 H ₂ O
00-054-1863	17	5,7-Dihydroxy-4H-4-chromenone	0,000	0,281	C ₉ H ₆ O ₄

Abbreviations: CHEM-TeNWs, chemically synthesized tellurium nanowires; XRD, X-ray powder diffraction.

**Figure S4** XRD pattern for GREEN-TeNWs.

Abbreviations: GREEN-TeNWs, green-synthesized tellurium nanowires; XRD, X-ray powder diffraction.

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