

Minimize the Risk of False Lab Test Results



Tosoh is Your Simple Solution to Biotin Interference

The increase in biotin supplementation use combined with the limitations in many immunoassays has led to false lab results, misdiagnosis and mismanagement of patients, triggering the FDA to issue a warning against biotin interfering with some lab tests¹⁻³.

Tosoh's ST AIA-PACK[®] Test Menu of immunoassays use a proprietary method that is **free from biotin interference**.

Not all immunoassays are the same. Using the right immunoassay gives you confidence in the result you deliver. **Choose wisely. Choose Tosoh.**

TOSOH BIOSCIENCE

www.tosohbioscience.us



Facts on Biotin

What is Biotin & what does it do?

- Vitamin B7
- Water soluble vitamin of the B-complex
- Essential vitamin
- Half life 8-16hrs
- It is involved in a wide range of metabolic processes, specifically in the utilization of fats, amino acids and carbohydrates
- Essential for skin, nerve and digestive health as well as embryonic development

Where can it be found?

- Naturally occurring in meat, fish, eggs, seeds
 - 35 to 70 mcg daily recommended
- Multi & prenatal vitamins
 - 30-150 mcg of biotin
- Supplements:
 - 2000-10,000 mcg of biotin
 - Often packaged as hair and nail beauty treatment

Who is using it?

- Over 100 million people in U.S. use vitamin/mineral supplements: > 66% of US adults⁴
- Megadoses 10-20mg per day prescribed for patients with:
 - Inherited metabolic diseases
 - Inflammatory diseases
 - Multiple sclerosis



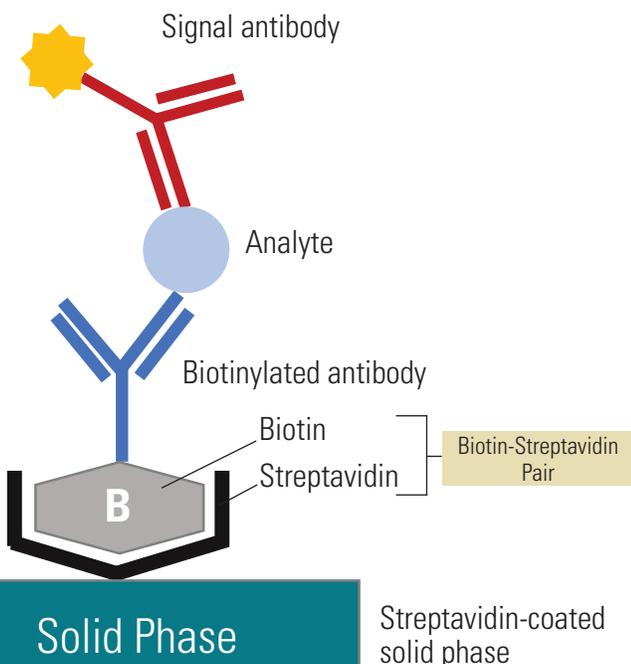
Prevalence of Biotin Supplement Use

Biotin mainstream use is growing rapidly due to increased awareness of its benefits to hair, skin and nails. Now a \$30 billion dollar industry, its placements in beauty-related supplementation has led to increasing sales, particularly in the 5,000 to 10,000 mcg dosages³.

Surveys⁵ have shown that approximately:

- 41.8% of patients reported taking multivitamins
- 7.7% reported taking biotin supplements
 - 79.2% of them were female
- 7.4% of emergency department patients had biotin in their blood at or above the lowest known threshold for interference

What is Biotin Interference



- Biotin is a small molecule and it can be attached to a variety of other molecules such as large antibodies to tiny steroid hormones with no/minimal effect on their biological activity.

Biotin-Streptavidin Pair:

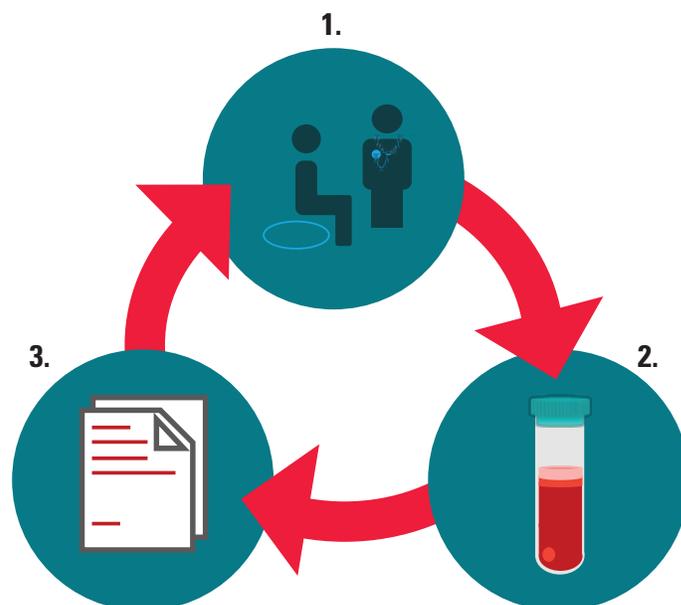
- The high affinity binding of biotin to streptavidin is a popular assay basis for many molecular tests and immunoassay platforms.
- This pair is used to capture and amplify the assay readout in immunoassays.

When exogenous biotin is present in a sample due to ingestion from supplements, it too will bind to streptavidin and prevent the assay's Biotin-Streptavidin Pair from binding and acting as a signal isolation and amplification tool. This is called **biotin interference**^{5,6}.

The Impact of Biotin Interference in Laboratory Tests

The Cycle of Biotin interference:

1. Patient taking biotin supplements gives a blood sample containing unbound biotin.
2. Blood test is performed with method susceptible to biotin interference leading to erroneous results.
3. Physician is misguided with false results leading to improper treatment and continued patient health concern⁷.



Limitations of Current Protocol for Mitigating Risks of Biotin Interference

Current Protocol Requires:

Communication

- Biotin protocol in place requires patients to declare ingestion of biotin-containing supplements.

Awareness

- Lab directors need to communicate the warnings.
- Lab personnel must be made aware of the reality of biotin interference.

Compliance

- Patients are instructed to refrain from taking biotin for 48 hours and to return before a blood draw⁸.
- Lab personnel to comply with filling out the necessary information and complying to the recommendations.

Alternative Testing

- A specimen suspected of biotin interference, those above or below clinical thresholds, should be analyzed with an alternate platform that is free from biotin interference.

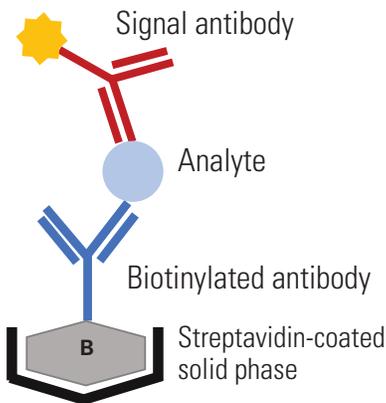
Limitation:

- Patients may not be able to recall exact details on supplementation.
- Emergency department patients may not be in appropriate physical health to communicate any information.
- Clinicians need to be made aware of the methodologies that are susceptible to biotin interference as well as solutions for susceptible samples.
- Some assays require up to 7 days for normalization⁹.
- Difficult to attain full compliance.
- Due to evidence of biotin accumulation in the blood, period of cessation from biotin ingestion is dependent on assay type, biotin dosage and patient physiological factors such as kidney function¹⁰⁻¹¹ etc.
- Increases turnaround time or may not be feasible due to availability of appropriate testing platforms.
- Samples that are seemingly normal due to false elevation or false lowering of the actual value are overlooked and not flagged for alternate testing.

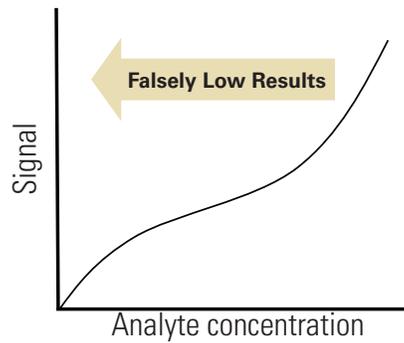
Mechanism of Biotin Interference in Laboratory Tests^{5,6}

Sandwich Immunoassay

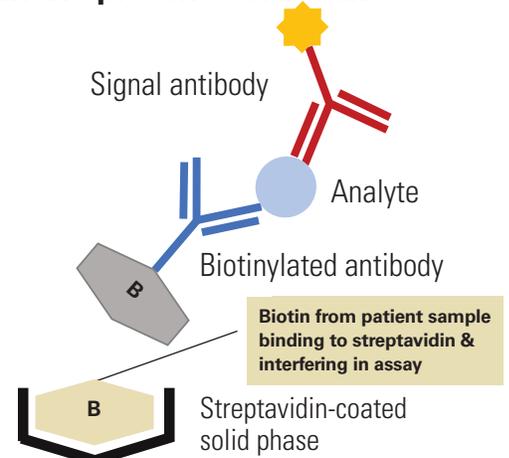
No biotin



Solid Phase



In the presence of biotin



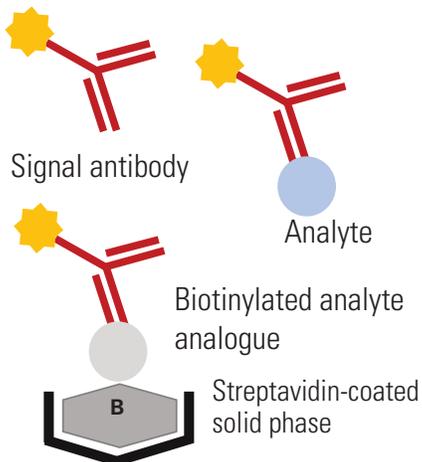
Solid Phase

Excess biotin in a sandwich assay leads to a falsely low result

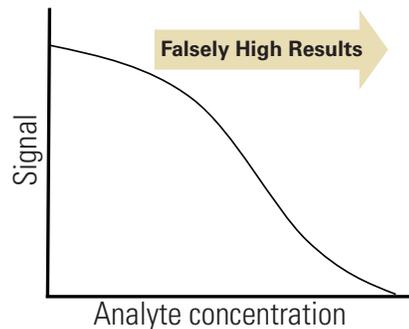
In a biotin-based sandwich immunoassay, the analyte is isolated by being sandwiched between a signaling antibody and the biotinylated antibody which is in turn bound to a streptavidin-coated solid phase. This complex is measured and the signal intensity is directly related to the analyte concentration in the sample. In the presence of exogenous biotin in the sample which binds to the streptavidin-coated solid phase in the place of the signaling complex, the signal is lost through washing steps. This leads to a falsely low result.

Competitive Immunoassay

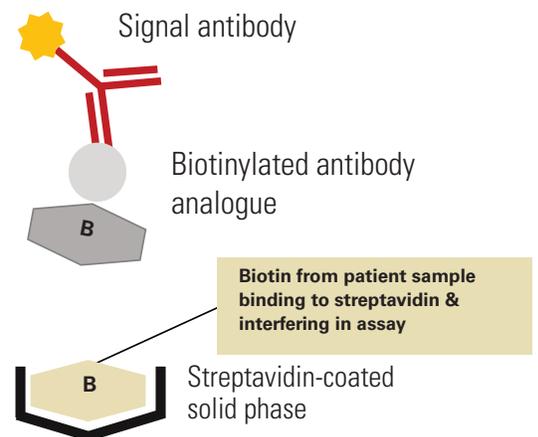
No biotin



Solid Phase



In the presence of biotin



Solid Phase

Excess biotin in a competitive immunoassay leads to a falsely high result

In a biotin-based competitive immunoassay, the analyte competes with an biotinylated analyte analogue for binding to the signal antibody. The solid phase-bound complex of biotinylated analyte analogue and signaling antibody is isolated and measured. Hence, the signal being measured is captured from the biotinylated analyte analogue which is indirectly related to the analyte concentration in the sample. In the presence of exogenous biotin which binds to streptavidin on the solid phase, the signaling complex is prevented from binding leading to a falsely high result.

Biotin Interference in Widely Used Biotin-based Immunoassays

A study published in September 2016, looked at how a 10 mg daily dose of biotin affected test results in six healthy adults. Results showed that biotin supplementation caused errors in nearly 40 percent among the 23 lab tests⁷. The table below summarizes the extent of biotin interference in immunoassays.

Assays	Company A	Company B	Company C	Company D	Company E	Tosoh's AIA-PACK
FT3	✓		No Biotin	✓	✓	No Biotin
FT4	✓		No Biotin	✓	✓	No Biotin
Total T3	No Biotin		No Biotin	✓		No Biotin
Total T4	No Biotin		No Biotin	✓	No Biotin	No Biotin
TSH	No Biotin		✓	✓	✓	No Biotin
TRAb				✓		
SHBG	✓			✓		No Biotin
Thyroglobulin	✓			✓		
PTH	No Biotin	✓	✓	✓		No Biotin
25 OH vit D	No Biotin	✓	✓	✓		No Biotin
Cortisol	No Biotin		✓	✓		No Biotin
ACTH				✓		No Biotin
Testosterone	No Biotin		✓	✓		No Biotin
Estradiol	No Biotin		✓	✓	✓	No Biotin
FSH	No Biotin		✓	✓	✓	No Biotin
LH	No Biotin		✓	✓	✓	No Biotin
Prolactin	No Biotin		✓	✓	✓	No Biotin
IGF1		✓				
GH	No Biotin	✓		✓		No Biotin
C peptide				✓		No Biotin
Insulin	No Biotin			✓		No Biotin

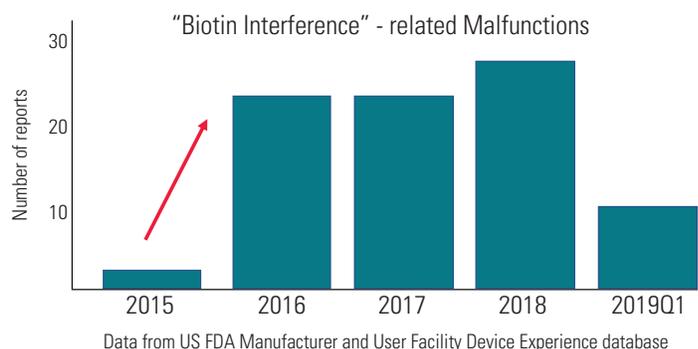
 Assay not available
 No Biotin
 No Biotin in Assay
 Biotin-Streptavidin use in assay

Table adapted from Piketty et al. (2016)⁷ & contains company names

Reports of Biotin Interference in Immunoassays

First Author (Ref)	Year	Analytes Affected	Clinical Consequences
Henry (6)	1996	FT4 TSH	Delay in treating hypothyroidism
Meany (7)	2009	PTH	Delay in treating severe secondary hyperparathyroidism
Kwok (8)	2012	FT4 FT3 TSH	Nil
Wijeratne (9)	2012	FT4 FT3	Nil
Wijeratne (9)	2012	FT4 FT3 TG DHEAS E ₂ T Ferritin	Peak interference at 2 h, duration and magnitude varied according to analyte
Waghray (10)	2013	PTH	Nil
Waghray (10)	2013	PTH	Nil
Barbesino (11)	2016	FT4 FT3 TSH TRAb	Nil
Charles	2019	TSH	Nil
Charles	2019	TSH	Non-toxic goiter confused for toxic nodular goiter
Charles	2019	TSH	Erroneous Graves' disease diagnosis
Charles	2019	TSH	Mistaken clinical assessment

- Reports of biotin-related laboratory errors have increased in recent years.

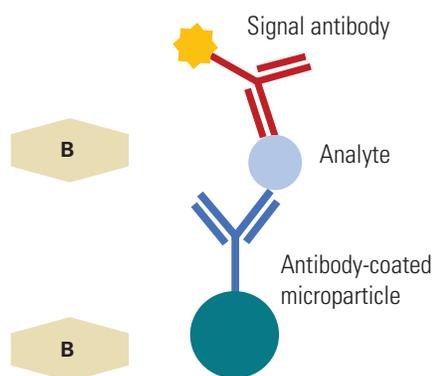


- This has led to misdiagnoses, inappropriate or delayed treatment.
- Increase economic burden and time wasted due to confusion when results do not match clinical picture and subsequent testing cascade.

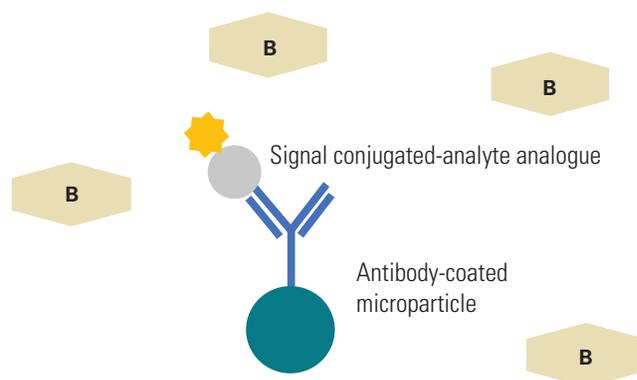
Table adapted from Elston MS et al. (2016)¹²

Tosoh's Immunoassays are Free from Biotin Interference

Sandwich Immunoassay



Competitive Immunoassay



Biotin does not affect Tosoh assays because our assays do not employ the biotin-streptavidin pair to isolate our signal. Our antibodies are coated on microparticles and form the basis of our proprietary dry-reagent **Unit Dose Test Cup Technology**.

Tosoh's Unit Dose Test Cup Technology

Tosoh Bioscience's proprietary dry-reagent, unit dose test cup technology is **free from biotin interference**, offers calibration stability of up to 90 days, and achieves consistency and accuracy with reduced wasted. The test cup is interchangeable across Tosoh's portfolio of automated immunoassay analyzers. Tosoh analyzers are suited for a variety of different throughput requirements, from small physician office labs to large reference labs, and are easy to use, robust, and precise, and offer a simplified workflow with minimal downtime.



Choose Wisely. Choose Tosoh.

References

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For more information, call 1.800.248.6764

Tosoh products are for Prescription use only as In-Vitro Diagnostics

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Part # AIA-BIO-BR01 Rev. 01/0719



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