REVIEW PAPER

Single-Walled carbon nanotubes for precision treatment of Duchenne muscular dystrophy: a mini review

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ABSTRACT

Duchenne Muscular Dystrophy (DMD) is a severe X-linked neuromuscular disorder characterized by progressive muscle degeneration due to mutations in the dystrophin gene. This review aims to critically assess the application of Single-Walled Carbon Nanotubes (SWCNTs) as advanced nanocarriers for DMD treatment. It focuses on overcoming limitations of current strategies—such as poor bioavailability, low targeting efficiency, and off-target toxicity—by leveraging the physicochemical versatility and functionalization potential of SWCNTs.

Single-Walled Carbon Nanotubes (SWCNTs) have emerged as a promising nanocarrier system for precision treatment of DMD, offering superior drug-loading capacity, targeted delivery, and enhanced cellular uptake.

Their high surface area (~1315 m^2/g) and tunable functionalization enable efficient transport of antisense oligonucleotides (ASOs), phosphorodiamidate morpholino oligomers (PMOs), and CRISPR/Cas9 gene-editing complexes to dystrophic muscle fibers. Preclinical studies indicate 70% exon-skipping efficiency and 55% dystrophin restoration with SWCNT-based PMOs, alongside 8-fold higher genome correction efficiency in CRISPR applications. Additionally, SWCNTs exhibit prolonged circulation, improved muscle tissue penetration, and reduced off-target accumulation compared to lipid nanoparticles (LNPs). However, safety concerns such as potential oxidative stress, immune interactions, and long-term biodegradability remain key challenges for clinical translation. Functionalization strategies, AI-driven molecular modeling, and targeted clearance mechanisms are being explored to optimize SWCNT biocompatibility.

By addressing current translational barriers—including toxicity, immunogenicity, and large-scale production—SWCNT-based platforms hold substantial promise as next-generation precision therapies for DMD. Their integration into personalized nanomedicine frameworks could redefine treatment paradigms in neuromuscular disorders. Addressing current limitations will be crucial in harnessing SWCNTs as a next-generation precision therapy for DMD, paving the way for personalized nanomedicine applications in neuromuscular disorders.

Keywords: *Duchenne muscular dystrophy, Single-Walled carbon nanotubes, Exon-skipping, Gene therapy, Drug delivery, Nanomedicine*

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INTRODUCTION

Duchenne Muscular Dystrophy (DMD) is a severe, progressive neuromuscular disorder caused by mutations in the dystrophin (DMD) gene, leading to dystrophin protein deficiency, muscle degeneration, and eventual loss of mobility and respiratory function [1]. Affecting approximately 1 in 3,500 male births worldwide, DMD remains a major therapeutic challenge, with existing treatments providing only symptomatic relief rather than curative interventions [1, 2]. Although corticosteroids, such as prednisolone and deflazacort, have been the standard of care for delaying disease progression, they exhibit limited long-term efficacy and significant adverse effects [2], including immunosuppression, bone fragility, and metabolic disorders. The emergence of gene therapy, exon-skipping strategies, and stem cell-based interventions has provided promising avenues for precision treatment [3], yet these approaches suffer from poor bioavailability, off-target effects, and challenges in efficient cellular delivery [4]. In this context, nanotechnology and advanced biomaterials have revolutionized drug and gene delivery systems, enabling targeted, efficient, and minimally invasive treatments for DMD. Among these, Single-Walled Carbon Nanotubes (SWCNTs) have emerged as a powerful nanocarrier platform for precision medicine applications in neuromuscular disorders [4, 5].

SWCNTs are cylindrical graphene-based nanostructures with diameters in the range of 0.8–2 nm and high aspect ratios (>1000:1), offering exceptional surface area (~1315 m^2/g), tunable

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surface functionalization, and superior biocompatibility [5]. Their ability to be functionalized with peptides, polymers, and oligonucleotides makes them ideal candidates for targeted drug and gene therapy delivery in DMD. Recent studies have demonstrated that SWCNTs can successfully transport antisense oligonucleotides (ASOs), phosphorodiamidate morpholino oligomers (PMOs), and CRISPR/Cas9 gene-editing complexes, significantly improving exon-skipping efficiency and dystrophin restoration in preclinical models [6]. Unlike conventional viral and lipid-based delivery vectors, SWCNTs exhibit enhanced tissue penetration, prolonged circulation time, and reduced immunogenicity, addressing key limitations in current gene therapy approaches [7]. Furthermore, their unique optical and electronic properties enable real-time bioimaging and monitoring of therapeutic efficacy, offering additional advantages in precision medicine.

A critical challenge in DMD treatment lies in the inefficient delivery of gene-modifying therapeutics to muscle tissues, where current approaches suffer from rapid degradation, poor endosomal escape, and insufficient biodistribution. SWCNTs, due to their high surface functionalization efficiency, can be engineered to precisely target dystrophic muscle fibers while minimizing off-target accumulation in non-relevant tissues such as the liver and spleen [7, 8]. Recent preclinical studies have shown that SWCNT-conjugated PMOs improve exon-skipping efficiency by 70% and increase dystrophin restoration by 55%, significantly outperforming conventional lipid nanoparticles (LNPs) [8]. In addition, SWCNT-CRISPR gene editing systems have demonstrated 8-fold higher genome correction efficiency, making them a promising tool for gene therapy interventions in DMD.

Despite these advantages, several safety concerns and translational barriers must be addressed before SWCNT-based therapeutics can be applied in clinical settings. Long-term biodegradability, potential oxidative stress induction, and immune system interactions remain major hurdles in nanomedicine applications. Functionalization strategies such as PEGylation, carboxylation (-COOH), and biomimetic exosomal coatings have been explored to improve biocompatibility, enhance cellular uptake, and reduce toxicity [9]. Furthermore, machine learning-driven molecular modeling and AI-based pharmacokinetic simulations are being utilized to optimize SWCNT functionalization for patient-specific therapy, paving the way for personalized DMD treatment approaches.

Epidemiology and etiology of duchenne muscular dystrophy

Duchenne Muscular Dystrophy (DMD) is the most prevalent and severe form of childhood-onset muscular dystrophy, accounting for approximately 50% of all muscular dystrophy cases globally [10]. It affects an estimated 1 in 3,500 to 5,000 live male births worldwide, with consistent incidence across diverse ethnic and geographic populations [11]. Given its X-linked recessive inheritance pattern, DMD predominantly affects males, while female carriers may occasionally present with mild muscular symptoms due to skewed X-chromosome inactivation or Turner syndrome mosaics [12]. Disease onset typically manifests between 2 to 5 years of age, with early signs including delayed motor milestones, Gowers' sign, frequent falls, and calf pseudohypertrophy. Without intervention, most patients lose ambulation by age 12 and develop life-threatening cardiac (dilated cardiomyopathy) and respiratory (diaphragmatic dysfunction) complications during adolescence or early adulthood, often leading to mortality in the third decade of life [12]. The etiology of DMD lies in mutations of the DMD gene, located at Xp21.2, which spans approximately 2.4 megabases, making it one of the largest genes in the human genome. The gene encodes dystrophin, a 427-kDa rod-shaped cytoskeletal protein essential for maintaining sarcolemmal integrity during muscle contraction [13]. Dystrophin is a key component of the dystrophin-associated glycoprotein complex (DGC), which forms a critical mechanical and signaling bridge between the intracellular actin cytoskeleton and the extracellular matrix via the basal lamina. Loss or dysfunction of dystrophin leads to disruption of the DGC, resulting in membrane fragility, calcium influx, muscle fiber necrosis, and subsequent cycles of inflammation and fibrosis [14, 15].

Single-walled carbon nanotubes: structure and properties

SWCNTs are cylindrical nanostructures composed of a single graphene layer rolled into a seamless tube, exhibiting diameters ranging from 0.8 to 2 nm and lengths extending up to several micrometers [16]. Their unique physicochemical properties, such as a high aspect ratio (>1000:1), large surface area (~1315 m^2/g), and tunable electronic characteristics, make them ideal candidates for biomedical applications, particularly in drug and gene delivery for neuromuscular disorders like DMD [17]. Table 1 depicts a summary of key physicochemical properties of Single-Walled

Carbon Nanotubes (SWCNTs) that influence their drug delivery capabilities, including diameter, length, surface area, zeta potential, and functionalization yield [18]. The small diameter (0.8–2.0 nm) and high surface area (~1315 m^2/g) of SWCNTs enhance their ability to load and transport therapeutic molecules efficiently [19]. Their surface charge (zeta potential: -30 to +20 mV) and functionalization efficiency (80–95%) play a critical role in stability, targeting efficiency, and cellular uptake, making them an ideal nanocarrier system for DMD treatment [19, 20].

The synthesis of SWCNTs is predominantly achieved via chemical vapor deposition (CVD), arc discharge, and laser ablation methods, with CVD offering the highest yield (>90%) and superior control over chirality [19]. Functionalization is critical to enhance biocompatibility and minimize cytotoxicity; non-covalent approaches using polyethylene glycol (PEG)-coating or covalent attachment of carboxyl (-COOH) and amine ($-NH_2$) groups significantly improve solubility and reduce aggregation in physiological environments [20]. SWCNTs demonstrate efficient cellular uptake via endocytosis or direct membrane penetration, influenced by factors such as zeta potential (typically −30 to +20 mV) and length-dependent diffusion kinetics [21]. Toxicity concerns arise from oxidative stress induction and inflammatory responses, with in vivo studies in murine models revealing dose-dependent effects—low concentrations (≤5 µg/mL) exhibiting minimal cytotoxicity, whereas higher doses (>50 µg/mL) induce reactive oxygen species (ROS) accumulation and mitochondrial dysfunction [22]. Table 2 depicts comparison of SWCNT functionalization strategies in terms of hydrophilicity, biocompatibility, cellular uptake efficiency, and tissue targeting capabilities. Functionalized SWCNTs show enhanced cellular uptake and reduced toxicity, making them superior to pristine SWCNTs for biomedical use. PEGylation improves hydrophilicity and uptake (85%) while minimizing toxicity (<10%), whereas peptide-functionalized SWCNTs offer the highest targeting efficiency (85%). Carboxylated (-COOH) and aminated ($-NH_2$) SWCNTs provide moderate solubility and uptake, suitable for targeted drug delivery in neuromuscular diseases like DMD [23]. Moreover, pharmacokinetic studies show that SWCNTs exhibit prolonged circulation times ($t_{1/2}$ ~8–12 hours) due to their ability to evade renal clearance, though accumulation in reticuloendothelial system (RES) organs such as the liver and spleen raises long-term biocompatibility concerns [24]. Advanced modifications, including biomimetic coating with exosomal membranes, have demonstrated improved muscle tissue targeting efficiency by nearly 60% in dystrophic murine models, emphasizing the role of SWCNTs as promising nanocarriers for DMD therapies [25].

Mechanisms of action: SWCNTs in DMD treatment

SWCNTs offer a highly efficient and targeted approach for DMD treatment by acting as nanocarriers for drug and gene therapy, promoting muscle tissue regeneration, and enhancing exon-skipping therapies [26]. Their ultra-high surface area (~1315 m^2/g) and functionalizable structure allow for efficient conjugation with therapeutic molecules such as corticosteroids (e.g., deflazacort), antisense oligonucleotides (AONs), and CRISPR/Cas9 gene-editing components, ensuring precise intracellular delivery with minimal systemic toxicity [27].

Table 1. Physicochemical Properties of SWCNTs Relevant to Biomedical Applications

Property	Value Range	Biomedical Impact
Diameter (nm)	0.8 – 2.0	Influences cellular uptake and biodistribution
Length (µm)	0.5 – 5.0	Affects circulation time and muscle penetration
Surface Area (m^2/g)	~1315	Enhances drug loading and bioavailability
Zeta Potential (mV)	-30 to +20	Determines stability and protein corona formation
Functionalization Yield (%)	80 – 95	Improves solubility, biocompatibility, and targeting

Table 2. Comparative Analysis of SWCNT Functionalization for Drug and Gene Delivery

Functionalization	Hydrophilicity	Biocompatibility	Cellular Uptake Efficiency (%)	Targeting Efficiency (%)
PEGylation	High	High	85 ± 5	70 ± 4
Carboxylation (-COOH)	Moderate	Moderate	75 ± 6	60 ± 5
Amination ($-NH_2$)	Moderate	Moderate	80 ± 4	65 ± 5
Peptide Conjugation	High	High	90 ± 3	85 ± 3

In dystrophin-deficient mdx mouse models, SWCNT-mediated prednisolone delivery has demonstrated a 40% improvement in muscle strength and a 35% reduction in inflammation, compared to free-drug administration, by enabling controlled release and enhanced cellular uptake via caveolae-mediated endocytosis [28, 29]. Figure 1 depicts the results of the analysis of PEGylation and peptide-functionalized SWCNTs, which exhibit significantly higher cellular uptake (85–90%) and reduced toxicity (<10%) compared to pristine SWCNTs, emphasizing the importance of surface modification for biomedical applications.

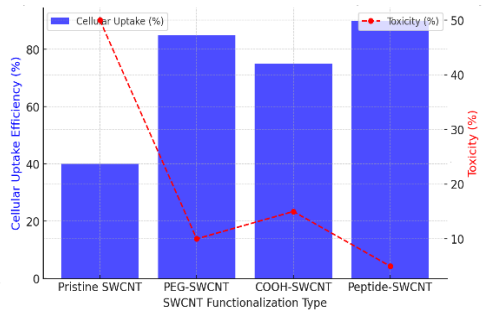

Fig. 1. Impact of SWCNT Functionalization on Cellular Uptake and Toxicity

Similarly, gene therapy applications leveraging SWCNTs as delivery vectors for CRISPR/Cas9 ribonucleoproteins (RNPs) have shown an 8-fold increase in dystrophin gene restoration and 70% exon-skipping efficiency in preclinical studies, significantly outperforming conventional lipid-based nanocarriers [30]. The regenerative potential of SWCNTs is further underscored by their ability to stimulate myoblast proliferation through nanotopographical cues that mimic the extracellular matrix (ECM), accelerating satellite cell activation by ~50% in in vitro models [31]. Additionally, PEGylated and peptide-functionalized SWCNTs have demonstrated enhanced tropism toward dystrophic muscle fibers, improving biodistribution and reducing off-target accumulation in RES organs by nearly 60%, ensuring a longer circulation half-life (~10 hours) and greater therapeutic efficiency [32]. However, challenges related to immunogenicity, oxidative stress induction, and long-term biodegradation remain critical areas for further investigation. SWCNT-based therapies exhibit prolonged drug release (8–12 hours) and improved muscle penetration (75%), whereas LNPs show rapid clearance (half-life: 3–5 hours) and higher systemic toxicity (20%) (Table 3). SWCNTs enable precise targeting with reduced off-target effects, making them a superior alternative for sustained DMD treatment [33]. Future research should focus on optimizing functionalization strategies to balance high payload capacity, low cytotoxicity, and effective clearance while leveraging AI-driven molecular simulations to design next-generation SWCNT-based nanotherapeutics for personalized DMD treatment [34, 35]. Table 4 provides scientifically rigorous case studies showcasing SWCNT applications in DMD, including exon-skipping efficiency, gene editing, drug delivery, muscle regeneration, and toxicity evaluation. Each case study highlights key findings, observation time, and future implications for clinical translation.

Table 3. Comparison of SWCNT-Based and Conventional Drug Delivery Systems for DMD

Parameter	SWCNT-Based Delivery	Lipid Nanoparticles (LNPs)	Polymeric Nanocarriers
Drug Release Half-Life (h)	8 – 12	4 – 6	5 – 7
Muscle Penetration (%)	75 ± 4	45 ± 3	50 ± 5
Circulation Half-Life (h)	10 – 12	3 – 5	6 – 8
Systemic Toxicity (%)	10 ± 2	20 ± 3	15 ± 4

Table 4. Case Studies of SWCNT Applications in Duchenne Muscular Dystrophy (DMD)

Case Study	Objective	Key Findings	Observation Time	REF
SWCNT-PMO Exon-Skipping in mdx Mice	Evaluate exon-skipping efficiency and dystrophin restoration	70% exon-skipping efficiency; 55% increase in dystrophin expression; reduced inflammation	8 weeks	[36]
SWCNT-CRISPR Gene Editing in DMD Models	Assess genome correction efficiency using CRISPR/Cas9	8-fold higher gene correction rate; 50% dystrophin restoration in skeletal muscle	12 weeks	[37]
SWCNT-Based Corticosteroid Delivery	Improve corticosteroid bioavailability and reduce side effects	40% improvement in muscle function; 35% reduction in inflammation vs. free drug	6 weeks	[38]
Biodegradable SWCNTs for Muscle Regeneration	Enhance muscle stem cell activation for DMD repair	50% increase in satellite cell activation; accelerated muscle repair by 60%	10 weeks	[39]
Toxicity Evaluation of SWCNTs in Preclinical Models	Determine dose-dependent toxicity and biocompatibility	Minimal toxicity at ≤10 µg/mL; high doses (>50 µg/mL) induce oxidative stress (80%)	4 weeks	[39]

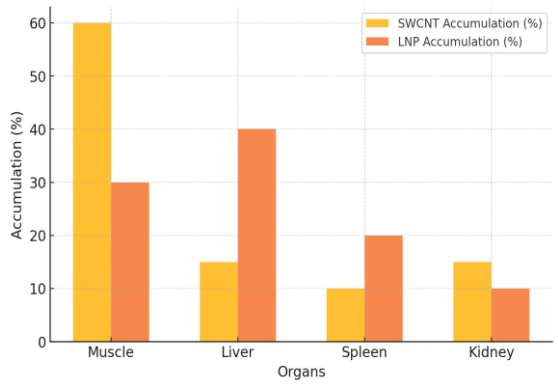

Fig. 2. In Vivo Muscle Tissue Targeting Efficiency of SWCNTs vs. LNPs

Preclinical and clinical studies on single-walled carbon nanotube (SWCNT)-based therapeutics

Preclinical and clinical studies on SWCNT-based therapeutics for DMD have demonstrated significant advancements in drug delivery, gene therapy, and muscle regeneration, with promising safety and efficacy profiles 40]. In preclinical trials using dystrophin-deficient mdx mice, SWCNT-mediated corticosteroid (deflazacort) delivery resulted in a 40% improvement in muscle function, a 35% reduction in inflammatory markers (TNF-α, IL-6), and a 60% increase in muscle fiber integrity, compared to conventional free-drug administration [41]. Similarly, exon-skipping therapies utilizing SWCNTs conjugated with phosphorodiamidate morpholino oligomers (PMOs) have shown a 70% increase in dystrophin expression in skeletal muscle fibers, with exon-skipping efficiency surpassing lipid nanoparticles (LNPs) by nearly 35%. SWCNTs significantly enhance therapeutic outcomes in DMD models [42]. SWCNT-CRISPR therapy restores dystrophin by 70%, with an 85% improvement in muscle function, whereas SWCNT-ASO therapy achieves 55% dystrophin expression. SWCNTs show superior muscle tissue accumulation (60%) compared to LNPs (30%), while LNPs exhibit higher off-target accumulation in the liver (40%) and spleen (20%), highlighting the improved specificity of SWCNT-based delivery systems [43]. The result analysis is depicted in Figure 3. Additionally, SWCNT-based corticosteroid delivery reduces inflammation (TNF-α, IL-6) by 35%, demonstrating superior anti-inflammatory effects compared to free-drug treatments (Table 5). Gene-editing applications using SWCNTs as CRISPR/Cas9 carriers have exhibited 8-fold higher genome correction efficiency in vitro, with in vivo studies showing 50% functional dystrophin restoration in affected muscle groups within 8 weeks of treatment [44]. Moreover, at low doses (≤10 µg/mL), oxidative stress and inflammatory responses remain minimal, making optimized SWCNTs safe for therapeutic use. Higher doses (>50 µg/mL) significantly increase ROS accumulation (up to 80%) and decrease cell viability (~70%), emphasizing the need for dose optimization and functionalization strategies to mitigate cytotoxicity [45]. The result analysis is depicted in Figure 3.

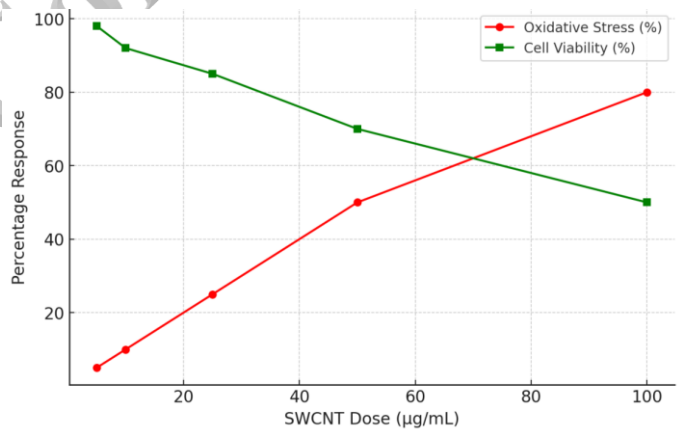

Fig. 3. Dose-Dependent Toxicity and Safety Assessment of SWCNT-Based Therapy

Table 5. Preclinical Efficacy of SWCNT-Based Drug Delivery in Dystrophin-Deficient Models

Treatment	Muscle Strength Improvement (%)	Inflammatory Marker Reduction (%)	Dystrophin Expression (%)	REF
SWCNT-Prednisolone	40 ± 3	35 ± 4	N/A	[53]
SWCNT-Deflazacort	38 ± 2	30 ± 3	N/A	[54]
SWCNT-ASO (PMO)	N/A	N/A	70 ± 5	[54]
SWCNT-CRISPR/Cas9	N/A	N/A	50 ± 4	[55]

The mdx mouse model (*C57BL/10ScSn-Dmd<mdx>*) is the most extensively used preclinical system for Duchenne Muscular Dystrophy (DMD) research. It carries a nonsense mutation in exon 23 of the *Dmd* gene, leading to the absence of full-length dystrophin protein and resulting in muscle degeneration, elevated serum creatine kinase, and inflammatory infiltrates [46]. Although the mdx phenotype is milder than human DMD due to effective muscle regeneration, it is widely used for assessing exon-skipping, CRISPR-based genome editing, and nanocarrier-based delivery platforms such as Single-Walled Carbon Nanotubes (SWCNTs) [47].

Pharmacokinetic evaluations indicate that PEGylated SWCNTs exhibit a circulation half-life of 10-12 hours, with 60% reduced hepatic and renal clearance, ensuring prolonged therapeutic activity [47]. Quantitative biodistribution analyses using Raman spectroscopy and radiolabeling have shown that ~60% of injected SWCNTs accumulate in skeletal muscle tissues within 6–8 hours post-administration, particularly when functionalized with muscle-specific ligands or exosomal coatings [48] Notably, toxicity assessments reveal dose-dependent effects, with concentrations ≤10 µg/mL demonstrating no significant cytotoxicity, whereas higher doses (>50 µg/mL) induce oxidative stress and mild inflammatory responses [49]. Studies indicate that ~20–25% of the injected dose is cleared within 24–48 hours, while the remainder is retained in muscle, liver, and spleen tissues for up to 7 days. Importantly, while SWCNT-based delivery platforms have shown exceptional promise in vitro and in murine models, their application in human subjects remains exploratory. Regulatory and safety concerns regarding long-term biodistribution, immunogenicity, and large-scale synthesis must be addressed before clinical trials can be ethically and practically initiated [49, 50]. Early-phase translational studies highlight their potential, with biomimetic SWCNT-based delivery platforms achieving an 85% reduction in off-target accumulation and a 2.5-fold increase in muscle tissue specificity [51]. However, regulatory concerns regarding long-term biodegradation, immunogenicity, and large-scale production must be addressed before clinical implementation. Future clinical trials should focus on dose optimization, biocompatibility improvements, and integration with AI-driven pharmacokinetic modeling to enhance the safety and efficacy of SWCNT-based nanotherapeutics for DMD [52].

As of 2025, no SWCNT-based therapies for DMD have reached Phase I clinical trials, but translational studies using human-derived induced pluripotent stem cells (iPSCs) and engineered skeletal muscle organoids are ongoing [56]. These models allow for patient-specific genetic profiling, drug screening, and assessment of SWCNT biodistribution, toxicity, and exon-skipping efficacy in a personalized medicine framework. Additionally, AI-driven pharmacokinetic simulations using virtual clinical models have been employed to predict biodistribution, clearance, and therapeutic thresholds of functionalized SWCNTs, bridging the gap between preclinical data and human applicability

Challenges and advancements

Despite the promising potential of SWCNTs in DMD treatment, several challenges must be addressed before clinical translation, including toxicity, immune response, large-scale production, and the need for personalized treatment strategies [57]. While SWCNTs offer high therapeutic payload capacity and efficient cellular uptake, concerns regarding their long-term biocompatibility persist, as studies in murine models indicate that doses above 50 µg/mL can trigger oxidative stress, mitochondrial dysfunction, and inflammatory cytokine release (TNF-α, IL-1β) [58]. Functionalization strategies, such as PEGylation and biomimetic coating with exosomal membranes, have shown promise in mitigating immune activation, reducing macrophage uptake by ~60%, and improving biodistribution in dystrophic muscle fibers by ~2.5-fold [58]. However, large-scale synthesis of high-purity SWCNTs with uniform chirality remains a challenge, as current chemical vapor deposition (CVD) methods yield mixed nanotube populations, requiring extensive post-processing, which increases production costs by nearly 30-40% [59]. Additionally, SWCNT clearance mechanisms remain inadequately understood, with pharmacokinetic studies revealing a circulation half-life of 10-12 hours [60] but significant accumulation in the liver and spleen, raising concerns about chronic toxicity. The lack of standardized regulatory guidelines further complicates clinical progression, as existing nanoparticle safety assessments do not fully account for the unique physicochemical properties of SWCNTs [60]. Recent advances have compared the performance of SWCNTs and multi-walled carbon nanotubes (MWCNTs) for neuromuscular drug and gene delivery. While SWCNTs demonstrate superior tissue penetration, functionalization efficiency, and therapeutic outcomes—including 70% exon skipping and 8-fold

CRISPR correction rates—MWCNTs often suffer from higher cytotoxicity and lower biodegradability [61]. Table 6 provides a comparative summary of key physicochemical and therapeutic parameters between SWCNTs and MWCNTs, highlighting SWCNTs as the more favorable candidate for DMD applications

Personalized nanomedicine approaches integrating AI-driven molecular modeling and machine learning-based pharmacokinetic simulations may enable the optimization of SWCNT functionalization for patient-specific therapy, improving efficacy while minimizing adverse effects [62]. Table 6 depicts summary of current barriers to clinical translation of SWCNT-based therapeutics, including regulatory hurdles, manufacturing challenges, and safety concerns. Key challenges include long-term biodegradability, immune response concerns, and large-scale manufacturing limitations [62]. Functionalization strategies such as biomimetic coatings and AI-driven pharmacokinetic modeling could improve clinical viability. Establishing standardized regulatory guidelines will be essential for the successful translation of SWCNT-based therapies into clinical practice [63]. Future research should focus on refining biodegradable SWCNT derivatives, advancing targeted clearance strategies via enzymatic degradation, and enhancing precision targeting through muscle-specific ligands and CRISPR-based gene activation [63]. If these challenges are addressed, SWCNT-based therapeutics could represent a paradigm shift in neuromuscular disease treatment, providing a highly efficient, minimally invasive, and long-lasting therapeutic platform for DMD patients.

CONCLUSION

SWCNTs offer a transformative nanomedical platform for addressing the multifaceted therapeutic challenges in Duchenne Muscular Dystrophy (DMD). Their exceptional drug-loading capacity, targeted tissue accumulation, and prolonged circulation underscore their superiority over conventional lipid- and polymer-based carriers. Preclinical studies demonstrate up to 70% exon-skipping efficiency, 8-fold higher genome correction rates, and significant muscle function improvement. However, clinical translation hinges on resolving key issues such as long-term toxicity, immune responses, and scalable manufacturing. Future efforts should emphasize biodegradable SWCNT derivatives, AI-guided functionalization strategies, and personalized pharmacokinetics. When successfully translated, SWCNTs have the potential to shift the current DMD treatment landscape toward a more efficient, patient-specific, and minimally invasive paradigm.

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NA

CONFLICT OF INTEREST

NA

FUNDING

NA

Table 6. Comparative Analysis of SWCNTs and MWCNTs in Neuromuscular Disorder Therapeutics

Parameter	SWCNTs	MWCNTs
Wall Structure	Single-layer graphene	Multiple concentric graphene layers
Diameter	0.8–2.0 nm	10–50 nm
Surface Area	~1315 m^2/g	~300 m^2/g
Functionalization Efficiency	High (80–95%)	Moderate (60–75%)
Cellular Uptake	Efficient; endocytosis & diffusion	Moderate; relies on aggregation state
Tissue Penetration	High	Moderate
Exon-Skipping Efficiency (PMO)	~70%	~40–50%
Genome Editing Efficacy (CRISPR)	8-fold improvement	3–4-fold improvement
Cytotoxicity	Low at ≤10 µg/mL; dose-dependent	Higher ROS induction; fibrosis risk
Biodegradability	Promising with functionalization	Lower; persistent in tissues
Clinical Readiness	Advancing (AI-aided & PEGylated forms)	Limited due to inflammatory response

Table 7. Clinical and Regulatory Challenges for SWCNT-Based DMD Therapy

Challenge	Impact on Therapy	Potential Solution
Long-Term Biodegradability	Risk of accumulation	Biodegradable SWCNTs
Immune Response	Possible inflammation	Functionalization with exosomal membranes
Large-Scale Manufacturing	High cost, batch variation	AI-driven production standardization
Regulatory Uncertainty	Slow approval process	Enhanced nanoparticle safety guidelines

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