# Mushrooms, gut microbiota and cancer: a scoping review with qualitative synthesis

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## BACKGROUND

Cancer is a leading cause of death worldwide [1], and treatment places a complex burden on the individual and on healthcare [2].

Immune dysregulation is a hallmark of cancer progression [3]. Mushrooms have demonstrated immunomodulatory properties [4], and a systematic review of mushroom supplements used in cancer reported improved survival, side effects and quality of life [5].

A possible mechanism is their prebiotic activity, influencing the balance of gut microbiota and subsequent production of short chain fatty acids (SCFAs) [6].

## AIM

The aim of this paper is to map and synthesise the evidence that examines the impact of mushrooms on cancer-related immunological processes due to their potential interaction with the gut microbiota.

## METHODOLOGY

A scoping review was chosen due to the lack of clinical trials [7]. PubMed, the Cochrane Library and the Allied and Complementary Medicine Database were searched using the primary search terms “Cancer”, “Microbiota” and “Mushrooms”.

This identified 23 papers:
- 20 murine *in vivo* studies
- 1 *in vitro* experiment
- 1 *in silico* study
- 1 cross-sectional human study

Data was extracted, tabulated and qualitatively synthesised. Murine studies lacked transparency in blinding protocols, but otherwise performed well in critical appraisal.

## FINDINGS

The literature was heterogeneous, with no human clinical trials. The mushroom and cancer most frequently studied were *Ganoderma lucidum* and colorectal cancer (CRC), respectively (Figure 1).

Among murine studies:
- **17** found significant evidence of tumour reduction;
- **12** found significant changes to cytokines.

Twenty-two studies analysed gut microbiota:
- **8** found significant changes in diversity;
- **2** reported significant changes to the F/B ratio, a comparison of the phyla *Firmicutes/Bacteroidetes* (see Figure 2 for taxonomy);
- **4** found significantly restored cancer-related pathways in gene pathway enrichment analysis;
- **6** found increased short chain fatty acid (SCFA) production;
- **1** identified cancer-preventative pathways via computer modelling of mushrooms and human gut microbiota.

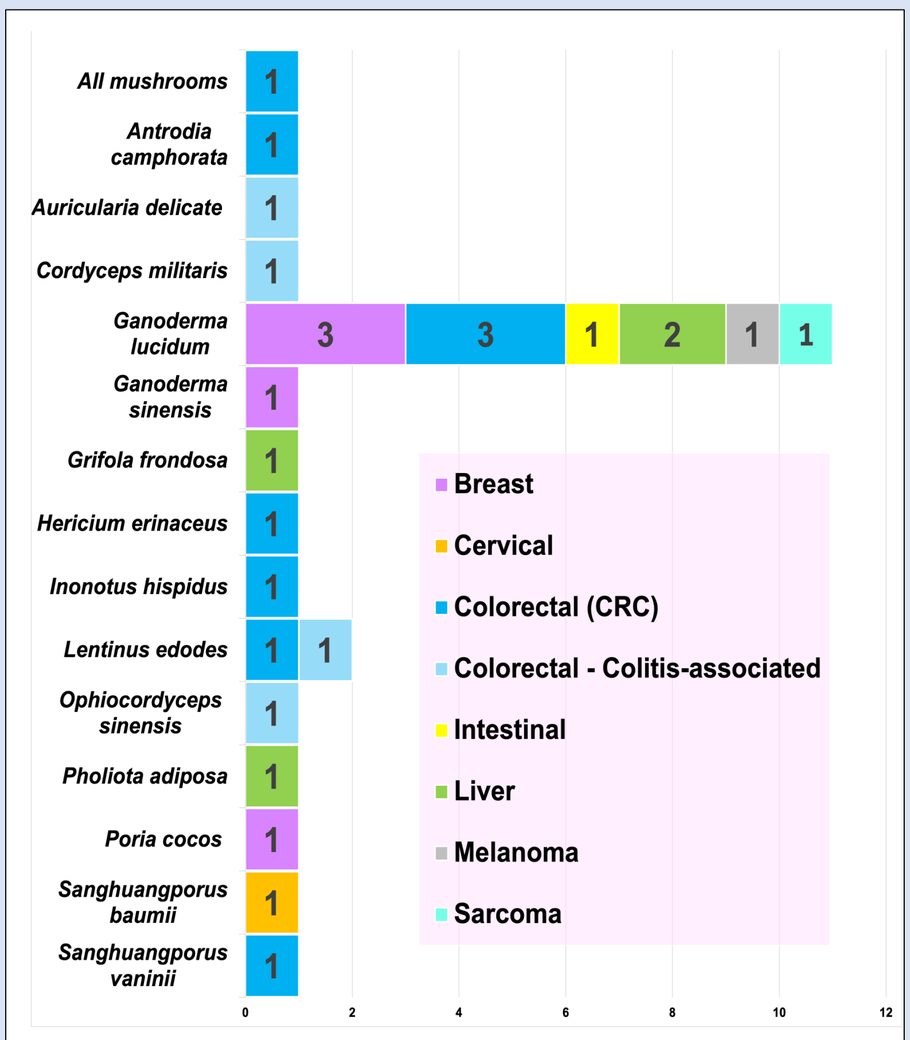


***Figure 1. Number of studies by mushroom and cancer type***


***Figure 2. Taxonomy of microbiota***

## DISCUSSION

**Why was *Ganoderma lucidum* so frequently used?** Possibly due to the promising results of a Cochrane Review [8], and to its global availability.

**Why was CRC so frequently studied?** Possibly because the colon comes into direct contact with mushrooms and gut microbiota. However, ten studies examined non-GI cancers, despite poor absorption of key mushroom compounds [9, 10]. Eight of these found tumour reductions with mushroom treatment, suggesting a possible systemic impact on cancer prevention.

**Evidence of systemic impact:** Some alterations to cytokine production with mushroom treatment followed known anti-inflammatory or anti-tumour trends, while others were inconsistent or difficult to interpret.

**Gut microbiota:** Mushrooms were associated with changes to gut microbiota in most studies, but the complex and dynamic nature of gut microbiota makes changes to diversity, F/B ratios and other measurements difficult to interpret.

**F/B ratio:** Different cancer types have demonstrated opposing influences on F/B ratio [11,12]. Additionally, most of the data was from mice, and while there are similarities, the F/B ratio is significantly lower than in humans, and there are also differences at family and genus level (see Figure 2 for taxonomy) [13].

**SCFAs:** production was increased in mice in this present review, while previous human cancer studies examining SCFAs have shown mixed results [14].

**Gene pathway enrichment analysis:** gut microbiota was altered by mushroom ingestion in a way that may influence cancer progression. The most prominent pathways were different in each study, possibly due to the different mushroom extracts and cancers studied.

## CONCLUSION

Mushroom-associated changes to microbiota and their potential impact on cancer are difficult to interpret. Results from murine studies are difficult to extrapolate to humans, and human studies are lacking. *In silico* research may prove invaluable in its ability to rapidly examine the impact of multiple mushroom and cancer types and interpret the potential role of human gut microbiota in cancer prevention. Cancer clinical trials using mushrooms could consider taking stool samples to analyse for gut microbiota and SCFAs. The findings of this review are too heterogeneous to inform any kind of treatment protocol, and further research is recommended.

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