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“Enhance the Loading Capacity of Carbon Containing Nano-Carriers through Surface Modification”

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ABSTRACT

Introduction: Drug delivery systems (DDS) aim to enhance drug release by targeting tissues and reducing dosages. Carbon nanotubes (CNTs), with superior mechanical, electrical, optical, and thermal properties, show promise for DDS. It can improve polymer matrices' thermal and mechanical properties. However, current DDS have drug loading capacities below 10%. CNTs' high surface area offers potential for large-scale delivery. Modifying CNT surfaces with hydrophilic or amphiphilic polymers can boost loading capacity, and chemical functionalization can enhance biocompatibility.

Objective: This study investigates improving CNT-based drug delivery systems by enhancing drug loading capacity, solubility, and biocompatibility through surface modifications. It aims to boost loading capacity with various surface modifications, increase biocompatibility via chemical functionalization, and evaluate covalent functionalization's impact on solubility and dispersibility, advancing the development of more effective CNT-based drug delivery systems.

Method: Single-walled carbon nanotubes (SWCNTs) were oxidized using sulfuric acid (H_2SO_4) and nitric acid (HNO_3) at 100°C for 2 hours. The oxidized SWCNTs were then converted into acyl chloride groups with thionyl chloride ($SOCl_2$) in tetrahydrofuran (THF), followed by amino-functionalization. Infrared (IR) spectroscopy was used to analyze the functionalized CNTs and identify characteristic peaks indicating successful carboxylation.

Results: IR spectra indicate successful SWCNT oxidation, showing peaks for carboxyl groups (C=O at 1633.76 cm^{-1}). This functionalization enhances solubility and dispersibility, improving SWCNT suitability for drug delivery applications.

Conclusion: The study demonstrates CNTs' potential in DDS, showing improved drug loading capacity, solubility, and biocompatibility via surface modifications, with functionalized SWCNTs as promising drug carriers.

Keywords: *Carbon nanotubes (CNT), Single-walled carbon nanotubes (SWCNT), graphene, nano-diamond, drug delivery system, surface modification.*

Introduction

Drug delivery system (DDS) aim to improve drug release efficiency and effectiveness. Drug delivery systems that are able to precisely target the right tissue and reduce the dosage required to produce the therapeutic effect of treatment make it possible to achieve DDS.(1) Since CNTs have exceptional mechanical, electrical, optical, thermal, and electrical conductivity qualities in addition to having a large surface area, they are a hot issue in study. The incorporation of CNTs into polymer bulk materials will surely enhance their thermal and mechanical properties.(2)Drug release occurs at a reasonably fast initial burst release time, and the drug loading capacity of the drug delivery system is still below 10%. The process of identifying and altering materials with the potential to serve as drug carrier materials will improve this system. Carbon nano tubes (CNTs) are one substance that shows promise as a carrier (CNTs)(3).

Drug loading is the process of mixing the active medication with the carriers to be delivered to the intended cells or tissues; CNTs are commonly used for this purpose because of their spherical shape and high surface area to volume ratio, which offer enormous potential for large-scale drug delivery(4). Moreover, by changing the hydrophilic or amphiphilic polymers on their surface, CNTs’ loading capacity can be increased (5). CNTs’ biocompatibility could also be improved by chemically functionalizing their surface.(2) Covalent anchoring of PEG layers(6), amphiphilic de-block co-polymers (7), or PAMAM dendrimers (8) on the surface of CNT’s can be used to change them in a hyluronic acid matrix.(9).

Cylindrical tubes made of one or more coaxially stacked layers of grapheme sheets with sp2 hybridized carbon atoms organized in a honeycomb lattice can be used to present the structure of carbon atoms organized in a honeycomb lattice can be used to represent the structure of carbon nano tubes(CNTs). As a result, carbon nanotubes (CNTs) can be divided into two categories: Single-walled CNTs (SWCNTs) and Multi-walled CNTs (MWCNTs), which are composed of multiple concentric grapheme sheets.(10) These tubes have quite small and uniform diameter, on the order of 1nm =10-9m(11).

APPLICATIONS OF CNTs IN DRUG DELIVERY:

CNTs are nanometer in size and are long cylindrical formed by covalent bonds between carbons. CNTs has as large ratio of length to diameter so that it can provide a large surface area. It is easy for CNTs to absorb drugs, DNA, vaccines, or antibodies on the surface or cavity of the tube.(1)The applications of CNTs as drug excipients are of interest, given their capacity to interact with macromolecules such as proteins and DNA. The salient characteristics of an efficient dug delivery system include its ability to perform controlled and targeted drug delivery, which CNTs have been shown to exhibit (4).

Functionalization of CNTs:

Researchers in the fields of synthetic chemistry and materials science find it interesting to add “chemical functionalities” to the nano tubes in order to functionalize them in way that would enable them to overcome such challenges(9). Functionalization can increase the solubility and processibility of nanotubes (12) by combining their unique features with those of other materials. A variety of the CNT functionalization such as carboxyl-, hydroxyl-, amine-, and amino- functionalization of CNTs have been reported. As a result of this surface modification, CNTs’ hydrophobic and intact surface change into hydrophilic and active surfaces, which improves their compatibility and distribution across a wide range of solvents and media.(13)

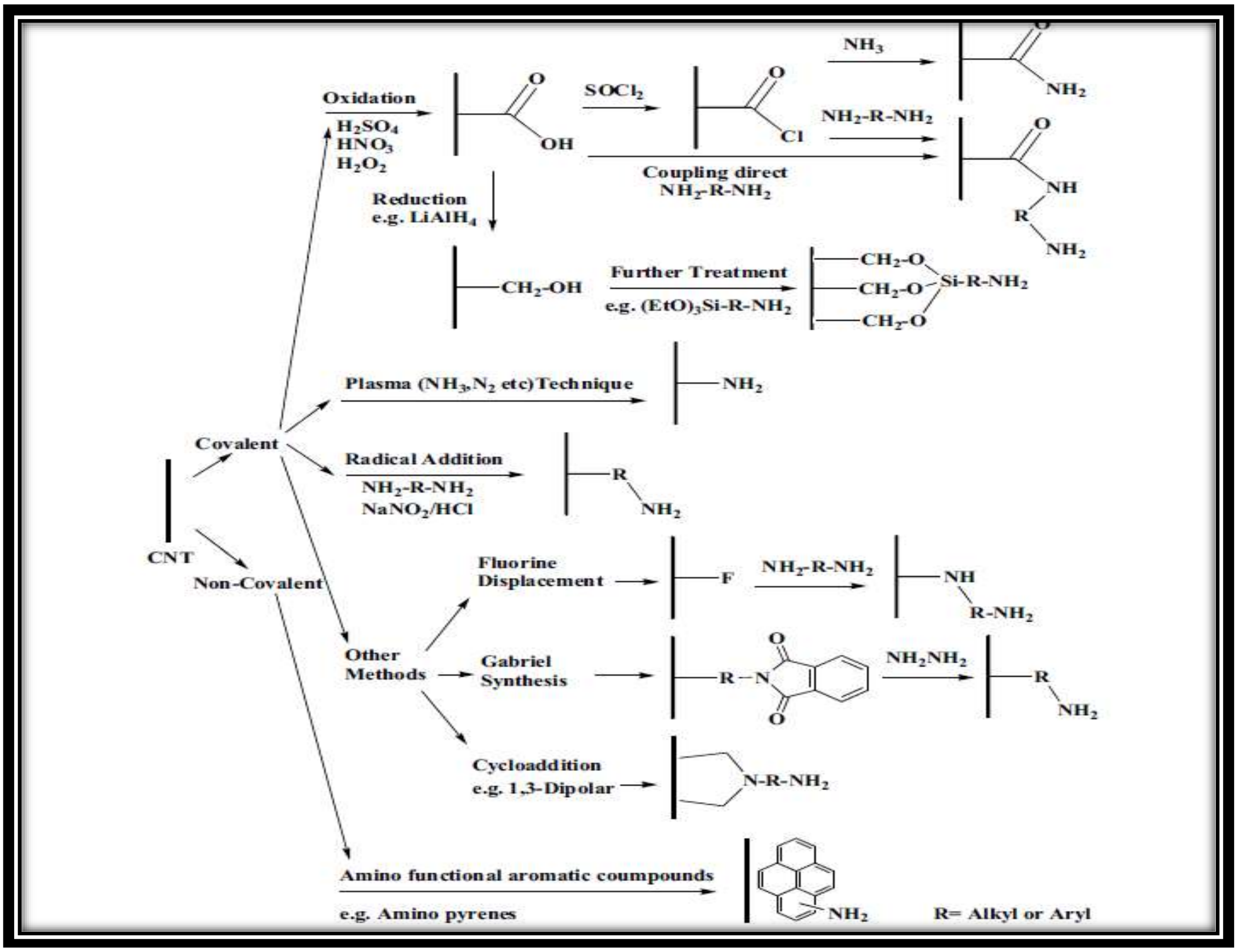

Fig:1 *Strategies for covalent and non-covalent functionalization* (13)

Covalent Functionalization:

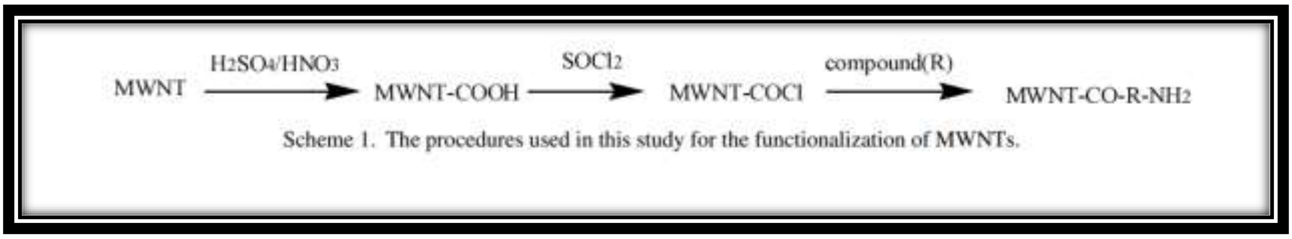

Fig:2 *The Procedure Used In This Study For The Functionalization Of SWNT.*

The covalent functionalization of MWNT and SWNT open ends can be used to build chemically sensitive proximal probe tips capable of imaging surfaces at high resolution. Specifically, the carboxylic acid groups at the open nano tube ends can be linked to a variety of chemical groups to give the ends basic or hydrophobic activity. When scanned across OH-terminated self-assembled mono-layers, proximal probe microscopes use carbon nano tube tips that have been chemically modified with either amines (-NHx $_5$) or phenyl ($-C_6H_{55}$) groups to measure distinct adhesive forces. Reactions with gas molecules driven by a transient arc generated at the MWNT ends can also functionalize unopened MWNT proximal probe tips. Different gases react differently with functionalized metal-organic frameworks (MWNTs). MWNTs exhibited acidic properties when they reacted with O_2, pH-independent properties when they reacted with H_2, and basic properties when they reacted with N_2 (13).

Among the many reactions that can be used to derivative carboxy (-COOH) functional groups, we have concentrated on nano-tube chemical modification that involves the coupling of amines to the carboxyl group at the tip ends to form amide-linked groups (Fig: 3). The broad applicability of this coupling reaction to aqueous and non-aqueous chemistry makes it especially attractive for nano-tube functionalization. (14)

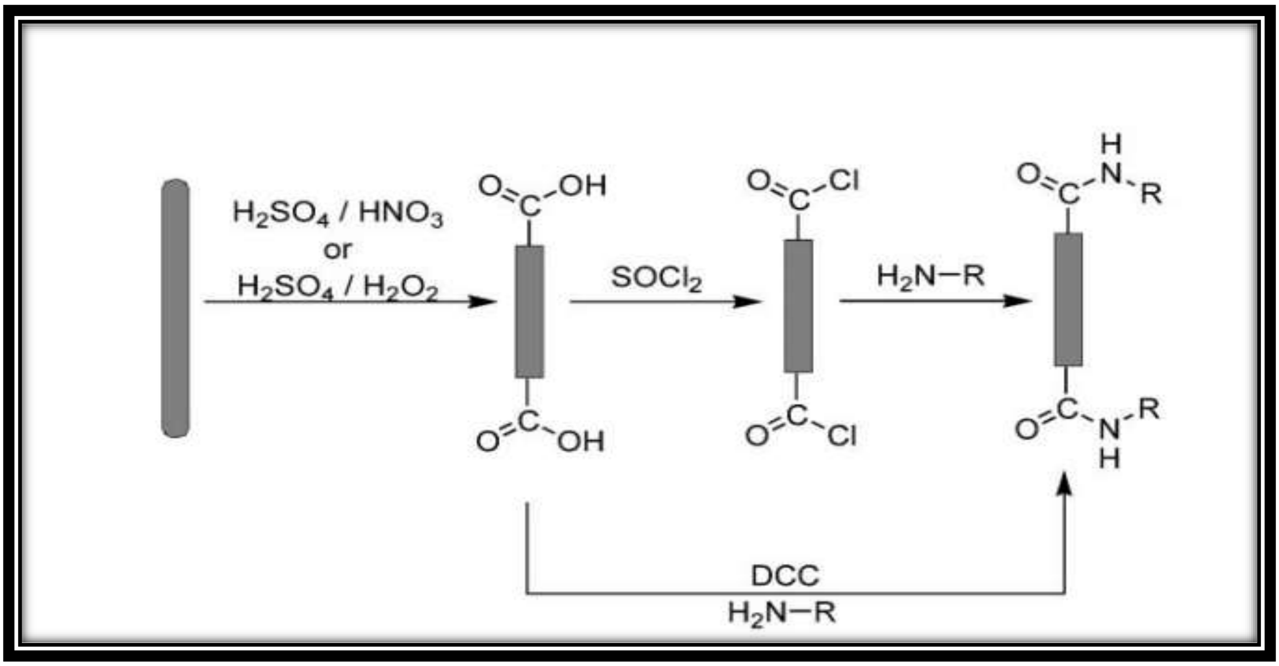

Fig:3 *Schematic depiction of oxidative etching of swcnts followed by treatment with thionyl chloride, and subsequent amidation. The depiction here is for simplicity, and in deference to the difficulty in accurately determining the nature and location of oxygenated functionalities. It is understood that these oxidations also result in the introduction of moieties at defect sites along the sidewalls, and that functionalities other than carboxylic acids are formed (such as esters, quinines, and anhydrides). Additionally, although only one per end is shown, there are expected to be multiple functionalities at each end. Also shown is the dicyclohexyl carbodiimide coupling of a primary amine and swcnt carboxy groups. Alcohols have also been employed as the nucleophile, resulting in the formation of ester linkages (15).*

Covalent Sidewall Functionalization:

Covalent functionalization is predicated on changing sp2 carbon atoms to sp3 carbon atoms, which breaks the translational symmetry of carbon nanotubes. CNTs are highly reactive and can be grafted with other chemical species to potentially increase the adhesion between the polymer and CNTs, leading to increased mechanical performance. This is especially true because of the p-orbitals of the sp2-hybridized C atoms. COOH and OH moieties are typically covalently induced through various mechanisms, including oxidation with oxygen, air, aqueous hydrogen peroxide, concentrated sulfuric acid, nitric acid, or other acid combinations (16-17).

Covalent side wall functionalization is a chemical process used to modify carbon nanotubes (CNTs) to enhance their properties : such as solubility in organic solvents, dispersion stability , chemical reactivity , electronic properties [like conductivity etc], and compatibility with other materials. This method involves the formation of covalent bonds between functional groups and the carbon atoms on the sidewalls of the CNTs. The functionalization can be achieved through various reactions, such as oxidation, amidation, esterification, and cycloaddition.

One common approach involves treating CNTs with strong acids, such as sulfuric acid (H2SO4) and nitric acid (HNO3), which introduces carboxyl (–COOH) and hydroxyl (–OH) groups on the sidewalls. These groups can then react with other molecules to attach different functional groups, improving solubility, dispersibility, and reactivity. Covalent functionalization is crucial for applications in nanocomposites, sensors, drug delivery, and other areas where enhanced interaction between CNTs and other materials is desired.

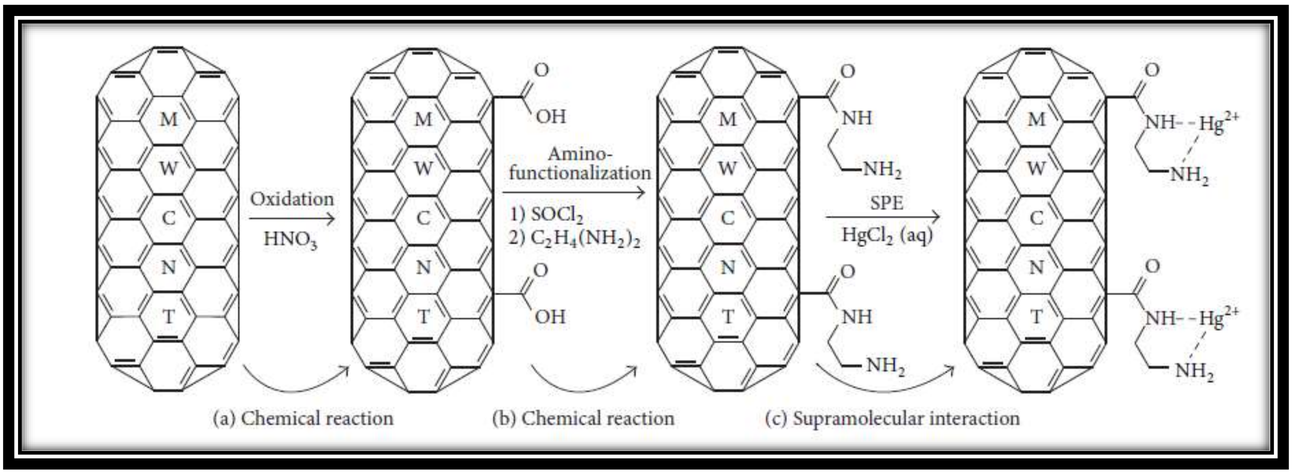

Fig:4 *Covalent Sidewall Functionalization*

MATERIALS AND METHOD:

MATERIALS:

Methanol (HPLC grade), ethanol, propanol, Cu(NO3)2·4H2O, Pb(NO3)2, Cd(NO3), ethylenediaminetetraacetic acid (EDTA), and HgCl2.Ca(NO3)2· 4H2O, MgCl2· 6H2O, DMF, THF, SOCl2, HCl (35%), HNO3 (65%), and Thiourea.

METHOD:

The oxidation process involved treating the CNTs with H2SO4 and HNO3 at 100°C for 2 hours.

Preparation of Oxidized CNTs.

The oxidized CNTs are created by oxidizing raw CNTs. CNTs (0.1 g) are spread in a flask with 30mL of H2SO4 (65%). The mixture is refluxed at 100℃ for 120 minutes to oxidize CNTs (fig:5). After cooling to ambient temperature, the mixture is filtered through a 0.45 μm PTEE filter and rinsed with deionized water until the pH of the filtrate reaches 7. The filtered material is then dried at 70℃ for 2 hours. The resultant solid is employed as purified CNTs in the subsequent phase (18).

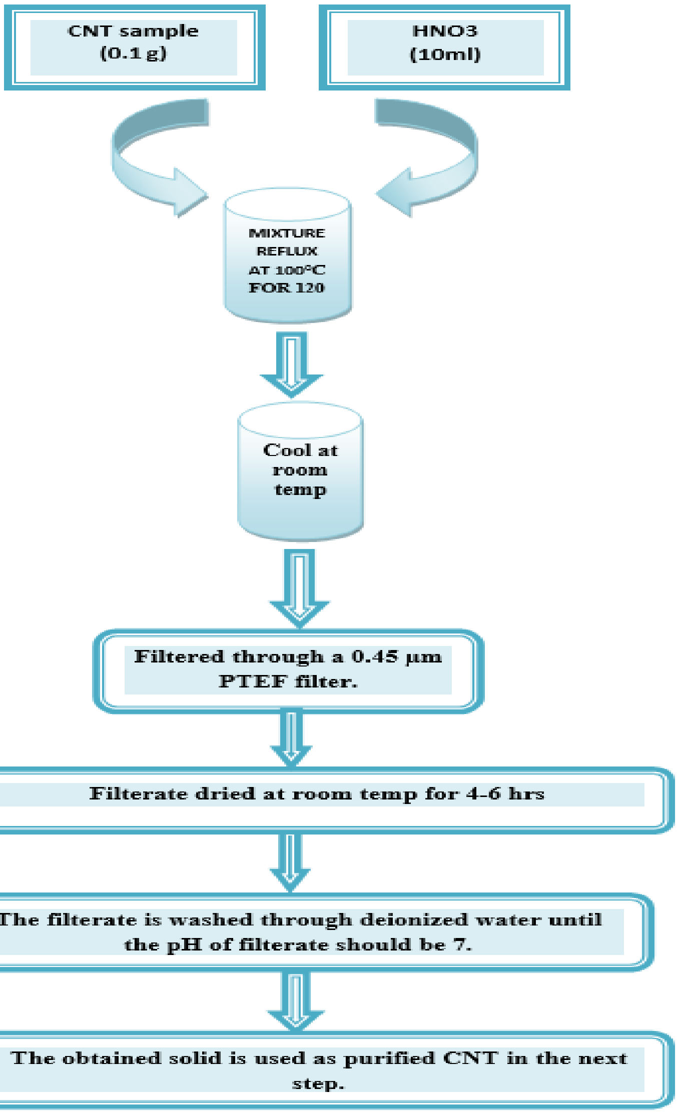

Fig:5 *Oxidised SWCNT Preparation.*

Preparation of Acyl chloride CNTs:

To make acyl chloride CNTs, the oxidized CNTs (0.1g) are suspended in 50ml of SOCL$_2$ and 16.6 ml of THF (tetrahydrofuran). To convert surface-bond carboxyl groups into acyl chloride groups, the suspension is treated with an ultrasonic bath (40 kHz) foe 30 minutes, followed by 24 hours of stirring at 70°C. The solid is subsequently filtered and washed with anhydrous THF. It is then dried in a hoover at ambient temperature for hours. The resulting solid is used in the amino-functionalization process (19-20).

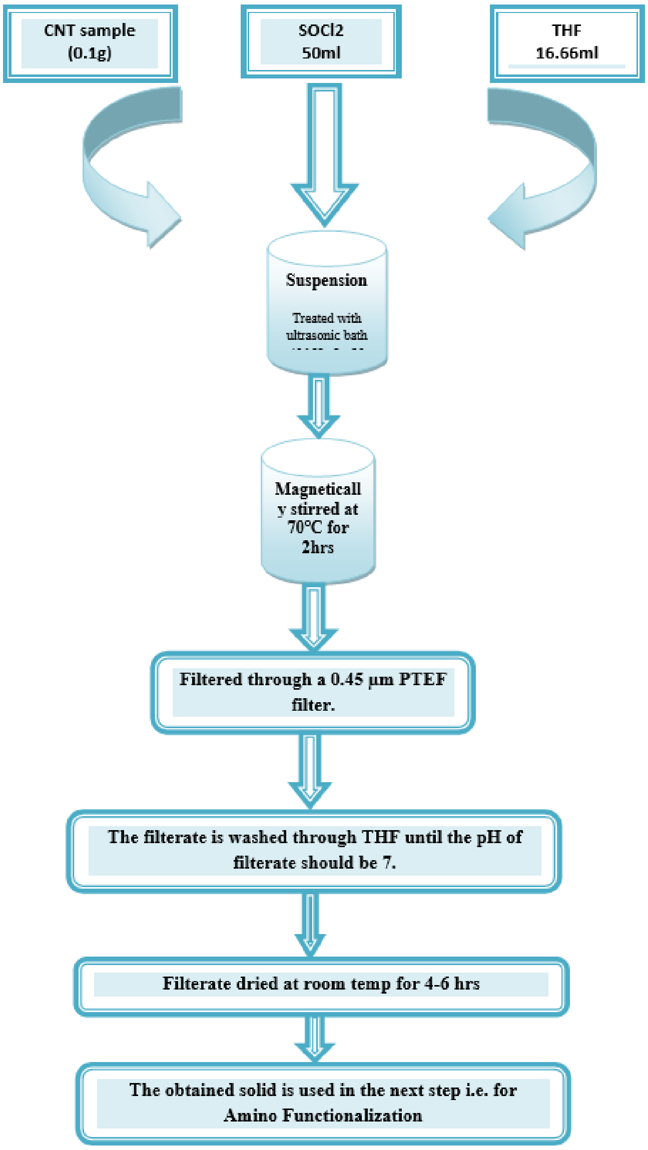

Fig:6 *Synthesis Of Acyl* Chloride *CNTs*

RESULT:

IR spectra of raw & oxidized CNTs:

All the IR spectra of SWCNTs, GRAPHENE, NANODIAMOND recorded using the KBr pellet method, reveal significant changes post-oxidation.. The IR spectra of raw &oxidized CNTs showed characteristic peaks.

Sample 1: *SWCNT'S*

SWCNTs are insoluble in water and for the improvement in solubility and dispensability in different solvent it is treated with conc. H2SO4 and HNO3 at 100^{o}C, so that it will open its carboxylic moiety and the identification of carboxylated SWCNTs have the characteristic peaks of at N-H at 3464.27cm^{-1}, C-H at 2858.60 cm^{-1} , C=C at 2002.18 cm^{-1} , C=O at 1633.76 cm^{-1}.

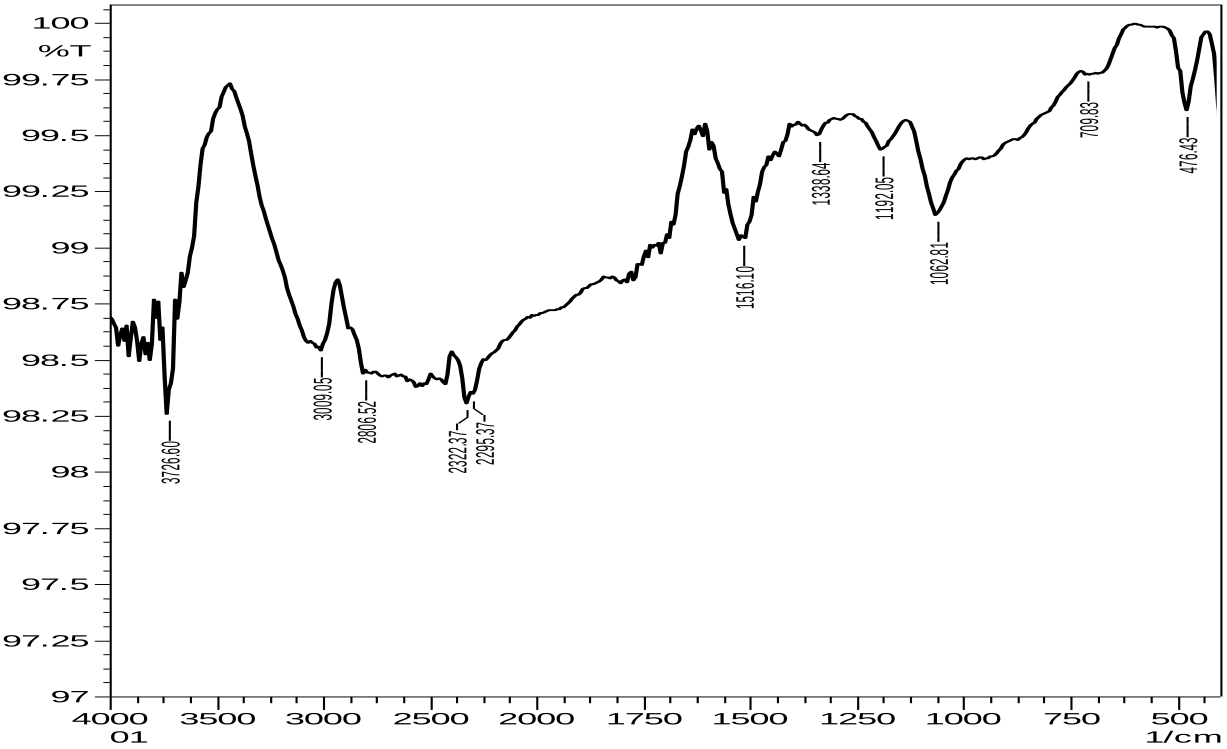

Fig:7 *IR spectra of Raw SWCNTs.*

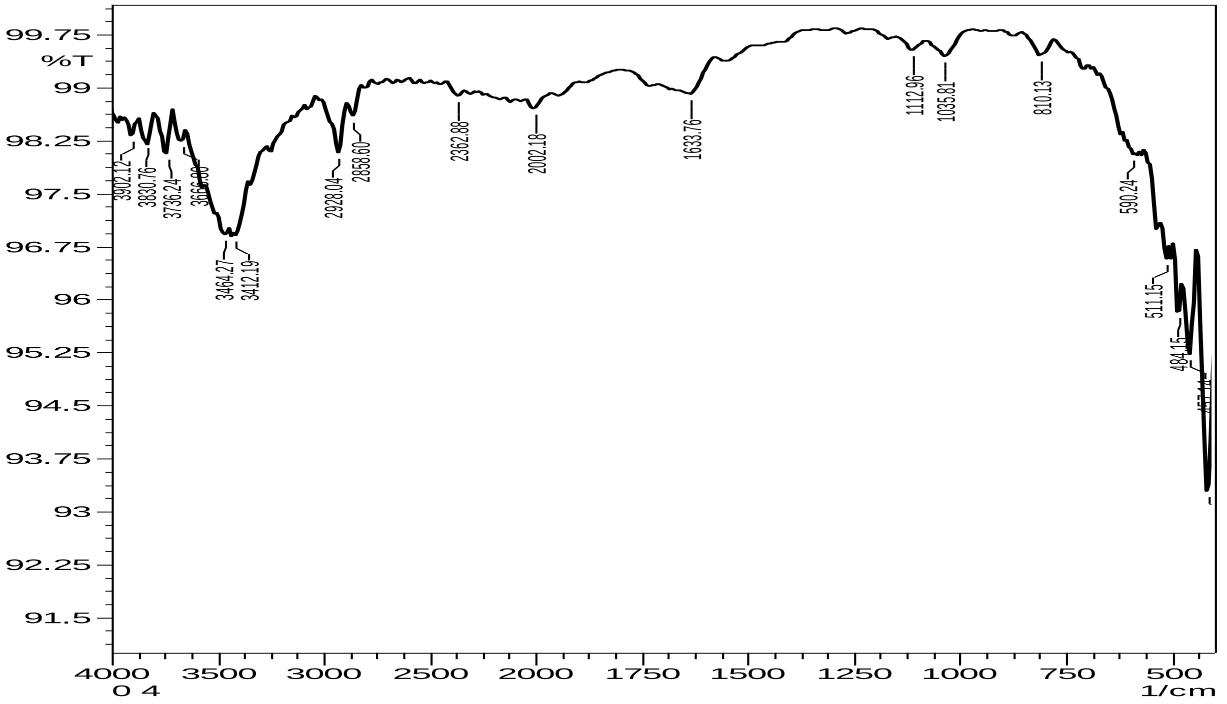

Fig:8 *IR spectra of Oxidized SWCNTs*

Sample 2: NANO-DIAMOND

Nano-diamond are undissolved in water, they are treated with concentrated H2SO4 and HNO3 at 100$_{β}$C to open up their carboxylic moiety. The distinctive peaks of carboxylated nano-diamond are C=O at 1703.20 cm-1, CONH at 1626.05 cm-1, C-N at 1176.62 cm-1, C-O-C at 1033 cm-1, and C-O at 1111.03 cm-1 that can be used to identify them.

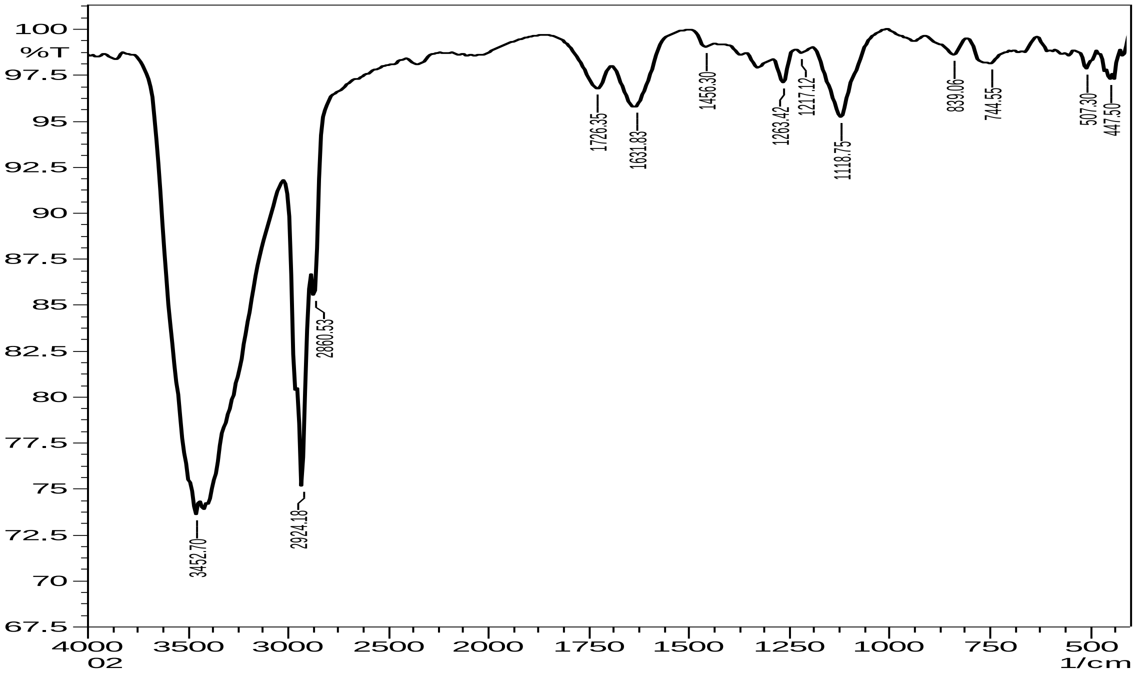

Fig:9 *IR spectra of Raw Nano-diamond CNTs.*

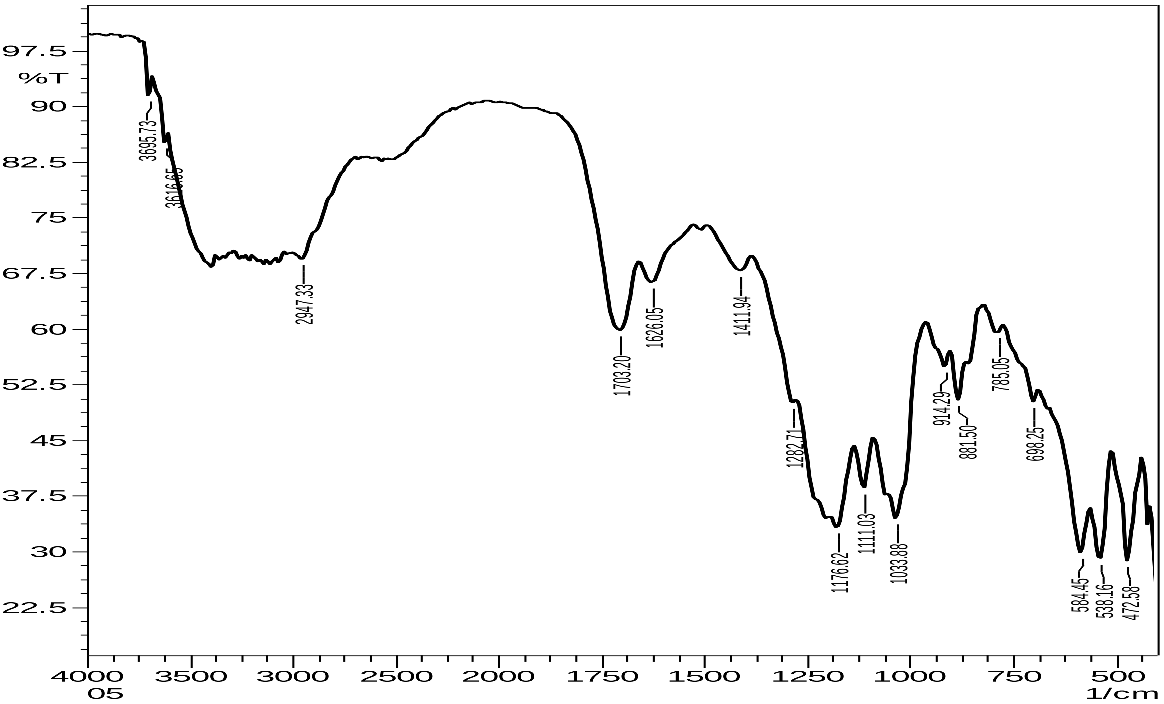

Fig:10 *IR spectra of Oxidized Nano-diamond CNTs.*

Sample 3: GRAPHENE

Graphene is insoluble in water, so it is treated with concentrated H2SO4 and HNO3 at 100°C to open its carboxylic moiety. Carboxylated graphene has characteristic peaks at C-N at 1286.56 cm-1, C=C-CH at 3055.35 cm-1, and C-H at 2949.26 cm-1.

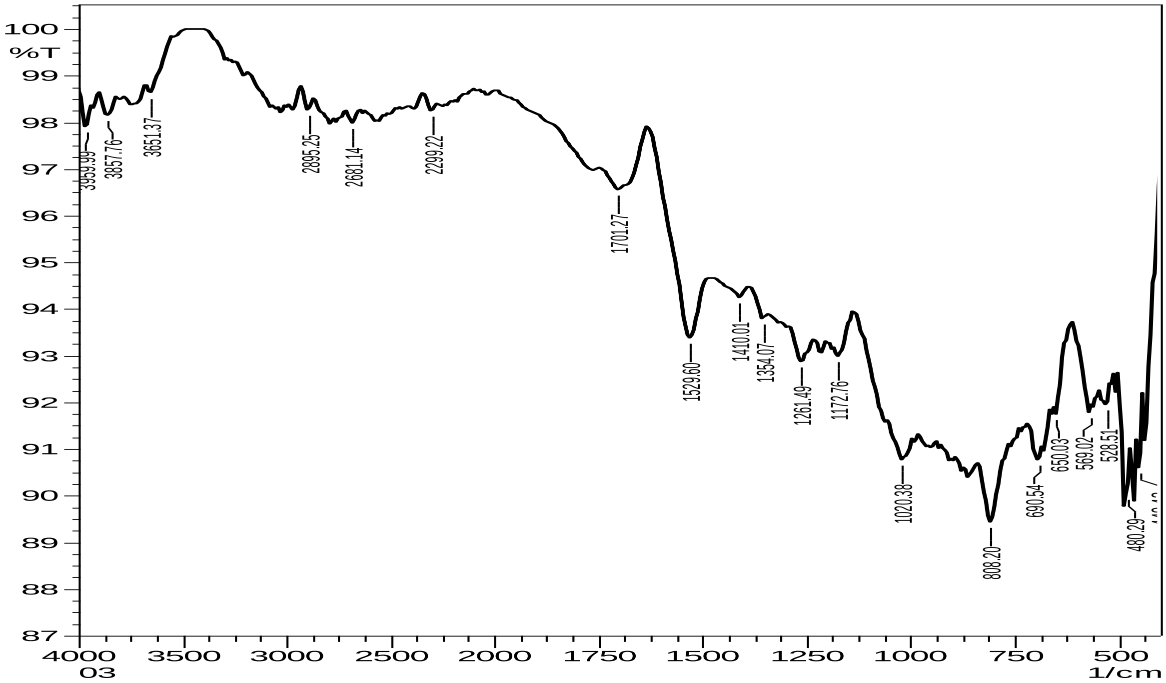

Fig:11 *IR spectra of Raw Graphene CNTs.*

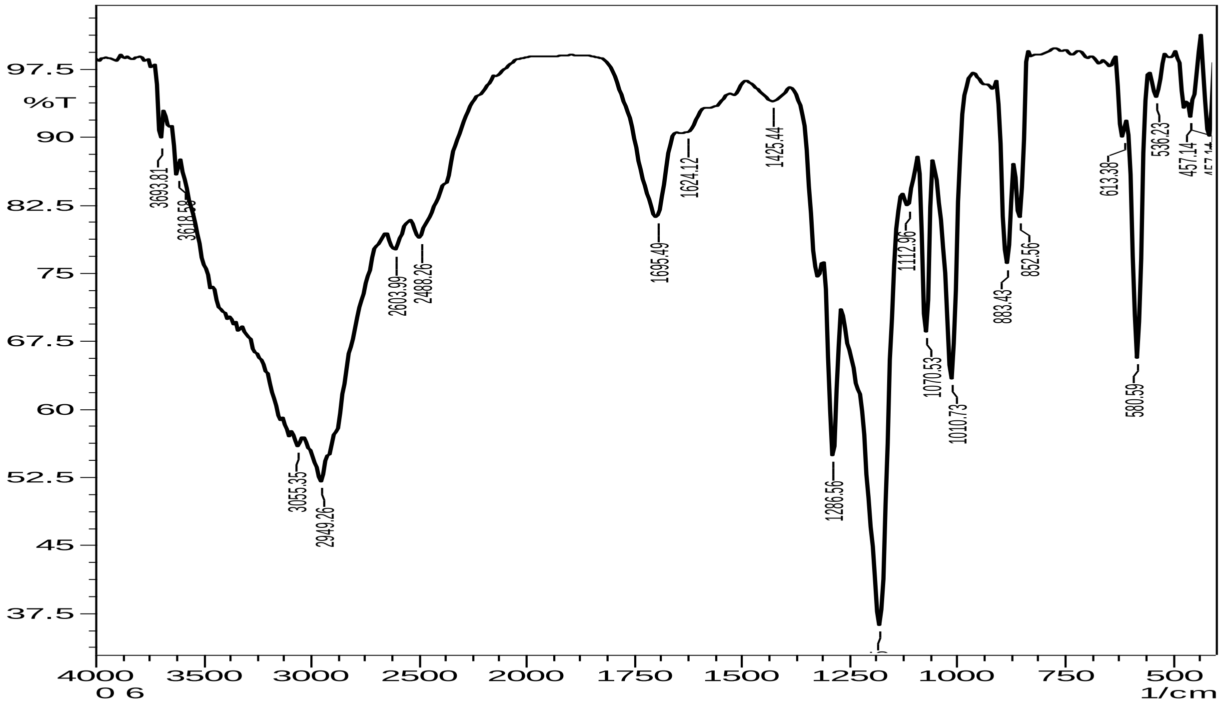

Fig:12 *IR spectra of Oxidized Graphene CNTs.*

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