European Journal of Molecular & Clinical Medicine
ISSN 2515-8260 Volume 07, Issue 07, 2020

Carbon Nanotubes In Treatment Of Arthritis: An Overview

Manvendra Singh, Pallavi Nayak, Vijay Mishra*

[1]*School of Pharmaceutical Sciences, Lovely Professional University, Phagwara, India*

*Corresponding author
Dr. Vijay Mishra
School of Pharmaceutical Sciences,
Lovely Professional University, Phagwara, (Punjab), India
Email: vijaymishra2@gmail.com

Abstract: Arthritis is a type of joint dysfunction that includes one or more joint inflammation like rheumatoid or psoriatic arthritis, and associated autoimmune disorders. The biggest concern about arthritis is that the discomfort is always persistent and may be confined to the injured joint due to swelling that happens throughout the joint, trauma to the joint induced by illness, regular wear and tear, muscle strains triggered by vigorous action toward hard sore joints and exhaustion, which in effect contributes to inflexibility, immobility and muscle weakening. Carbon nanotubes with unusual physicochemical properties (cell membrane penetration, large surface area and drug payload, biocompatibility, simple surface alteration, photoluminescence properties and non-immunogenicity) are employed to conquer the challenges of inflammation.

Keywords: Arthritis, Inflammation, Carbon nanotubes, Rheumatoid arthritis

1. Introduction

Nanomedicines actually display an unplausible capacity to resolve the challenges posed by gene therapy, cancer therapies, as well as certain life-threatening illnesses. Researchers are now investigating the special characteristics of carbon nanotubes (CNTs) worldwide to harness their ability. Various forms of CNTs demonstrate the capacity to move drugs, bioactives, and nucleic acids far within the cell to previously unattainable targets. CNTs would have enormous use as an industrial and freely accessible biomaterial (Mishra et al., 2018). Carbon nanotubes (CNTs), with their strange physical chemical properties, have been shown to have a promising potential in their targeting on a receptor basis (cell membrane penetration, surface strong and drug useful power, biocompatibility, simple modulation of surface, the ability of photologic illuminance and non-immunoscopicity (Mehra et al 2014). The CNTs were first discovered and thoroughly identified in his TEM discovery by Sumio Iijima (Japanese Microscopist), though some scientists assumed that it had been found earlier by Bacon (Sharma et al., 2019; Nayak et al., 2019). Based on their composition, diameter and length CNTs can be categorized as single-walled CNTs (SWCNTs), double-walled CNTs (DWCNTs), triple-walled CNTs (TWCNTs) and multi-walled carbon nanotubes (MWCNTs) (Figure 1) (Kesharwani et al., 2015).

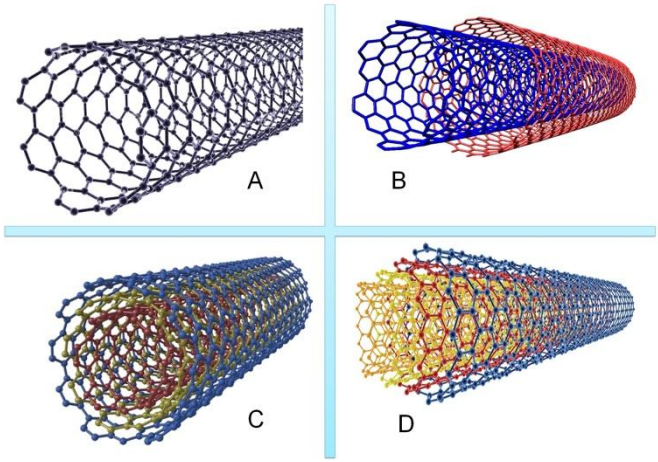

Figure 1: Different categories of CNTs

2. Arthritis

It is a category of diseases which harm the body joints of a person or animal. "Arthritis" indicates bone or muscle joint inflammation. Arthritis has the ability to inflict discomfort, swelling and stiffness. Getting moved with arthritis will hurt. Arthritis is a chronic disease. The most severe type of arthritis is osteoarthritis. This can impact both the body's bigger and smaller joints, like elbows, ankles, feet, spine, hip, and knee. Essentially, the condition is one developed by regular wear and tear of the joint; however, osteoarthritis can also arise as a consequence of injury(Bhatia *et al*., 2013; Sharma *et al*., 2019). Osteoarthritis occurs in the cartilage, allowing the two opposite bones to erode towards each other. Typically, during operations, the disorder begins with mild discomfort, but eventually the discomfort may be constant, and also manifest when in a state of rest. Solid tissue bonds, or ligaments, bind the bones, which tend to support the joint. Both muscles and tendons protect the joints and help to travel. The region inside or near a joint becomes inflamed with arthritis, causing inflammation, weakness and even trouble moving (Shweta et al., 2014). Rheumatoid arthritis (RA) is a hereditary inflammatory condition marked by persistent inflammation of the joint that eventually results in serious impairment and premature death. The disease's pathogenesis includes preclinical RA, hereditary factors and environmental factors (Thakur et al., 2016).

The first documented signs of human arthritis date to 4500 BC (Joel et al., 2005; Blumberg and Sokoloff, 1961). Arthritis was sometimes referred to in early literature as the most prevalent ailment among prehistoric inhabitants (Diplodocus, 1992). It was reported in Native American skeletal remains discovered in Tennessee (Wayback Machine Medical News 2010).

3. Classification of Arthritis

3.1. Osteoarthritis

Osteoarthritis is the world's most severe joint condition, impacting an estimated 10 % of men and 18 % of women over the age of 60. The pain and loss of function that weaken; the resulting socio-economic burden in developing countries is high, costing between 1-2.5% of gross domestic product. Traditionally, therapy for osteoarthritis consists of pain reduction with end-stage joint replacement. Osteoarthritis was previously treated as a solely mechanical cartilage loss disorder, but it is now understood to be a dynamic illness involving the whole joint, in which matrix protease activation plays a crucial function. The likelihood that multiple risk factors can give rise to osteoarthritis via a specific end pathway offers possible

therapy. Cartilage, subchondral bone and synovium potentially all play a vital role in pathogenesis of the disorder, and there might even be correlations with systemic inflammation (Glyn-Jones et al., 2015).

3.2. Adult-onset Still's disease

Adult-onset Still's disease (AoSD) was first identified by Bywaters in the early 1970s as an inflammatory disorder that appeared in young adults, very close to the childhood-onset Still's disease, currently named systemic-onset juvenile idiopathic arthritis (SoJIA), identified by Sir Still a century earlier. While the disease's precise pathogenic pathways remain unclear, significant progress was made first to validate the homology between AoSD and SoJIA, and then the condition became the model of non-family, or intermittent, systemic autoinflammatory disorders (SAID) (Efthimiou et al., 2020). The AoSD is a severe, auto-inflammatory, idiopathic, neurological condition. Patients may pose with "Still's triad," inflammation, salmon-colored evanescent rash, and regular or double regular fevers, but there are numerous atypical instances. Described by George Still in children as early as 1896 and further defined in 1971 by Eric Bywaters who had an adult onset of symptoms, "Still's disease" has come to describe a continuum between chronic juvenile idiopathic arthritis (SJIA) at one end and AoSD at the other, depending on age between emergence of symptoms (Mitrovic et al., 2019).

3.3. Gout and pseudo-gout

Gout and Pseudogout are popular forms of aged inflammatory joint disease. In comparison, the concomitant pseudogout diagnosis was focused primarily on the radiological findings of calcification, with few studies in the literature documenting the unique microscopic findings of both forms of crystals in the same joint. Gout, one of the most common types of inflammatory arthritis, is marked by extreme joint discomfort, which sometimes interferes with everyday operations or avoids them. A great deal has been achieved to elucidate the symptoms, diagnosis, and gout prevention. The gout usually occurs in the joints because of the aggregation of monosodium urate crystals leading to elevated amounts of serum uric acid. Successful therapies have been well developed, in the form of urate reduction drugs (Todd and Wright, 2020).

3.4. Ankylosing spondylitis

It is a chronic inflammatory rheumatic condition that involves the axial spine, triggering inflammatory back pain signature, which may contribute to structural and functional impairments and reduction in quality of life. Ankylosing spondylitis is the main subtype and a significant consequence of an interrelated rheumatic disorder community currently called spondyloarthritides. The group's health characteristics include acute back pain, asymmetric peripheral oligoarthritis (mostly in the lower limbs), enthesitis, and particular involvement of the organ such as anterior uveitis, psoriasis, and persistent inflammatory bowel disease. Rare symptoms of ankylosing spondylitis include the aortic root presence and conduction disorders. Clinically distinguished are five subgroups: reactive spondyloarthritis, psoriatic spondyloarthritis, ankylosing spondylitis, inflammatory bowel disorder induced undifferentiated spondyloarthritis, and spondyloarthritis. The MHC class I molecule HLA B27 is the best known contributing factor, but many have yet to be found (Braun and Sieper, 2007).

3.5. Rheumatoid arthritis

Rheumatoid arthritis (RA) is a significant cause of impairment. It occurred some thousand years ago in the early Native American populations but could not have originated in Europe until the 17th century. Early studies of RA pathogenesis focused on autoantibodies and immune complexes. More specifically, autoantibodies 'involvement has been moving back to the forefront. Relevant clinical approaches may be developed depending on the pathogenic

pathways to inhibit synovial inflammation and joint damage (Firestein, 2003; Thakur et al., 2016).

3.6. Septic arthritis

Chronic bacterial septic arthritis is a serious illness with a death rate of 15% and a strong likelihood of permanent loss of operation. The causative species are numerous, the most specific being contamination with *Staphylococcus aureus* (Baillet et al., 2019). In infants, septic arthritis is a serious problem, involving rapid treatment, synovial space drainage, and antimicrobial therapy to avoid bad outcomes. Hematogenous diffusion through the synovial joint is the most common form of transmission. Septic arthritis is usually seen in boys and involves more the weight-bearing joints (Alarcón et al., 2019).

3.7. Juvenile idiopathic arthritis

It is a heterogeneous syndrome that describes childhood's most severe rheumatological disorder. In juvenile idiopathic arthritis (JIA) a number of cardiac manifestations were identified. The most severe systemic form is pericarditis and myocarditis, and heart failure is a life-threatening consequence of the macrophage activation syndrome. Among rheumatoid factor-positive polyarthritis and developmental ankylosing spondylitis, valvular cardiac disorder, the most usually aortic insufficiency, has arisen. The nature of the reported weakness in the role of the systolic and diastolic ventricle is uncertain because JIA is not correlated with an elevated incidence of ischemic heart disease or cardiac failure. There's always an unknown chance of early atherosclerosis. While several tests have indicated endothelial and vascular impairment, it has not been observed that the carotid intima-media thickness was reliably thicker than in stable samples. Despite reduced anaerobic health, the workout ability of children with chronic arthritis is preserved independent of the level of illness operation (Figure 2) (Ravelli et al., 2017).

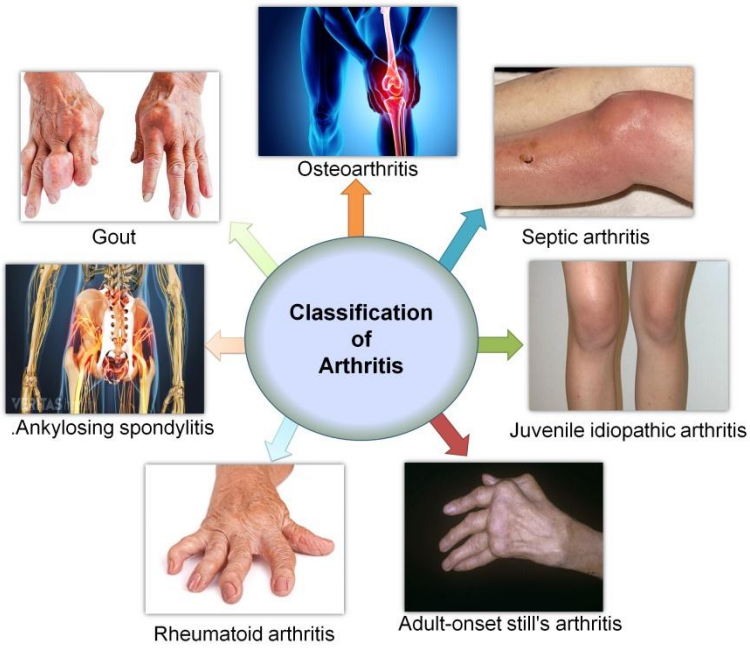

Figure 2: Classification of arthritis

4. Carbon nanotubes in treatment of Arthiritis

Lee et al., a non-particulate glucocorticoid (GC) treated dexamethasone (DEX) to suppress anti-inflammatory reaction, has been extensively used in the diagnosis of numerous diseases such as inflammation, obesity, asthma, chronic obstructive pulmonary disorder, cerebral edema, and multiple sclerosis; However, repeated and/or high-dose GC therapy can cause some severe adverse effects (arthropathy of Charcot, hyperglycemia, osteoporosis,

syndrome of Cushing and adrenal insufficiency etc.). Throughout this analysis, DEX-carbon nanotube (CNT) integrates enhanced intracellular drug distribution by increased caveolin-dependent endocytosis, and eventually suppressed the production of large pro-inflammatory cytokines throughout human fibroblast-like synoviocytes (FLS)-stimulated tumor necrosis factor-α (TNF-α) at low concentrations (Lee et al., 2017).

Lee et al., examined the repeated intra-articular corticosteroid treatments for the diagnosis of synovial inflammation in advanced arthritis are unavoidable. Nevertheless, the application of corticosteroids in the short and long term typically causes severe adverse effects. This research shows that corticosteroid (triamcinolone) conjugation on polyethyleneglycol (PEG)-modified MWCNTs improves intracellular drug distribution by enhanced lysosome transport and eventually suppresses the production of significant pro-inflammatory cytokines (i.e., TNF-a, IL-1b, and IL-6) and fibroblast-like synoviocyte matrix-1 and -3. In summary, low-dose triamcinolone conjugation with carbon nanotubes greatly reduced fibroblast-like synoviocyte inflammatory reaction by achieving extremely effective intracellular shipping, and proposed a possible drug candidate to overcome side effects correlated with traditional low-dose arthritis therapy (Lee et al., 2016).

Kayat et al., studied the CNTs anchored by folate to target an anti-arthritic medication, Methotrexate (MTX) to the arthritic inflammatory area. In vitro drug release in PBS (pH 7.4) was observed to be 66.35 ± 2.3 and 56.88 ± 1.9% in 24 h, from pristine MWCNTs and folate conjugated MWCNTs formulation, respectively. Folate conjugated MWCNTs greatly improved the %age inhibition of arthritis, biological half-life, and MTX delivery rate relative to naked MWCNTs filled with MTX, as well as free MTX. The current findings illustrate the ability of drug-loaded functional MWCNTs to alter the pharmacokinetics as well as the stable and optimized drug delivery mechanism (Kayat et al., 2015).

De et al. researched the manufacture and efficiency of a basic amperometric immunosensor system that could theoretically be used for the identification of autoimmune disease serum anti-citrullinated peptide antibodies (ACPAs). A synthetic peptide (CFFCP1) chimeric filaggrin-fibrin was used as a detector bolted to the surface of the multi-wall electrical transducer (MWCNT–PS) mounted on a CNT-polystyrene. Initially, the subsequent immunosensor technique was evaluated in sera of rabbits previously inoculated with the synthetic peptide and subsequently introduced in human sera to identify ACPAs. A comparative research was performed using blood donor control serum, which revealed the selectivity of the immunosensor response and its susceptibility to anti-CFFCP1 antibodies in RA patients (De et al., 2011).

5. Conclusion

Carbon nanotubes have gained significant interest in the areas of medicinal and biomedicine. Important progress has been made in developing and optimizing medicines for the treatment of different diseases. Exploration of CNTs in biomedical applications is continuing, however has tremendous potential. Because a significant portion of the human body is made up of biomass, this is commonly known as a very biocompatible substance. Cells have been seen to develop on CNTs and no toxic impact occurs. The MWCNT – PS composite-based electrodes can be used to create an electrochemical immunosensor to rapidly diagnose arthritis.

6. References

[1]. Alarcón, A. E., Shetty, A. K., and Gedalia, A. (2019). Septic Arthritis in Children: Clinical Update. In *Infections and the Rheumatic Diseases* (pp. 29-40). Springer, Cham.
[2]. Arthritis History Archived 2010-01-30 at the Wayback Machine Medical News

[3]. Baillet, A., Trocmé, C., Romand, X., Nguyen, C. M., Courtier, A., Toussaint, B., Gaudin, P., and Epaulard, O. (2019). Calprotectin discriminates septic arthritis from pseudogout and rheumatoid arthritis. *Rheumatology*, *58*(9), 1644-1648.
[4]. Blumberg, B. S., and Sokoloff, L. (1961). Coalescence of caudal vertebrae in the giant dinosaur Diplodocus. Arthritis and Rheumatism: Official Journal of the American College of Rheumatology, 4(6), 592-601.
[5]. Braun, J., and Sieper, J. (2007). Ankylosing spondylitis. The Lancet, 369(9570), 1379-1390.
[6]. Bridges, P. S. (1992). Prehistoric arthritis in the Americas. Annual Review of Anthropology, 21(1), 67-91.
[7]. de Gracia Villa, M., Jiménez-Jorquera, C., Haro, I., Gomara, M. J., Sanmartí, R., Fernández-Sánchez, C., and Mendoza, E. (2011). Carbon nanotube composite peptide-based biosensors as putative diagnostic tools for rheumatoid arthritis. Biosensors and Bioelectronics, 27(1), 113-118.
[8]. Efthimiou, P., and Yadlapati, S. (2019). Adult-Onset Still's Disease. In Auto-Inflammatory Syndromes (pp. 261-276). Springer, Cham.
[9]. Firestein, G. S. (2003). Evolving concepts of rheumatoid arthritis. Nature, 423(6937), 356-361.
[10]. Glyn-Jones, S., Palmer, A. J. R., Agricola, R., Price, A. J., Vincent, T. L., Weinans, H., and Carr, A. J. (2015). Osteoarthritis. The Lancet, 386(9991), 376-387.
[11]. DeLisa, J. A., Gans, B. M., and Walsh, N. E. (Eds.). (2005). Physical medicine and rehabilitation: principles and practice (Vol. 1). Lippincott Williams and Wilkins.
[12]. Kayat, J., Mehra, N. K., Gajbhiye, V., and Jain, N. K. (2016). Drug targeting to arthritic region via folic acid appended surface-engineered multi-walled carbon nanotubes. Journal of drug targeting, 24(4), 318-327.
[13]. Kesharwani, P., Mishra, V., and Jain, N. K. (2015). Validating the anticancer potential of carbon nanotube-based therapeutics through cell line testing. Drug discovery today, 20(9), 1049-1060.
[14]. Lee, Y. K., Choi, J. K., Kang, Y. J., Kim, H. W., Kim, S. W., Park, C. K., Khang, D., and Kim, S. H. (2016). Triamcinolone–carbon nanotube conjugation inhibits inflammation of human arthritis synovial fibroblasts. Journal of Materials Chemistry B, 4(9), 1660-1671.
[15]. Lee, Y. K., Kim, S. W., Park, J. Y., Kang, W. C., Kang, Y. J., and Khang, D. (2017). Suppression of human arthritis synovial fibroblasts inflammation using dexamethasone-carbon nanotubes via increasing caveolin-dependent endocytosis and recovering mitochondrial membrane potential. International journal of nanomedicine, 12, 5761.
[16]. Mehra, N. K., Mishra, V., and Jain, N. K. (2014). A review of ligand tethered surface engineered carbon nanotubes. Biomaterials, 35(4), 1267-1283.
[17]. Mishra, V., Kesharwani, P., and Jain, N. K. (2018). Biomedical applications and toxicological aspects of functionalized carbon nanotubes. Critical Reviews™ in Therapeutic Drug Carrier Systems, 35(4).
[18]. Mitrovic, S., Feist, E., and Fautrel, B. (2020). Adult-Onset Still's Disease. In Periodic and Non-Periodic Fevers (pp. 93-132). Springer, Cham.
[19]. Nayak, P., Singh, M., and Mishra, V. (2019). Carbon-Based Nanotheranostics. *Think India Journal*, *22*(16), 925-934.
[20]. Ravelli, A., Schiappapietra, B., Verazza, S., and Martini, A. (2017). Juvenile idiopathic arthritis. In The Heart in Rheumatic, Autoimmune and Inflammatory Diseases (pp. 167-187). Academic Press.
[21]. Sharma, N., Mishra, V., Singh, M., and Nayak, P. (2019). Carbon nanotubes in delivery of curcumin: An overview. Think India Journal, 22(16), 935-946.

[22]. Shweta, B., and Badola, A. (2015). Possible approaches for evaluating arthritis and its management. The Journal of Nursing Trendz, 6(2), 32-39.
[23]. Thakur, S., Riyaz, B., Patil, A., Kaur, A., Kapoor, B., and Mishra, V. (2018). Novel drug delivery systems for NSAIDs in management of rheumatoid arthritis: An overview. Biomedicine and Pharmacotherapy, 106, 1011-1023.
[24]. Todd, E., and Wright, A. (2020). Gout: origin, treatment, and prevention. Bios, 91(1), 66-73.
[25]. Bhatia, A., Singh, B., Raza, K., Wadhwa, S., & Katare, O. P. (2013). Tamoxifen-loaded lecithin organogel (LO) for topical application: development, optimization and characterization. International Journal of Pharmaceutics, 444(1-2), 47-59.
[26]. Sharma, A., Shahzad, B., Kumar, V., Kohli, S. K., Sidhu, G. P. S., Bali, A. S., & Zheng, B. (2019). Phytohormones regulate accumulation of osmolytes under abiotic stress. *Biomolecules*, *9*(7), 285.