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Role of Nutraceuticals in Tuberculosis Management: A Comprehensive Review

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ABSTRACT

Tuberculosis (TB) is still one of the biggest infectious killers in the world, and it is closely linked to how well-nourished a person is. Poor nutrition makes a person more likely to get active TB in the first place, and once someone has TB, the disease itself makes their nutrition worse — so it becomes a cycle that is hard to break. Along with the usual TB medicines (the DOTS regimen), researchers have been looking at nutraceuticals — that is, vitamins, minerals and natural plant compounds that do more than just basic nutrition — as extra support to help the immune system, lower drug side effects, and improve how well patients respond to treatment. This review looks at what is currently known about the more commonly studied nutraceuticals in TB, such as vitamin D, vitamin A, zinc, selenium, vitamin C, omega-3 fatty acids, curcumin, and probiotics. It also talks about bigger nutrition-support programmes like the RATIONS trial, mentions some drug–nutrient interactions relevant to TB medicines, and points out the gaps that still need more research before any of these can be officially recommended.

Keywords: Tuberculosis; nutraceuticals; vitamin D; curcumin; malnutrition; host-directed therapy; RATIONS trial

1. INTRODUCTION

Tuberculosis is caused by a bacteria called Mycobacterium tuberculosis, and it is still among the top ten causes of death across the world. It is actually the leading cause of death from a single infectious disease. Even though we have the DOTS (Directly Observed Treatment, Short-course) strategy and effective antibiotics, TB treatment does not always go smoothly. The main problems are that the treatment takes a long time (usually 6 months or more), the drugs can be toxic to organs like the liver, patients often find it hard to stay adherent to such a long course, and drug-resistant TB strains keep appearing.

Because of these problems, researchers have started paying more attention to the host side of things — meaning the patient's own body and immune system — rather than only focusing on new drugs. This is where nutraceuticals come in. Nutraceuticals are substances that sit somewhere between food and medicine: vitamins, minerals, amino acids, plant polyphenols, and probiotics that can have a real physiological effect on the body. In TB, the hope is that these compounds can act as “host-directed therapy,” meaning they help the body's own defences fight the infection better, rather than attacking the bacteria directly like antibiotics do. This review tries to put together what is currently known about nutraceuticals in TB, from prevention to use alongside treatment.

2. HOW NUTRITION AND TB ARE CONNECTED

The connection between malnutrition and TB has been known for a very long time, but recent studies have put actual numbers on it. According to Cochrane reviews, being undernourished roughly doubles a person's risk of developing active TB disease. The WHO's Global Tuberculosis Report also states that undernutrition is responsible for a very large share of new TB cases every year, making it the single biggest population-level risk factor for TB — bigger than most people realise. Patients with TB who are also malnourished have a much higher chance of dying compared to those who are well-nourished.

This relationship works both ways. When a person is undernourished for a long time, their cell-mediated immunity (the part of the immune system that is most important for controlling TB) becomes weaker, so the bacteria are more likely to become active. On the other hand, once a person actually has active TB, the disease itself causes weight loss and micronutrient deficiencies because of poor appetite, higher energy needs from the illness, and ongoing inflammation. So poor nutrition leads to more TB, and TB leads to worse nutrition — it becomes a loop that is difficult to break without outside help.

This is not just a medical issue but also a social one. Since TB mostly affects working-age adults in low- and middle-income countries, families often lose income at the same time as facing high treatment costs, which pushes them further into food insecurity. Because of this, studies like the RATIONS trial in India — which gave patients and their household members food and micronutrients — found lower TB rates among contacts and better survival in patients, especially when patients gained weight early in treatment. This kind of evidence is why the WHO and other health bodies now say that checking and supporting a patient's nutrition should be a regular part of TB care, not just an extra step.

3. WHY NUTRACEUTICALS ARE BEING STUDIED AS HOST-DIRECTED THERAPY

Host-directed therapy (HDT) is a newer idea in TB treatment. Instead of trying to kill the bacteria directly (which is what antibiotics do), HDT tries to make the patient's own immune system work better — for example, helping macrophages (a type of immune cell) destroy the bacteria more effectively, or reducing the extra inflammation that damages lung tissue and causes cavities to form. Since many nutraceuticals already have known effects on the immune system and act as antioxidants, they have been proposed as cheap, generally safe options for this kind of therapy. If they work, they could potentially shorten treatment time, lower the chance of relapse, reduce drug-related organ damage, and simply make the long months of TB treatment easier for the patient.

That said, it's important to be honest that the evidence for most nutraceuticals in TB is still at an early stage compared to approved HDT drugs. A lot of what we know comes from lab experiments and animal studies, and the human trials that do exist are often small, use different doses, and measure different outcomes, which makes it hard to compare results across studies. The next sections go through what is known for each nutraceutical individually.

4. MICRONUTRIENTS STUDIED IN TB

4.1 Vitamin D

Vitamin D is probably the most studied nutraceutical in TB. It helps turn monocytes (a type of white blood cell) into macrophages that are better at fighting mycobacteria, and it triggers the production of natural antimicrobial peptides like cathelicidin. Several observational studies have found that people with low vitamin D levels are more likely to get TB and tend to have more severe disease. Clinical trials giving vitamin D along with normal TB treatment have shown some patients clear the bacteria from their sputum faster, especially those who were deficient to begin with, and the side effects are minimal even at higher doses. However, bigger reviews that combine many studies together have found that it's still not clear whether vitamin D actually reduces relapse or death rates — the benefit seems to mainly apply to correcting an existing deficiency rather than helping everyone equally.

4.2 Vitamin A

Vitamin A helps keep the lining of the airways healthy and supports a type of immune response (Th1) that is important for containing TB bacteria. It works through some of the same pathways as vitamin D, so some researchers have suggested giving both together might work better. But just like with vitamin D, the actual trial results in TB patients have been mixed, and the clearest benefit is seen in patients who were already deficient rather than in the general TB population.

4.3 Zinc

Zinc is needed by many immune enzymes and is important for T-cells and neutrophils to do their job properly. A lot of TB patients, especially in poorer settings, are found to be low in zinc, so correcting this seems like it should help. But when researchers have actually tested zinc supplementation in TB patients, most trials and reviews have not found a clear benefit on treatment outcomes. This is a good example of how something that makes sense biologically doesn't always show up as a real benefit in clinical trials.

4.4 Selenium

Selenium is part of an antioxidant enzyme (glutathione peroxidase) and may help reduce the tissue damage caused by ongoing inflammation in TB. There isn't a lot of TB-specific research on selenium compared to other nutrients, so most of what we know is either theoretical or borrowed from studies in other infections.

4.5 Vitamin C

Vitamin C is a well-known antioxidant and may help neutrophils and other immune cells work better. It has been studied more in viral respiratory infections than in TB specifically, so the direct evidence for TB is still quite limited and mostly observational.

4.6 Omega-3 Fatty Acids

Omega-3 fats can change the type of inflammatory molecules the body produces, which in theory could help reduce excess lung inflammation in TB. Actual TB-specific clinical data is still very limited, and, as seen in other fields where omega-3s have been studied, higher doses need to be used carefully because of possible side effects.

5. PLANT-BASED COMPOUNDS (PHYTOCHEMICALS)

5.1 Curcumin

Curcumin, the main active compound in turmeric (Curcuma longa), is one of the most talked-about plant compounds for TB. Lab studies show that curcumin can directly kill both normal and drug-resistant strains of M. tuberculosis, and it also works together with standard TB antibiotics to help clear the bacteria from infected macrophages better than antibiotics alone. It also seems to boost helpful immune signals like IL-12. In mice with TB, combining curcumin with regular antibiotics reduced the amount of bacteria in the lungs more than antibiotics by themselves. On top of that, curcumin is known to protect the liver, which is useful because common first-line TB drugs like isoniazid and rifampicin can be hard on the liver.

The biggest problem with curcumin is that it is very poorly absorbed when taken by mouth — the body breaks it down and gets rid of it quickly, so very little actually reaches the bloodstream. To get around this, scientists have been developing special formulations, like curcumin wrapped in nanoparticles or coated with chitosan, to improve how well it is absorbed. Some early animal studies suggest that these improved formulations might even help antibiotics work faster, which could reduce the chances of the bacteria becoming drug-resistant. But human trials are still very limited, and curcumin is not an approved TB treatment at this point.

5.2 Other Plant Compounds

Apart from curcumin, many other plant-based compounds — flavonoids, alkaloids, terpenoids and similar molecules from traditional medicinal plants — have been tested for their ability to fight TB bacteria or support the immune system. The idea behind studying these is mainly to shorten the long DOTS treatment course, reduce drug side effects, and boost the body's natural defences. However, almost all of this evidence still comes from lab and animal studies, so proper human trials are needed before any of these can be recommended in practice.

6. PROBIOTICS AND GUT HEALTH

Long-term use of multiple TB drugs together often upsets the stomach and gut, causing nausea and disturbing the normal gut bacteria. This can make it harder for patients to stick to their treatment, which is already a long six-month (or longer) course. Probiotics have been suggested as a way to keep the gut bacteria balanced during treatment, and through what is called the gut–lung axis, they might also help support the immune system more broadly. There isn't much TB-specific clinical evidence for probiotics yet, but the idea of using them to make TB treatment more tolerable, and therefore easier to complete, is gaining some interest.

7. NUTRITION SUPPORT PROGRAMMES AND WHAT THEY SHOW

Looking at single micronutrients only tells part of the story. Some of the strongest evidence we have actually comes from larger nutrition support programmes rather than giving one vitamin or mineral alone. The WHO clearly recognises food insecurity and undernutrition as major, structural risk factors for TB, and recommends that nutrition assessment and support be built into routine TB care rather than treated as optional. Community-based feeding programmes for malnourished and food-insecure populations, including people with TB and HIV, have shown moderate benefits according to Cochrane reviews.

The RATIONS trial mentioned earlier is one of the best examples of this kind of evidence. It gave TB patients and their household contacts food rations (about 1200 kcal and 52 grams of protein per day) plus micronutrients, and this reduced both TB deaths in patients and new TB cases among their contacts — with patients who gained weight early in treatment having a much better chance of survival. Similar programmes, like the INSTITUT study in Benin, are looking at how built-in nutritional support within national TB programmes affects outcomes. Overall, this evidence suggests that general nutrition — enough calories and protein — should be prioritised alongside, not instead of, more specific micronutrient or plant-compound supplementation.

8. PROBLEMS AND OPEN QUESTIONS

- Results are inconsistent: for zinc, vitamin A and even vitamin D, several well-designed trials have shown no clear benefit compared to placebo, even though the biological reasoning makes sense. This shows a gap between "should work in theory" and "actually works in patients."

- Poor absorption: compounds like curcumin are not well absorbed by the body, so advanced formulations (like nanoparticles) are needed, and these are not always affordable or available in the low-resource settings where TB is most common.

- Dosing is not well defined: for most nutraceuticals, we still don't know the ideal dose to use alongside TB treatment, and some (like high-dose zinc or omega-3s) may even cause problems at higher doses.

- Drug–nutrient interactions: TB drugs can affect nutrition and vice versa. For example, isoniazid can interfere with vitamin B6 levels in the body, and poor nutrition can change how well drugs are absorbed — so nutrition support needs to be planned carefully alongside the drug regimen, not separately.

- Most positive results are in deficient patients only: the benefit of supplementation is usually seen in patients who were already low in that nutrient, so it may not help patients whose levels are already normal.

- Quality and regulation: like other supplement markets, TB-related nutraceutical products can vary a lot in quality, and there is a risk of exaggerated claims reaching patients through misinformation.

9. SUMMARY TABLE OF KEY NUTRACEUTICALS

Nutraceutical	What it is thought to do	How strong is the evidence
Vitamin D	Helps macrophages (immune cells) fight the TB bacteria better	Fairly good lab evidence; human trials show faster sputum clearance in patients who were deficient, but not proven to cut deaths or relapse
Vitamin A	Keeps the lung lining healthy and supports the immune response	Mixed results; seems to help mainly if the patient was already low in vitamin A
Zinc	Needed for immune cells like T-cells and neutrophils to work properly	Not consistent; correcting a deficiency may help, but giving it to everyone hasn't shown clear benefit
Selenium	Antioxidant that may reduce tissue damage from inflammation	Very limited TB-specific data so far
Vitamin C	Antioxidant, may support immune cell function	Mostly small/observational studies, not strong trial evidence
Omega-3 fatty acids	May lower excess inflammation in the lungs	Still early-stage; more research needed
Curcumin	Direct antibacterial action plus immune-boosting and liver-protecting effects	Promising in animal/lab studies; poor absorption in the body is a big problem, nano-formulations being tested
Probiotics	May reduce stomach-related side effects of TB drugs	Very early evidence, not much clinical data yet

10. WHAT FUTURE RESEARCH SHOULD FOCUS ON

Going forward, a few things seem important. First, we need larger, well-designed clinical trials with standard doses and outcomes that actually matter, like relapse rate, death rate, or time taken for sputum to become culture-negative — especially for the more promising options like vitamin D and curcumin. Second, future studies should try to identify which specific groups of patients (for example, those who are deficient, those with drug-resistant TB, or those with HIV co-infection) are most likely to actually benefit, instead of testing everyone as one group. Third, more work is needed on improving how compounds like curcumin are absorbed by the body, along with studies on whether these approaches are actually affordable and practical in high-burden countries. Lastly, even while this more specific research is ongoing, health systems should keep investing in basic nutrition support and screening as part of standard TB care, since this is where the evidence is already the strongest.

11. CONCLUSION

Nutrition and tuberculosis are closely tied together in a cycle where poor nutrition increases the risk and severity of TB, and TB in turn worsens a person's nutritional status. Nutraceuticals — including vitamin D and other micronutrients, plant compounds like curcumin, and probiotics — offer a reasonable, generally low-cost and low-risk way to support the immune system, reduce drug side effects, and make TB treatment a bit easier to get through. However, at this point in time, the evidence for most individual nutraceuticals is still early-stage or mixed. The clearest and most consistent benefit so far has not come from single supplements but from broader nutritional support given as part of TB care, as shown in large trials like RATIONS. Going forward, better clinical trials, more targeted use in patients who are actually deficient or high-risk, and continued work on improving absorption of promising compounds will be needed before nutraceuticals can become a standard part of TB treatment guidelines.

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