

Thrush: Zinc may prevent yeast infections—new research

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Candida albicans. Credit: Wikipedia.

Around a half-billion women experience a vaginal yeast infection (thrush) every year—with around 140 million women suffering from multiple infections <u>throughout their lifetime</u>.

While treatments do exist for thrush, for many <u>women</u> these aren't effective (or they only have <u>short-term effects</u>). But new research has discovered that zinc could be used to <u>treat vaginal yeast infections</u> by



limiting how the fungus grows in the vagina.

The majority of vaginal yeast infections are caused by the fungus *Candida albicans*. For most of us, this fungus exists as a normal part of our microbiome and is harmless. But when the microbiome is disturbed (for example, as a result of <u>antibiotic use</u>), this can change how C. albicans grows—making it more likely to cause an infection.

This fungus has also evolved strategies to help it acquire the nutrients it needs to grow, even in the harsh environments of mammalian tissues. In the human vagina, for example, the fungus finds itself in an environment that's acidic, with lots of competition from local bacteria for nutrients.

One <u>key nutrient</u> this fungus needs to grow and multiply is the metal zinc. When C. albicans cannot find zinc in its immediate surroundings, it instead makes a protein called Pra1 that helps it find the metal in <u>nearby cells</u> and the vaginal mucus. This was one of the key findings of this latest study.

The researchers also found that in women who had a <u>vaginal yeast</u> <u>infection</u> caused by C. albicans, the levels of inflammation in the vagina were higher than in women who did not have thrush. This meant their <u>immune system</u> was activated against the fungi.

These inflammation levels also positively correlated with the amount of Pra1 produced. This is important, because inflammation causes many of the symptoms of thrush—including itching, a burning feeling and swelling.

Since Pra1, rather than C. albicans itself, appeared to be causing many of the symptoms of thrush, the researchers then wondered whether adding zinc back into the vagina would stop the fungus making Pra1 and thus reduce inflammation.



They gave a commercially available vaginal gel that contains zinc (currently used for vaginal dryness) to six women who had experienced multiple yeast infections. The women self-applied the gel every night for two weeks, followed by twice a week thereafter for up to three months.

The results showed that the zinc-containing gel stopped the symptoms of thrush in five of the six women. While this still needs to be tested in a bigger group, the results are promising—and may provide a new way to treat vaginal yeast infections, particularly for recurrent sufferers.

Exactly how the zinc gel works to stop yeast infections needs to be figured out. But it's likely because providing the fungus with enough zinc stops it producing Pra1. This in turn reduces inflammation—and symptoms.

So instead of getting rid of the fungus, the gel may be helping the fungus to grow alongside the other microbes that make up the vaginal microbiome in a more balanced, harmonious way.

Heavy metals

Many fungi that cause infections in humans make proteins to help them grow when nutrients, such as <u>zinc</u> or copper, are in short supply. Pra1 is one example.

Another is the fungus Cryptococcus neoformans, which causes meningitis in people with Aids. This fungus makes a protein called Ctr4, which helps it grow even when copper levels are limited. Our <u>recent</u> work also showed that C. neoformans will hide inside the brain's <u>immune cells</u> in order to find copper, helping to promote infection.

But when we deleted Ctr4 from the fungus's genes, this limited how much the fungus was able to grow—helping to <u>prevent brain infection</u>.



Zinc and copper are not only important for how fungi grow—they're also important metals that help our immune system. Zinc can fuel the killer functions of neutrophils, a type of immune cell that detects and destroys bacteria and fungi.

Copper helps maintain the number of immune cells in your blood. It's also found within <u>anti-microbial peptides</u>—small proteins in your saliva and gut that protect against invading microbes.

Because our immune cells use metals to function, they can be rich sources of these nutrients. Some microbes, such as C. neoformans, may target immune cells to acquire these nutrients, as can bacteria that live inside our immune cells—including Mycobacteria, which causes tuberculosis. Immune cells will sometimes attempt to limit a microbe's access to these nutrients to prevent infection, a process known as "nutritional immunity".

Given the way metals can influence the outcome of infections and immune responses, it's no wonder there's growing interest in this aspect of immunology research.

Better understanding how metals can be used to prevent and treat thrush could have a significant benefit for all who suffer from it. Vaginal thrush is one of the most common fungal infections worldwide. It is associated with a high-economic cost, due to the amount of drugs needed to treat recurrent infections and loss of productivity due to time off work. Moreover, recurrent thrush causes a poor quality of life for patients.

Antifungal drug resistance is also a growing problem. The development of drug resistance in the C. albicans <u>fungus</u> can be one reason that <u>standard treatments don't work</u> for some women.

Harnessing what we've learned from recent studies that have examined



how fungi use and acquire nutrients to cause <u>infection</u> can help us identify new strategies to treat not only thrush, but other fungal infections which are a growing problem <u>around the world</u>.

More information: Elena Roselletti et al, Zinc prevents vaginal candidiasis by inhibiting expression of an inflammatory fungal protein, *Science Translational Medicine* (2023). DOI: 10.1126/scitranslmed.adi3363

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