Inhibition of TNF-α Promoter Activity and Synthesis by A11-99-1, a New Cyclopentenone from the Ascomycete Mollisia melaleuca

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In a search for inhibitors of the inducible tumor necrosis factor-α (TNF-α) promoter activity and synthesis, a new chlorinated cyclopentenone was isolated from fermentations of the ascomycete Mollisia melaleuca. The structure was determined by a combination of spectroscopic techniques. The compound blocked the inducible human TNF-α promoter activity and synthesis with IC50-values of 2.5–5 µg/ml (8.1–16.1 µM). Studies on the mode of action of the compound revealed that the inhibition of TNF-α promoter activity is caused by an inhibition of the phosphorylation of the IκB protein which prevents the activation of the transcription factor NF-κB. No cytotoxic, antibacterial and antifungal activities could be observed up to 100 µg/ml (323 µM) of the compound.

Key words: Mollisia melaleuca, Cyclopentenone, TNF-α, NF-κB