THE ROLE OF HERBAL PLANT PRODUCTS IN THE TREATMENT OF SICKLE CELL ANAEMIA

Dr. R. Santosh Kumar*

Assistant Professor, Department of Pharmaceutics, GITAM School of Pharmacy, GITAM (Deemed to be University), Visakhapatnam-530045, Andhra Pradesh, India.

BONI SAI YASHWANTH

GITAM School of Pharmacy,
GITAM (Deemed to be University), Visakhapatnam-530045, Andhra Pradesh, India.

ABSTRACT:

In impoverished countries, medicinal plants have been utilized to treat different variations of illnesses, including sickle cell disease. Because of their cultural connection and inability to pay for the care offered by conventional medical practitioners, few populations in the evolving nations mainly hang on to traditional medicine. Traditional healers adhere to the idea of holistic therapy, and the bioactive components of medicinal plants utilized in traditional medicine that have therapeutic benefits are typically unknown. The term "active principle" refers to compounds found in medicinal plants that have therapeutic qualities. As a result, herbal plants imply a crucial role in the treatment of sickle cell anemia. Males are more affected by the condition because its causative gene is very expressive and dominant. Females, on the other hand, are frequent carriers since they are recessive and lack self-expression. It has been demonstrated that Pterocarpus santolinoides and Aloe vera extracts increase sickle cell blood's gelling time and decrease sickling in vitro.

KEYWORDS: Herbal medicines, Sickle cell Anemia, Traditional medicine, Antisickling activity, Antidrepanocytary activity, Anti-oxidants activity, sickle cell hemoglobin.

INTRODUCTION:

Sickle cell anemia is a hereditary condition expressed by uneven crescent-shaped red blood cells. (Generally, red blood cells develop in the shape of a disc.) Myths fostered by cultural ideals are dangerous. Childhood deaths within a family, for example, were generally associated with bad spirits in traditional African culture. When the underlying causes of many of these deaths were discovered, the entrance of Western medicine changed everything. People in numerous places, mainly in Africa and Asia, have learned to deal with the sickle cell disease problem by utilizing plants. Since the beginning of time, raw plant extracts have been utilized to treat a variety of illnesses.; however, in most cases, it is unknown what makes these plants bioactive. The advantages of conventional medicine and the reasons for its use have been demonstrated by several developments in a scientific study on the use of plants and herbs. The purpose of this research is to emphasize traditional healers' Utilization of herbal remedies in the treatment of sickle cell disease (SCD), as well as the underlying principles in their usage [1]. Several medicines have been researched for their anti-sickling properties. Inhibiting sickle

cell hemoglobin (HbS) polymerization, enhancing the Fe2+/Fe3+ status, and lowering lactate dehydrogenase (LDH) activity in blood plasma have all been reported to be possible by using the extracts of dry prawn (Astacus red) and dried fish (Tilapia). Because LDH is a sensitive indicator of hemolysis, the quantity of LDH in this disordered patient's blood impacts the severity of the disease. There have also been stories of SCD patients receiving excellent prenatal treatment. [2,3]

CAUSES, OCCURRENCE, AND RISK FACTORS INCLUDE:

Hemoglobin S, a defective kind of hemoglobin, causes sickle cell anemia. Red blood cells contain the oxygen-transporting protein hemoglobin. When exposed to low oxygen levels, hemoglobin S changes the structure of red blood cells. Red blood cells resemble crescents or sickles. The sickle-shaped cells are fragile and provide less oxygen to the tissues of the body. They can very readily become entangled in tiny blood vessels and break into shards that impair healthy blood flow [4]. Sickle cell anemia is inherited from both parents. You will have sickle cell trait if you inherit the normal hemoglobin (A) gene from one parent and the hemoglobin S gene from the other. Sickle cell trait does not cause sickle cell anemia in those who carry it. People of African and Mediterranean descent are far more prone to suffer from sickle cell disease. South and Central Americans, Caribbean residents, and Middle Easterners are also affected.[5]

SYMPTOMS AND TESTS:

Symptoms usually occur after four months. Common symptoms include stomach pain episodes, bone discomfort, shortness of breath, delayed growth and puberty, exhaustion, fever, high heart rate, and lower leg ulcers (in adolescents and adults).

The following tests are often used to detect and monitor sickle cell anemia patients: Hemoglobin electrophoresis and complete blood count (CBC) Test for sickle cell disease. A treatment's main objective is to manage and reduce symptoms while minimizing casualties. A sickle cell crisis requires blood transfusions, pain medications, and plenty of fluids. Acute chest syndrome, anemia, blindness/vision impairment, brain, and nerve system (neurologic) symptoms and stroke, mortality, illness of several organ systems (kidney, liver, lung), and drug (narcotic) use are all complications.[6]

PREVENTION:

Only when parents with the sickle cell trait produce a child together may sickle cell anemia be avoided. All sickle cell trait carriers should obtain genetic counseling. One out of every twelve African Americans has the sickle cell trait. You can avoid the change in the shape of red blood cells if you drink the optimum level of fluids, and obtain sufficient oxygen and treat infections as soon as possible if you have SCA.[7]

THE WESTERN LITERATURE ON SICKLE CELL DISEASE:

A Chicago physician, James B. Herrick, first mentioned sickle cell disease in the western literature in 1910, when he noted a patient from one of the Caribbean islands with anemia characterized by unique red cells that were "sickle-shaped." Red Cell Sickling and Oxygen: In 1927, Hahn and Gillespie determined that red cell sickling was caused by a lack of

oxygen [8]. Sherman (a Johns Hopkins Medical School student) observed birefringence in deoxygenated red cells in 1940, showing that the structure of hemoglobin in the molecule was changed by low oxygen. [9]

THE ISSUE:

A glutamic acid to valine substitution in the sixth position of the beta-globin chain of hemoglobin S (HbS) results in sickle cell disease, and multiple amino acids can be altered at once. Sickle cell disease variants which include only one defective gene has never been considered a disease [10]. In hypoxic environments, deoxy-HbS molecules polymerize, resulting in rigid, sickled cells. As a result, the usual disc biconcave RBC deforms. The red cell membrane loses its functional capacities due to sickle cell polymerization, resulting in a loss of K+ and water and a proportional increase of Na+. During sickling, there is an increase in intracellular free Ca2+, which results in a loss of K+ and the flow of Cl- and water [11]. The clumping of sickled RBCs blocks small blood arteries, restricting blood delivery to numerous organs. Deoxygenation damages the endothelium of tissue capillaries, resulting in plasma exudation into the surrounding soft tissue. This describes the majority of sickle cell disease patients' soft tissue edema in general [12].

CLINICAL SIGNS AND SYMPTOMS:

The phenotype of SCA differs hugely across individuals and throughout time in the same patients. Anemia, illnesses that cause pain, and organ failure are the three main groups of sickle cell disease's clinical symptoms, which are wide and diverse. Acute painful episodes or "crises" can be caused by clogged blood vessels and damaged organs. Sickle cell crisis can occur by occluding the artery as a result of membrane distortion. SCD patients are afflicted with various disorders, including acute chest syndrome (ACS), one of the leading causes of hospitalizations, stroke, and acute splenic sequestration. This condition also causes hyposthenuria, priapism, vascular necrosis, proliferative retinopathy, delayed growth, and sexual maturation, chronic pulmonary sickness, chronic nephropathy, etc. [13]

TABLE: LIST OF PLANTS USED TRADITIONALLY IN HERBAL MEDICINE TO TREAT SICKLE CELL ANAEMIA [14]

S.NO	Biological source	Part used	Therapeutic Action
	Picrorhiza kurroa	Extract	Antioxidant Activity
	Scoparia dulcis	Extract	Antioxidant Activity
	Camellia sinensis	Extract	Antioxidant Activity
	Adansonia digitata	Extract	Antisickling Activity
	Cissus populnea	Root Extract	Antisickling Activity
	Carica papaya	Extract	Antisickling Activity
	Aged garlic	Extract	Suppresses hemolysis and prevents reduced membrane deformability.
	Cajanus cajan	Seed Extract	Effective in restoring normal morphology of erythrocytes.

	Bridelia ferruginea	Extract	Antidrepanocytary activity
.	Ceiba pentandra	Extract	Antidrepanocytary activity
.	Morinda Lucida	Extract	Antidrepanocytary activity
.	Terminalia catappa	Extract	Human erythrocytes' osmotically induced hemolysis is effectively inhibited by an antisickling agent.
.	Aloe vera	Extract	Sickling is inhibited in vitro and the gelling time of sickle cell blood is increased.
.	Pterocarpus santolinoides	Extract	Sickling is inhibited in vitro and the gelling time of sickle cell blood is increased.
.	Eugenia caryophyllala	Fruit	Antisickling Activity
.	Pterocarpa Osun	Stem	Antisickling Activity
.	Piper guineensis	Seeds	Antisickling Activity

ORTHODOX THERAPEUTIC OPTIONS INCLUDE:

The most promising line of traditional treatment employed in managing sickle cell disease has been the induction of fetal hemoglobin. It is believed that polymerized globin chains are affected by fetal hemoglobin., whose contact leads to cell stiffness. In randomized adult patient studies, HU therapy decreased acute chest syndrome and the requirement for blood transfusions while lowering unpleasant crises by up to 50%.

HU has also been used successfully in children. Blood transfusions have aided in managing sickle cell disease, although with inevitable consequences. In some instances, bone marrow transplantation in youngsters has resulted in cures. Anti-adhesion and anti-oxidative therapy are two more traditional avenues of treatment being investigated. [15]

MEDICINAL PLANT POTENTIALS:

Extracts of Piper guineensis, Pterocarpa Osun, and Eugenia caryophyllala, were reported to be used to treat sickle cell disease [16]. In vitro studies have shown that the extracts of Pterocarpus santolinoides and Aloe vera lengthen the sickle cell blood gelling period and reduce sickling. This demonstrates that using these herbs to treat sickle cell disease may be quite effective. It has also been suggested that Fagara zanthoxyloides root extracts help reverse sickling [17,18]. One lady used Scoparia dulcis to treat sickle cell disease for over two decades, and the plant's effectiveness in treating sickle cell disease was proposed. Two-hydroxybenzoic acid was extracted and identified as the anti-sickling agent produced by the root of the plant Zanthoxylum macrophylla, which was also recognized as an anti-sickling agent in a crude aqueous extract of the plant's roots. Garcinia kola, often known as 'bitter kola,' is a popular seed among Nigerians. It may be beneficial in the treatment of sickle cell disease. An investigation of Garcinia kola aqueous extracts to support the aforesaid claim indicated that it was more effective and efficient on membrane stability than phenylalanine [19]. In comparison to Garcinia kola, the membrane stabilizing activity of Zanthoxylum macrophylum roots aqueous extract was lower than that of phenylalanine. Both Cassia alata and Senna podocarpa having the ability to stabilize the membrane; however, Senna alata has a higher amount of stabilizing effect. Pharmacological medicines that alter membrane stability might be utilized to influence

the sickling process of erythrocytes, a common physiological sign of sickle cell disease [20]. Additionally, it has been asserted that erythrocytes from sickle cell anemia patient blood samples retained their normal shape by treating with the extract of Cajanus cajan seed [21]. As a result of its capacity to reduce hemolysis and prevent membrane deformability, aged garlic may be useful in sickle cell treatment. [22]. Adansonia digitata L (Bambacaceae), which has been claimed to be useful in the treatment of sickle cell anemia, did not function as an anti-sickling substance in vitro. The properties of these plants contribute to the ability to care for sickle cell disease patients [23].

TREATING SICKLE CELL DISEASE WITH BIOACTIVE COMPONENTS OF MEDICINAL PLANT:

The furanoditerpene component of Sphenocentrum jollyanun has been used to treat inflammation-related illnesses such as sickle cell [24]. A rearranged limonoid derived from Khaya senegalensis was discovered to be an antisickling agent. [25] Scoparia dulcis is rich in flavonoids and terpenes. By allosterically moving oxygen equilibrium curves to the left, the naturally occurring aldehyde 5-hydroxymethyl-2-furfural (5HMF) reduces red cell sickling. Green tea epigallocatechin gallate and Zanthoxyllum macrophyla 2-dihydroxy benzoic acid are two more helpful compounds [26]. The Nigerian Zanthoxylum has gotten a lot of interest [27]. Derivatives of dihydroxybenzoic acid, p-hydroxybenzoic acid, and 4-fluoro benzoic acid were the bioactive substances in charge of the anti-sickling characteristics. Low quantities of them were demonstrated to make them active, with the latter being the most active.[28]

ANTIOXIDANTS' FUNCTION:

In sickled erythrocytes, KCL-cotransport is thought to be activated as a result of oxidative cell damage [29]. Because sickle cell RBC are weak and loss of water makes it necessary to give minerals, antioxidants on a constant basis to maintain hydration and membrane integrity. As a result, the Micronutrients and antioxidant capabilities of numerous tropical plants have been studied. Scoparia Dulcis, aged garlic, and Picrorhiza kurroa have all been researched, as have M. charantia, Cymbropogon citratus, and Camellia sinensis [30].

CONCLUSION:

The most common blood disorder is Sickle cell anemia which affects a vast majority of the world's population, spanning nations and races. However, we can observe that the bioactive chemicals found in plants have a wide range of therapeutic actions that are used in traditional medicine and are mostly used as traditional healers for sickness treatment. Because most plants have medicinal properties, their efficacy in treating sickle cell anemia must be exploited. Males are also more affected by the illness because the implicated gene is dominant and very expressive. Females are typically carriers because the condition is recessive and does not show symptoms.

REFERENCES:

1. Evans, WC. Trease and Evans. Pharmacognosy 15th ed. W.B Saunders, Edinburgh; 585pp, 2002.
2. Roopen, A; Paul E. R; Raymond W: Tucaresol increases oxygen affinity and reduces hemolysis in subjects with sickle cell anemia. British.J. of Hematology.1996; 93: 817 – 821
3. Mou Sun P; Wilburn W; Denise Raynor B; Jamieson D. Sickle cell in pregnancy: Am.J. Obstet Gynecol.2001; 184(6):1127-1130.
4. Sumner J. The natural History of Medicinal Plants. 1st ed. Timber Press. Portland; 235pp, 2000.
5. Elujoba AA, Odeleye OM, Ogunyemi CM. Traditional medicine development for medical and dental primary health care delivery system in Africa. African Journal. Traditional, Complementary and Alternative Medicines 2005; 2(1): 46-61.
6. Ryan K, Bain BJ, Worthington D, et al. Significant hemoglobinopathies: guidelines for screening and diagnosis. Br J Haematol 2010; 149: 35–49.
7. Rees DC, Williams TN, Gladwin MT. Sickle-cell disease. Lancet 2010; 376: 2018–31.
8. Ataga KI, Moore CG, Hillery CA, et al. Coagulation activation and inflammation in sickle cell disease-associated pulmonary hypertension. Haematologica 2008; 93:20–6.
9. Kato GJ, McGowan V, Machado RF, et al. Lactate dehydrogenase as a biomarker of hemolysis-associated nitric oxide resistance, priapism, leg ulceration, pulmonary hypertension, and death in patients with sickle cell disease. Blood 2006; 107:2279–85.
10. Gladwin MT, Sachdev V, Jison ML, et al. Pulmonary hypertension as a risk factor for death in patients with sickle cell disease. N Engl J Med 2004; 350:886–95.
11. Kato GJ, Hsieh M, Machado R, et al. Cerebrovascular disease associated with sickle cell pulmonary hypertension. Am J Hematol 2006; 81:503–10.
12. Sun K, Xia Y. New insights into sickle cell disease: a disease of hypoxia. Curr Opin Hematol 2013; 20:215–21.
13. Ballas SK, Gupta K, Adams-Graves P. Sickle cell pain: a critical reappraisal. Blood 2012; 120:3647–56.
14. Hillery CA, Kerstein PC, Vilceanu D, et al. Transient receptor potential vanilloid 1 mediates pain in mice with severe sickle cell disease. Blood 2011; 118:3376–83.
15. Hassell K. Hematology/Oncology clinics in North America .2005; 19(5): 903- 916
16. Adebanjo AO, Adewunmi CO, Essien EE. Anti-infective agents of higher plants. 5th International Symposium in Medicinal Plants, University of Ife (OAU), Nigeria, 1983; 152-158.
17. Goldberg, A.M; Brugnara, C; Dover J. l: Hydroxyurea and erythropoietin therapy in sickle cell anemia. Seminars in Oncology.1992;19 (3): 74 – 81.
18. Sofowora, A. Medicinal plants and traditional medicine in Africa. Spectrum Books, Ibadan; 289pp,1993
19. Herrick JB. Peculiar elongated and sickle-shaped red blood corpuscles in a case of severe anemia. Arch. Intern. Med. 1910; 6: 517 – 520.
20. Dapa D, Gil T. Sickle cell Disease in Africa. Current opinion in Hematology 2002; 9 (2):111-116
21. Svarch E, Vilorio P, Nordet I , Chesney A, Batista JF, Torres L, Gonzalez A, de la Torre E. Partial splenectomy in children with sickle cell disease and repeated episodes of splenic sequestration. Hemoglobin 1996; 20:393-400

22. Svarch E, Hernández P, Ballester JM. Sickle Cell Disease in Cuba. Institute de Hematologia e Inmunologia (IHI) La Habana, Cuba. 2001.
23. Bianchi N, Zuccato C, Lampronti I, Borgatti M, Gambari R. Fetal Hemoglobin Inducers from the Natural World: A Novel Approach for Identification of Drugs for the Treatment of β-Thalassemia and Sickle-Cell Anemia.2007,
24. Mack AK, Kato GJ. Sickle cell disease and Nitric oxide: A paradigm shift Internat J. Biochem and Cell Biol.2006; 38(8):1237-1243.
25. Okochi, V.I, Okpuzor, J, Alli, L. A comparison of an African herbal formula with commercially available haematinics. African Journal of Biotechnology 2003; 2 (8) :237-240
26. Fleming, AF. Sickle-cell disease. A handbook for the general clinician. 1st ed church Livingstone Inc. New York. 145pp, 1982
27. Mgbemene CN, Ohiri FC. The anti-sickling potential of Terminalia catappa leaf extract. Pharmaceutical biology 1999; 37(2):152-154.
28. Orhue NEJ, Nwanze EAC, Okafor A. Serum total protein, albumin and globulin levels in Trypanosoma brucei infected rabbits: Effects of orally administered Scoparia Dulcis 2005. African Journal of Biotechnology. 4(10):1152-1155
29. Elekwa I, Monanu MO, Anosike EO Studies on the effect of aqueous extracts of Garcinia kola seed on the human erythrocyte's adenosine triphosphatase of HbAA, HbAS, and HbSS genotypes. Global J. Med Sci. 2003; 2(2). 107-114.
30. Okpuzor J, Adebesin O. Membrane stabilizing effect and antisickling activity of Senna podocarpa and Senna alata. 31st congress for European biochemical societies, Instanbul, Turkey, July 25-29, 2006.