

Division of Biochemical
Pharmacology, Department of
Basic Medical Research,
Graduate School of Medicine,
Ehime University, Shitsukawa,
Toon City, Ehime 791-0295,
Japan

Yoshiyuki Kimura

Division of Functional Histology,
Department of Functional
Biomedicine, Graduate School of
Medicine, Ehime University,
Shitsukawa, Toon City, Ehime
791-0295, Japan

Maho Sumiyoshi, Masahiro
Sakanaka

Research and Development,
Daiso Co. Ltd. Amagasaki City,
Hyogo 660-0842, Japan

Takahiro Suzuki, Toshio Suzuki

Correspondence: Y. Kimura,
Division of Biochemical
Pharmacology, Department of
Basic Medical Research,
Graduate School of Medicine,
Ehime University, Shitsukawa,
Toon City, Ehime 791-0295,
Japan. E-mail: yokim@m.ehime-u.
ac.jp

Effects of water-soluble low-molecular-weight β -1, 3-D-glucan (branch β -1, 6) isolated from *Aureobasidium pullulans* 1A1 strain black yeast on restraint stress in mice

Yoshiyuki Kimura, Maho Sumiyoshi, Takahiro Suzuki, Toshio Suzuki and Masahiro Sakanaka

Abstract

It is well known that different stress paradigms are able to rapidly induce corticosterone production and immune function through the activation of the hypothalamic–pituitary–adrenal axis. It has been reported that glucocorticoids suppress natural killer (NK) activity and interleukin (IL)-1 production and, on the other hand, that IL-1 and IL-6 stimulate the release of corticotrophin-releasing-hormone from the rat hypothalamus. Moreover, it has been reported that IL-12 plays a central role in the initiation of cell-mediated immunity, directly and via its induction of interferon (IFN)- γ and activation of NK cells. In this study, we examined the effects of water-soluble low-molecular-weight β -glucan isolated from *Aureobasidium pullulans* 1A1 strain on the corticosterone levels and immune function, such as NK activity and IL-6 and IL-12 production, using a restraint stress-induced mouse model. The water-soluble low-molecular-weight β -glucan at a dose of 50 or 100 mg kg⁻¹ inhibited the increases in the blood corticosterone level and the reduction of NK activity induced by restraint stress. Furthermore, the water-soluble low-molecular-weight β -glucan (100 mg kg⁻¹) prevented the reduction of IL-6 and IL-12 production by splenocytes caused by restraint stress. These findings suggest that the inhibitory actions of water-soluble low-molecular-weight β -glucan on the increase in corticosterone level and reduction of NK activity induced by restraint stress may be associated with the abrogation of the IL-6 and IL-12 reduction caused by the stress. Thus, water-soluble low-molecular-weight β -glucan may be an effective dietary supplement for the prevention of stress.

Introduction

It has been established that stress can affect immune function through the activation of the hypothalamic–pituitary–adrenal axis resulting in the production of a number of neuroendocrine mediators (Riley 1981; Zwillig et al 1993). Some of these mediators, such as corticosterone in rodents or cortisol in man, have been shown to be immunosuppressive in both rodents and man (Dhabhar et al 1994). It is well known that glucocorticoids are major mediators of the stress response and modulate many signalling events in the immune response. Glucocorticoids modulate antigen presentation, cytokine production, T-cell expansion and natural killer cell activity (Belsito et al 1982; Synder & Unanue 1982; Chrousos & Gold 1992; Bonneau et al 1997; Maes et al 1998; Steer et al 1998; Wieggers & Reul 1998). Plasma corticosterone levels have been used for many years as an indicator of stress in mice. Thus, stress causes various disorders in relation to the bio-regulatory, autonomic nervous, endocrine and immune systems. In general, (1 \rightarrow 3) or (1 \rightarrow 6) β -glucans isolated from basidiomycetes mushrooms have high viscosity and high molecular weight (over 2000 kDa) and are water-insoluble. In addition, β -glucan easily forms gels containing high-order structures of single spirals or triplet spirals due to its unique primary structure; therefore, its purification is extremely difficult, and consequently crude β -glucan fractions have been used in many reported studies rather than purified β -glucan. We succeeded in the isolation and industrial-scale production of water-soluble low-molecular-weight β -(1,3–1,6) D-glucan from *Aureobasidium pullulans* GM-NH-1A1 strain (black yeast, a mutant of the strain K-1)