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Inulin stimulates NO synthesis via activation of PKC-α and protein tyrosine kinase, resulting in the activation of NF-κB by IFN-γ-primed RAW 264.7 cells

Hyun-Na Koo[a,b,*], Seung-Heon Hong[b] and Hyung-Min Kim[a]

[a] *Department of Pharmacology, College of Oriental Medicine, Kyung Hee University, 1 Hoegi-Dong, Dongdaemun-Gu, 130-701, Seoul, South Korea*

[b] *Department of Oriental Pharmacy, College of Pharmacy, Wonkwang University, Iksan, Jeonbuk 570-749, South Korea*

Inulin, an active component of Chicorium intybus root, has been shown to stimulate the growth of bifidobacteria, and inhibit colon carcinogenesis. NO mediates a number of the host-defense functions of activated macrophages, including antimicrobial and tumoricidal activity. We examined the effect of inulin on the synthesis of NO in RAW 264.7 cells. Inulin alone had no effect, whereas inulin with IFN-γ synergistically increased the NO production and inducible NO synthase (iNOS) expression in RAW 264.7 cells. Synergy between IFN-γ and inulin was mainly dependent on inulin-induced TNF-α secretion. Also, protein kinase C (PKC)-α was involved in the inulin-induced NO production. Inulin-mediated NO production was inhibited by the protein tyrosine kinase (PTK) inhibitor, tyrphostin AG126. Since iNOS gene transcriptions have been shown to be under the control of the NF-κB/Rel family of transcription factors, we assessed the effect of inulin on NF-κB/Rel using an EMSA. Inulin produced strong induction of NF-κB/Rel binding, whereas AP-1 binding was slightly induced in RAW 264.7 cells. Inulin stimulated phosphorylation and degradation of IκB-α. These results suggest that in IFN-γ-primed RAW 264.7 cells inulin might stimulate NO synthesis via activation of PKC-α and PTK, resulting in the activation of NF-κB.

Keywords: Inulin; Nitric Oxide (NO); Nuclear factor-κB (NF-κB); Protein kinase C (PKC)-α; Protein tyrosine kinase (PTK); RAW 264.7 cells