

# HASIL CEK\_Supplemental Efficacy

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## Supplemental Efficacy in Tuberculosis Patients: A Systematic Review

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### ABSTRACT

**Background:** Tuberculosis is a disease that continues to be a global issue because it contributes to high death and morbidity rates. To minimize the severity of tuberculosis, nutritional supplements should be given to tuberculosis patients. However, there are only a few studies in the literature that evaluate the impact of supplementation on overall clinical improvement in tuberculosis patients. This study aimed to update the current evidence of supplementation's clinical benefit for tuberculosis patients. **Method:** The databases Pubmed, Science Drive, and Sage were utilized to search for references to the publications included in this study. Following inclusion and exclusion extraction, seven of the 14,249 items discovered remained. **Result:** Six of the seven publications found that extra supplementation for tuberculosis patients led to clinical improvement, while one article found no benefit. Vitamin D1000IU, Vitamin D5000IU, Vitamin D2, *Channa striata* extraction, Calcitrol supplements, *Baihe gujin* (traditional herbs), and probiotic *Lactobacillus casei* are just a few of the supplements included in these seven pieces. **Conclusion:** Supplements can be given to tuberculosis patients in conjunction with anti-tuberculosis therapy because they have been shown to be effective in providing clinical improvement in patients, but their effectiveness is dependent on the type and dose given.



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### Introduction

Tuberculosis cases were recorded in Southeast Asia (43%), Africa (25%), and the West Pacific (18%) in 2020. Out of the 30 countries that contribute the most to tuberculosis worldwide, eight countries account for two-thirds of the total, with India accounting for 26%, China 8.5%, Indonesia 8.4%, the Philippines 6.0%, Pakistan 5.8%, Nigeria 4.6%, Bangladesh 3.6%, and South Africa 3.3% [4]. A significant close relationship was discovered between nutritional deficiencies and the incidence of tuberculosis. Patients with tuberculosis often have poor nutritional status [8].

Several previous literature reviews have indicated that neuropathy prevention in tuberculosis patients can be achieved through the administration of additional micronutrients, such as vitamin B6 [17]. In addition, previous studies utilizing systematic reviews and meta-analyses to evaluate the efficacy and safety of vitamin D supplements in tuberculosis patients concluded that vitamin D had no impact on the improvement of tuberculosis patients [26]. Although several additional supplements for clinical improvement in tuberculosis patients have been studied by previous



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researchers, only specific micronutrient and macronutrient supplements like vitamin D and vitamin B6 have been discussed [7,16,19]. While many previous studies have examined the effectiveness of various types of supplements. For example, the addition of *Channa striata* extract supplements, which are snakehead fish extracts, supplementation of a type of probiotic containing the *Lactobacillus casei* strain known in *Yakult* packaged beverages, and additional supplementation of herbal plants for clinical improvement in tuberculosis patients [13,14,21]. Therefore, the purpose of this study was to update the existing evidence of supplementation's clinical efficacy for tuberculosis patients.

## Materials and Method

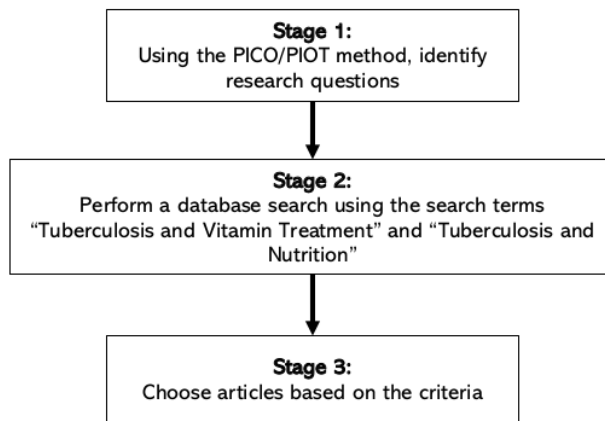
The research was conducted utilizing a systematic literature review approach, with data collected systematically by identifying, evaluating, and interpreting all findings to answer research questions (Table 1). Modeling a clinical question form known as PICO/PIOT, which is used to answer research questions, is the first step in the research process. P=patient/population/problem, I=intervention/prognostic factor/Issue, C=comparison/intervention, and O=outcome/result. Following the PIOT method, a research question was developed to carry out this systematic review: *is there any clinical improvement in patients with tuberculosis who are given additional supplementation?*

**Table 1.** Research Questions Using PIOT/PICO

PICO	Explanation
Population (P)	All patients with tuberculosis are receiving anti-tuberculosis medication with supplements and/or vitamins
Issue (I)	Is there any clinical improvement in patients with tuberculosis who receive additional supplementation?
Outcome (O)	Patient recovery/clinical advancement
Type Of Study (T)	RCT, Case-Control, Cohort, Experimental study

## Database keyword search phases

The keywords "tuberculosis and vitamin treatment" and "tuberculosis and nutrition" were used to search three databases (Pubmed, Direct research, and Sage) for publications published between 2018 and 2022 with the keywords "tuberculosis and vitamin treatment" and "tuberculosis and nutrition." Articles that could be accessed, additional intervention research, research designs using RCTs, case-control, cohort, and experimental studies, and study subjects who had been diagnosed with tuberculosis were used as criteria for inclusion. Articles that use a literature review, case report, cross-sectional, or descriptive research method are not allowed. Database keyword search procedures are shown in Figure 1.



**Figure 1.** Database Keyword Search Procedures

The original search yielded 14,249 articles, which were reduced by 1 to 14,248 articles. The remaining 3,503 articles and 24 publications that met the research design criteria were omitted because they could not be obtained. Studies that met the following inclusion criteria were included: they were published in English, were available in full text, were submitted via digital media platforms, and had sufficient data; then, we found as many as 10,745 articles. Seventeen studies were removed because the study participants did not have tuberculosis, and there was no extra supplemental medication; the remaining seven articles were included in this analysis (Figure 2).

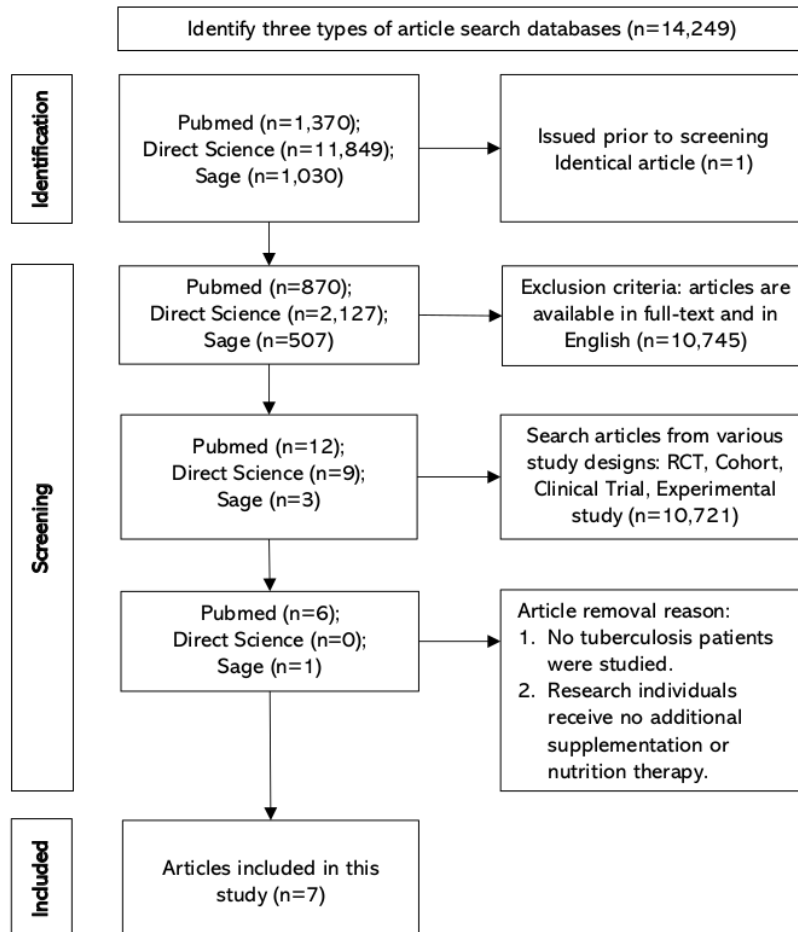


Figure 2. Articles Search Databases

## Results and Discussion

### Results

The subjects in the seven articles were tuberculosis patients undergoing anti-tuberculosis treatment (control group), and patients undergoing anti-tuberculosis treatment and supplementation (case group) (Table 2). Males and females varied from 6 to 65 years of age. Four articles incorporate Body Mass Index characteristics (BMI), one article made use of the nutritional status measurement and 1 other article did not include body mass index characteristics [2, 6, 13, 14, 23, 25]. Three articles measured serum vitamin levels [2, 23, 27]. While four other articles did not [2, 6, 13, 14]. Blood tests, chest X-rays, sputum culture, lung function, vitamin levels, and tuberculosis symptom

scoring were performed on subjects before and after the study, as shown in Table 3. There are only three articles that report on the findings of research on supplement side effects (Table 4.1; Table 4.2) [2, 25, 27].

**Table 2.** Summary of Searching Article

Authors	Evaluation of success criteria for adding supplements							Assess side effect	Treatment status
	Blood test	Sputum test	BMI	Vitamin test	Thorax test	Lung performance	symptoms		
Wen et al.,2022 [15]	√	√	x	√	√	x	√	√	It reduced sputum culture conversion time and chest X-ray lesions.
Tamara et al.,2022 [13]	x	√	√	√	x	x	√	x	Vitamins reduce discomfort and boost nutrition.
Ma'rufi et al., 2022 [8]	x	x	√	x	x	x	x	x	Supplement users gained weight
Ge and Zhu, 2020 [14]	√	x	x	x	x	√	√	x	<i>Baihe gujin</i> supplements alleviate symptoms and safeguard kidney function.
Bekele et al., 2018 [12]	√	√	√	√	x	x	√	√	Increased vitamin D and reduced TB symptoms.
Lan Jiang et al., 2022 [9]	√	x	x	x	x	x	x	x	In tuberculosis, probiotics suppress inflammatory cytokines.
Wallis et al., 2021 [11]	x	√	x	x	x	√	x	√	Lung function was unchanged and side effects required additional study.

**Table 3.** Evaluation of Success Criteria for Adding Supplements

Authors	Type of supplement	Side effect	Note
Wen et al., 2022 [15]	Calcitriol	Increased uric acid 20 (66.7%), nausea and reflux 11 (33.3%)	Symptomatic therapy reduces mild side effects.
Bekele et al., 2018 [12]	VitD3+PBA	Anemia (5(2.8), night sweats (3(1.7), and breast abscess (1(0.6)) were all greater than placebo.	Other side effects such as chest pain, dyspnea, numbness, flank pain, arthralgia, and skin rash were found to be less than placebo.
Wallis et al., 2021 [11]	Ergocalciferol	Side effects 210th day after the onset of tuberculous spondylitis	Side effect is regarded as a paradoxical reaction to treatment (the cause is unknown)

## Discussion

Four journals used Vitamin D supplements as research trial materials, while three other studies used traditional Chinese, probiotic probiotics *Lactobacillus casei*, and *Channa striata* extract (contains snakehead fish) [2, 6, 13, 14, 23, 25, 27].

According to the prevalence of tuberculosis patients who suffer more vitamin D deficit than the group without tuberculosis, vitamin D deficiency is linked to the incidence of tuberculosis [24]. Furthermore, vitamin D deficiency in tuberculosis patients results in higher levels of sputum smears

**Table 4.1** Observed Adverse Effects in Supplement studies

Authors (year)	Country	Study design	Age sample	Sample size	Supplement	Dose	Follow up	The effect of adding supplements
Tamara et al., 2022 [13]	Indonesia	RCT	Median (min-max) 9.1 (6-16.8)	Sample size for placebo = 40, Vit D = 40	Vitamin D	Vitamin D 1000IU daily while on standard anti-tuberculosis medication	symptom assessment weekly, anthropometric measurements six months after therapy, and nutritional status measurements monthly throughout therapy	Fever length 2 weeks median/range (1-3), cough duration 2 weeks median/range (1-6), increased vitamin D compared to placebo, before intervention median 21.7 range 20-28.3, after intervention median 13.4 range 10.2-21.5 (p<0.001). Improved nutritional status compared to placebo: z score for median age/range 0.5 (-0.62-1.7), z_score for body weight 0.79 (0.15-1.8), z_score for height and weight 0.7 (0.15-1.8) (0.13-1.22)
Ma' ruf et al., 2020 [8]	Indonesia	RCT	Age ranged: <20 (7.22); 20-29 (16.49); 30- samples of treatment, supplement 39 (17.53); 40-49 (19.59); >50 (39.18)	A total sample of 200, the case group received 103 (16.49); 30-samples of treatment, supplement 39 (17.53); and the control group 97 respondents	<i>Chianna striata</i> extract	500mg for 4 weeks of study	0-4 weeks	Supplement group BMI increase: week 0: mean 17.43 16.82-18.04 CI 95%; week 1: 17.65 17.05-18.24 95%; week 2: 17.90 17.28-18.47 95%; week 3: 18.04 17.44-18.64 95%; week 4: 18.22 17.62-18.82 95%; overall P value = 0.000.
Lan et al., 2022 [9]	Cina	RCT	Low dose: 26.1 (SD=10.8) High dose: 26.1 (SD=10.6)	Sample for control group = 15, low dose = 16, high dose = 16	<i>L. casei</i> strain probiotic supplement bottles) daily for 4 weeks of anti-tuberculosis treatment.	1x10 <sup>10</sup> CFU (1 bottle) and 2x10 <sup>10</sup> CFU (2 supplement bottles) daily for 4 weeks of anti-tuberculosis treatment.	Over 4 weeks	The high-dose group had more white blood cells and fewer inflammatory cytokines than the other groups: white blood cell count (109/L) 6.16 (4.39, 7.51; p value= 0.580); neutrophil count 3.34 (2.47, 4.63; p value= 0.733); lymphocyte count 1.91 (1.42, 2.35; p value= 0.210); monocyte count 0.55 (0.43, 0.67; p value= 0.798); eosinophil count 0.10 (0.06, 0.23; p value= 0.113)
Ge and Zhu, 2020 [14]	Cina	RCT	Mean ± SD= 63.1 ± 12.1	Anti-tuberculosis treatment included 58 participants, whereas combined treatment had 42.	<i>Baihe Gujjin</i> stew	Baihe Gujjin decoction 200 ml orally daily for 6 months.	2-4 weeks after treatment	Cough symptom mean ± SD 38.8 ± 4.1; Mean ± SD from Negative sputum after 2 weeks of treatment= 85.5 ± 0.4; Mean ± SD_Breathless = 3.6 ± 1.3; Mean ± SD_chest pain= 3.1 ± 0.9; Mean ± SD from Leukocytes 4 weeks after therapy = 6.9± 1.5; Hb 4 weeks after therapy=127.3 ± 7.0; Creatinine after 4 weeks of therapy= 74.7 ± 6.1 a.b; TNF-α 2 weeks after therapy = 123.12±8.56; When compared to the control group, symptoms, white blood cells, creatinine levels, and cytokine markers all decreased.



Table 4.2 Observed Adverse Effects in Supplement studies

Authors (year)	Country	Study design	Age sample	Sample size	Supplement	Dose	Follow up	The effect of adding supplements
Wen et al., 2022 [15]	Cina	RCT	Mean $\pm$ SD= 56.7 $\pm$ 14.0; Nilai p <0.05	90 participants were included in the following groups: a) Normal-25(OH)D=30; Low-25(OH)D=30; Low-25(OH)D-Calcirol=30.	Calcirol	The 0.25 $\mu$ g bid dose was stopped when the 25-(OH) D level reached normal levels ( $\geq$ 75 nmol/L)	Weeks 1,4,2 month,6 months after therapy	Results after 6 months of therapy: Sputum culture 3.20 $\pm$ 1.35; 50% lesion absorbed 7.38 $\pm$ 1.47; chest cavity pictures missing 29 (96.7%). The low 25-(OH)D group that underwent calcirol therapy performed similarly to the normal group. Calcirol boosted CD4+ T cell counts more than placebo.
Bekele et al., 2018 [12]	Ethiopia	RCT	Mean= 0.31	150 vitamin D3+PBA and 146 placebo participants completed the research.	Vitamin D3 +PBA	5000 IU vitamin D3 (5 tablets/day) and 500 mg PBA (1x2 tablets); placebo vitamin D3 and placebo PBA.	Symptoms = 0-8th week; Modified TB score = 0,4,8,16, and 24; Sputum microscopy = 0-4, and 8; TB = weeks 0-8; Vitamin D3 levels and chest X-rays are 0,4,8,16, and 24.	Week 8: -0.93 to -0.10; week 16: -0.65 to 0.00. In the therapy group, severe tuberculosis symptoms decreased significantly. The primary TB score reduced at week 8 (p-value = 0.005) while the modified tuberculosis score fell at weeks 8 and 16. Sputum-positivity (mITT) week 4 OR 0.49; 95% CI = 0.037-8. Low plasma 25(OH)D3 improved at week 4 (mean 38.6 vs 91.5 nmol/l) compared to placebo. Week 8 (38.4 vs 109.4 nmol/l) and week 16 (4.4 nmol/l vs 92.7nmol) mean values
Wallis et al., 2021 [11]	Afrika	RCT	Mean 37 (29-49)	Completed study participants: 1) Control = 18; 2) CC-11050 = 18; 3) Everolimus = 21; 4) Auranofin = 21; 5) Ergocalciferol (vitamin D group) = 20.	Ergocalcifero 1 (Vit D)	vitamin D 5 mg on day 1, 2.5 mg on days 28 and 56.	Day 0,1,7,14,21,28,35,42, 56,84,112,140,180 sputum culture. Spirometry on days 1,14,28,56,84,112,140, and 180 more to 540.	On the 28th day, the sputum culture results showed no difference between groups: number of hazards 37, day 56 amount of risk 30, day 84 amount of risk 15, day 112 amount of risk 6, day 140 amount of risk 1, and day 180 amount of risk 0. Pulmonary function test FEV1% day 56 - amount of risk 0. Pulmonary function test FEV1% day 180 2.28% mean (-9.65 to 4.00) 95% CI value p 0.42, day 180 0.61% mean (-5.64 to 6.86) p-value 0.85, day 540th - 0.52% mean (-9.91 to 8.87) p-value 0.91, and FVC/L day 56 -0.05 mean (-0.29 to 0.20) p-value 0.72, day 180 - 0.04 mean (-0.31 to 0.23) p-value 0.78, and day 540 - 0.14 mean (-0.55 to 0.28) FVC, L had worse pulmonary function than other groups

as well as more extensive lung lesions, indicating the severity of the disease [11]. Vitamin D is a fat-soluble vitamin that can be obtained from the sun or foods such as egg yolks, liver, butter, and fish oil. Vitamin D is absorbed by the skin (from sunshine), processed in the liver, and excreted in the kidneys before it can be carried in the blood and released to have its full effect on the body [3]. Vitamin D receptors, CYP27B1 enzymes, and CYP24A1 enzymes are required for vitamin D metabolism, which is influenced by inflammatory mediators in immune cells and epithelial cells. Serum 25 (OH) 2 D levels in the body can be influenced, particularly by cigarette smoke and the inflammatory cytokines TNF- $\alpha$ , IL-1 $\beta$ , IL-17A, and TGF $\beta$ 1 [20]. Activating macrophages and monocytes, and regulating the development of antigen-presenting cells and natural killer cells, which are used to combat viruses and bacteria, are just a few of the functions of vitamin D in the body in addition to maintaining bone health. [5].

*Lactobacillus casei* is a type of good bacteria that can be found in a variety of foods. *Lactobacillus casei* has the ability to control the expression of cytokines such as interleukin-6, interleukin-12, and interferon-g [15]. According to a prior study, *Lactobacillus casei* increases the activity of macrophages, which lowers the risk of infection [18]. *Lactobacillus casei* has been shown to prevent elderly weight loss by producing organic acids in the digestive system that convert fiber into energy-producing substances [10]. A database search on the effects of probiotics revealed that they could provide health benefits such as lowering the risk of heart disease, acting as an anti-carcinogen, and lowering the risk of sepsis and lung infections, making probiotics a therapeutic option in the future [30]. Furthermore, previous research using prebiotic and antibiotic-treated rats found that they reduced interleukin-1 $\alpha$  serum levels compared to the control group and also protected the balance of digestive tract microorganisms after antibiotic therapy [31].

Snakehead fish called *Channa striata*, which inhabits fresh water, has 70% protein [12]. This fish has a lot of protein, which helps wounds heal, and has anti-inflammatory and fever-reducing effects. (Snakehead Fish (*Channa striata*) and Its Biochemical Properties for Therapeutics and Health Benefits, 2018). *Baihe gujin* is a traditional Chinese medicine that is used to cure lung problems. It is composed of many herbal plants, including *Lilii bulbis*, *Ophiopogonis radix*, *Rehmannio viride radix*, *Rehmannia praep radix*, *Paeonia alba radix*, *Fritillariae cirrhosae bulbis*, *Platycodi radix*, *Scrophulariae*. It has been demonstrated that *Ophiopogonis radix* is widely utilized in conjunction with contemporary therapy to cure tuberculosis [29]. Numerous ingredients found in conventional medicines have been found to have biological effects on the body, such as anti-inflammatory and anti-cancer capabilities [28]. In pulmonary fibrosis research on rats, *Lilii bulbis* was discovered to have an anti-inflammatory and pro-macrophage impact [1].

Ferulic sodium is one of the parts of this herb. Previous research findings on mice have shown that ferulic acid has an anti-inflammatory effect and speeds up the healing process [32]. One of the components of this herb, angelica sinensis clam root, stimulated the immune system's helper T cells and promoted macrophages' production of IL-2, IL-4, IL-6, and interferon- $\gamma$  [9].

Several weaknesses were acknowledged in this study: first, small doses of vitamins did not affect patients; second, the treatment group received a mixture of vitamins; third, the number of samples was insufficient; and fourth, numerous articles failed to mention any negative effects. However, some of the strengths of this article are as follows: first, the supplements in the article are more diverse; second, the supplements or additional nutrients that are used can be easily obtained, such as good fish (*Channa striata* extract) and *Lactobacillus casei* found in *Yakult* packaged drinks; and third, the age characteristics of the population in the article are more diverse, so that additional supplementation can be used by more than one age group. Therefore, we argue that this article's findings can be applied to tuberculosis patients.

## Conclusion

According to the results of this comprehensive review study, adding supplements to the regimens of patients with tuberculosis provided variable degrees of clinical benefit. The dosage and kind of supplement used will determine how well it works when added. It is envisaged that numerous researchers will carry out studies on supplemental or supplementary nourishment for tuberculosis patients, particularly dietary supplements or herbal plants that are simple to obtain.



### Declaration

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**Conflicts of Interest:** We affirm that we do not compete with anyone's interests.

### References

- Ahn, J., Joo, H., Park, J., Park, J.-W., Kim, K.-I., Jung, H.-J., Bu, Y., & Lee, B.-J. The Effects of Lung-Moistening Herbal Medicines on Bleomycin-Induced Pulmonary Fibrosis Mouse Model. *Processes*, 2020 8(1), 102. <https://doi.org/10.3390/pr8010102>
- Mazur A, Koziorowska K, Dynarowicz K, Aebisher D, Bartusik-Aebisher D. Vitamin D and Vitamin D3 Supplementation during Photodynamic Therapy: A Review. *Nutrients*. 2022 Sep 15;14(18):3805. doi: 10.3390/nu14183805. PMID: 36145180; PMCID: PMC9502525.
- Buonsenso D, Pata D, Turriziani Colonna A, Ferrari V, Salerno G, Valentini P. Vitamin D and tuberculosis in children: a role in the prevention or treatment of the disease? *Monaldi Arch Chest Dis*. 2022 Mar 30;92(4). doi: 10.4081/monaldi.2022.2112. PMID: 35352542.
- Chakaya, J., Petersen, E., Nantanda, R., Mungai, B. N., Migliori, G. B., Amanullah, F., Lungu, P., Ntouni, F., Kumarasamy, N., Maeurer, M., & Zumla, A. The WHO Global Tuberculosis 2021 Report – not so good news and turning the tide back to End TB. *International Journal of Infectious Diseases*, 2022 124, S26–S29. <https://doi.org/10.1016/j.ijid.2022.03.011>
- Charoenngam, N., & Holick, M. F. Immunologic Effects of Vitamin D on Human Health and Disease. *Nutrients*, 2020 12(7), 2097. <https://doi.org/10.3390/nu12072097>
- Ge, H.-B., & Zhu, J. Clinical efficacy of Baihe Gujin decoction combined with anti-tuberculosis therapy for pulmonary tuberculosis with Yin-deficiency and Fire-hyperactivity syndrome. *Journal of International Medical Research*, 2020 48(5), 030006051987553. <https://doi.org/10.1177/0300060519875535>
- Ganmaa D, Uyanga B, Zhou X, Gantsetseg G, Delgerekh B, Enkhmaa D, Khulan D, Ariunzaya S, Sumiya E, Bolortuya B, Yanjmaa J, Enkhsetseg T, Munkhzaya A, Tunsag M, Khudyakov P, Seddon JA, Marais BJ, Batbayar O, Erdenetuya G, Amarsaikhan B, Spiegelman D, Tsolmon J, Martineau AR. Vitamin D Supplements for Prevention of Tuberculosis Infection and Disease. *N Engl J Med*. 2020 Jul 23;383(4):359-368. doi: 10.1056/NEJMoa1915176. PMID: 32706534; PMCID: PMC7476371.
- Benjumea-Bedoya D, Marín DM, Robledo J, Barrera LF, López L, Del Corral H, Ferro BE, Villegas SL, Díaz ML, Rojas CA, García LF, Arbeláez MP. Risk of infection and disease progression in children exposed to tuberculosis at home, Colombia. *Colomb Med (Cali)*. 2019 Dec 30;50(4):261-274. doi: 10.25100/cm.v50i4.4185. PMID: 32476692; PMCID: PMC7232949.
- Firdaus FZ, Skwarczynski M, Toth I. Developments in Vaccine Adjuvants. *Methods Mol Biol*. 2022;2412:145-178. doi: 10.1007/978-1-0716-1892-9\_8. PMID: 34918245.
- Ishikawa, H., Mutoh, M., Yoshimura, K., Fujii, G., Nakamura, T., Takeshita, T., Wakabayashi, K., & Sakai, T. Very Long-Term Treatment with a Lactobacillus Probiotic Preparation, Lactobacillus Casei Strain Shirota, Suppresses Weight Loss in the Elderly. *Nutrients*. 2020 12(6), 1599. <https://doi.org/10.3390/nu12061599>
- Jaimni, V., Shasty, B. A., Madhyastha, S. P., Shetty, G. V., Acharya, R. V., Bekur, R., & Doddamani, A. Association of Vitamin D Deficiency and Newly Diagnosed Pulmonary Tuberculosis. *Pulmonary Medicine*, 2021, 1–6. <https://doi.org/10.1155/2021/5285841>
- Karnila, R., Edison, Suharman, I., Sidauruk, S. W., & Mahardika, N. Nutritional Characteristics of Protein Isolated from Snakehead (*Channa striata*) Using the pH-Shift Method. *IOP Conference Series: Earth and Environmental Science*, 2020 430(1), 012004. <https://doi.org/10.1088/1755-1315/430/1/012004>
- Lan Jiang, Jinyu Wang, Lei Xu, Jing Cai, Shanliang Zhao, & Aiguo Ma. Lactobacillus casei modulates inflammatory cytokines and metabolites during tuberculosis treatment: A post hoc randomized controlled trial. *Asia Pacific Journal of Clinical Nutrition*, 2022 31(1). [https://doi.org/10.6133/apjcn.202203\\_31\(1\)0008](https://doi.org/10.6133/apjcn.202203_31(1)0008)
- Ma'rufi, I., Ali, K., Jati, S. K., Sukmawati, A., Ardiansyah, K., & Ningtyias, F. W. Improvement of Nutritional Status among Tuberculosis Patients by *Channa striata* Supplementation: A True Experimental Study in Indonesia. *BioMed Research International*, 2020, 1–9. <https://doi.org/10.1155/2020/7491702>
- Minervini, F., & Calasso, M. Lactobacillus casei Group. In P. L. H. McSweeney & J. P. McNamara (Eds.), *Encyclopedia of Dairy Sciences* (Third Edition) 2022 (pp. 275–286). *Academic Press*. <https://doi.org/10.1016/B978-0-08-100596-5.00853-2>
- Patti, G., Pellegrino, C., Ricciardi, A., Novara, R., Cotugno, S., Papagni, R., Guido, G., Totaro, V., De Iaco, G., Romanelli, F., Stolfi, S., Minardi, M. L., Ronga, L., Fato, I., Lattanzio, R., Bavaro, D. F., Gualano, G., Sarmati, L., Saracino, A., ... Di Gennaro, F. (2021a). Potential Role of Vitamins A, B, C, D and E in TB Treatment and Prevention: A Narrative Review. *Antibiotics*, 10(11), 1354. <https://doi.org/10.3390/antibiotics10111354>
- Setyawan, D.A., & Wiwik S. Spatial Distribution of Dengue Hemorrhagic Fever (DHF) Cases in Sragen. *Dis. Prev. Pub. Heal. J*, 2021 15 (1). <https://doi.org/10.12928/dpphj.v15i1.2178>
- Rocha-Ramirez, L. M., Hernández-Ochoa, B., Gómez-Manzo, S., Marcial-Quino, J., Cárdenas-Rodríguez, N., Centeno-Leija, S., & García-Garibay, M. Impact of Heat-Killed Lactobacillus casei Strain IMAU60214 on the Immune Function of Macrophages in Malnourished Children. *Nutrients*, 2020 12(8), 2303. <https://doi.org/10.3390/nu12082303>
- Safitri, E. A., Siagian, P., Sinaga, B. Y. M., & Eyanoe, P. C. Vitamin C Supplementation Improves Pulmonary Tuberculosis Patients' Sputum Conversion During Intensive Phase Category I Treatment in Medan. *Respiratory Science*, 2022 2(2), Article 2. <https://doi.org/10.36497/respirsci.v2i2.30>
- Schrumpf, J. A., van der Does, A. M., & Hiemstra, P. S. Impact of the Local Inflammatory Environment on Mucosal Vitamin D Metabolism and Signaling in Chronic Inflammatory Lung Diseases. *Frontiers in Immunology*, 2020 11, 1433. <https://doi.org/10.3389/fimmu.2020.01433>
- Getachew S, Medhin G, Asres A, Abebe G, Ameni G. Traditional medicinal plants used in the treatment of tuberculosis in Ethiopia: A systematic review. *Heliyon*. 2022 May 18;8(5):e09478. doi: 10.1016/j.heliyon.2022.e09478. PMID: 35647341; PMCID: PMC9130528.
- Prachom N, Yuangsoi B, Pumnuan J, Ashour M, Davies SJ, El-Haroun E. Effects of Substituting the Two-Spotted Cricket (*Gryllus bimaculatus*) Meal for Fish Meal on Growth Performances and Digestibility of Striped Snakehead (*Channa striata*) Juveniles. *Life (Basel)*. 2023 Feb 20;13(2):594. doi: 10.3390/13020594. PMID: 36836949; PMCID: PMC9962915.

23. Tamara, L., Kartasasmita, C. B., Alam, A., & Gurnida, D. A. Effects of Vitamin D supplementation on resolution of fever and cough in children with pulmonary tuberculosis: A randomized double-blind controlled trial in Indonesia. *Journal of Global Health*, 2022 12, 04015. <https://doi.org/10.7189/jogh.12.04015>
24. Chang SW, Lee HC. Vitamin D and health - The missing vitamin in humans. *Pediatr Neonatol*. 2019 Jun;60(3):237-244. doi: [10.1016/j.pedneo.2019.04.007](https://doi.org/10.1016/j.pedneo.2019.04.007).
25. Wallis, R. S., Ginindza, S., Beattie, T., Arjun, N., Likoti, M., Edward, V. A., Rassool, M., Ahmed, K., Fielding, K., Ahidjo, B. A., Vangu, M. D. T., & Churchyard, G. Adjunctive host-directed therapies for pulmonary tuberculosis: A prospective, open-label, phase 2, randomised controlled trial. *The Lancet Respiratory Medicine*, 2021 9(8), 897-908. [https://doi.org/10.1016/S2213-2600\(20\)30448-3](https://doi.org/10.1016/S2213-2600(20)30448-3)
26. Suffeld CR, Mugusi F, Muhihi A, Aboud S, Nagu TJ, Ulenga N, Hong B, Wang M, Fawzi WW. Efficacy of vitamin D3 supplementation for the prevention of pulmonary tuberculosis and mortality in HIV: a randomised, double-blind, placebo-controlled trial. *Lancet HIV*. 2020 Jul;7(7):e463-e471. doi: [10.1016/S2352-3018\(20\)30108-9](https://doi.org/10.1016/S2352-3018(20)30108-9). PMID: 32621874; PMCID: PMC7433214.
27. Wen, Y., Li, L., & Deng, Z. Calcitriol supplementation accelerates the recovery of patients with tuberculosis who have vitamin D deficiency: A randomized, single-blind, controlled clinical trial. *BMC Infectious Diseases*, 2022 22(1), 436. <https://doi.org/10.1186/s12879-022-07427-x>
28. Xie, R., Song, Z., Xu-shao, L., Huang, J., Zhao, T., & Yang, Z. The mechanism of Bai He Gu Jin Tang against non-small cell lung cancer revealed by network pharmacology and molecular docking. *Medicine*, 2022 101(52), e32555. <https://doi.org/10.1097/MD.00000000000032555>
29. Xu, Y., Dai, G., Tang, S., Yang, H., & Sun, Z. Changes of Anti-tuberculosis Herbs Formula During Past Three Decades in Contrast to Ancient Ones. *Chinese Journal of Integrative Medicine*, 2021 27(5), 388-393. <https://doi.org/10.1007/s11655-020-3475-y>
30. Yadav, M. K., Kumari, I., Singh, B., Sharma, K. K., & Tiwari, S. K. Probiotics, prebiotics and synbiotics: Safe options for next-generation therapeutics. *Applied Microbiology and Biotechnology*, 2022 106(2), 505-521. <https://doi.org/10.1007/s00253-021-11646-8>
31. Yao, G., Cao, C., Zhang, M., Kwok, L.-Y., Zhang, H., & Zhang, W. Lactobacillus casei Zhang exerts probiotic effects to antibiotic-treated rats. *Computational and Structural Biotechnology Journal*, 2021 19, 5888-5897. <https://doi.org/10.1016/j.csbj.2021.10.026>
32. Lv Y, Wang Y. Chemical constituents from *Oldenlandia diffusa* and their cytotoxic effects on human cancer cell lines. *Nat Prod Res*. 2023 Feb;37(3):397-403. doi: [10.1080/14786419.2021.1974434](https://doi.org/10.1080/14786419.2021.1974434). Epub 2021 Dec 22. PMID: 34933627.

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