Tosoh's Biotin-Free Immunoassays Signify Zero Biotin Interference Risk

Endogenous biotin in patient samples can cause interference because many immunoassays use the biotin-streptavidin interaction. Tosoh has a full menu of 100% biotin-free immunoassays compatible with AIA® systems.

Protect your Immunoassay Results from Biotin-Induced Laboratory Errors

- Over 66% of adults in the U.S. take dietary supplements[1] which can include biotin to support healthy hair, skin and nails
- Biotin treatment has been also reported to potentially benefit patients with a wide range of conditions such as multiple sclerosis, inherited metabolic diseases, and diabetes mellitus[2]
- Reports of biotin-related laboratory errors have been increasing over recent years

Using Tosoh's AIA-PACK® assays can eliminate your risk of biotin interference.

TOSOH BIOSCIENCE
www.tosohbioscience.us

TOSOH

Biotin Interference

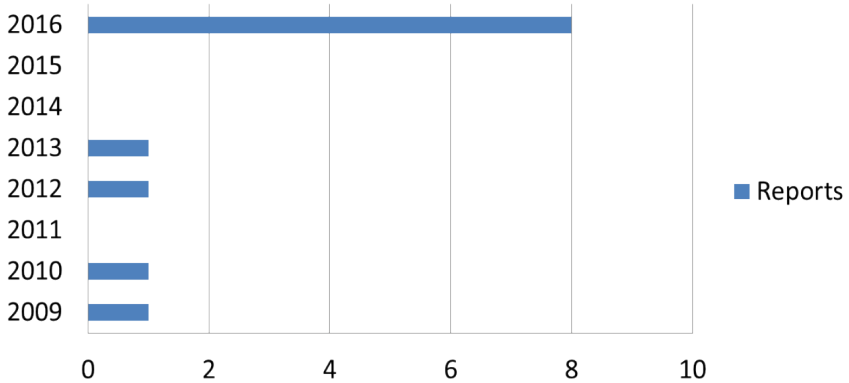
Popular Assay Design Meets Vitamin Megatrend

- Over 100 million people in the U.S. use vitamin/mineral supplements[3]
- Many over-the-counter vitamin supplements include significant amounts of biotin, up to 10 mg (10,000 mcg) per pill, to improve hair and nails[4]
- "Use of vitamin D, magnesium, iron, CoQ10 and biotin were at historically high levels" - Sloan Trends, Inc. (2014)[3]
- Biotin megadoses are also being used to manage various diseases[2]
- Biotin can cause test interference because many immunoassays are designed to use biotin-streptavidin interactions[5]

Misdiagnosis Reports Have Been Increasing

- "Our core laboratory has recently identified several Mayo Clinic patients with erroneous thyroid function test results... due to biotin supplement consumption….In one case, the patient was scheduled for radioiodine thyroid ablation due to erroneous thyroid function results." — Katzman, B.M. et al. (2016), Mayo Clinic[6]
- "...laboratory findings suggested a diagnosis of severe Graves' disease. All of the assays yielding abnormal results employed the biotin-streptavidin affinity in their design. The patient had no symptoms of hyperthyroidism, and a detailed review of his medications revealed intake of megadoses of biotin." — Barbesino, G. (2016), Massachusetts General Hospital[7]
- "Two patients presented with surprising low parathyroid levels — one during preoperative evaluation for hyperthyroidism and another during post-operative follow-up after subtotal parathryroidectomy. The patients were found to be taking 1,500 mcg and 5,000 mcg of biotin per day, respectively. The role of biotin was confirmed in one of the patients…" — Waghray, A. et al. (2013), Cleveland Clinic[8]
- "...increased intact PTH result from the reference laboratory (786 ng/L) was more consistent with the patient's clinical picture, suggesting that the 48 ng/L value obtained in our clinical laboratory was falsely low… Further review of the patient's medical history revealed that she was ingesting 10 mg biotin per day for restless leg syndrome..." — Meany, D. L. et al. (2009), Johns Hopkins Medical Institutions[9]

Biotin Interference Report Trend[4, 5-15]



Megadoses May Lead to Misdiagnosis

Examples of widely used hormone immunoassays using streptavidin-biotin* compared with Tosoh's AIA-PACK® Immunoassays

Assays	Company 1	Company 2	Company 3	Company 4	Company 5	Tosoh's AIA-PACK
FT3	√		No Biotin	√ (286)	√ (205)	No Biotin
FT4	√		No Biotin	√(82)	√(205)	No Biotin
Total T3	No Biotin		No Biotin	√(41)		No Biotin
Total T4	No Biotin		No Biotin	√(409)	No Biotin	No Biotin
TSH	No Biotin		√(20.5)	√(102)	√(2050)	No Biotin
TRAb				√(41)		
SHBG	√			√(246)		No Biotin
Thyroglobulin	√			√(327)		
PTH	No Biotin	√	√(20.5)	√(205)		No Biotin
25-OH vit D	No Biotin	√(300)	√(61)	√(286)		No Biotin
Cortisol	No Biotin		√(41)	√(123)		No Biotin
ACTH				√(246)		No Biotin
Testosterone	No Biotin		√(41)	√(123)		No Biotin
Estradiol	No Biotin		√(20.5)	√(147)	√	No Biotin
FSH	No Biotin		√(41)	√(246)	√	No Biotin
LH	No Biotin		√(20.5)	√(205)	√	No Biotin
Prolactin	No Biotin		√(41)	√(164)	√	No Biotin
IGF-1		√(300)				
GH	No Biotin	√(300)		√(123)		No Biotin
C-peptide				√(246)		No Biotin
Insulin	No Biotin			√(246)		No Biotin

Assay not available | √ Streptavidin-biotin use in assay design | No Biotin in assay

() Biotin concentrations in nmol/L above which an erroneous result can happen, based on company reagent notices

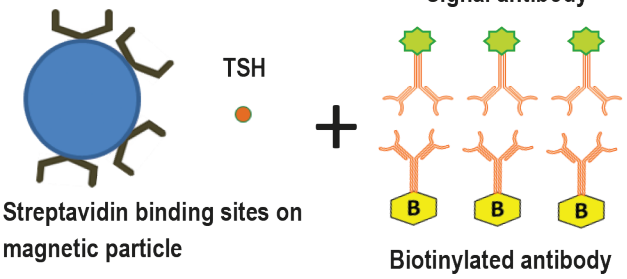
*Table with five companies' immunoassay information adapted from Piketty et al. (2016) *CCLM*[10]

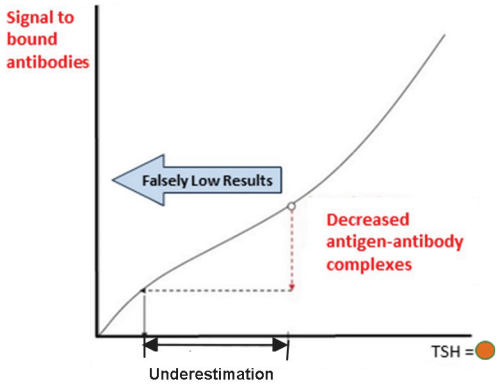
Tosoh Has a Full Menu of Biotin-Free Immunoassays

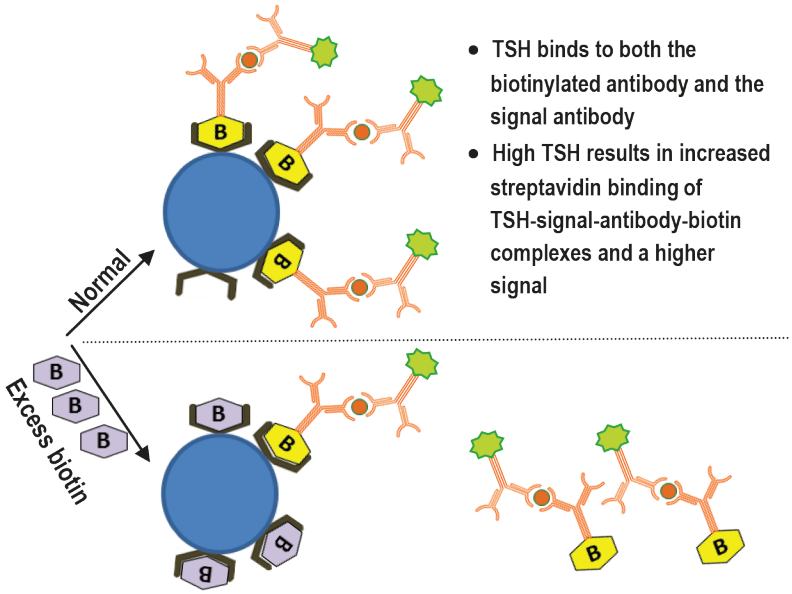
How Does Biotin Cause Immunoassay Interference?[10,16]

Sandwich Immunoassay

Excess biotin can lead to a false LOW result





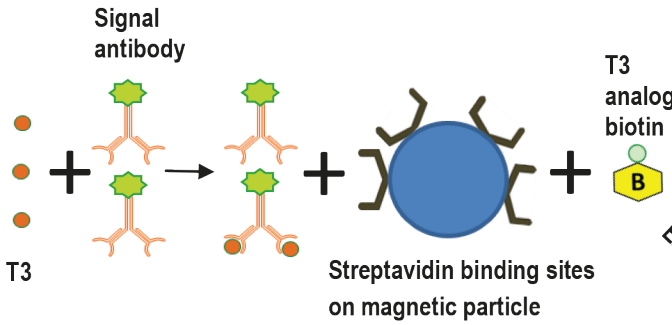


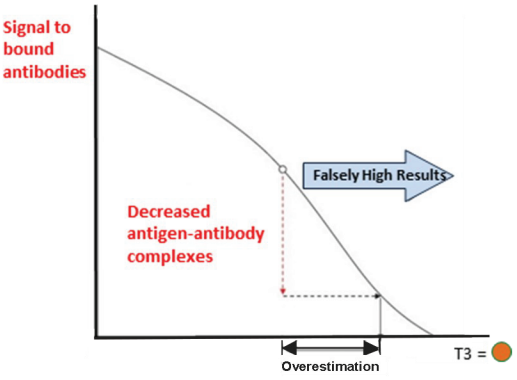
- TSH binds to both the biotinylated antibody and the signal antibody
- High TSH results in increased streptavidin binding of TSH-signal-antibody-biotin complexes and a higher signal

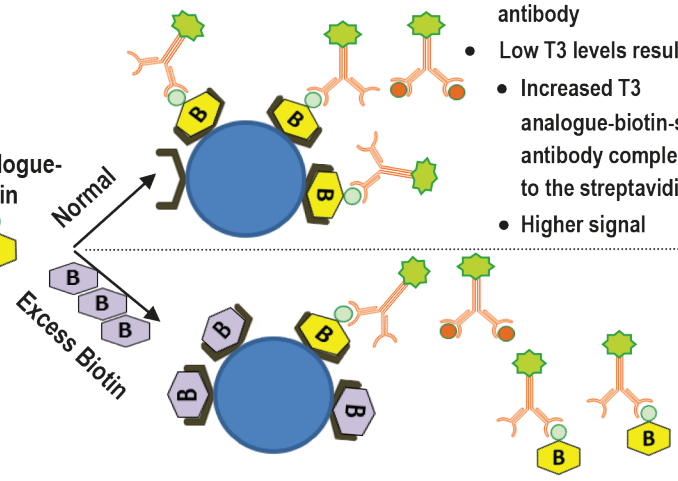
- Excess biotin bind to the streptavidin sites
- This blocks the TSH-signal-antibody-biotin complexes from binding.
- The resulting very low signal is misinterpreted as a low TSH

Competitive Immunoassay

Excess biotin can lead to a false HIGH result







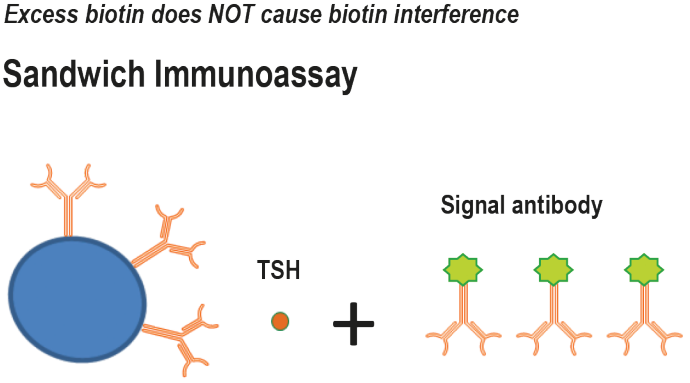
- T3 competes with T3 analogue-biotin to bind with the signal antibody
- Low T3 levels result in:
  - Increased T3 analogue-biotin-signal antibody complex binding to the streptavidin
  - Higher signal

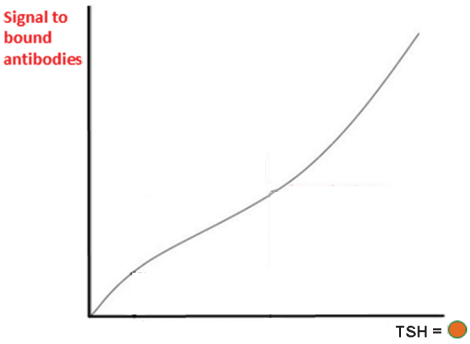
- Excess biotin binds to the streptavidin sites blocking the T3 analogue-biotin-signal antibody complex from binding
- The low signal is misinterpreted as high T3

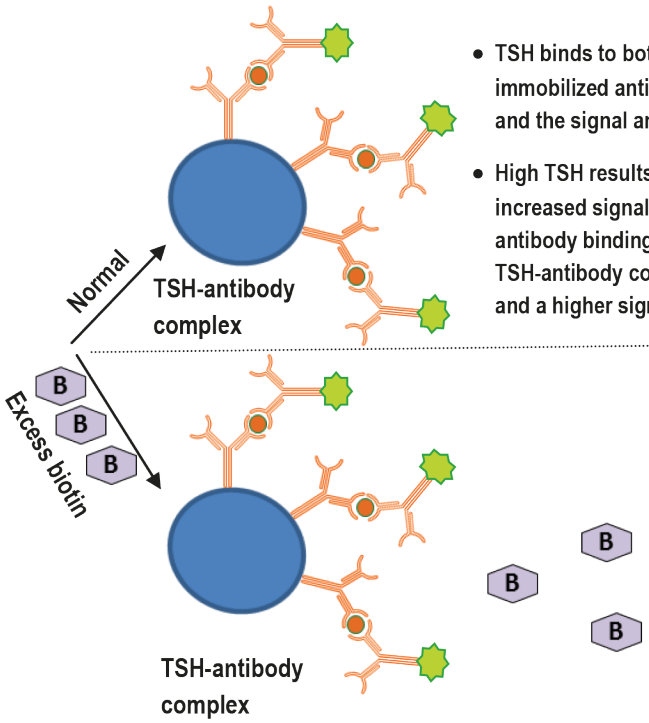
Tosoh's Immunoassays are 100% Biotin-Free[10]

Excess biotin does NOT cause biotin interference

Sandwich Immunoassay



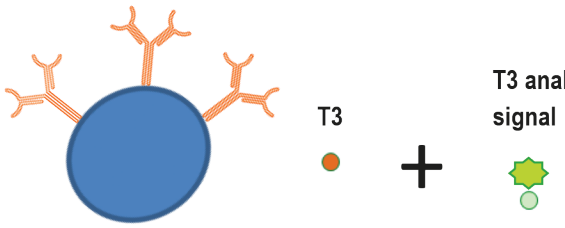


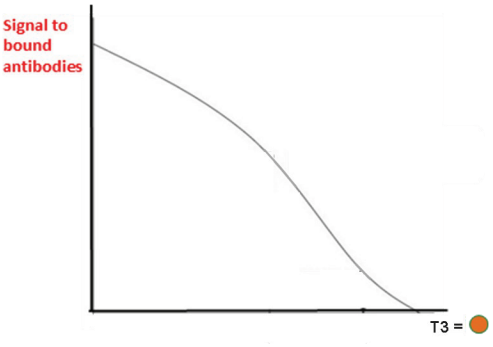


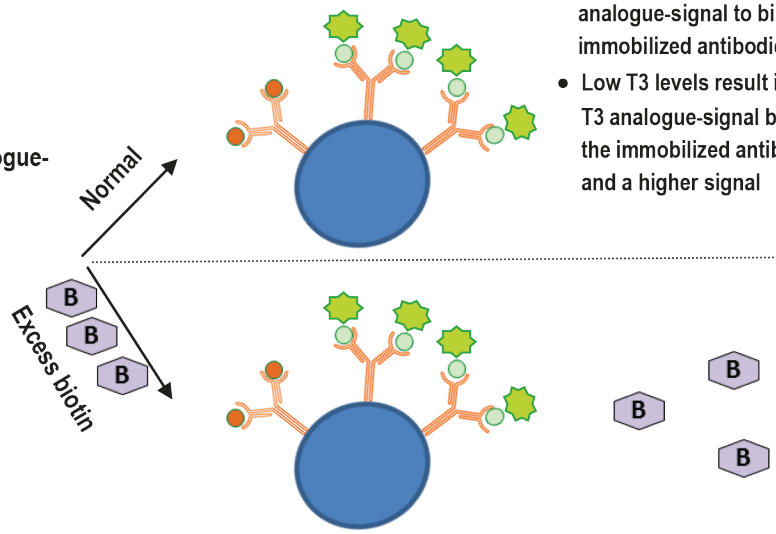
- TSH binds to both the immobilized antibody and the signal antibody
- High TSH results in increased signal antibody binding of TSH-antibody complexes and a higher signal

A biotin-free sandwich immunoassay design has ZERO (0) risk of biotin interference.

Competitive Immunoassay







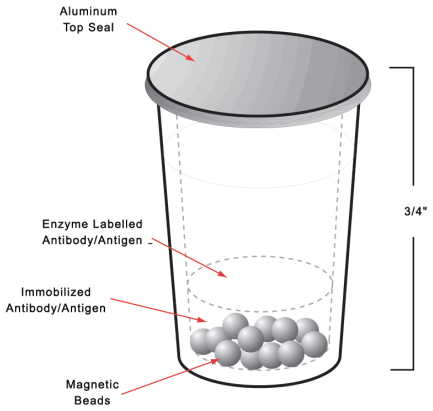
- T3 competes with T3 analogue-signal to bind with immobilized antibodies
- Low T3 levels result in more T3 analogue-signal binding to the immobilized antibodies and a higher signal

A biotin-free competitive immunoassay design has ZERO (0) risk of biotin interference.

Tosoh's Biotin-Free Immunoassays feature...

Unit Dose Test Cup Reagents

- Single, unitized cups use a dry reagent format that requires no pre-mixing, no pre-measuring, no on-board refrigeration and no waste
- Dry reagent format ensures calibration stability of up to 90 days for most assays
- Reagents have a one year shelf life from date of manufacture
- The AIA test cups and trays are labeled with code and lot number for automated scheduling and inventory management on the AIA-2000 and AIA-900 sorter models
- ST AIA-PACK reagents provide a faster turnaround time due to a 10 minute incubation protocol
- Extensive test menu provides a wide range of immunoassay tests including thyroid, cardiac markers, tumor markers, reproductive hormones, anemia markers, metabolic markers, diabetes, kidney markers and more



Test Cup Diagram
Actual Test Cup Size:
1.25 W x 2.0 H cm

Tosoh AIA Test Menu

10 minute incubation unless otherwise noted.

Tumor Markers
AFP
CEA
PSA
CA 125
CA 27.29
CA 19-9

Diabetes Assays
C-Peptide II
HbA1c •
Insulin

Thyroid
TSH
TT3
T4
FT3
FT4
T-Uptake
TSH 3rd Gen ◆
TPO Ab ◆
Tg Ab ◆

Cardiac Markers
CKMB
Troponin I 2nd Gen
Myoglobin

Anemia
Ferritin
Vitamin B12 ◆
Folate ◆
RBC Folate ◆

Reproductive
β-HCG
HCG
DHEA-S
Estradiol (E2)
hs Estradiol (hs E2) ◆
FSH
LH II
Prolactin
Progesterone II
Progesterone III
SHBG
Testosterone

Kidney Marker Assays
β-2 Microglobulin
Cystatin C
iPTH

Metabolic
Cortisol
HGH

Additional Assays
ACTH
Homocysteine
IgE II
PAP
25-OH vitamn D ◆

Reagent Tray - 20 Test Cups/tray

• Available on AIA-360 and AIA-900 only.

◆ > 10 minute incubation. Not available for use on AIA-360.

Tosoh - Your Simple Solution to Biotin Interference

Eliminate your false result risk due to biotin megadoses by switching to our highly flexible and advanced immunoassay platforms.

AIA-900 Benchtop

AIA-900 Loader Model

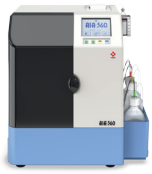
AIA-900 with 9 Tray Sorter

AIA-900 with 19 Tray Sorter

AIA-900 Automated Immunoassay Analyzer

- Max. 90 tests per hour
- Intuitive operations for advanced testing
- Three interchangeable system configurations

Available for Labs and Workloads of All Sizes



Instrument image size not proportional

AIA-360

AIA-360 Automated Immunoassay Analyzer

- 36 tests per hour
- First result—20 minutes

AIA-2000

AIA-2000 Automated Immunoassay Analyzer

- Max. 200 tests per hour
- Load 960 tests (48 trays)
- Walk away time — 4 hours
- Full-featured and flexible for high throughput testing

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