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Turkey tail for pets: A CLOSER LOOK



Lack of transparency on labels for animal health products can result in a pet owner unknowingly buying a "mushroom" supplement that contains no actual mushrooms.



The use of functional mushrooms with health benefits in animals has increased exponentially over the past 10 years. Products marketed as dietary supplements for animals, however, are not regulated by the FDA in the same way as are those marketed for humans. The can be sold without manufacturer proof of quality control and without guaranteed transparency regarding label language.

This could lead to undesired outcomes, such as a pet owner purchasing a product incorrectly labeled as "mushrooms for pet use" that doesn't actually contain mushroom. This could delay essential medical treatment for a pet with a terminal disease, because the pet owner may think that the supplement will work for their pet's illness.

Many mushrooms possess benefits from their active compounds. In particular, the β -glucans (a type of polysaccharide) support immunity; they are considered to have antibiotic, antiviral, and antineoplastic properties. Unfortunately, not all products labeled as "mushrooms" contain mushroom.

This article examines the growing interest in mushroom use for animals, familiarizes veterinarians with the terminology and methods of mushroom production, and discusses a recent double-blind study that analyzed 10 commercially available pet supplements labeled as containing "turkey tail" for their digestible starch and β-glucan content.

The goal here is to help inform veterinarians about potential misrepresentation of mushroom products and provide guidance on what to look for if they decide to offer mushrooms to their patients.

THE GROWING INTEREST IN **MUSHROOM USE FOR ANIMALS**

One factor contributing to the growing interest in mushrooms by veterinarians and the pet-owning public was the publication in 2012 of a double-blind, randomized pilot study using the polysaccharopeptide (PSP) pharmaceutical extract of Trametes versicolor (turkey tail). Investigators measured median survival times for dogs with splenic hemangiosarcoma "whose owners opted not to pursue chemotherapy following splenectomy." Findings showed that "high-dose PSP significantly delayed the progression of metastases and afforded the longest survival times reported in canine hemangiosarcoma." As a result of this small study, pet owners and veterinarians started to use turkey tail for their pets with cancer.

The second factor contributing to the increased interest in mushrooms was the COVID-19 pandemic. As fears of this potentially fatal infection increased, people searched for any means to boost their immune systems and for supplements with antiviral properties. Functional mushrooms can provide both antiviral activity and immunomodulation. Studies have been published concerning the use of immune-modulating mushroom species as both preventives and treatments for COVID-19 infection.²



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As a result of these 2 factors, the number of companies selling mushroom-labeled supplements for pets has increased substantially. A Google search on October 25, 2022, for pet mushroom products using the search parameter "mushroom products for pets" delivered 23,600,000 results. When that search was repeated in February 2023, Google returned 34,700,000 results. That's an increase of 11,100,000 results—32% more in 4 months.

Currently, use of cannabis and cannabidiol is a regulatory nightmare. On the other hand, the only mushrooms considered to be controlled substances are those containing psilocybin—a Schedule 1 substance under the Controlled Substances Act. States and municipalities in both the United States and Canada, however, are "decriminalizing" the possession and use of psilocybin amid a growing body of research into its therapeutic uses.

Lastly, the FDA does not regulate animal supplements in the same way that it does human supplements. In 1996, the agency determined that the Dietary Supplement Health and Education Act of 1994 didn't apply to products for use in animals, so the FDA regulates products marketed as dietary supplements for animals as either food for animals or animal drugs, depending on their composition of ingredients and intended use.³

The legal status of mushrooms, the more straightforward regulatory environment for the fungi vs cannabidiol, and the few published studies of mushrooms in veterinary species have contributed to the current proliferation of companies selling mushroom products for pets.

As a result, the lack of language guidelines for the labeling of animal health supplements could lead a consumer to unknowingly purchase a "mushroom" supplement that contains no actual mushrooms.

INVESTIGATIONS INTO MUSHROOM PRODUCTS FOR PET USE

For the reasons previously noted, many animal health products labeled as mushrooms for pet use have become available in the online marketplace and in brick-and-mortar retailers. The cultivation process for mushrooms can take as long as 6 months for a harvestable crop. A relatively recent, fast-track production method grows fungal mycelium from medicinal mushrooms on sterile grain, which is then dried; it is then marketed as a mushroom product. The product, however, contains diluted mycelium and very few to no mushrooms.

This fast-track method is cause for concern.

The amount of β -glucans and other compounds with medicinal value is much higher in the mushroom (the fruiting stage of its life cycle) vs the mycelium (vegetative stage) when grown on grain. Mushrooms naturally contain very little digestible starch, and they can have as much as 50% β -glucans. Mycelium grown on grain, however, is low in β -glucans—approximately 10% or less (in some cases, only 1%)—and high in starch (35%-40%) due to the dilutional effect of the grain carbohydrates on mycelium-derived β -glucans.

Several peer-reviewed published studies have examined the content of digestible starch and β -glucans in human dietary supplements labeled as containing mushrooms. In a 2016 study validating a β -glucan analysis methodology, McCleary et al measured the comparative amounts of these 2 polysaccharides in 12 products purchased on Amazon. Based on their β -glucan vs digestible starch (α -glucan) content, just 2 of the 12 products analyzed were made with mushrooms.

A second study published in 2017 examined the quality of *Ganoderma lucidum* (reishi) dietary supplements collected in the United States.⁷ High-performance, thin-layer chromatography fingerprints of triterpenes, colorimetric assay of polysaccharides, saccharide mapping, and gas chromatography coupled with mass spectrometry fingerprints of polysaccharides were studied. Of 19 samples analyzed, only 5 samples met their label claims of containing *G lucidum* mushroom.

Pet Mushroom Product Analysis Study

To assess the percentage of pet health products that contained mushroom or mycelium on grain, Real Mushrooms funded the double-blind Pet Mushroom Product Analysis Study that evaluated 10 commercial mushroom products labeled as containing "turkey tail mushroom for pets" and purchased on the Internet. Each product was evaluated for its polysaccharide content by a third-party International Organization for Standardization/International Electrotechnical Commission 17025–accredited laboratory experienced in the McCleary β -glucan testing methodology. The findings of this study are published here for the first time.

The investigators analyzed how many of 10 animal health supplements identified as containing mushroom actually contained mushrooms. The mushroom products were purchased from Amazon in December 2022. Upon receipt, their labels were taped over, and each product was assigned a number at random (001-010). These blinded products were submitted to the

third-party laboratory; the results were returned by the number, not product name. An employee at Real Mushrooms who was not involved in the study kept the key to product identification.

The objectives of this study were 2-fold:

- 1. to analyze mushroom products labeled for pet use for both their β -glucan content and digestible starch content (measured as α -glucans); and
- 2. to compare label claims with the testing results to determine how many claims on labels from the 10 products analyzed were accurate.

The results are detailed in the **Table**. Of the 10 blinded products analyzed, 6 had relatively high α -glucan (starch) content and lower β -glucan content. The high starch and low β -glucan levels indicated that these products were derived from the mycelial-grain biomass, as found in myceliated grain. Conversely, 4 products had substantially higher β -glucan content than α -glucan content, indicating that these 4 products were derived from the mushroom itself.

TRADITIONAL VS NONTRADITIONAL CULTIVATION

Modern pharmaceutical technology has harnessed the metabolic power of fungal mycelium grown in liquid culture to produce drugs (eg, penicillin, cyclosporin) and powerful compounds (eg, proteoglycan PSP). The liquid cultivation approach maximizes the growth potential of mycelium and allows separation of the liquid growth medium from the mycelium.⁸ With this in mind, it is important for veterinarians to understand the 2 commercial cultivation methods for mushroom-labeled products and the role that the fungal life cycle plays in mushroom quality and production.

Traditional Commercial Mushroom Cultivation

There are 2 steps for traditional commercial mushroom cultivation. In the first, mycelium from the desired fungal species is cultured on sterile grain. The mycelium spreads completely throughout the grain but leaves quite a bit of grain and grain starch in the myceliated biomass. This myceliated grain is called "grain spawn." Creating grain spawn is the first step in all mushroom cultivation practices.

The second step in traditional commercial mushroom cultivation uses grain spawn to inoculate an appropriate substrate material for that fungal species. Dead or dying wood, straw,

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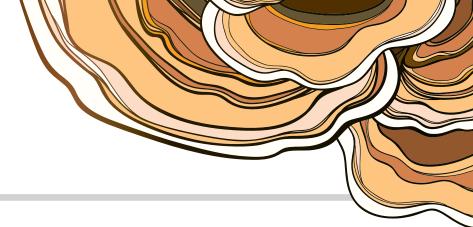


TABLE. Analysis of α - and β -Glucan Content in 10 Commercially Available Online Products for Pet Use Labeled as Containing Turkey Tail Mushroom^a

Brand ^b	Label claim of type of fungal extract	Measured β-glucan	Measured α-glucan	Mush or mog ^c
PET-001	TT + other mushrooms	1.8%	19.5%	Mog
PET-002	Mushroom complex	3.1%	39.2%	Mog
PET-003	Organic mushroom blend	40.4%	2.3%	Mush
PET-004	Mushroom complex	8.1%	21.8%	Mog
PET-005	TT mushrooms	35.7%	2%	Mush
PET-006	Organic TT mushrooms	10.3%	15.7%	Mog
PET-007	TT certified organic mushroom powder	7%	24.7%	Mog
PET-008	Pure TT mushroom powder	1.1%	66.6%	Mog
PET-009	TT mushroom	29.4%	4.7%	Mush
PET-010	TT mushroom + 4 other species	21.3%	3.5%	Mush

IEC. International Electrotechnical Commission; ISO. International Organization for Standardization; mog. mycelium grown on grain; mush, mushroom; TT, turkey tail.

^bFor this double-blind Pet Mushroom Product Analysis Study, product labels were taped over, and each was assigned a code number. The 10 blinded products were sent to an ISO/IEC 17025-accredited laboratory with experience in the McCleary $\beta\text{-glucan testing methodology.}^6\text{ The blinded results were tabulated using their numerical code without knowledge of the}$

^cOf the 10 products for pet use labeled as containing turkey tail mushroom, only 4 products (40%) had percentages of β -glucans and α -glucans (starch) consistent with actual mushroom.

compost, or manure are typical fungal substrates. When the mycelium has grown throughout the substrate and environmental conditions are conducive, the mycelium organizes itself into the mushroom fruiting body. The end product of traditional commercial cultivation methods is the mushroom.9

Nontraditional Cultivation

A nontraditional methodology is being used to commercially manufacture products labeled as mushrooms. The grain spawn used in traditional mushroom cultivation is not inoculated onto its appropriate substrate. Instead, the dried and powdered grain spawn is called a "mushroom product." These nontraditionally cultivated products may be incorrectly labeled as "mushrooms" or correctly labeled as "mycelium biomass cultivated on a grain."

Differences Between Products

Producers that sell grain spawn as their end product instead of mushrooms claim that their powdered mycelium grown on grain also has medicinal benefits. These products, however, have significantly reduced β-glucan content, and they may contain 50% or greater starches from the grain spawn (see the Table). As discussed

previously, mushrooms naturally contain very small amounts of α -glucan (starch). When α -glucans in amounts greater than 5% are found in a product labeled as "mushroom," the source of the α -glucans commonly is grain spawn.

It was beyond the scope of the Pet Mushroom Product Analysis Study to compare the clinical benefits of the 2 cultivation methodologies directly. However, a search on Google Scholar for "mushroom β -glucans" brings up thousands of published studies that have evaluated the role of mushroom β -glucans in promoting health and treating disease.

Results of a published in vitro study suggested that the mycelial elements and mycelial digestion products of rice flour have immune-modulating properties. 10 In addition, arabinoxylans— α -glucans found in the fiber of grains—have mild immunomodulating properties.¹¹ It is likely, this author conjectured, that observed medicinal benefits from mycelium grown on grain result from postbiotic properties related to solid fermentation of the grain.

The mycelium digests the grain to derive its own nourishment for growth. The mycelium does not completely digest the grain in the grain spawn. If Lugol iodine is used to evaluate a mycelium grown on grain product for starch content, it will turn the characteristic purple color associated with a starch reaction.

More definitive studies of mycelium grown on grain may better identify the exact molecules or food components responsible for its postbiotic activity. The best way to compare mushrooms with mycelium grown on grain in terms of bioactivity would be to test mushrooms head-tohead with mycelium grown on grain in vitro or in a clinical trial using a crossover design.

It is possible that mycelium grown on grain contains beneficial compounds from the mycelium along with those derived from the fungal digestion of the grain; however, separation of mycelium from the grain that it has grown into is impossible. 10 This could pose a problem for a pet that depends on a grain-free diet for its continued health.

The differences between these 2 cultivation methodologies in terms of their measured content of active constituents are substantial. Similarly, the starch content of each methodology is clearly different.5-7

IMPROVING QUALITY AND CONSISTENCY OF ANIMAL **HEALTH SUPPLEMENTS**

The National Animal Supplement Council (NASC) was established in 2001 to work with the FDA Center for Veterinary Medicine, state regulators, and the Association of American Feed Control Officials (AAFCO) to develop a responsible path forward for products similar to human dietary supplements marketed for use in dogs, cats, and horses. The NASC now has nearly 300 member companies; it plays a critical role in the animal supplement industry, helping companies follow NASC guidelines developed with input from regulators.

For member companies to display the NASC Quality Seal on their product labels, they must pass an independent audit that includes a review of FDA Current Good Manufacturing Practices; they also must follow proper labeling guidelines and have an adverse event reporting system in place. Compliance with FDA label language standards, including the absence of medical claims, is essential for transparency and consumer safety. To that end, NASC will purchase a member company's product from a random retail source and submit it for third-party analysis to ensure that it meets labeling claims for potency.

President, board chairman, and founding member of the NASC Bill Bookout noted, "AAFCO has been working to support label consistency with human food by updating the information on pet food labels. Under the AAFCO Pet Food Label Modernization project, major regulatory labeling changes or updates are in

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progress, and these changes will take place over the next 5 to 7 years to make labeling on pet nutritional products (dog food, cat food, and nutritional supplements) more closely aligned with human nutritional labeling—so labels will say 'Pet Nutrition Facts' instead of 'Guaranteed Analysis,' which is the current requirement" (email communication, as of February 1, 2023).

THE ROAD AHEAD

Product transparency is essential for consumers. Every product marketed as mushrooms for pets should identify its production method to allow consumers to make an informed decision about the product they select for their pet.

Perils of Labeling

Mislabeling of myceliated grain powder can lead pet consumers to purchase a product that they think contains mushrooms when, in fact, they are purchasing a product with 10% to 20% fungal mycelium, 60% starch from grains, and water content for the remainder.⁶

Because some consumers feed their pets grain-free or low-carbohydrate diets, they try to avoid supplying their pets with calories from carbohydrates. Importantly, cancer cells derive their energy mainly from simple sugars and carbohydrates, less so from protein sources, and not at all from fat sources. This means that certain diets could nourish cancer cells. As a result, veterinarians may recommend that a dog with cancer be fed a diet lower in carbohydrates and higher in protein and fats.¹¹

Label transparency is crucial so pet owners can, if necessary, avoid carbohydrate-based products from mycelium grown on grain. No guidelines, much less regulatory language, currently clarify the type of fungal product that consumers purchase for their pets. As mentioned previously, human mushroom and mycelial biomass products are regulated under the Dietary Supplement Health and Education Act of 1994. In addition, the American Herbal Products Association, which promotes responsible commerce of human herbal supplements, published a guidance policy on label content to differentiate between mushroom and mycelial biomass products. 12

In the absence of regulatory legislation—or even guidance regarding label language for mushroom and mycelial biomass products for animal health—it may be up to an established trade group such as the NASC to help clarify label language for these products to provide better product transparency to pet owners/consumers.

In the meantime, veterinarians can do the following regarding products labeled as containing turkey tail mushrooms for pets:

- understand the label terminology and production methods for a product that they may consider using in their practice; and
- be aware of potential misrepresentation and lack of transparency currently related to use of these fungal supplements.

In addition—and just as importantly—veter-inarians should educate pet parents on this potential misrepresentation of mushroom products (**Box**^{7,13-15}) and how they can make informed decisions that are appropriate for their animal's health needs.
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AUTHOR DISCLOSURE

Silver is a paid consultant for Real Mushrooms.

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REFERENCES

- Brown DC, Reetz J. (2012). Single agent polysaccharopeptide delays metastases and improves survival in naturally occurring hemangiosarcoma. Evid Based Complement Alternat Med. 2012;2012:384301. doi:10.1155/2012/384301
- Arunachalam K, Sasidharan SP, Yang X. A concise review of mushrooms antiviral and immunomodulatory properties that may combat against COVID-19. Food Chem Adv. 2022;1:100023. doi:10.1016/j. focha.2022.100023
- Inapplicability of the dietary supplement health and education act to animal products. Fed Regist. 1996;61(78):17706-17708. Accessed March 1, 2023. www.govinfo.gov/content/pkg/FR-1996-04-22/pdf/96-9780.pdf
- Saari M, Prange A, Lelley JI, Hambitzer R. Screening of beta-glucan contents in commercially cultivated and wild growing mushrooms. Food Chem. 2017;216:45-51. doi:10.1016/j.foodchem.2016.08010
- Chilton JS. A new analytical fingerprinting method for quality control of medicinal mushroom products. In: Baars JJP. Science and Cultivation of Edible Fungi: Proceedings of the XIXth International Congress on the Science and Cultivation of Edible Fungi, Amsterdam, the Netherlands, 30 May-2 June 2016. International Society for Mushroom Science; 2016:267-270.
- McCleary BV, Draga A. Measurement of β-glucan in mushrooms and mycelial products. J AOAC Int. 2016;99(2):364-373. doi:10.5740/ jaoacint.15-0289
- Wu DT, Deng Y, Chen LX, Zhao J, Bzhelyansky A, Li SP. Evaluation on quality consistency of *Ganoderma lucidum* dietary supplements collected in the United States. *Sci Rep.* 2017:7(1):7792. doi:10.1038/ s41598-017-06336-3
- Stamets P, Chilton JS. Grain culture. In: The Mushroom Cultivator: A Practical Guide to Growing Mushrooms at Home. Agarikon Press; 1983:42.
- Benson KF, Stamets P, Davis R, et al. The mycelium of the *Trametes versicolor* (turkey tail) mushroom and its fermented substrate each show potent and complementary immune activating properties in vitro. *BMC Complement Altern Med*. 2019;19(1):342. doi:10.1186/s12906-019-2681-7
- Zannini E, Nuñez AB, Sahin AW, Arendt EK. Arabinoxylans as functional food ingredients: a review. Foods. 2022;11(7):1026. doi:10.3390/foods11071026
- 11. Leeson J. Dog cancer diet: food recommendations and feeding tips.

 Covetrus Great Pet Care. February 22, 2023. Accessed February 23, 2023. www.greatnetcare.com/dog-putrition/dog-cancer-diet/
- 2023. www.greatpetcare.com/dog-nutrition/dog-cancer-diet/
 12. AHPA guidance policies: labeling of dietary supplements containing fungi dietary ingredients. American Herbal Products Association. March 2019. Accessed October 25, 2022. www.ahpa.org/Files/Document%20 Library/AHPAGuidancePolicies/AHPA_Guidance_on_fungi_labeling.pdf
- Why growing mushrooms in North America is not economical for health products. Nammex. Accessed March 3, 2023. www.nammex.com/why-growingmushrooms-in-north-america-is-not-economical-for-supplements/
- Grimm D, Wösten HAB. Mushroom cultivation in the circular economy. Appl Microbiol Biotechnol. 2018;102(18):7795-7803. doi:10.1007/s00253-018-9226-8
- Royse DJ, Baars J, Tan Q. Current overview of mushroom production in the world. In: Diego CZ, Pardo-Giménez, A, eds. Edible and Medicinal Mushrooms. 2017;5-13. https://doi.org/10.1002/9781119149446.ch2

BOX. Is It Mushroom or Myceliated Grain?^{7,13-15}

Too often, supplements marketed as mushrooms for pets do not contain any mushroom, because they are made from myceliated grain. Many US manufacturers of mushroom supplements are growing mycelium on sterile grain, because the process is fairly inexpensive (far less so than growing mushrooms in a controlled setting), and it allows for mass production. The result is a product often advertised as a mushroom supplement that doesn't contain any mushrooms, is low in β -glucans, and is high in starch.

It can be difficult to determine whether a mushroom product for pets contains grain, because the labeling of many of these supplements does not properly indicate ingredients. This mislabeling may or may not be intentional. In some cases, the supplement company itself may not know what it's selling, because it's working with a third-party supplier of ingredients. Regardless, this lack of transparency is misleading.

To determine whether a mushroom product for pets contains myceliated grain, consider the following:

- Where is it made? Myceliated grain, when sold as a supplement, is almost always grown in the United States, because it is too costly to grow mushrooms for supplements in North America.¹⁴ Pure mushroom extracts come from China, which produced 87% of the world's cultivated mushrooms in 2013.¹⁵
- What does the label say? Products made from myceliated grain are often described by words that include "fermented," "full spectrum," "made in the USA" or "USA grown," "mycelium," "mycelial biomass," "myceliated brown rice," "polysaccharides," and "primordia."
- Does the label mention polysaccharides?
 Myceliated grain products often tout high polysaccharide content as proof of effectiveness rather than mentioning β-glucan levels. Because grain contains inert polysaccharides—mainly α-glucan (starch)—polysaccharides are a poor measure of quality.
- What does the Lugol iodine starch test show?
 Confirm the presence of grain by mixing
 1 g of the mushroom product into 3 tbsp of
 water and adding 10 drops of Lugol iodine.¹⁵
 If the test sample turns purple or black,
 it contains starch.

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