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Original Article

Phytochemicals As Therapeutic Agents For Sickle Cell Disease: A Review Of Current Evidence

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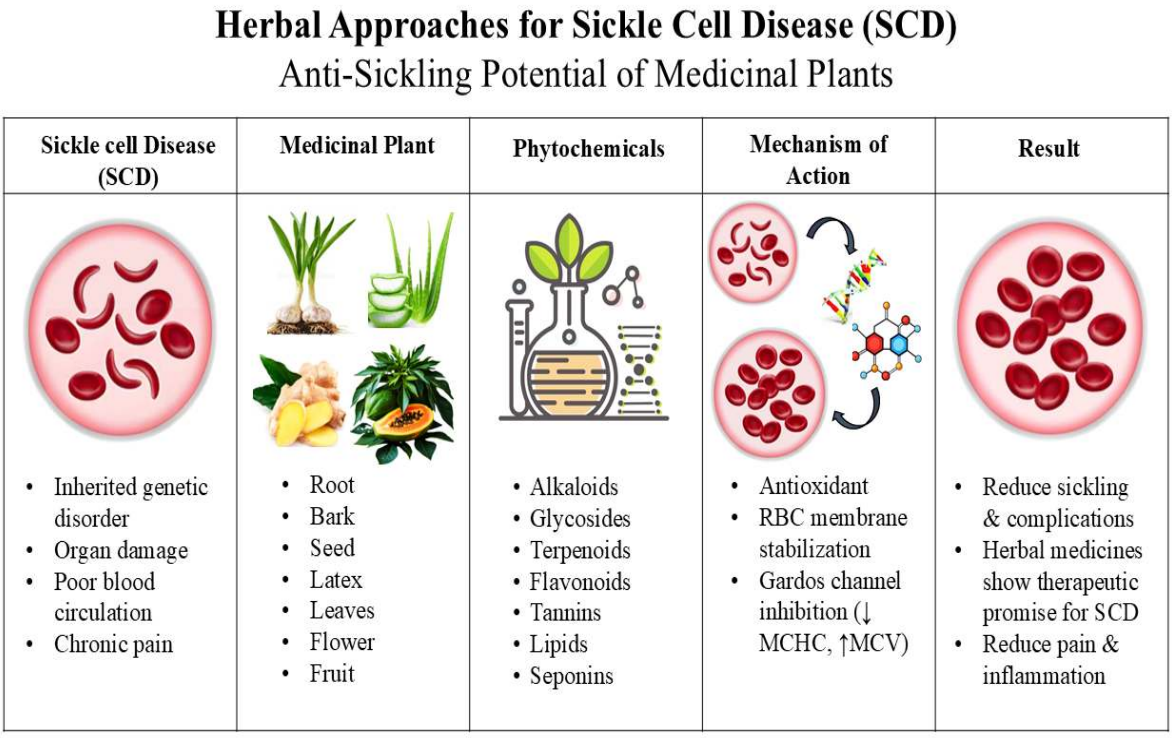
ABSTRACT

The severe genetic condition known as sickle cell disease (SCD) affects both babies and children and causes damage to several organs, poor blood circulation, and chronic discomfort. This study looks at how medicinal plants can prevent red blood cell sickling by using their fruits, leaves, seeds, bark, and latex. A systematic review and meta-analysis assess the efficiency and safety of herbal remedies for sickle cell disease (SCD) throughout the continent. Herbal therapies, including ginseng products, *Zingiber officinale, Cymbopogon citratus*, *Aloe barbadensis miller*, and Forever Living products. The pharmacological data for sickle cell treatment was thoroughly evaluated in this study, with a focus on phytochemicals Haemoglobin polymerization and sickling reversal were the assays with the most reports. Many plant species have been found to offer anti-sickling qualities. Herbal treatments for sickle cell illness are covered in this review article.

Keywords: Organ damage, Sickle cell disease, Phytochemicals, Polymerization, Haemolysis, Mutation.

INTRODUCTION

Graphical Abstract:



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The genetic blood condition known as SCD, or SCA, is inherited in in a recessive autosomal way(Inusa et al., 2019). It is identified by red blood cells that stiffen and take on the shape of a sickle. Haemoglobin clumps (polymerizes) when oxygen is lost, giving it this aberrant form(Ghusoon G Al- Janabi et al., 2021). According to Balgir (2006), people with this illness frequently suffer from recurrent pain crises, persistent anemia, splenic enlargement, frequent severe infections, and substantial organ damage. Because these sickled cells carry less oxygen, they thicken the blood and interfere with normal blood flow, particularly in small blood arteries, which may result in cell death (infarction) and tissue damage (ischemia) (Elendu et al., 2023). An abnormal β-globin gene mutation causes sickle cell disease (SCD), a hereditary illness that is characterized by the production of aberrant HbS, which deforms red blood cells by forming polymers in low oxygen environments(Gbotosho et al., 2021). The World Health Organization (WHO) claims that anemia is the state in which a person's blood haemoglobin content is low, namely less than 110, less than 120, or less than 130 g/L for males, women who are not pregnant, and kids between the ages of 6 and 59 months(Baldi & Pasricha, 2022). Worldwide, anemia affects 30% of women between the ages of 15 and 49, 37% of pregnant women, and 40% of babies between the ages of 6 and 59 months, according to the World Health Organization. Additionally, anemia cost 50 million years of good life in 2019. In India and other nations, especially wealthy ones, the high prevalence of anemia is a serious problem. By 2025, the World Health Organization hopes to cut anemia in women of reproductive age by 50% (Chakrabarty et al., 2023). However, during the past 20 years, the frequency of anemia has stayed constant worldwide, and the goal might not be accomplished by 2030 (Merid et al., 2023).

1.1. Genetics of SCD:

In order to acquire sickle cell disease (SCD), One defective copy of the gene must be inherited from each parent18. A hereditary condition that affects red blood cells, sickle cell disease (SCD) is inherited in an autosomal recessive manner(Quintana-Bustamante et al., 2022). If a person inherits only one gene, they are a carrier, often known as possessing the sickle cell trait, and typically show no symptoms(William Coetzee et al., 2022). If two carriers have a kid, in addition to having a 25% probability of having SCD, the child has a 50% chance of also being a carrier and a 25% chance of inheriting two normal genes(Skrypnyk et al., 2024). The beta-globin gene, it contributes to the formation of red blood cells' haemoglobin, is mutated in sickle cell disease (SCD)(Lattanzi et al., 2021). The mutation results in the beta-globin chain's sixth position, which transports oxygen throughout the body, changing from glutamic acid to valine(Dorneles et al., 2025). Thus, an abnormal form of haemoglobin called haemoglobin S (HbS) is created(Alfeel et al., 2025). When blood oxygen levels drop, red blood cells are twisted into a sickle or crescent shape when HbS molecules stick to each other to form long fibers(Wise et al., 2024). These rigid sickled cells have the ability to obstruct blood arteries, which can decrease or even prohibit oxygen from reaching various bodily areas(Conran & Embury, 2021). This results in tissue and organ damage, as well as excruciating events called vaso-occlusive crises(Jang et al., 2021). Because sickled red blood cells degrade more readily than healthy ones, a chronic deficiency of healthy red blood cells exists, which causes chronic anemia and exhaustion(Barua et al., 2023). An individual who gets the sickle cell gene from both parents has HbS illness, the most prevalent and severe kind of sickle cell disease(Khamees et al., 2021). This kind is common in North America and frequently results in major health issues(Hessburg et al., 2021). However, each person's sickle cell disease (SCD) symptoms might differ significantly(Ballas et al., 2010). There are many who have milder illnesses with less obvious symptoms, while others have regular pain episodes and frequently require medical service(Davis et al., 2011). Both genetic composition and environmental factors contribute to the variation in the disease's impact on individuals(K. Wang et al., 2017). Because HbF helps keep red blood cells from sickling, those who naturally make larger amounts of foetal haemoglobin (HbF) typically experience less severe symptoms (Donaldson et al., 2001).

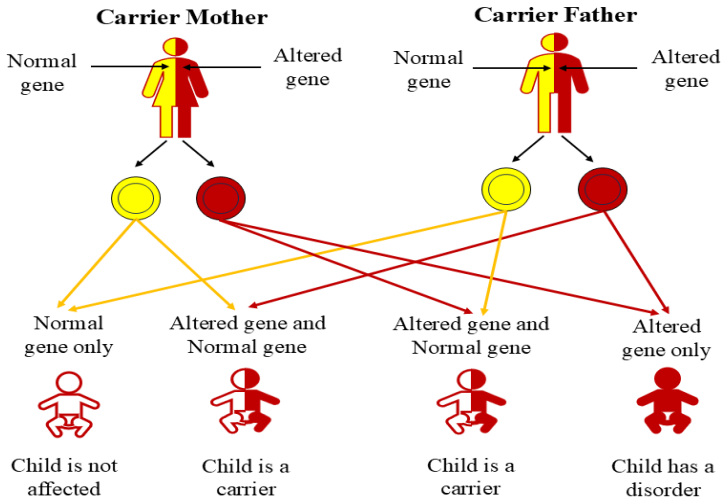


Figure 1: Illustrates a pattern of autosomal recessive inheritance where two carrier parents have a 25% chance of producing an unaffected child, a 50% chance of having a carrier child, and a 25% chance of having an affected child.

Alpha-thalassaemia, which lowers the quantity of another kind of globin, is one genetic disorder that can impact the development of sickle cell disease(Higgs et al., 1982). Hereditary variations in inflammation and blood coagulation may also impact the severity of the illness(Ratnoff & Bennett, 1973). In addition to genetics, environmental and societal variables are important(Bouchard & McGue, 2003). Economic stability, family support, a good diet, and frequent access to healthcare can all aid in symptom management and the avoidance of problems. People who live in places with greater healthcare tend to have better overall health outcomes and fewer emergencies. Conversely, a lack of support and therapy can make managing the illness far more challenging(Jeon et al., 2009). Sickle cell disease can afflict persons of any ethnic origin, However, people with African, Middle Eastern, Mediterranean, and Indian ancestry are most likely to have it. One of the most common genetic blood disorders worldwide is sickle cell disease (SCD)(Saraf et al., 2014). In spite of being brought on by a single, minor gene alteration, it affects many parts of the body. Thankfully, many SCD patients are living longer, healthier lives thanks to increased awareness, advancements in medicine, and supportive care. Symptoms and effects can be lessened with the use of drugs such as hydroxyurea, blood transfusions, antibiotics, pain management, and routine medical examinations(Chan et al., 2022). Newer gene treatments or bone marrow transplants may be able to help in certain situations(Moore, 2002). Better treatments and even cures for the illness are still being investigated by researchers(Cox et al., 2009).

1.2. Pathophysiology of SCD:

The pathophysiology of SCD is shown in the schematic illustration. **(Figure 2)** Vaso-occlusive crises (VOC), haemolysis, polymerization, oxidative stress, sterile inflammation, and endothelial dysfunction are the main characteristics of sickle cell anemia.

Haemolysis: The haemoglobin S (HbS) molecule is more likely to form stiff, elongated chains when oxygen levels are low because of a beta haemoglobin mutation in the gene(Yu, 2022). Because oxygen availability varies early in the illness process, red blood cells with HbS may alternate between their typical disc-like form and a sickle or crescent shape. However, some of these cells eventually become irreversibly sickled as they lose their capacity to return to their original shape(Padilla et al., 1973). Because of this irreversible deformity, they are more likely to hemolyze (break apart) and obstruct tiny blood arteries, which might result in vaso-occlusive crisis (VOC)(Camus et al., 2012).

Vaso-occlusive crises (VOC): Red blood cells impacted by aberrant haemoglobin S undergo vaso-

occlusive crises (VOCs) when they become rigid and curled in low-oxygen situations(Ahmed & Ibrahim, 2017). Due to their decreased flexibility, these malformed cells frequently group together or adhere to the linings of microscopic blood arteries, resulting in blockages in the microcirculation(Michel, 2020). The outcome is a localized shortage of oxygen (ischemia), severe discomfort, and the possibility of tissue damage since blood flow is constrained and oxygen cannot adequately reach some tissues(Sjöberg & Singer, 2013). Additionally, the obstruction triggers the immune system and endothelium, which worsens the obstruction by releasing inflammatory cytokines and encouraging additional platelet and white blood cell adhesion(Granger & Kubes, 1994). Free haemoglobin is released during haemolysis of fragile sickled cells, which lowers nitric oxide levels and causes vasoconstriction and endothelial dysfunction, both of which increase VOC(Ahmed, 2011). Several acute and chronic sickle cell disease issues are brought on by this sickling cycle, vascular obstruction, inflammation, and ischaemia, which is the foundation of VOC pathophysiology(Osunkwo et al., 2020).

Polymerization: Haemoglobin S (HbS), an abnormal type of haemoglobin is produced when the beta-globin gene is mutated(R. Das & Sharma, 2019). The propensity of HbS molecules to adhere to one another and form inflexible, rod-like structures when oxygen levels fall is called polymerization. Because of this, red blood cells lose their typical round form and take on a sickle-like curvature(Pauling et al., 1949). These cells can initially regain their original form if oxygen is reintroduced, but repeated instances over time cause the sickling to become permanent(Nash et al., 1986). Anemia can result from these malformed cells' rigidity and fragility, as well as their ability to obstruct tiny blood arteries, which lowers blood flow and increases pain, organ damage, and other disease consequences(Metivier et al., 2000).

Oxidative stress: An aberrant form of haemoglobin known as haemoglobin S (HbS) is produced when the beta-globin gene is mutated(Fujii et al., 2021). The tendency of HbS molecules to cling to one another and create rigid, rod-like structures when oxygen levels fall is called polymerization. Because of this, red blood cells lose their typical round form and take on a sickle-like curvature(Herrick, 1910). These cells can initially regain their original form if oxygen is reintroduced, but repeated instances over time cause the sickling to become permanent.Aanemia can result from these malformed cells' rigidity and fragility, as well as their ability to obstruct tiny blood arteries, which lowers blood flow and increases pain, organ damage, and other disease consequences(Graham, 1924).

Sterile inflammation: Sterile inflammation, which happens even in the absence of infection, is a major factor in the consequences of the illness(Rock et al., 2010). Hazardous materials such as free haemoglobin and as sickled red blood cells break down, heme is released into the bloodstream. These compounds function as warning signs that trigger synthesis of substances that cause inflammation from immunological and blood vessel cells. Sickled cells and other blood components adhere more firmly to vessel walls as a result of this inflammation, obstructing blood flow and resulting in damage(Hebbel et al., 2004). Reactive oxygen species are dangerous chemicals produced by repeated bouts of blood artery obstruction and reopening, which exacerbate tissue damage and inflammation. In sickle cell disease, this ongoing cycle of inflammation and destruction exacerbates organ issues and discomfort(Nader et al., 2020).

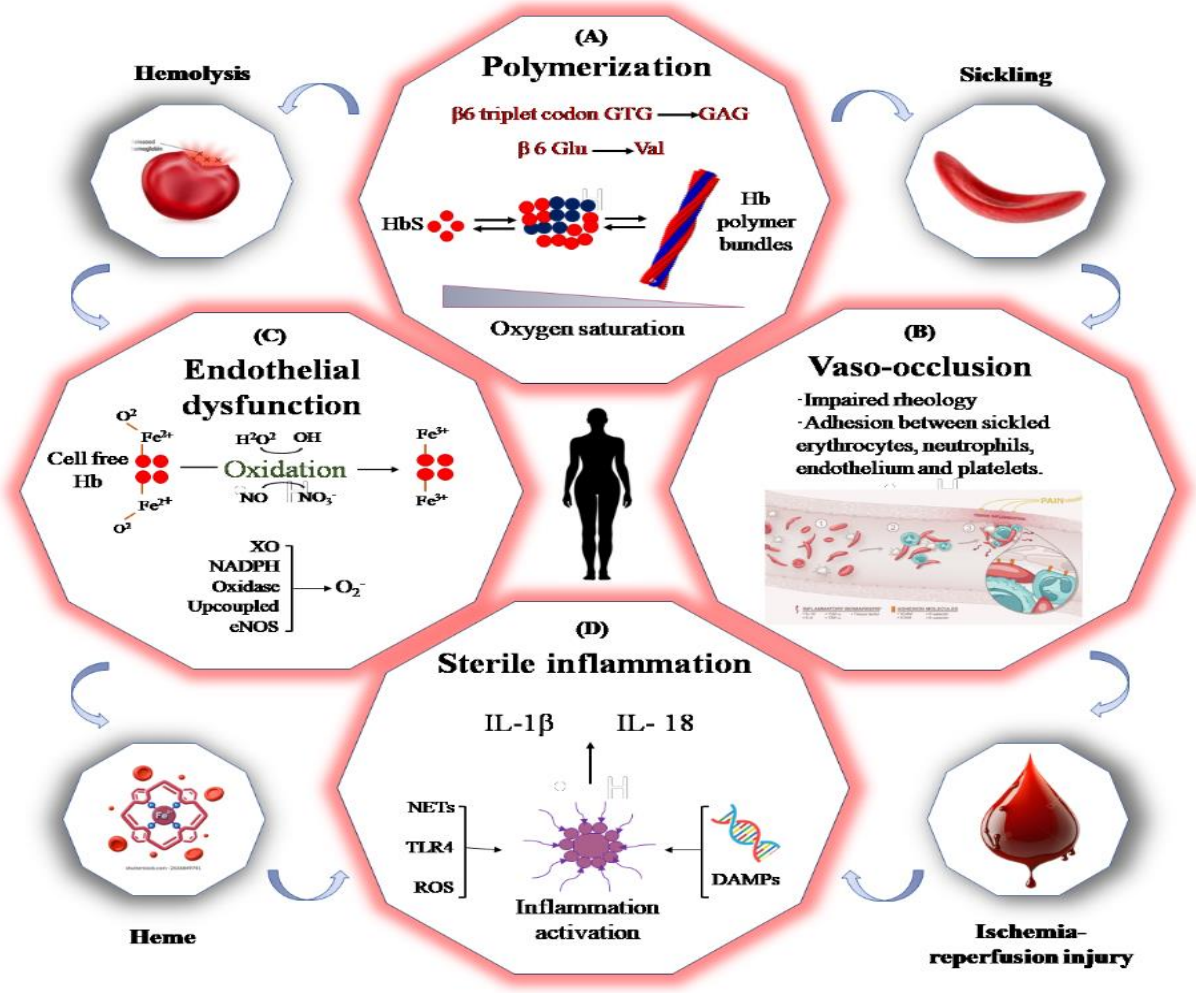


Figure 2: Pathophysiology of Sickle Cell Anemia

2. Traditional Herbal Management of SCA:

Natural plants are used in herbal treatment for sickle cell anemia to assist control the disease's symptoms, which include low blood count, discomfort, and oedema. Carica papaya, Hibiscus sabdariffa, Vernonia amygdalina, Aloe barbadensis miller, Telfairia occidentalis, Bryophyllum pinnatum, Anacardium occidentale, and Fagara zanthoxyloides are a few traditional herbs that contain natural compounds that may help improve blood health by avoiding red blood cells with sickles. (Table 1&2) These herbs' antioxidant and anti-inflammatory qualities assist reduce discomfort and cell damage during a sickle cell crisis(Okpuzor et al., 2008a). Standard medical treatments should not be replaced by herbal medicines, even if they might improve a patient's health and are frequently more affordable and accessible in rural regions(Wardle et al., 2012). Rather, they can be taken in conjunction with medications such as folic acid, as well as pain relievers and lots of water. However, before these herbal remedies may be widely suggested, further research and safety testing are required(Rousseaux & Schachter, 2003).

2.1 *Carica papaya Linn* (Papaya)

Carica papaya Linn is thought to function by decreasing erythrocyte sickling and stabilizing red blood cell membranes(Kamilla et al., 2021). Bioactive substances with antioxidant qualities, including flavonoids, alkaloids, and phenolic compounds, are present in its leaf extract and aid in reducing oxidative stress, a major contributor to the sickling process. By improving red blood cell hydration and flexibility, the extract may reduce haemoglobin polymerization and sickle cell development(Munir et al., 2022).

An in vitro investigation assessed the antisickling properties of aqueous *Carica papaya* leaf extract at 2, 4, 6, 8, and 10 mg/mL dosages using blood samples from 50 confirmed HbS sickle cell patients. With the

greatest effectiveness shown at the 10 mg/mL concentration, the findings showed that the percentage of sickled red blood cells decreased in a dose-dependent manner, that previously sickled cells reversed, and that the osmotic fragility of red blood cells significantly decreased ($p < 0.05$)(Naiho et al., 2015).

2.2 *Hibiscus sabdariffa* (Roselle)

Roselle, also known as *Hibiscus sabdariffa*, is thought to function by shielding red blood cells from oxidative damage and lowering their sickling. The extract has demonstrated the ability to prevent haemoglobin S polymerization, which is the process that gives red blood cells their sickle shape(Mohamed et al., 2012). For sickle cell anemia, *Hibiscus sabdariffa* may help preserve normal cell shape, enhance blood flow, and lessen consequences including discomfort and organ damage by stabilizing the red blood cell membrane and lowering oxidative stress(Peter et al., 2017). *Hibiscus sabdariffa* leaf extract was tested at 0.1, 1.0, and 10 mg/mL concentrations to assess its potential antisickling properties in a laboratory (in vitro) study involving blood samples from 11 sickle cell anemia patients. According to the findings, the extract considerably reduced red blood cell sickling, with the biggest impact shown at the highest concentration (10 mg/mL)(Pereye et al., 2022).

2.3 *Aloe barbadensis miller* (Aloevera)

Aloe barbadensis miller is believed to aid in lowering the sickling process by stabilizing red blood cell membranes and lowering oxidative stress. It includes bioactive substances that function as antioxidants, preventing free radical damage to red blood cells(N, 2010). These substances include vitamins A, C, and E, polysaccharides, flavonoids, and phenolic compounds. These antioxidants have the potential to enhance red blood cell hydration and flexibility while preventing haemoglobin polymerization, a crucial step in sickle cell development(Krasias, 2021). Consequently, aloe vera may contribute to the preservation of red blood cells' typical form and function, enhancing circulation and lowering the incidence of sickle cell-related problems(Ejele & Njoku, 2008).

Aloe vera leaf extracts were examined at to evaluate 2.5 mg/mL, 5 mg/mL, and 10 mg/mL its antisickling ability in vitro research utilizing blood samples from people with sickle cell anemia. The results showed that aloe vera had antisickling efficacy that was dose-dependent, indicating that larger concentrations made it more effective. The 10 mg/mL dosage exhibited the highest amount of sickling inhibition among the tested levels. It also indicated a substantial capacity to reverse red blood cells that had previously become sickled(Cotoraci et al., 2021).

2.4 *Telfairia occidentalis* (Fluted Pumpkin)

Telfairia occidentalis prevents red blood cells from deforming into sickles by blocking deoxygenated haemoglobin S polymerization(Cyril-Olutayo et al., 2019). This is main way that it works to improve sickle cell anemia. Antioxidants like flavonoids and phenolic chemicals, which are abundant in it, help stabilize red blood cell membranes and lessen oxidative stress, both of which support the preservation of normal cell form and function(Atabo et al., 2016). The plant's rich iron and vital vitamin content also boost hematopoiesis and encourage the reversal of cells that have already begun to sickle(Osuntoki & Sanusi, 2007). Red blood cell integrity and function are enhanced by these combined actions, which makes *Telfairia occidentalis* a potentially useful adjuvant in medication for sickle cell anemia(Salman et al., 2018). Studies on animals and in laboratories have demonstrated the potential antisickling properties of *Telfairia occidentalis*. For up to 95% of HbS red blood cells, ethanol leaf extracts (1–16 mg/mL) restored sickling in vitro. Additionally, sickled cells' membrane stability was enhanced by saline extracts. RBC count, haemoglobin, and red cell fragility were all enhanced in rats given oral dosages of 10–20 mg/day and 80–400 mg/kg/day without causing any harm(Salman et al., 2018).

2.5 *Bryophyllum pinnatum* (Patharchatta)

The "miracle leaf" or "life plant", *Bryophyllum pinnatum*, has anti-sickling properties through a variety of ways. Flavonoids, triterpenoids, and phenolics are some of its bioactive substances that aid in preventing deoxygenated haemoglobin S polymerization, the main factor causing sickling in RBC(Fürer et al., 2013). Along with being strong antioxidants, Red blood cell membrane stability and oxidative stress reduction are provided by these phytochemicals, which stops haemolysis and

preserves proper cell structure(Morais Fernandes et al., 2021). Furthermore, under the right circumstances, *Bryophyllum pinnatum* has been shown to encourage sickled cells to return to their typical biconcave form The plant helps to control sickle cell anemia overall by enhancing red blood cell integrity and lowering vaso-occlusive consequences(Andrade et al., 2020).

A leaf extract from *Bryophyllum pinnatum* was tested for antisickling properties in vitro. The aqueous extract's content of 10 mg/mL was assessed using blood samples from sickle cell patients. The extract prevented more sickling under low oxygen tension and dramatically restored sickled cells to their original form. This suggests that it could be used to treat sickle cell anemia in a supportive manner(Elufioye et al., 2022).

2.6 *Anacardium occidentale* (Cashew)

The phytochemicals found in Anacardium occidentale (cashew trees), such as flavonoids, tannins, and phenolic compounds, have a strong anti-sickling effect on sickle cell anemia (Omoboyowa et al., 2018). These bioactive components lessen red blood cell sickling by preventing deoxygenated haemoglobin S (HbS) from polymerizing (P. C. Chikezie et al., 2020). The plant's antioxidant qualities aid in the neutralization of reactive oxygen species (ROS), shielding red blood cells against membrane instability and oxidative damage. Furthermore, Anacardium occidentale increases red blood cells' hydration and deformability, which helps sickled cells reverse and lengthens their lifespan. Through these processes, the plant helps people with sickle cell anemia have better blood flow and have fewer vaso-occlusive crises (Q. Wang & Zennadi, 2021).

Anacardium occidentale (cashew) leaf extract was tested for its potential to treat sickle cell anemia by treating blood from sickle cell patients with extract concentrations ranging from 1 to 10 mg/ml. The study's findings showed that the extract, especially at the 10 mg/mL concentration, could help preserve better cell morphologies under low oxygen levels, lessen sickling, and even restore the proper shape of malformed red blood cells (Out, n.d.).

2.7 *Moringa oleifera* (Drumstick)

Moringa oleifera, sometimes referred to as the drumstick tree, has anti-sickling properties for sickle cell anemia because of its rich phytochemical makeup, which includes flavonoids, phenolic compounds, vitamins (particularly vitamin C), and minerals like iron and zinc ("In Vitro Evaluation of Moringa Oleifera Leaf Extracts Used in Managing Sickle Cell Patients in South West Nigeria," 2018). By inhibiting the polymerization of deoxygenated haemoglobin S (HbS), these components help stop red blood cells from deforming into sickles (Ohiagu et al., 2021a). By stabilizing RBC membranes and reducing oxidative stress, its potent antioxidant qualities enhance cell flexibility and stop haemolysis (Azeem et al., 2023). Moreover, its hematopoietic potential improves the synthesis of red blood cells, hence treating anemia frequently linked to sickle cell disease (Azeem et al., 2023). All of these activities work together to improve red cell health and lessen difficulties for sickle cell anemia patients (Obeagu & Obeagu, 2024).

In vitro, Moringa oleifera leaf ethanol extracts have demonstrated potent antisickling efficacy; in deoxygenated erythrocytes, 4 mg/mL inhibited HbS sickling by about 95.6% and reversed it by approximately 79.4% (Adejumo et al., 2012). There are currently no documented human clinical studies involving sickle cell patients. For 14 days, Wistar rats given oral ethanol extract 50–100 mg/kg body weight showed better haematologic parameters, elevated antioxidant gene activity, and altered sickle-cell-related gene expression without causing appreciable harm (Ameh & Alafi, n.d.). In sickle cell disease, dosage is still determined via human trials until safety and effectiveness are established (Suzana et al., 2017a).

2.8 *Hymenocardia acida Tul* (Heart tree)

The anti-sickling properties of Hymenocardia acida Tul., a medicinal plant used in traditional African medicine, are mainly due to its bioactive phytochemicals, which include flavonoids, alkaloids, tannins, and phenolic compounds (Amom et al., 2013). Red blood cell sickling is caused by deoxygenated haemoglobin S (HbS) polymerization, which is inhibited by these substances (Dash et al., 2013). The plant's potent antioxidants aid in lowering

oxidative stress, preserving the structural integrity of red blood cell membranes and preventing damage (Biochemical_Changes_in_Haematological_an, n.d.). Under some circumstances, Hymenocardia acida has also been shown to aid in membrane stabilization and encourage sickled cells to return to their normal form (A. Kumar et al., 2024). Through these processes, it enhances blood rheology, lessens haemolysis, and may even lessen sickle cell crisis symptoms. Hymenocardia acida Tul. leaf extract's anti-sickling properties were evaluated in a lab-based study utilising sickle cell anemia patients' blood. The extract was given in concentrations of 2.5, 5.0, and 10.0 mg/mL. The results showed that, in a way that is depending on dosage, the plant extract dramatically decreased the quantity of sickled red blood cells. The most effective dosage, which improved red cell shape and decreased sickling, was 10 mg/ml. These results validate the custom of using H. acida to treat sickle cell crises (P. K. Das et al., 2007).

2.9 *Azadirachta indica* (Neem)

The phytoconstituents of Azadirachta indica, sometimes referred to as neem, including flavonoids, triterpenoids (such as nimbin and azadirachtin), tannins, and polyphenols, may have anti-sickling properties in sickle cell anemia (Verma et al., 2021). These substances aid in avoiding sickle-shaped red blood cell formation by blocking Haemoglobin S (HbS) polymerisation from deoxygenation. Neem's strong antioxidant qualities help red blood cell membranes stay flexible and structurally intact by reducing oxidative stress and lipid peroxidation (Sarkar et al., 2021). Neem's anti-inflammatory qualities may also lessen the intensity of vaso-occlusive crises (Orisakwe et al., 2020). All of these effects work together to enhance red blood cell activity and lessen sickle cell anemia-related problems. An in vitro investigation examined the effects of Azadirachta indica ethanol leaf extract at 0.5%, 1.0%, and 2.0% w/v on sodium metabisulphite-induced sickling in human HbS blood (Elufioye et al., 2019). In a dose-dependent way, the extract reversed sickling; at 2.0%, HbS polymerization decreased to 1.8% from 37% in controls (Braga et al., 2021). It was just as effective as saline + p-hydroxybenzoic acid. These findings suggest that the antioxidant and membrane-stabilizing chemicals found in A. indica leaves may be beneficial for the management of sickle cell anemia(P. Chikezie, 2006).

2.10 *Allium sativum* (Garlic)

Garlic, or Allium sativum, is a well-known medicinal herb with a number of health advantages. It has also had encouraging results in the treatment of SCA (Tesfaye & Mengesha, 2015). A blood condition known as sickle cell anemia causes red blood cells, which are typically soft and spherical, to take on a sickle shape (Arihan et al., 2021). Blood vessel obstructions brought on by its irregular form might cause anemia, pain, and other problems. Haemoglobin S (HbS), an aberrant form of haemoglobin that prefers to aggregate when blood oxygen levels drop, is the primary cause of this sickling (Shahab Uddin et al., 2016). Natural substances found in garlic, such as S-allyl cysteine, diallyl disulphide, and allicin, aid in halting haemoglobin S's polymerisation or clumping Duncan Maina, 2017). Garlic lowers the likelihood of sickle-shaped red blood cells by halting this process (Moriguchi et al., 2001). Furthermore, because garlic is a potent antioxidant, it aids in the removal of harmful substances called free radicals from the body (Banerjee et al., 2003). These free radicals can weaken red blood cells' membranes, which makes them more fragile. Garlic protects cells by strengthening their membranes and increasing their stability and flexibility (Iciek et al., 2009). Garlic also increases blood flow by lowering inflammation and relaxing blood arteries (Ried & Fakler, 2014). Garlic has a lot of potential as a supportive, natural therapy for this illness, but additional clinical research is required (Ansary et al., 2020). Allium sativum (garlic) treated with 2% sodium metabisulphite was evaluated for its antisickling properties in an in vitro investigation utilizing HbS blood samples. 200, 400, and 600 mg/mL of aqueous garlic extract dramatically decreased sickled cells in a way that is dependent on dosage; the highest impact was noticed at 600 mg/ml. The effect was attributed to allicin, an organosulfur component found in garlic that has antioxidant and red cell membrane-stabilizing properties. These results provide credence to garlic's potential as an antisickling remedy (Colín-González et al., 2012).

S. No.	Name	Scientific Name	Family	Part use	Phyto-constituent	Benefits	Ref.
1.	Papaya	*Carica papaya Linn*	Caricaceae	Leaves	Flavonoids, Phenolic compounds, Alkaloids, Saponins, and Glycosides.	Papaya leaf extract lowers oxidative stress and increases RBCs and immunity.	(Sharma et al., 2022)
2.	Roselle	*Hibiscus sabdariffa*	Malvaceae	Leaves	Anthocyanins, Flavonoids, and organic acids.	Hibiscus tea lessens sickle crises and provides antioxidant protection.	(González-Stuart, 2011)
3.	Aloe vera	*Aloe barbadensis miller*	Liliaceae	Juice or gel	Barbaloin, Anthraquinones and Flavonoids	Offers healing, immune-supporting, and anti-inflammatory properties.	(Alamgir, 2018)
4.	Fluted Pumpkin	*Telfairia occidentalis*	Cucurbitaceae	Leaves	Phenols, Flavonoids, Alkaloids, Tannins, and Saponins,	Iron and folate-rich, increases the formation of haemoglobin.	(Elechi et al., 2022)
5.	Patharchatta	*Bryophyllum pinnatum*	Crassulaceae	Leaves	Alkaloids, Flavonoids, Glycosides, Triterpenes, Cardenolide.	Lessens weakness, discomfort, and inflammation in sickle cell crises.	(Oladejo et al., 2022)

6.	Cashew	*Anacardium occidentale*	Anacardiaceae	Leaves	Flavonoids.	Cashew leaves that are anti-sickling encourage the production of good haemoglobin.	(P. C. Chikezie, 2011)
7.	Drumstick	*Moringa oleifera*	Moringaceae	Leaves, Seed, Flowers	Flavonoids, Alkaloids, Phenols, Terpenes, Saponins, Tannins.	Red blood cell sickling is prevented by moringa's reduction of oxidative stress.	(Suzana et al., 2017b)
8.	Heart tree	*Hymenocardia acida Tul*	Phyllanthaceae	Leaves	Tannins, Saponins, Flavonoids, Terpenes, Steroids, and Resins.	Sickling is reversed and HbS polymerisation is prevented by Hymenocardia acida.	(Mpiana et al., 2009)
9.	Neem	*Azadirachta indica*	Meliaceae	Neem oil extracted from the seeds	Flavonoids, Tannins, and Saponins.	Neem enhances oxygen transport and lessens pain crises and sickling.	(Kotue TC et al., 2016)
10.	Garlic	*Allium sativum*	Alliaceae	Garlic bulb	Phenolic, Saponins, Anthosyanins Vinyldithiins.	Garlic improves cellular activity and shields red	(Takasu et al., 2006)

						blood cells.	
11.	Lemon Grass	*Cymbopogon citratus*	Poaceae	Leaves	Citral is an acyclic monoterpene aldehyde combination of geranial.	Red blood cell sickling may be prevented by lemongrass extracts.	(Awor et al., 2024)
12.	Pigeon Pea	*Cajanus cajan*	leguminosae	Seeds	Flavonoids, Stilbenes, Saponins, Tannins.	Extracts of Cajanus cajan may prevent vaso-occlusion and sickling.	(Akinsulie et al., 2005)
13.	Gambian Mahogany	*Khaya senegalensis*	Meliaceae	Stem, Bark and Leaves	Alkaloids, Tannins, Saponins, Steroids, Flavonoids, Terpenoids.	Improves haemoglobin function and cell flexibility to reverse sickling.	(Christianah et al., 2020)
14.	Prickly ash	*Fagara zanthoxyloides*	Rutaceae	Roots, Bark, and Leaves	Alkaloids, Amides, Lignans, Coumarins, and Volatile oils	Red cell shape is preserved by reducing sickling using root and bark extracts.	(Christianah et al., 2020; Okagu et al., 2021)
15.	Ginseng	*Panax quinquefolius L.*	Araliaceae	Root	Polysaccharides, Alkaloids, Polyacetylenes, Phenolic acids, and Saponins.	In sickle cells, ginsenosides lessen discomfort, inflammation, and sickling.	(X. Wang et al., 1999)

16.	African Black pepper	*Piper guineensis*	Piperaceae	seeds	Alkaloids, flavonoids, phenols, tannins, saponins, and glycosides.	Inhibiting red blood cell sickling and reversing sickled cells.	(Wambebe et al., 2001)
17.	Camwood	*Pterocarpa osun*	Fabaceae	Stem	Flavonoids, Tannins, Terpenoids, Alkaloids, and Glycosides	Inhibiting haemoglobin S polymerization and reducing vaso-occlusive crises in sickle cell anemia.	(Okpuzor et al., 2008b)
18.	Clove	*Eugenia caryophyllala*	Myrtaceae	Fruit	Sesquiterpene β-caryophyllene and eugenol derivatives like eugenyl acetate.	May help manage pain, a key symptom of sickle cell crises, and anti-sickling properties.	(Sani et al., 2021)
19.	Jowar	*Sorghum bicolor*	Gramineae	Leaves	Tannins, Flavonoids, Phenolic Acids, and Anthocyanin	increases haemoglobin, stops sickling, and guards against harm.	(Saha et al., 2025)
20.	Mututi / Rosewood	*Pterocarpus santolinoides*	Fabaceae	Entire plant	Alkaloids, Flavonoids, Saponins, Tannins, Terpenoids, Steroids, Coumarins and Phenols.	Prevents sickling and may raise haemoglobin levels.	(Okparauka & Ojimelukwe, 2025)

21.	Almond	*Terminalia catappa*	Combretaceae	Leaves	Phenols, Tannins, Flavonoids, Alkaloids, Saponins, Steroids, Terpenoids, and Carotenoids	Antisickling properties, increasing haemoglobin levels, and stabilizing red blood cell membranes	(Mgbemene & Ohiri, 1999)
22.	Liquorice Weed, Sweet Broom Weed, and Goatweed	*Scoparia dulcis*	Plantain	Leaves	Alkaloids, tannins, phenols, terpenoids, and flavonoids.	Antisickling properties, inhibiting sickling and restoring normal red blood cell morphology.	(Karjavkar et al., 2025)
23.	Bitter Wood	*Quassia afr icana*	Simaroubaceae	Root, Bark	β-carbolines, scopoletin, and cathine-6-one.	Reversing red blood cell (RBC) sickling and preventing cell aggregation in vitro.	(Kolawole & Emmanuel, n.d.)
24.	Christmas bush	*Alchornea cordifolia*	Euphorbiaceae	Leaves	Terpenoids, alkaloids, phenols, flavonoids, tannins, and saponins.	Suppression of HbS erythrocyte sickling.	(Oyedeji et al., n.d.)
25.	Grape-seeded amomum	*Afromomum albo violaceum*	Zingiberaceae	Leaves and seeds.	Terpenes, alkaloids, tannins, phenolics, and flavonoids.	Inhibits oxidative damage and restores the structure of red	(Valentin et al., 2024)

						blood cells.	
26.	Custard-Apple	*Annona senegalensis*	Annonaceae	Leaves	Alkaloids, Saponins, Tannins, Flavonoids, Steroids, Calcium, Potassium, and Iron.	Prevent red blood cell sickling and haemolysis in sickle cell anemia patients.	(J et al., 2025)
27.	Guinea Pepper	*Aframomum melegueta*	Zingiberaceae	Seed, Bark	Gingerol, Paradol, Shogaol, Terpenoids, Flavonoids, Tannins, Alkaloids, Saponins, Cardiac Glycosides, And Phenolic Compounds.	Antioxidant effects that reduce oxidative stress, and its anti-inflammatory properties that can alleviate pain associated with the condition.	(Adeniyi et al., 2024)
28.	Bridelia, Blackbird tree, or Shea nut tree	*Bridelia ferruginea*	Phyllanthaceae	Leaves	Flavonoids, Phenolics, Triterpenes, Saponins, Alkaloids, Cardiac, Glycosides, Steroids.	Antioxidant, Anti-inflammatory, Analgesic effects, supportive role in managing Sickle Cell Disease.	(Ayodele et al., 2024)

29.	Kapok Tree	*Ceiba pentandra*	Malvaceae	Trunk bark and branches	Alkaloids, Tannins, Flavonoids, Saponins, Terpenoids, Phenols, Glycosides, Carbohydrates.	Anti-sickling effect, reducing thrombin activity, and potentially increasing foetal haemoglobin levels.	(Asigbaase et al., 2024)
30.	Brimstone tree	*Morinda lucida*	Rubiaceae	Stem bark, leaves, root.	Alkaloids, Tannins, Saponins, Phenols, Flavonoids, Steroids, Terpenoids, Anthraquinones, and Polyphenols.	In vitro anti-sickling activity by reducing sickled red blood cells and increasing resistance to haemolysis.	(Marcelin et al., 2025)
31.	Coleus	*Coleus kilimandcharis*	Lamiaceae	Entire part	Phenolic acids, Flavonoids, Terpenoids, Sterols.	Anti-sickling activity	(Mpiana et al., 2007a)
32.	African pear, plum, safou	*Dacryodes edulis*	Burseraceae	Fruit	Alkaloids, carotenoids, flavonoids, tannins.	Anti-sickling potential	(Mpiana, Ngbolua, et al., n.d.)
33.	Welwitschia, Bush Mango	*Caloncoba welwithsii*	Achariaceae	Leaves	Friedelane triterpenoids, Flavanols, and Phytosterols.	stabilizing red blood cell membranes and promoting flexibility.	(Mpiana et al., 2007b)

34.	Cowpea, Black-eyed pea, Southern pea	*Vigna unguiculata*	Fabaceae	Seeds	Friedelane Triterpenoid, Flavonoids Phytosterols	Improves the shape and longevity of red blood cells and has antisicklin g properties.	(Mpiana, Mudogo, et al., n.d.)
35.	African satinwood	*Zanthoxylu m macrophyll a*	Rutaceae	Root	Alkaloids (Benzophenant hridines), Flavonoids, Phenols, Lignans, and Saponins.	Helps stabilize erythrocyt e membrane s and reduces red blood cell deformatio n.	(Elekwa et al., 2005)
36.	Bitter kola	*Garcinia kola*	Clusiaceae or Guttiferae	Seed, leaves, seed pods.	Alkaloids, Flavonoids, Terpenoids, Coumarins, Lignans, and Phenols.	Stabilize the membrane s of sickle-shaped RBC, help restore their normal shape.	(Elekwa et al., 2004)
37.	Candle bush	*Senna alata*	Fabaceae	Leaves, root.	Alkaloids, terpenoids, anthraquinones , flavonoids, and tannins.	Anti-sickling activity, which helps to stabilize red blood cell membrane s and restore their normal shape.	(Atanu et al., 2022)

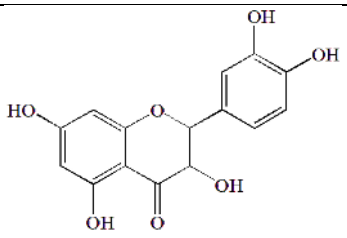
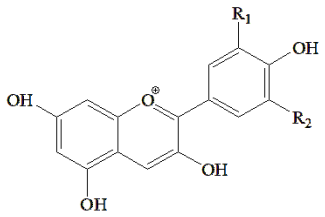
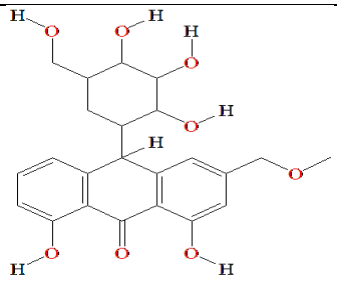
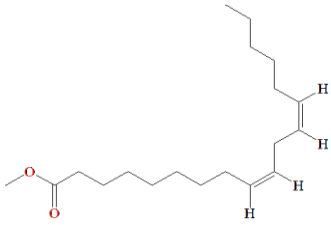
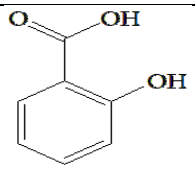
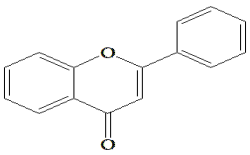
38.	Podocarp Senna, Sicklepod Senna	*Senna podocarpa*	Fabaceae	Leaves, root	Alkaloids, tannins, terpenoids, anthraquinones, and flavonoids.	Antioxidant and anti-inflammatory properties, oxidative stress in SCA.	(Ogunniyi et al., 2023)
39.	Ajara, Dafara, Latutuwa	*Cssus populnea L.*	Vitaceae	Root	Alkaloids, Flavonoids, Saponins, Terpenoids, Carotenoids.	Anti-oxidative and anti-sickling properties.	(Moody et al., 2003)
40.	Baobab	*Adansonia digitata L*	Bambacaca e	Bark, Fruit, Leaves, Seed.	Alkaloids, Flavonoids, Saponins, Tannins, Terpenoids.	Antisickling, antioxidant properties lessen dehydration and oxidative stress.	(Adesanya et al., 1988)
41.	Akerejupon	*Sphenocentrum jollyanun*	Menisperm aceae	Root	Glycosides, alkaloids, flavonoids, tannins, and saponins.	Increases the synthesis of red blood cells and keeps them stable.	(Omoyajowo et al., 2025)
42.	Bitter melon	*M. charantia*	Cucurbitac eae	Leaves	Cucurbitacin flavonoids, saponins, triterpenes, charantin.	antioxidant, anti-inflammatory, neuroprotective properties.	(Semiz & Sen, 2007)
43.	Tea plant, tea shrub.	*Camellia sinensis*	Theaceae	Leaves	Amino acids, alkaloids, polyphenols, flavonoids.	prevent red blood cell haemolysis.	(Ojo et al., 2006)

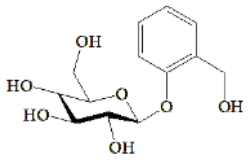
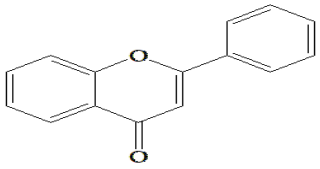
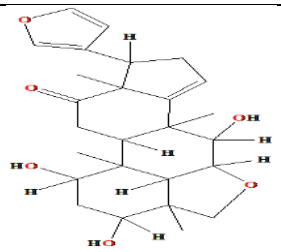
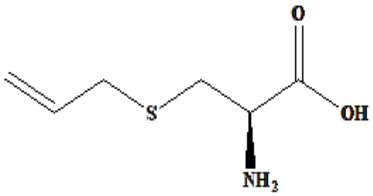
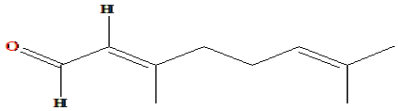
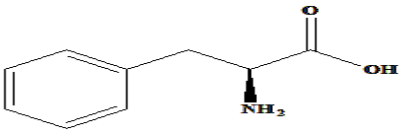
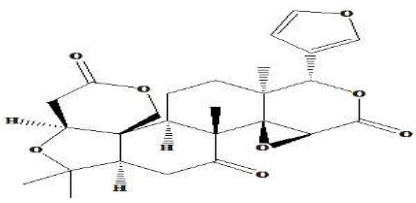
44.	Kutki, Katuk, Kardu	*Picrorhiza kurroa*	Plantaginaceae	Rhizomes	Iridoid glycosides cucurbitacins (triterpenoid) phenolic compounds.	ameliorate anemia, improve haemoglobin levels, RBC counts.	(Shinder et al., 2008)
45.	Avocatier	*Persea americana*	Lauraceae	Seeds	Alkaloids, terpenoids and steroids, saponins, tannin, flavonoids, glycosides, tannins.	Antisickling properties and may help improve haemoglobin levels in anemia.	(Borive Amani et al., 2025)
46.	Kouoptche	*Harungana madagascariensis*	Clusiaceae	Leaves	Alkaloids, saponins, flavonoids, anthrones, anthraquinones, xanthones, essential oils	Anti-sickling activity, which reverts sickle-shaped red blood cells to their normal biconcave form.	(Iinuma et al., 1995)
47.	Yamafzelia a	*Ficus thonningii*	Moraceae	Leaves	Alkaloids, polyphenols, tannins, saponosides, flavonoids	Antioxidant properties, which help combat oxidative stress in SCA patients.	(Chauke et al., 2025)
48.	Chrysanthe	*Chrysanthellum americanum*	Asteraceae	Leaves	Tannins, saponosides, flavonoids	Stabilizing red blood cell membranes and improving erythrocyte	(Gamo et al., 2024)

						morpholog y.	
49.	Djansang	*Ricinodend ron heudelotii*	Euphorbiac eae	Bark	Tannins, saponins, flavonoids, alkaloids, carotenoids, phenols.	The shape of the erythrocyt es was reversed and became normal.	(Edo et al., 2025)
50.	Jouon	*Brideliamic rantha*	Phyllanthac eae	Bark	Flavonoids, polyphenolic compounds.	reduces tissue damage and inflammati on in sickle cell disease.	(Lubisi et al., 2025)
51.	Viande de biche	*Lannea kerstingii*	Anacardiac eae	Bark	Alkaloids, Flavonoids, Saponins, Steroids, Tannins, Triterpenoids Polyphenols.	Increase haemoglo bin levels and improve the osmotic resistance of red blood cells.	(Pomaa et al., 2024)
52.	Pion d'inde	*Jatrophacu rcas*	Euphorbiac eae	Leaves	Alkaloids, glycosides, flavonoids, saponins, tannins and terpenoids	Significant in vitro normalizat ion of sickle cell erythrocyt es at 87%.	(Mbadiko et al., 2025)

53.	Faux manioc	*Jatropha gossypiifolia*	Euphorbiaceae	Leaves	Alkaloids, glycosides, flavonoids, saponins, tannins and terpenoids	Enhances red cell stability, lessens sickling, and prevents HbS polymerisation	(Mireille et al., 2025)
54.	Cajanus	*Piptadenia trump africanum*	Mimosaceae	Seeds	Flavonoids, tannins, alkaloids, saponins, cyanogenic glycosides, glycosides.	Enhances membrane stability and shields erythrocytes from oxidative damage.	(Ahajumobi & Asika, 2024)
55.	Bolongo	*Fagara tessmannii*	Rutaceae	Bark	Alkaloids, lignans, phenols, amide, acidic phenol, coumarins.	Red cells are stabilized and sickling is avoided by antioxidant qualities.	(Chalotra et al., 2023)
56.	Curcuma	*Curcumalonga*	Zingiberaceae	Rhizomes	Triterpenes, flavonoids, phenols, anthraquinones, saponins, anthrocyanines	Anti-sickling properties, which help to correct sickled red blood cells and normalize their function.	(Hatairaktham et al., n.d.)

Table 1: Summary of Medicinal Plants with Their Scientific Classification and Therapeutic Significance

S. No.	Name	Individual Constituent	Structure	Mechanism of Action	Ref.
1.	Papaya	Quercetin, Kaempferol		Antioxidant, Membrane stabilization, Anti-sickling	(N. O. A. Imaga et al., 2009)
2.	Roselle	Anthocyanins		Antioxidant, RBC membrane stabilization, Gardos channel inhibition (↓ MCHC, ↑ MCV), anti-sickling	(Manzano-Pech et al., 2025)
3.	Aloe vera	Barbaloin		minimizes pain, oxidative stress, inflammation in sickle crises.	(Naini et al., 2021)
4.	Fluted Pumpkin	Methyl linoleate ester		Inhibits HbS polymerization ; anti-sickling; enhances membrane fluidity	(Ohiagu et al., 2021b)
5.	Patharchatta	Phenolics & flavonoids		Antioxidant, membrane stabilization, anti-haemolytic	(S. Kumar & Judi, 2404)
6.	Cashew	Flavonoids		↓HbS polymerization ; RBC membrane stabilization; antioxidant	(Anorue & Joshua, 2025)

7.	Drumstick	Glycoside		↑NO→ vasodilation; improve Fe^{2+}/Fe^{3+} ratio; inhibit HbS polymerization	(Vishwakarma et al., n.d.)
8.	Heart tree	Flavonoids		Anti-sickling (RBC reversal), membrane stabilization, antioxidant	(Kumar Pandey et al., 2025)
9.	Neem	Nimbidin		Direct inhibition of HbS polymerization (anti-sickling)	(Amponsah et al., 2024)
10.	Garlic	S-allyl cysteine (SAC)		Antioxidant, Stabilizes (RBC) membranes, Inhibits formation of dense sickle cells	(Netshiluvhi, 2025)
11.	Lemon Grass	Citral		Antioxidant, vasodilatory, anti-inflammatory	(Nambiar & Matela, 2012)
12.	Pigeon Pea	Phenylalanine		Direct HbS polymerization inhibitor; reverses sickling	(N. A. Imaga et al., 2013)
13.	Gambian Mahogany	Limonoid		Direct HbS polymerization inhibition; reverses sickling without RBC damage	(Obodozie et al., 2010)

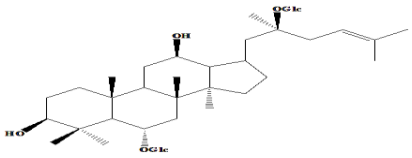
15.	Ginseng	Ginsenosides		Neutralize free radicals, reduce oxidative stress in cells (especially RBCs).	(Cai et al., 2025)
16.	Prickly ash	Amides & alkaloids		Bind HbS and inhibit polymerization	(Mawthoh et al., 2023)

Table 2: Medicinal Plants Their Phytoconstituents and Mechanisms of Action in Sickle Cell Disease Management.

CONCLUSION

The study's findings demonstrate the potential of medicinal plants as safe and efficient substitutes for the treatment of sickle cell disease (SCD). As evidenced by the results of several tests, especially those on sickling reversal and hemoglobin polymerization inhibition, many plant species have strong anti-sickling capacity. Aloe barbadensis miller, ginseng, Zingiber officinale, and Cymbopogon citratus are among the herbs that contain phytochemicals that greatly improve blood circulation and lessen organ damage. Overall, herbal treatments are a useful, affordable, and supplementary strategy for reducing SCD problems and improving patients' quality of life; hence, they merit additional clinical testing and pharmacological investigation.

Future directions:

Future studies on herbal treatments for sickle cell disease (SCD) should concentrate on identifying, defining, and standardizing the bioactive phytochemicals that have anti-sickling properties. To confirm their effectiveness, safety, and modes of action, further thorough pharmacological and clinical research is required. Novel plant-based formulations or medications that successfully lower haemoglobin polymerisation and avoid organ damage can be developed by fusing contemporary biotechnology with traditional expertise. In order to guarantee the quality, dose, and long-term therapeutic potential of these herbal remedies in the management of SCD worldwide, extensive clinical trials and regulatory assessments will also be necessary.

ABBREVIATION:

SCD - Sickle Cell Disease

WHO - World Health Organization

ATP - Adenosine Triphosphate

Hb - Haemoglobin

HbS - Haemoglobin S

HbF - Foetal Haemoglobin

VOC - Vaso-occlusive crises

CBC - Complete Blood Count

CVS - Chorionic Villus Sampling

ROS - Reactive Oxygen Species

SOD - Superoxide Dismutase

CAT - Catalase

GPx - Glutathione Peroxidase

NF-κB - Nuclear Factor-Kappa B

EPO - Erythropoietin

PCV - Packed Cell Volume

RBC - Red Blood Cell

TNF-α - Tumor Necrosis Factor Alpha

EGCG - Epigallocatechin Gallate

MCHC - Mean Corpuscular Haemoglobin Concentration

MCV - Mean Corpuscular Volume

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