

Review Article

Vitamin B12 in Modern Therapeutics: Emerging Applications and Clinical Benefits Review

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Abstract

An indispensable micronutrient with clear roles in DNA synthesis, erythropoiesis, and neurological activity is vitamin B12 (cobalamin). Emphasizing its mechanisms of action, clinical benefits, and challenges in modern therapeutics, this review explores the expanding therapeutic uses of vitamin B12. Recent research shows that it can have uses other than only filling in for shortages. It may also protect neurons, lower inflammation, and control chronic disorders including diabetic neuropathy, Parkinson's disease, and multiple sclerosis. Because it promotes one-carbon metabolism, methylation events, and energy generation in the mitochondria, vitamin B12 helps heal. It has been shown to reduce side effects from chemotherapy, control glycemic control in those with diabetes, and treat dermatological disorders including vitiligo and eczema. Still, barriers including bioavailability issues, malabsorption syndromes, and disagreement on ideal dosing levels limit its broad use. Although vitamin B12 is usually considered safe, concerns about too high supplementation and its long-term effects remain not sufficiently investigated. This review points to research gaps including the need for more study on gene-nutrient interactions, the need of customizing dosage, and the long-term effects of high supplement intake. The most current data showing the need for vitamin B12 in modern medicine is gathered in this review. It also supports more studies to find the best uses for different patient groups.

Keywords: Vitamin B12, Cobalamin, Therapeutic Applications, Experimental Applications, DNA synthesis, Homocysteine

Introduction

Background on Vitamin B12 (Cobalamin): Vitamin B12, sometimes known as cobalamin, is essential for many physiological activities including DNA synthesis, erythropoiesis, and neurological function¹. Structurally one of the most complex vitamins, vitamin B12 is defined by a cobalt ion at its core surrounded by a corrin ring (**Fig.1**) and it is water soluble.

Its unusual arrangement allows involvement in two important chemical reactions: methylmalonyl-CoA mutase converts homocysteine to succinyl-CoA², and methionine synthase converts homocysteine to methionine. Energy generation, nucleotide synthesis, and the preservation of myelin sheaths in the nervous system all depend on these reactions³. Not produced by plants, vitamin B12 is mostly found in animal-derived foods, including meat, fish, eggs, and dairy products⁴. Starting in the stomach, absorption proceeds in several phases where gastric acid and intrinsic factor (IF) help the ileum to absorb them².

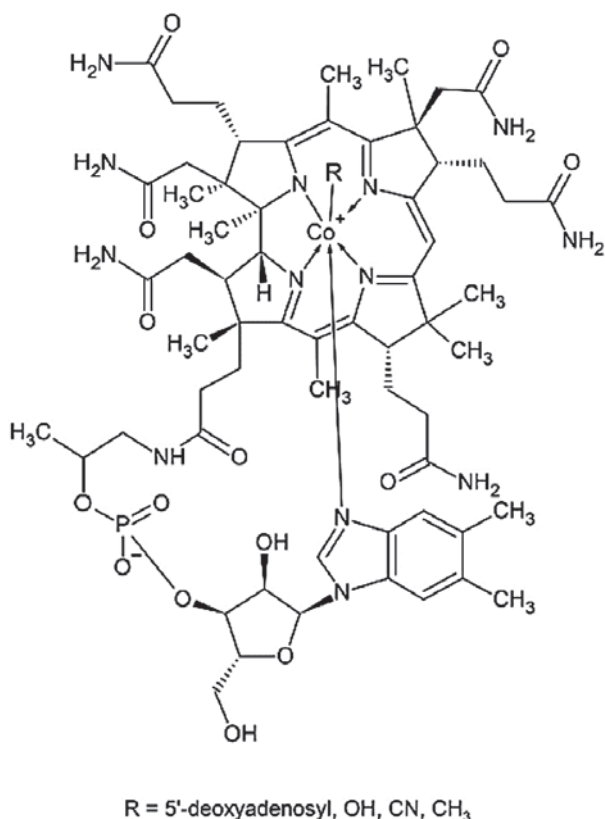


Figure 1: The chemical structure of vitamin B12.

Significance in Metabolism, DNA Synthesis, and Neurological Function: The biologically active form

of vitamin B12, holotranscobalamin (holoTC), helps it to be delivered to cells all around the body by binding with transcobalamin II in the bloodstream. Cellular metabolism, particularly the synthesis of DNA and RNA, depends on vitamin B12. It facilitates the reactivity of methionine synthase in activating tetrahydrofolate, a required molecule in nucleotide synthesis³. Inadequate vitamin B12 lowers DNA replication, leading to megaloblastic anaemia and other haematological issues². Moreover, vitamin B12 is essential for neurological activity since it helps myelin sheaths preserve and synthesize neurotransmitters. A deficit can lead to peripheral neuropathy as well as subacute combined degeneration of the spinal cord cognitive decline¹.

Historical Perspective: Vitamin B12 has therapeutic use going back to early in the 20th century; Sobczyńska-Malefora et al.² first identified it as the "anti-pernicious anaemia factor". Discovering vitamin B12 changed the course of treatment for pernicious anaemia, a fatal condition marked by megaloblastic anaemia and neurological damage. Before being injected with pure vitamin B12, the raw liver was used for treatment¹. It is used to treat a wider spectrum of diseases including neuropathies, cognitive disorders, and even psychiatric illnesses as scientists have found more about its function in metabolism and neurology³.

Rationale for the Review: Vitamin B12 is important for treating deficits, but new studies show it can solve many health issues. Vitamin B12 may have therapeutic uses. It may protect neurons, lower inflammation, and help people with Parkinson's disease and multiple sclerosis¹. In these new therapeutic environments, we don't know how it works, the optimal dose, or its duration. Vitamin B12 deficiency is also rising, especially in the elderly, vegetarians, and malabsorption patients. So, it is crucial to explore all therapeutic options². This review intends to investigate the latest developments in vitamin B12 research, underline new therapeutic uses, and point up areas requiring more study to maximize its clinical use.

Recent Therapeutic Applications of Vitamin B12: Traditionally, deficiencies and related disorders including pernicious anaemia and neurological problems have been treated with vitamin B12. However, recent studies reported some therapeutic possibilities like the management of chronic diseases,

anti-inflammatory actions, and neuroprotection. We discuss the most current therapeutic uses of vitamin B12 in several clinical settings below.

1. Neuroprotection and Neurological Disorders

1.1 Multiple Sclerosis (MS): Vitamin B12 has shown successful implementation in treating demyelination and neurodegeneration-marked chronic autoimmune disease, multiple sclerosis. Studies revealed that this vitamin can reduce homocysteine levels, which are usually raised in MS sufferers and aggravate their condition. Additionally, it helps to repair myelin and lowers oxidative stress, slows the course of the disease, and improves neurological features^{5,6}.

1.2 Parkinson's Disease: Vitamin B12 has been looked at in Parkinson's disease in terms of lowering oxidative stress and enhancing mitochondrial activity. By reducing the plasma homocysteine level, vitamin B12 (mostly methylcobalamin) helps Parkinson's sufferers with their motor symptoms⁷⁻⁹.

1.3 Cognitive Decline and Alzheimer's Disease: By supporting methylation processes and lowering homocysteine levels, which are linked to cognitive decline and Alzheimer's disease, vitamin B12 is absolutely important for cognitive health. Often in conjunction with folate and vitamin B6, vitamin B12 supplements have been shown in clinical studies to slow cognitive decline and boost memory in elderly patients^{10,11}.

2. Anti-Inflammatory and Immunomodulatory Effects

2.1 Rheumatoid Arthritis: Because of its anti-inflammatory qualities, vitamin B12 has been investigated as an addition to rheumatoid arthritis medication. By consuming vitamin B12, rheumatoid arthritis sufferers may experience less pain and inflammation in their joints since it modulates the synthesis of cytokines and reduces oxidative stress¹².

2.2 Inflammatory Bowel Disease (IBD): Vitamin B12 malabsorption and deficiency have been linked to inflammatory bowel disease including ulcerative colitis and Crohn's disease. Research revealed that extra vitamin B12 to IBD sufferers has been shown to improve their health by reducing inflammation and improving the healing of mucosal surfaces^{1,2}.

3. Cardiovascular Health

3.1 Cardiovascular Disease and Hyperhomocysteinemia: Raised homocysteine levels have been linked to heart disease, stroke, atherosclerosis, and other cardiovascular diseases. Together with folate and vitamin B6, vitamin B12 reduces homocysteine levels and hence decreases the risk of cardiovascular events in high-risk populations³.

3.2 Heart Failures: Common in those with heart failure, vitamin B12 deficiency is associated with a poor prognosis. Presumably because of its involvement in energy metabolism and homocysteine reduction. Moreover, vitamin B12 supplements have also been shown to enhance cardiac function and lower hospitalisations for heart failure sufferers¹.

4. Mental Health and Psychiatric Illnesses

4.1 Depression and Anxiety: Serotonin and dopamine are synthesized from vitamin B12, which regulates mood and emotional well-being. Particularly in patients with deficient or suboptimal levels, clinical studies have reported that vitamin B12 supplementation can help to improve symptoms of depression and anxiety².

4.2 Psychosis and Schizophrenia: The study found that a deficiency of vitamin B12 has been linked to psychiatric illness including psychosis and schizophrenia. Supplements of vitamin B12 combined with other B vitamins have been shown in patients with schizophrenia to improve psychiatric symptoms and cognitive performance^{3,13}.

4.3 Autism Spectrum Disorder: A systematic review and meta-analysis reported that the subcutaneous injection of methylcobalamin (mB12) may improve ASD-related metabolic abnormalities and clinical symptoms¹⁴.

5. Chronic Pain and Neuropathy

Many studies have been carried out worldwide recently in search of substitutes for conventional analgesic medications to either replace them or at least shorten the length of drug therapy, thus minimizing their side effects¹⁵.

5.1 Diabetic Neuropathy: Investigated for its ability to control diabetic neuropathy, a common diabetes complication marked by nerve damage and chronic pain, is vitamin B12. Patients with diabetic neuropathy

have seen improved nerve conduction velocity and pain reduction by methylcobalamin, a bioactive form of vitamin B12¹⁶⁻¹⁸.

5.2 Chemotherapy-Induced Neuropathy: One crippling side effect of cancer treatment is chemotherapy-induced peripheral neuropathy (CIPN). Some research shows improvements in nerve function and pain relief by addition of vitamin B12 in the treatment plan that additionally prevents or lessens CIPN^{19,20}.

6. Fertility and Pregnancy

6.1 Female Fertility: By helping DNA synthesis and methylation processes, vitamin B12 is absolutely important for reproductive health. Recurrent pregnancy loss and infertility have been linked to a vitamin B deficiency. Therefore, in women with a deficiency, vitamin B12 supplements have been shown to increase fertility outcomes^{2,21,22}.

6.2 Pregnancy and Fetal Development: Both fetal brain development and the prevention of neural tube defects depend on vitamin B12. Adverse effects linked to maternal vitamin B12 deficiency during pregnancy have included low birth weight and preterm birth. Particularly in vegetarian and vegan mothers, vitamin B12 supplementation has been shown to improve mother and fetal health outcomes²³⁻²⁵.

7. Endocrine and metabolic diseases

Metabolic problems including type 2 diabetes and insulin resistance are closely associated with vitamin B12 deficiency. In diabetic patients, vitamin B12 supplements lowered homocysteine levels and improved glycemic control, according to a randomized controlled trial²⁶. Moreover, vitamin B12's advantages in controlling polycystic ovary syndrome (PCOS), especially in terms of metabolic and hormonal imbalance correction, especially in light of metabolic and hormonal imbalance²⁶.

8. Dermatological Reversals

In dermatology, especially in treating inflammatory skin disorders, topical vitamin B12 has shown promising performance in lowering the symptoms of psoriasis and eczema²⁷, presumably because of its function in melanin synthesis. Other studies showed

that vitamin B12 supplementation enhanced skin repigmentation in vitiligo sufferers^{28,29}.

9. Low back pain and Other Musculoskeletal pain

A double-blind, randomised, placebo-controlled study reported that intramuscular injection of vitamin B12 supplementation improved low back pain in lumbago sciatica or sciatic neuritis patients³⁰. An anti-inflammatory, antinociceptive, neuroprotective, and neuromodulating action on the descending pain system explains this effect³⁰⁻³². On pain relief in patients with knee osteoarthritis, a clinical trial looked at the effectiveness of vitamins B and E in concert with diclofenac. According to the study, adding vitamins B and E along with diclofenac might help osteoarthritis sufferers find better pain relief³³.

10. Acute and subacute herpetic neuralgia

In patients with subacute herpetic neuralgia and subacute ophthalmic herpetic neuralgia, studies reported that local methylcobalamin injections reduced pain and improved quality of life^{34,35}. In addition, vitamin B12 supplementation improved the quality of life for postherpetic neuralgia patients by reducing pain^{20,36}.

11. Temporomandibular disorders

A randomised clinical trial evaluating the orofacial pain and temporomandibular disorders (TMD) investigating the treatment efficacy of laser punctures coupled with vitamin B12 revealed that the combined laser and B12 group had the fastest pain relief by the fourth session³⁷.

12. Chronic Post-Thoracotomy Pain Syndrome (CPTPS)

Patients in a clinical trial provided with the pregabalin and methylcobalamin combination reported far less pain than those treated with diclofenac potassium. The pregabalin and methylcobalamin combination was found to be safe and effective for lowering CPTPS with low side effects and high patient compliance³⁸.

13. Aphthous Ulcers

Another clinical study looked at aphthous ulcers using vitamin B12 ointment. Compared to the placebo group, patients receiving vitamin B12 ointment showed a significant reduction in pain³⁹.

Experimental Uses of Vitamin B12: Animal Model Neuropathic Pain

The combined use of vitamin B12 with metformin reduced neuropathic pain in diabetic rats⁴⁰. Another study showed that vitamin B12 can improve the analgesic effects of opiates⁴¹ and nonsteroidal anti-inflammatory drugs (NSAIDs). Vitamin B12 significantly lowered the formalin-induced jerking frequency and flexing-licking duration, ultimately exhibiting antinociceptive effects when combined with ketorolac^{42,43}.

Conclusion

Previously used to prevent deficiencies, vitamin B12 is now used in endocrinology, dermatology, neurology, and oncology. Important mechanisms show their relevance in both cellular and systemic equilibrium. Recent studies show its potential in neuroprotection, modulation of inflammation, and management of chronic diseases, as well as supporting new clinical interventions. Still, problems with bioavailability, malabsorption syndromes, and different dosages call for more research. The growing prevalence of vitamin B12 deficiency, especially among elderly people, vegetarians, and those with gastrointestinal problems, emphasises the need to address these differences. Priority areas for the next studies would focus on improving bioavailability, looking at gene-nutrient interactions, and creating evidence-based supplementation programs. Long-term studies are needed to assess the safety and effectiveness of high-dose vitamin B12 in different populations.

Finally, vitamin B12 has a great medicinal value. A multidisciplinary study can fully realise its ability to improve health outcomes in different diseases. This review argues for the inclusion of vitamin B12 into modern therapeutic approaches to ensure that everyone can benefit from it.

References

1. Wolffenbuttel BH, Owen PJ, Ward M, Green R. Vitamin B₁₂. *BMJ*. 2023 Nov 20;e071725.
2. Sobczyńska-Malefora A, Delvin E, McCaddon A, Ahmadi KR, Harrington DJ. Vitamin B₁₂ status in health and disease: a critical review. *Diagnosis of deficiency and insufficiency – clinical and laboratory pitfalls*. *Crit Rev Clin Lab Sci*. 2021 Aug 18;58(6):399–429.
3. Green R, Allen LH, Bjørke-Monsen AL, Brito A, Guéant JL, Miller JW, et al. Vitamin B12 deficiency. *Nat Rev Dis Primer*. 2017 Jun 29;3(1):17040.
4. Watanabe F, Bito T. Vitamin B₁₂ sources and microbial interaction. *Exp Biol Med*. 2018 Jan;243(2):148–58.
5. Miller A, Korem M, Almog R, Galboiz Y. Vitamin B12, demyelination, remyelination and repair in multiple sclerosis. *J Neurol Sci*. 2005 Jun;233(1–2):93–7.
6. Nozari E, Ghavamzadeh S, Razazian N. The Effect of Vitamin B12 and Folic Acid Supplementation on Serum Homocysteine, Anemia Status and Quality of Life of Patients with Multiple Sclerosis. *Clin Nutr Res*. 2019;8(1):36.
7. Lamberti P, Zoccolella S, Armenise E, Lamberti SV, Fraddosio A, De Mari M, et al. Hyperhomocysteinemia in L -dopa treated Parkinson's disease patients: effect of cobalamin and folate administration. *Eur J Neurol*. 2005 May;12(5):365–8.
8. McCaddon A. Vitamin B12 in neurology and ageing; Clinical and genetic aspects. *Biochimie*. 2013 May;95(5):1066–76.
9. Rekik A, Santoro C, Poplawska-Domaszewicz K, Qamar MA, Batzu L, Landolfo S, et al. Parkinson's disease and vitamins: a focus on vitamin B12. *J Neural Transm*. 2024 Dec;131(12):1495–509.
10. Lauer AA, Grimm HS, Apel B, Golobrodska N, Kruse L, Ratanski E, et al. Mechanistic Link between Vitamin B12 and Alzheimer's Disease. *Biomolecules*. 2022 Jan 14;12(1):129.
11. Smith AD, Smith SM, De Jager CA, Whitbread P, Johnston C, Agacinski G, et al. Homocysteine-Lowering by B Vitamins Slows the Rate of Accelerated Brain Atrophy in Mild Cognitive Impairment: A Randomized Controlled Trial. *Bush AI, editor. PLoS ONE*. 2010 Sep 8;5(9):e12244.

12. Dułak NA, Rytlevska M, Jaskólska M, Chmielewski M. A new perspective on vitamin B12 deficiency in rheumatology: a case-based review. *Rheumatol Int.* 2024 Jan 31;44(4):737–41.
13. Roffman JL, Lamberti JS, Achtyes E, Macklin EA, Galendez GC, Raeke LH, et al. Randomized Multicenter Investigation of Folate Plus Vitamin B₁₂ Supplementation in Schizophrenia. *JAMA Psychiatry.* 2013 May 1;70(5):481.
14. Rossignol DA, Frye RE. The Effectiveness of Cobalamin (B12) Treatment for Autism Spectrum Disorder: A Systematic Review and Meta-Analysis. *J Pers Med.* 2021 Aug 11;11(8):784.
15. Rouf MA, Begum S, Ali T, Rahman MM, Masood S. ?-Tocopherol and Ketorolac on Pain in Long Evans Rats. *J Bangladesh Soc Physiol.* 2017 Sep 9;12(1):21–7.
16. Didangelos T, Karlafti E, Kotzakioulafi E, Margariti E, Giannoulaki P, Batanis G, et al. Vitamin B12 Supplementation in Diabetic Neuropathy: A 1-Year, Randomized, Double-Blind, Placebo-Controlled Trial. *Nutrients.* 2021 Jan 27;13(2):395.
17. Karedath J, Batool S, Arshad A, Khalique S, Raja S, Lal B, et al. The Impact of Vitamin B12 Supplementation on Clinical Outcomes in Patients With Diabetic Neuropathy: A Meta-Analysis of Randomized Controlled Trials. *Cureus [Internet].* 2022 Nov 22 [cited 2025 May 24]; Available from : <https://www.cureus.com/articles/126132-the-impact-of-vitamin-b12-supplementation-on-clinical-outcomes-in-patients-with-diabetic-neuropathy-a-meta-analysis-of-randomized-controlled-trials>
18. Sun A li, Ni Y hong, Li X bo, Zhuang X hua, Liu Y tao, Liu X hua, et al. Urinary Methylmalonic Acid as an Indicator of Early Vitamin B12 Deficiency and Its Role in Polyneuropathy in Type 2 Diabetes. *J Diabetes Res.* 2014;2014:1–6.
19. Jeenia FT, Sojib FA, Rahman MS, Ara T, Khan R, Tanin MJU. Neuroprotective effect of vitamin B₆ and vitamin B₁₂ against vincristine- induced peripheral neuropathy: A randomized, double-blind, placebo controlled, multicenter trial [Internet]. *Oncology;* 2021 [cited 2025 May 24]. Available from: <http://medrxiv.org/lookup/doi/10.1101/2021.05.18.21257296>
20. Julian T, Syeed R, Glasgow N, Angelopoulou E, Zis P. B12 as a Treatment for Peripheral Neuropathic Pain: A Systematic Review. *Nutrients.* 2020 Jul 25;12(8):2221.
21. Cirillo M, Fucci R, Rubini S, Coccia ME, Fatini C. 5-Methyltetrahydrofolate and Vitamin B12 Supplementation Is Associated with Clinical Pregnancy and Live Birth in Women Undergoing Assisted Reproductive Technology. *Int J Environ Res Public Health.* 2021 Nov 23;18(23):12280.
22. Zhang L, Wu L mei, Xu W hai, Tian Y qing, Liu X ling, Xia C yun, et al. Status of maternal serum B vitamins and pregnancy outcomes: New insights from in vitro fertilization and embryo transfer (IVF-ET) treatment. *Front Nutr.* 2022 Nov 11;9:962212.
23. Behere RV, Deshmukh AS, Otiv S, Gupte MD, Yajnik CS. Maternal Vitamin B12 Status During Pregnancy and Its Association With Outcomes of Pregnancy and Health of the Offspring: A Systematic Review and Implications for Policy in India. *Front Endocrinol.* 2021 Apr 12;12:619176.
24. Pepper MR, Black MM. B12 in fetal development. *Semin Cell Dev Biol.* 2011 Aug;22(6):619–23.
25. Rogne T, Tielemans MJ, Chong MFF, Yajnik CS, Krishnaveni GV, Poston L, et al. Associations of Maternal Vitamin B12 Concentration in Pregnancy With the Risks of Preterm Birth and Low Birth Weight: A Systematic Review and Meta-Analysis of Individual Participant Data. *Am J Epidemiol.* 2017 Jan 20;amjepid;kww212v1.
26. Satapathy S, Bandyopadhyay D, Patro BK, Khan S, Naik S. Folic acid and vitamin B12 supplementation in subjects with type 2 diabetes mellitus: A multi-arm randomized controlled clinical trial. *Complement Ther Med.* 2020 Sep;53:102526.

27. Agnihotri S, Kaur J, Masand P, Anurag, Parihar VK, Sharma A. Vitamins strategies for psoriasis: An update on current scientific evidence. *J Holist Integr Pharm.* 2023 Dec;4(4):299–309.
28. Brescoll J, Daveluy S. A Review of Vitamin B12 in Dermatology. *Am J Clin Dermatol.* 2015 Feb;16(1):27–33.
29. Shakhbazova A, Wu H, Chambers CJ, Sivamani RK. A Systematic Review of Nutrition, Supplement, and Herbal-Based Adjunctive Therapies for Vitiligo. *J Altern Complement Med.* 2021 Apr 1;27(4):294–311.
30. Mauro GL, Martorana U, Cataldo P, Brancato G, Letizia G. Vitamin B12 in low back pain: a randomised, double-blind, placebo-controlled study. *Eur Rev Med Pharmacol Sci.* 2000;4(3):53–8.
31. Feily A. Successful Treatment of Isotretinoin Induced Musculoskeletal Pain by Vitamin B12 and Folic Acid. *Open Access Maced J Med Sci.* 2019 Oct 10;7(21):3726–7.
32. Nava-Mesa MO, Aispuru Lanche GR. Papel de las vitaminas B, tiamina, piridoxina y cianocobalamina en el dolor de espalda y otras condiciones musculoesqueléticas: revisión narrativa. *Med Fam SEMERGEN.* 2021 Nov;47(8):551–62.
33. Dehghan M. Comparative Effectiveness of B and E Vitamins with Diclofenac in Reducing Pain Due to Osteoarthritis of the Knee. *Med Arch.* 2015;69(2):103.
34. Xu G, Lv ZW, Feng Y, Tang WZ, Xu GX. A Single-Center Randomized Controlled Trial of Local Methylcobalamin Injection for Subacute Herpetic Neuralgia: Methylcobalamin Injection for Subacute Herpetic Neuralgia. *Pain Med.* 2013 Jun;14(6):884–94.
35. Xu G, Zhou CS, Tang WZ, Xu J, Xu G, Cheng C, et al. Local Administration of Methylcobalamin for Subacute Ophthalmic Herpetic Neuralgia: A Randomized, Phase III Clinical Trial. *Pain Pract.* 2020 Nov;20(8):838–49.
36. Wang JY, Wu YH, Liu SJ, Lin YS, Lu PH. Vitamin B12 for herpetic neuralgia: A meta-analysis of randomised controlled trials. *Complement Ther Med.* 2018 Dec;41:277–82.
37. Reis LNC, Falabella MEV, Carvalho FRD, Camargos GL. The effectiveness of laserpuncture associated with vitamin B12 in the treatment of temporomandibular disorders and orofacial pain. *Res Soc Dev.* 2023 May 17;12(5):e17812541593.
38. Metin SK, Meydan B, Evman S, Dogruyol T, Baysungur V. The Effect of Pregabalin and Methylcobalamin Combination on the Chronic Postthoracotomy Pain Syndrome. *Ann Thorac Surg.* 2017 Apr;103(4):1109–13.
39. Liu HL, Chiu SC. The Effectiveness of Vitamin B12 for Relieving Pain in Aphthous Ulcers: A Randomized, Double-blind, Placebo-controlled Trial. *Pain Manag Nurs.* 2015 Jun;16(3):182–7.
40. Pecikoza U, Tomić M, Nastić K, Micov A, Stepanović-Petrović R. Synergism between metformin and analgesics/vitamin B12 in a model of painful diabetic neuropathy. *Biomed Pharmacother.* 2022 Sep;153:113441.
41. Buesing S, Costa M, Schilling JM, Moeller-Bertram T. Vitamin B12 as a Treatment for Pain. *Pain Physician.* 2019 Jan;22(1):E45–52.
42. Rahman MM, Begum N, Ali T, Rouf MA, Masood S. Vitamin B12 and ketorolac on pain in Long Evans rats. *J Bangladesh Soc Physiol.* 2016 Dec 14;11(2):63–9.
43. Rahman MdM, Begum N, Abdur Rouf M, Masood S. Synergistic Antinociceptive, Anti-inflammatory Interaction between Vitamin B12 and Ketorolac in Long Evans Rats. *Eur J Clin Med.* 2021 Jul 9;2(3):105–10.