Evaluating the Effects of Curcumin-Coated Gold Nanoparticles on Survival and Motor Functions in a Parkinson's *C. elegans* Model

Parkinson's disease (PD) is an age-related neurodegenerative disease that is the second most common neurodegenerative disorder globally, after Alzheimer's (Córneo et al., 2020). PD mainly affects people older than the age of 60 and is characterized by various motor and non-motor symptoms, such as low blood pressure, mood swings, tremors in the body, slower movement, and posture instability (Thirugnanam & Santhakumar, 2022). These symptoms majorly result from the death of dopamine-producing (dopaminergic) neurons, leading to a significant decline in dopamine levels as the disease progresses. A hallmark of PD is the accumulation of Lewy bodies, which contain toxic α-synuclein aggregates—misfolded proteins that disrupt cellular homeostasis and contribute to neuronal death. The overexpression of α-synuclein leads to toxicity and the degeneration of dopaminergic neurons in both in vivo and in vitro models (Hu et al., 2018).

PD pathology is also associated with mitochondrial dysfunction, apoptosis (programmed cell death, neuroinflammation, and oxidative stress, which play a key role in the development of the disease (Thirugnanam & Santhakumar, 2022). Additionally, oxidative stress in the brain directly contributes to elevated ROS levels – reactive oxygen species-- promoting dopamine neurodegeneration. Excess production of ROS in Parkinson's leads to cellular dysfunction and neuroinflammation, further worsening neuronal damage. Although there are individual treatments synthesized for the symptoms of Parkinson's, no treatment has been discovered to halt the progression of the disease completely. Drugs such as Levodopa and various monoamine oxidase inhibitors, that are currently prescribed for PD, have significant side effects and do not have a lasting effect. (Xue et al., 2019). Hence ongoing research is focused on utilizing natural compounds and nanomedicine as a therapeutic treatment for Parkinson's disease.

Several natural compounds are currently being investigated for their potential in neurodegenerative diseases. Curcumin, also known as diferuloylmethane, is a natural compound found in turmeric with strong antioxidant and anti-inflammatory properties. Traditionally used in India and Asia as medicine, it has several health benefits: protection against infections, diabetes, skin diseases, and high cholesterol. Recent studies have shown that testing curcumin on PC12 cells expressing the A53T a-synuclein mutation may have neuroprotective effects for A53T-linked PD models (Liu et al., 2011). Since neuroprotective agents prevent or slow the progression of neuronal damage, the study highlights how curcumin significantly reduced ROS levels and protected the cells against neuronal death (Liu et al., 2011). However, one major limitation of curcumin is its low bioavailability—the rate at which it enters the bloodstream and reaches targeted tissues. To enhance its therapeutic potential, researchers are exploring ways to improve curcumin's delivery, including its combination with nanoparticles for pathological diseases.

Nanomedicine, an emerging field that applies nanotechnology to medical treatments, is rapidly advancing the development of innovative therapies. Metal nanoparticles, specifically gold nanoparticles (AuNPs), have gained increasing interest due to their optical and biocompatible properties. Additionally, gold nanoparticles are synthesized in nanoscale sizes with tunable surfaces, allowing them to deliver drugs in a controlled manner across the blood-brain barrier. These nanoparticles have unique properties that, at specific concentrations, enable them to have neuroprotective effects or sometimes even induce toxicity. (Grancharova et al., 2024). Since they have majorly been shown to promote the regeneration of neurons in various model organisms, gold nanoparticles may have positive implications in neurodegeneration research. For instance, the Paeonia moutan extract-coated gold nanoparticles were tested in Parkinson-induced mice, whose DA neuronal levels were depleted due to exposure to MPTP, a neurotoxin. The results demonstrate signs of increased dopamine levels and reduced neurotoxicity, as the grip strength and footprint patterns of the treated mice returned to approximately normal levels

after nanoparticle treatment. Additionally, ROS levels of the mice were reduced, proving that gold nanoparticles are in fact, anti-inflammatory and can be used as therapeutic agents (Xue et al., 2019).

6-OHDA, also known as 6-hydroxydopamine, is widely used in preclinical research to model Parkinson's disease. This neurotoxin induces and further amplifies the degeneration of dopaminergic neurons, neuronal damage, generation of cytotoxic species, and the onset of various motor dysfunctions (Simola et al., 2007). More importantly, 6-OHDA triggers oxidative stress and therefore increases ROS levels, promoting neurotoxicity. Due to these properties, 6-OHDA makes the ideal neurotoxin to create a Parkinson's model. Furthermore, recent research has shown that administering curcumin in a 6-OHDA-induced PD model reduced oxidative stress and lowered the α-synuclein levels (Grancharova et al., 2024). These findings further suggest curcumin's potential as a therapeutic agent for Parkinson's disease in a 6-OHDA-induced model.

To evaluate the effects of curcumin-coated gold nanoparticles on Parkinson's disease, we used the model organism *Caenorhabditis Elegans* (C. *elegans*). C. elegans is a worm model that is commonly used for studying neurodegenerative diseases due to its simplicity, short lifespan, small size, and similarity to the human genome (Hu et al., 2018). Hermaphrodite C. elegans has 302 neurons in total, eight of which are dopaminergic neurons that control locomotion and various behaviors. This study utilizes the C. elegans strain NL5901 expressing alpha-synuclein in the muscles and oxidative stress markers, as well as the yellow fluorescent protein (YFP). These worms are suitable for fluorescent imaging when looking at alpha-synuclein levels. Thus, the NL5901 Parkinson's strain is used as a positive control while the N2 Wildtype strain is used as a negative control. By comparing the treated groups of the Parkinson's strain to both a wild-type control and PD control, this study is focused on assessing curcumin-coated gold nanoparticle worm behavior and alpha-synuclein levels.