IJPSR (2019), Volume 10, Issue 8 **(Research Article)**

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 22 November 2018; received in revised form, 03 March 2019; accepted, 08 March 2019; published 01 August 2019

SURFACE MODIFICATION AND NON-COVALENT FUNCTIONALIZATION OF SINGLE-WALLED CARBON NANOTUBES AND THEIR CHARACTERIZATION

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Keywords:

Single-walled carbon nanotubes, Functionalization, Cytotoxicity, Biocompatibility

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ABSTRACT: Single-walled carbon nanotubes (SWNTs) though emerged as a promising material for delivery of biomolecules into various cells, due to their high cytotoxicity, they are limited in use in many biological systems and also in humans. The present research explores the preparation of functionalized SWNTs of low cytotoxicity and biocompatibility by altering the size and surface functionalization. Noncovalent amine functionalization improves their biocompatibility, solubility and alters their cellular interaction pathways resulting in reduced cytotoxic effects so that the biomolecule will be preferably released from the carbon nanotube when the complex has been taken up by endocytosis into the cells. The noncovalent functionalization of SWNTs was carried out by using polymer 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-N-[amino (polyethylene glycol) - 2000] (ammonium salt) (DSPE-PEG 2000 amine) which makes the hydrophobic lipid chains of PEG to get strongly anchored onto the nanotube surface, whereas the hydrophilic chain renders SWNTs water soluble and biocompatible which results in the development of NH_2-PEG-SWNTs. The functionalized SWNTs were further characterized by FE-SEM, Raman spectroscopy, FT-IR and UV-VIS-NIR, and zeta potential. So these functionalized SWNTs can be used as effective carbon materials with enhanced solubility properties and has potential biomedical applications in the delivery of biomolecules to disease target sites.

INTRODUCTION: Carbon nanotubes (CNTs) are a hexagonal array of carbon atoms rolled up into thin, long, seamless cylinders of graphene sheets [1]. Application of Carbon nanotubes in biomedicine has been increasing rapidly because of unique intrinsic properties like mechanical strength, thermal and electrical conductivity [2-6].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.10(8).3816-24

The article can be accessed online on www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.10(8).3816-24

As CNTs have a smaller diameter and their ability to penetrate cells and tissues, they play a vital role in drug delivery and other medical applications. Depending on the number of graphene layers, they are categorized into single-walled carbon nanotubes and multi-walled carbon nanotubes (MWNTs). Due to structural complexity in MWNTs, they are not well defined compared to SWNTs.

SWNTs have well defined atomic structure with high length to diameter ratio [7, 8]. Also, because of strong van der Waals interactions SWNTs tend to aggregate into bundles estimated to be~500eV per micrometer of tube-tube contact [9].

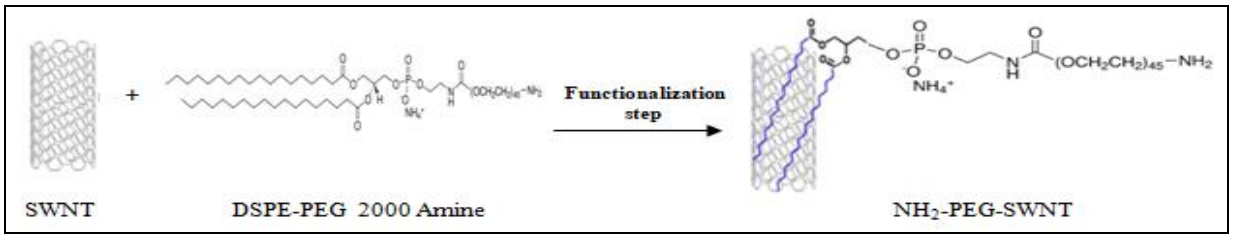
This strongly affects the electronic structure of the nanotubes and obstructs them in separating according to their diameter and chirality. The applications of SWNTs are limited due to their poor dispersion in most of the solvents and polymer matrixes [10]. Henceforth to enhance the solubility, SWNTs are functionalized either noncovalently (like polymer- wrapping or π-π stacking) or covalently (like defect-targeted or side-wall-targeted) [11-18]. These non-covalently functionalized carbon nanotubes are generally easier to disperse in water [19-20] and organic solvents [21] which enhances the homogeneity and dispersion of SWNTs within the polymer and resulting in the improvement of biocompatibility and reduces the toxicity [22]. Many studies showed that for the effective and safe delivery of biomolecules into different cells, functionalized carbon nanotubes act as potential nanocarriers [23-26]. Amine functionalized carbon nanotubes were used for different applications like photodynamic therapy using $NaNo_2$ and ethylenediamine [27], to adsorb anionic dyes in single and binary systems using diethylenetriamine [28], for efficient gene delivery using 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-N-[amino (poly-ethylene glycol) - 2000] carboxylic acid [26]. Different methods for the characterization of functionalized SWNTS include solid phase techniques like Raman spectroscopy, solution-based spectroscopic methods like UV-VIS-NIR and FT-IR, and microscopy and other related tools like FE-SEM to analyse the surface structure of functionalized carbon nanotubes.

The present work is part of a wider research which reports the preparation of non-covalently functionalized single walled carbon nanotubes using DSPE-PEG 2000 amine which is a cationic lipid used to condense and deliver anionic nucleic acids through electrostatic interactions and have been characterized by FE-SEM, Raman spectroscopy, Fourier transform infrared spectroscopy, UV-VIS-NIR measurements and Zeta (ζ) -potential of functionalized SWNT samples has also been performed to evaluate the stability. This study provides a simple and efficient surface modification approach furnishing amine containing functionality non-covalently bonded to the surface of the SWNTs that are used for other practical applications.

MATERIALS AND METHODS: Materials and Reagents: Hipco Single-walled carbon nanotubes (SWNTs) were purchased from Nopo nanotechnologies, Bangalore were prepared by Chemical Vapour Deposition. The diameter and length of the Single-walled carbon nanotubes were ~0.6 - 1.2 nm and ~400 - 1000 nm, respectively, with purity higher than 97%, 1,2-distearoyl-*sn*-glycero- 3- phosphoethanolamine- N- [amino (polyethyleneglycol)- 2000] (ammonium salt) was purchased from Avanti polar lipids Inc., Alabama and stored at -20 ºC, Hydrochloric acid (HCl), Nitric acid (HNO_3) and Ultra-pure water.

Purification and Oxidation of SWNTs: SWNTs were purified by acid treatment method which was a slight modification from the method reported by Liu *et al*. [29] In this method, H_2SO_4 was substituted by HCl and other alterations were as explained below. SWNTs were treated in a mixture of HNO_3 and HCl in 3:1 (v/v) ratio in an ultrasonic water bath for 4 h. Now the SWNTs were separated from the acid by washing several times with distilled water until the filtrate acquires a pH of 7. Then the SWNTs were oven dried at 105 ºC and stored in desiccators for further use.

Methodology: SWNTs and DSPE-PEG 2000 amine were taken in a ratio of 1:4 in a 20 ml Scintillation glass vial and 5 ml of ultrapure water was added and mixed well. Firstly, sonication was done by using ultrasonic bath sonicator (PCI analytics) by placing in a central location in the sonication tank filled with 1400 ml of distilled water at 33 KHz in an ice-bath cooling system for 90 min by maintaining the temperature not exceeding 20 ºC ± 5 ºC.



Now the SWNTs suspension was centrifuged using ultracentrifuge (Sorvall Discovery M150 SE) for 6 h at 4 ºC, 23,000 rpm and the supernatant was collected and stored at 4 ºC. Now the supernatant was characterized by using FE-SEM, Raman Spectroscopy, FT-IR, UV-VIS-NIR, and Zeta potential.

Characterization:

FE-SEM Analysis: The morphology of functionalized single-walled carbon nanotubes were carried out by Field Emission Scanning Electron Microscopy. FE-SEM (Zeiss, Supra55) images were recorded by Signal A = In Lens mode and WD = 3.7 mm, EHT = 5.00 kV and at different magnifications.

Raman Analysis: Raman Spectra were measured on an In Photonics Raman Spectrometer Model (DV420-OE) and the excitation wavelength of the laser was 532nm. The samples for the observation were prepared by forming a thin film of SWNTs aqueous solution on the slide, then allowing them to dry in a desiccator.

FTIR Analysis: FTIR spectra of the produced SWNTs samples were recorded by a Bruker Alpha-T. Samples were pelletized in KBr using a 25-ton ring press under the pressure of 10 ton. The background spectrum of control KBr was subtracted from that of the SWNTs spectrum. In the employed configuration it has been possible to cover the 400-4000 cm^{-1} range with a resolution of 4 cm^{-1}.

UV-VIS-NIR Analysis: UV-VIS-NIR absorption spectra were recorded with UV-Vis-NIR Spectrophotometer (UV-3600, Shimadzu) to determine the SWNT concentration in the suspension.

Zeta Analysis: A 100 µl aliquot of NH_2-SWNTs was diluted in 1.9 ml of ultra-pure H_2O, the Zeta potential and size were analyzed in triplicate using Malvern Zeta sizer Nano ZS 90 based on quasi-elastic light scattering.

RESULTS AND DISCUSSION: Recent studies showed that to obtain an efficient and non-cytotoxic SWNT-based delivery system, the length, bounded functional groups, metal contaminants in impure SWNTs, the degree of aggregation and type of functionalization may be the key parameters [30-32]. Carbon nanotubes with these optimized physicochemical parameters can be used in biomedical applications as biocompatible materials [33]. In the present study, firstly Hipco SWNTs were treated with acids (HNO_3 and HCl) and sonicated which resulted in the metal contaminants removal, shortening the length and oxidized ends reduce the aggregation. The introduced carboxylic group on the surface of SWNTs were used as reaction precursors in the functionalization which allows the possibility of SWNTs to combine with DSPE-PEG 2000 amine that enhances the solubility and biocompatibility of SWNTs. **Fig. 1a** & **b** shows the aqueous solution of SWNTs before and after Sonication.

BEFORE SONICATION **AFTER SONICATION**

FIG. 1: ULTRA SONICATION OF SWNTs

FE-SEM Analysis of Purified SWNTs: SWNTs were characterized by using Scanning Electron Microscopy which provides the morphological information of SWNTs and impurities by EDAX analysis. The SEM images and corresponding EDAX image analysis results of the sample were represented in **Fig. 2A** & **B**. The SEM images showed that the carbon nanotubes were single walled and the lengths of the SWNTs were 400nm to 1000 nm. EDAX analysis of non functionalized SWNTs shown in **Table 1** represents the composition and amounts of the elements present in the SWNTs.

Spectrum Processing: No peaks omitted, Processing option: All elements analyzed (Normalised)

Number of iterations = 3

Standard:

C $CaCO_3$ 1-Jun-1999 12:00 AM
Fe Fe 1-Jun-1999 12:00 AM

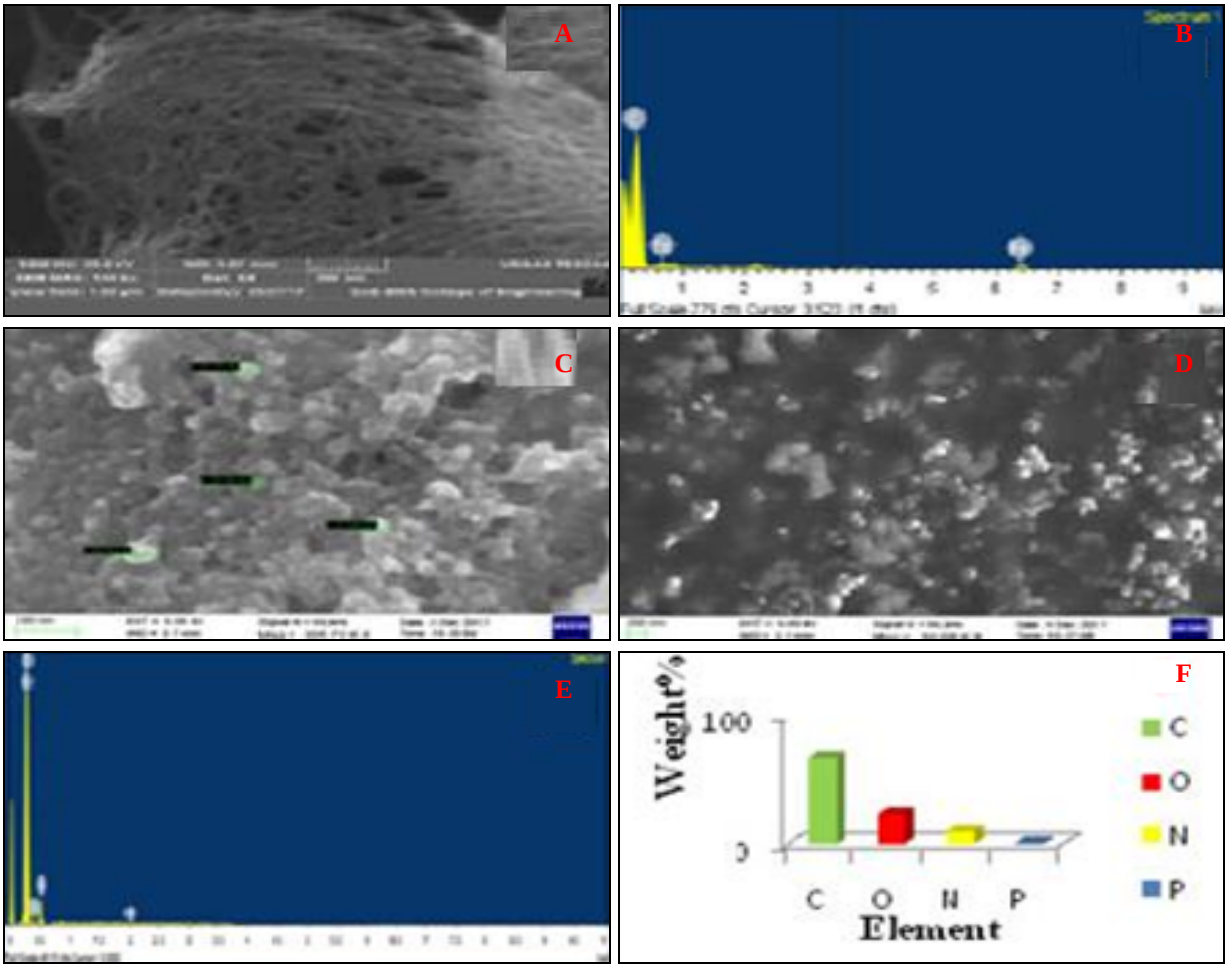


FIG. 2: A) SEM IMAGE OF HIPCO SWNTs AT 130KX. B) EDAX IMAGE REPRESENTING THE PRESENCE OF DIFFERENT ELEMENTS IN NOPO HIPCO SWNTs. C) FESEM ANALYSIS OF SAMPLE AT 305.72KX (FUNCTIONALIZED SWNTS SIZE ON AVERAGE OF 100 TO 120 nm). D) FESEM ANALYSIS OF SAMPLE AT 50.08KX (UNIFORM DISTRIBUTION OF SWNTS IN DSPE PEG 2000 AMINE POLYMER) E) EDAX IMAGE REPRESENTING THE PRESENCE OF DIFFERENT ELEMENTS. F) QUANTITATIVE ANALYSIS OF WEIGHT % ELEMENTS IN THE SAMPLE

TABLE 1: REPRESENTS WEIGHT % AND ATOMIC % OF SWNTs

Element	Weight %	Atomic %
C K	98.87	99.25
Fe K	1.13	0.75
Total	100.00	100.00

Fe SEM Results of Functionalized SWNTs: Field Emission Scanning Electron Microscope (FESEM) is a familiar microscopic method to understand the morphological structure and subsurface composition of nanomaterials with EDAX analysis [34]. **Fig. 2C** represents the morphological study of the functionalized SWNTs. The Field Emission Scanning Electron Micrographs showed that after sonication, the length of the SWNTs was reduced to an average of 100 nm to 120 nm and **Fig. 2D** represents that the functionalized SWNTs were uniformly distributed in DSPE PEG 2000 amine polymer.

EDAX analysis of functionalized SWNTs was carried out for 7 iterations. The composition analysis for various components like C, O, N, and P in terms of weight % and atomic %. Numerical values are tabulated Table 2 & 3 and represented graphically in **Fig. 2F**.

Spectrum Processing: Peak possibly omitted: 4.517 kev, Processing option: All elements analyzed (Normalised)

Number of iterations = 7

TABLE 2: REPRESENTS THE STANDARDS OF THE ELEMENTS

C	$CaCO_3$
N	Not defined
O	SiO_2
P	GaP
Fe	Fe
Cl	KCl

TABLE 3: REPRESENTS WEIGHT % AND ATOMIC % OF ELEMENTS IN THE SAMPLE

Element	Weight %	Atomic %
C K	67.36	73.34
O K	22.38	18.29
N K	9.37	8.03
P K	0.89	0.34
Total	100.0	100.00

From the EDAX analysis **Fig. 2E Table 1** & **3** of non functionalized and functionalized SWNTs, it was confirmed that the weight % of carbon is reduced from 98.87 to 67.36 along with the appearance of new atoms indicating that the functional groups (N, O, P) were attached to SWNTs. So from this analysis, it was confirmed that the size of SWNTs was reduced and the SWNTs were non covalently functionalized by using DSPE-PEG 2000 amine.

Raman Spectroscopic Analysis: Raman spectroscopy is one of the well-established technique to analyze the vibrational properties and electronic structures, particularly for the characterization of the diameter of carbon nanotubes and helps to identify SWNTs and MWNTs along with purity of the samples. The G/D ratio is a good index to measure the quality of SWNT purity [35-37]. Raman spectroscopy analysis of carbon nanotubes monitors peaks such as Radial Breathing Mode (RBM) according to the diameter of the SWNTs. RBM intensity is more sensitive to the chirality and diameter for SWNTs with a diameter of 0.6 ~ 1.4 nm. The intensity and shape of D-mode at 1290-1320 cm^{-1} relates to the SP^3 hybridized carbon atoms which in turn corresponds to the extent of defects inside wall of the carbon nanotubes and sidewall functionalization. Raman spectroscopy at 532 nm excitation was done, and measurement parameters were maintained at the same excitation wavelength. Raman spectra's of the purified and functionalized SWNTs are presented in **Fig. 3A** & **B**.

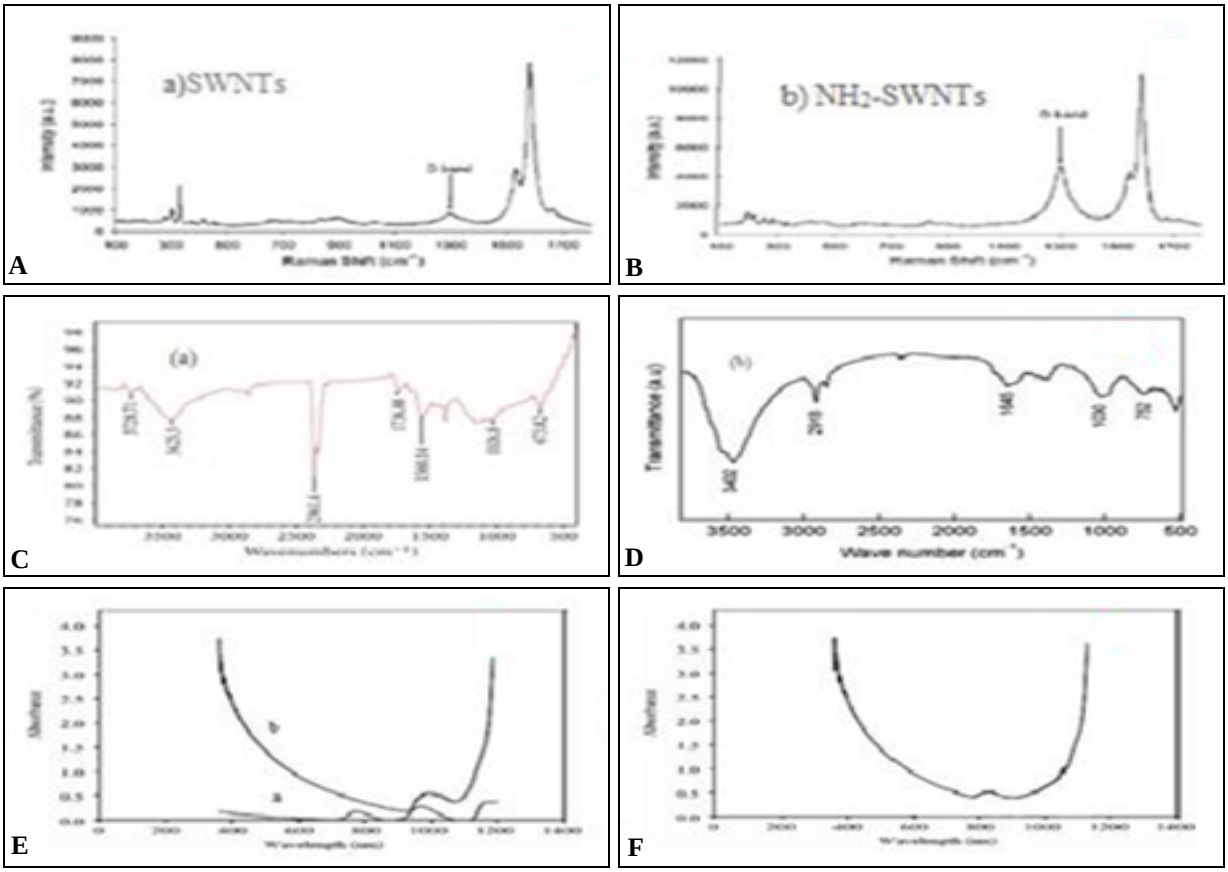


FIG. 3: A) RAMAN SPECTRA OF PURIFIED HIPCO SWNTs B) RAMAN SPECTRA OF FUNCTIONALIZED SWNTs. C) FT-IR SPECTRUM OF PURIFIED AND OXIDIZED SWNTs. D) FT-IR SPECTRUM OF FUNCTIONALIZED SWNTs. E) UV-VIS-NIR ABSORPTION SPECTRUM OF PURIFIED AND OXIDIZED HIPCO SWNTs. F) UV-VIS-NIR ABSORPTION SPECTRUM AFTER FUNCTIONALIZATION WITH DSPE-PEG 2000 AMINE

In the spectra, RBMs, D-band and the G-band were observed between 100~ 300cm^{-1}, 1250~ 1350 cm^{-1}, and 1500~ 1600 cm^{-1} respectively [38]. From the Spectrum, RBM peaks were observed at 272, 236, 186 cm^{-1} and it was observed that the intensities of the RBM were decreased after functionalization. The D- band represents the disorganization in the hexagonal framework of the carbon nanotubes and D-band, and G-band relative intensities represent the defects introduced upon functionalization [39]. D-band peak at 1300 cm^{-1} and G-band peaks at 1526 cm^{-1} and D/G ratio were 0.056 which confirms that the sample was Single-walled carbon nanotubes having high purity **Fig. 3A**. From **Fig. 3B**, the D/G ratio was 0.42, indicating an increased disorder in the structure of the functionalized carbon nanotubes and a significant increase in the intensity of the D-band due to the electronic resonance confirms amine functionalization.

FT-IR Analysis: Fourier Transform-Infrared Spectroscopy (FTIR) is an analytical technique used to identify organic and in some cases inorganic materials also. The change in the nature of bonding and impurities in SWNTs are studied using FTIR spectroscopy. Unknown IR absorption spectrum is compared with standard spectra to identify the polymer or other constituents in the sample. Absorption bands in the range of wavelengths from 1500 cm^{-1} - 4000 cm^{-1} are typically due to functional groups and from 400 cm^{-1} to 1500 cm^{-1} represents the fingerprint region. Absorption bands in this region are due to intramolecular phenomena and are highly specific to each material [27]. The alterations in the functional groups that occur in the functionalized SWNTs were analyzed by FTIR and compared with the purified and oxidized SWNTs. The intensities of the broad bands in the region 3500 cm^{-1} - 3400 cm^{-1} can be assigned to –OH and N-H stretching vibrations. The FTIR spectra of oxidized show four major peaks, located at 3728, 3425, 2361, and 1560 cm^{-1} respectively.

From **Fig. 3C**, peak at 3728 cm^{-1} is attributed to free hydroxyl groups, a broad peak at ~3425 cm^{-1} which is a characteristic of the O-H stretch of the hydroxyl group which is attributed to the oscillation of carboxyl groups. The peak at 2361 cm^{-1} can be associated with the O−H stretch from strongly hydrogen-bonded −COOH. The peak at 1736 cm^{-1} is associated with the stretch mode of carboxylic groups as observed in the IR spectrum of the acid-treated SWNTs indicating that carboxylic groups are formed due to the oxidation of some carbon atoms on the surface of the SWNTs by nitric acid. The peak at 1560 cm^{-1} is related to the carboxylate anion stretch mode. From **Fig. 3D** a broad and strong peak at 3402 cm^{-1} was assigned to stretching vibration of the N-H bond which increased after functionalization. The peak at 2918 cm^{-1} was attributed to C-H stretching which is absent in the IR spectrum of the purified SWNTs.

The peak at 1645 cm^{-1} was attributed to C=C stretching of SWNTs and N-H bond bending of the amine group due to amine functionalization and indicating that the functional groups were introduced on to the sidewall of SWNTs. The peak at 1030 cm^{-1} was assigned to stretching vibration of C-O bond increased after functionalization. A small peak in the range 1100-1000 cm^{-1} indicates the presence of inorganic phosphate ion and indicating the functional groups were introduced on to the sidewall of SWNTs. Thus the presence of amine groups in the functionalized SWNTs can be expected [40, 41].

UV-VIS- NIR Spectroscopy: UV-VIS-NIR absorption spectroscopy is a powerful tool to determine the concentration of dispersed SWNTs [42, 43]. The dispersed SWNTs reveal the maximum UV-VIS-NIR absorbance of the solution corresponds to the maximum concentration of dispersed SWNTs. Using higher polymer concentration, the dispersion rate of SWNTs increases and maximum dispersion can be achieved by sonication at low temperature. Longer sonication time is required for the dispersion of higher SWNT concentrations [44]. From **Fig. 3E**-(a) two distinct peaks were observed at 960 nm and 750 nm in absorption spectra of Hipco SWNTs, and they represent the first and second pair of van Hove singularities of the carbon nanotubes. In **Fig. 3E**-(b), peak at 760 was disappeared, and the surface modification in the SWNTs resulted in the disruption of the aromatic ring which in turn showed changes in conductivity. As a result, changes were observed in van Hove singularities in the absorption spectrum. This represents that damage on the sidewall after acid treatment.

From **Fig. 3F**, distinct peak was observed at 808nm observed after functionalization using DSPE-PEG 2000 amine. The concentration of functionalized SWNTs was recorded, and the dispersed SWNT sample concentration was found to be 152 mg/L at 808nm.

Size and Zeta Potential Measurement: The surface charge and the stability of the SWNTs were determined by Zeta potential analysis. The zeta potential of the purified SWNTs and NH_2-SWNTs were tested individually. **Fig. 4A** & **B** represents the zeta potential and sizes of purified SWNTs were -12.6 ± 1.4mV and 128.43 ± 9.2 respectively. Furthermore, after non-covalent functionalization using DSPE-PEG 2000 amine, SWNTs were dispersed into a stable aqueous suspension, and their solubility is gradually improved, and the zeta potential and size of NH_2- SWNTs were 39.35 ± 2.1mV and 158.56 ± 8.7 respectively as shown in **Fig. 4C** & **D**. It was observed that the zeta potential and diameter obtained with SWNT-cur using PVP K30 was found to be -12.5 ± 1.1 mV and 170.4 ± 8.5 nm [45]. This shows that the size and stability were improved using DSPE PEG 2000 amine. Compared with the purified SWNTs, the amine functionalized SWNTs size was smaller and the zeta potential reversed from negative to positive which indicates the SWNTs were amine functionalized and as the zeta potential is 39.35 ± 2.1 mv indicates the functionalized SWNTs are more stable without any aggregation. The nanoscale size and strong interparticle repulsion suggest that the cationic amine functionalized SWNTs may be further linked with anionic biomolecules like RNA and DNA which makes the formulation suitable for *in-vivo* administration [46].

Size and Zeta Potential Measurement (Before Functionalization):

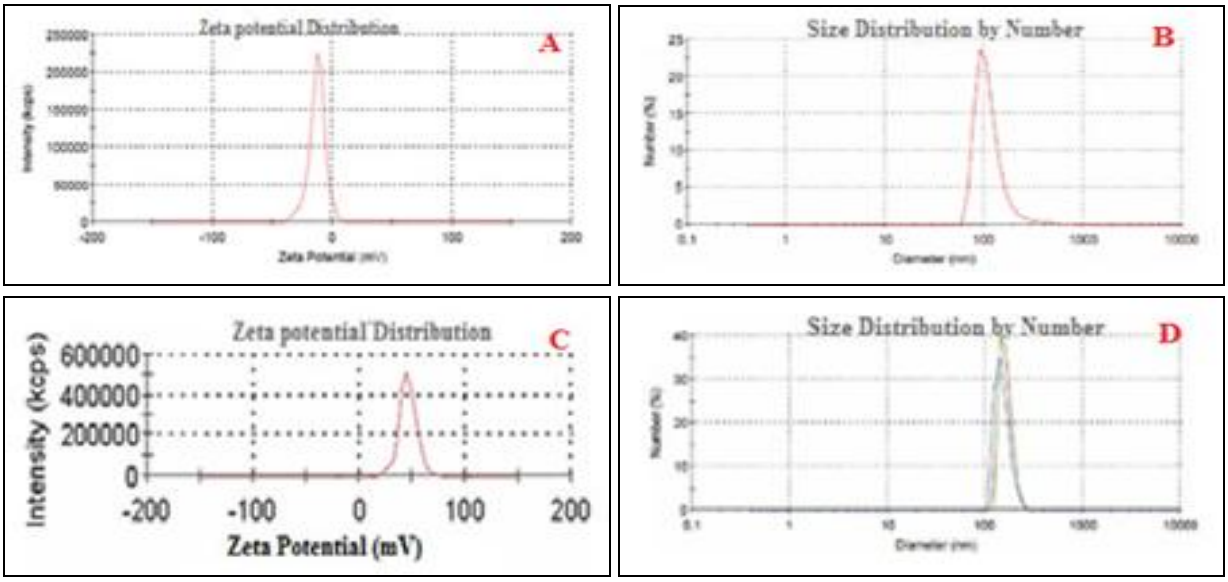


FIG. 4: A) ZETA POTENTIAL OF PURIFIED SWNTs. B) PARTICLE SIZE DISTRIBUTION OF PURIFIED SWNTs. C) ZETA POTENTIAL OF NH_2- SWNTs. D) PARTICLE SIZE DISTRIBUTION OF NH_2- SWNTs.

CONCLUSION: Single-walled carbon nanotubes functionalized with DSPE-PEG 2000 amine was successfully prepared and characterized using different techniques like FE-SEM, Raman Spectroscopy, FT-IR, UV-Vis-NIR and Zeta potential measurements. The morphological study using FESEM showed that the functionalized single-walled carbon nanotubes were embedded and well dispersed within the polymer matrix. Raman analysis confirms the Single-walled carbon nanotubes are of high purity and amine functionalized. Functionalization of SWNTs was further confirmed through FTIR spectroscopy by comparing the spectral differences between purified SWNTs and functionalized SWNTs.

UV-VIS-NIR corresponds to the concentration of dispersed SWNTs. Zeta potential measurement confirmed the stability and improved solubility of NH_2-SWNTs. Henceforth these functionalized SWNTs can be used as a carrier in many biomedical applications which also implies the

effective capability and possibility of using such surface to load and deliver a variety of therapeutic agents, enzymes, proteins and biomolecules to the disease target sites.

ACKNOWLEDGEMENT: The author(s) greatly acknowledges DST (Women Scientist –A), New Delhi for financial support to carry out this research.

CONFLICT OF INTEREST: The authors declared no conflicts of interest.

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How to cite this article:
Lalitha KN, Mohan GK and Uma A: Surface modification and noncovalent functionalization of single walled carbon nanotubes and their characterization. Int J Pharm Sci & Res 2019; 10(8): 3816-24. doi: 10.13040/IJPSR.0975-8232.10(8).3816-24.