

Effects of PPAR α -ligand-Clofibrate- on NO Production: Role of PKC and PKA

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Abstract

Nitric oxide (NO), an endogenous vasodilator, is a key regulator of basal vascular tone. Peroxisome proliferator activated receptor α (PPAR α) ligand, clofibrate, has been reported to increase production of NO. Protein kinases C (PKC), a family of protein kinase enzymes, is involved in controlling the function of proteins through phosphorylation of hydroxyl groups of serine and threonine amino acid residues. Protein kinases A (PKA) is a cAMP-dependent protein kinase. There are evidence in support of clofibrate effect on NO production/availability independent of NO synthesis. Production of NO has been linked to protein kinases PKA and C-mediated signaling mechanisms. Therefore, we postulated that clofibrate-mediated increase in NO production might be attributed to PKA/PKC signaling pathway. We examined clofibrate mediated increase in NO production/availability in renal proximal tubular cells isolated from PPAR α knockout (KO) mice and the role of PKA/PKC signaling pathways using PKA 14-22 and chelerythrine, PKA and PKC inhibitors, respectively. Effect of clofibrate on eNOS and iNOS gene/protein expression was examined. Our result indicated reduced NO production in PPAR α KO mice compared to the WT. Addition of clofibrate enhanced NO production in both groups, which was abolished by L-NAME. Both PKC and PKA inhibitors reduced clofibrate-mediated NO production in both groups. Clofibrate increased eNOS and iNOS mRNA and iNOS protein expression in the KO but not in WT. Clofibrate did not affect PKA/PKC protein expression in either group. Our data suggest that clofibrate effect on NO production is through induction of iNOS gene and it is PPAR α -independent mechanism.

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Biography:

Dr. Yousefipour received her PhD in Environmental Toxicology from Texas Southern University (TSU) in 2003. At the present time, she is a tenure full professor at TSU. Yousefipour has been studying the effect of environmental pollutants on cardiovascular system and has authored or co-authored more than 25 scientific papers in prominent journals. Yousefipour has been the recipient of Caroline Tum Sudan Professional Opportunity Award from American Physiological Society as well as several awards from TSU Research Week program. She is a member of several professional organizations including American Heart Association, American Physiological Society, and Society of Toxicology.