**Bioprospecting of Macula Carotenoids for Targeted Interaction with Underexplored Retinopathy Proteins from a Mouse Dataset: An *In-silico* Exploration for Diagnosis and Treatment Intervention**

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**Background and aims.** Retinopathy is a progressive retina disorder, affecting millions with and without diabetes, hypertension or by frequent radiation exposure. For safe pharmacological intervention, phytochemicals specifically macular carotenoids (MC); lutein, meso-zeaxanthin and zeaxanthin (LMZ) are vital in retinal health due to its high bioaccumulation (80-90%) in the macula (1), however, the mechanistic cause-effect benefit of LMZ are restricted to interleukin 6 (IL-6), heme oxygenase-1 (HO-1), superoxide dismutase (SOD), tumor necrosis factor alpha (TNF-α), and vascular endothelial growth factor (VEGF) for mice (2). The aim of this study was to bioprospect LMZ for underexplored retinopathy-related proteins.

**Methods.** Network pharmacology was performed to identify the therapeutic correlation of LMZ against underexplored proteins in angiogenic, apoptotic, inflammatory, oxidative stress, and retinal neurodegeneration mechanisms of early retinopathy in a mouse dataset. A protein-protein interaction (PPI) and enrichment analysis was performed to identify common pathways and then advanced to molecular docking for binding interaction and affinity.

**Results.** A total of six key underexplored proteins were identified by network pharmacology. Notably, cyclin-dependent kinase 1 (cdk1), integrin beta-1 (itgb1), phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (pik3ca), phosphoinositide-3-kinase regulatory subunit 1 alpha (pik3r1), platelet-derived growth factor receptor beta (pdgfrb), and protein kinase c zeta type (prkcz) were related to AGE-RAGE, mTOR, PIK3-Akt, and VEGF signalling pathways, based on enrichment analysis, and the functional association was supported by PPI. With docking, LMZ had affinity within -2.722 to -6.664 kcal/mol of known inhibitors, roniciclib (cdk1), risuteganib (itgb1), imatinib (pdgfrb), palomid529 (pik3ca), dactolisib (pik3r1), and stat (prkcz), demonstrating LMZ suitability to target these proteins.

**Conclusion/Discussion.** These results proposed LMZ could selectively stimulate the underexplored proteins for early retinopathy treatment compared to inhibitors. These findings provide insight useful for experimentation of LMZ benefit from mice to human trials in early retinopathy.

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**References**

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