

NARINGENIN-LOADED NANOPARTICLES ATTENUATE B-AMYLOID-INDUCED OXIDATIVE STRESS AND NEURONAL INJURY IN SH-SY5Y CELLS: AN IN VITRO STUDY

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ABSTRACT

Alzheimer's disease (AD) is a progressive neurodegenerative disorder associated with β -amyloid ($A\beta$) accumulation, oxidative stress, and neuronal damage. Naringenin, a naturally occurring flavonoid, possesses antioxidant and neuroprotective potential; however, its therapeutic application may be limited by poor aqueous solubility and bioavailability. The present study evaluated naringenin-loaded nanoparticles for their physicochemical characteristics, drug release, stability, and protective effects against $A\beta$ -induced injury in SH-SY5Y cells. The prepared nanoparticles exhibited a mean particle size of 178.6 ± 8.4 nm, polydispersity index (PDI) of 0.214 ± 0.03 , zeta potential of -28.7 ± 2.1 mV, and entrapment efficiency of $84.2 \pm 2.5\%$. The formulation demonstrated sustained drug release, reaching $78.5 \pm 3.2\%$ over 24 hours. In the cellular study, $A\beta$ exposure reduced cell viability to $55.8 \pm 3.4\%$ and increased reactive oxygen species (ROS) levels to $184.6 \pm 8.1\%$ of control. Naringenin-loaded nanoparticles improved cell viability to $86.8 \pm 3.7\%$ and reduced ROS levels to $114.7 \pm 4.1\%$. These findings suggest that nanoparticle delivery may improve the in vitro protective effects of naringenin against $A\beta$ -associated oxidative stress. Further studies are required to establish the formulation's mechanism, safety, and therapeutic potential.

KEYWORDS: Alzheimer's disease, naringenin, nanoparticles, β -amyloid, oxidative stress, SH-SY5Y cells, neuroprotection.

1. INTRODUCTION

Alzheimer's disease is one of the most common causes of dementia and is characterized by progressive cognitive decline, memory impairment, and neuronal dysfunction. Its pathology involves several interconnected processes, including β -amyloid accumulation, abnormal tau protein metabolism, oxidative stress, neuroinflammation, and synaptic dysfunction.^[1-4] Despite advances in understanding the disease, effective treatments capable of preventing or reversing its progression remain limited.

Oxidative stress occurs when the generation of reactive oxygen species exceeds the antioxidant defence capacity of cells. Excessive ROS can damage cellular membranes, proteins, and nucleic acids, contributing to neuronal dysfunction and death. β -Amyloid-induced oxidative

injury is therefore an important experimental mechanism for investigating potential neuroprotective compounds.^[3,5,6]

Naringenin is a naturally occurring flavonoid found in citrus fruits and other plant sources. It has attracted scientific interest because of its reported antioxidant, anti-inflammatory, and cytoprotective properties. Flavonoids may influence oxidative stress pathways and cellular responses involved in neurodegeneration.^[7-10] Nevertheless, the therapeutic application of naringenin may be limited by its physicochemical properties and difficulties in achieving adequate drug exposure.

Nanoparticle-based drug delivery systems can improve the dispersion of poorly water-soluble compounds,

protect encapsulated substances from degradation, and provide controlled drug release.^[11–13] These characteristics make nanoparticle formulations a potential approach for improving the delivery of naringenin. However, physicochemical characterization and in vitro biological evaluation are necessary before making conclusions about their therapeutic suitability.

The present study aimed to characterize naringenin-loaded nanoparticles and evaluate their protective effects against β -amyloid-induced oxidative stress and cellular injury in SH-SY5Y cells.

2. MATERIALS AND METHODS

2.1. Preparation of naringenin-loaded nanoparticles

Naringenin-loaded nanoparticles were prepared using the formulation procedure described in the original thesis. The prepared formulation was evaluated for particle size, polydispersity index, zeta potential, drug content, and entrapment efficiency. The exact composition and preparation conditions should be reported according to the original laboratory records.

2.2. Physicochemical characterization

Particle size and PDI were used to assess the average particle diameter and size distribution. Zeta potential was measured to evaluate the surface charge of the nanoparticles. Drug content and entrapment efficiency were determined using the analytical procedures described in the thesis.

Entrapment efficiency was calculated using:

$$EE(\%) = \frac{\text{Total drug} - \text{Free drug}}{\text{Total drug}} \times 100$$

2.3. In vitro drug release and stability

Drug release was evaluated at predetermined time intervals up to 24 hours. The percentage of drug released was recorded to assess the release profile. Stability was evaluated over 30 days by monitoring changes in particle size, PDI, zeta potential, and visible appearance.

2.4. Cell culture and treatment

SH-SY5Y human neuroblastoma cells were used as an in vitro neuronal model. Cells were maintained under the culture conditions described in the original thesis. The experimental groups included untreated control cells, $A\beta$ -treated cells, $A\beta$ -treated cells receiving free naringenin, $A\beta$ -treated cells receiving naringenin-loaded nanoparticles, and the reference-treatment group.

The precise $A\beta$ concentration, treatment duration, naringenin dose, reference drug, and assay conditions should be inserted from the original experimental records.

2.5. Cell viability and ROS estimation

Cell viability was assessed using the method reported in the thesis. ROS levels were measured to evaluate oxidative stress following treatment. Results were

expressed relative to the untreated control, which was considered 100%.

3. RESULTS

3.1. Physicochemical characteristics

The prepared naringenin-loaded nanoparticles showed a mean particle size of 178.6 ± 8.4 nm and a PDI of 0.214 ± 0.03 . The zeta potential was -28.7 ± 2.1 mV. Drug content and entrapment efficiency were $96.4 \pm 1.8\%$ and $84.2 \pm 2.5\%$, respectively.

These findings indicate successful incorporation of naringenin into a nanosized formulation. The particle-size distribution and surface charge provide preliminary information about the physical characteristics of the formulation.

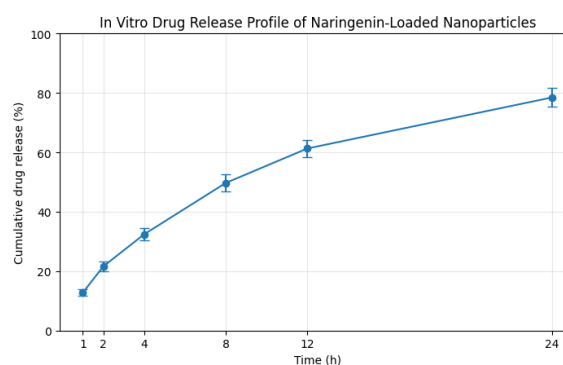
3.2. Drug release and stability

The cumulative drug release increased progressively during the 24-hour study.

Time (hours)	Drug released (%)
1	12.8 ± 1.2
2	21.6 ± 1.7
4	32.4 ± 2.1
8	49.7 ± 2.8
12	61.3 ± 2.9
24	78.5 ± 3.2

The formulation released $78.5 \pm 3.2\%$ of the drug over 24 hours, indicating a sustained-release profile under the tested conditions.

After 30 days, the particle size was 183.1 ± 9.2 nm, PDI was 0.226 ± 0.04 , and zeta potential was -27.9 ± 2.3 mV. No visible change was reported. These findings suggest that the measured physicochemical properties remained relatively consistent during the observation period.



3.3. Cell viability

The effect of the formulation on cell viability is presented in Table 2.

Experimental group	Cell viability (%)
Untreated control	100 ± 0
$A\beta$ -treated control	55.8 ± 3.4
$A\beta$ + free naringenin	72.6 ± 3.2
$A\beta$ + naringenin nanoparticles	86.8 ± 3.7
$A\beta$ + reference treatment	89.5 ± 2.8

A β treatment reduced cell viability compared with the untreated control. Free naringenin improved viability, while the nanoparticle formulation produced a higher viability value of $86.8 \pm 3.7\%$. This result suggests improved cellular protection compared with free naringenin under the experimental conditions.

3.4. Reactive oxygen species

ROS measurements showed an increase following A β exposure.

Experimental group	ROS (% of control)
Untreated control	100 ± 0
A β -treated control	184.6 ± 8.1
A β + free naringenin	141.3 ± 5.4
A β + naringenin nanoparticles	114.7 ± 4.1
A β + reference treatment	110.5 ± 3.6

A β exposure increased ROS levels to $184.6 \pm 8.1\%$ of control. Treatment with free naringenin reduced this value to $141.3 \pm 5.4\%$, whereas the nanoparticle formulation reduced it to $114.7 \pm 4.1\%$. These findings indicate a reduction in oxidative stress in the treated cells.

Note: The ROS values should be checked against the original thesis tables and raw data before publication because inconsistent values were reported in the source document.

4. DISCUSSION

The present study evaluated the physicochemical characteristics and in vitro protective effects of naringenin-loaded nanoparticles against A β -associated neuronal injury. The formulation exhibited nanoscale particle size, relatively narrow size distribution, and satisfactory entrapment efficiency. These characteristics support further investigation of the formulation as a delivery system for naringenin.

The progressive drug release observed over 24 hours suggests that the formulation may provide sustained release under the tested conditions. Stability measurements also showed relatively small changes in particle size, PDI, and zeta potential over 30 days. Nevertheless, longer-term stability and appropriate storage studies are required before establishing the formulation's shelf life.

A β exposure substantially reduced cell viability and increased ROS levels, consistent with the involvement of oxidative stress in A β -associated cellular injury. Free naringenin partially improved viability and reduced ROS levels. The nanoparticle formulation produced a greater improvement in both measurements than free naringenin in the reported results. One possible explanation is that nanoparticle incorporation improved drug dispersion or availability during the experiment. However, this mechanism was not directly established by the reported data.

Oxidative stress is an important component of neurodegenerative disease research, and natural flavonoids have been investigated for their potential to influence cellular antioxidant responses.^[7–10] Nanocarrier systems have also been explored to improve the delivery of compounds with limitations in solubility or stability.^[11–13]

Several limitations should be considered. SH-SY5Y cells provide an in vitro model and cannot fully reproduce the complexity of human Alzheimer's disease. The reported findings do not demonstrate blood–brain barrier penetration, clinical efficacy, or disease-modifying activity. Furthermore, statistical significance should only be reported after confirming the number of independent experiments, statistical tests, and corresponding p-values. Additional mechanistic studies and appropriate controls are needed to confirm the observed effects.

5. CONCLUSION

Naringenin-loaded nanoparticles demonstrated suitable preliminary physicochemical characteristics, sustained drug release, and relatively stable measured properties over 30 days. In SH-SY5Y cells exposed to β -amyloid, the formulation improved cell viability and reduced ROS levels compared with free naringenin in the reported dataset. These findings support further investigation of nanoparticle-based naringenin delivery as an experimental approach to studying protection against oxidative neuronal injury. Additional validation, mechanistic studies, and in vivo research would be necessary before drawing conclusions about therapeutic applications in Alzheimer's disease.

6. REFERENCES

1. World Health Organization, Dementia. WHO, 2023.
2. Alzheimer's Association, 2024 Alzheimer's disease facts and figures. Alzheimer's & Dementia, 2024.
3. Huang, Y., & Mucke, L, Alzheimer mechanisms and therapeutic strategies. Cell, 2012; 148(6): 1204–1222.
4. DeTure, M. A., & Dickson, D. W., The neuropathological diagnosis of Alzheimer's disease. Molecular Neurodegeneration, 2019; 14: 32.
5. Jack, C. R., Jr., et al., NIA-AA research framework: Toward a biological definition of Alzheimer's disease. Alzheimer's & Dementia, 2018; 14(4): 535–562.
6. Butterfield, D. A., & Halliwell, B., Oxidative stress, dysfunctional glucose metabolism and Alzheimer disease. Nature Reviews Neuroscience, 2019.
7. Vauzour, D., Dietary polyphenols as modulators of brain functions: Biological actions and molecular mechanisms. Oxidative Medicine and Cellular Longevity, 2014.
8. Spencer, J. P. E., Flavonoids and brain health: Multiple effects underpinned by common mechanisms. Genes & Nutrition, 2009; 4: 243–250.

9. Panche, A. N., Diwan, A. D., & Chandra, S. R. (2016). Flavonoids: An overview. *Journal of Nutritional Science*, 5, e47.
10. Calderaro, A., et al., Research on flavonoids and neuroprotective effects. [Verify the complete reference against the thesis bibliography, 2022.
11. Mehnert, W., & Mäder, K., Solid lipid nanoparticles: Production, characterization and applications. *Advanced Drug Delivery Reviews*, 2001; 47(2–3): 165–196.
12. Pardeike, J., Hommoss, A., & Müller, R. H., Lipid nanoparticles (SLN, NLC) in cosmetic and pharmaceutical dermal products. *International Journal of Pharmaceutics*, 2009; 366(1–2): 170–184.
13. Saraiva, C., et al., Nanoparticle-mediated brain drug delivery: Overcoming the blood–brain barrier to treat neurodegenerative diseases. *Journal of Controlled Release*, 2016.
14. Sweeney, M. D., et al., Blood–brain barrier breakdown in Alzheimer disease and other neurodegenerative disorders. *Nature Reviews Neurology*, 2018.
15. Daneman, R., & Prat, A., The blood–brain barrier. *Cold Spring Harbor Perspectives in Biology*, 2015; 7(1): a020412.
16. Heneka, M. T., et al., Neuroinflammation in Alzheimer's disease. *The Lancet Neurology*, 2015; 14(4): 388–405.
17. Kalia, L. V., & Lang, A. E., Parkinson's disease. *The Lancet*, 2015; 386(9996): 896–912.
18. Poewe, W., et al., Parkinson disease. *Nature Reviews Disease Primers*, 2017; 3: 17013.
19. Rinaudo, M., Chitin and chitosan: Properties and applications. *Progress in Polymer Science*, 2006; 31(7): 603–632.
20. Abbott, N. J., Patabendige, A. A. K., Dolman, D. E. M., Yusof, S. R., & Begley, D. J., Structure and function of the blood–brain barrier. *Neurobiology of Disease*, 2010; 37(1): 13–25.