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A Review On Biotin Deficiency

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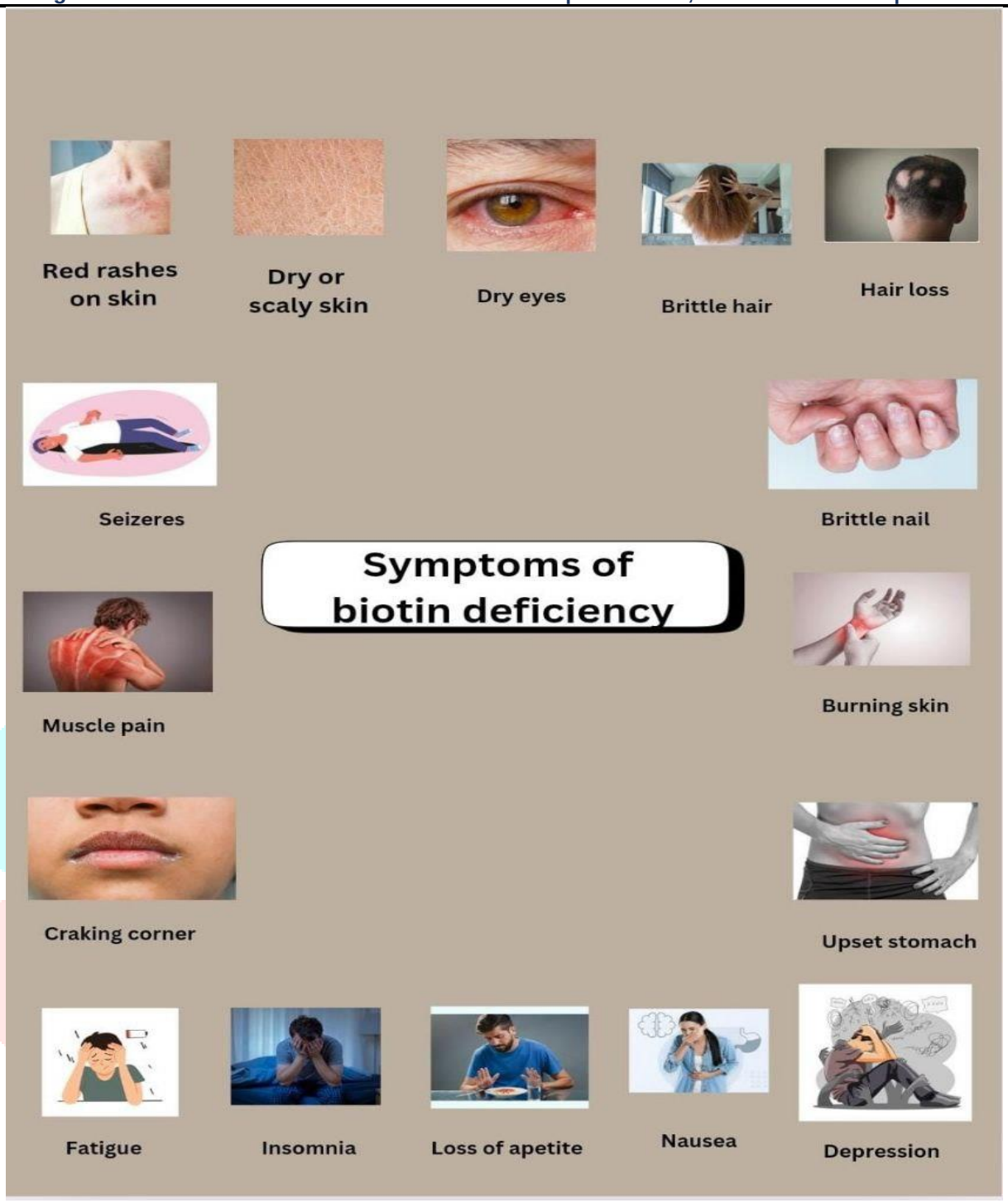
Abstract:- Biotin, a B vitamin essential for various metabolic processes in humans, has been investigated as a treatment for several nail disorders based on findings from in vitro and animal studies involving hooves and claws. This review discusses the pharmacology, mechanism of action, and research on the use of biotin in treating brittle nails, triangular worn down nails, trachyonychia, and habit tic nail deformity, teratogenicity, BTBGD , alopecia, periorficial deformities, insomnia, depression, fatigue, loss of appetite.

Keywords:- Biotin, Biotin deficiency ,brittle nails, trachyonychia, and habit tic nail deformity, teratogenicity, BTBGD, alopecia, periorficial deformities, insomnia, depression, Biotidinase, fatigue, loss of appetite

Introduction:- Biotin is a water-soluble B vitamin obtained from dietary sources such as cereals, walnuts, peanuts, milk, and egg yolks, as well as synthesized by intestinal bacteria. Its discovery originated from experiments where rats fed a diet high in raw egg whites exhibited symptoms including hair loss, dermatitis, and neuromuscular dysfunction. These symptoms were alleviated by a substance initially referred to as "Protective Factor X," later identified as biotin. It was also discovered that raw egg whites contain avidin, a glycoprotein that binds to biotin and prevents its absorption. Biotin is a bicyclic compound with eight potential stereoisomers, but only the d-(+)-biotin stereoisomer is naturally occurring and biologically active.

Nominal biotin deficiency has been observed in pregnant and breastfeeding women, but its clinical significance remains unclear. Biotin supplements are marketed for enhancing nail, hair, and skin health, though solid evidence supporting these claims is lacking. Additionally, biotin supplementation can interfere with certain laboratory tests, leading to false-positive or false-negative outcomes. Some studies have reported the effectiveness of high-dose biotin in treating neurological conditions like multiple sclerosis, but the underlying mechanism is not well understood.



Disease caused By Biotin Deficiency :

1.Brittle nail

*** Ethology of Brittle Nail Syndrome**

*** Lifestyle factors**

An increased risk for these nail abnormalities has been attributed to patients who manicure frequently, have occupations that require frequent handwashing or manipulation of the hands, and those who smoke tobacco.

- **Dermatologic diseases:-**

Brittle nail syndrome has been associated with pemphigus vulgaris, psoriasis, eczema, lichen planus, alopecia areata, lichen striatus, scleroderma, Darier disease, discoid lupus erythematosus, and pityriasis rubra pilaris, among other conditions.

- **Genetic diseases**

It has been associated with numerous genodermatoses, including punctate palmoplantar keratoderma, as well as congenital hemidysplasia with ichthyosiform erythroderma (or nevus) and limb defects (CHILD) syndrome, among many others.

- **Systemic diseases:-**

Onychorrhexis has been described in a wide variety of systemic diseases. It has been associated with liver disease (most commonly hepatitis C virus infection and cirrhosis),thyroid disease, hypoparathyroidism, and chronic renal failure. It has also been associated with vascular diseases such as peripheral arterial disease, arteriosclerosis, microangiopathy, Raynaud disease, anaemia, and polycythaemia vera, as well as rheumatologic diseases such as gout, osteoarthritis, polyarteritis nodosa, rheumatoid arthritis, systemic lupus, and systemic sclerosis. Onychorrhexis can also be seen in graft versus host disease, sarcoidosis, primary systemic amyloidosis, and chronic immunosuppressed disorders such as severe combined immunodeficiency or AIDS.

- **Mineral abnormalities**

It has been associated with iron-deficiency anaemia, arsenic poisoning, and zinc deficiency.

- **Medication adverse effects**

Brittle nails have been documented as an adverse effect of cancer therapy, including the Bruton tyrosine kinase inhibitor ibrutinib. It has also been associated with azidothymidine, etanercept, hydroxyurea, itraconazole, and retinoid use.

- **Pathophysiology**

Biotin stimulates keratin hence biotin deficiency leads to keratin deficiency

Brittle nails can be of primary origin or develop secondary to an underlying condition. Primary brittle nails are speculated to develop from the impairment of intercellular adhesive factors of the nail matrix or abnormalities in epidermal growth and keratinization. Brittle nails of secondary origin are typically linked to disordered keratinization from dermatologic disease or systemic disorders, such as endocrine, metabolic, or vascular abnormalities. Other precipitating factors for brittle nails include the repetitive wetting and drying of the hands, direct contact with chemicals (nail polish remover), trauma to the nail, and onychomycosis

2.In Pregnancy [Teratogenic]

Maternal Biotin Status During Pregnancy

Evidence of Marginal Biotin Deficiency:

Studies Conducted: Three recent studies indicate that a marginal biotin deficiency develops in a substantial proportion of pregnant women.

Indicators of Biotin Status:

Four validated indicators in nonpregnant women induced to have marginal biotin deficiency by egg white feeding include:

• Urinary excretion of 3-hydroxyisovaleric acid (3HIA)

• Urinary excretion of biotin

• Serum concentration of biotin

• Urinary excretion of biotin metabolites (bisnorbiotin, biotin-d,l-sulfoxide)

• Best Indicators:

Urinary 3HIA and biotin were the most reliable indicators.

2. Cross-Sectional and Longitudinal Studies:

1.Cross-Sectional Study: Urine samples collected at early (17 weeks) and late (36 weeks) prenatal visits showed increased 3HIA excretion in both periods, suggesting reduced biotin enzyme activity.

2.Longitudinal Study: Blood and urine samples collected at early (10 weeks) and late (36 weeks) pregnancy confirmed increased 3HIA excretion. Biotin serum concentrations were higher in early pregnancy compared to nonpregnant controls but decreased significantly in late pregnancy, sometimes falling below normal levels.

3.Biotin Catabolism:

Accelerated biotin catabolism was suggested by the increased urinary ratio of bisnorbiotin to biotin in both early and late pregnancy, likely due to increased steroid hormone concentrations during gestation.

Biotin Supplementation: A randomized, placebo-controlled trial with biotin supplementation (300 µg) in pregnant women significantly decreased 3HIA excretion, indicating improved biotin status.

Teratogenic Effects of Biotin Deficiency

1. Mouse Studies:

Maternal and Fetal Biotin Status: Biotin deficiency in mice, induced by varying egg white content in the diet, showed that fetal biotin status significantly correlated with maternal biotin status. Reduced activity of the biotin-dependent enzyme propionyl-CoA carboxylase (PCC) was observed.

Fetal Malformations:

Rates of cleft palate and limb hypoplasia were dependent on egg white concentration. Control diets (mouse chow, 0% egg white, and biotin-supplemented high egg white) showed low malformation rates, indicating that malformations were due to biotin deficiency rather than other factors.

Mechanism: Reduced carboxylase activity in biotin-deficient fetuses was mediated by decreased biotinylation of carboxylases rather than decreased mRNA expression for these enzymes.

2.Conclusions from Mouse Studies:

Marginal maternal biotin deficiency leads to significant fetal biotin deficiency, causing severe reductions in biotinylated enzyme mass and activity in fetuses.

This deficiency results in teratogenic effects, such as cleft palate and limb hypoplasia, primarily due to inadequate biotinylation of carboxylases despite normal gene expression for these enzymes.

Summary

Human Implications: Although the clinical significance of marginal biotin deficiency during pregnancy in humans remains unclear, the animal studies raise concerns about potential teratogenicity.

Recommendations: Ensuring adequate biotin intake during pregnancy through diet or supplementation is important to prevent possible developmental abnormalities in the fetus

3.Biotin-thiamine-responsive basal ganglia disease (BTBGD)

- **Childhood Presentation (Age 3-10 Years)**

•**Symptoms:** Recurrent subacute encephalopathy characterized by confusion, seizures, ataxia, dystonia, supranuclear facial palsy, external ophthalmoplegia, and/or dysphagia. Without treatment, this can progress to coma and death.

•**Neurological Signs:** Nearly universal presence of dystonia and cogwheel rigidity; common occurrences of hyperreflexia, ankle clonus, and Babinski responses. Hemiparesis or quadriparesis may be observed.

•**Triggers:** Episodes can be triggered by febrile illness, mild trauma, or stress**.**

Seizure Control: Seizures are typically manageable with anti-seizure medications.

Early-Infantile Presentation

Symptoms:

Occurs within the first three months of life, presenting with poor feeding, vomiting, acute encephalopathy, and severe lactic acidosis.

Prognosis: Poor outcome even after supplementation with biotin and thiamine.

Adult-Onset Presentation

Symptoms: Wernicke-like encephalopathy with acute onset of status epilepticus, ataxia, nystagmus, diplopia, and ophthalmoplegia typically occurring in the second decade of life**.**

Response to Treatment: Partial or complete improvement with early administration of biotin and thiamine.

- **Diagnosis**

Genetic Testing: Diagnosis is confirmed by identifying biallelic pathogenic variants in the SLC19A3 gene through molecular genetic testing.

Management

Treatment of Manifestations

Medications: Oral administration of biotin (5-10 mg/kg/day) and thiamine (up to 40 mg/kg/day, max 1500 mg daily) should begin early in the disease course and continue lifelong.

Acute Management: Intensive care may be needed for acute encephalopathic episodes, with increased doses of thiamine administered intravenously. Anti-seizure medications are used to control seizures.

Dystonia Treatment: Symptomatic treatment includes trihexyphenidyl or L-dopa.

Supportive Therapies: Rehabilitation, physiotherapy, occupational therapy, and speech therapy. Educational programs should be adapted to individual needs.

F**amily Education:** Emphasis on the importance of lifelong adherence to medical therapy.

Prevention of Primary Manifestations

Early Intervention: Prompt administration of biotin and thiamine early in the disease course.

Surveillance

Neurological Reviews: Every six months to assess neurologic status**.**

Developmental and Educational Assessments: Annually, with social support and care coordination during each visit.

Avoidance Recommendations

Risk Factors: Avoid infections, stress, intense exercise, and trauma.

Evaluation of Relatives at Risk

Genetic Screening: It is recommended to clarify the genetic status of at-risk relatives to identify those who may benefit from early treatment with biotin and thiamine and preventive measures.

Pregnancy Management

Medication Continuation: Affected women should continue taking thiamine and biotin during pregnancy.

Genetic Counselling

Inheritance Pattern: Autosomal recessive**.**

Risk to Siblings: At conception, each sibling has a 25% chance of being affected, a 50% chance of being an asymptomatic carrier, and a 25% chance of being unaffected and not a carrier.

Testing Options: Carrier testing for at-risk family members, and prenatal and preimplantation genetic testing for pregnancies at increased risk, are possible if SLC19A3 pathogenic variants are known in the family**.**

4.Hairloss (Alopesia)

Biotin Deficiency and Hair Loss in Women

Introduction

Biotin, a vital coenzyme involved in metabolic processes crucial for skin and hair health, has gained popularity as a supplement for treating hair loss. However, limited data exists on biotin deficiency prevalence among the general population and individuals experiencing hair loss not attributable to metabolic disorders. This review aims to explore the frequency of biotin deficiency in women with hair loss and the efficacy of oral biotin supplementation for non-metabolic-related hair loss.

Risk Factors and Clinical Manifestations

Recognized risk factors for biotin deficiency include gastrointestinal disorders and medications interfering with biotin metabolism. Clinical signs often encompass hair loss and seborrheic-like dermatitis.

Diagnostic Approaches

Serum biotin levels exhibit variability, with urine 3-hydroxyisovaleric acid excretion serving as a reliable marker for deficiency. Classification based on serum levels: optimal (>400 ng/L), suboptimal (100–400 ng/L), deficiency (<100 ng/L).

Findings

Among women with hair loss, 38% exhibited biotin deficiency, while 13% had optimal levels. Trichograms showed telogen effluvium in both groups, but the presence of seborrheic-like dermatitis correlated with biotin deficiency.

Clinical Implications

Indiscriminate oral biotin supplementation for hair loss is discouraged unless deficiency is confirmed. Hair loss in women may stem from multifactorial causes, necessitating a thorough clinical evaluation.

Conclusion

Treating hair loss with oral biotin warrants caution, as deficiency is not universal. Clinical assessment, serum biotin determination, and addressing underlying causes are essential. Biotin supplementation, if indicated, typically involves 5 mg/day.

Future Directions

Further research is needed to elucidate the interplay between biotin deficiency and hair loss, considering potential confounding factors such as nutritional deficiencies and endocrine disorders.

Key Takeaways

Biotin deficiency is prevalent in a significant proportion of women with hair loss. Clinical evaluation, serum biotin assessment, and consideration of risk factors are crucial for appropriate management. Oral biotin supplementation should be tailored to individual cases, accounting for underlying causes of hair loss.

5.Periofercialdermatitis (also called as biotin deficient face)

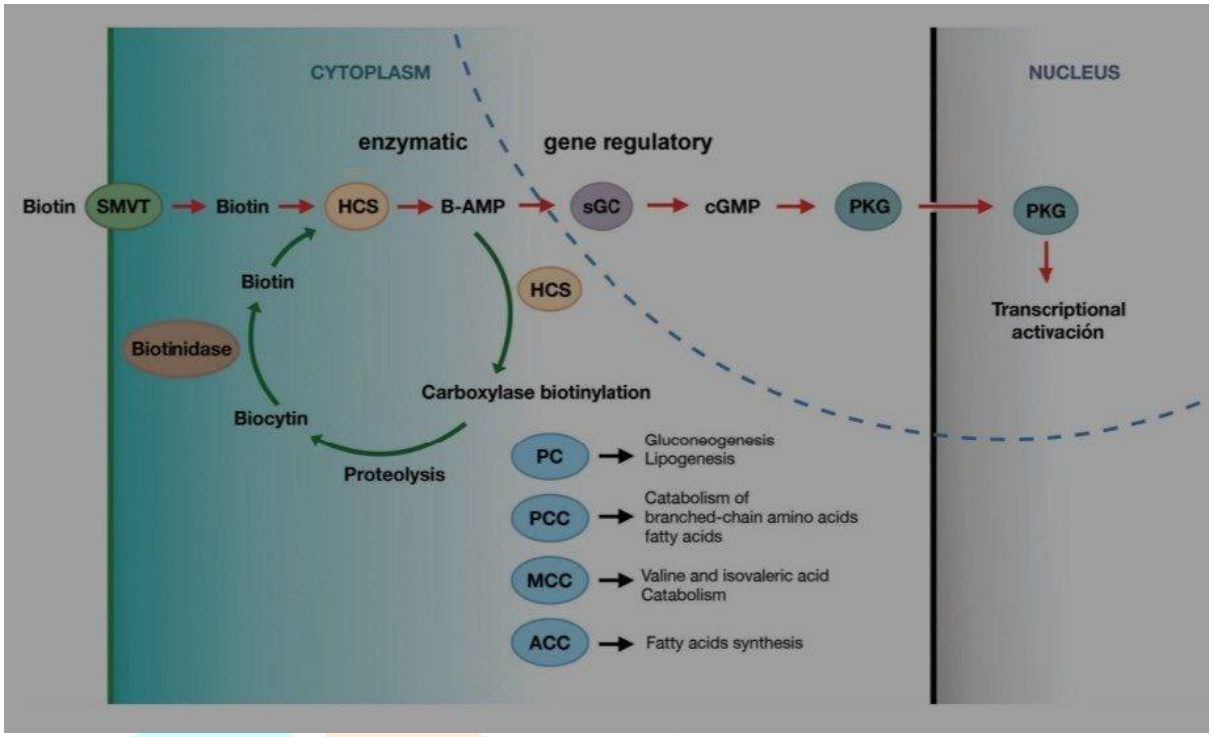
Periorifecialdrrmatatitis face biotin deficiency

Biotin, a water-soluble vitamin, serves as a crucial cofactor for four carboxylases, each catalysing essential steps in intermediary metabolism. For instance, acetyl-CoA carboxylase facilitates the pivotal step in fatty acid elongation. In individuals of all ages, biotin deficiency results in alopecia and a distinctive scaly, erythematous dermatitis occurring around body openings. This rash bears resemblance to that seen in zinc deficiency, with Candida albicans frequently isolated from the affected skin lesions. Biotinidase deficiency, an inherited metabolic disorder, leads to biotin deficiency, likely due to impaired intestinal absorption, cellular salvage, and renal reabsorption of biotin. Dermatologic symptoms akin to biotin deficiency are observed in individuals with biotinidase deficiency. Evidence suggests that compromised fatty acid metabolism, stemming from diminished activities of biotin-dependent carboxylases, particularly acetyl-CoA carboxylase, contributes to the dermatologic manifestations of biotin deficiency. Additionally, Candida infections resulting from compromised immune function may exacerbate dermatitis associated with biotin deficiency.

6.Depression

B vitamins have vital roles in the development, maintenance, and functioning of the brain, while severe deficiencies have been linked to increased psychological disorders. However, no published studies have examined the association between dietary intake of vitamin B and depression, anxiety, and stress symptoms in a general population

7. Biotinidase Deficiency



Biotinidase deficiency is an autosomal recessive disorder caused by mutations in the gene responsible for producing biotinidase. This condition, also known as the juvenile form or late-onset multiple carboxylase deficiency (MCD), occurs in approximately 1 in 61,067 births. The disorder is highly variable, with patients showing either profound or partial biotinidase deficiency. Affected individuals cannot release biotin from dietary proteins or recycle the vitamin within cells during carboxylase turnover. Consequently, their cells exhibit a significant reduction in the activity of all biotin-dependent carboxylases.

Clinically and biochemically, biotinidase deficiency presents with symptoms such as alopecia, developmental delays, organic aciduria, seizures, skin rashes, mild hyperammonemia, and respiratory issues. Some patients also develop neurological issues, including intellectual disabilities, hearing loss, optic nerve atrophy, myelopathy, and Leigh syndrome. Symptoms typically manifest between 2 weeks and 2 years of age, though some individuals may develop the condition later in life. Most clinical and biochemical symptoms, except for neurological damage, can be improved or reversed with pharmacological doses of biotin (5-20 mg/day). The lifelong need for biotin and the specific neurological symptoms unique to biotinidase deficiency (and not seen in holocarboxylase synthetase (HCS) deficiency) are not fully understood.

In vitro studies using fibroblasts deficient in biotinidase have shown that reduced biotin availability disrupts the HCS-cGC-PKG pathway and the transcription of the HCS gene. This combined deficiency in HCS and biotinidase might lead to neurological disorders by impairing the metabolism in brain regions with high biotin demand, such as the auditory and visual centers, including the dorsal and ventral cochlear nuclei, the superior olivary complex, and the vestibular nucleus.

Other minor effects of biotin deficiency

- **Swallon and painful tongue that is magenta in colour**
- **Dry eyes**
- **Loss of apetite**
- **Fatigue**

- **Sources of biotin**

Biotin, also known as vitamin B7, is an essential nutrient that supports metabolic functions, skin health, and the nervous system. It is found in various foods, Given in below table

Food Category	Specific Foods	Biotin Benefits
Eggs	Egg yolk	Rich source, best consumed cooked to avoid avidin.
Nuts and Seeds	Almonds, peanuts, walnuts, sunflower seeds	High in biotin, healthy fats, and protein.
Legumes	Peanuts, soybeans, lentils, chickpeas	Good amounts of biotin, protein, and fiber.
Whole Grains	Oats, barley, whole wheat	Biotin content may reduce during processing.
Organ Meats	Liver, kidneys	Among the richest sources of biotin.
Dairy Products	Milk, cheese, yogurt	Good sources of calcium and biotin.
Fish	Salmon, sardines	Provide biotin and omega-3 fatty acids.
Vegetables	Sweet potatoes, spinach, broccoli	Excellent plant-based sources of biotin.
Fruits	Bananas, avocados, raspberries	Lower in biotin compared to other sources.
Yeast	Brewer's yeast, nutritional yeast	Highly concentrated sources of biotin.

Including a variety of these foods in your diet can help ensure adequate biotin intake.

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