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Investigate the carboxylation in carbon containing nano-carriers for drug delivery systems

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Abstract

Introduction: This study explores the versatile properties of carbon nanotubes (CNTs), emphasizing their exceptional mechanical, thermal, electrical, and optical characteristics, particularly in drug delivery applications. Synthesis methods, like low-temperature chemical vapor deposition (CVD), are favored for precise control. Challenges, such as working with small structures, high production costs, and implementation uncertainties, are acknowledged. Detailed discussions on CNT properties, including mechanical strength and thermal conductivity, underscore their suitability for drug delivery systems. Specific challenges of single-walled carbon nanotubes (SWNTs), focusing on purity and dispersibility, are addressed. The outlined plan involves a literature review, carboxylation method selection, post-carboxylation identification, and characterization steps, exploring SWCNTs' conversion, curcumin-loaded delivery systems, amino-functionalization, and targeted drug delivery functionalization. The chosen carboxylation method involves H_2O_2/UV oxidation, with applicable procedural steps for both SWCNTs and multi-walled CNTs (MWCNTs).

Summary and Conclusion: This investigation aims to advance the understanding of carbon-based nano-carriers, particularly CNTs, for drug delivery. The abstract encapsulates the exploration of CNT properties, diverse applications, challenges, and the proposed systematic methodology for carboxylation, providing a succinct overview of the study's objectives and significance.

Keywords: Carbon nanotubes, SWCNTs**,** MWCNTs, CVD

Introduction

Carbon (C) is one of the most versatile elements in the periodic table, known for its tetra velent shell [2]. In the earth's crust, carbon ranks as the 15th naturally occurring element [1]. Its unique electronic structure makes it difficult to completely gain or lose electrons for forming fully occupied orbital's in chemical reaction. By combining various hybridization of sp3, sp2 and sp1 or embedding other foreign atoms in carbon hybrids the desired properties can be modified and researchers working with carbon materials have been doing this for a considerable time [2]. Since carbon has a tetra valency and an sp3 hybridization, it can form a wide range of crystalline structures [1]. There are two naturally occurring crystalline forms of pure carbon: diamond and graphite. Carbon atoms in diamond in diamond exhibit sp3 hybridization, which occurs when four, are pointed towards the corners of a regular tetrahedron. One of the reasons for its hardness is the ensuring three-dimensional network, or diamond, which is incredibly stiff. In graphite, sp2 hybridization occurs, in which each atom is bonded evenly to three carbons (120) in the x-y plane, and a weak bond exists in the z axis. A graphite sheet's characteristic hexagonal (honeycomb) lattice is formed by the sp2 set [3].

In 1985, researches led by Korto and associates discovered Buckminster fullerence (C60), a novel type carbon. In addition to fullerene (C60), diamond, and graphite, quasione-dimensional nanotubes are another type of carbon that was first identified by Ijima in 1991 when he found multiwalled carbon nanotubes (MWCNTs) in carbon soot produced using an arc-discharge technique. Allotropes of carbon are carbon nanotubes, or CNTs [3].

Carbon Nanotubes

Carbon nano tubes (CNT) are the fundamental building blocks of nanotechnology. Carbon with an atomic number of 6 plays a vital role in nanotechnology [4]. Carbon nano tubes (CNTs) have unique atomic arrangement and band structure [5]. CNTs have outstanding mechanical, thermal, electrical, and optical properties that are being used exclusively or in mix to deliver keen sensors or on other hand multifunctional materials [6].

These extraordinary properties make CNTs one of the most revered interconnect materials in current nano scale technology [5]. Carbon nano tubes are the allotropes of carbon [3]. Carbon nanotubes are made up of carbon and it is a tube shape material which have very small diameter [7]. The diameter of nanotube is about 10 thousand times smaller than the diameter of human hair [8]. The diameter of carbon nanotube is measured by nano scale [7].

In recent years carbon nanotubes are the most exciting areas of research [9]. The nano sized carbon (or nano carbons) which comprise fullerenes, graphene and CNT [10]. Special priority is given to graphenes and CNTs, as they play into current advances based on nano materials, including conductive and high-strength composites, artificial implants, sensors, drug delivery systems, energy conversion and storage devices, radiation source, and field emission displays, hydrogen storage media, and nanometer-sized semiconductor devices, probes, and interconnects [4].

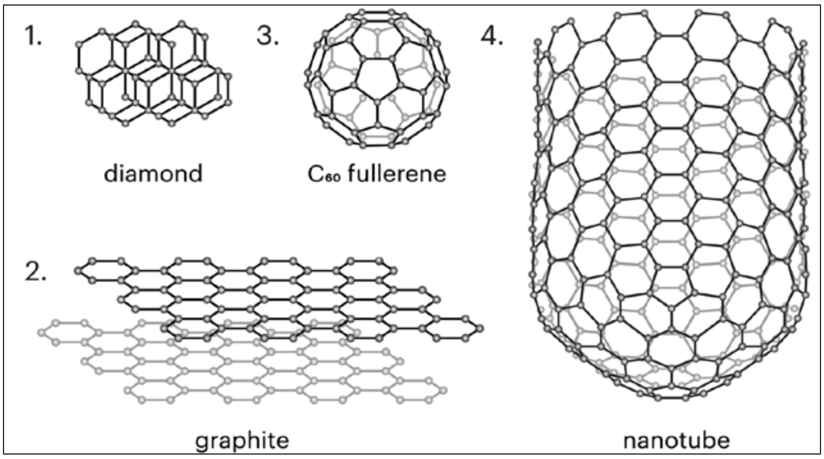

Fig 1: Types of carbon nanotubes

Structure of carbon nanotubes

Carbon nanotubes, also known as tubular fullerenes. CNTs are cylindrical [13] sheets of graphite [12] of sp^2 bonded carbon atoms [13] that have been rolled into tube. CNTs are considered as nearly one dimensional structure (1D bucky-tube shape) according to their high length to diameter ratio [12]. Carbon nanotubes are bucky-tubes, in carbon nanotubes, carbon molecules are in cylindrical shape and have unique properties that make carbon nanotubes used in different areas [11]. Graphenes which are rolled into cylinder that forms carbon nano tubes [5].

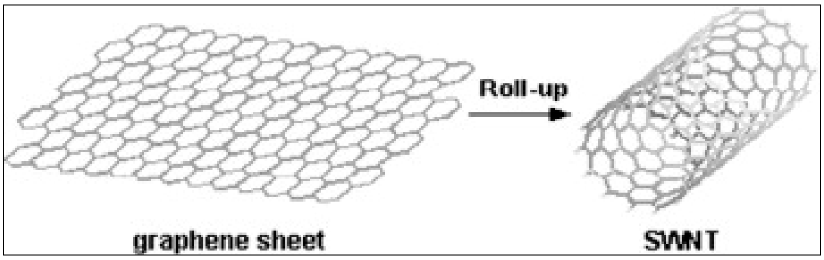

Fig 2: Structure of carbon nanotubes

Classification of carbon nano tubes

Carbon nano tube are classified in the following two types:

- SWCNTs- Single-walled carbon nanotubes
- DWCNTs- Double walled carbon nanotubes
- MWCNTs-Multiple-walled carbon nanotubes

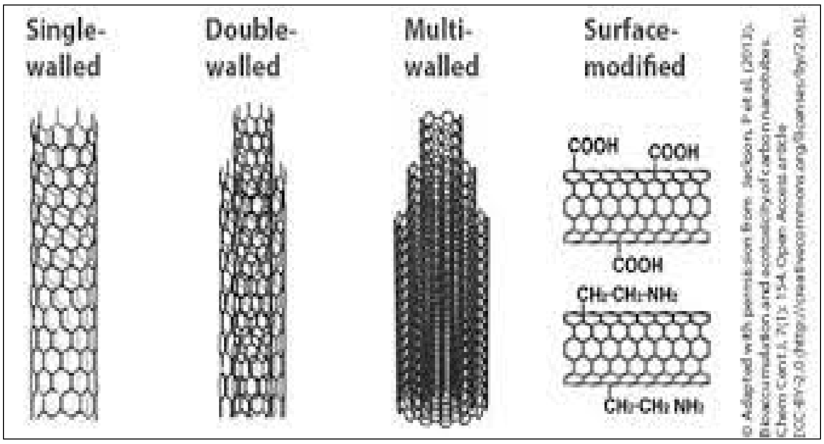

Fig 3: Classification of carnon nanotubes

SWCNTs- Single-walled carbon nanotubes

Single-walled CNTs (SWCNTs) are made of a single graphene sheet rolled upon itself with a diameter of 1-2nm [14]. Comprised entirely of carbon, the structure of pure SWCNT can be visualized as rolled-up tubular shell of grapheme sheet which is made up of benzene type hexagonal rings of carbon atoms. Graphene sheets are seamless cylindrical derived from a honeycomb lattice, representing a single atomic layer of crystalline graphite [3].
CNTs generally have a length to diameter ratio of about 1000 and more so they can be considered as nearly one-dimensional structure [12]. The length can vary depending on the preparation methods [14].

DWCNTs- Double walled carbon nanotubes

Double-wall nanotubes (DWNTs) indeed exhibit unique properties that make them promising candidate for various applications DWNTs, as the name suggests, consist of two concentric nanotube walls. These structures offer a combination of properties from both single-wall nanotubes (SWNTs) and multi-wall nanotubes (MWNTs).
Here are some key points about DWNTs and their potential applications:

Chemical Resistance: One of the notable feature of DWNTs is their superior resitance to chemicals. This property can be crucial in application where exposure to harsh environments or chemicals reaction is a concern. The outer wall of DWNTs can act as a protective layer, preventing the internal properties of the nanitube from being compromised.

Functionalization: The ability to modify the outer wall of DWNTs while maintaining or chemical properties allows for functionalization. Functional groups can be attached to outer surface to impart specific properties or enable theattachment of molecules for Targeted applications. This makes DWNTs versatile for various functional modifications.

Dielectrics: DWNTs can be employed in delectric applications. Dielectric are materials that do not conduct electricity but a support the formation of an electric field. The unique structure of Dwnts may offer advantages in term of dielectric properties, making them suitable for use in electronic devices and capacitors.

Gas sensors: The chemical resistance and surface modification of DWNTs make them suitable for gas sensing applications. The interaction between gases and the modifies surface of DWNTs can lead to detectable changes in their properties, enabling the development of sensitive and selective gas sensors.

Nano sensor: DWNTs can be used in nanosensors due to their size & sensitivity. The ability to finctionalize the outer wall allows for the detection of specific molecules or changes in the surrounding environment at the nanoscale. This is valuable in fields such as medical diagontics and environmental monitoring.

Nano composite materials: Incorporation DWNTs into composite materials can enhance their mechanical, thermal, and electrical properties. The dual-wall structure provides an additional dimension for tailoring material properties, making DWNTs useful in the development of advanced nanocomposites.

Field-Emission displays: The unique properties of DWNTs, including their electrical conductivity and structural stability, make them suitable for applications in field-emission displays. These displays use the phenomenon of field emission for producing images, and the properties of DWNTs can contribute to the efficiency & performance of ssuch displays [15].

Synthesis of double-wall nanotubes (DWNTs) via CCVD

- The synthesis of DWNTs involves the chemical vapor deposition (CCVD) technique, a common method for growing carbon nanotubes.
- The CCVD process for DWNTs was first proposed in 2003. In this technique, the selective reduction of oxide solutions in a mixture of methane and hydrogen takes place. The reduction process facilities the growth of carbon nanotubes.
- The selective reduction of oxide solutions suggest that certain precursor materials containing oxides are used, and the reduction step is a key aspect of the synthesis [4].

MWCNTs-Multiple-walled carbon nanotubes

MWCNTs consist of multiple concentric layers of graphene rolled up into a tube-like structure. These layers are cylindrical and can range from a few to hundreds layers.
The distance between adjacent layers in MWCNTs is typically around 0.34 nanometers. This distance reprents the within a single graphene sheet [4].

Structure of MWNTs

- MWNTs consist of multiple layers of graphene sheets rolled upon themselves to form a cylindrical
- The layers are arranged concentrically, with each layer representing tub. The no. of layers (tubes) can vary, and it determines the diameter of the nanotube.

Diameter Range

- The diameter of MWNTs can vary, and it typically falls within the range of 2 to 50 nanometers.
- The variation in diameter is attributed to the no. of graphene tubes (Layers) present in the nanotube structure. Nanotubes with large diameters usually have a higher no. of concentric layers.

Inter-layer distance

- The inter-layer distance in MWNTs, or the distance adjacent graphene layers/ is mentioned as approximately 0.34 nanometers.
- The distance represents the separation between and properties of MWNTs [14].

Synthesis of CNTs

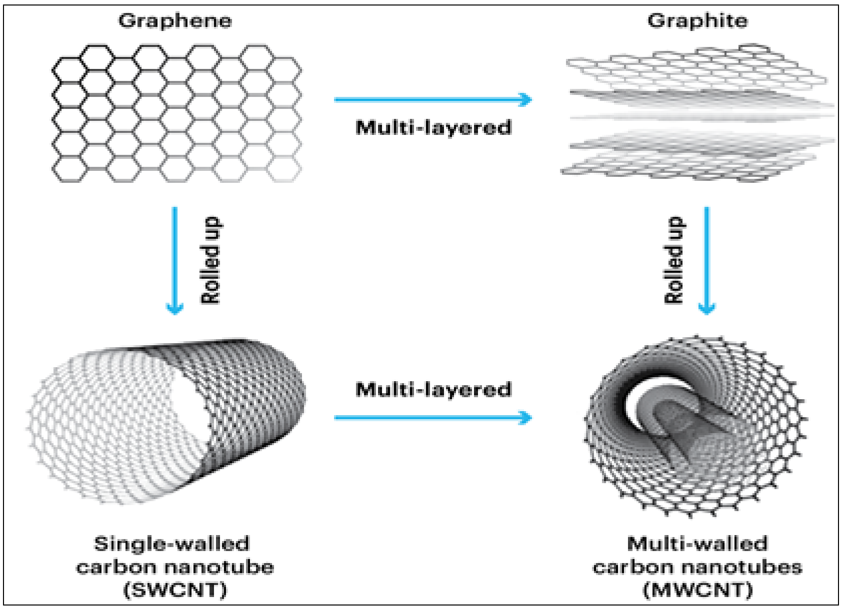

Fig 4: Formation of graphene sheets.

High-quality nanotube materials are essential for both fundamental research and technological applications. In this context, “high-quality” refers to the absence of structural and chemical defects over a considerable length scale, typically ranging from 1 to 10 microns along the tube axes. The increasing no. of patents and publications on carbon nanotube (CNT) synthesis indicates the growing interest and advancements in this field. However, despite the progress, numerous challenges persist that need resolution, particularly in achieving the synthesis of CNTs with the desired high quality and extended length scales. Addressing these challenges is crucial to fully realize the potential of carbon nanotubes in various applications, from electronics to material science [3].

CNTs can be prepared by various methods, such as

a) Arc discharge method
b) Chemical vapor deposition
c) Laser ablation
d) Flame synthesis method

Arc discharge method: Two vertical, thin electrodes positioned in the chamber’s centre make up the arc-discharge assembly. A tiny bit iron can be held in the shallow dip of the lower electrode, or cathode, while reaction is evaporating. By applying a DC current of 200 A at 20V between the two electrodes, an arc-discharge can be produced. For the production of SWNTs, the three elements argon, iron, and methane must be used. When creating nanotubes by arc-discharge synthesis [14], narrow electodes with drilled holes used as anodes, and filled with a mixture of graphite and pure powdered metals (Fe,Ni, or Co). At 100-500 Torr in a He environment, the electrodes were vaporized at a comparatively modest current of 95-105 A. There was a large production of CNTs [15]. Two graphite electrodes in a reactor with a helium environment (660mbar) produced the arc [16].

Chemical vapor deposition: This procedure involves adding a mixture of hydrocarbon gas, acetylene, methane, or ethylene, and nitrogen to the reaction chamber. The hydrocarbon breaks down at temperatures between 700 ℃ and 900 ℃ while the reaction is going on, forming nanotubes on the substance at atmospheric pressure [17]. This processmay create a huge no. of nanotubes and control the direction in which the nanotubes develop on the substrate [18]. This method offers two main advantages. Although the quality of the nanotubes is inferior, they can be produced at a much lower temperature and can take on well-organised shapes thanks to the catalyst’s ability to be deposited on the top of the substrate [16].

Laser ablation

This process involves blasting the graphite target with laser light, growing the tube until too many catalyst atoms aggregate on the end of the nanotube, and allowing the large particles to either detach or become over-coated with enough carbon to poison the catalysis, allowing the tube to terminate with a catalyst particle or with a fullerene like tip [16].

Flame synthesis method

The method of Flame synthesis is another way to make CNTs. Hydrocarbon flames are used in this process. The formation and expansion of CNTs are aided by these fires. Rich sources of carbon are gases found in the post-flame area, such as CO, CH_4, C_2H_2, C_2H_4 and C_2H_6. The process is exothermic, and endothermic carbon deposition reactions are supported by chemical energy produced in the flame as heat. The provision of reactions sites for the deposition of solid black carbon is another necessity for catalysts. The growth of CNTs is similar to that of CVD. It is possible to obtain significant quantities of CNTs for commercial use if the right catalyst, flame, and reaction conditions are given [19].

Carboxylation

Carboxylation (Carbonylation) is the combination of an organic compound with carbon monoxide & carboxylation refers to reactions that introduce carbon monoxide into organic and inorganic compounds. The carboxylation refers to reaction that introduce carbon monoxide into organic and inorganic compounds. The carboxylation reaction is used to make aldehydes and alcohols containing carbon one additional carbon atom-the major product involves the introduction of the carbonyl group (>CO) into the starting materials to produce aldehydes (CHO), carboxylic acids (CO_2H), and esters (CO_2R).

Carboxylation of CNTs

Method 1: H_2O_2/UV Oxidation

In a typical process 1g of as received FWcnt was dispersed in 25ml hydrogen peroxide 30% w/v (100 vol.) in an open culture disk beaker, immersed in an ultrasonic bath and irridiated

With a UV LIGHT (Philips Lighting 250HPLN 250W without filter) at 15e 20 cm lamp distance during 15min. The resulting dispersion was diluted in distilled water, cleaned and filtered several times. Before drying, the wet sample was ground for 20mi in an agate motar and finally lyophilized. Nanotubes treated in this way will be called oxidized FWCNT all along this paper in order to avoid confusion with as received or pristine FWCNT that also contain traces of acid groups. This method was also applied to multiwall nanotubes: GS and NCL [26].

H_2O_2 /hv 2OH

Method 2

MWCNT done by adding concentrated H2SO4, and concentrated HNO3 in (1:1) ratio. The reaction mixture is sonicated for one hour. The (1:1) reaction mixture is refluxedat 120 °C foe 3 hours. After the reaction, the mixture was diluted with distilled water and allowed to sediment. The process repeated several times remove the acid and schematic illustration of carboxylation of MWCANT [20].

Functionalization of CNTs

The process of functionalizing carbon nanotubes (CNTs) improves their dispersion in solvents and polymeric materials by preventing agglomeration and bundle formation. To improve CNT's levels of reactivity and homogeneous dispersion, it is essential to purify or functionalize them. Purification is the process of getting rid of undesirable perticles that are left over from the synthesis process, while functionalization is the process of adding a particular functional group to the ends or side chains of CNTs (16&25). The Process of functionalizing carbon nanotubes involves adding different types of chemical functional groups, like carbonyl, hydroxyl, amine, and/or amino, to the structure. Because of this surface modification, CNTs' hydrophobic and intact surfaces change into hydrophilic and active surfaces, which improves their compatibility and distribution across a wide range of solvents and media [21-24]. CNT functionalization can result in more effective interaction and compatibility withnthe polymer matrix. CNT sidewalls can be carboxylated through oxidative treatments with acid mixes. Acid mixes that are often employed include HNO_3, HNO_3-H_2SO_4,$KMnO_4$,H_2O_2 and KMO_4-H_2SO_4.The oxidative treatments modify the side walls of CNT with carboxyl and hydroxyl groups (-COOH and -OH).Several researches have used these oxidative treatments to improve the surface functionality of CNTs [20].

Techniques and methods for amino functionalization CNTs: Numerous investigation have been carried out to produce amino group on the surface of carbon nanotubes (CNTs), and different techniques for amino functionalization of CNTs have been devised. A variety of research groups have extensively employed four main functionalization of CNTs oxidation, plasma and radical addition as covalent processes, and functionalization based on π-π interactions in pyrene derivatives as a non-covalent method [27].

Additional techniques for the amino functionalization of carbon nanotubes (CNTs) include the direct substitution of diamines for the fluoride(F) group [28], the synthesis of Gabriel [29] and formation of amides [34], as well as 1,3 dipolar and [4+2] cycloadditions [30-32]. These methods demonstrate a variety of covalent and non-covalent amino functionalization strategies for CNTs.

Conclusion

The conclusion of this investigation signifies a significant stride in advancing our comprehension of carbon nano-carriers, with a specific focus on carbon nanotubes (CNTs) and their potential in drug delivery applications. The abstract encapsulates a comprehensive exploration of CNT properties, their diverse application, encounted challenges, and proposed systematic methodoly for carboxylation. Elaborating on these aspects will provide a more in-depth understanding of study's objectives and its broader significance in the field of nanotechnology and drug delivery.

The study commences with an in-depth examination of the versatiles properties exhibited by CNTs, emphasizing their exceptional mechanical, thermal, electrical, and optical characteristics.

This foundational understanding establishes the groundwork for their exploration in various applications, positioning them as promising candidates for drug delivery systems. The categorization of CNTs into single-walled (SWCNTs) and multi-walled (MWCNTs) structures further refines their utility in specific contexts, fostering a nuanced understanding of their capabilities.

Synthesis methods, particularly low-temperature chemical vapor deposition (CVD), emerge as crucial contributes to the precision and control necessary for harnessing CNT's properties.

Despite the inherent advantages, the investigation conscientiously acknowledges challenges associated with the utilization of CNTs, such as navigating the intricacies of working with small structures, grappling with high production costs, and addressing uncertainties in implantation.

These challenges underscore the importance of developing comprehensive methodologies to maximize the potential of CNTs while mitingating potential drawbacks.

The proposed systematic methodology for carboxylation, employing H_2O_2 /UV oxidation, is a pivotal aspect of this investigation. This method is meticulously outlines, demonstrating its applicability to both SWCNTs and MWCNTs. This planned approach encompasses a literature review, method selection, post-carboxylation identification, and characterization steps, providing a clear roadmap for researchers interested in exploring CNTs for drug delivery.

In essence, this investigation's comprehensive exploration of CNYs for drug delivery not only deepens our understanding of their properties and challenges but also offers a strategic methodology, paving the way for future advancements in the utilization of carbon-based nano-carriers in the pharmaceutical field.

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