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Perspective

Beyond Protein: *Neurospora crassa* as an Underrecognized Dietary Source of Ergothioneine and Spermidine

Paul Shapiro

BMC Ingredients, West Sacramento, CA 95691, USA; paul.shapiro@bmcingredients.com

Abstract

Neurospora crassa has a long history of human consumption in fermented foods and is now produced by submerged fermentation as a whole-mycelium food ingredient. Its protein, fiber, and safety profile have been established, but two smaller constituents—ergothioneine and spermidine—have received little attention. This narrative review places those compounds in context and reports third-party measurements from one commercial lot of dried *N. crassa* biomass. The lot contained 0.604 mg/g ergothioneine and 20.3 mg/100 g spermidine as received. Sample moisture was not reported, so dry-weight concentrations could not be calculated. The ergothioneine result is numerically within published dry-weight ranges for *N. crassa* and several cultivated mushrooms, but different moisture bases and methods preclude a direct comparison. The spermidine result is similar to a published soybean value (20.7 mg/100 g), below a wheat-germ value (35.4 mg/100 g), and higher than values reported for several foods in one survey. Studies in model organisms and observational human studies provide a rationale for further research on healthy aging, but neither compound has been shown to extend human life when consumed in *N. crassa*. Replicated lot testing, moisture measurement, and bioavailability studies are needed before health claims can be made.

Keywords: *Neurospora crassa*; mycoprotein; ergothioneine; spermidine; fungi; fermented foods; healthy aging; food composition

1. Introduction

Fungi occupy a unique place in modern food culture. They are neither plants nor animals, yet nutrition is still commonly discussed as if those were the only two choices. Mushrooms are familiar, but foods made from fungal mycelium remain unfamiliar to many consumers even when they have a long record of use. *Neurospora crassa* is a useful example. The organism is best known as a laboratory workhorse, but it has also been eaten for generations in fermented foods in Asia and Africa and is now grown as a whole-biomass food ingredient [1–4].

Most recent discussion of *N. crassa* as food has centered on protein. That focus makes sense. Commercial dried biomass is approximately 50% protein and about 30% fiber on a dry basis, with a complete essential-amino-acid profile and useful amounts of several minerals [4,5]. But a protein-first description is incomplete. Fungi make metabolites that are rare or unevenly distributed elsewhere in the food supply. Two of them—ergothioneine and spermidine—are especially relevant because both have been discussed in the biology of aging.

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The word longevity invites overstatement. Ergothioneine has been proposed as a "longevity vitamin," and spermidine extends lifespan in several model organisms, but neither observation establishes that a food containing either compound will extend human life. The more defensible question is narrower: does food-grade *N. crassa* contain nutritionally meaningful amounts of these compounds, and how do the measured amounts compare with familiar foods?

This paper addresses that question as a narrative review and perspective. It combines published work on *N. crassa*, ergothioneine, and spermidine with a transparent single-lot case example from commercially produced dried *N. crassa* mycelium. The aim is not to make a clinical claim. It is to identify a neglected part of the organism's composition, show where it sits within the existing food literature, and define the next experiments worth doing.

2. Scope and Approach

2.1. Narrative Literature Review

A targeted narrative search was conducted through August 2026 using PubMed, publisher databases, DOI-linked records, and reference lists. Search terms combined "*Neurospora crassa*," "mycoprotein," "food," "ergothioneine," "spermidine," "polyamines," "mushroom," "wheat germ," "bioavailability," "autophagy," "mortality," and "longevity." Priority was given to primary compositional studies, human studies, authoritative reviews, and public regulatory records. This was not a systematic review or meta-analysis; the food-composition literature is too heterogeneous in sampling, moisture basis, extraction, and analytical method for pooled inference. OpenAI ChatGPT-5 was used to assist with literature organization and figure preparation; the author selected and interpreted the evidence and verified the reported data and citations.

2.2. Existing Compositional Analyses

A single production lot of heat-treated, dried *N. crassa* Bstr 26 mycelial biomass (commercial name Rhiza; lot 2025021209KLB; manufactured 12 February 2025) was analyzed by an independent commercial laboratory, Twin Arbor Analytical. Ergothioneine was reported as 0.6040 mg/g using LC–MS (laboratory SOP TM0055; accession 15559; report dated 3 July 2025). Spermidine was reported as 20.3 mg/100 g using laboratory SOP TM0042 (accession 16155; report dated 13 August 2025). Results are presented as reported, on an as-received basis. The certificates note that not all methods are accredited to ISO/IEC 17025:2017. Each certificate reports one result for its analyte and provides no replicate results, limit of quantification, measurement uncertainty, or sample moisture value. No replicate lots were tested. A dry-weight concentration cannot be calculated without moisture data, and no statistical inference was attempted. The analytical results are summarized in Table 1.

Table 1. Existing analytical results for one commercial lot of dried food-grade *N. crassa* mycelium.

Analyte	Reported Result	Method and Record	Interpretation and Limitation
Ergothioneine	0.6040 mg/g as received (60.4 mg/100 g)	LC–MS; SOP TM0055; accession 15559; 3 July 2025	One result; no replicates, limit of quantification, uncertainty, or sample moisture. Dry-weight value unavailable.
Spermidine	20.3 mg/100 g as received (0.203 mg/g)	SOP TM0042; accession 16155; 13 August 2025	One result; no replicates, limit of quantification, uncertainty, or sample moisture. Dry-weight value unavailable.

For comparison, published ergothioneine values were retained in mg/g and labeled by basis. Wheat-germ and soybean spermidine values of 2437 and 1425 nmol/g, respectively, were taken from a review that compiled the underlying food-composition literature and were converted to mg/100 g using a molecular weight of 145.25 g/mol [6]. Other spermidine values were taken from a literature-based food database [7]. These comparisons are deliberately descriptive. A number printed beside another number does not make the underlying measurements equivalent.

3. *N. crassa* Is Already a Food with a Long History of Safe Consumption

Commercial *N. crassa* is a technological novelty, not a biological one. People have been eating this genus in fermented foods for generations. Traditional uses include red oncom, fermented okara, and HongJun tofu; *N. crassa* has also been identified in traditional cassava heap fermentations, although it was not reported as the dominant fungus [1]. These foods are not identical to purified mycelial biomass. Modern metagenomic work has also shown that the related species *N. intermedia* dominates oncom produced from soymilk byproducts in Western Java [2]. Even so, the record matters: humans did not begin encountering this genus when fermentation companies arrived in the twenty-first century.

The safety case is also broader than traditional use. Perkins and Davis found no evidence that *Neurospora* causes human infection despite extensive laboratory and environmental exposure [3]. A modern safety evaluation of food-grade *N. crassa* biomass included genomic, toxicological, nutritional, allergenicity, and tolerability evidence [4]. In 2024, the U.S. Food and Drug Administration issued a "no questions" response to GRAS Notice 1117 for mycelial biomass from *N. crassa* Bstr 26 for specified food uses [5]. A no-questions letter is not a blanket health endorsement, but it is a meaningful regulatory milestone.

This distinction between safety and health should remain clear. The safety dossier supports use of the biomass as food under the notified conditions. The presence of ergothioneine and spermidine adds compositional interest; it does not alter the terms of that conclusion and does not, by itself, prove a physiological effect.

4. Ergothioneine

4.1. A Fungal Metabolite That Humans Retain

Ergothioneine is a sulfur-containing derivative of histidine synthesized by certain fungi and bacteria. Animals obtain it from diet and concentrate it in selected tissues through the transporter encoded by SLC22A4 [8–10]. That dedicated uptake system is one reason the compound has attracted attention. Another is chemical: ergothioneine is comparatively stable at physiological pH and can participate in redox and metal-chelation chemistry [8,9].

In *N. crassa*, the biology is not speculative. Deletion of *egt-1* eliminates ergothioneine production, and the mutant is more sensitive to peroxide during conidial germination and has shorter conidial survival [11]. Biochemical work later clarified the compact fungal biosynthetic route [12]. Those experiments describe fungal physiology, not human nutrition; the germination-survival benefit that egt-1 confers on conidia has no established human analog.

4.2. Comparison with Mushrooms

Mushrooms are the best-known dietary source of ergothioneine, but their concentrations vary widely. Dubost and colleagues reported 0.4–2.0 mg/g dry weight across cultivated mushrooms, with white button mushrooms at the low end and specialty mushrooms higher [13]. Kalaras and colleagues later found a wider 0.15–7.27 mg/g dry-weight range across a broader set of species [14]. Species, tissue, cropping conditions, and analytical method all matter.

The 0.604 mg/g as-received result for this commercial *N. crassa* lot is numerically within the published cultivated-mushroom range and earlier estimates for *N. crassa* of 0.466–0.850 mg/g dry weight [11,13]. These are contextual comparisons, not equivalent measurements: the literature values are expressed on a dry-weight basis, whereas sample moisture was not reported for the commercial lot. Samples also came from different studies with different extraction and analytical methods. The data therefore do not establish a relative ranking between this lot and mushrooms. Figure 1 presents these contextual comparisons.

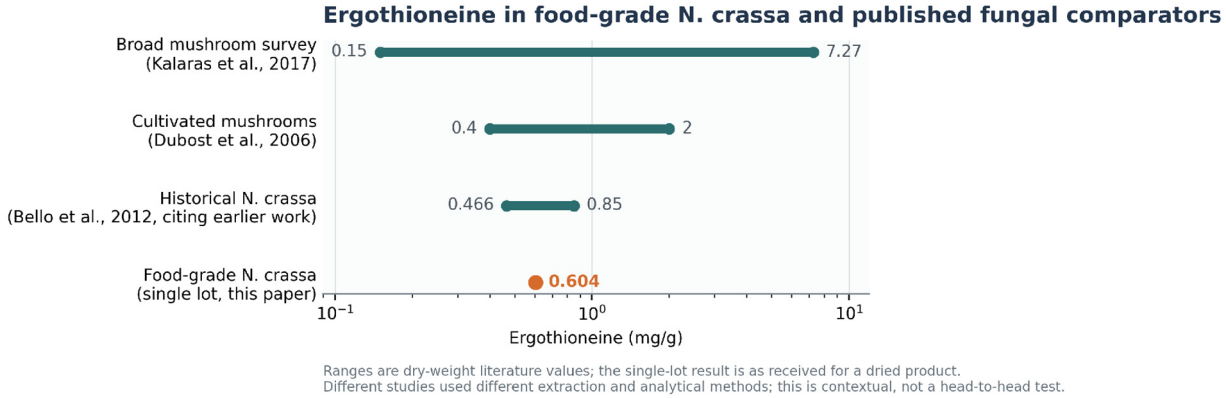

Figure 1. Ergothioneine concentrations in one food-grade *N. crassa* lot and published fungal comparators [11,13,14]. Horizontal lines show published ranges; the orange point is the single-lot value. Literature ranges are dry-weight values. The commercial result is as received for a dried product and was not moisture-corrected. Methods were not harmonized. The horizontal concentration axis uses a logarithmic scale.

4.3. What the Longevity Literature Does—And Does Not—Show

Ames included ergothioneine in a proposed class of "longevity vitamins": compounds whose long-term insufficiency might not cause an acute deficiency disease but could increase late-life risk [15]. It is a hypothesis, not a recognized nutrient requirement. In a Swedish cohort, higher circulating ergothioneine was associated with lower risks of cardiovascular disease and mortality [16]. This observational result does not establish causation: reverse causation and residual confounding remain possible, and circulating ergothioneine could be a marker of other dietary or health differences.

Human absorption is more directly supported. In a small crossover study, ergothioneine from *Agaricus bisporus* mushrooms was bioavailable and appeared in red blood cells after consumption [17]. Our search identified no comparable study of food-grade *N. crassa*. It is reasonable to infer that chemically identical ergothioneine can be released from different fungal foods, but the surrounding matrix and processing may change bioaccessibility. That question can be tested without invoking lifespan.

5. Spermidine

5.1. A Common Metabolite with Uncommon Interest

Spermidine is a polyamine found in all living cells. It participates in nucleic-acid stabilization, translation, cell growth, and stress responses. Food is one contributor to exposure, alongside endogenous synthesis and microbial metabolism in the gut [6,18]. Plant foods generally contain more spermidine than spermine, with wheat germ, legumes, soy foods, mushrooms, peas, and several green vegetables among the commonly cited sources [6,7,18,19].

The composition literature is messy. Concentrations change with cultivar, maturity, fermentation, processing, and storage; published surveys also differ in extraction and chromatography [6,7,19]. This variability is precisely why comparisons should be used to set context rather than rank foods with false precision.

5.2. Comparison with Wheat Germ and Other Foods

The commercial *N. crassa* lot contained 20.3 mg spermidine per 100 g as received. Muñoz-Esparza and colleagues summarized published values of 2437 nmol/g for wheat germ and 1425 nmol/g for soybeans [6]. Converted using a molecular weight of 145.25 g/mol, those values are approximately 35.4 and 20.7 mg/100 g, respectively. The single-lot *N. crassa* result is numerically below the cited wheat-germ value and similar to the cited soybean value. These values came from different studies and cannot establish a reliable ranking of foods or of *N. crassa* production lots.

A literature-based Turkish food database reported 8.86 mg/100 g for mushrooms, 6.52 mg/100 g for green peas, and 3.24 mg/100 g for broccoli [7]. The measured *N. crassa* lot is numerically higher than these values from one survey; other studies have reported higher mushroom values. Moisture basis, sample selection, processing, and analytical methods differ, so the comparisons describe context rather than relative nutritional superiority. Figure 2 presents the selected spermidine values, and Table 2 lists the source values and measurement bases used in both comparative figures.

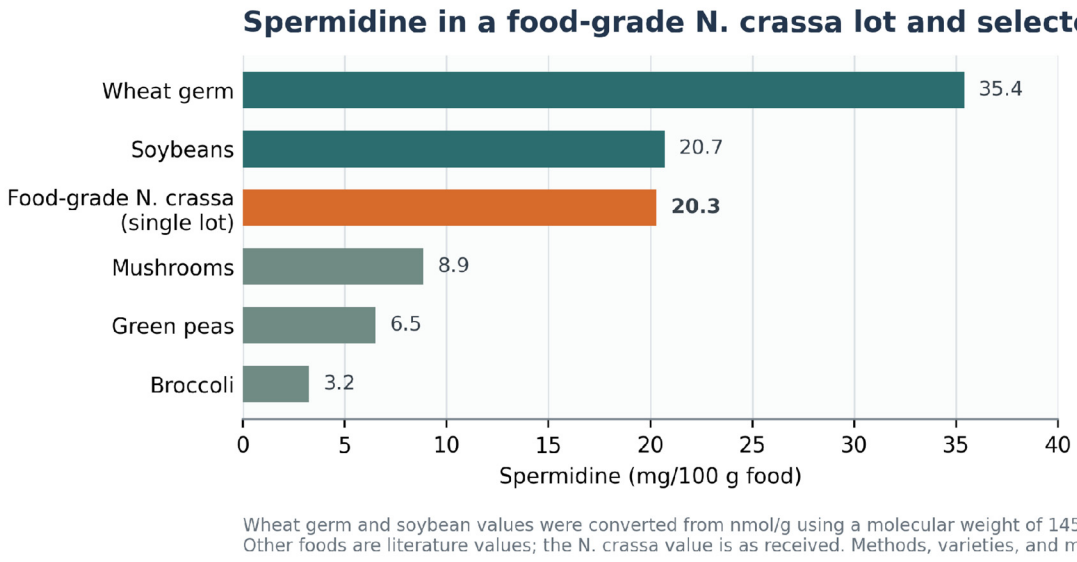

Figure 2. Spermidine in one food-grade *N. crassa* lot and selected foods [6,7]. Wheat-germ and soybean values were converted from nmol/g using 145.25 g/mol. The figure combines values from different studies and is not a controlled comparison. Food form, moisture, processing, and analytical method differ. The single-lot *N. crassa* value is as received for a dried product; literature values were obtained on different bases and by non-harmonized methods.

Table 2. Source values used in the comparative figures.

Food or Material	Reported or Converted Value	Basis	Source
Food-grade *N. crassa*, one lot	Ergothioneine 0.604 mg/g	As received; dried product	Independent commercial analysis; Table 1
Historical *N. crassa*	Ergothioneine 0.466–0.850 mg/g	Dry weight	Bello et al. [11], citing earlier work
Cultivated mushrooms	Ergothioneine 0.4–2.0 mg/g	Dry weight	Dubost et al. [13]

Table 2. *Cont.*

Food or Material	Reported or Converted Value	Basis	Source
Broad mushroom survey	Ergothioneine 0.15–7.27 mg/g	Dry weight	Kalaras et al. [14]
Wheat germ	Spermidine 35.4 mg/100 g	Compiled value; converted from 2437 nmol/g	Muñoz-Esparza et al. [6]
Soybeans	Spermidine 20.7 mg/100 g	Compiled value; converted from 1425 nmol/g	Muñoz-Esparza et al. [6]
Food-grade *N. crassa*, one lot	Spermidine 20.3 mg/100 g	As received; dried product	Independent commercial analysis; Table 1
Mushrooms	Spermidine 8.86 mg/100 g	Compiled literature value	Buyukuslu et al. [7]
Green peas	Spermidine 6.52 mg/100 g	Compiled literature value	Buyukuslu et al. [7]
Broccoli	Spermidine 3.24 mg/100 g	Compiled literature value	Buyukuslu et al. [7]

5.3. The Longevity Evidence Is Promising but Incomplete

Spermidine entered the longevity discussion because it induces autophagy and extends lifespan in yeast, flies, worms, and other experimental systems [20,21]. More recent work places endogenous spermidine within the autophagic response to fasting across several species [22]. These findings say nothing about dose, though; lifespan extension in yeast and flies does not translate into a known effective human intake.

Human evidence has two different faces. In the Bruneck cohort, higher estimated dietary spermidine intake was associated with lower all-cause mortality over long-term follow-up [23]. In contrast, a 12-month randomized trial in 100 older adults with subjective cognitive decline found that a wheat-germ extract providing 0.9 mg/day of spermidine did not improve the primary memory outcome or most secondary biomarkers compared with placebo [24]. The trial tested cognition rather than longevity and used a modest supplemental dose, but it remains a useful restraint on broad claims.

Polyamine biology also resists simple "more is better" messaging. Polyamines are required for normal growth, yet dysregulated polyamine metabolism is characteristic of many tumors and is itself a therapeutic target [25]. Ordinary spermidine-containing foods are not implicated by this; polyamine biology is just complicated enough that a nutrition paper should not flatten it into one direction of effect. At present there is no established recommended intake for spermidine [6].

6. Why the Co-Occurrence Matters

Mushroom fruiting bodies can supply ergothioneine, and wheat germ can supply spermidine. This single lot of food-grade *N. crassa* contained both compounds in a biomass that also contains protein and fiber [4,5]. Whether both concentrations are typical of other *N. crassa* lots remains to be established.

Co-occurrence does not demonstrate biological synergy. A concentration per gram also says little about actual dietary exposure without a serving size. As an illustrative calculation, a 30 g serving of this dried lot would contain approximately 18.1 mg ergothioneine (0.604 mg/g × 30 g) and 6.1 mg spermidine (20.3 mg/100 g × 30 g). This is not an established serving recommendation or an estimate of absorbed dose. Moisture, recipe formulation, preparation, stability, and bioavailability could change practical exposure.

The co-occurrence of these compounds raises testable questions about consistency across production lots, stability during storage and cooking, and release from the mycelial matrix during digestion. The existing measurements cannot establish physiological effects or consumer responses.

7. Limitations and a Proportionate Research Agenda

The largest limitation is obvious: the new compositional evidence comes from one lot. A single measurement can establish presence and approximate magnitude, but not a product specification, a manufacturing average, or species-wide composition. The reports provide one result per analyte and do not report replicate measurements, limits of quantification, measurement uncertainty, or sample moisture; dry-weight concentrations cannot be calculated. Cross-food comparisons combine different laboratories and methods. Finally, concentration is not bioavailability, and bioavailability is not clinical benefit.

This is a review and perspective with an illustrative case example, not a definitive compositional survey. Its claims should remain at that level.

A proportionate next phase would proceed in four steps. First, test multiple nonconsecutive production lots for ergothioneine and spermidine, with moisture measured on the same samples and methods run under an appropriate quality system. Second, test stability through storage and representative cooking conditions. Third, use an in vitro digestion model to estimate release from the mycelial matrix. Fourth, if exposure remains nutritionally relevant, conduct a human bioavailability study that measures plasma or red-blood-cell ergothioneine and appropriate polyamine endpoints. A longevity trial is neither the first nor the most useful next experiment.

8. Conclusions

One commercial dried lot of food-grade *N. crassa* mycelium contained 0.604 mg/g ergothioneine and 20.3 mg/100 g spermidine as received. Published biology establishes that the organism can synthesize ergothioneine [11,12]. The measured ergothioneine concentration is numerically within published fungal-food ranges, and the measured spermidine concentration is similar to one published soybean value and higher than values reported for several foods in one survey. Differences in moisture basis, sampling, and analytical methods limit these comparisons.

These observations establish the presence and approximate magnitude of both compounds in one lot; they do not establish species-wide concentrations, bioavailability, or health benefits. Replicated composition measurements with sample moisture data, stability testing, and bioavailability studies are needed to assess the nutritional significance of food-grade *N. crassa*.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/applmicrobiol6100116/s1: Table S1, Certificate of analysis for ergothioneine (Twin Arbor Analytical accession 15559); Table S2, Certificate of analysis for spermidine (Twin Arbor Analytical accession 16155).

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Data Availability Statement: The two third-party analytical results from one commercial production lot are reported in the article. The supporting certificates of analysis, including the lot, accession numbers, methods, results, and report dates, are provided as Tables S1 and S2 in the Supplementary Materials. Further inquiries can be directed to the corresponding author.

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figures. The author verified the cited sources and reported data, and takes full responsibility for the content.

Conflicts of Interest: As sole author and as CEO of the funding company, P.S. was solely responsible for the study's design, data interpretation, manuscript writing, and the decision to submit for publication. P.S. is co-founder and chief executive officer of BMC Ingredients, which manufactures and markets the *N. crassa* ingredient discussed in this article. BMC Ingredients paid the independent laboratory to perform the compositional analyses; the laboratory did not control the interpretation or the decision to submit. The comparative literature values were selected from public sources, and the limitations of the single-lot data and cross-study comparisons are stated throughout the article.

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