SPINRAZA 2.0 ENHANCED EFFICACY WITH GRAPHENE QUANTUM DOTS

ABSTRACT:

Spinal muscular atrophy is an inherited autosomal recessive disease of avarying phenotype that is characterized by progressive muscle weakness, reduced tone with associated destruction of alpha m units. In 95% of cases, SMA results from a homozygous deletion of SMN1 on chromosome 5q13; how this does not explain how there can be significant clinical heterogeneity in phenotype. SMA incidence has been estimated at 1 in 6000 to 11000, with a carrier frequency in the of mutations in SMN1 of 2 t (1 in 40) in the general population. To treat the underlying causes of SMA, the Food and Drug Administration (FDA) has recentlyapproved three specific therapies:
Nusinersen (Spinraza): This is to treat SMA in children and adults. It's designed to boost the pproved t treat SMA in children under 2 years old.Risdiplam (Evrysdi): This is approved to treat SMAproduction of the sensor motor neuron (SMN) protein, which is insufficient in people with most types of SMA. Th protein helps motor nerves survive.Onasemnogene abeparvovec-xioi (Zolgensma): This is a in individ ages 2 months and older. Spinraza (nusinersen) can be formulated as Graphene Quantum Dots (GQDs . Researchers have explored the use of GQDs as a delivery platform for various therapeutic agents, in oligonucleotides like Spinraza.. ormulating Spinraza as Graphene Quantum Dots (GQDs) aims to over the drawbacks of conventional Spinraza. It increases Bioavailability , Reduces toxicity , Targeted deliv Overcomes Blood Brain Barrier.

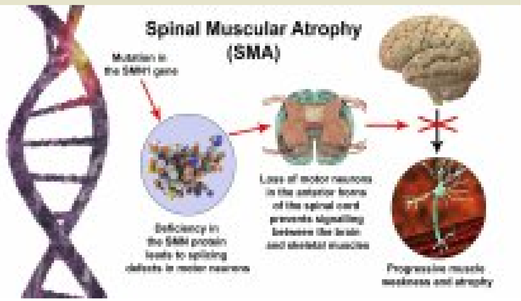
KEY WORDS: Spinraza,Graphene Quantum Dots, Bioavailability, Toxicity,Targeted delivery

INTRODUCTION

Spinal muscular atrophy (SMA) is a devastating genetic disorder characterized by progressive muscle weakness and atrophy. Spinraza (nusinersen), an antisense oligonucleotide therapy, has revolutionized SMA treatment by targeting the underlying genetic cause. However, conventional Spinraza administration is hindered by limitations, including frequent intrathecal injections, limited bioavailability, and potential immunogenicity.Recent advances in nanotechnology have led to the emergence of Graphene Quantum Dots (GQDs) as a versatile platform for therapeutic delivery. GQDs offer exceptional biocompatibility, photostability, and tunable surface chemistry, making them an attractive candidate for enhancing Spinraza delivery.This project aims to develop and characterize a novel formulation of Spinraza as Graphene Quantum Dots, leveraging the synergistic benefits of both technologies to overcome the limitations of conventional Spinraza administration. By optimizing the design and functionality of GQD-formulated Spinraza, we seek to improve treatment outcomes, reduce adverse effects, and enhance patient compliance for SMA patients worldwide.:

MECHANISM OF ACTION

- Cellular Uptake
- Endosomal uptake
- Spinraza Release and Distribution
- SMN Protein Production
- Motor neuron Survival
- Clearance and Biodiversity



FORMULATION PROCESS

Step 1: Synthesis of Graphene Quantum Dots- Use a top-down approach, such as chemical exfoliation or hydrothermal treatment, to synthesize GQDs from graphene oxide.- Alternatively, use a bottom-up approach, such as molecular beam epitaxy or chemical vapor deposition, to synthesize GQDs from molecular precursors
.Step 2: Functionalization of Graphene Quantum Dots- Functionalize the GQDs with hydrophilic groups, such as carboxyl, hydroxyl, or amino groups, to improve their solubility and biocompatibility.- Use techniques such as diazonium chemistry, click chemistry, or electrochemical functionalization to introduce functional groups onto the GQDs.
Step 3: Loading Spinraza onto Graphene Quantum Dots- Use techniques such as electrostatic adsorption, π-π stacking, or covalent conjugation to load Spinraza onto the functionalized GQDs.- Optimize the loading efficiency and capacity by adjusting parameters such as the concentration of Spinraza, the ratio of Spinraza to GQDs, and the incubation time.
Step 4: Characterization of Spinraza-Loaded Graphene Quantum Dots- Use techniques such as transmission electron microscopy (TEM), atomic force microscopy (AFM), and dynamic light scattering (DLS) to characterize the size, shape, and surface morphology of the Spinraza-loaded GQDs.- Use techniques such as Fourier transform infrared spectroscopy (FTIR), Raman spectroscopy, and X-ray photoelectron spectroscopy (XPS) to characterize the chemical composition and bonding of the Spinraza-loaded GQDs.
Step 5: In Vitro and In Vivo Evaluation- Evaluate the toxicity, cellular uptake, and efficacy of the Spinraza-loaded GQDs in vitro using cell cultures and in vivo using animal models.- Assess the pharmacokinetics, biodistribution, and therapeutic efficacy of the Spinraza-loaded GQDs in animal models.

CONCLUSION

Formulating Spinraza as Graphene Quantum Dots represents a promising strategy to overc the limitations of conventional Spinraza administration. The unique properties of GQDs, includingtheir small size, biocompatibility, and tunable surface chemistry, enable enhanced cellular uptake, endosomal escape, and sustained release of Spinraza.This novel formulationhas the potential to:
1.Improve bioavailability and reduce dosing frequency
2. Enhance SMN protein production and motor neuron survival
3. Reduce immunogenicity and toxicity4. Improve patient compliance and quality of lifeWhile further research is needed to optimize the design and functionality of GQD-formulated Spinraza, this innovative approach holds great promise for Revolutionizing the treatment of spinal muscular atrophy (SMA).

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