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An insight into the anti-inflammatory properties of edible and medicinal mushrooms

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ABSTRACT

Background: Mushrooms have been valuable as edible and medical provisions for humankind. It is attributed not only to the quality of their taste but also to their biological activities. The extracts, compounds, and metabolites have a lot of biological activities such as antidiabetic, antioxidative, antitumor, and anti-inflammatory effects. The potent anti-inflammatory activity is associated with a multitude of signaling pathways. However, there are a few review papers on the anti-inflammatory activity of mushrooms.

Scope and approach: Herein, the anti-inflammatory potential of mushroom is critically discussed using *in vitro* and animal models. Moreover, the mechanisms of anti-inflammatory activity are summarized. The current status of clinical studies evaluating anti-inflammatory activity of mushroom is also presented.

Key findings and conclusion: It is believed that insights about these advances may encourage researchers to discover new phytochemical components and further study specific bioactivities of mushroom.

1. Introduction

Mushrooms have been used as food and medicine in different countries for centuries. They are rich in many bioactive compounds such as proteins, dietary fiber, lectins, polysaccharides, phenolic and polyphenolics, terpenoids, ergosterols, and volatile organic compounds (El Enshasy & Hattikaul, 2013; Kalač, 2013). They also contain micro- and macro-nutrients including minerals, protein, vitamins, amino acids, etc. Moreover, mushrooms are an important source of biologically active compounds with potential medicinal values such as beta-glucans (Du, Lin, Bian, & Xu, 2015). Furthermore, some of the known chemopreventive agents present in mushrooms include terpenoids, phenolic compounds, peptides and steroids. Mushrooms are also high in antioxidants, which are important because antioxidants protect human cells against diseases like cancer and heart disease by fighting free radicals. Mushrooms are considered as valuable health foods since they have a significant amount of dietary fiber and are poor in calories and fat (Mattila, Suonpää, & Piironen, 2009). Inflammation is the body's natural immune response against heart disease, chronic pain, age-related diseases, memory loss, and autoimmune diseases. Inflammation is a critical component of tumor progression. Many cancers arise from sites of infection, chronic irritation, and inflammation. Therapy that directly targets apoptosis and inflammation could be highly effective for the treatment of cancer (Iman et al., 2017). Many types of inflammation have long-term effects, but we can minimize inflammation within the body with proper diet. Consumption of functional foods, such as mushroom (Taofiq, Martins, Barreiro, & Ferreira, 2016), berries (Joseph, Edirisinghe, & Burtonfreeman, 2014), vegetables, legumes (Zhu, Du, & Xu, 2018), and fish (Wall, Ross, Fitzgerald, & Stanton, 2010) with anti-inflammatory properties, is one of the possible strategies to suppress inflammation. Although the immuno-stimulant activity of mushrooms has been largely demonstrated, their potential anti-inflammatory activity has been scarcely reviewed. In this work, the available *in vitro*, animal, and clinical studies were reviewed to clarify the potential of mushroom in inflammation prevention and treatment.

2. Inflammation

Inflammation is the natural protective response of the innate immune system to tissue injury or damaging external stimuli such as

Abbreviations: CD, Crohn's disease; ConA, concanavalin A; COX-1, cyclooxygenase-1; COX-2, cyclooxygenase-2; DAI, disease activity index; DSS, dextran sulfate sodium; G-CSF, granulocyte colony-stimulating factor; GM-CSF, granulocyte-macrophage colony stimulating factor; IFN-γ, interferon-γ; IL-6, interleukin-6; Inos, inducible nitric oxide synthase; LOX, lipoxygenase; LPS, lipopolysacharide; MAPKs, mitogen-activated protein kinases; MCP, monocyte chemotactic protein; MMPs, matrix metalloproteinases; NO, nitric oxide; NF-κB, nuclear factor kappa-B; PGE 2, prostaglandin E 2; ROS, reactive oxygen species; STAT, signal transducers and activators of transcription; TNF-α, tumor necrosis factor-α; UC, ulcerative colitis

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pathogens, allergens, infections, irritants, and ultraviolet light irradiation (Joseph, Edirisinghe, & Burton-Freeman, 2016; Phull & Kim, 2017). Chronic inflammation increases the risk of various cancers. Thus, it is important to investigate the relationship between inflammation and cancer. Inflammation is closely linked to cancer, and many anti-cancer agents are also used to treat inflammatory diseases (Rayburn, Ezell, & Zhang, 2009). Inflammation is a complex process mediated by cytokines, chemokines, adhesion molecules, and cytoplasmic nuclear receptors (Talero, Ávila-Roman, & Motilva, 2012). Cytokines are immune-modulatory molecules that control the inflammatory response (Joseph et al., 2014). A high production of nitric oxide (NO) and some pro-inflammatory cytokines, such as tumor necrosis factor-α (TNF-α), interferon-γ (IFN-γ), interleukin-6 (IL-6), and interleukin-1β, have been closely related with a deficient activation of macrophages and the pathogenesis of several inflammatory diseases (Alvarez-Suarez et al., 2017).

3. *In vitro* studies

For *in vitro* models, lipopolysaccharide (LPS)-induced macrophages, concanavalin A (ConA)-stimulated mouse splenocytes, and IFN-γ activated murine macrophages (Gunawardena et al., 2014) have been investigated in recent years.

The anti-inflammatory activities of mushroom on macrophages are mediated through the inhibition of some signaling pathways, such as nuclear factor kappa-B (NF-κB) (Chang, Lur, Lu, & Cheng, 2013), pro-inflammatory cytokines, prostaglandins release, reactive oxygen species (ROS) production (Talero et al., 2012), signal transducers and activators of transcription 1 (STAT1), and STAT6. Many mechanisms have been identified for the anti-inflammation activity of mushroom, including inhibition of secretion of inflammatory cytokine, prevention of oxidation, regulation of the host immune system, and changes in cellular signaling. A common denominator in the pathogenesis of most chronic inflammatory diseases is the involvement of oxidative stress, related to ROS production by all aerobic organisms (Gasparrini et al., 2017). The mechanisms of action in *in vitro* studies follow a more complicated process.

3.1. Anti-inflammatory properties of mushrooms

Several *in vitro* studies have been carried out to evaluate the chemopreventive and anti-inflammatory potential of various mushrooms (Fig. 1). For cyclooxygenase-1 and cyclooxygenase-2 enzymes (COX-1 and COX-2) model, the ethyl acetate extracts from mushroom indicated a higher inhibitory activity against both enzymes than 70% ethanolic extracts. The ethyl acetate extracts of *Ganoderma applanata*, *Naematoloma sublateritium*, *Pleurotus eryngii*, and *P. salmoneostramineus* also showed higher COX-2 inhibitory effects compared to COX-1 inhibition (Elgorashi, Maekawa, & Satoh, 2008). Kobori, Yoshida, Ohnishi-Kameyama, and Shinmoto (2007) found that ergosterol peroxide and ergosterol from edible or medicinal mushrooms suppress LPS-induced inflammatory responses through the inhibition of NF-κB and CCAAT/enhancer-binding protein beta transcriptional activity and phosphorylation of mitogen-activated protein kinases (MAPKs) (shown in Fig. 2).

In another study, Dudhgaonkar, Thyagarajan, and Sliva (2009) investigated that triterpene extract from *Ganoderma lucidum* that markedly suppressed the secretion of inflammatory cytokine TNF-α and IL-6 and inflammatory mediator NO and prostaglandin E 2 (PGE 2) from LPS-stimulated murine RAW264.7 cells. In addition, triterpene extract from *G. lucidum* also down-regulated LPS-dependent expression of inducible nitric oxide synthase (iNOS) and COX-2 in RAW264.7 cells.

Jo et al. (2010) determined the *in vitro* anti-inflammatory potential of hot water extract from *Cordyceps militaris* fruiting bodies on LPS-stimulated NO production, TNF-α and IL-6 release in RAW 264.7 cells. The treatment of macrophages with various concentrations of hot extract significantly reduced LPS-induced production as well as NO, TNF-

Fig. 1. The mushroom varieties with anti-inflammatory activity. (Fresh white mushrooms: *Agaricus bisporus*; oyster mushroom: *Pleurotus ostreatus*; crimini: Portabella; enoki: *Flammulina velutiper* (Fr.) Sing; maitake: *Grifola frondosa*; beech: *Hypsizygus tessellatus*; shiitake: *Lentinus edodes*).

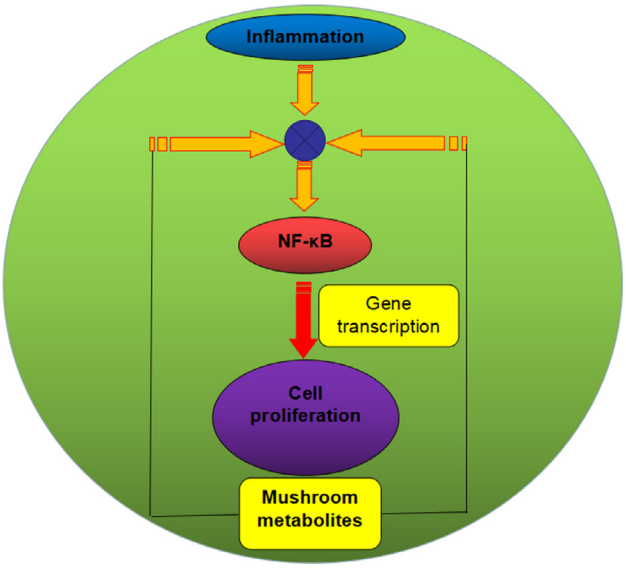

Fig. 2. Mmushrooms exert anti-inflammation effect via NF-κB pathway.