Siegesbeckia pubescens (Compositae) is an annual herb indigenous to Korean mountainous regions. Recent reports have been issued on some compounds derived from S. pubescens for its anti-inflammatory activity or mode of action. The quercetin 3,7-O-dimethyl ether (QDE) isolated from the herbs of S. pubescens suppressed the lipopolysaccharide (LPS)-induced nitric oxide and inducible nitric oxide synthase (iNOS) protein production in mouse macrophages. QDE downregulated pro-inflammatory cytokines such as interleukin (IL)-6, IL-1?, tumor necrosis factor -? levels in LPS-stimulated macrophages. Also, QDE decreased the expression of LPS-induced iNOS and cyclooxygenase-2 (COX-2) protein and the production of IL-8 in LPS-induced HT-29 cells. Macrophages and colon epithelial cells are important for regulating the colon immune systems, thus QDE may regulate inflammatory colon disease via LPS-induced inflammation in macrophages and colon epithelial cells. QDE, anti-inflammatory constituent of S. pubescens herbs, can be expected to be a potential candidate for therapeutics against inflammatory bowel disease.