Biotin

bw	body weight
CNS	Chinese Nutrition Society
CRN	Council for Responsible Nutrition
DRI	dietary reference intake
EC SCF	European Commission Scientific Committee on Food
EFSA	European Food Safety Authority
EVM	Expert Group on Vitamins and Minerals
ICMR-NIN	Indian Council of Medical Research - National Institute of Nutrition
IOM	Institute of Medicine
IU	international unit
JECFA	Joint FAO/WHO Expert Committee on Food Additives
KNS	Korean Nutrition Society
LOAEL	lowest observed adverse effect level
LOEL	lowest observed effect level
NDA	EFSA Panel on Nutrition, Novel Foods and Food Allergens
NIH	National Institute of Health
NOAEL	no observed adverse effect level
NOEL	no observed effect level
RCT	randomized clinical trial
SUL	safe upper level
UF	uncertainty factor
UL	tolerable upper intake level

Introduction

Biotin is a water-soluble B vitamin consisting of an ureido ring fused with a tetrahydrothiophene ring with a valeric acid side chain (Mock 2014; NIH 2022). The only active form found in nature is the D(+)-biotin isomer (Mock 2014). Biotin functions as a cofactor for five carboxylase enzymes, including acetyl-CoA carboxylase 1 and 2, propionyl-CoA carboxylase, methylcrotonyl-CoA carboxylase, and pyruvate carboxylase (Zemplen and Mock 1999a; Drake 2022; NIH 2022; Solvik and Strand 2024). Biotin plays a critical role in fat synthesis, branched-chain amino acid catabolism, gluconeogenesis, and cell signaling (NIH 2022; Chungchunlam and

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Moughan 2024).

Unlike plants and microorganisms, animals and humans cannot synthesize biotin and require dietary or supplemental intake (Solvik and Strand 2024; EFSA 2014). Dietary biotin consumed by animals is stored in tissues, which in turn provide a rich source of biotin for the human diet. Biotin can be found in milk, liver, grains, soy, nuts, meat, fish, poultry, egg, some cheeses, and some vegetables (Drake 2022; Staggs et al. 2024). Dietary biotin is ingested primarily in protein-bound forms (e.g., covalently bonded to lysine residues of a protein or peptide) but is also available in unbound form (Zempleni and Mock 1999a; NIH 2022). In food, the proportion of free versus bound biotin varies with the majority of biotin in meat and cereals bound to protein (Zempleni and Mock 1999b; Solvik and Strand 2024).

Bioavailability

Biotin has been shown to be fully absorbed after oral supplementation (EFSA 2006). Inter-individual variability in biotin absorption and clearance has been observed, particularly at supplemental intakes of 5 mg per day and higher. This variability is influenced by renal function, age, and dose, and may result in substantially higher serum biotin concentrations in some individuals at the same oral dose (Grimsey et al. 2017; EMA 2019). Free biotin is readily absorbed in the intestine via a sodium-dependent multivitamin transporter; at pharmacological doses (i.e., 150-300 mg per day) it is absorbed via passive diffusion (Jungert et al. 2022; Solvik and Strand 2024). In the plasma, biotin is transported as free biotin or bound covalently or reversibly to plasma proteins (Mock 2014; Solvik and Strand 2024). Uptake of biotin to the liver and peripheral tissues occurs via a sodium-dependent multivitamin transporter and the monocarboxylate transporter (EFSA 2014; Solvik and Strand 2024). Biotin can be stored in muscles, liver, and brain in limited concentrations; the liver is the main site of biotin utilization and metabolism (Chungchunlam and Moughan 2024; NIH 2022). Biotin and biotin metabolites are excreted primarily in the urine, while biliary excretion is thought to be nearly negligible (Zempleni et al. 1999b; Zempleni and Mock 1999c).

Safety Considerations

No direct toxic effects of oral biotin have been reported in humans. However, clinically relevant

indirect safety risks have been identified related to interference with laboratory diagnostic tests, including at supplemental doses commonly found in consumer products (FDA 2019; EMA 2019).

Clinical Trial Safety Data

No toxic effects of oral biotin have been reported in humans, including in studies administering up to 300 mg biotin per day for up to three years. This pharmaceutical dose of biotin (i.e., "high-dose biotin" or HDB) has been used in the treatment of certain hereditary metabolic disorders, such as biotinidase deficiency (biotin transport deficiency), holocarboxylase synthetase deficiency, and biotin-thiamine-responsive basal ganglia disease (Avery 2019; Drake 2022; NIH 2022). In addition, biotin has been investigated for its potential beneficial effects in patients with multiple sclerosis (MS) (Sedel et al. 2016; Drake 2022). RCTs conducted with HBD in patients with MS, amyotrophic lateral sclerosis, or chronic demyelinating peripheral neuropathy have been published since CRN's 3rd edition (e.g., Tourbah et al. 2016, 2018; Cree et al. 2020; Sedel et al. 2015; Birnbaum et al. 2017; Guillevin et al. 2019; Juntas-Morales et al. 2020; Créange et al. 2023). For example, two large, phase III RCTs, known as the MS-SPI and SPI2 trials, were conducted with MD1003 (HDB, 300 mg per day) (Tourbah et al. 2016; Cree et al. 2020). In the MS-SPI study, 154 patients with progressive MS were first administered placebo or 300 mg biotin per day (100 mg three times per day) for 12 months. Subsequently, all patients received 300 mg biotin per day for an additional 12 months (Tourbah et al. 2016). The authors reported that most adverse events were mild to moderate, and that the incidence and distribution of adverse events was similar between the treated and placebo groups. The only serious adverse events occurring in more than one patient were MS-related (Tourbah et al. 2016). The SPI2 study randomized 642 patients with primary and secondary progressive MS to receive placebo or biotin (100 mg three times per day) for 12 months (Cree et al. 2020). The SPI2 trial was designed to investigate the efficacy and safety of MD1003 in a larger cohort than that of the MS-SPI trial. The authors concluded that biotin was well tolerated in this study, with a safety profile similar to that of the earlier MS-SPI trial (Cree et al. 2020). However, incorrect clinical laboratory data due to biotin interference were observed in the SPI2 trial (see *Laboratory Testing Interference* below); as such, the study authors also concluded that "high dose biotin when used offlabel could lead to deleterious health consequences to patients from misleading laboratory tests that, in turn, could lead to inappropriate medical interventions such as mismanagement of thyroid or cardiac

conditions." Although HDB (300 mg per day) has not been associated with intrinsic toxicity, these studies were conducted under controlled clinical conditions and included risk-mitigation strategies for laboratory test interference. Consequently, their relevance for assessing consumer safety at lower, unsupervised supplemental intakes is limited (Cree et al. 2020; FDA 2019).

Given that the 300 mg daily dose of HDB investigated in these trials is 7,500 to 10,000 times greater than the Adequate Intake (AI) levels for adults defined by the EFSA (2014) and the IOM (1998), respectively, HDB is considered an active pharmaceutical (Sedel et al. 2016). In addition, trials with HDB are limited to pharmacological treatment in patients with specific neurological disorders. As such, studies with HDB were determined by CRN not to be an appropriate basis from which to derive its supplemental UL for the general population. Therefore, these studies were excluded from CRN's inclusion criteria for the current update. In addition, the risk of biotin assay interference increases with dose and serum/blood concentration (see *Laboratory Testing Interference* below). Despite employing multiple risk mitigation interventions during the SPI2 trial, inaccurate laboratory results occurred with a dose of 300 mg per day in patients with progressive MS (Cree et al. 2020). While assay interference is not relevant to biotin's effects in the body, the potential risk to the consumer relative to biotin dose was considered. The increase in risk of interference at pharmacological doses of biotin provided further support for excluding HDB when determining CRN's supplemental UL.

Given the absence of known adverse effects at any observed level of intake, CRN derived a supplemental UL of 2.5 mg per day in its 3rd edition based on market data for supplement products at that time (5 mg and 7.5 mg) and the lack of adverse events reported by the United States (US) Food and Drug Administration (FDA). This UL was further supported by the NOAEL of 9 mg per day reported in the clinical trial published by Maebashi et al. (1993), in which no adverse effects were reported in patients with non-insulin dependent diabetes mellitus who received placebo or 9 mg per day (in three doses) of supplemental biotin for one month. In this same study, 20 patients received the same 9 mg biotin per day in combination with an anti-microbial drug for up to four years without "undesirable side effects."

Five human clinical trials published since the 3rd edition (i.e., 2014) were identified that met the inclusion criteria (see CRN Methodology Chapter) and were conducted at biotin doses relevant to

dietary supplement levels.[1,2] No serious adverse effects associated with biotin were reported across these studies, in which biotin doses ranged from 2.5-20 mg per day (Li et al. 2017; Garbers et al. 2021; Ylli et al. 2021; Valentim et al. 2024; Himmelreich et al. 2026). In an open, parallel study published by Garbers et al. (2021), healthy volunteers (n=38) were administered topical minoxidil 5% twice daily, oral biotin 2.5 mg per day, or both for 28 days; a control group was also included. The study authors stated that no adverse effects were reported (Garbers et al. 2021). Valentim et al. (2024) conducted a cross-over trial in healthy men (n=10) who were given topical minoxidil, oral biotin (5 mg per day), and both each for two weeks. While no adverse effects were reported, this publication did not specify monitoring for such.

One long-term study administering 10 mg biotin per day was identified in the updated search for this review that met the inclusion criteria (see Methodology Chapter). In this study published by Himmelreich et al. (2026), patients with congenital disorders of glycosylation (n=19) received 10 mg biotin per day for 12 months. No adverse effects were reported throughout the study. Two small, short-term studies were also identified that administered 10 mg biotin per day in healthy volunteers for 7-8 days (Li et al. 2017; Ylli et al. 2021). No specific safety data were reported in these studies, which were designed specifically to investigate the potential interference of biotin supplementation with laboratory assays (see *Laboratory Testing Interference* below). One additional study was identified that utilized oral biotin in the control group (Gupta 2022). In this study, healthy males (n=40) with a history of hair loss were orally administered 10 mg biotin per day (as part of a combination product) with or without intradermal platelet rich plasma. The combination product in this study also contained calcium pantothenate, N-Acetylcysteine, zinc, copper, and selenium; as such, this study was excluded based on CRN's inclusion criteria. This study (Gupta 2022) is included in this discussion for contextual purposes, as biotin supplementation was concluded to be safe by the author.

Laboratory Test Interference

As mentioned above, laboratory test interference represents the primary identified consumer

[1] CRN's established methodology was followed; the only deviation was the exclusion of studies conducted with HDB (e.g., 300 mg per day).
[2] Literature search conducted April 2026

safety risk for biotin supplementation and is considered an important safety consideration from a public health perspective, despite not reflecting intrinsic toxicity of the nutrient (FDA 2019; EMA 2019). Supplemental biotin can cause interference with certain laboratory tests informing medical diagnoses (EMA, 2019; FDA, 2019; Karibi et al. 2021; NIH 2022). While this is not a toxic effect of biotin in the body, the risk of interference increases with biotin dose. Thus, this indirect safety concern is considered in the overall assessment for biotin.

Various assays used in the clinical setting utilize the reaction between biotin and streptavidin to assess key parameters, including thyroid and cardiac function (Gifford et al. 2018; Avery 2019; FDA 2019; Karibi et al. 2021; Collinson 2020;). Circulating biotin levels higher than those associated with biotin from diet alone have been shown to yield falsely low or falsely high results, depending on the test system employed. For example, false diagnosis of hyperthyroidism is associated with inaccurate immunoassay results for thyroid stimulating hormone, thyroxine, and triiodothyronine (Gifford et al. 2018; Avery 2019; NIH 2022). Missed diagnosis and underdiagnosis of heart attack and heart failure are associated with falsely low results for markers due to biotin interference, such as cardiac troponin (Avery 2019; FDA 2019). In 2019, the US FDA updated its original 2017 warning that biotin from dietary supplements can interfere with lab results, noting particular concern for falsely low results for troponin and the associated risk of missed diagnosis of heart attacks.

The risk of biotin assay interference increases with dose (EMA 2019). Generally, interference in these assays has been associated with intake levels starting at 10 mg biotin per day and serum or blood biotin levels starting at 30 ng per mL (Avery 2019; Frame et al. 2019; Collinson 2020). However, interference with cardiac troponin assays has been demonstrated with biotin concentration of 20 ng per mL (corresponding to intakes in the 5 to 10 mg per day range). In more sensitive assays, some data suggest that biotin serum concentration as low as 10 ng per mL may cause interference (Avery 2019). For reference, normal dietary intakes have been shown to correlate with serum biotin levels ranging from 0.1 to 0.8 ng per mL, whereas doses of 5 to 10 mg biotin per day result in serum concentrations averaging approximately 15 to 30 ng per mL (Avery 2019). Meanwhile, biotin doses of 20 mg per day and pharmaceutical doses of 300 mg per day have been reported to result in approximate peak serum concentrations of 200 and 1,200 ng per mL, respectively (Avery 2019; FDA 2019). Of note, serum biotin concentrations resulting

from supplemental intakes vary between individuals and depend on renal function; due to decreased clearance, biotin half-life and serum levels are often higher in patients with renal impairment (EMA 2019; Grimsey et al. 2017).

While the risk of biotin interference has been established, real-world data on the prevalence of biotin interference with laboratory assays vary. For example, one study reported that 7.4% and 2% of patients in an emergency department had biotin concentrations at or above 10 and 20 ng per mL, respectively, with an estimated clinical risk of missed diagnosis of 0.8% in this population (Katzman et al. 2018). In a study designed specifically to assess interference with the Roche Diagnostics high-sensitivity cardiac troponin T assay, the authors concluded no cases of interference in 572 patients (Vroemen et al. 2019). Conversely, the SPI2 trial concluded that, despite employing multiple risk mitigation interventions during the study, inaccurate laboratory results still occurred with a dose of 300 mg per day in patients with progressive MS (Cree et al. 2020). Cree et al. (2020) was also one of three studies included in a meta-analysis of RCTs administering HDB (300 mg per day) in patients with MS (Espiritu and Remalante-Rayco 2021). The authors determined that 4.7% of 662 pooled patients administered HDB across these studies had laboratory test interference, while zero incidence of interference was reported in the pooled placebo group.

Recommendations for a washout period between stopping supplemental biotin intake and testing in these assays vary from waiting 8 hours to 2 to 3 days, often depending on biotin dose or patient health status (Grimsey et al. 2017; Li et al. 2017; Avery 2019). One study concluded 8 hours after dosing to be sufficient for mitigating risk of biotin interference from intakes of up to 10 mg biotin per day, but longer periods (up to 73 hours) to be necessary for higher intakes (Grimsey et al. 2017). Conversely, the FDA (2019) stated that available data are "insufficient to support recommendations for safe testing using affected tests in patients taking high levels of biotin, including about the length of time for biotin clearance from the blood." In addition, while some manufacturers have successfully modified their technology to address the issue of biotin interference in their assay (e.g., restoring assay accuracy by using biotin depletion protocols), others have not (FDA 2019; Collinson 2020; Vroemen et al. 2019). Also, significant differences in biotin tolerance between assays from different manufacturers were reported in a recent study (Chiu et al. 2025).

Therefore, despite advancements in mitigating potential interference of biotin with these clinical laboratory assays, some risk remains, particularly with higher, pharmaceutical doses of biotin (i.e., HDB), in individuals with renal insufficiency (including age-related decline), and/or in acute emergency situations where tests cannot be delayed. Individuals taking biotin-containing supplements or medications should inform their healthcare providers and laboratory staff, where relevant.

Official Reviews

IOM (1998). The IOM (1998) set an AI of 30 µg for biotin. The IOM noted that no adverse effects had been reported in humans, including in patients treated with up to 200 mg per day (Mock 1996). The IOM concluded that the data on adverse effects of biotin were insufficient for a quantitative risk assessment and, therefore, an UL value could not be derived.

EC SCF (2001). The EC SCF (2001) summarized the limited data available at that time and concurred that the available data were insufficient to support a quantitative risk assessment and therefore did not set an UL value. The EC SCF (2001) report was republished by the EFSA (2006), which stated that "there are insufficient data to draw any conclusions concerning the safety of very high-level supplements."

EVM (2003). Similarly, the UK's EVM concluded that the data from studies on humans and animals were not sufficient to establish a SUL. In the absence of established toxicity at any observed intake level, the EVM identified the Maebashi et al. (1993) clinical trial that involved oral administration of 9 mg per day of supplemental biotin without adverse effects as the basis for a guidance level. Citing the low number of individuals studied and the lack of a control group in the 4-year study,[3] the EVM applied an UF of 10 to conclude that biotin supplements of 0.9 mg per day should be considered safe. Considering the likely intake from food, the EVM set a guidance level for consumption from all sources at 0.97 mg per day.

[3] The one-month study included a placebo control group.

Chinese Nutrition Society (CNS 2023). The CNS determined AI levels for biotin but did not derive ULs "due to insufficient data on adverse effects resulting from excessive intake."

Indian Council of Medical Research - National Institute of Nutrition (ICMR-NIN 2020). The ICMR-NIN did not derive an UL for biotin.[4]

Korean Nutrition Society (KNS 2020). The KNS published its general approach to evaluating data for setting DRI values. The KNS determined AI levels for biotin but did not derive ULs.[5]

CRN Recommendations

CRN previously developed a supplemental UL of 2.5 mg per day for biotin in adults. The goal of the current chapter was to determine whether more recent human clinical data are available that might impact the conclusions published in the 3rd edition. A total of six new trials were identified that administered biotin at doses relevant to dietary supplement levels.[6] While not all human clinical trials are specifically designed to evaluate adverse effects, no new trials were identified following CRN's updated methodology that reported any serious adverse effects associated with biotin. As with any assessment in which not all available data are reviewed, inherent uncertainties with the risk assessment and selection of the UL are recognized. The table below summarizes human clinical studies considered in reviewing the supplemental UL by CRN according to its principal points of departure for risk assessment (as described in the Methodology Chapter).

[4] No additional information was provided.
[5] Table 4 of KNS (2020) states that biotin was included in the 2020 update to update the AI only.
[6] Five trials meeting CRN's inclusion criteria were identified. Gupta (2022) administered biotin as part of a combination product but is discussed in this review for additional context.

Studies Considered for the CRN UL for Biotin in Adults

Reference	Study Design	Participant Description	No. of Subjects	Supplemental Dose(s) (mg/day)	Duration	NOAEL (mg/day)
Key study from 3rd edition						
Maebashi et al. (1993)[a]	Randomized, placebo-controlled	Patients with non-insulin dependent diabetes mellitus	28	0, 9	1 month	9
	Open-label		20	9	Up to 4 years	9
Key studies identified in update						
Himmelreich et al. (2026)	Open-label	Patients with congenital disorders of glycosylation	19	10	12 months	10
Gupta (2022)	Randomized	Healthy men with hair loss	40	10[b]	3 months	10
Li et al. (2017)	Crossover	Healthy adults	6	10	1 week	10
Ylli et al. (2021)	Prospective	Healthy adults	13	10	1 week	10
Valentim et al. (2024)	Crossover	Healthy men	10	5[c]	2 weeks	5
Garbers et al. (2021)	Open-label, parallel	Healthy adults	38	0, 2.5[c]	4 weeks	2.5

[a] Patients (n = 28) received placebo or 9 mg per day for one month; twenty patients received the same 9 mg biotin per day in combination with an anti-microbial drug for up to four years (no placebo group).

[b] Biotin was provided as a combination product that also contained calcium pantothenate, N-Acetylcysteine, zinc, copper, and selenium. Volunteers were randomized to receive supplementation with or without intradermal platelet rich plasma.

[c] Treated volunteers were administered topical minoxidil, oral biotin, or both.

ULs for biotin have not been established by authoritative agencies, such as the IOM (1998), EFSA (2006), and the EVM (2003) due to insufficient data from which to conduct a risk assessment (see *Official Reviews*). At the time of these reviews, only a small number of human clinical studies conducted with biotin were available, all of which consistently demonstrated a lack of adverse effects. Noting the absence of established toxicity at any observed intake level, the EVM (2003) set a guidance level for supplemental intake of 0.9 mg per day based a single clinical trial in which no adverse effects were observed up to a dose of 9 mg per day (Maebashi et al. 1993). Similarly, oral intakes of up to 10 mg were previously noted by the Select Committee on GRAS Substances (SCOGS, 1978) to lack adverse effects, demonstrating that

biotin must have an extremely low order of toxicity.[7]

In its 3rd edition, CRN concurred with these agencies and concluded that adverse effects were not observed at any level of intake. Thus, the CRN UL was based on market data for supplement products at that time (5 mg and 7.5 mg) and the lack of adverse events reported by the US FDA. The previous CRN UL was further supported by the NOAEL of 9 mg per day from the Maebashi et al. (1993) study. Additional human clinical studies published since the 3rd edition were identified as part of this update at doses up to 10 mg biotin per day; no serious adverse effects were reported (Li et al. 2017; Garbers et al. 2021; Ylli et al. 2021; Gupta 2022; Valentim et al. 2024; Himmelreich et al. 2026). Taken individually, each trial has limitation(s) in its design that reduce its utility to serve as the basis of the UL, including small size, short duration, and/or lack of a placebo control group. However, when considered together, the data support the safety of doses up to 10 mg biotin per day. In addition, data from trials with HDB (300 mg per day) can be used to address any uncertainties associated with the limitations identified.

Therefore, based on the human studies available, 10 mg per day is selected as the supplemental NOAEL for biotin for adults following the CRN process. Given that ample data are available demonstrating that serious adverse effects were not observed with administration of 300 mg biotin per day, application of additional UFs was determined to be unnecessary. Despite the lack adverse effects directly related to biotin, the indirect safety concern of biotin assay interference warrants additional consideration at higher doses; therefore, an UL is selected for biotin instead of an HOI. Consistent with CRN's methodology, an UF of 1 is applied to the NOAEL to yield an UL of 10 mg per day for supplemental biotin in adults.

As discussed in *Safety Considerations*, supplemental biotin has been shown to interfere with various clinical laboratory tests used in the diagnosis of different medical conditions, including thyroid disease and cardiac conditions. This risk increases with increasing doses of biotin. Individuals taking biotin-containing supplements or medications should inform their healthcare providers and laboratory staff prior to laboratory testing. Particular caution is warranted for cardiac and thyroid testing and in emergency medical situations where testing cannot be delayed

[7] In the US, biotin is generally recognized as safe (GRAS) as a nutrient in food with no limitations other than good manufacturing practice (21 CFR §182.8159).

(FDA 2019; EMA 2019).

Quantitative Summary for Biotin in Adults

CRN (2026) UL, supplemental intake	10 mg (10,000 µg)/day
IOM (1998) UL, total intake	Not determined
EFSA (2006) UL, total intake	Not determined
EVM (2003), guidance level, supplemental intake	0.9 mg (900 µg)/day
CNS (2023), total intake	Not determined
ICMR-NIN (2020), total intake	Not determined
KNS (2020), total intake	Not determined

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