**Carbon Dots as a Therapeutic Strategy for Harnessing Quercetin's Anti-Alzheimer’s Potential**

**Shourya Tripathi1,2,** Manish Kumar Chourasia1,3.

Division of Pharmaceutics and Pharmacokinetics, CSIR-Central Drug Research Institute1, Lucknow, Uttar Pradesh, India;

Jawaharlal Nehru University2, New Delhi, India;

Academy of Scientific and Innovative Research3, Ghaziabad, India

**Background and aims.** Alzheimer’s disease (AD), the predominant cause of dementia, affects over 55.2 million individuals globally, with current treatment modalities only providing symptomatic relief without altering the disease progression. Quercetin, a bioactive flavonoid, has long been studied for its neuroprotective properties, through various mechanisms such as inhibiting amyloid beta aggregation and tau phosphorylation, reducing neuronal oxidative stress and neuroinflammation and regulating calcium homeostasis. However, its therapeutic potential is limited by poor bioavailability and inefficient blood brain barrier (BBB) penetration. Carbon dots, an emerging class of nanomaterials, present an ideal drug delivery platform due to their high aqueous solubility, biocompatibility and low toxicity.

**Methods.** Quercetin conjugated carbon dots (QCDs) were synthesized using a microwave-assisted method, followed by characterization for size, fluorescence properties, and cytotoxicity. Cellular uptake was investigated in neonatal rat brain astrocytes via flow cytometry and confocal microscopy. ROS scavenging activity was evaluated, and amyloid beta (Aβ) aggregation inhibition was assessed using circular dichroism spectroscopy, Thioflavin-T kinetics, and microscopy. The ability of QCDs to cross the BBB was examined using an *in vitro* BBB model, and pharmacokinetics and *in vivo* biodistribution was assessed in C57BL/6 mice. The therapeutic efficacy was further evaluated in an AD transgenic *Caenorhabditis elegans* model (CL4176 strain) *in vivo.*

**Results.** QCDs demonstrated uniform nanoscale size, stable fluorescence, and low cytotoxicity. Efficient cellular internalization in astrocytes was confirmed by both flow cytometry and confocal microscopy. QCDs exhibited significant ROS scavenging activity and markedly inhibited Aβ fibril formation. *In vitro* BBB model experiments revealed the capacity of QCDs to traverse endothelial barriers, while *in vivo* studies in mice confirmed successful brain delivery. QCD treatment in *Caenorhabditis elegans* models demonstrated a significant reduction in both oxidative stress, and amyloid burden, with markedly lower amyloid-β aggregation in the transgenic CL4176 strain, confirming its anti-amyloidogenic and neuroprotective potential.

**Conclusion/Discussion.** QCDs exhibit promising multifunctional properties, including antioxidative and anti-amyloidogenic effects, effective BBB penetration, and effective brain delivery. These findings highlight the potential of QCDs as a novel nanotherapeutic platform for modulating AD pathology.