Stimulation of TNF-α Release by Fungal Cell Wall Polysaccharides

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Z. Naturforsch. 60c, 921–926 (2005); received July 13/August 8, 2005

Carboxymethylated derivatives were prepared from the (1→3)-β-d-glucan isolated from the cell wall of baker’s yeast Saccharomyces cerevisiae and from the chitin-glucan complex of the mycelium of the industrial filamentous fungus Aspergillus niger. The polysaccharides were applied to peritoneal mouse macrophages and after a 2-h incubation the release of TNF-α by the stimulated macrophages was measured using an enzyme-linked immunosorbent assay. As the third polysaccharide stimulant, a water-soluble derivative of chitin was assayed and the observed cytokine release was compared with the control experiment. In three concentrations of the polysaccharides applied, carboxymethyl glucan revealed a dramatic increase in the TNF-α release, while addition of carboxymethyl chitin-glucan resulted only in a moderate enhancement, and carboxymethyl chitin was inactive. The results indicate that fungal polysaccharides, especially (1→3)-β-d-glucan, are potent macrophage stimulators and activators of TNF-α release, which implies their potential application in antitumor therapy.

Keywords: Tumor Necrosis Factor-α, Glucan, Chitin

Introduction

Fungal cell walls consist predominantly of polysaccharides (up to 90%), the most abundant of which is β-d-glucan (50–60% of all cell wall polysaccharides), which plays the role of a skeletal carcass defining rigidity and stability of the cell and its morphological shape (Bartnicki-Garcia, 1968; Farkaš, 1979). Glucans having a backbone built of (1→3)-β-glycosidically linked d-glucose units with variable (1→6)-β-d-glucosyl branching have been isolated from various fungal, bacterial and algal sources and in the recent decades increased attention has been paid to these compounds due to their ability to act as non-specific modulators of the immune system (Williams, 1997; Kogan, 2000). Glucans belong to the class of drugs known as biological response modifiers (Bohn and BeMiller, 1995) and numerous studies have shown that (1→3)-β-d-glucans enhance the functional status of macrophages and neutrophils (Williams et al., 1996), modify immunosuppression (Browder et al., 1990), increase resistance to infections by Gram-negative bacteria (Pretus et al., 1991), as well as exert antitumor activity (Sherwood et al., 1986, 1987).

In our previous work we have reported on antibacterial (Kogan et al., 1989), antimutagenic (Čiřáková et al., 2001), antioxidant (Babincová et al., 1999; Slameňová et al., 2003, Kogan et al., 2005), and antitumor activities (Kogan et al., 2002; Khabikova et al., 2005) of the prepared water-soluble derivatives of (1→3)-β-d-glucan isolated from the cell walls of baker’s yeast Saccharomyces cerevisiae. Now we have demonstrated that at least some of its immunomodulatory activities could be explained by an increased release of specific cytokines from the activated immunocompetent cells, e.g., macrophages. At the same time, we compared its activity with that of the carboxymethylated derivative of the chitin-glucan complex from the mycelium of Aspergillus niger, in which β-d-glucan constitutes about 80%, and with carboxymethyl chitin (CM-C), the second polysaccharide component of the chitin-glucan complex.