Agaricus blazei ,Grifola frondosa Extracts

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Contributor: Geir Hetland

Extracts of the mushrooms also appear to be safe in preclinical and clinical studies. Whereas special focus has been on their antitumor effects, the mushrooms' anti-allergic properties have also been investigated. The anti-allergic mechanism was amelioration of a skewed Th1/Th2 balance. Here, a brief review is given of the preclinical and clinical findings with AbM and GF.

Keywords: Antiallergic ; Agaricus blazei ; Grifola frondosa ; mushrooms ; clinical studies

1.Introduction

During the last 40 years medicinal effects of the related *Basidiomycetes* mushrooms, *Agaricus blazei* Murill (AbM) and *Grifola frondosa* (GF) from Brazilian and Eastern traditional medicine, respectively, have been documented scientifically.

2. Antiallergic Effects

An *Agaricus blazei* (AbM) extract has been shown[1] to inhibit induced anaphylactic reaction, including passive immunization, i.e., ear-swelling, in a mouse model by a treatment effect on the mast cell reaction (Table 1). In another mouse allergic asthma model with orally administered AbM extract, reduced levels were observed of specific immunoglobulin (Ig)E, IgG1 and bronchial eosinophils owing to amelioration of skewed T helper cell (Th)1/Th2 balance[2]. This was confirmed by us with the AbM-based and GF-containing extract, Andosan™, in the similar ovalbumin (OVA)-induced allergic sensitization mouse model, in which specific IgE and IgG1 were also reduced and Th1 response increased relative to Th2[3]. By use of this OVA sensitization mouse model for allergy, the mechanism behind the reduced specific IgE and improved Th1/Th2 balance was found to be AbM promotion of epithelial cell-induced macrophage (MΦ) activation and naïve T cells differentiation to Th1 cells[4]. Recently, we undertook a placebo-controlled randomized clinical study where blood donors with self-reported and specific IgE-confirmed birch allergy and asthma, were given Andosan™ orally for 2 months prior to the pollen season. They had less general allergy and asthma ailments and used less medication for the diseases[5]. This was caused by reduced specific IgE levels and reduced mast cell sensitization, as shown indirectly by the basophil activation test, a surrogate for mast cell activation (Table 2)[5].

Table 1. Anti-allergic Effects of *Agaricus blazei* Murill and *Grifola frondosa* (*Human study).

Product, Admin.	Study In, Of	Effects	Mechanism	Author, Year
AbM mycelia water extract incl. HE, GF, p.o. (Andosan)	Placebo-ctr RCT in blood donors, Pollen allergy & asthma (*n* = 60)	↓ General symptoms, and medication	↓ Spec. IgE, reduced basophil sensitivity	*Mahmood et al., 2019[5]

Water AbM extract, p.o.	Mice, Allergy	↓ OVA sensitization	↓ Spec. IgE, improv. Th1/Th2 balance via MF activ. by epithelial cc, diff. promotion of naïve T cc to Th1 cc	Bouike et al., 2011[4]
AbM mycelia water extract incl. HE, GF, p.o. (Andosan)	Mice, Allergy	↓ OVA sensitization	↓ Spec. IgE, IgG1 and improved Th1/Th2 balance	Ellertsen & Hetland 2009[3]
AbM water extract, p.o.	Mice, Asthma	↓ Spec. IgE, IgG1 and bronchial eosinophils	Amelioration of skewed Th1/Th2 balance	Takimoto et al., 2008[2]
AbM water extract, p.o.	Mice, Anaphylaxis	Inhib. of induced anaphylactic reaction and ear swelling	Treatment of mast cell mediated anaphylactic reaction	Choi et al., 2006[1]
GF alcohol extract and ergosterol, p.o.	Mice, Allergic inflammation	Inhib. mast cc degranulation, alleviated anaphylactic cutaneous response	↓ Type 1 allergic reaction by suppression of mast cc degranulation	Kawai et al., 2019[6]
GF polysacch, p.o.	Mice, AD	Inhib. AD-like skin lesion	↓ IgE, mast cc infiltr., cytokine express. controlling Th1/Th2	Park et al., 2015[7]

Abbreviations: immunoglobulin (Ig), ovalbumin (OVA), atopic dermatitis (AD)，Grifola frondosa （GF）.Form Hetland et al., 2020[8] .

Table 2. Basophil maximal (peak) reactivity during intervention in birch pollen allergic blood donors before and after the pollen season

	Placebo		Andosan	
Bet v 1 conc. (ng/ml)	Peak before	Peak after	Peak before	Peak after
100	1 (5.2 %)			1 (4.1)
10	7 (36.8)		4 (16.6)	1 (4.1)
1	11 (57.8)	17 (89.4)	20 (83.3)	19 (79.1)
0.1		2 (10.5)		3 (12.5)
Mean	9.52 ±5.12	0.90* ±0.06	2.50 ±0.69	5.38^ ±4.12
Total	19 (100%)	19 (100)	24 (100)	24 (100)

*p=0.004 vs. before pollen season, ^p=0.062 vs. before pollen season. Abbreviation: Bet v 1 is the major birch pollen allergen. Modified from Mahmood et al, 2019[5].

Moreover, in mice with orally administered GF polysaccharide or extract (Table 1), antiallergic effects have also been observed: Atopic dermatitis-like skin lesions and mast cell degranulation were inhibited due to alleviated anaphylactic cutaneous response[6][7]. This was found to be caused by reduced IgE and mast cell infiltration, a cytokine expression that ameliorated the Th1/Th2 imbalance[7], and a reduced type I allergic response by suppression of mast cell degranulation[6]. Hence, GF polysaccharides could be used as a novel therapeutic drug instead of corticosteroids or as supplementary treatment[7].