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Aquasome Based Nanocarriers for Improved Brain Delivery of DDI-90: A Novel Neuroprotective Approach for Alzheimer's Disease

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INTRODUCTION & AIM

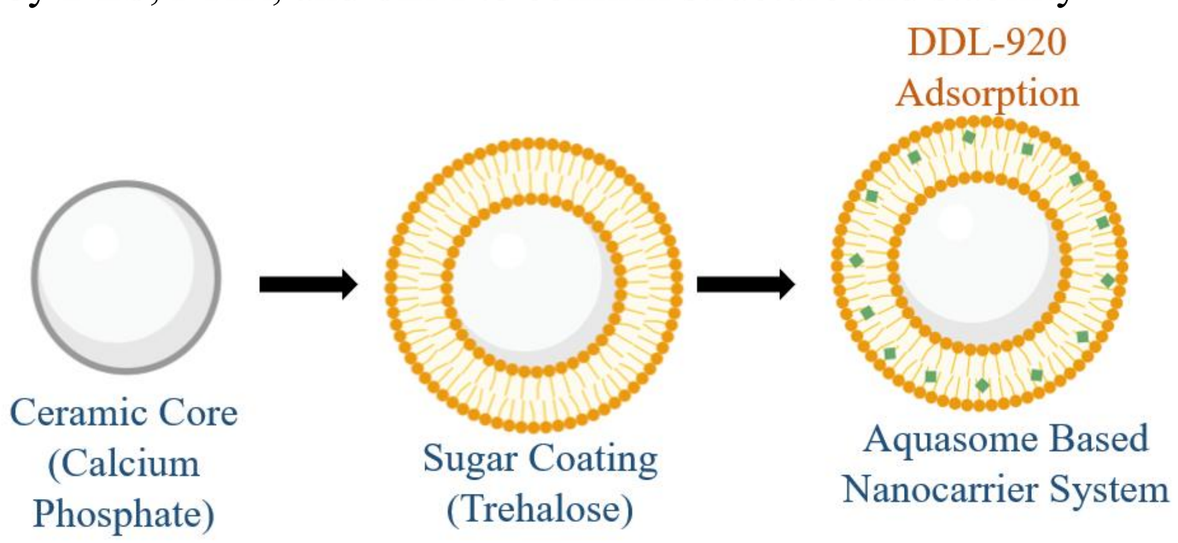
Alzheimer's disease remains a major neurodegenerative challenge, marked by progressive cognitive decline and the accumulation of amyloid plaques. Despite decades of research, the available treatments offer only limited symptomatic benefit, largely because most therapeutic molecules fails to reach the brain in sufficient concentrations.

DDl-920, a small molecule with strong neuroprotective activity, has shown promising preclinical data, including improved spatial memory and reduced amyloid plaque load in experiment models, Hower, its **poor solubility (<0.5 µg/mL), low oral bioavailability (~12%)**, and restricted **brain penetration (brain/plasma ratio <0.08)** have limited its clinical use.

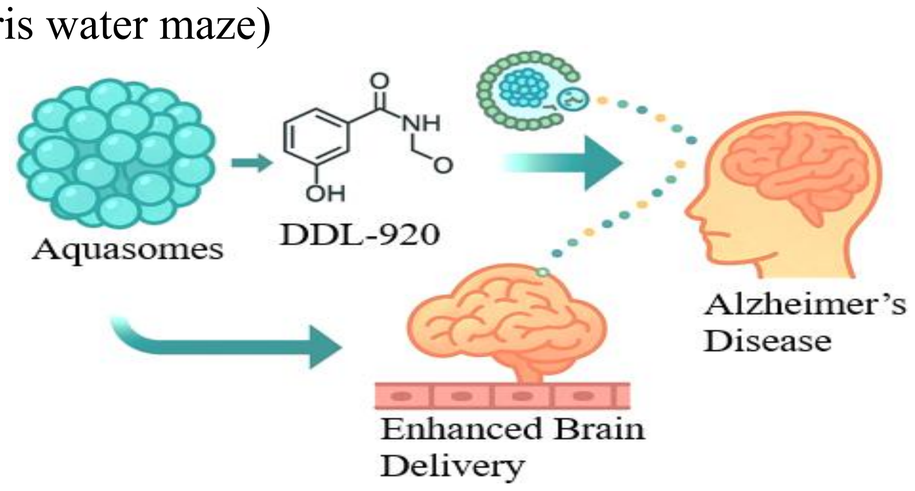
Objective: The study was designed to develop **aquasome based nanocarriers** to improve the solubility, bioavailability, and brain uptake of DDL-920 for potential use in Alzheimer's therapy.

METHOD

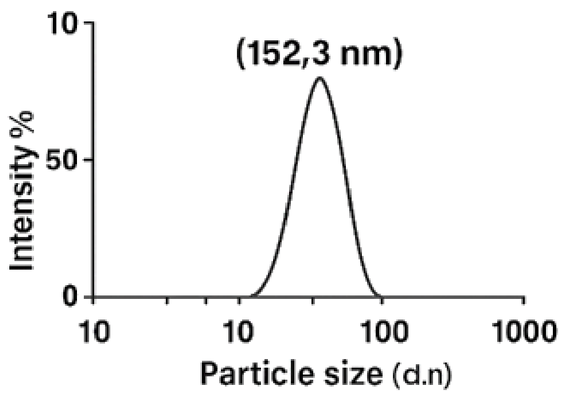
Aquasomes were formulated as a three-tiered system consisting of a calcium phosphate core, a trehalose coating, and DDL-920 adsorbed onto the surface. Optimization was carried out using a factorial design approach to balance particle size, surface charge, and drug loading. The formulations were characterized by DLS, FTIR, and SEM to confirm structure and stability

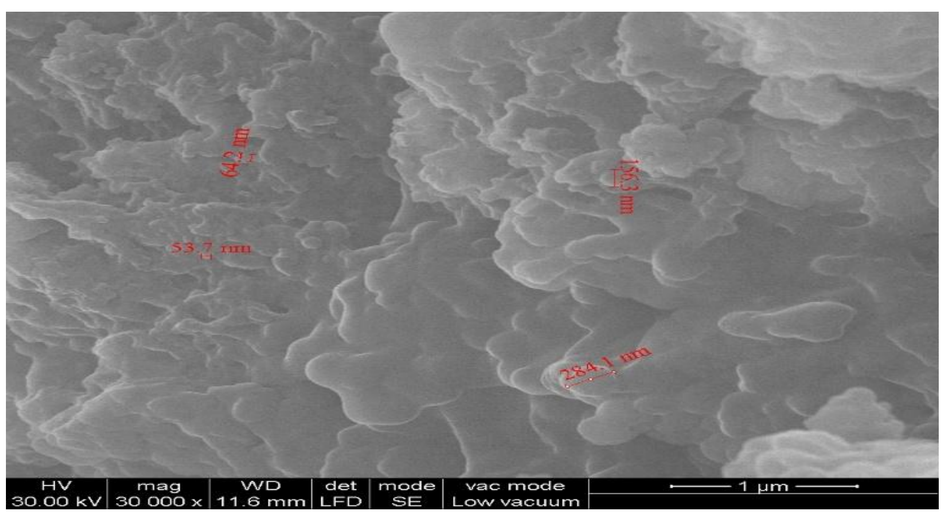


Drug Release and solubility were evaluated under physiological conditions. *Invitro* BBB permeability was examined using the hCMEC/D3 cell model. Further, pharmacokinetic and biodistribution studies in Alzheimer's induced mice assessed brain uptake, while behavioural studies (Morris water maze)



RESULTS & DISCUSSION





The optimized aquasome formulation achieved a particle size of **152.3 ± 6.4 nm**, **zeta potential of –21.6 ± 2.3 mV, and encapsulation efficiency of 82.4 ± 3.5%**. The formulation produced a 12-fold increase in solubility and exhibited sustained release up to 74.

Transport studies through the BBB model revealed **4.3 times higher permeability** compared to the free drug. In vivo analysis confirmed **enhanced brain drug accumulation (2.6 ± 0.4 µg/g)**, while behavioural evaluation demonstrated **a 65% improvement in memory scores,** in contrast to **28%** observed with the unformulated compound.

These outcomes highlight the capacity of aquasome to overcome physicochemical and biological barriers, enhancing DDL-920 therapeutic impact.

CONCLUSION

Aqusome based nanocarriers significantly improved the solubility, and brain delivery of DDL-920, into enhanced neuroprotective activity in Alzheimer's models. This system represents a feasible platform for CNS-targeted delivery of small molecule drugs with poor bioavailability.

FUTURE WORK / REFERENCES

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