Atrovirinone inhibits proinflammatory mediator synthesis through disruption of NF-kappaB nuclear translocation and MAPK phosphorylation in the murine monocytic macrophage RAW 264.7.

ABSTRACT

In a previous communication we showed that atrovirinone, a 1,4-benzoquinone isolated from the roots of Garcinia atroviridis, was able to inhibit several major proinflammatory mediators of inflammation. In this report we show that atrovirinone inhibits NO and PGE2 synthesis through inhibition of iNOS and COX-2 expression. We also show that atrovirinone inhibits the secretion of IL-1β and IL-6 in a dose dependent fashion whereas the secretion of IL-10, the anti-inflammatory cytokine, was enhanced. Subsequently we determined that the inhibition of proinflammatory cytokine synthesis and inducible enzyme expression was due to a dose-dependent inhibition of phosphorylation of p38 and ERK1/2. We also showed that atrovirinone prevented phosphorylation of I-κBα, which resulted in a reduction of p65NF-κB nuclear translocation as demonstrated by expression analysis. We conclude that atrovirinone is a potential anti-inflammatory drug lead that targets both the MAPK and NF-κB pathway.

Keyword: Atrovirinone; Garcinia atroviridis; INOS; COX-2; Cytokines; MAPK; NF-kB.