WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
Coden USA: WJPRAP Impact Factor 8.63
Volume 15, Issue 22, 354-371. Review Article ISSN 2277–7105

NETWORK PHARMACOLOGY AND ANTI-INFLAMMATORY POTENTIAL OF *AGARICUS BISPORUS* (BUTTON MUSHROOM): AN INTEGRATIVE REVIEW

Diptendu Sarkar*

Assistant Professor & Head, Department of Microbiology, Ramakrishna Mission Vidyamandira (An autonomous UG and PG College, Affiliated to University of Calcutta), Belur Math, Howrah, Pin-711202, West Bengal, India.

Article Received on 15 Oct. 2026,
Article Revised on 05 Nov. 2026,
Article Published on 16 Nov. 2026,

https://doi.org/10.5281/zenodo.24272686

***Corresponding Author**

Diptendu Sarkar

Assistant Professor & Head, Department of Microbiology, Ramakrishna Mission Vidyamandira (An autonomous UG and PG College, Affiliated to University of Calcutta), Belur Math, Howrah, Pin-711202, West Bengal, India.

How to cite this Article: Diptendu Sarkar* (2026). Network Pharmacology And Anti-Inflammatory Potential Of Agaricus Bisporus (Button Mushroom): An Integrative Review. World Journal of Pharmaceutical Research, 15(22), 354–371
This work is licensed under Creative Commons Attribution 4.0 International license.

ABSTRACT

One of the most popular edible mushrooms worldwide is *Agaricus bisporus* (button mushroom). It has many nutritional value. It contains several bioactive compounds such as polysaccharides, β-glucans, phenolic compounds, flavonoids and ergothioneine, which may exhibit antioxidant, immune regulating, antimicrobial along with antiinflammatory potentiality. Several diseases such as diabetes, cancer, cardiovascular disorders and neurodegenerative diseases are commonly associated with chronic inflammation. Important cellular pathways such as NF-κB, MAPK, PI3K/Akt, JAK/STAT and Nrf2 are associated with antiinflammatory effects of *A. bisporus*. It may control inflammation, oxidative stress and immune responses. Network biology and network pharmacology help us to understand how mushroom compounds interact with human proteins and influence different biological pathways. This review discusses the active compounds in *A. bisporus* and how they may help reduce inflammation. The review also describes how different computational tools can be used to identify the molecular targets and pathways responsible for the potential anti-inflammatory effects of *A. bisporus.* However, these findings need further confirmation through laboratory and animal experiments.

KEYWORDS: Agaricus bisporus; button mushroom; anti-inflammatory activity; network pharmacology; network biology; phytochemicals; NF-κB; MAPK; molecular docking; systems biology.

INTRODUCTION

Inflammation is the body's natural protective response to infections, injuries and harmful substances. It helps protect the body and repair damaged tissues. However, long lasting inflammation can damage healthy cells and contribute to several chronic diseases. Different immune cells, proteins and signalling molecules may control the inflammatory process. TNF-α, IL-1β, IL-6, COX-2, iNOS and PGE2 are the major inflammatory mediators.[1] There are two major signalling pathways named as NF-κB and MAPK which play important roles in controlling inflammation by regulating the production of the mediators.[2] Inflammation may be increased and cellular damage may have occurred due to the excessive production of reactive oxygen species (ROS).[3] Many natural products from plants, mushrooms, marine organisms and microorganisms are found to have potential anti inflammatory effects. Because of high nutritional value and bioactive compounds present in an edible mushrooms *Agaricus bisporus* (button mushroom), it become more attractive in pharmaceutical research. It belongs to the family Agaricaceae. Many proteins, dietary fibres, polysaccharides, vitamins, minerals, phenolic compounds and other antioxidant substances are found in *Agaricus bisporus.*[4] Important bioactive constituents include β-glucans, ergothioneine and phenolic acids, which may help regulate oxidative stress and immune responses. Although the nutritional and antioxidant properties of *A. bisporus* are well known, but its exact role in controlling inflammation and the molecular pathways involved are still not fully understood.[5] Network biology helps us understand how the active compounds interact with different proteins and regulate inflammation related pathways.[6] This review focuses on the antiinflammatory potential of *Agaricus bisporus* and uses network based approaches to explore how its bioactive compounds may control inflammation.

NUTRITIONAL PROPERTIES AND PHYTOCHEMICAL COMPOSITION OF *AGARICUS BISPORUS*

Agaricus bisporus contains several natural bioactive compounds that may contribute to its antioxidant, immune-regulating and anti-inflammatory properties. These compounds include polysaccharides, β-glucans, phenolic acids, ergothioneine, lectins, proteins, sterols, fatty acids and other small molecules.[7] Among these, polysaccharides are particularly important

because they form a major part of the mushroom cell wall and may influence different biological activities. β-glucans are important mushroom polysaccharides made up of glucose units connected through specific chemical bonds. Their biological activities depend on their molecular size, chemical structure, branching pattern and solubility. β-glucans may interact with different receptors present on immune cells, such as Dectin-1, complement receptor 3 (CR3) and certain Toll-like receptors (TLRs).[8] These interactions may influence macrophage activity and regulate the production of inflammatory molecules called cytokines. Macrophages are important immune cells that help the body fight infections and remove damaged cells. β-glucans may activate these cells and modify their immune responses.[9] However, their effects are not always anti-inflammatory, as some β-glucans can also stimulate immune activity depending on their structure and the surrounding cellular conditions.[10] Another important group of compounds present in *A. bisporus* is phenolic compounds, which are widely known for their antioxidant properties. Important phenolic acids reported in mushrooms include gallic acid, caffeic acid, p-coumaric acid, ferulic acid, protocatechuic acid and chlorogenic acid.[11] These compounds may help protect cells from oxidative damage by reducing harmful free radicals and supporting the body's natural antioxidant defence system. Excessive production of reactive oxygen species (ROS) can damage cellular components, including proteins, lipids and DNA, and may also activate inflammatory pathway[12]s. Some phenolic compounds have shown the ability to influence important inflammatory signalling pathways, particularly NF-κB and MAPK, in experimental studies. These pathways control the production of inflammatory cytokines and other mediators. Therefore, phenolic compounds may help reduce oxidative stress and regulate inflammatory responses.[13] However, the amount and activity of individual phenolic compounds in *A. bisporus* may vary depending on the mushroom variety, growing conditions, maturity and extraction methods. Ergothioneine is another important bioactive compound found in *A. bisporus*. It is a naturally occurring sulphur-containing amino acid derivative that has attracted considerable attention because of its antioxidant and cell-protective properties.[14] Unlike many other antioxidant compounds, ergothioneine enters cells through a specific transporter known as organic cation transporter novel type 1 (OCTN1), which is produced by the SLC22A4 gene.[15] Once inside the cells, ergothioneine may help protect proteins, lipids and other cellular components from oxidative damage. It may also support mitochondrial function and help maintain normal cellular activities under stressful conditions. Since excessive ROS production can activate inflammatory responses, the antioxidant activity of ergothioneine may indirectly help regulate inflammation.[16] In

addition to polysaccharides and phenolic compounds, *A. bisporus* also contains different proteins and lectins that may have important biological functions. Lectins are special types of proteins that can recognize and bind to specific sugar molecules present on cell surfaces. Through these interactions, some mushroom lectins may influence cell communication, immune responses and cell growth.[17] However, the biological activities of individual lectins and proteins depend on their structure and concentration, and their specific effects need further investigation. The mushroom also contains several other nutritional and bioactive substances, including amino acids, fatty acids, nucleotides, vitamins and sterols. Among the sterols, ergosterol is particularly important because it is a major fungal sterol and can be converted into vitamin D2 (ergocalciferol) when exposed to suitable ultraviolet light.[19] Fatty acids and amino acids also contribute to the nutritional value and normal biological functions of the mushroom. Collectively, these compounds make A. bisporus an important source of natural bioactive substances with possible antioxidant, immune-regulating and anti-inflammatory activities.[20] Studying these compounds individually and in combination may help explain their effects on inflammatory mediators, oxidative stress and important cellular signalling pathways.[21] Network biology and network pharmacology can further help identify the possible interactions between these mushroom-derived compounds and human proteins, providing a better understanding of their potential role in controlling inflammation.[22] However, these possible biological effects require further confirmation through biochemical, cellular and animal experiments.

Table 1: Major Bioactive Compounds of *Agaricus bisporus* and Their Possible Biological Activities.

Bioactive compounds	Examples / Major types	Possible biological activities
Polysaccharides	Structural polysaccharides	Support immune regulation and may influence inflammatory responses.[5,7]
β-glucans	β-(1→3) and β-(1→6) glucans	Interact with immune-cell receptors such as Dectin-1 and CR3; regulate macrophage activity and cytokine production.[10,14]
Phenolic acids	Gallic acid, caffeic acid	Antioxidant activity; may help regulate oxidative stress and inflammation.[15,21]
Phenolic acids	Ferulic acid, p-coumaric acid	Free-radical scavenging and potential cellular protection.[7,16]
Phenolic acids	Chlorogenic acid, protocatechuic acid	May influence oxidative and inflammation-related signalling pathways.[18,20]
Ergothioneine	Sulphur-containing amino acid derivative	Protects cells against oxidative damage and may support mitochondrial function.[17,22]
Lectins	Carbohydrate-binding	May influence cell communication,

	proteins	immune responses and cell growth.[10,19]
Other proteins	Mushroom proteins and enzymes	Contribute to nutritional value and may have different biological functions.[10,21]
Sterols	Ergosterol	Acts as a fungal membrane component and can be converted into vitamin D2 following UV exposure.[19,21]
Fatty acids	Linoleic acid, oleic acid and other fatty acids	Contribute to nutritional value and cellular functions.[20]
Amino acids	Essential and non-essential amino acids	Support protein synthesis, tissue repair and normal metabolism.[19,22]
Vitamins	Riboflavin (B2), niacin (B3), pantothenic acid (B5), vitamin D2	Support energy metabolism, cellular functions and normal physiological activities.[17,19,22]
Minerals	Potassium, phosphorus, selenium and copper	Support normal cellular functions, mineral balance and antioxidant enzyme activity.[21,22]

MOLECULAR MECHANISMS OF ANTIINFLAMMATORY ACTIVITY OF *AGARICUS BISPORUS*

The antiinflammatory activity of *A. bisporus* may involve several molecular pathways rather than a single target. Its different bioactive compounds may interact with immune cell receptors and influence inflammatory enzymes, signalling proteins and transcription factors. These interactions may help regulate the production of inflammatory cytokines and reduce oxidative stress. However, the overall biological effects depend on the type of bioactive compounds present, their concentration and the method used to prepare the mushroom extract.[23] The antiinflammatory effects of *Agaricus bisporus* may involve several important molecular pathways that control immune responses, inflammation and oxidative stress. One of the major pathways is the nuclear factor-kappa B (NF-κB) pathway, which regulates the production of inflammatory substances such as TNF-α, IL-1β, IL-6, COX-2 and iNOS.[24] During infection or tissue injury, bacterial components such as lipopolysaccharide (LPS) can activate Toll-like receptor 4 (TLR4), which further activates the IκB kinase (IKK) complex.[25] This leads to the breakdown of inhibitory proteins called IκB and allows NF-κB proteins, particularly p65 and p50, to enter the nucleus and increase the production of inflammatory molecules.[26] An experimental study reported that pretreatment of human and mouse macrophages with button mushroom powder reduced NF-κB activation and inflammatory cytokine production following LPS and β-glucan stimulation.[27] The study also showed reduced inflammation in a mouse model of colitis, suggesting that *A. bisporus* may help regulate excessive inflammatory responses. Another important pathway is the mitogen activated protein kinase (MAPK) pathway, which includes three major proteins like ERK1/2,

JNK and p38 MAPK.[28,29] These proteins control cell growth, survival, stress responses and the production of inflammatory substances. Their activation can stimulate another protein called AP-1, which increases the expression of inflammatory genes.[30] However, mushroom compounds do not always suppress inflammation. Many researchers reported that a polysaccharide called TJ3, isolated from *A. bisporus*, activated ERK/MAPK and NF-κB signalling in macrophages and increased the production of iNOS, COX-2, IL-1β, IL-6 and TNF-α.[31,32] This indicates that some mushroom polysaccharides may stimulate immune responses rather than reduce inflammation. The phosphoinositide 3-kinase/protein kinase B (PI3K/Akt) pathway is another important signalling system involved in cell survival, metabolism, immune responses and inflammation. It mainly works through proteins such as PI3K and Akt, which regulate several cellular activities and interact with other inflammatory pathways, including NF-κB.[33,34] Mushroom derived bioactive compounds may influence this pathway through their effects on cellular stress and immune regulation. Important proteins such as AKT1, PIK3CA, PIK3R1, MTOR and PTEN can therefore be considered potential targets for further investigation, although their direct regulation by *A. bisporus* compounds has not yet been clearly established.[35] Oxidative stress is also closely associated with inflammation because excessive production of reactive oxygen species (ROS) can damage proteins, fats and DNA and increase inflammatory responses. The nuclear factor erythroid 2-related factor 2 (Nrf2) pathway protects cells against this damage by controlling the production of antioxidant proteins.[36] Under normal conditions, Nrf2 is controlled by a protein called KEAP1. During oxidative stress, Nrf2 becomes active, enters the nucleus and increases the expression of protective genes such as HMOX1, NQO1, GCLC, GCLM, SOD1 and GPX1.[37,38] Ergothioneine and phenolic compounds present in *A. bisporus* may help protect cells against oxidative damage and influence this antioxidant pathway. An experimental study using *A. bisporus* extracts in intestinal Caco-2 cells reported increased Nrf2 expression and reduced levels of IL-6 and COX-2, suggesting a possible connection between antioxidant activity and inflammation control.[39] Toll-like receptors (TLRs) are another important group of proteins involved in the body's first line of immune defence. Among them, TLR4 plays a major role in recognising bacterial LPS and activating inflammatory responses. After activation, TLR4 interacts with signalling proteins such as MYD88, TIRAP, TRIF and TRAM, which further activate IRAK1, TRAF6, TAK1, IKK and NF-κB.[40,41] This process leads to the production of inflammatory cytokines. Experimental findings with button mushroom powder suggest that some mushroom components may influence these immune receptors and reduce excessive inflammatory responses. The Janus

kinase/signal transducer and activator of transcription (JAK/STAT) pathway also plays an important role in inflammation.[42] When IL-6 binds to its receptor, it activates JAK proteins, which then activate STAT proteins. Activated STAT proteins enter the nucleus and control the expression of genes involved in inflammation and immune responses. Proteins such as JAK1, JAK2, STAT1, STAT3, IL6 and IL6R are therefore important potential targets for studying the effects of *A. bisporus,* although their direct interaction with mushroom compounds requires further confirmation.[43,44] In addition to these signalling pathways, two important inflammatory enzymes, cyclooxygenase-2 (COX-2) and inducible nitric oxide synthase (iNOS), are also involved in inflammation. COX-2 produces prostaglandins, which contribute to pain, fever and swelling, while iNOS produces nitric oxide (NO).[45] Excessive production of NO can increase cellular damage and oxidative stress. Some mushroom extracts have shown the ability to reduce NO production in experimental studies, and comparative research on edible mushrooms has reported antiinflammatory activity in NO-production assays.[46] Cinnamic acid was identified as one of the compounds contributing to the activity of the tested extracts. Finally, inflammatory cytokines are important signalling molecules that control communication between immune cells. Major proinflammatory cytokines include TNF-α, IL-1β, IL-6, IL-17A and IFN-γ. Excessive production of these molecules can increase inflammation and contribute to tissue damage. The potential anti-inflammatory activity of *A. bisporus* can therefore be investigated by studying its effects on cytokine production, inflammatory enzymes and the above signalling pathways in macrophages and other relevant cells.[33,47] Overall, these findings suggest that *A. bisporus* may influence inflammation through several interconnected molecular pathways. However, its effects may vary depending on the type of bioactive compound, its concentration and the experimental conditions. Therefore, further studies are required to identify the specific compounds, molecular targets and signalling mechanisms responsible for its anti-inflammatory activity.

Table 2: Important interpretation of the pathway.

Signalling pathway	Important molecular targets	Possible biological effect
NF-κB	IKK, IκB, RELA, NFKB1	Regulation of inflammatory cytokines[22,27]
MAPK	ERK1/2, JNK, p38, AP-1	Regulation of inflammatory and stress responses[11, 28]
PI3K/Akt	PIK3CA, PIK3R1, AKT1, MTOR, PTEN	Cellular survival and immune regulation[29,31]

Nrf2/ARE	NFE2L2, KEAP1, HMOX1, NQO1	Antioxidant defence[40,42]
TLR signalling	TLR4, MYD88, IRAK1, TRAF6	Recognition of microbial molecules and immune activation[43,44]
JAK/STAT	JAK1, JAK2, STAT1, STAT3	Cytokine-mediated inflammatory regulation[44,46]
Inflammatory enzymes	PTGS2 (COX-2), NOS2 (iNOS)	Regulation of prostaglandin and nitric oxide production[45,47]

INTEGRATED NETWORK BIOLOGY MODEL OF *AGARICUS BISPORUS* MEDIATED ANTI INFLAMMATORY ACTIVITY

Network biology is a research approach that helps scientists understand how different biological molecules, proteins, and signalling pathways work together inside cells. Unlike traditional drug research, which mainly focuses on the interaction between one compound and one target, network biology studies how several bioactive compounds can interact with multiple proteins and influence different biological processes. This approach is particularly useful for studying *Agaricus bisporus* (button mushroom), which contains several beneficial substances, including polysaccharides, β-glucans, phenolic compounds, ergothioneine, sterols, and other metabolites.[48] Network pharmacology combines chemical, genetic, protein, and biological information to identify these compounds, predict their possible molecular targets, and understand the pathways involved in their biological activities. For this purpose, databases and computational tools such as PubChem, LOTUS, FooDB, NPASS, SwissTargetPrediction, SEA, UniProt, GeneCards, DisGeNET, Open Targets, STRING, Cytoscape, CytoHubba, DAVID, ShinyGO, AutoDock Vina, RCSB Protein Data Bank, GROMACS, SwissADME, and ProTox can be used. These tools help identify mushroom compounds, predict their protein targets, construct protein interaction networks, identify important proteins, analyse biological pathways, study molecular binding, and predict drug-like properties and toxicity.[49] However, small-molecule target prediction tools should not be directly applied to large polysaccharides such as β-glucans; specialised carbohydrate–protein interaction studies and experimental methods are more suitable for these compounds. To investigate the antiinflammatory properties of *A. bisporus*, inflammation-related genes can be collected from databases using terms such as inflammation, chronic inflammation, inflammatory response, macrophage activation, colitis, and oxidative stress. The predicted targets of mushroom compounds can then be compared with these inflammation related genes to identify common molecular targets. Important candidate proteins include TNF, IL6, IL1B, PTGS2 (COX-2), NOS2 (iNOS), TLR4, MYD88, RELA, NFKB1, AKT1, MAPK1,

MAPK14, STAT3, NFE2L2 (Nrf2), KEAP1, HMOX1, CASP1, and NLRP3.[50] These are proposed research targets and should not be considered confirmed targets of *A. bisporus* without experimental evidence. Protein–protein interaction analysis using STRING and Cytoscape can help understand how these proteins are connected and identify important proteins in the network. Parameters such as degree centrality, betweenness centrality, closeness centrality, MCODE, and MCC can be used to identify highly connected proteins and important functional groups. Proteins such as TNF, IL6, RELA, AKT1, MAPK1, TP53, and STAT3 may be investigated as possible hub proteins, although their actual importance must be determined from the obtained network data.[44,48] A compound–target–pathway network can also be developed to show how different mushroom constituents, such as β-glucans, ergothioneine, phenolic acids, and ergosterol, may be associated with inflammatory proteins and signalling pathways, including NF-κB, MAPK, PI3K/Akt, Nrf2, and JAK/STAT. These interactions may help explain possible effects on inflammatory cytokines, oxidative stress, macrophage activity, and intestinal health. Molecular docking can further be used to study the possible binding of small mushroom-derived compounds, such as ergothioneine, ergosterol, caffeic acid, ferulic acid, p-coumaric acid, gallic acid, chlorogenic acid, and chrysin, with selected inflammatory proteins such as COX-2, iNOS, TLR4, AKT1, MAPK1, p38α, JAK2, STAT3, KEAP1, and NLRP3.[47,49] However, the presence of these compounds in the particular mushroom sample should first be confirmed through HPLC or LC-MS/MS analysis. For docking studies, protein structures can be obtained from the RCSB Protein Data Bank, prepared by removing unwanted water molecules and adding hydrogen atoms and suitable charges, and then analysed using AutoDock Vina.[46,48] The binding energy and different interactions, such as hydrogen bonds, hydrophobic interactions, π–π interactions, π–alkyl interactions, and electrostatic interactions, can be examined using Discovery Studio Visualizer or PyMOL. More negative docking scores may indicate better predicted binding under the same computational conditions, but they cannot prove that a compound activates or inhibits a protein.[43,47] Molecular dynamics simulation using GROMACS for 50–100 ns can provide additional information about the stability of protein–compound complexes by analysing RMSD, RMSF, radius of gyration, hydrogen bonds, solvent-accessible surface area (SASA), and binding free energy through MM-PBSA or MM-GBSA analysis. In addition, Gene Ontology (GO) and KEGG pathway enrichment analyses using DAVID or ShinyGO can help identify the biological processes, molecular functions, cellular locations, and signalling pathways associated with the selected genes.[48,49] Important biological processes may include regulation of inflammation, cytokine production,

macrophage activation, oxidative stress responses, apoptosis, and cellular responses to bacterial components such as lipopolysaccharide. Relevant molecular functions may include cytokine binding, protein kinase activity, transcription factor binding, antioxidant activity, and enzyme binding, while important cellular locations may include the cytoplasm, nucleus, plasma membrane, mitochondria, and extracellular region. The major signalling pathways for investigation include NF-κB, TNF, Toll-like receptor, MAPK, PI3K/Akt, JAK/STAT, NOD-like receptor, HIF-1, apoptosis, and glutathione metabolism. Finally, the findings from phytochemical identification, target prediction, protein interaction analysis, molecular docking, molecular dynamics, and pathway enrichment can be combined to develop an integrated network biology model of the possible anti-inflammatory activity of *A. bisporus*.[50] This model may involve four major mechanisms: modulation of innate immune signalling through TLR4, NF-κB, and MAPK pathways; reduction of oxidative stress through ergothioneine, phenolic compounds, and Nrf2-associated antioxidant mechanisms; regulation of inflammatory mediators such as TNF-α, IL-1β, IL-6, COX-2, and iNOS; and improvement of intestinal immune responses and epithelial barrier function. These mechanisms may work together because oxidative stress can increase inflammatory signalling, while inflammatory responses can also increase the production of reactive oxygen species.[47,49,50] Therefore, network biology and network pharmacology provide useful computational approaches to understand the possible molecular mechanisms of the antiinflammatory properties of *Agaricus bisporus*. However, all predicted interactions and mechanisms require further laboratory and experimental validation.

Table 3: Proposed network pharmacology workflow.

Step 1	Phytochemical identification
Step 2	Chemical structure retrieval
Step 3	Target prediction
Step 4	Inflammatory target identification
Step 5	Identification of common targets
Step 6	Protein–protein interaction analysis
Step 7	Network visualization and hub identification
Step 8	Functional enrichment analysis
Step 9	Molecular docking
Step 10	Molecular dynamics simulation
Step 11	Experimental validation

Table 4: Proposed candidate targets of *A. bisporus* associated with inflammatory signalling.

Gene/protein	Biological role	Associated pathway
TNF	Inflammatory cytokine	TNF signalling
IL6	Inflammatory cytokine	JAK/STAT
IL1B	Pro-inflammatory cytokine	NF-κB
PTGS2	COX-2 enzyme	Prostaglandin synthesis
NOS2	iNOS enzyme	Nitric oxide production
TLR4	Innate immune receptor	TLR signalling
MYD88	Adaptor protein	TLR signalling
RELA	NF-κB p65	NF-κB signalling
NFKB1	NF-κB p50	NF-κB signalling
AKT1	Protein kinase	PI3K/Akt
MAPK1	ERK2	MAPK signalling
MAPK14	p38 MAPK	Inflammatory signalling
STAT3	Transcription factor	JAK/STAT
NFE2L2	Nrf2 transcription factor	Antioxidant response
KEAP1	Nrf2 regulatory protein	Oxidative stress regulation
HMOX1	Heme oxygenase-1	Antioxidant defence
CASP1	Inflammatory caspase	Inflammasome signalling
NLRP3	Inflammasome component	NLRP3 inflammasome

Table 5: Selection of protein targets from *A. bisporus.*

Protein	UniProt accession	Research significance
COX-2	P35354	Prostaglandin production [42]
iNOS	P35228	Nitric oxide production [47]
TLR4	O00206	Innate immune recognition [33,44]
AKT1	P31749	Cellular signalling [45]
MAPK1	P28482	ERK signalling [49]
p38α	Q16539	Inflammatory signalling [34,44]
JAK2	O60674	Cytokine signalling [38,47]
STAT3	P40763	Inflammatory gene regulation [41,49]
KEAP1	Q14145	Nrf2 regulation [48,50]
NLRP3	Q96P20	Inflammasome signalling [44,49]

Table 6: KEGG pathway analysis to identify important signalling pathways associated with with inflammatory processes of *A. bisporus*.

KEGG pathway	Major molecular components	Relevance
NF-κB signalling	RELA, NFKB1, IKBKB	Inflammatory gene regulation [44]
TNF signalling	TNF, MAPK8, RELA	Cytokine-mediated inflammation [42]
Toll-like receptor signalling	TLR4, MYD88, TRAF6	Innate immune activation [47]
MAPK signalling	MAPK1, MAPK14, MAPK8	Cellular stress and inflammation [48]
PI3K/Akt signalling	AKT1, PIK3CA, MTOR	Cellular survival and metabolism [49]

JAK/STAT signalling	JAK1, JAK2, STAT3	Cytokine responses[48,50]
NOD-like receptor signalling	NLRP3, CASP1, IL1B	Inflammasome activation[49,50]
HIF-1 signalling	HIF1A, AKT1	Cellular stress responses[49,50]
Apoptosis	CASP3, BCL2, BAX	Cell survival and death [42,47]
Glutathione metabolism	GCLC, GCLM, GPX1	Antioxidant defence [38,47]

LIMITATIONS AND RESEARCH CHALLENGES

Although *Agaricus bisporus* shows promising antiinflammatory and antioxidant properties, some important limitations must be considered before using it for therapeutic purposes. The amount of bioactive compounds present in this mushroom may vary depending on the mushroom strain, stage of development, cultivation conditions, growing medium, harvesting time, storage, and processing methods. Therefore, proper chemical analysis and standardization are necessary to obtain consistent results. Another important concern is that different mushroom compounds may produce different effects on the immune system. Some compounds may reduce excessive inflammation, while others may activate macrophages and increase the production of inflammatory cytokines. For example, the TJ3 glucogalactomannan obtained from *A. bisporus* has been reported to activate NF-κB and MAPK signalling pathways, showing that individual mushroom compounds may have different biological effects. Therefore, the activity of one compound should not be considered representative of the entire mushroom. Computational methods also have certain limitations because target-prediction databases depend on previously available chemical and biological information and may not accurately predict all interactions of mushroom derived compounds. These methods are also not directly suitable for predicting the protein targets of large polysaccharides. In addition, some mushroom compounds may be changed during digestion, intestinal microbial activity, or liver metabolism, so their effects inside the human body may differ from those observed in laboratory experiments. Although several experimental studies have reported promising antioxidant, immune regulating, and antiinflammatory activities, more well-designed human studies are required to confirm their safety and therapeutic effectiveness. Different extraction methods may also produce mushroom preparations with different chemical compositions and biological activities. Therefore, standardized extracts based on their chemical composition and biological effects are essential for reliable research and future applications.

FUTURE PERSPECTIVES

Network pharmacology and network biology provide useful approaches for understanding the possible anti-inflammatory properties of *Agaricus bisporus*. Future research should combine LC-MS/MS-based metabolomics with network pharmacology to identify the actual chemical compounds present in mushroom extracts and investigate their possible molecular targets and signalling pathways. Further studies should also examine the relationship between mushroom-derived polysaccharides, intestinal microorganisms, short chain fatty acids, and inflammation to understand their possible effects on gut health. The influence of different mushroom compounds on macrophage activation and M1 and M2 macrophage polarization should be investigated to understand their immunomodulatory properties. Another important research area is the regulation of the NLRP3 inflammasome pathway, particularly its effects on CASP1 activation and IL-1β production. Molecular docking and molecular dynamics studies can be used to investigate the possible binding interactions and stability of selected small mushroom-derived compounds with suitable inflammatory proteins. Different mushroom extracts, including aqueous, ethanolic, polysaccharide-rich, and phenolic-rich fractions, should also be studied separately to identify the compounds responsible for specific biological activities. Furthermore, important proteins identified through network analysis using Cytoscape should be experimentally examined through techniques such as qPCR, Western blotting, and ELISA to confirm their involvement in inflammatory pathways. Finally, properly standardized and scientifically evaluated mushroom preparations may have potential for development as functional food ingredients. However, their safety, chemical composition, and biological effectiveness must be established through appropriate laboratory, animal, and human studies before considering their use in health related applications.

CONCLUSION

Agaricus bisporus, commonly known as the white button mushroom, is a good source of nutrients and bioactive compounds that may help regulate immune responses and reduce inflammation. It contains several beneficial substances, including β-glucans, ergothioneine, phenolic acids, sterols, proteins, and other natural compounds that may influence different biological activities. Experimental studies suggest that mushroom extracts may help control inflammation by regulating macrophage activity, NF-κB and MAPK signalling pathways, and antioxidant defence mechanisms. Some studies have also reported changes in inflammatory markers and Nrf2 expression in intestinal cells. However, certain isolated mushroom polysaccharides may stimulate immune responses and activate inflammatory signalling

pathways, indicating that the biological effects of this mushroom depend on its chemical composition and preparation methods. Network biology and network pharmacology provide useful approaches to understanding these complex activities by combining phytochemical analysis, molecular target prediction, protein–protein interaction networks, hub protein identification, GO and KEGG pathway analysis, molecular docking, and molecular dynamics simulations. These computational approaches can help identify important mushroom compounds, their possible protein targets, and the signalling pathways involved in inflammation. Combining computational studies with laboratory and animal experiments will be essential to confirm these findings and understand the actual molecular mechanisms. Overall, *A. bisporus* is a promising mushroom for investigating natural anti-inflammatory compounds, but further experimental and clinical studies are required to establish its safety, effectiveness, and potential use in the prevention or management of inflammatory diseases.

REFERENCES

1. Muszyńska, B., Kała, K., Rojowski, J., Grzywacz, A., Opoka, W., Composition and biological properties of Agaricus bisporus fruiting bodies – a review. Pol. J. Food Nutr. Sci, 2017; 67: 173–181. https://doi.org/10.1515/pjfns-2016-0032.
2. Blumfield, M., Abbott, K., Duve, E., Cassettari, T., Marshall, S., Fayet-Moore, F., Examining the health effects and bioactive components in Agaricus bisporus mushrooms: a scoping review. J. Nutr. Biochem, 2020; 84: 108453. https://doi.org/10.1016/j.jnutbio.2020.108453.
3. Ramos, M., Burgos, N., Barnard, A., Evans, G., Preece, J., Graz, M., et al., Agaricus bisporus and its by-products as a source of valuable extracts and bioactive compounds. Food Chem, 2019; 292: 176–187. https://doi.org/10.1016/j.foodchem.2019.04.035.
4. Feng, Y., Zhang, J., Wen, C., Dzah, C.S., Juliet, I.C., Duan, Y., et al., Recent advances in Agaricus bisporus polysaccharides: extraction, purification, physicochemical characterization and bioactivities. Process Biochem, 2020; 94: 39–50. https://doi.org/10.1016/j.procbio.2020.04.010.
5. Muszyńska, B., Grzywacz, A., Kała, K., Gdula-Argasińska, J., Anti-inflammatory potential of in vitro cultures of the white button mushroom, Agaricus bisporus (Agaricomycetes), in Caco-2 cells. Int. J. Med. Mushrooms, 2018; 20: 129–139. https://doi.org/10.1615/IntJMedMushrooms.2018025408.
6. Jeong, S.C., Koyyalamudi, S.R., Jeong, Y.T., Song, C.H., Pang, G., Macrophage immunomodulating and antitumor activities of polysaccharides isolated from Agaricus

bisporus white button mushrooms. J. Med. Food, 2012; 15: 58–65. https://doi.org/10.1089/jmf.2011.1704.

7. Zhao, X., Hou, P., Xin, H., Zhang, Y., Zhou, A., Lai, C., et al., A glucogalactomanan polysaccharide isolated from Agaricus bisporus causes an inflammatory response via the ERK/MAPK and IκB/NF-κB pathways in macrophages. Int. J. Biol. Macromol, 2020; 151: 1067–1073. https://doi.org/10.1016/j.ijbiomac.2019.10.148.
8. Yin, X., You, Q., Zhou, X., Complex enzyme-assisted extraction, purification, and antioxidant activity of polysaccharides from the button mushroom, Agaricus bisporus. Int. J. Med. Mushrooms, 2015; 17: 987–996. https://doi.org/10.1615/IntJMedMushrooms.v17.i10.80.
9. Dubost, N.J., Ou, B., Beelman, R.B., Quantification of polyphenols and ergothioneine in cultivated mushrooms and correlation to total antioxidant capacity. Food Chem, 2007; 105: 727–735. https://doi.org/10.1016/j.foodchem.2007.01.030.
10. Ghahremani-Majd, H., Dashti, F., Chemical composition and antioxidant properties of cultivated button mushrooms (Agaricus bisporus). Hortic. Environ. Biotechnol, 2015; 56: 376–382. https://doi.org/10.1007/s13580-015-0124-z.
11. Hammann, S., Vetter, W., Method development for the determination of free and esterified sterols in button mushrooms (Agaricus bisporus). J. Agric. Food Chem, 2016; 64: 3437–3444. https://doi.org/10.1021/acs.jafc.6b00383.
12. Muszyńska, B., Grzywacz-Kisielewska, A., Kała, K., Gdula-Argasińska, J., Anti-inflammatory properties of edible mushrooms: a review. Food Chem, 2018; 243: 373–381. https://doi.org/10.1016/j.foodchem.2017.09.149.
13. Moro, C., Palacios, I., Lozano, M., D'Arrigo, M., Guillamón, E., Villares, A., et al., Anti-inflammatory activity of methanolic extracts from edible mushrooms in LPS activated RAW 264.7 macrophages. Food Chem, 2012; 130: 350–355. https://doi.org/10.1016/j.foodchem.2011.07.049.
14. Gunawardena, D., Bennett, L., Shanmugam, K., King, K., Williams, R., Zabaras, D., et al., Anti-inflammatory effects of five commercially available mushroom species determined in lipopolysaccharide and interferon-γ activated murine macrophages. Food Chem, 2014; 148: 92–96. https://doi.org/10.1016/j.foodchem.2013.10.015.
15. Dempsey, E., et al., Protective properties of the white button mushroom, Agaricus bisporus, in a mouse model of colitis. Mol. Nutr. Food Res, 2025.

16. Negative regulation of innate immune signaling by components of the button mushroom Agaricus bisporus. Mol. Nutr. Food Res, 2023; 67: 2200845. https://doi.org/10.1002/mnfr.202200845.
17. Zhang, M., Zhao, L., Tang, F., Gao, J.M., Qi, J., Chemical structures, biological activities, and biosynthetic analysis of secondary metabolites from Agaricus mushrooms: a review. J. Agric. Food Chem, 2024; 72: 12387–12397. https://doi.org/10.1021/acs.jafc.4c01861.
18. Yang, Q., Fan, S., Wang, M., Ye, L., Yang, Z., Tan, W., et al., Extraction techniques, structural characteristics, and biological functions of Agaricus bisporus polysaccharides: a review. Int. J. Biol. Macromol, 2025; 313: 144229. https://doi.org/10.1016/j.ijbiomac.2025.144229.
19. Du, B., Lin, C., Bian, Z., Xu, B., An insight into anti-inflammatory effects of fungal beta-glucans. Trends Food Sci. Technol, 2015; 41: 49–59. https://doi.org/10.1016/j.tifs.2014.09.002.
20. Goodridge, H.S., Wolf, A.J., Underhill, D.M., Beta-glucan recognition by the innate immune system. Immunol. Rev, 2009; 230: 38–50. https://doi.org/10.1111/j.1600-065X.2009.00793.x.
21. Brown, G.D., Gordon, S., Fungal beta-glucans and mammalian immunity. Immunity, 2003; 19: 311–315.
22. Brown, G.D., Dectin-1: a signalling non-TLR pattern-recognition receptor. Nat. Rev. Immunol, 2006; 6: 33–43.
23. Brown, G.D., Herre, J., Williams, D.L., Willment, J.A., Marshall, A.S.J., Gordon, S., Dectin-1 mediates the biological effects of beta-glucans. J. Exp. Med, 2003; 197: 1119–1124.
24. Brown, G.D., Gordon, S., Immune recognition of fungal beta-glucans. Cell. Microbiol, 2005; 7: 471–479.
25. Goodridge, H.S., Underhill, D.M., Fungal recognition by dectin-1. Handb. Exp. Pharmacol, 2012; 204: 87–109.
26. Vetvicka, V., Thornton, B.P., Ross, G.D., Soluble beta-glucan polysaccharide binding to the lectin site of neutrophil or natural killer cell complement receptor type 3 stimulates iC3b-mediated cellular cytotoxicity. J. Clin. Invest, 1996; 98: 50–61.
27. Chan, G.C.F., Chan, W.K., Sze, D.M.Y., The effects of beta-glucan on human immune and cancer cells. J. Hematol. Oncolm, 2009; 2: 25.

28. Volman, J.J., Ramakers, J.D., Plat, J., Dietary modulation of immune function by beta-glucans. Physiol. Behav, 2008; 94: 276–284.
29. Chen, J., Seviour, R., Medicinal importance of fungal beta-(1→3), (1→6)-glucans. Mycol. Res, 2007; 111: 635–652.
30. Wasser, S.P., Medicinal mushrooms as a source of antitumor and immunomodulating polysaccharides. Appl. Microbiol. Biotechnol, 2002; 60: 258–274.
31. Wasser, S.P., Current findings, future trends, and unsolved problems in studies of medicinal mushrooms. Appl. Microbiol. Biotechnol, 2011; 89: 1323–1332.
32. Lull, C., Wichers, H.J., Savelkoul, H.F.J., Antiinflammatory and immunomodulating properties of fungal metabolites. Mediators Inflamm, 2005; 2005: 63–80.
33. Rop, O., Mlcek, J., Jurikova, T., Edible mushrooms as functional foods and their antioxidant properties. Int. J. Mol. Sci, 2009; 10: 531–537.
34. Guillamón, E., García-Lafuente, A., Lozano, M., Rostagno, M.A., Villares, A., Martínez, J.A., Edible mushrooms: role in the prevention of cardiovascular diseases. Fitoterapia, 2010; 81: 715–723.
35. Finimundy, T.C., Dillon, A.J.P., Henriques, J.A.P., Ely, M.R., A review on general nutritional compounds and pharmacological properties of the *Lentinula edodes* mushroom. Food Nutr. Sci, 2013; 4: 2–12.
36. Lawrence, T., The nuclear factor NF-κB pathway in inflammation. Cold Spring Harb. Perspect. Biol, 2009; 1: a001651.
37. Karin, M., Nuclear factor-κB in cancer development and progression. Nature, 2006; 441: 431–436.
38. Hayden, M.S., Ghosh, S., NF-κB, the first quarter-century: remarkable progress and outstanding questions. Genes Dev, 2012; 26: 203–234.
39. O'Neill, L.A.J., Golenbock, D., Bowie, A.G., The history of Toll-like receptors—redefining innate immunity. Nat. Rev. Immunol, 2013; 13: 453–460.
40. Medzhitov, R., Origin and physiological roles of inflammation. Nature, 2008; 454: 428–435.
41. Nathan, C., Points of control in inflammation. Nature, 2002; 420: 846–852.
42. Reuter, S., Gupta, S.C., Chaturvedi, M.M., Aggarwal, B.B., Oxidative stress, inflammation, and cancer: how are they linked? Free Radic. Biol. Med, 2010; 49: 1603–1616.

43. Ferrero-Miliani, L., Nielsen, O.H., Andersen, P.S., Girardin, S.E., Chronic inflammation: importance of NOD2 and NALP3 in interleukin-1β generation. Clin. Exp. Immunol, 2007; 147: 227–235.
44. Libby, P., Inflammatory mechanisms: the molecular basis of inflammation and disease. Nutr. Rev, 2007**;** 65: S140–S146.
45. Hopkins, A.L., Network pharmacology: the next paradigm in drug discovery. Nat. Chem. Biol, 2008; 4: 682–690. https://doi.org/10.1038/nchembio.118.
46. Gfeller, D., Grosdidier, A., Wirth, M., Daina, A., Michielin, O., Zoete, V., SwissTargetPrediction: a web server for target prediction of bioactive small molecules. Nucleic Acids Res, 2014; 42: W32–W38. https://doi.org/10.1093/nar/gku293.
47. Shannon, P., Markiel, A., Ozier, O., Baliga, N.S., Wang, J.T., Ramage, D., et al., Cytoscape: a software environment for integrated models of biomolecular interaction networks. Genome Res, 2003; 13: 2498–2504. https://doi.org/10.1101/gr.1239303.
48. Szklarczyk, D., Gable, A.L., Nastou, K.C., Lyon, D., Kirsch, R., Pyysalo, S., et al., The STRING database in 2021: customizable protein-protein networks, and functional characterization of user-uploaded gene/measurement sets. Nucleic Acids Res, 2021; 49: D605–D612. https://doi.org/10.1093/nar/gkaa1074.
49. Huang, D.W., Sherman, B.T., Lempicki, R.A., Systematic and integrative analysis of large gene lists using DAVID bioinformatics resources. Nat. Protoc, 2009**;** 4: 44–57. https://doi.org/10.1038/nprot.2008.211.
50. Zhou, Y., Zhou, B., Pache, L., Chang, M., Khodabakhshi, A.H., Tanaseichuk, O., et al., Metascape provides a biologist-oriented resource for the analysis of systems-level datasets. Nat. Commun, 2019; 10: 1523. https://doi.org/10.1038/s41467-019-09234-6.