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Bionanocomposites: Drug Delivery System

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Abstract - The drug's solubility, subsequent transport through the intestinal membrane, and transit through the liver affect the pace of absorption and, therefore, the commencement of action. The bioavailability and, finally, the solubility of a drug's molecules determine its therapeutic efficacy. One crucial factor in achieving the optimum medication concentration in the bloodstream so that a pharmacological reaction may be seen is solubility. Only 8% of potential new drugs now in development have good solubility and permeability. The low water solubility of many medications is a major obstacle to the creation of highly effective formulations. When developing formulations, conducting clinical trials, or evaluating novel chemicals for medicinal efficacy, poor solubility is a concern. The bioavailability and absorption of such novel chemical are constrained by poor water solubility. Methodical formulation approaches are necessary to increase the bioavailability of such drugs due to their poor solubility. Such medications must have a high enough absorption rate after oral administration or be given intravenously in order to be considered bioavailable.

Keywords - Bionanocomposites, Drug Delivery System, Pharmacological, Medicines.

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INTRODUCTION

Nanotechnology is the practise of engineering working systems at the molecular level. The fast development of science and technology towards the end of the 20th century spawned not just novel, forward-thinking concepts, but also tools that allow us to literally see atoms in the material around us. Science especially that which was accomplished towards the end of the 20th century, may take credit for the amazing development of nanotechnology, Collaboration amongst chemists, biologists, physicists, computer scientists, and others in the scientific community made this outcome all but inevitable. As a result, the humanities, including philosophy, economics, and ethics, as well as the hard sciences, such as chemistry, electronics, mechanics, biotechnology, medicine, pharmacy, and computer science, have contributed to the fast development of nanotechnology.

We have covered such topics as an introduction to bionanocomposites, the Drug Delivery System, some applications of the Drug Delivery System, and the Multifunctionalism of Drug Carrier. Also, we stress the importance of the background information and the goals of the investigation. [1]

BIONANOCOMPOSITES

Bionanocomposites are a new class of nanostructured hybrid materials that have been created via the convergence of many different scientific disciplines. They consist of inorganic or environmentally friendly matrices and polymers with at least one dimension on the nanoscale scale. These biohybrid materials have significant practical value due to structural and functional features that are superior to those of conventional nanocomposites fabricated from synthetic polymers. Biopolymers' inherent biocompatibility and biodegradability provide new possibilities for these hybrid materials, especially in regenerative medicine and environmentally beneficial applications (green nanocomposites). The development of novel bionanocomposites, which add multifunctionality by synergistically mixing biopolymers with inorganic/green matrices and nanometer-sized materials, might be an interesting topic of research. [2]

Polylactic Acid/Cellulose Composites

The biodegradable agricultural raw material maize is used to create the versatile biopolymer polylactic acid (PLA), which has promising applications in the packaging, automotive, and biomedical sectors. PLA's potential in the packaging industry is significant because of its many desirable properties, including its high clarity and stiffness, excellent printability, and ability to be made using widely available production technology. The polymer PLA is now available for use in a wide range of food packaging contexts, including containers, cups, overwrap, and laminating sheets, all of which are designed to lengthen the life of perishable goods. However, PLA's thermal, water vapour, and gas barrier qualities are inferior to those of conventional petroleum-based polymers. In order to tailor the properties of the polymer, it is best to make green

composites out of the PLA and reinforcing elements like cellulose and its derivatives. [3]

Properties of Polylactic Acid/Cellulose Composites

Natural fibres and cellulose derivatives have been the subject of much study as reinforcements for PLA since the turn of the decade, with the goal of developing environmentally friendly composites with desirable properties. Due to their superior mechanical properties, such as exceptionally high bending strength and stiffness, nanoscale cellulose fibres show more promise as reinforcing fillers in polymer matrices. Nanoscale cellulose has been extensively explored for its potential in polymer composites, It may be made from a variety of organic materials like cotton, tunicate, bacteria, ramie, and wood. The high aspect ratio and strong dispensability of cellulose improve barrier characteristics to gases and vapours, which is especially helpful given that the presence of the impermeable crystalline fibres could lengthen the channel for gas or vapour movement through the composite, resulting in slower diffusion processes.

Natural Rubber/ Cellulose Composites

Elastomers are a significant family of polymers due to their unique properties, which include resistance to abrasion, chemical breakdown, temperature extremes, and other forms of environmental stress. One-third of the demand for the elastomer natural rubber (NR) is met. Natural rubber, a biopolymer, is often used as a matrix component in polymer nanocomposites. As the second most widely used biopolymer, it has seen more study than any other elastomer. Using NR in large quantities while developing eco-friendly composites is technologically critical. There was a 62% increase in production of natural rubber from 2000 to 2012, and in that year, natural rubber accounted for almost 42% of all rubber produced worldwide. NR is elastic, supple, and impervious to water. Among the numerous possible uses for this material are erasers for pencils and parts for spacecraft. Extracting the latex, aqueous emulsion, or saplike dispersion from the Hevea Brasiliensis tree yields this remarkable high molecular weight polymer. Since the polymer tends to remain amorphous below a temperature of around -70 degrees Celsius, its cis form is the most practical. They act like elastomers because a portion of their C=C saturations have been chemically crosslinked (vulcanised).

Mechanical Properties

Modulus increases, strength increases with good bonding at high fibre concentrations, elongation at failure decreases, creep resistance greatly improves compared to particulate-filled rubber, hardness increases, and cut, tear, and puncture resistance also improve noticeably are the primary effects of bio-fibre reinforcement on the mechanical properties of NR composites.

Analysed the raw coir fibre's potential for use in micro-reinforcing NR. The addition of sisal fibres to an NR matrix has also been investigated by scientists. The incorporation of oil palm fibre into the rubber matrix has been tried before with positive results. Examined the effect on mechanical properties of oil palm fibres being added to NR composites, In contrast to what had been found in earlier studies, they found that increasing the concentration of fibres often decreased the tensile and tear strengths. Implications of grass fibre (bagasse) on NR, It has been demonstrated that pineapple and kenaf fibres may serve as reinforcements in NR. In 2002, the first bamboo fiber-reinforced NR composites were produced using a wide range of bamboo fibre loadings. Research has been conducted on composites with and without a bonding agent. The addition of filler loads and bonding agents can increase the tensile modulus and hardness of composites. In order to further solidify the bond between the bamboo fibre and NR, a bonding chemical is used. Because of its amorphous nature, bamboo fibre has trouble adhering to the NR matrix, which may explain why filler loading decreases tensile and tear strengths.

Thermal Degradation Analysis

Potentially helpful data on optimal production and operating temperatures could be gleaned from a thermal analysis of nanocomposites. Rubber/cellulose whiskers nanocomposites were compared to a clean rubber matrix using rmogravimetric analysis to determine thermal stability (TGA). Thermal degradation of rubber in a nitrogen atmosphere started around 380 degrees Celsius, progressed through primary volatilization and pyrolysis with significant weight loss, and was finished at around 550 degrees Celsius. Bringing the degradation start temperature down from 275 degrees Celsius to 265 degrees Celsius, the addition of 10% cellulose whiskers to NR nanocomposites. A possible reason why nanocomposites made of rubber and cellulose whiskers have a longer service life is that the degradation initiation temperature of cellulose whiskers is lower than that of rubber.

When gases like carbon dioxide, carbon monoxide, formic acid, and acetic acid are created, the cellulose breakdown process begins. Both single-component NR and nanocomposites displayed multi-step deterioration in their TGA curves. Composites of NR and nanocellulose have greater degradation temperatures (between 268 and 360°C) than pure NR (between 242 and 315°C). Inflammable breakdown byproducts are no longer found at temperatures over 400 degrees Celsius. Nanocomposites outperformed the employed matrix and reinforcement when subjected to heat deterioration, as shown by their study. Researchers believe that the cellulose nanofibres embedded in the NR matrix will be safe from fast decomposition. [4]

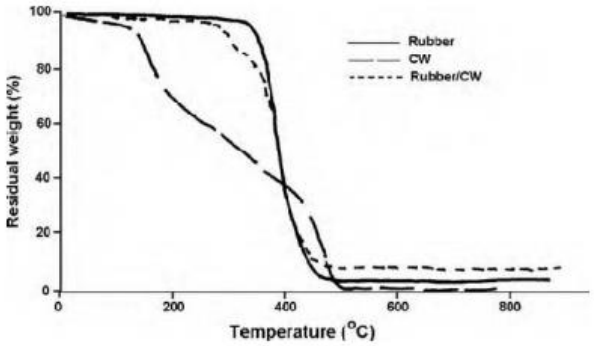

Figure 1: TGA curve of rubber, bagasse cellulose whiskers (CW), and rubber/cellulose whiskers nanocomposites

DRUG DELIVERY SYSTEM

Many cutting-edge medical devices now use DDS because of its widespread interest and usefulness. With DDS, it is feasible to improve the efficacy and safety of using modified medicines over their unmodified counterparts by administering medicinal substances by managing their rate, duration, and place of release within the body. The most effective medication delivery system keeps tabs on the dosage and adjusts the rate of release as needed throughout treatment. In addition to reducing variations in plasma levels and extending the onset of action, optimal drug carriers play a number of other crucial functions. Possible results include better medication compliance and less frequent dosing.

Successful transport of biological molecules and pharmaceutical medications has been achieved using a wide variety of biocompatible nanomaterials. Carbon nanotubes, polymeric nanoparticles, mesoporous silica, and gold nanoparticles are other often used drug carriers alongside liposomes and dendrimers. Both liposomes and polymeric NPs have been the focus of intense research as potential drug delivery systems. One of the first and only liposomal drug delivery formulations (Doxil®) approved by the FDA for use in the treatment of human cancer. Hydrophilic drugs may be transported via the liposome's water core, whereas lipophilic drugs can be transported through the lipid bilayer. [5]

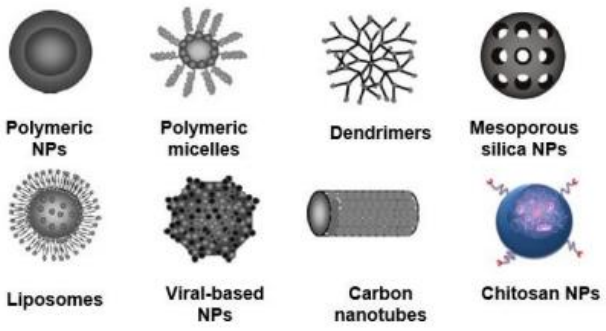

Figure 2: Different types of nanocarrier systems for drug delivery

Particle size, surface charge, and hydrophobicity all have a role in how easily drug carriers are ingested by phagocytic cells. Particles between 200 nm and several microns in size were found to have the greatest phagocytic uptake and opsonin adsorption. Coated particles are less likely to interact with environmental proteins like opsonins when hydrophilic polymers like poly (ethylene glycol) are used.

Polymeric Matrices

Biodegradable polymers are the state-of-the-art in the medical profession at the moment when it comes to creating effective drug delivery systems. Polymers that degrade into innocuous substances like carbon dioxide and water are one kind of biomaterial. Cellulose, chitosan, polypeptides, and proteins are just few of the numerous natural substances that may be converted into biodegradable polymers. Synthetic polymers include poly(lactic acid), poly(glycolic acid), poly(caprolactone), and poly(styrene-butadiene-styrene) (glycolic acid). 39 Condensation polymerization between diols and diacids or ring opening polymerization (ROP) of lactones and lactides are common routes for making biodegradable polymers such poly esters from their respective monomers (for example, ROP of -caprolactone monomer in Fig. 2). The biodegradability of polymers is greatly affected by whether or not they include an active linkage (ester, amine, urethane, and enolketone) that may be hydrolyzed and/or reduced to tiny compartments under hydrolysis or enzymatic activity. The two primary byproducts of PLA and PGA degradation lactic acid and glycolic acid are biocompatible and quickly flushed from the body. Hydrophobicity, molecular weight, crystallinity, surface area, type of repeating units, and polymer compositions are only few of the variables that affect the rate of degradation of bulk polymers. [6]

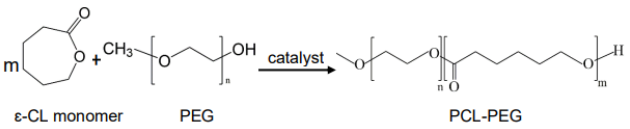

Figure 3: Scheme of ring opening polymerization of ε-caprolactone (ε -CL) monomer

Biodegradable drug carriers may now include slow-release polymers. Particularly useful for hydrophobic drugs, polymeric nanospheres provide protection from the physiological milieu of the body. Polymeric nanoparticles' stability is improved and their drug delivery window is expanded by PEGylation. The medical community has advanced to a point where biodegradable polymers are the gold standard for developing safe and efficient drug delivery systems. Biodegradable polymers, for example, are completely safe to use since they decompose into inert chemicals like carbon dioxide and water.

Micellar Nanostructures

Many self-assembling nanoscale materials include functional components at their centre, such as micelles and core-shell structures. Micelles may be

synthesised from block copolymers, which are strong macromolecules with potential use in the administration of drugs. In order to categorise block copolymer micelles, one possible approach is to measure the intermolecular force between the micelle core and the surrounding water. While amphiphilic block micelles (ABM) are generated when the core's hydrophobic blocks are connected hydrophobically, polyion complex micelles (PICM) are formed when a polycation and polyanion, such plasmid DNA, come into electrostatic contact. Metal complexation led to the formation of micelles. Micelles form a tight shell with the help of hydrophilic blocks like polyethylene oxide (PEO), which may form hydrogen bonds with the surrounding water. When the amphiphilic block copolymer reaches or above the critical micelle concentration, it may give rise to stable micelles (CMC). Increasing entropy by releasing water molecules into the bulk aqueous phase facilitates the bonding of polymer chains. Micelle stability could be improved by core-shell crosslinking. Drug release from the micelle's core is regulated by its coronal permeability, which may be changed by cross linking.

Magnetic Nanoparticles

Magnetized nanoparticles have several medical applications, including targeted drug administration, thermogenesis, and MRI contrast agents (MNPs). Superparamagnetic minerals like magnetite (Fe3O4) and maghemite (-Fe2O3) are used to manufacture MNPs for medicinal purposes. The ability to miniaturise MNPs and transform them into super paramagnetic materials with improved magnetic characteristics is one of their primary benefits. Attaching different ligands and payloads to MNPs just requires a simple surface functionalization. To facilitate the transfer of medications and biomolecules, MNPs may be coated with polymers such as dextran, polysaccharides, polyethylene glycol, and mesoporous silica. The particles are shielded from environmental hazards thanks to the covering. Carboxyl, amino, biotin, and carbodi-imide groups may be attached to the particle's surface to increase its functionality. [7]

Quantum Dots

To effectively treat cancer, tumours must be found at an early stage. As a result of their unique optical, electrical, or magnetic properties, certain inorganic NPs may be scanned in a number of ways to evaluate drug carrier effectiveness in addition to neoplastic tissues. In terms of fluorescence quantum yield, semiconductor nanocrystals (QDs) are superior to traditional organic dyes for use in biological imaging because they are both more luminous and more photostable. Although quantum dots (QDs) are only about 10 nm in size, the quantum confinement effect has a major impact on the visible region across which QDs absorb and emit light. It was proven to be possible to create high-quality photoluminescent semiconductors that are also biocompatible. Changes were made to the surface chemistry of QDs in a variety of ways to make them more biocompatible. Surface modification of QDs with biomolecules including antibodies, nucleic acids, and peptides has the potential to reduce their toxicity and increase their utility in medical applications, particularly in vivo imaging, by making them safer to employ. Depending on the circumstances, these biomolecules may form covalent or non-covalent bonds with the QDs. QDs containing surface functional groups like carboxylic acid, primary amine, and thiol may bind antibodies and peptides thanks to the cross-linking abilities of carboxydiimide, maleimide, and succinimide. Stock shift, thermal and environmental stabilities, and decreased toxicity are just a few of the ways in which doped semiconductor nanocrystals excel above their undoped forebears.

APPLICATION TO DRUG DELIVERY

Drugs may be included into nanogels or covalently linked to polymer chains to act as hydrophobic moieties and self-assembly catalysts. The drug release mechanism may be affected by the diffusion rate of the drug from the carrier, the stability of the aggregate, and/or the biodegradation rate of the copolymer. Good stability and slow biodegradation mean that kinetics will be influenced by things like material-drug interactions, the molecular weight of the copolymer, the hydrophobic-hydrophilic balance, the placement of the drug inside the nanogel, the quantity loaded, and the size of the nanogels. [8]

Dextran

Dextran is a polysaccharide with a high molecular weight that is mostly synthesised by the enzymes of some types of bacteria. It is made up of 1,3-branched, 1,6-linked D-glucopyranoses. Not only is it non-toxic, biodegradable, and resistant to protein adsorption, but it also has good water solubility. Because of its high concentration of hydroxyl groups per monomer unit, it is also accessible to chemical modification through reactive hydroxyl chemistries. [9]

i. Dextran modified with polycaprolactone

The formation of nano-aggregates from dextran-Poly (-caprolactone) copolymers is a well-documented phenomenon. Hydrophobic polyester PCL, also known as poly(-caprolactone), has great tensile and thermoplastic qualities and is biodegradable, biocompatible, minimally immunogenic, and nontoxic. Also employed as the hydrophobic component in micelle-forming materials, as well as an implantable biomedical material and a sustainable bionanocomposite.

ii. Dextran modified with poly (D,L-lactide)

Polylactide (PLA) is a polymer that has several applications in the medical field due to its biodegradability and biocompatibility. It has been shown that particles with core-shell topologies may be generated from the self-assembling block copolymer dex-b-PLA, which is made of dextran and

poly(D,L-lactide). By adjusting their molecular weights, the blocks' diameters may be accurately tuned in the range of 15-70 nm. Nanogels were able to carry up to 21% (weight-to-weight) of the drug payload of doxorubicin, resulting in sustained release for over 6 days. With careful manipulation of the copolymer's molecular weight, we were able to produce nanoparticles with a circulation lifespan more than eight times longer than PEG-coated ones.

iii. Dextran modified with cholesterol

Dextran that had been grafted onto polylactic acid (dex-g-PLLA) with varied levels of hydrophobic units was compared to dextran that had been treated with cholesterol (dex-chol). Dex-chol self-assembled into 125 nm nanogels using a CAC of 12.6x104 weight percent. Cholesterol cores shrank precipitously as a result of ester bond hydrolysis.

iv. Protein release from Dex-g-PLLA and Dex-Chol

The capacity of Dex-g-PLLA and Dex-Chol self-aggregates to entrap proteins and then release them was investigated in a study published in Science in 1977. It was demonstrated that lysozyme could be entrapped more efficiently during the production of the nanogel than by soaking, and that the hydrophobic component of the nanogel could be altered to affect the loading efficiency and release kinetics. Higher initial protein concentrations led to more protein encapsulation, suggesting that lysozyme loading potential existed inside the nanogels' interior. Dex-g-PLLA showed a loading capacity of 5.1-6.3% at 3 mg/mL protein, whereas Dex-Chol showed a capacity of around 8.2% at the same concentration.

Chitosan

Chitosan is a N-acetyl-D-glucosamine and b-(1,4)-linked D-glucosamine linear heteropolymer with variable molecular weights. After cellulose, chitin is the most abundant polysaccharide in nature. Chitin is partially deacetylated to create chitinase. Animal and human studies have demonstrated that chitosan has no health risks. Enzymes might break it down into harmless amino sugars that the body can use in full. Chitosan, in contrast to chitin, which is insoluble in aqueous and many organic solvents, is soluble in water at low pH levels due to protonation of the free amine groups. Although N-acetyl groups are generally hydrophilic, they may lead to a small degree of hydrophobic behaviour in certain contexts. Because of its positive charge, chitosan is the only naturally occurring polysaccharide capable of binding mucus via ionic contact with the quaternary amino and sialic acid groups of mucin. It is also helpful for cellular uptake and the relaxation of tight junctions because of its interactions with the negative charges carried by membrane proteins. Furthermore, chitosan's cationic characteristics may be modified to impart pH sensitivity. The antibacterial properties of chitosan are well-established due to its shown toxicity against a wide variety of bacteria, fungi, and parasites. [10]

i. Chitosan derivative with phosphorylcholine and deoxycholic acid moieties

A biodegradable amphiphilic chitosan derivative (DCA-PCCs) was developed by grafting hydrophilic phosphorylcholine (PC) and hydrophobic deoxycholic acid (DCA) moieties along its backbone. An optimal hydrophilic-hydrophobic balance may be attained by modifying both DS levels. This copolymer self-assembled when treated with DCA. Proteins like bovine serum albumin were employed as stand-ins. In comparison to the 213 nm BSA-loaded nanocomplexes, the size and size distribution of the blank nanoparticles were 285 nm and 0.235, respectively. These results suggest that interaction between the copolymer and the protein resulted in less massive aggregates. Biphasic release of BSA was observed, with 45% being released rapidly in the first 12 hours and the remaining 75% being released gradually over the following 72 hours, consistent with first order exponential decay kinetics. [11]

ii. Poly(p-dioxanone) end-modified chitosan

It was found that synthesising a block copolymer of chitosan and poly(p-dioxanone) (PPDO) with two distinct MW of PPDO-macromers resulted in an amphiphilic material with enhanced properties. The polymer surfactant had a CAC of 5-9.10-2 mg/mL and could self-assemble into pH-responsive chitosan micelles. Both the short and long PPDO copolymers had micelles of 115 and 77 nm, respectively. This unexpected finding was due to the fact that the short PPDO chain had inferior crystallisation capabilities, which led to a looser core, the opposite of what was predicted based on the influence of the length of the hydrophobic block in polymer surfactant. When the pH was lowered, the micelle diameter grew, indicating that the chitosan had become more hydrophilic and had swollen.

iii. Biotinylated N-palmitoyl chitosan

Hydrophobic palmitoyl chloride-modified chitosan was biotinylated for enhanced tumour cell targeting. The copolymer aggregated itself into positively charged spheres with a restricted size distribution (300–400 nm) across the range of their dimensions. Their diameter was smaller because to the low biotin concentration compared to N-palmitoyl chitosan-based assembly reports of 429 nm, but the CAC was only slightly lowered from 0.083 mg/mL to 0.081 mg/mL. Encapsulation efficiency for docetaxel loading into the carriers was 79%, and drug loading was 8.92%, both increases above the 68% and 5.84% reported for N-palmitoyl chitosan. Their drug release was biphasic, with an initial 6-hour burst followed by a prolonged release phase. It was shown that there was a little pH dependence, with the release being slower at pH5.5 compared to pH7.4. Release rates for the biotinylated copolymer were substantially lower; in comparison to the non-biotinylated copolymer, it only managed to achieve a rate of 10-20% after 72 hours. Additional properties

of the particles were biodegradability and compatibility with human blood.

iv. Chitosan functionalized with N -acetyl cysteine and vitamin E succinate

N-acetyl cysteine (NAC) was used to provide hydrophilic groups to the modified chitosan, while vitamin E succinate was used to add hydrophobic groups. Upon hydrodynamic aggregation, the resultant copolymer formed particles with a hydrodynamic diameter of 220–250 nm. The paclitaxel was loaded onto the carriers, and compared to a plain paclitaxel solution; the nanoparticle system had a relative bioavailability of 425%. [12]

CONCLUSION

The water-insoluble medication Ibuprofen's solubility, dispersion, and bioavailability were all improved by using acacia and ghatti gum as natural carriers in a microwave-generated nanobiocomposite. Extensive in vitro testing has shown that IBUACNBC improves both solubility and dissolution. Particle size distribution, scanning electron microscopy, transmission electron microscopy, Fourier transform infrared spectroscopy, and differential scanning calorimetry all show that the drug and excipients are compatible with one another, and that the drug's crystalline structure has been significantly modified into a nanobiocomposite. Transforming Ibuprofen into a Nanobiocomposite may account for the drug's enhanced solubility and dissolution. The effectiveness of the Nanobiocomposite depends on the medicine being evenly dispersed throughout the polymer.

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