Anti-Inflammatory Effects of Resveratrol and Nicotinamide are Mediated through the Activation of PARP-1

Yanez, M.[1], Jhanji, M.[4], Sajish, M.[5] and [*]Jabbarzadeh, E.[2,3]

[1] Postdoctoral Fellow, Department of Chemical Engineering, University of South Carolina, Columbia, SC 29208, USA ;[2]Associate Professor, Department of Chemical Engineering, and Biomedical Engineering Program, University of South Carolina, Columbia; [3]Associate Professor, Department of Orthopedic Surgery, University of South Carolina School of Medicine, Columbia SC, 29209, USA; [4]Graduate Research Assistant, Department of Drug Discovery and Biomedical Sciences, University of South Carolina, Columbia SC 29208 USA; [5]Assistant Professor, Department of Drug Discovery and Biomedical Sciences, University of South Carolina, Columbia SC 29208 USA.
ehsan@sc.edu

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Inflammation is the response of body to injuries and foreign materials and plays an important role in the effective management of diseases. The cascade of inflammatory response begins with the recruitment of neutrophils that produces inflammatory cytokines to stimulate the recruitment and differentiation of monocytes into macrophages. The phenotypes of macrophages, generally classified as pro-inflammatory (M1 macrophages) and wound healing (M2 macrophages), are the key targets in the anti-inflammatory drug discovery approaches. In the present work, we studied the combinatorial role of nicotinamide and resveratrol in the phenotypic regulation of inflammatory macrophages. Consistent with previous works, we also observed that both nicotinamide and resveratrol could suppress the expression of pro-inflammatory cytokines including TNFα and IL-6 and could up regulate the expression levels of the anti-inflammatory mediators (IL-10 and MRC1). Strikingly, the effects of nicotinamide were more profound than resveratrol while co-treatment with resveratrol further modulated the effects of nicotinamide. The results suggest that a combination of resveratrol with nicotinamide would trigger the conversion of nicotinamide into NAD^+ through the salvage pathway and would result in a favorable immune response for a longer period of time. Further investigations into the molecular mechanisms of action demonstrated that Poly [ADP-ribose] polymerase 1 (PARP-1)-mediated activation of Bcl-6 was primarily responsible for the observed anti-inflammatory effects. Our work further delineates the potential of pharmacologically active natural compounds to modulate inflammation with broad applicability in regenerative medicine and drug discovery.