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Double functionalized biodegradable Riluzole nanoparticles with therapeutic potential for neurodegenerative diseases

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Double functionalized biodegradable Riluzole nanoparticles with therapeutic potential for neurodegenerative diseases

Graphical Abstract



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Abstract:

Neurodegenerative diseases (ND) represent a major health problem in the global population and cause progressive neuronal death in the central nervous system (CNS) or peripheral system, leading to cognitive malfunction. Furthermore, there are currently no effective treatments for ND. The blood-brain-barrier (BBB) is one of the most restrictive physiological barriers and is responsible for protecting the CNS hindering the transport of drugs to the brain. Riluzole (RLZ) has proven to possess high neuroprotective capacity. However, its transport through the BBB is limited. Moreover, polymeric nanoparticles (NPs) improve the transport of drugs through the BBB and providing a prolonged drug release. Therefore, in this work double functionalized PLGA-NPs encapsulating RLZ have been developed using Polyethylene glycol (PEG) and a Cell Penetrating Peptide (CPP).

The preparation of the NPs was carried out using the solvent displacement method and they were optimized using the design of experiments approach. Subsequently, optimized NPs were prepared by incorporating custom synthesized PLGA-PEG and PLGA-CPP. CPP was synthesized by Solid-Phase Peptide Synthesis by an orthogonal strategy of amino acids protection (Fmoc-tButyl) and subsequently attached to PLGA.

The physicochemical characterization studies of the NPs showed RLZ entrapment efficiency higher than 90%, average size below 200 nm and a monomodal population.

In conclusion, functionalized NPs loaded with RLZ obtained present suitable physicochemical parameters, to initiate the drug delivery studies for treatment of ND.

Keywords: Polymeric nanoparticles; drug delivery; Riluzole;
Neurodegenerative diseases



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Introduction



World Health
Organization



In 2040
2nd cause of death
globally

Neurodegenerative diseases



Figure Adapted of siemens-healthineers



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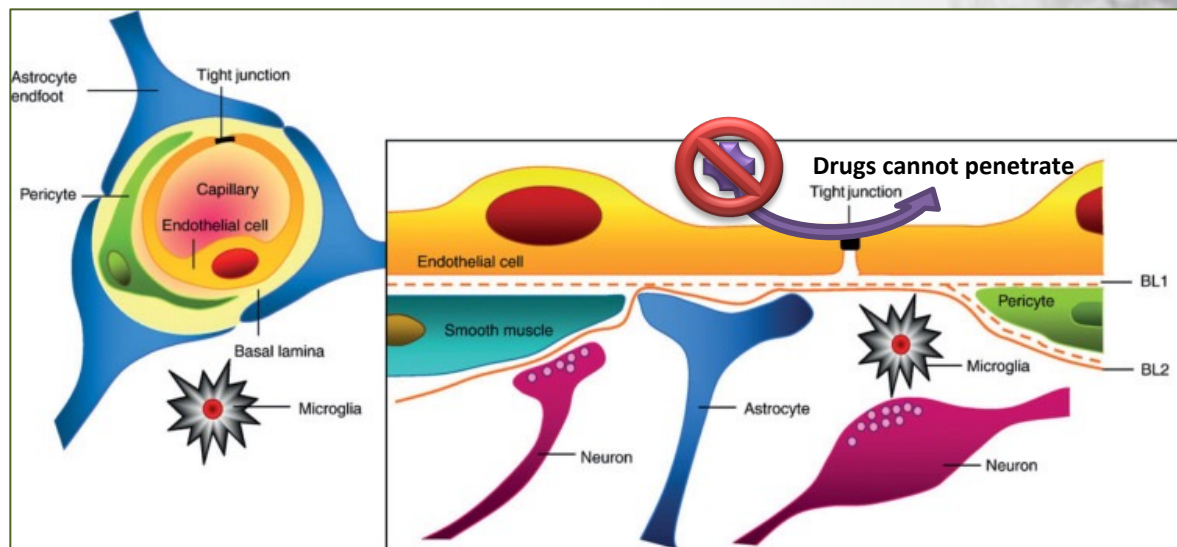
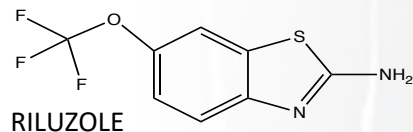


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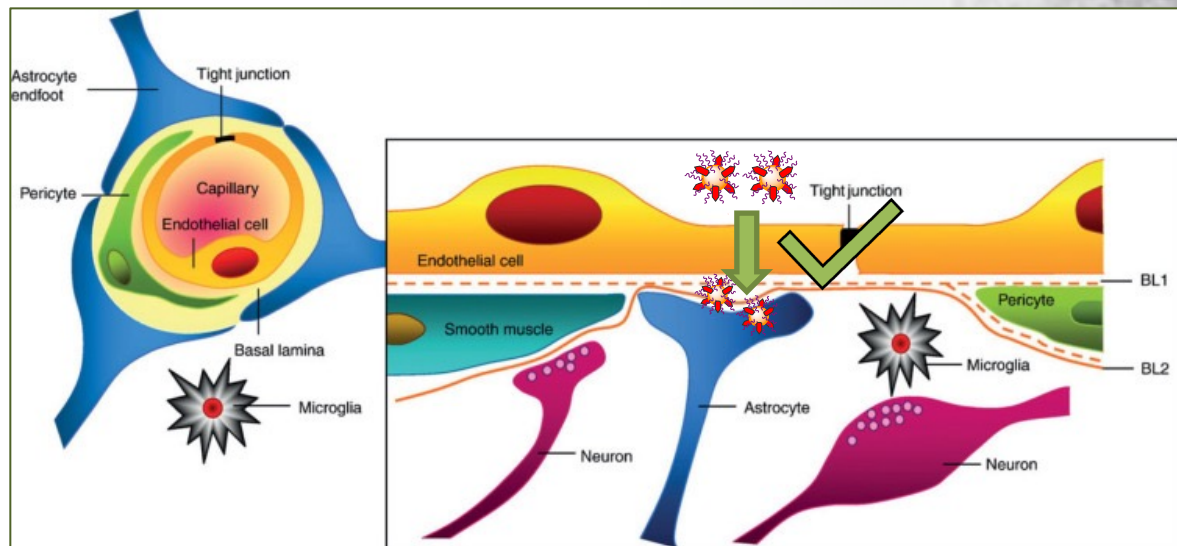
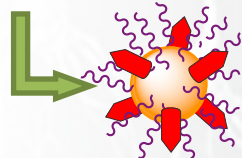
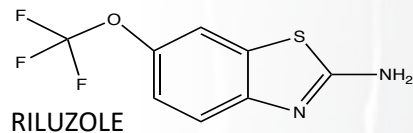
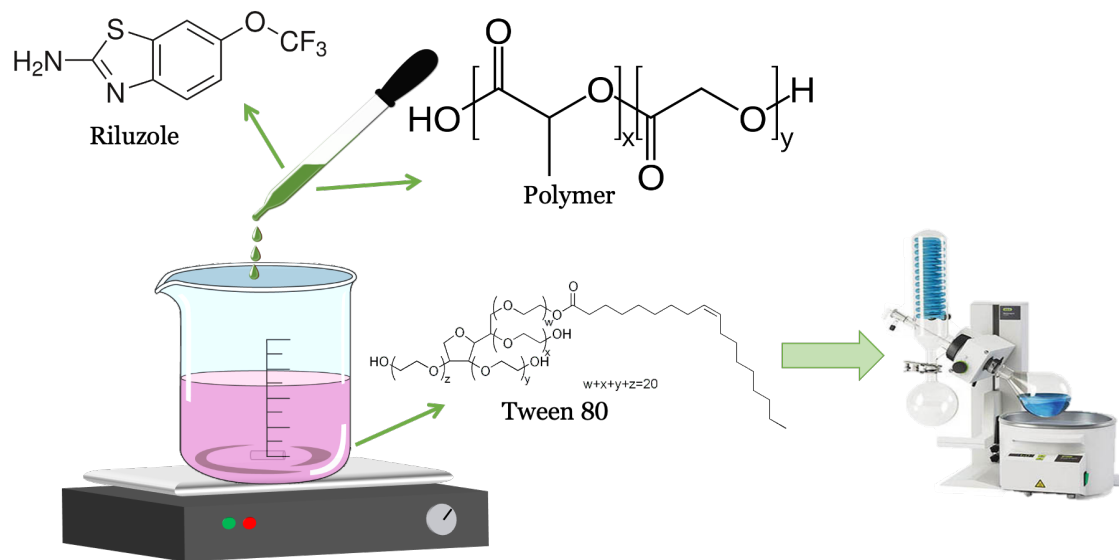


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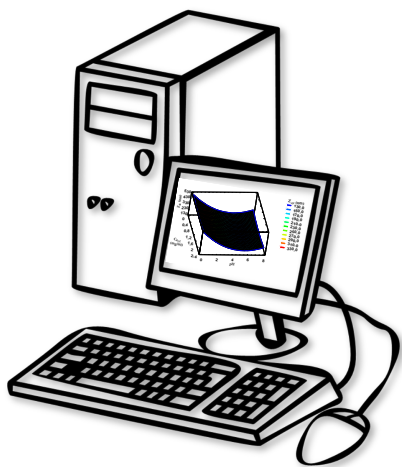


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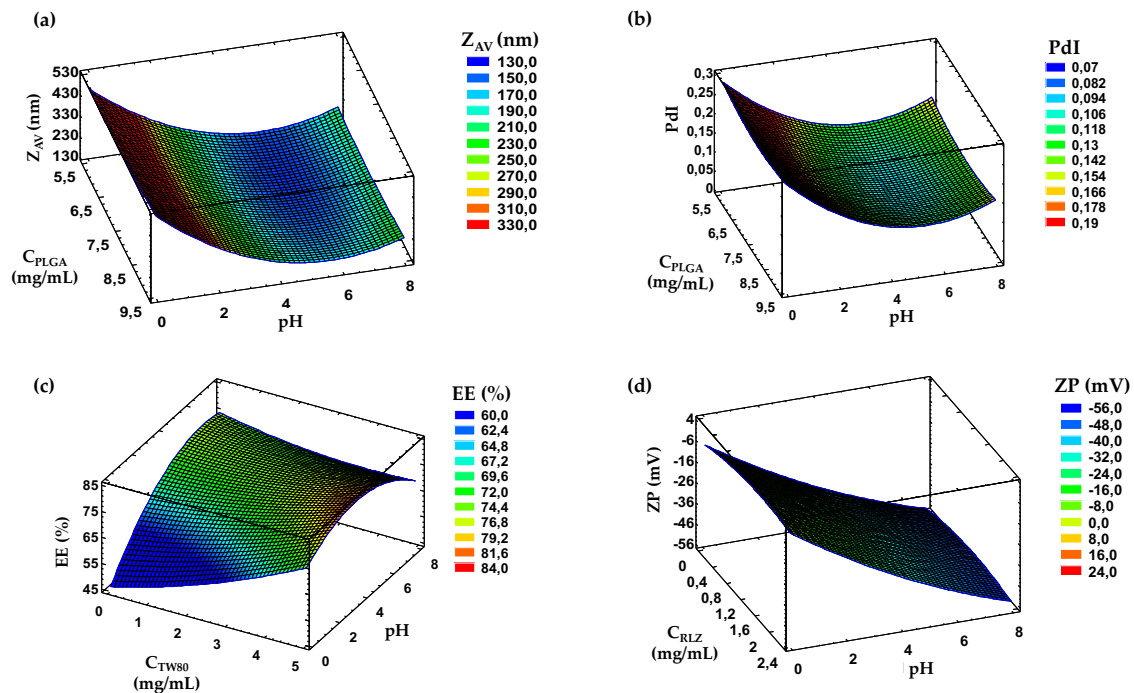
Results and discussion



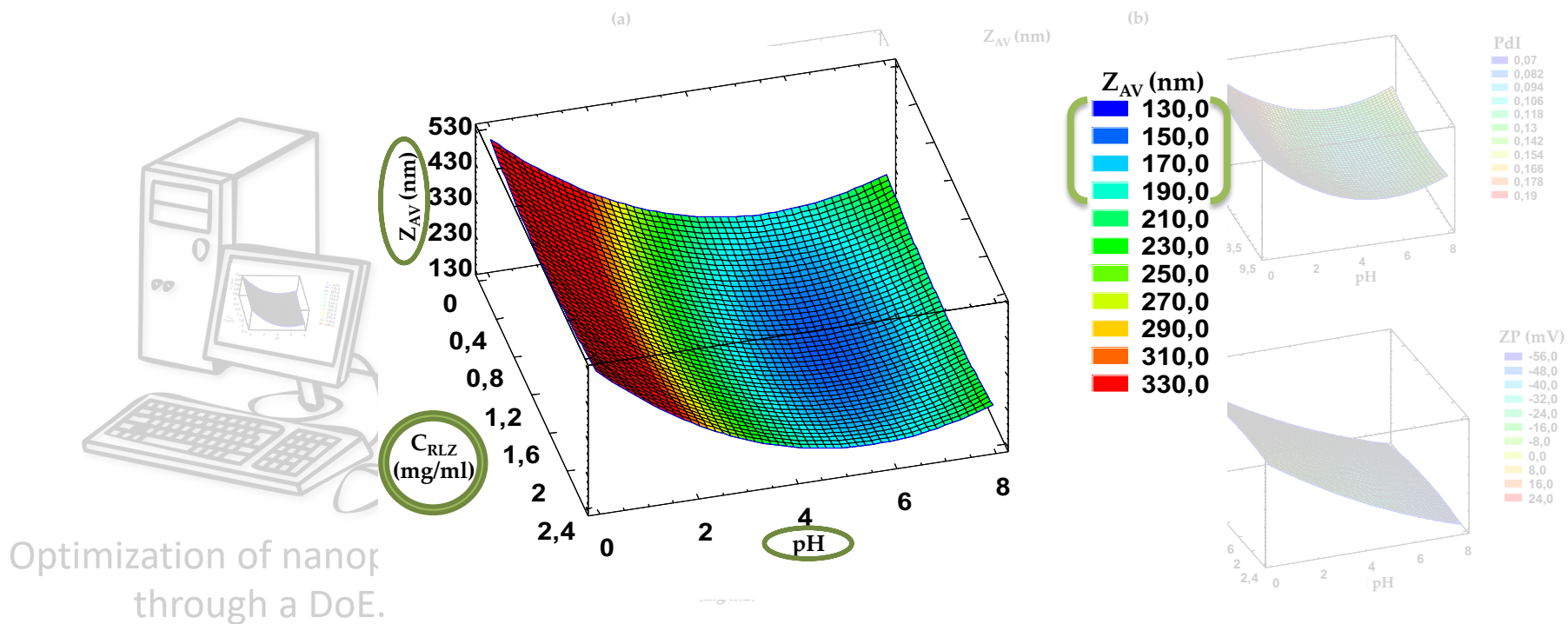
Results and discussion



Optimization of nanoparticles through a DoE.



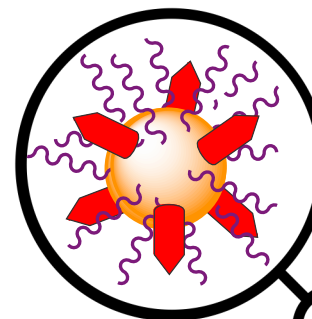
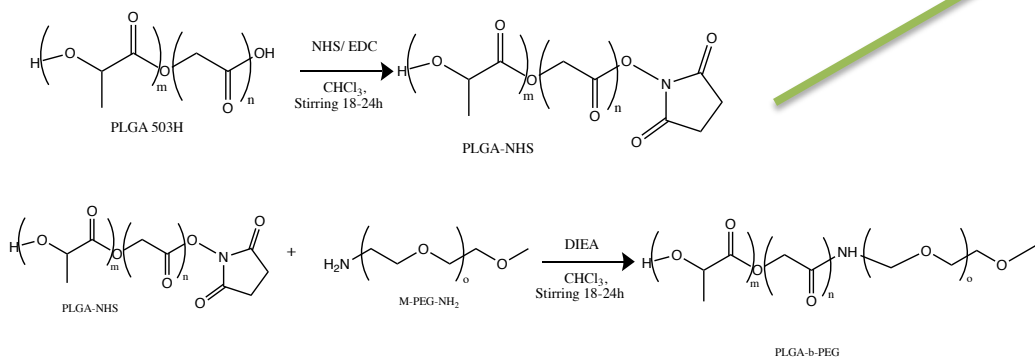
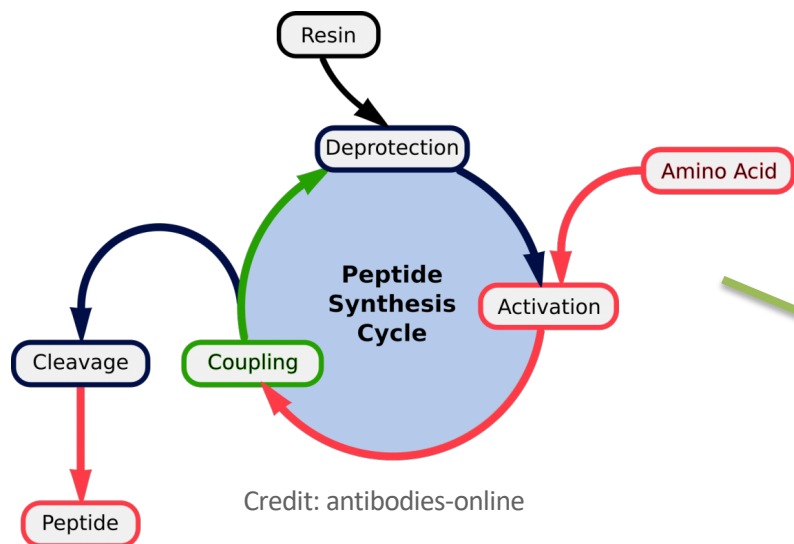
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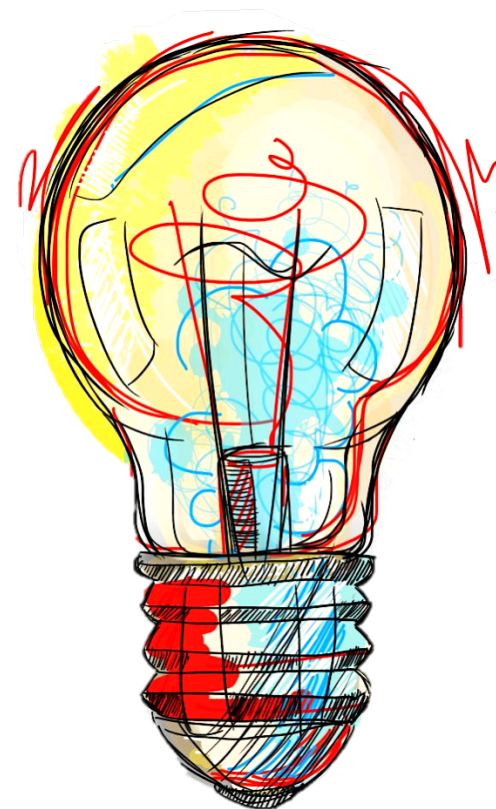
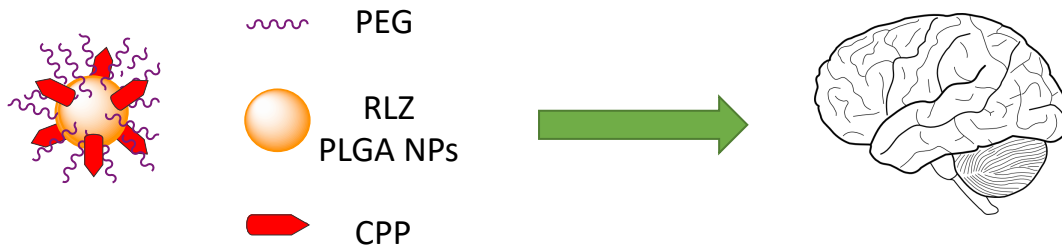


Optimized formulation	
Z _{AV}	<200 nm
PdI	Monomodal population
EE	>90%



Conclusions

- In conclusion, functionalized NPs loaded with RLZ obtained present suitable physicochemical parameters, to initiate the drug delivery studies for treatment of ND



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