

PDF issue: 2025-05-08

Novel anti-inflammatory property of polysaccharides from Lentinula edodes on colitis through necroptosis inhibition

ALAGBAOSO CHIDUBE ANTHONY

<mark>(Degree)</mark> 博士(学術)

(Date of Degree) 2021-03-25

(Date of Publication) 2023-03-25

(Resource Type) doctoral thesis

(Report Number) 甲第8081号

(URL) https://hdl.handle.net/20.500.14094/D1008081

※ 当コンテンツは神戸大学の学術成果です。無断複製・不正使用等を禁じます。著作権法で認められている範囲内で、適切にご利用ください。



別紙様式3(博士論文審査等内規第2条関係)

博士論文内容の要旨

氏 名_____ALAGBAOSO CHIDUBE ANTHONY

専攻・講座 APPLIED CHEMIST<u>RY IN BIOSCIENCE, AGROBIOSCIENCE</u>

論文題目(外国語の場合は,その和訳を併記すること。)

Novel anti-inflammatory property of polysaccharides from Lentinula edodes on

colitis through necroptosis inhibition

シイタケ由来多糖類によるネクロトーシスを介した新規腸炎抑制効果

指導教員 MASASHI MIZUNO

Chapter 2: Inhibitory Effect of Polysaccharides from *Lentinula edodes* (shiitake) against Ulcerative Colitis

Inflammatory bowel disease (IBD) is a chronic inflammation of the gastrointestinal tract, with an increasing global incidence and prevalence. It is subdivided into Crohn's disease and ulcerative colitis, and it affects people of all age groups, and negatively impacts on every aspect of lives of the victims. There is currently no cure for the disease, and the pathogenesis is not completely understood. Edible mushrooms have long served as a source of food and medicinal compounds in many parts of the world. Many of the beneficial health effects derived from mushrooms are triggered by their polysaccharide contents. In this chapter polysaccharide extracted from *Lentinula edodes* was orally administered to ulcerative colitis mice to investigate whether the polysaccharide sample inhibited ulcerative colitis. It was observed that the anti-inflammatory activity was demonstrated to be dependent on the carbohydrate-rich fraction.

Chapter 3: Differential Activity of Polysaccharides from Strains of *Lentinula edodes* against Ulcerative Colitis

The physiological properties of polysaccharides are dependent on the primary structure, solubility, degree of branching, molecular weight, charge of polymer, and structure in aqueous media. In this chapter, the anti-inflammatory activity of crude polysaccharides extracted from two strains of *Lentinula edodes* were investigated. It was observed that they differentially affected ulcerative colitis in mice. Also, column chromatographic separation of the crude polysaccharide indicated different peaks on the elution profiles. This suggested that the anti-inflammatory activities of the crude polysaccharide extracts may be strain-dependent.

Chapter 4: Anti-necroptosis Activity of Polysaccharides from Lentinula edodes

Necroptosis is a caspase-independent form of pro-inflammatory programmed cell death. It plays active role in the etiology, pathogenesis, and progression of ulcerative colitis. Inhibition of necroptosis also inhibited ulcerative colitis, which is an indication that necroptosis resulted in colitis. In this chapter, it was demonstrated that the polysaccharide sample from *Lentinula edodes* inhibited necroptosis in both *in vitro* and

in vivo models, suggesting that its anti-necroptosis activity may partly be responsible for its activity against ulcerative colitis.

Chapter 5: Effect of *Lentinula edodes* Polysaccharides on the Expression of Inflammatory Cytokines in Ulcerative Colitis

Necroptosis signaling stimulates the expression of inflammatory cytokines which together with DAMPs (damage associated molecular patterns) are released into the extracellular environment upon cell membrane rupture, and which results in the promotion and worsening of inflammatory conditions. In this chapter, it was observed that the expression of inflammatory cytokines (TNF- α , IL-6, IL-1 β , IFN- γ , and CCL-2) was up-regulated in the colon of ulcerative colitis mice and in Caco-2 cells (IL-8) undergoing necroptosis, which may have resulted from the activation of necroptotic signaling pathways in the colon and Caco-2 cells. However, the polysaccharide extracts down-regulated the expression of inflammatory cytokines may have directly resulted from the inhibition of necroptosis by the polysaccharide sample. It was also demonstrated that the anti-necroptosis activity of the polysaccharide sample and its inhibitory effects on the expression of inflammatory cytokines were independent of the expression of TNFR1 on the cell surface, thereby suggesting a direct effect on necroptosis mediators.