Synthesis and Characterization of Carbomer-Agarose Hydrogel for Sustained Melatonin Release to Promote Traumatic Brain Injury Recovery

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Traumatic brain injury (TBI) remains a leading cause of death and disability. Although the primary injury occurs at impact, long-term neurological damage results from secondary injury mechanisms, including neuroinflammation, oxidative stress, and progressive neuronal death. Despite extensive research, no FDA-approved therapies currently exist to directly repair TBI. Melatonin is a promising neuroprotective candidate due to its ability to cross the blood–brain barrier, reduce inflammation and oxidative stress, inhibit apoptosis, and restore disrupted circadian rhythms after injury. However, its clinical utility is limited by rapid metabolism within four to five hours. This study therefore investigates (1) melatonin's neuroprotective effects following TBI and (2) evaluates a biocompatible carbomer–agarose hydrogel as a sustained-release delivery platform to overcome melatonin's limitations. Using a Drosophila melanogaster closed-head TBI model, locomotor recovery was assessed with the Rapid Iterative Negative Geotaxis (RING) assay. Notably, melatonin treatment at a 4 mM concentration, for five days after injury, significantly improved locomotor performance relative to untreated injured flies ($P < 0.0001$). To extend melatonin's therapeutic window, a carbomer–agarose hydrogel was developed. FTIR spectroscopy confirmed successful melatonin encapsulation. Release studies showed sustained diffusion over seven days, reaching 80–90% cumulative release. Swelling peaked at physiological pH, and degradation reached 64% by day seven, supporting controlled biodegradation. Ultimately, these findings highlight the combined promise of melatonin and hydrogel-based delivery for enhancing functional recovery after TBI.

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