

Alendronate Enhances and Etidronate Inhibits *Porphyromonas gingivalis*-or
Toll-like Receptor 2 Ligand-induced IL-6 Production
by Mouse Macrophage-like J774.1 Cells

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Bisphosphonates are synthetic pyrophosphate analogues that inhibit bone resorption and thus are used to treat various diseases associated with increased bone resorption. Bisphosphonates can be divided into two different pharmacological classes based on whether or not they contain nitrogen. Nitrogen-containing bisphosphonates (NBPs), including alendronate, are more potent in inhibiting bone resorption, but have undesirable inflammatory side effects.

The present study examined the effects of alendronate and etidronate, a non-NBP, on IL-6 production by murine macrophage-like J774.1 cells incubated with *Porphyromonas gingivalis* or Pam₃ Cys-Ser-(Lys)₄ (Pam₃ CSK₄). While pretreatment of J774.1 cells with alendronate increased the production of IL-6, pretreatment with etidronate inhibited it. Furthermore, etidronate decreased alendronate-induced IL-6 production by J774.1 cells incubated with *P. gingivalis* or Pam₃ CSK₄. Enhanced IL-6 production by alendronate may promote the development of bisphosphonate-related osteonecrosis of the jaws (BRONJ), a side effect of alendronate treatment. In contrast, the findings that etidronate inhibited IL-6 production may explain why BRONJ is not observed in those who do not take NBPs.

Key words : nitrogen-containing bisphosphonates (NBPs), alendronate, etidronate, toll-like receptor (TLR) 2, interleukin-6 (IL-6)