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Review Article

Thalassaemia: An Overview of Pathophysiology, Diagnosis, and Management

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Abstract

The β-globin chain of haemoglobin is encoded by the HBB gene. Ineffective erythropoiesis, severe anaemia, and progressive iron overload are caused by an imbalance between α- and β-globin chains. Blood transfusions and iron chelation therapy are examples of conventional management techniques that have greatly increased survival; however, they are linked to a number of complications, such as organ toxicity, restricted accessibility, and low compliance. Because of their diverse biological activities, including antioxidant, iron-chelating, hepatoprotective, and foetal haemoglobin (HbF)-inducing qualities, phytocompounds have become promising therapeutic substitutes in recent years. With a focus on formulation development and therapeutic evaluation, this review examines the genetic and clinical basis of β-thalassemia, the limitations of current treatments, and the potential role of bioactive compounds derived from plants in its management.

Keywords: Iron chelation, foetal haemoglobin, oxidative stress, phytocompounds, β-thalassemia.

Introduction

Beta thalassemia is a hereditary blood disorder characterized by a defect in the production of beta-globin chains, which are vital components of hemoglobin. Hemoglobin is the iron-containing protein in red blood cells responsible for transporting oxygen from the lungs to body tissues[1]. In individuals with beta thalassemia, reduced or absent beta-globin synthesis leads to the formation of abnormal hemoglobin, resulting in ineffective red blood cell production and chronic anaemia. Beta thalassemia is inherited in an autosomal recessive pattern, meaning that an individual must receive the defective gene from both parents to develop the severe form of the disease. The condition is most commonly found in populations from the Mediterranean region, the Middle East, South Asia, Southeast Asia, and parts of Africa. This geographic distribution is believed to be linked to historical protection against malaria in carriers of the trait[2]

Based on the severity of the genetic defect, beta thalassemia is classified into three main types: beta thalassemia minor, beta thalassemia intermedia, and beta thalassemia major. Beta thalassemia minor usually causes mild or no symptoms, while beta thalassemia major is a severe condition that presents in early childhood and often requires lifelong blood transfusions and medical care. If left untreated, severe forms can lead to complications such as growth retardation, bone deformities, and organ damage due to iron overload.Beta thalassemia remains a major public health challenge worldwide, emphasizing the importance of early diagnosis, genetic counselling, and advancements in treatment strategies[3,4].

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- β-Thalassemia major: severe, transfusion-dependent anaemia manifesting in infancy.
- β-Thalassemia intermedia: moderate anaemia may not require regular transfusions.
- β-Thalassemia minor (trait): asymptomatic carrier state with mild microcytosis.

Thalassaemia is a group of inherited haemoglobin disorders characterized by defective synthesis of one or more globin chains, leading to chronic anaemia, ineffective erythropoiesis, and various systemic complications. Beta thalassaemia, the most common form, results from reduced or absent production of beta-globin chains. Conventional management primarily includes regular blood transfusions, iron chelation therapy, folic acid supplementation, and in selected cases, bone marrow transplantation or gene therapy. However, long-term treatment is associated with complications such as iron overload, oxidative stress, organ damage, and reduced quality of life. In recent years, herbal drugs and natural products have gained attention as supportive therapies in thalassaemia management. While herbal medicines do not cure thalassaemia or replace standard treatment, they may help improve haemoglobin levels, reduce oxidative stress, enhance immunity, and support liver and cardiac function. Many of these remedies are derived from traditional systems of medicine such as Ayurveda, Unani, and folk medicine[6,5].

2. Pathophysiology of β-thalassemia

Red cell survival is shortened and erythropoiesis is ineffective in β-thalassemia due to the relative excess of α-globin[8].

The β-thalassemia are genetic disorders of haemoglobin synthesis characterized by deficient (β+) or absent (β0) synthesis of the β-globin subunit of the haemoglobin molecule (Weatherall and Clegg 2001). The vast majority of individuals with thalassemia inherit their disorder as a Mendelian recessive. As will be covered in more detail below, homozygous people have severe anaemia of varying degrees and are classified as having homozygous β-thalassemia or

thalassemia major or intermedia, while heterozygous people have mild anaemia and microcytosis and are classified as having thalassemia minor or trait. Dominantly inherited β-thalassemia, which affects heterozygous people due to the synthesis of a highly unstable β-globin variant, is much less common (Thein 1999). Rare deletional mutations can eliminate one or more of the other genes on chromosome 11, resulting in forms of the disease known as δβ-, γδβ-, or εγδβ-thalassemia. Normally, the disruption is limited to β-globin synthesis.

3. Role of Herbal Therapy in Thalassaemia

The rationale behind using herbal drugs in thalassaemia lies in their antioxidant, immunomodulatory, anti-inflammatory, hepatoprotective, and hematinic properties. Chronic anemia and iron overload lead to excessive production of free radicals, causing oxidative damage to red blood cells and vital organs. Herbal antioxidants may help neutralize these free radicals and reduce tissue injury. Additionally, some herbs are believed to stimulate erythropoiesis or improve overall nutritional status[9].

1. Wheatgrass (*Triticum aestivum*)

Wheatgrass is one of the most widely studied herbal supplements used in thalassaemia patients. It is rich in chlorophyll, vitamins, minerals, amino acids, and enzymes. Chlorophyll has a chemical structure similar to haemoglobin, which has led researchers to explore its role in blood disorders[10].

Several clinical studies have suggested that regular consumption of wheatgrass juice may help increase haemoglobin levels, reduce transfusion frequency, and improve general well-being in thalassaemia patients. Wheatgrass also exhibits strong antioxidant activity, helping to reduce oxidative stress caused by iron overload. It is commonly administered as fresh juice, powder, or tablets[11].

2. Amla (*Emblica officinalis*)

Amla, also known as Indian gooseberry, is a potent antioxidant and one of the richest natural sources of vitamin C. It plays an important role in reducing oxidative damage and improving immune function. In thalassaemia patients, amla may help protect red blood cells from oxidative hemolysis and support liver health, which is often compromised due to iron overload.

Although vitamin C enhances iron absorption, controlled doses of amla are used carefully under medical supervision in thalassaemia to avoid worsening iron overload. Its rejuvenating (Rasayana) properties make it valuable in long-term supportive care[12].

3. Turmeric (*Curcuma longa*)

Turmeric contains curcumin, a bioactive compound with powerful antioxidant, anti-inflammatory, and iron-chelating properties. Curcumin has been studied for its ability to bind excess iron and reduce iron-induced oxidative stress. This makes turmeric particularly useful in managing complications related to iron overload in transfusion-dependent thalassaemia.

Additionally, curcumin supports liver and cardiac health and may reduce inflammation associated with chronic disease. Turmeric is typically used as a dietary supplement or in standardized curcumin formulations[13].

4. Guduchi (*Tinospora cordifolia*)

Guduchi is a well-known immunomodulatory herb in Ayurveda. It enhances immune response, improves antioxidant defence mechanisms, and supports liver function. Thalassaemia patients often suffer from recurrent infections due to anaemia and repeated transfusions; Guduchi may help strengthen immune resistance[14]. Its hepatoprotective effect is particularly beneficial in preventing liver damage caused by iron overload and long-term chelation therapy[15].

5. Tulsi (*Ocimum sanctum*)

Tulsi, also called holy basil, is valued for its adaptogenic, antioxidant, and anti-inflammatory properties. It helps the body adapt to chronic stress and improves overall vitality. In thalassaemia patients, Tulsi may help reduce fatigue, improve immunity, and protect red blood cells from oxidative damage[16]. Regular consumption of Tulsi extracts or tea is believed to improve respiratory health and general well-being in chronically ill patients[17].

6. Moringa (*Moringa oleifera*)

Moringa is a nutrient-rich plant containing iron, calcium, vitamins, amino acids, and antioxidants. Although iron supplementation must be used cautiously in thalassaemia, moringa may help improve general nutritional status, muscle strength, and immunity. It is sometimes used to combat mild anaemia and fatigue, especially in thalassaemia minor or intermedia patients[18].

7. Ashwagandha (*Withania somnifera*)

Ashwagandha is an adaptogenic herb known for improving stamina, reducing stress, and enhancing overall health. In thalassaemia patients, it may help manage weakness, fatigue, and stress associated with chronic illness. Its antioxidant and immunomodulatory properties support long-term health and recovery[19].

Advantages of Herbal Drugs in Thalassaemia

- Natural and generally well tolerated
- Reduce oxidative stress and inflammation
- Support liver, heart, and immune function[20]
- Improve quality of life and energy levels
- May reduce complications associated with iron overload

Limitations and Precautions

- They do not cure thalassaemia
- Scientific evidence is limited and variable
- Risk of interaction with iron chelators and other medications[21]
- Iron-containing herbs may worsen iron overload
- Dosage standardization is often lacking[22]

Table 1:Drugs used

S.no	Herbal drug	Botonical name	Chemical constituents	Pharmacological action
1.	Wheatgrass	Triticum aestivum	Chlorophyll, flavonoids, vitamins (a, c, e), minerals (mg, fe), amino acids	Hematinic, antioxidant, erythropoiesis supportive, reduces transfusion requirement[23]
2.	Amla	Emblica officinalis	Ascorbic acid (vitamin c), tannins (emblicanin a & b), flavonoids, polyphenols	Antioxidant, immunomodulatory, hepatoprotective, protects rbcs from oxidative damage[24]
3.	Turmeric	Curcuma longa	Curcumin, demethoxycurcumin, bisdemethoxycurcumin, volatile oils	Antioxidant, anti-inflammatory, iron-chelating, hepatoprotective[25]
4.	Guduchi	Tinospora cordifolia	Alkaloids (berberine), diterpenoids, glycosides, polysaccharides	Immunomodulatory, antioxidant, hepatoprotective[26]
5.	Tulsi	Ocimum sanctum	Eugenol, ursolic acid, rosmarinic acid, flavonoids	Adaptogenic, antioxidant, anti-inflammatory
6.	Moringa	Moringa oleifera	Vitamins (a, c), flavonoids, phenolics, amino acids, minerals	Nutritional support, antioxidant, anti-inflammatory[27]

Future Perspective and Challenges

Novel curative treatments for beta-thalassemia, such as gene therapy and gene editing, are anticipated in the future with the goal of minimizing or doing away with the need for blood transfusions[28]. The main obstacles are the high cost and restricted availability of these novel treatments, the need for improved access to and administration of current treatments like iron chelation and transfusions, and the complicated and ongoing financial, psychological, and physical burden on patients and their families.

Conclusion

Herbal drugs play a supportive role in the management of thalassaemia by improving antioxidant defences, enhancing immunity, protecting vital organs, and improving overall well-being. Among these, wheatgrass, amla, turmeric, Guduchi, Tulsi, moringa, and Ashwagandha are commonly used in traditional medicine systems. While they offer promising benefits, herbal therapies should not replace standard treatments such as blood transfusions and chelation therapy. Future scientific research and clinical trials are necessary to establish their efficacy, safety, and standardized dosing. When used responsibly, herbal drugs can complement modern medicine and help improve the quality of life of individuals living with thalassaemia.

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