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News & Comments

# Effect of Nonylphenol (NP) on Human Preadipocytes

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Metabolic syndromes such as obesity, diabetes, and hypertension are on the rise, posing a public health issue. Consumption of contaminated food and drink, as well as inhalation of airborne particles, are the main routes of human exposure to ENDRs. ENDRs have been shown to increase the emergence of obesity in humans by causing excessive adipogenesis and disrupting energy balance and lipid metabolism. Adipogenesis involves a variety of signal transduction mechanisms. The MAPK/ERK signalling pathways must be activated for preadipocyte differentiation. ERK1 knockout (KO) mice had fewer adipocytes and lower adiposity than WT mice, and preadipocyte retrieved from ERK1 KO animals have less differentiation in vitro than WT preadipocyte under equal differentiation culture conditions. Activation of MEK/MAPKs in preadipocyte causes PPAR expression.

Accelerating lipolysis, on the other hand, necessitates increased lipase expression/activity to hydrolyse triglycerides into glycerol and free fatty acids. Phosphorylation of serine by cAMP-dependent Protein Kinase A (PKA) is required for lipase action. The mechanisms underlying the adipogenicity effect of NP on human preadipocyte were investigated in this work.

This research project was implemented at the Department of Chemical and Materials Engineering, Chinese Culture University, Taipei, Taiwan. All other reagents were acquired from Sigma Chemical Co., while NP was purchased from Fluka (Buchs, Switzerland) and dissolved in methanol as a 0.5 M stock solution (St. Louis, MO, USA). GeneTex Inc. (San Antonio, TX, USA) provided anti-fatty acid synthase (FASN), anti-glyceraldehyde-3-phosphate dehydrogenase (GAPDH), and anti-vinculin antibodies, while Cayman Chemical (Ann Arbor, MI, USA) provided anti-proliferator-activated receptor-a (PPAR-") and anti-proliferator-activated receptor- (PPAR-). Human preadipocyte were donated by Cell Application (San Diego, CA, USA).

PAM was used to keep human preadipocyte at 37 °C in a 5% CO2 environment. Human preadipocyte were seeded onto plates or pans at 48000 cm2 G1 in PAM medium for 2 days, then cultured in PADM for 6 days, with medium exchange every two days, to differentiate into adipocytes. The gels were transferred to Immobilon-P PVDF membranes using 6-12% acrylamide sodium dodecyl sulphate-polyacrylamide gels. The target protein bands were detected using enhanced chemiluminescence (ECL) detection reagents (Amersham Pharmacia Biotech) after membranes were blotted with the relevant antibodies.

Incubation of NP human preadipocyte cells with or without U0126 has been studied in two ways. For

the first series of experiments, the cells were cultured for 6 days in a PADM medium with NP (0 or 20 M) and U0126 (0 or 10 M). For the second set of experiments, the cells were cultured with NP (0 or 20 M) mixed with U0126 (10 M) in PADM medium for 0-1 day, then with NP (0 or 20 M) in PADM medium only for the next 2-6 days.

The c/EBP" mRNA expression in human preadipocyte exposed with U0126 for the full 6 days was constant, however, FASN mRNA expression was increased (p0.05), and PPAR" mRNA expression was decreased (p<0.01). Preadipocyte cells treated with U0126 for 0-1 day, on the other hand, had lower PPAR levels. Human preadipocyte cultures were treated. NP alone increased FASN mRNA expression (p<0.05, decreased PPAR" mRNA expression (p<0.05, and increased PPAR mRNA expression (p<0.05, H89, on the other hand, boosted the mRNA expression levels of FASN (p<0.01, and PPAR (p<0.05, demonstrating that inhibiting PKA activity can stimulate lipogenesis. H89, on the other hand, did not increase NP-stimulated FASN and PPAR mRNA expression, implying that NP may suppress PKA activity at rest, negating any effects of H89 on FASN or PPAR gene expression.

Nonylphenol works as an environmental contaminant by altering homeostatic control of cellular activities, including lipid metabolism, at least in part through interfering with endocrine signalling. Previously, it has been shown that NP exposure throughout the embryonic period increased 11b-HSD1 activity in the liver and adipose tissues, as well as corticosterone and aldosterone plasma concentrations in adult rats.

In conclusion, the findings suggest that NP increases lipogenesis transiently via ERK activation, as evidenced by U0126-mediated inhibition during the early stages of therapy. Surprisingly, sustained ERK inhibition alone enhances lipogenesis but not NP-stimulated lipogenesis, indicating that the NP-induced effect is transitory. Blocking PKA increases the NP-induced lipogenesis by lowering the PPAR" protein expression. All evidence suggests that NP can help with adipogenesis. These behaviours can be observed in both rat and human models.

JOURNAL REFERENCE

Chang, L.L., W.S.A. Wun and P.S. Wang, 2022. Mechanisms mediating the lipogenic effect of nonylphenol in human preadipocytes. Int. J. Pharmacol., 18: 144-152.

KEYWORDS

Nonylphenol(NP), human preadipocytes, metabolic syndromes, ENDRs, lipolysis, adipogenicity effect, ERK activation