



Biotin Interference With Laboratory Test Results

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SUMMARY

Introduction: Biotin interference in laboratory tests is a growing concern, particularly due to the widespread use of biotin not only as a therapeutic agent but also as a supplement in the cosmetic industry. Immunoassays utilizing biotin-streptavidin technology are especially susceptible to interference, which can result in inaccurate test results, misdiagnosis, and inappropriate treatment.

Methodology: This review synthesizes information from scientific literature available through databases like PubMed and Google Scholar. Keywords such as „biotin”, „interference” and „immunoassay” were used to identify relevant studies.

Topic: This review addresses the risk of biotin interference in various immunoassays, particularly its impact on thyroid function tests (TSH, FT3, FT4), parathyroid hormone (PTH), testosterone, human chorionic gonadotropin (hCG), and cardiac markers including troponin. It explores the pharmacokinetics of biotin elimination and the prevalence of elevated biotin levels in patient populations. The clinical consequences of falsely high or low results, potentially leading to misdiagnosis, are highlighted. Methods for mitigating biotin interference, such as serial dilution, biotin depletion, and advancements in biotin-resistant immunoassays, are also discussed.

Conclusion: Biotin interference presents a significant challenge in laboratory diagnostics, particularly with the growing use of high-dose biotin supplements. Tests most susceptible include those assessing thyroid function, reproductive hormones, and cardiac markers. Raising awareness among healthcare professionals and patients, along with implementing biotin depletion protocols and improving immunoassay designs, are key strategies to mitigate interference. Continued research into biotin-resistant immunoassays is critical for enhancing diagnostic accuracy and preventing clinical misinterpretation.

Keywords: Biotin Supplementation, Diagnostic Accuracy, Immunoassay, Biotin-Streptavidin Technology, Thyroid Function Tests, Biotin Depletion Protocols

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INTRODUCTION

Definition and Classification of Interference

Interference in laboratory tests represents a critical problem in clinical diagnostics, where the accuracy and reliability of results are essential for effective patient treatment. In the context of laboratory medicine, interference is defined as the effect of a substance present in the sample that alters the true value of the result, usually expressed as the concentration or activity of the analyte [1]. This effect can lead to misinterpretation, potentially resulting in incorrect diagnoses, inadequate treatment, and unfavorable patient outcomes. Interference may originate from various sources, both endogenous and exogenous. Endogenous substances, such as hemoglobin, bilirubin, lipids, and paraproteins, are natural components of bodily fluids and represent the most common interferents in laboratory test results [2]. Exogenous sources are substances not normally found in biological samples and originate from external sources. Significant exogenous contributors to interference include pharmaceutical drugs prescribed to patients, herbal medications, dietary supplements, contrast agents, and others. These substances may interact with analytical reagents or detection systems used in tests, leading to falsely elevated or reduced results. Addressing the problem of interference is essential to maintaining the integrity of laboratory results, ensuring that the right patient receives the correct result at the right time [3].

Discovery of Biotin and Avidin

Like many scientific breakthroughs, the discovery of biotin (also known as vitamin H or vitamin B7) stemmed from a simple observation: eating raw egg whites was toxic, but this toxicity could be neutralized by an unknown substance found in egg yolks. In 1927, biochemist Margaret Avril Boas from the Lister Institute in London found that young rats fed dried raw egg whites as their main protein source quickly developed severe dermatitis, alopecia, and a stiff, spastic walk that made them resemble kangaroos. The rats died within 4 to 6 weeks, and Boas called this condition „egg white injury“. She also discovered a „protective factor X“ in yeast and raw liver that could cure this disease [4]. In 1937, nutritionist and pedi-

atrician Paul György, along with his colleagues, discovered a substance he called „vitamin H“ (from the German „Haut“, meaning „skin“), which prevented the pathological changes that developed in rats and chickens fed raw egg whites [5]. Later studies determined that „egg white injury“ occurs when biotin from food is ingested along with a protein in raw egg whites that binds strongly to it. This does not occur if the protein is denatured by heat. In 1940, biochemist Esmond Snell from the University of Texas at Austin isolated this protein, originally named avidalbumin (literally, „hungry albumin“), but it was later renamed avidin due to its high affinity for biotin (from „avidity“ + „biotin“) [6]. Liver and yeast provided protection against „egg white injury“ because they contain large amounts of biotin, sufficient to saturate avidin, leaving excess biotin available for absorption [4].

Biotin

Biotin (vitamin H, B7, coenzyme R) is an essential water-soluble vitamin of the Bcomplex [7]. It consists of a tetrahydrothiophene ring, a valeric acid side chain, and a ureido (tetrahydroimidazalone) ring. Its primary biological role is to act as an enzymatic cofactor necessary for carbon dioxide transfer [8]. This function is carried out by five carboxylases in the human body (acetyl-CoA carboxylase (ACC) 1 and 2, pyruvate carboxylase (PC), propionyl-CoA carboxylase (PCC), and 3-methylcrotonyl-CoA carboxylase (MCC)) to which biotin is covalently bound. These carboxylases are involved in various cellular metabolic processes, such as the synthesis and oxidation of fatty acids, gluconeogenesis, and the degradation of branched-chain amino acids and odd-chain fatty acids. In addition to these roles, new functions have been discovered that are not associated with carboxylases, including cellular signaling, epigenetic regulation of gene expression, and chromatin structure, as well as involvement in the immune response [7]. The recommended daily intake of biotin is 30 µg, which is typically obtained through diet. Normal circulating biotin concentrations typically range from 0.1 to 0.8 ng/mL [9]. Biotin is abundant in everyday foods such as egg yolk, cereals, soy, avocado, cauliflower, leafy green vegetables, pork, liver, and others [10].

The typical daily intake of biotin in Western populations ranges from 35 to 70 µg/

day. Biotin is absorbed from the gastrointestinal tract and reaches its maximum blood concentration approximately two hours after oral intake. Only a small portion of biotin undergoes catabolism, while the excess is excreted through urine [11]. Oral doses of biotin at 10 mg result in maximum plasma concentrations ranging from 55 to 140 ng/mL (225–573 nmol/L). Biotin accumulation occurs with daily administration, with circulating concentrations being twice as high on the seventh day compared to the first. Steady-state concentrations are achieved after 3 days of continuous supplementation. Biotin concentrations drop below 20 ng/mL within 1 to 146 hours, depending on the dose (1–300 mg), but elimination may be impaired in individuals with renal dysfunction [12]. Biotin deficiency is extremely rare and occurs only in severely malnourished children or individuals with inborn errors of metabolism [13].

Avidin

Avidin (66,000 Da) is a tetrameric glycoprotein found in egg whites [14]. The first bacterial avidin, streptavidin, was isolated in 1964 from the bacterium *Streptomyces avidinii*, which produces antibiotics [15]. To date, numerous avidins have been discovered in both eukaryotic and prokaryotic species [16]. Structurally, avidins contain four binding sites for biotin. Biotin binds to avidin with a dissociation constant (K_d) of approximately 10^{-15} M, and to streptavidin with a K_d of approximately 10^{-14} M [17]. This bond represents the strongest known non-covalent interaction between a protein and a ligand. The unique properties of the streptavidin-biotin pair have led to their widespread application in biotechnology, including immunoassays, immunohistochemistry, protein and nucleic acid purification, cell biology studies, live-cell imaging, and more recent applications in imaging techniques and

drug delivery [18]. The strength of their bond is crucial for these applications, as it forms almost instantly and remains extremely stable under conditions of extreme temperatures, pH changes, detergents, denaturing agents, and organic solvents [11].

Immunoassay

Immunoassays are bioanalytical methods in which the determination of analyte concentration is based on antigen-antibody reactions [19]. They are most commonly used to measure hormones, oncology markers, and cardiology markers. Immunoassays utilize highly specific antibodies to target and quantify particular molecules of interest [20]. Immunoassays are divided into two types: non-competitive and competitive assays.

Non-competitive „Sandwich” Immunoassay

The non-competitive „sandwich” immunoassay is an immunometric technique that uses two antibodies, with each binding to a different site on the antigen. The first antibody, called the capture antibody, is highly specific for the target antigen and is immobilized on a solid surface. After the antigen is added, a second antibody, known as the detection antibody, is introduced. This detection antibody is labeled with an enzyme or fluorophore and binds to another site on the antigen. In this process, the antigen is „sandwiched” between the two antibodies (Figure 1). When a substrate is added to the reaction mixture or the fluorophore is excited, a signal is produced, and its intensity directly proportional to the concentration of the analyte. The sensitivity of the immunoassay depends largely on how well the antibodies bind to the antigen. As the antigen concentration in the sample increases, more detection antibodies bind, resulting in a stronger signal. The standard (calibration) curve for a

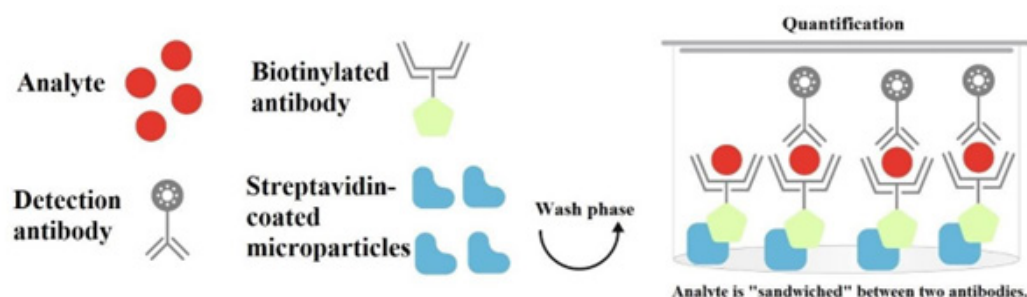
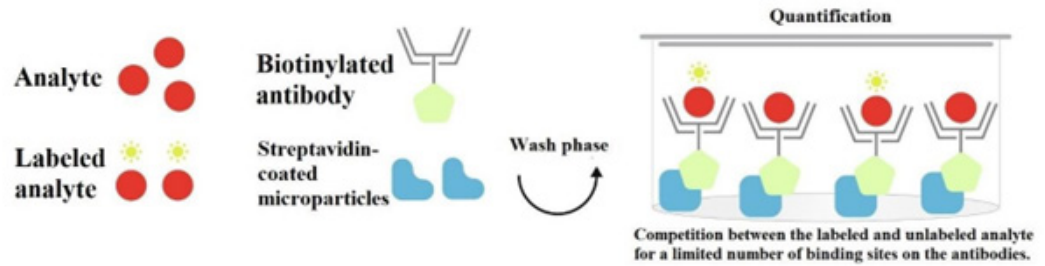


Figure 1. Non-competitive „sandwich” immunoassay

Figure 2. Competitive immunoassay



sandwich immunoassay shows a positive slope [21]. *Sandwich* immunoassays are commonly used to measure larger molecules such as thyroid-stimulating hormone (TSH), cardiac troponin, and other proteins [22].

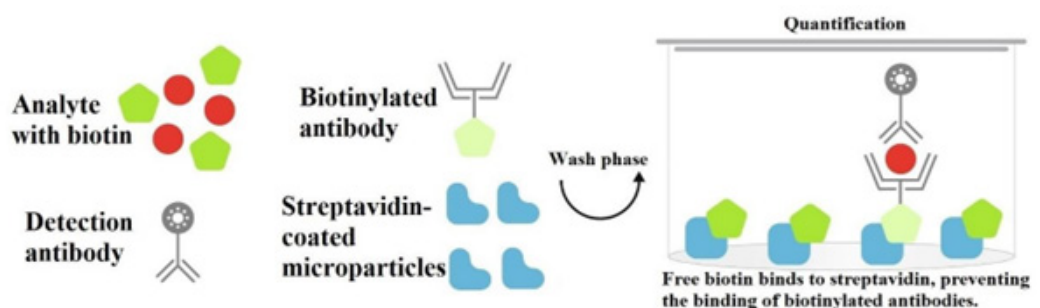
Competitive Immunoassay

The competitive immunoassay is based on competition between the labeled analyte and the unlabeled analyte from the sample for a limited number of binding sites on the antibodies (Figure 2). In this type of immunoassay, only one antibody is used. The antibodies are incubated simultaneously with a known concentration of the labeled analyte and the unlabeled analyte present in the sample. According to the law of mass action, the amount of labeled ligand that binds to the antibody depends on the total concentration of both the labeled and unlabeled ligands. As the concentration of the unlabeled ligand increases, less of the labeled ligand can bind to the antibody, resulting in a decrease in the intensity of the detected signal. Therefore, the lower the signal, the higher the concentration of unlabeled analyte in the sample. The standard (calibration) curve for a competitive immunoassay has a negative slope. Competitive immunoassays are often used to measure small analytes such as thyroid and steroid hormones, or when a specific pair of antibodies for the analyte is not available [21,22].

Application of the Streptavidin-Biotin Complex in Immunoassays

Biotin can be covalently attached to various macromolecules with minimal alteration to their biological activity. This process is known as biotinylation. When biotin is bound to another molecule, its affinity for streptavidin is greater than to avidin [11]. By biotinylating an antibody, it becomes „bivalent“, allowing it to bind both the target component and streptavidin. Since the detection limit is largely influenced by the number of captured signal molecules, incorporating the biotin-streptavidin pair into immunoassays significantly increases the sensitivity of the analysis [24]. Research shows that 59% of immunoassays in the United States use the biotin-streptavidin in their formulations [25]. Commercial immunoassay systems are fully automated, featuring storage compartments for reagents and supplementary materials, along with mechanisms to process multiple patient samples simultaneously. These analyzer systems employ simple and rapid methods for automated quantitative analyte determination [11]. The risk of inaccurate patient results due to biotin interference can vary significantly between different immunoassays, and depends on the concentration of biotin and the analyte in the sample, as well as the specific test used. All immunoassays based on the biotin-streptavidin interaction may be susceptible to biotin interference [23].

Figure 3. Biotin interference in non-competitive immunoassays



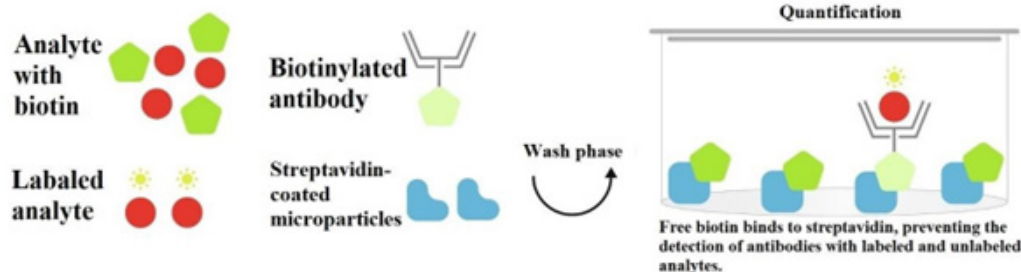


Figure 4. Biotin interference in competitive immunoassays

Mechanism of Interference at Elevated Biotin Concentrations

In non-competitive „sandwich” immunoassays, when excess biotin is present in the sample, free biotin will saturate the streptavidin binding sites incorporated in the solid phase, preventing the binding of the biotinylated (capture) antibody (Figure 3). In this case, the detection antibody will bind to the analyte, but the analyte itself will not be attached to the solid phase and will be washed away during the wash phase, leading to a falsely reduced signal and result. In competitive immunoassays, excess biotin in the sample binds to the streptavidin solid phase and prevents the binding of antibodies linked to both the labeled and unlabeled analytes (Figure 4). The unbound antibody is removed during the washing process, resulting in a reduced signal and a falsely elevated result [22]. Non-competitive tests are theoretically less prone to interference because there are excess binding sites for the analyte, while in competitive tests, the binding sites for analytes are limited [26]. The presence of the biotin-streptavidin complex does not necessarily indicate that the test will be susceptible to biotin interference. In certain methods, streptavidin and biotin are pre-combined during the production process. Tests that use such „pre-bound” reagents, rather than mixing individual reagents with the patient sample during the analysis, are considered resistant or insensitive to biotin interference [27].

Therapeutic Use of High Doses of Biotin

Inherited metabolic disorders affecting biotin metabolism include holocarboxylase synthetase deficiency and biotinidase deficiency. Both conditions result in impaired function of all biotin-dependent carboxylases, culminating in multiple carboxylase deficiencies. The characteristic manifestation of these diseases include metabolic acidosis associated with

neurological abnormalities and dermatological manifestations. The clinical and biochemical presentation varies between these two inherited disorders. The onset of biotinidase deficiency can be gradual and subtle, and the presentation is often highly variable. Neurological symptoms frequently dominate, without metabolic acidosis or significant abnormalities in the excretion of organic acids. After treatment with pharmacological doses of biotin (5–20 mg daily), nearly all symptomatic children show clinical improvement. In both diseases, therapy is lifelong [13].

Biotin-responsive basal ganglia disease (BTBGD) is an autosomal recessive hereditary disorder that typically manifests in childhood, between the ages of 3 and 10 years. It is characterized by recurrent episodes of subacute encephalopathy, presenting with symptoms such as confusion, seizures, ataxia, dystonia, supranuclear facial paresis, external ophthalmoplegia, and/or dysphagia. If untreated, the disease can lead to coma or even death. Biotin (5–10 mg/kg/day) is administered orally as soon as possible, and treatment continues for life [28].

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) characterized by multiple isolated inflammatory lesions associated with demyelination and gliosis [29]. About 85% of all MS patients have the relapsing-remitting form (RRMS), characterized by unpredictable acute episodes of neurological dysfunction, known as relapses, followed by variable recovery and periods of clinical stability. Within ten years, more than 50% of patients with RRMS develop permanent disability with or without continued relapses, a form known as secondary progressive multiple sclerosis (SPMS). Around 15% of patients experience early permanent worsening of neurological function, which is called primary progressive multiple sclerosis (PPMS) [30]. Biotin administration may influence disease progression and long-term dis-

ability in patients with progressive MS [31]. In a pilot study, 21 out of 23 patients (91.3%) showed some clinical improvement. Similar positive results were reported in patients with SPMS and PPMS who suffered from optic neuropathies, hemianopsia, or spinal cord involvement. The conclusion was that a dose of 300 mg/day is the best clinical option. A randomized, double-blind, placebo-controlled study with a follow-up open-label phase, where all patients received high doses of biotin, reported a reduction in MS-related disability in 12.6% of patients, while no improvement was noted in the placebo group ($p = 0.005$). The treatment's efficacy was maintained for 24 months in 77% of patients who initially responded to the therapy. High-dose biotin also reduced the proportion of patients with confirmed disease progression. Among patients who switched from placebo to high-dose biotin, there was a halt in disease worsening, and in some cases, an improvement in MS-related disability was noted [32]. Although high doses of biotin are generally well tolerated and safe, they do not always lead to significant neurological improvement in patients. This raises the question of whether some patients in the MS study had biotinidase deficiency and therefore responded to biotin therapy [34]. However, the likelihood of this is minimal due to the discrepancy in the prevalence of these two diseases, as well as the fact that more patients showed improvement when the strict criteria of the primary study endpoint were excluded [35]. In any case, further studies and clinical research are needed to support the results obtained in the pilot study.

Biotin has gained significant commercial popularity due to claims that it promotes healthy hair and nail growth. In conditions like brittle nail syndrome and hair disorders such as uncombable hair syndrome, biotin supplementation has shown clinical improvements [36].

Small, uncontrolled studies suggest the benefit of 2.5 mg of biotin daily in treating brittle nails, while a dose of 5 mg daily has proven effective in patients with triangular worn-down nails [37]. Data from Switzerland show a 25% increase in nail plate thickness in patients with brittle nails who received biotin supplementation [38]. In uncombable hair syndrome, although no definitive therapy exists, biotin supplementation has shown a positive effect on hair strength and elasticity. Biotin

therapy is recommended as it has no adverse effects and can alleviate symptoms in young patients [39]. Despite these findings, no randomized controlled trials have been conducted to confirm biotin's efficacy in healthy individuals [36]. Nevertheless, biotin's popularity has risen significantly, not only due to its media promotion but also because it has become a „trendy” supplement among consumers. This popularity far exceeds the limited clinical evidence supporting its efficacy in hair improvement, highlighting a discrepancy between its actual benefit and current fame [40].

METHODOLOGY

Information for this review was gathered from scientific articles accessed through internet-based databases, including PubMed and Google Scholar. The search was conducted using key words such as „interference”, „biotin” and „immunoassay”. A total of 50 articles and case reports published to date were included in this study, all of which comprehensively addressed the inference of biotin and its relevance in the scientific field. A systematic literature search was conducted using only Serbian and English languages, which may represent a limitation of this study, potentially affecting the comprehensiveness of included research.

TOPIC

Risk Assessment of Interference in Automated Immunoassays

Many automated immunoassay systems from various manufacturers utilize the biotin-streptavidin interaction, making them susceptible to biotin interference (Table 1). The interference threshold represents the biotin concentration (in nmol/L) at which exogenous biotin in the sample causes a significant analytical error (greater than $\pm 10\%$ change) in test results [41]. The degree of interference depends on the interference threshold of the specific test and the concentration of biotin in the sample [22]. As the biotin concentration increases, the likelihood of deviations from true values also rises. While changes can occur within reference ranges, a more significant issue arises when results exceed these reference limits, potentially leading to clinical confusion, patient anxiety, unnecessary testing, or even inappropriate treatment [42].

Multi-Test Assay System	Total Immunoassays	Vulnerable to Biotin Interference	Biotin Interference Threshold (range, nmol/L)
Roche Elecsys®	81	81	21 - 491
Ortho Vitros®	43	29	10 - 82
Siemens Dimension®	26	21	205 - 8200 (3 n/a)
Siemens Centaur®	67	18	41 - 4090 (6 n/a)
Beckman Coulter Access®/DXI®	48	14	41 - 1000 (9 n/a)
Abbott Architect i2000®	46	2	120 (1 n/a)

Table 1. Biotin interference in tests of the most commonly used automated immunoassay systems [41]

n/a - not assessed

The Scientific Committee of the Association for Clinical Biochemistry and Laboratory Medicine (ACB) has suggested that tests with an interference threshold lower than 30 ng/mL (120 nmol/L) of biotin should be considered susceptible to interference, as this level corresponds to the expected maximum serum biotin concentration after taking over-the-counter (OTC) supplements in doses of 5–10 mg. Other authors have proposed that biotin concentrations as low as 10 ng/mL may pose a potential for interference, particularly in highly sensitive immunoassays [43]. Once a method's susceptibility to biotin interference and its interference threshold are established, the risk of inaccurate results depends on the biotin dose taken, the pharmacokinetics of the supplement, and the timing of the sample collection relative to the last taken dose [41].

Pharmacokinetic studies in a healthy population indicate that with a daily biotin intake of 2.5 mg (which is about 80 times the recommended daily allowance), serum biotin levels drop below 10 ng/mL within 2 hours. For doses of 10 mg per day, the threshold of 30 ng/mL is reached after 8 hours. After very high doses of biotin (≥ 20 mg per day), serum concentrations do not fall to 30 ng/mL even after 31 hours, and it takes 73 hours to drop to 10 ng/mL [12]. Based on this, it can be assumed that a single oral dose of less than 1 mg of biotin is unlikely to interfere with tests that have an interference threshold above 40 nmol/L (Table 2). On the other hand, a single oral dose of 300 mg can lead to serum biotin concentrations exceeding 3000 nmol/L, which surpasses the interference thresholds of sensitive tests listed in Table 1. In fact, the risk of inaccurate test results may last several days, depending on the interference threshold of the test itself, indicating that the use of sensitive methods should be avoided in patients taking more than 100 mg per day due to the significant risk of misdiagnosis. A recent evaluation of interference in a patient with multiple scler-

osis treated with a daily dose of 300 mg of biotin showed falsely elevated or decreased results in 12 different endocrine tests [41].

Recommendations for reducing the risk of biotin interference in tests that use streptavidin-biotin technology vary between manufacturers. Some manufacturers do not mention biotin at all in their instructions, while others provide specific guidelines on acceptable serum biotin concentrations that do not significantly affect results ($\leq 10\%$ variation). These thresholds range from 10 to 500 ng/mL, with most tests having a threshold above 50 ng/mL [12]. Piketty and colleagues studied the extent of biotin interference in several immunoassays (free triiodothyronine (FT3), free thyroxine (FT4), parathyroid hormone (PTH), thyroid-stimulating hormone (TSH), 25-hydroxyvitamin D, cortisol, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, and C-peptide) on the Cobas e411 system by Roche Diagnostics. Study participants received moderate (25–30 mg) and high doses of biotin (300 mg), and biotin and its metabolites (bisorbiotin and biotin sulfoxide) in serum were measured using liquid chromatography with mass spectrometry (LC-MS/MS), a method not susceptible to biotin interference. The study demonstrated that test results were most significantly altered in individuals taking ≥ 100 mg of biotin daily, with the extent of deviation showing a direct correlation with the serum biotin concentration. Even at lower doses (15 mg per day), a false increase of 10–20% was noted for 25-hydroxyvitamin D. Moreover, results that were outside the reference range returned to normal once biotin was removed, confirming that biotin was responsible for the noted interference. This study also demonstrated variable sensitivity of different assays to biotin interference. Prolactin results were the least affected, with about 10% negative deviation in results in 2 out of 23 patients, while 25-hydroxyvitamin D was the most susceptible, with positive devia-

Table 2. Thresholds for biotin-induced interference as stated in the Roche Elecsys manufacturer's instructions for use [summarized from 46]

Roche Elecsys®	Type of error	Interference threshold (ng/mL)
Anti-TPO	Increase	>10
Anti-Thyroglobulin, Elecsys	Increase	>60
Anti-TSH Receptor, Elecsys	Increase	>10
Anti-HBc IgM	Decrease	>100
Anti-HCV	Decrease	>50
C-Peptide	Decrease	>60
Calcitonin, Elecsys	Decrease	>40
Carcinoembryonic Antigen (CEA)	Decrease	>120
DHEA-S	Increase	>70
Estradiol III, Elecsys	Increase	>36
Folate III	Increase	>21
Free T4 II, Elecsys	Increase	>20
Free T3 III, Elecsys	Increase	>70
FSH, Elecsys	Decrease	>60
HCG STAT	Decrease	>40
HCG+B, Elecsys	Decrease	>80
Hepatitis B Antigen, Elecsys	Decrease	>40
Hepatitis B Core Antibody, Elecsys	Increase	>30
Hepatitis B Surface Antigen	Decrease	>44
Immunoglobulin E	Decrease	>100
Luteinizing Hormone, Elecsys	Decrease	>50
Parathyroid Hormone, Elecsys	Decrease	>50
Parathyroid Hormone STAT, Elecsys	Decrease	>50
NT-proBNP II	Decrease	>30
NT-proBNP II STAT	Decrease	>30
Procalcitonin, BRAHMS Elecsys	Decrease	>30
Progesterone III, Elecsys	Increase	>30
Prolactin II, Elecsys	Decrease	>40
PSA Total, Elecsys	Decrease	>60
Sex Hormone Binding Globulin, Elecsys	Decrease	>70
Triiodothyronine (T3), Elecsys	Increase	>10
Testosterone II, Elecsys	Increase	>30
Thyroid Stimulating Hormone, Elecsys	Decrease	>1200
Thyroxine (T4), Elecsys	Increase	>100
Troponin I, Elecsys	Decrease	>30
Troponin T	Decrease	>50
Troponin T STAT	Decrease	>50
Troponin T STAT Gen.5 (reformulated)	Decrease	>1200
Vitamin B12, Elecsys	Increase	>50
25-Hydroxyvitamin D	Increase	>70
Vitamin D Total II, Elecsys	Increase	>30

tions greater than 10% noted in 23 out of 23 patients [44].

Roche Diagnostics guidelines recommend that samples from patients taking high

doses of biotin (>5 mg daily) should not be tested for at least 8 hours after the last dose [45]. Research on the Vitros 5600 platform by Ortho Clinical Diagnostics found that non-

competitive immunoassays are more prone to errors at lower biotin concentrations compared to competitive tests. Immunometric methods showed a deviation of about -50% at a biotin concentration of 50 ng/mL, while competitive immunoassays showed smaller errors at lower concentrations (<12%) but larger positive deviations (>200%) at concentrations above 50 ng/mL [47].

Prevalence of Elevated Biotin Concentrations in Patient Populations

In 2018, Katzman and colleagues conducted the first study to provide data on the prevalence of elevated biotin concentrations in the blood of patients admitted to emergency departments in the United States. The threshold for interference was set at a concentration of 10 ng/mL, as stated in Roche Diagnostics guidelines as the minimum value at which interference may occur. In 7.4% of patients of 1,442 participants, biotin concentrations were ≥ 10 ng/mL [48]. In a similar study conducted in Australia, only 0.8% of 490 participants had biotin concentrations above 10 ng/mL. The authors were surprised by the large differences in biotin concentrations between the two studies [49]. Similar results were noted in the Netherlands, where only 0.2% of 1,000 participants had biotin concentrations ≥ 10 ng/mL. The conditions of this study differed slightly from previous ones, as it included a broader patient population, including patients from hospitals, clinics, primary care settings, and nursing homes [50].

The most recent study, which involved a larger and geographically diverse patient population from five different emergency department locations in the United States, showed that 4.1% of the 7,118 collected samples exceeded the interference threshold [51]. One possible explanation for the significantly different risk estimates in these studies is the variation in biotin supplementation rates among different populations or the presence of other sources of biotin in diets and supplements [50]. High-dose biotin can be purchased over the counter at pharmacies, and its popularity has partly increased due to promotion in holistic medicine and the cosmetic industry. The availability, awareness, and interest in the alleged health benefits of biotin may vary between populations, leading to different rates of biotin use among patients [51].

Impact of Biotin on Hormonal, Serological, and Cardiac Markers: Cases, Mechanisms, and Consequences of Interference

Thyroid Hormones (TSH, FT3, FT4)

In the literature, the majority of reported cases of biotin interference involve thyroid function tests. The first case, described in 1996, involved a newborn girl who was diagnosed with congenital hypothyroidism during a screening of umbilical cord blood, where her TSH level was 472 mIU/L and FT4 was 9.2 pmol/L. A repeated analysis two days later on a new sample showed TSH at 363 mIU/L and FT4 at 97 pmol/L, which contradicted the initial results. It was discovered that the baby had been given a vitamin cocktail (20 mg of thiamine, 10 mg of biotin, and 10 mg of riboflavin) immediately after birth because her brother had died of organic acidosis two years earlier. This discrepancy in TSH and FT4 levels was not noted when the samples were analyzed using a method that did not involve biotin-streptavidin interaction. On the fourth day, biotin therapy was discontinued, and two days later, the results showed TSH at 140 mIU/L and FT4 at 16.3 pmol/L, leading to the initiation of thyroxine therapy [52].

Another case from 2012, reported in China, involved a three-year-old girl with propionic acidemia whose condition stabilized after therapy, though she continued to exhibit mild developmental delay and poor weight gain. Laboratory tests showed TSH levels between 0.01–0.23 mIU/L (reference range 0.9–6.5 mIU/L), FT4 at 12.6–17.0 pmol/L (12.0–22.0 pmol/L), and FT3 at 6.2 pmol/L (2.8–7.1 pmol/L), measured on the Roche Modular Analytics E170 and Cobas e601 immunoassay systems. The girl did not show visible signs of thyrotoxicosis, and there was no family history of thyroid disorders. Repeated samples continued to show persistently low TSH levels with normal FT4 values. A clinical pathologist investigated the immunoassays used, and serial dilution showed a non-linear response, after which TSH increased to 3.3 mIU/L, indicating interference. Further investigation revealed that the patient was on oral biotin therapy (10 mg) and levocarnitine (300 mg), suggesting a potential role of biotin in the interference [53].

A similar case was noted in a one-week-old baby with signs of liver failure and lactic acidosis, who was being treated with

30 mg of biotin daily (10 mg every 8 hours). Thyroid function tests on a Beckman DxI analyzer showed FT4 >77.7 pmol/L, FT3 at 24.9 pmol/L, and TSH at 3.75 mIU/L, which was illogical. Repeated tests on Abbott Architect and Siemens Centaur systems showed normal values, confirming that the interference was specific to the Beckman DxI analyzer. After discontinuation of biotin therapy, the results normalized [54].

Biotin interference is frequently reported in patients with multiple sclerosis, which is understandable given that high doses of biotin, up to 300 mg daily, are used to treat this disease. Thyroid function tests in these patients may be misinterpreted due to a specific combination of falsely low TSH values in non-competitive immunoassays and falsely high FT3 and FT4 values in competitive immunoassays. Such results, combined with falsely elevated TSH receptor autoantibodies, can lead to a misdiagnosis of severe hyperthyroidism caused by Graves' disease [55]. This can result in inappropriate therapy [56–58], unnecessary thyroid ultrasounds [56, 58, 59, 65], radioactive iodine uptake tests [60–62, 66], and even masking of hypothyroidism with delayed treatment [52, 63]. There are several concerning scenarios. Hyperthyroidism in elderly patients is often asymptomatic, so physicians rely

on laboratory tests for diagnosis. Methimazole is the drug of choice for treating Graves' disease, but the frequency of side effects is dose-dependent and occurs in 13–24% of patients. Radioactive iodine therapy, the most common treatment in the U.S., leads to hypothyroidism requiring lifelong levothyroxine therapy [68]. Furthermore, patients with thyroid cancer may remain undiagnosed due to biotin interference, which lowers the level of thyroglobulin, a tumor marker. In severe cases, biotin interference can lead to the recommendation of thyroidectomy [61]. A comprehensive overview of these case reports is provided in Table 3.

Parathyroid Hormone (PTH)

In 2009, a 60-year-old woman with a history of osteopenia, bone fractures, and chronic renal insufficiency was evaluated for surgery due to primary hyperparathyroidism. Over the previous year, her PTH levels had been elevated, but at this evaluation, her PTH was undetectable, while calcium levels remained high. It was discovered that the patient had been taking 1.5 mg of biotin daily for hair growth. Her PTH normalized to 197 pg/mL one month after biotin use was discontinued. However, when biotin was resumed, her PTH again became

Table 3. Case reports of misdiagnosed hyperthyroidism due to biotin interference in laboratory tests

Authors	Country	Number of cases	Age	Dose (mg/day)	Reason for biotin use
Henry et al. [52]	S. Arabia	1	1 day	10	Organic acidemia
Kwok et al. [53]	China	1	3 years	10	Propionic acidemia
Wijeratne et al. [54]	Australia	1	1 week	30	Lactic acidosis
Barbesino [61]	USA	1	55 years	300	MS
Elston et al. [64]	New Zealand	1	63 years	300	MS
Kummer et al. [56]	Germany	6	<18 years	2-5	Metabolic disorder
Minkovsky et al. [62]	USA	1	74 years	300	MS
Bülöw Pedersen and Laurberg [65]	Denmark	1	1 day	5	Biotinidase deficiency
Al-Salameh et al. [57]	France	1	32 years	100	Adrenomyeloneuro pathy
Batista et al. [66]	Brasil	1	Not reported	5-300	Hair and nail growth
Cusini et al. [59]	Italy	1	69 years	300	MS
Lim et al. [67]	France	2	Not reported	300	MS
Sharma et al. [68]	USA	1	60 years	10	Not reported
Willeman et al. [69]	France	1	39 years	>0.05	MS
De Roeck et al. [70]	Belgium	1	Not reported	300	MS
Evans et al. [63]	Australia	1	15 months	15	Mitochondrial disorder
Koehler et al. [71]	Germany	1	47 years	300	MS
Stieglitz et al. [72]	USA	1	48 years	5	Hair and nail growth

undetectable. In the same study, a 62-year-old woman with a history of elevated calcium levels and subsequent nephrolithiasis was presented. She had undergone a subtotal parathyroidectomy for primary hyperparathyroidism. After surgery, her PTH was 21 pg/mL, and calcium was 9.9 mg/dL. However, at routine check-ups at 6- and 9-months post-surgery, her PTH was undetectable, even though her calcium levels remained normal. Further investigation revealed that the patient had been taking 5 mg of biotin daily for neuropathic pain. After discontinuing biotin, her PTH levels returned to normal, confirming that biotin had caused the falsely low results [73]. Another case involved a woman with end-stage renal disease, where falsely normal PTH levels of 48 ng/L were measured on a Roche Elecsys analyzer. In contrast, a Siemens Immulite 2000 analyzer showed much higher PTH levels of 786 ng/L, which better matched her clinical presentation. It was discovered that the woman had been taking 10 mg of biotin daily for restless legs syndrome, which caused the falsely low results on the Roche Elecsys test [74].

Testosterone

Biotin can affect total testosterone levels, but its impact on free testosterone is less understood. One documented case in the literature involves a 74-year-old woman who visited her primary care physician due to concerns about frontal hair loss (alopecia), acne, and mild hirsutism. Her total testosterone was elevated at 146 ng/dL (reference range 7.0–40 ng/dL), while her free testosterone was within normal limits at 4.2 pg/mL (<4.2 pg/mL), along with normal sex hormone-binding globulin (SHBG) levels of 48 nmol/L (14–73 nmol/L). Additionally, androstenedione was elevated at 161 ng/dL (17–99 ng/dL), but other values, including the complete metabolic panel (CMP), prolactin, DHEA-S, and 17hydroxyprogesterone, were within normal ranges. The patient had been taking 1 to 3 mg of biotin daily. After discontinuing biotin, repeat analysis showed elevated free testosterone at 12.7 pg/mL (0.2–3.7 pg/mL), and total testosterone at 120 ng/dL (2–45 ng/dL), with normal SHBG levels of 39 nmol/L (14–73 nmol/L). These results aligned more closely with her clinical presentation of postmenopausal hyperandrogenism [75].

Another case involved a 48-year-old woman who visited an endocrinology clinic

due to palpitations, difficulty losing weight, and hirsutism. The referring physician raised the question of whether these symptoms were related to thyroid dysfunction, which had been diagnosed three years earlier. The patient had subclinical hyperthyroidism of unclear etiology, with normal iodine uptake tests and negative autoantibodies. After being prescribed antithyroid therapy but discontinued it due to weight gain and fatigue. Significant findings included the absence of acne, central obesity, and hyperglycemia. Due to hirsutism, weight gain, and possible thyroid dysfunction, further endocrine testing revealed elevated morning cortisol and total testosterone levels at 115mg/dL and 232 ng/dL, respectively, while ACTH was low. FSH and LH concentrations were lower than expected for perimenopausal status. This prompted an investigation into possible medication or supplement use, leading to the disclosure that she had been taking 5 mg of biotin daily for the past six months, intermittently over the previous five years. Initial lab results were inconsistent with her clinical picture, suggesting potential biotin interference. Physicians advised her to stop taking biotin before a follow-up test scheduled for 3.5 weeks later. However, the repeat results still showed an unusual hormonal profile. Due to unexplained low pituitary hormone levels, including a lack of prolactin, an MRI of the pituitary was performed to rule out a nonfunctional adenoma, as well as a CT scan of the adrenal glands to exclude pathology. The patient was referred to a reproductive endocrinologist to consider a possible testosterone-secreting tumor or ovarian hyperthecosis as the source of high testosterone. A pelvic ultrasound was normal, but a small testosterone-secreting tumor could not be ruled out, leading to the recommendation for a hysterectomy with oophorectomy. Ten weeks after the initial visit, free and total testosterone were measured by LC-MS/MS and found to be within the reference range. The patient's sample was tested for biotin concentration, revealing a level of 38 ng/mL. The patient admitted that she had continued taking biotin. She agreed to completely discontinue biotin for retesting. Two weeks later (12 weeks after the initial testing), her total serum testosterone, measured by both immunoassay and LC-MS/MS, was within the reference range [72].

Human Chorionic Gonadotropin (hCG)

Due to its low clinical relevance, a systematic evaluation of biotin interference in urine has not been conducted. However, biotin is actively excreted through urine, often at higher concentrations than in blood. In sports, the use of hCG is prohibited in men because it stimulates testosterone production. In women, hCG is an indicator of pregnancy, but it is also known to be produced endogenously in men under certain pathological conditions, such as testicular cancer. Anti-doping organizations are required to investigate any suspicious findings and conduct a medical evaluation before making decisions about anti-doping rule violations. In the context of anti-doping analysis, it has not been sufficiently studied whether biotin supplementation could mask positive results for hCG in immunoassays using biotinylated antibodies. Research indicates that, regardless of the initial hCG concentration, its levels decrease almost linearly with increasing biotin concentrations in the range of 100 to 1,000 ng/mL. It has been determined that the Elecsys hCG STAT test can yield false-negative results if biotin is present in urine at supraphysiological concentrations. Laboratories should use a modified protocol to avoid this biotin effect, especially when its concentration exceeds 200 ng/mL. In a study involving samples from American athletes, approximately 4% of urine samples had biotin concentrations above this threshold [76].

Prostate-Specific Antigen (PSA)

The PSA test plays a crucial role in diagnosing and monitoring patients with prostate cancer. In 2023, a 78-year-old man visited his physician due to rising PSA levels. The patient had been diagnosed with prostate cancer in 2014, followed by a radical prostatectomy a year later. Despite a relapse with secondary bone metastases, his disease had been under control in the subsequent years. In June 2023, laboratory results from the Abbott PSA test indicated an increase in PSA levels to 7.8 µg/L, which further rose to 10.9 µg/L in August.

However, when the test was repeated in October 2023 at an oncology center using the Ortho Vitros PSA test, the result came back at 6.02 µg/L—significantly lower than expected and inconsistent with previous results, as Ortho values are typically higher than those from

Abbott for the same samples. Further investigation for potential interference revealed the presence of biotin in the patient's sample. The patient later disclosed that he had been taking 0.5 mg of biotin daily. He agreed to stop taking biotin, and after two weeks, the PSA test was repeated, now showing a value of 20.9 µg/L on the Ortho Vitros PSA test, consistent with the PSA increase detected by the Abbott test. Following this result, the patient immediately began chemotherapy with docetaxel. This case illustrates how biotin interference can delay necessary treatments, such as chemotherapy. The oversight occurred because OTC supplements like biotin are rarely questioned during therapy evaluations, leading to the initial unawareness of their potential impact on test results [77].

Hepatitis B and C Viruses (HBV, HCV) and Human Immunodeficiency Virus (HIV)

Several studies have investigated how biotin affects serological markers for viruses such as HBV, HCV and HIV in tests utilizing the biotin-streptavidin interaction. In one study, ten healthy volunteers were given a single dose of 100 mg of biotin to examine its effects on markers for hepatitis B. Antibodies produced in response to Hepatitis B surface antigen (anti-HBs), core antigen (anti-HBc), and envelope antigen (anti-HBe) indicate different stages of infection. Anti-HBs suggests immunity post-infection or vaccination, while anti-HBc IgM indicates recent infection and anti-HBc IgG signals past or chronic infection. Anti-HBe reflects reduced viral replication, marking a transition to a less infectious state.

The results showed that 40% of participants had falsely negative results for anti-HBs, falling below the critical threshold of 10 mIU/mL, which could potentially lead to unnecessary revaccinations. Additionally, 90% and 80% of participants had falsely positive results for anti-HBc and anti-HBe, respectively, which could result in unnecessary medical investigations, increased healthcare costs, and psychological stress for patients [78].

In another experiment, biotin at concentrations ranging from 12.5 to 400 ng/mL was added to serum and plasma samples containing 30 pg/mL of HIV p24 antigen. At biotin concentrations of 200 ng/mL or higher, the HIV p24 antigen could not be detected, leading to falsely negative results [79]. In the

first experiment, 50% of anti-HIV and 66.6% of anti-HCV antibodies were also falsely negative after the ingestion of 100 mg of biotin. These findings are especially critical in clinical settings like blood and organ donor screening and testing individuals with high-risk sexual behaviors, as undiagnosed infections can significantly increase the likelihood of further viral transmission [78].

Allergen-Specific IgE Antibodies (sIgE)

Biotin-based immunoassays are also used to detect sIgE in the diagnosis of allergies. While laboratory testing is not always helpful in diagnosing anaphylaxis, it is important to note that anaphylaxis is recognized by healthcare professionals in over 80% of cases in patients with skin manifestations, but only in 55% of cases in those without these symptoms [80]. In such situations, additional laboratory diagnostics may be crucial.

This study examined biotin interference at concentrations ranging from 300 to 1,200 ng/mL. Patient samples were divided into groups with low and high sIgE concentrations. Results showed that the addition of biotin significantly reduced sIgE values measured by the IMMULITE-2000 test, with an average decrease of $92\% \pm 6.1\%$. A biotin concentration of 300 ng/mL was sufficient to cause a significant reduction in sIgE signal, leading to false-negative results in samples with low sIgE levels. Samples with high sIgE levels also showed a decrease in values but did not return false-negative results.

The effect of biotin on sIgE was further examined in a group of 18 patients with anaphylaxis. The addition of biotin in the IMMULITE-2000 test resulted in significant interference in sIgE values, with reductions of 86% and 92% at biotin concentrations of 184 and 500 ng/mL, respectively. Among patients with anaphylaxis to inhaled allergens, 5 out of 6 had false-negative results at both biotin levels. Similarly, in patients with anaphylaxis to wasp stings, false-negative results were recorded in 3 out of 6 samples at a concentration of 184 ng/mL, and in 4 out of 6 samples at a concentration of 500 ng/mL. Among patients with peanut-induced anaphylaxis, a concentration of 184 ng/mL led to false-negative results in 3 out of 6 patients, while the higher concentration of 500 ng/mL increased the number of false negative results to 5 out of 6 samples [81].

Troponin

In 2017, the first study was published showing that biotin can affect the results of cardiac markers, such as troponin and N-terminal prohormone of brain natriuretic peptide (NT-Pro-BNP) [82]. Treatment strategies for patients with non-ST elevation myocardial infarction (NSTEMI) are based on measuring troponin levels. The development of highly sensitive troponin tests, defined as tests with less than 10% imprecision at the 99th percentile and capable of detecting at least 50% of the reference population, has led to their use in rapid diagnostic algorithms [83].

The latest fifth-generation cardiac troponin T test (Gen 5 Stat cTnT; Roche Diagnostics) was compared with the earlier cTnT test (Roche Diagnostics) and the highly sensitive cardiac troponin I (hs-cTnI) test (Abbott STAT; Abbott Diagnostics), both of which are globally available analyzers. The study involved a plasma mixture from healthy volunteers who were taking 10 mg of biotin daily, along with plasma samples known to have elevated troponin concentrations. The main conclusion was that biotin can significantly affect the results of the Gen 5 cTnT test, leading to falsely negative results. The interference thresholds for Gen 5 cTnT were significantly lower (31 ng/mL) compared to other tests like the older cTnT (315 ng/mL) and hs-cTnI (>2000 ng/mL) [84]. In response, Roche later reformulated the Gen 5 cTnT test, increasing the biotin interference threshold to 1200 ng/mL [85].

In cases of suspected acute myocardial infarction (AMI), it is recommended to conduct troponin testing over a longer period (e.g. the 0/3 hour protocol). The first blood sample for troponin measurement is taken immediately upon hospital admission, and the second after 3 hours [86]. Research has shown that the risk of falsely negative results due to biotin in patients suspected of having AMI, who are tested using the Gen 5 cTnT test, is very low. One study assessed the prevalence of elevated biotin in two cohorts. The first cohort included 850 patients from U.S. emergency departments who were tested for troponin due to suspected AMI. In this cohort, the prevalence of biotin levels above 20 ng/mL was 0.13% upon hospital admission, and the risk of falsely negative results was estimated at 0.026%. The second cohort included 2023 randomly selected samples from a commercial laboratory

network in the U.S., providing broader coverage of the general population. The prevalence of biotin levels above 20 ng/mL in this cohort was 0.74%. The data were expanded to estimate the risk in patients taking high doses of biotin, such as those being treated for multiple sclerosis. It was estimated that the risk of biotin interference with the Gen 5 cTnT assay is approximately 0.025% upon hospital admission, decreasing to less than 0.00001% after 6 hours. Although the likelihood of biotin interference is minimal, special caution is recommended for patients taking high doses of biotin or those with renal insufficiency [87].

Methods for Detecting and Preventing Biotin Interference

Raising Awareness of Biotin Interference

Raising awareness about the issue of biotin interference is a crucial first step in reducing the risk of false laboratory test results. Therefore, it is essential to develop educational strategies for both healthcare professionals and patients. To increase awareness among healthcare workers, strategies should include organizing lectures and panel discussions, adding alerts to test results, distributing informative brochures throughout healthcare facilities, and providing links to additional information on websites aimed at healthcare professionals. For patients, it is helpful to include biotin-related notices on laboratory test orders, post information on laboratory and healthcare websites, include reminders in appointment systems and email notifications, and display posters and informational materials at sample collection sites and in clinics [88].

Detection of Biotin and Rapid Analysis Methods in Clinical Diagnostics

Introducing a biotin test into the diagnostic process that can detect high doses of biotin would be highly beneficial. This would provide clinicians with a reliable and timely indicator of potential biotin interference, eliminating the need for additional confirmation methods. Currently, commercial ELISA tests are available for manual use, capable of detecting very low biotin concentrations, as low as 0.4 ng/mL. Developing rapid tests for use directly at the point of care would be particularly useful for detecting biotin in urgent clinical situations.

While laboratory methods such as liquid chromatography-mass spectrometry (LCMS/MS) can be used to measure biotin concentrations, they are not practical for processing large numbers of samples in routine clinical practice [89].

Serial Dilution Methods

In laboratory practice, when biotin interference is suspected, the first approach often involves serial dilution. Simple serial dilution reduces the concentration of biotin in the sample, and by adjusting the analyte concentration in proportion to the dilution factor, more accurate results can be obtained. The sample should show values consistent with the dilution factor; however, if an interferent is present, the results will not be linear. As the sample is diluted, the degree of interference decreases, allowing for more reliable results.

Caution is needed when diluting free hormones or when excessive dilution is performed, as this can lead to inaccurate results. Additionally, if biotin levels in the sample are extremely high, multiple rounds of serial dilution may be necessary, which can require extra time [23].

Biotin Depletion Protocols

Biotin depletion protocols involve using materials that bind to biotin and remove it from the sample before testing. One common approach is to add streptavidin-agarose particles to the sample, typically at a ratio of 10% of the sample volume. The sample is then incubated for one hour with periodic mixing. After incubation, the sample is centrifuged, and the supernatant (the liquid above the sediment) is used for testing. Biotin interference is confirmed if there is a significant difference in test results before and after the biotin depletion process. While this method can reliably confirm the presence of biotin in a sample, a thorough evaluation is necessary before routine application in clinical practice. It is also essential to emphasize that results obtained after streptavidin treatment should not be used for final diagnostic conclusions. Instead, they should serve as an indication that the patient should stop biotin supplementation. Once biotin intake is discontinued, the patient should return for a new blood sample and testing to obtain accurate results [23].

Additionally, biotin can be effective-

ly removed from serum using streptavidin-coated microparticles, which eliminate biotin interference in the samples. This method is simple and reliable, allowing for the removal of high concentrations of biotin and its metabolites, especially in patients undergoing high-dose biotin therapy. The biotin depletion protocol takes less than an hour, ensuring quick and efficient sample processing [90].

Biotin Elimination Period

For patients taking biotin supplements at doses up to 10 mg per day, it is estimated that biotin is eliminated from the body within 8–10 hours, allowing its levels to return to near physiological values, thereby reducing the risk of interference with laboratory tests. However, for patients taking high doses of biotin, such as 300 mg daily, the time required for biotin elimination can be significantly longer. Additionally, patients with impaired kidney function may experience an even longer biotin elimination period, which can extend to several days or even weeks. Given that the elimination period can vary among patients, it is recommended that biotin supplementation be discontinued at least 48 hours prior to blood sample collection for laboratory testing to minimize the risk of potential interference [11].

Redesign of Immunoassay Formats and Technological Advancements to Reduce Biotin Interference

Immunoassay manufacturers face the challenge of developing new tests or modifying existing ones to make them more resistant to biotin interference, in accordance with guidelines established by the Food and Drug Administration (FDA) and the Clinical & Laboratory Standards Institute (CLSI). According to these guidelines, the biotin sensitivity threshold should be set at 3,510 ng/mL. This threshold is three times higher than the highest physiological concentration of biotin, which is 1,160 ng/mL, noted in patients taking high doses of biotin for the treatment of multiple sclerosis [90].

One strategy for eliminating biotin interference is to completely remove the biotin-streptavidin system and replace it with another high-affinity system, such as the fluorescein isothiocyanate (FITC)-anti-FITC system. This method relies on the binding of FITC markers to anti-FITC antibodies for im-

mobilization and detection and is considered a sensitive alternative to the biotin-streptavidin system [91].

Another approach to reducing biotin interference involves pre-binding biotin and streptavidin before the sample is introduced into the test. This method significantly reduces the risk of interference, although it may be more expensive and complex [11].

Increasing the number of binding sites for streptavidin is yet another method to raise the biotin interference threshold. A study by Liu and colleagues demonstrated that the primary cause of interference was an insufficient amount of streptavidin. When the concentration of streptavidin-coated magnetic particles was increased, the number of available streptavidin binding sites also rose, allowing for more effective neutralization of biotin in the samples. This approach maintained accuracy and precision in both competitive and non-competitive immunoassays [92].

CONCLUSION

Biotin interference in laboratory tests presents a significant challenge, particularly in immunoassays that rely on biotin-streptavidin technology. The increasing use of high-dose biotin supplements heightens the risk of producing inaccurate test results. Tests most vulnerable to interference include those assessing thyroid function, along with hormonal, reproductive, serological, and cardiac markers. In patients consuming high doses of biotin, laboratory results may not accurately represent their actual health status, potentially leading to inappropriate treatment and severe clinical consequences. To reduce the likelihood of errors, raising awareness of this issue among laboratory technicians, physicians, and patients is essential. It is recommended that patients taking biotin discontinue its use at least 48 hours prior to testing. Additionally, laboratories should employ serial dilution techniques or use protocols to remove biotin from samples before analysis. Further research and the development of novel techniques, including biotin-resistant immunoassays, are essential for reducing the impact of biotin interference in the future.

CONFLICTS OF INTEREST

All authors declare no conflict of interest.

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Interferencija biotina sa rezultatima laboratorijskih testova

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KRATAK SADRŽAJ

Uvod: Interferencija biotina u laboratorijskim testovima postaje sve veći problem, naročito zbog široke upotrebe biotina, ne samo kao terapijskog sredstva već i kao suplementa u kozmetičkoj industriji. Imunoeseji koji koriste biotin-streptavidin tehnologiju posebno su podložni smetnjama, što može dovesti do netačnih rezultata testova, pogrešne dijagnoze i neodgovarajućeg lečenja.

Metodologija: Pregled literature vršen je pomoću baza podataka kao što su PubMed i Google Scholar. Korišćeni su ključni pojmovi kao što su „biotin“, „interferencija“ i „imunoesej“ za identifikaciju relevantnih studija.

Tema: U preglednom radu, razmotren je rizik interferencije biotina u različitim imunoesejima, posebno njegov uticaj na testove funkcije štitne žlezde (TSH, FT3, FT4), paratiroidni hormon (PTH), testosteron, humani horionski gonadotropin (hCG) i srčane markere kao što je troponin. Istražena je farmakokinetika eliminacije biotina i prevalencija povišenih nivoa biotina u populaciji pacijenata. Istaknute su kliničke posledice lažno visokih ili niskih rezultata, koje mogu dovesti do pogrešne dijagnoze. Takođe su razmatr metode za ublažavanje interferencije biotina, kao što su serijsko razblaživanje, uklanjanje biotina i razvoj naprednih imunoeseja koji ne interferiraju sa biotinom.

Zaključak: Interferencija biotina predstavlja značajan izazov u laboratorijskoj dijagnostici, posebno uz sve veću upotrebu suplemenata sa visokim dozama biotina. Testovi koji su najosetljiviji uključuju one za procenu funkcije štitne žlezde, reproduktivne hormone i srčane markere. Podizanje svesti među zdravstvenim radnicima i pacijentima, uz primenu protokola za uklanjanje biotina i unapređenje dizajna imunoeseja, ključni su koraci za smanjenje interferencija. Kontinuirano istraživanje imunoeseja otpornih na biotin je ključno za poboljšanje dijagnostičke tačnosti i sprečavanje kliničkih pogrešnih tumačenja.

Ključne reči: suplementacija biotinom, dijagnostička tačnost, imunoesej, biotin-streptavidin tehnologija, testovi funkcije štitne žlezde, protokoli za uklanjanje biotina

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