ISBN: 978-81-992034-2-6

ABSTRACT NO:ICCPPR-SPS-119

Melatonin: A Novel Target for Neuroinflammation in Multiple Sclerosis

SHREE VIGA. J*

B. Pharmacy, VII SEM, School of Pharmaceutical Sciences, VISTAS, Chennai, Tamil Nadu, India-600117.

Corresponding author: Dr. J. Priyanga, Assistant Professor, Dept of Pharmacology, SPS.

ABSTRACT

Melatonin, a neuro-endocrine hormone, secreted by pineal gland best known for the regulating our circadian rhythm, can act as a potent anti-inflammatory and immunomodulatory properties that may countervail the pathogenesis of multiple sclerosis (MS). MS is an autoimmune disorder where our immune system accidentally activates immune cells against the myelin protein residue. This activation mistakenly attacks the protective myelin covering of nerve fibres. Experimental and clinical studies reveal that melatonin modulates immune balance and reduce the action of pathogenic effector T cells (TH17/TH1) toward regulatory subsets such as FoxP3^{+} Tregs and IL-10 producing Tr1 cells. Acting mainly through MT1/MTNR1A and MT2 receptors and nuclear factors including ROR-α, melatonin activates ERK1/2 and C/EBPα to repress REV-ERBα, relieving NFIL3 and thereby suppressing ROR-γt dependent TH17 differentiation and key cytokines IL-17 and GM-CSF. In parallel, MTNR1A–ERK1/2 and ROR-α pathways enhance Tr1 development and IL-10 production, while dendritic cell IL-27 is increased, helping to reduce immune cells infiltration into the central nervous system through down-regulation of chemokines CCL20/CCL19 and adhesion molecules ICAM-1. Melatonin's antioxidant activity further limits NF-κB driven inflammation. Preclinical experimental autoimmune encephalomyelitis models show reduced disease severity, lower TH17 responses, and higher IL-10 across varied dosing regimens. Limited clinical studies reveal decreased nocturnal melatonin during relapses and elevations following interferon-β or natalizumab therapy. A proposed "seasonal paradox," characterized by spring-summer relapse peaks despite high vitamin D, may reflect melatonin suppression by longer daylight. However, causality remains unproven, optimal dosing and long-term safety require clarification, and interactions with vitamin D or Epstein-Barr virus are not fully explored. Overall, melatonin represents a biologically plausible yet still investigational target for immunomodulatory strategies in MS.

Keywords: Melatonin, Multiple Sclerosis, Immunomodulation, Neuroinflammation, T helper cells, Regulatory T cells.