



Herbal Medicine and Medicinal Herbs: Dominance in the Treatment of Sickle Cell Anaemia

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ABSTRACT

Sickle cell disease (SCD) is a genetic blood disorder impacting the shape and movement of red blood cells in the blood vessels, which leads to various health issues. Current drugs for SCD treatment often fall short in terms of effectiveness, safety, and affordability. Therefore, there's a growing need to explore indigenous plant-based remedies from traditional medicine. SCD affects millions globally, and due to limited progress in drug discovery, patients frequently turn to traditional Ayurvedic treatments utilizing plants and plants extracts. Complementary and alternative medicine (CAM) has gained global attention, particularly for chronic diseases like SCD. Sickle cell anaemia has been managed with natural products, including herbs and Ayurvedic medicines. Established treatments for SCA involve hydroxyurea, folic acid supplementation, but they can be expensive and pose certain risks. Research into medicinal plants with anti-sickling properties has shown promise, offering an alternative approach to reduce crises, reverse red blood cell sickling and improve the quality of life.[1] This paper discusses the substantial benefits of Phyto-medicine, nutraceuticals and ayurvedic herbs in managing SCD, with a focus on traditional Ayurvedic medicines.[2]

Keywords: Ayurvedic Medicines, herbal drug, Sickel Cell Anaemia, Haemoglobin.

INTRODUCTION: -

Red blood cells (RBCs) contain various components, with one of the crucial elements being Haemoglobin. Haemoglobin A (Hb A), the most common type, is made up of two alpha and two beta globin chains. These RBCs typically have a flexible, biconcave disk-like shape that allows them to smoothly navigate through small blood vessels, and they generally live for around 120 days. Their primary role is to transport oxygen throughout the body.

Sickle cell anaemia (SCA) is indeed a genetic haemoglobin disorder in which the sixth amino acid of the beta chain of haemoglobin, which is normally glutamic acid, is substituted by valine. This genetic mutation results in the formation of abnormal haemoglobin, known as haemoglobin S, leading to the characteristic sickle-shaped red blood cells. The disease is characterized by chronic homolytic anaemia, where the red blood cells are destroyed more rapidly than they can be produced.[3] Additionally, patients with SCA often experience fever, increased susceptibility to infections, and unpredictable painful crises. These crises occur due to Vaso-occlusion, where the sickle-shaped red blood cells become trapped in small blood vessels, leading to tissue damage and intense pain. Sickle cell anaemia is a lifelong condition that requires ongoing management and care.[4] In cases of low oxygen levels, haemoglobin S (HbS) forms polymers, resulting in the formation of rigid and distorted red blood cells known as "sickle cells." These abnormal cells can lead to issues like impaired microcirculation, haemolysis, and a reduced red blood cell lifespan. Sickle cell disease (SCD) exhibits various clinical symptoms, including pain, Vaso-occlusive crises, spleen enlargement, acute chest syndrome, aplastic anaemia, homolytic anaemia, and the risk of stroke.[5]

Sickle cell anaemia is a genetic disorder in which red blood cells lose their normal flexibility and become rigid and distorted, resembling sickles.[11] This altered shape impairs their ability to flow through narrow blood vessels, making them more vulnerable to osmotic lysis and decreasing their resistance to haemolysis. A red blood cell that is inflexible, deformed, and lacks elasticity can become delicate and susceptible to breaking under minimal stress.

This fragility is often observed in conditions like sickle cell anaemia.[6]

In sickle cell disease, the red blood cell membrane exhibits heightened ion permeability, leading to cellular dehydration primarily through processes such as Ca-activated K-efflux and K-Cl cotransport. This dehydration results in the formation of "dense cells," which have an elevated haemoglobin concentration (MCHC). This increased MCHC promotes haemoglobin polymerization and contributes to the characteristic sickling of red blood cells.

Traditional medicine, including herbal remedies, plays a significant role in public health in countries like India due to its widespread acceptance, cultural significance, affordability, and trust in traditional medicine practitioners.[7] This practice of traditional medicine is not limited to India but is spread worldwide. In industrialized countries, more than 50% of the population uses adaptations of traditional medicines, often referred to as complementary or alternative medicines (CAM). This demonstrates the global reach and influence of traditional and alternative medical practices in meeting the health needs of diverse populations.

Sickle cell disease (SCD) and thalassemia are genetic blood disorders that affect a significant portion of the global population. SCD causes abnormal red blood cells, leading to increased blood thickness, cell clumping, and various health issues, including pain, anaemia, and organ-related problems due to inadequate blood and oxygen supply. The body compensates by producing more red blood cells, resulting in characteristic physical changes associated with the disease. SCD crises can be triggered by stress and infections. Proper medical management and treatment are crucial for these conditions.[8]

The use of herbal remedies from medicinal plants has a long history across many cultures, commonly known as herbalism or botanical medicine. In light of the increasingly sophisticated lifestyles worldwide, it has become essential to consider herbal practices as alternative or complementary medicine, ensuring accessibility to people regardless of their cultural background. This approach to healthcare is gaining global recognition. Traditional medicine plays a vital role in treating and managing various diseases in regions like Africa, where the lack of basic healthcare infrastructure and medical personnel makes it challenging to provide medical care to rural populations.

RESULT AND DISCUSSIONS: -

Medicinal Plants and herbs	Medicine names	Results and Properties
Zanthoxylum zanthoxyloides (Lam.)	Niprisan	Hydro ethanol extracts of Facavr and Drepanostatvr showed low anti-sickling activity, inhibiting less than 10% of the sickling process
	Drepanostatvr	
	Facavr	
F. xanthoxyloides root	-	The amount of carboxylic acid present in an extract is used as an indication of the ant sickling potency. The report on quantitating the total acids in the ant sickling fraction of various Fagara species has provided a chemical index for evaluating the relative ant sickling activity of these species
Extractives from the seeds of Cajanus cajan plant	-	The extract containing a mixture of phenylalanine (0.69mg/ml) and p-hydroxybenzoic acid (10.5g/ml) showed effective sickling inhibition, comparable to the components found in bean extract.
Aged garlic extract (AGE)	-	The enormously stretched sickle-shaped cells are formed by the repeated deoxy cycling; the erythrocyte membrane becomes susceptible to oxidative injury by reactive oxygen species. The protection of the erythrocyte membrane from an oxidative injury would prevent the membranes from becoming leaky to the calcium ion, thus the activation of the calcium-activated potassium efflux channel and the formation of dense cells has been inhibited. And it also developed a new ex vivo method of studying the possible efficacy of antioxidants taken orally on the dense cell formation in sickle cell patients
The dried leaves of Calliandraportoricensis (Leguminosae), barks of Canariumschweinfurthii (Burseraceae) and roots of Uvariachamae (Annonaceae)	Hepacare	Hepacare is favourable in the prevention of CCl ₄ -induced hepatocellular injury, by scavenging reactive free radicals, and boosting endogenous antioxidant systems.
The extracts of the bark of trunk and branches of Ceiba pentandra		This study suggests that the aqueous extract of C. pentandra may contain active components that reduce the thrombin activity and prolong the plasma clotting time by affecting the coagulation intrinsic pathway.

Extract from the seeds of Piper guineense, the flower buds of Eugenia caryophyllata, the stem parts of Pterocarpus, the leaf stalk of Sorghum bicolor	NIPRISAN	Niprisan has started a Phase III clinical trial as there is sufficient safety and efficient data has been provided to USA FDA And also the US FDA Botanical Review Team (BRT) suggested a simpler formulation of Niprisan.
Extracts of the roots of a plant Cissus populnea.		It is concluded that there is justification for the use of this herbal formula in traditional medicine for the treatment of sickle cell anaemia patients.
Aqueous extracts of Cajanus leaf and seed, Zanthoxylum leaf, and Carica papaya leaf		The medicinal plant extracts were able to reduce the percentage of sickled cells, the rate of haemoglobin polymerization, and the osmotic fragility of human sickled RBCs.
Scoparia dulcis		In the management of Sickle cell disorders the ant sickling results confirmed traditional usage of Scoparia dulcis and also a candidate for further investigations.
Extracts from S. monostachyus, C. papaya seed oil and I. Involucrate		Extracts from S. monostachyus, C. papaya seed oil and I. involucrate exhibited particular anti sickling properties combined with the potential to reduce stress in sickle cell patients. Each plant individually or in combination may be useful for the management of sickle cell disease.
Dadima		antioxidant and antimicrobial activity, having pectin and fibre. polyphenols, flavonoids, anthocyanins, and punicalagins.
Sarpunkha		Hepatoprotective, antioxidants, immune modulator antipyretic, antihyperlipidemic (+)-tephorin B (+)-tephorosone 7,4-dihydroxy-3,5-dimethoxyisoflavone chang, rutin, purpurin, purpurenone, quercetin, retinoids, deguelin, elliptone, rotenone, sitosterol, and tephrosin. Sharapunkha is the best medicine to treat splenomegaly. Anti-epileptic activity, anticarcinogenic, anti hypercholesterolemic, anxiolytic activity, Diuretic activity, Anti diarrheal, Hepatoprotective activity
Punarnava		Beta ecdysone – increase protein synthesis, antistress, immunomodulation, antihyperglycemic, hepatoprotective, Ant sickling, antimicrobial, antioxidant, immunomodulator, anti-inflammatory, 15 amino acids, hypoxanthine-9-L-arabiofuranoside, boerhaviorol, boeravilanosteny benzoate, - cardiotonic, beta-ecdysone-increase protein synthesis, antistress and immunomodulation, hepatoprotective. it is useful in disorders of liver and haematological conditions. Anti-
		sickling, Antimicrobial, Antioxidant, Hepatoprotective, Immunomodulator, Anticancer, Antifibrinolytic, Anti-Inflammatory, Diuretic, Spasmolytic.
Vikantaka		phenolic glucoside, -2-(4,6 -dibenzoyl-beta-glucopyranosyloxy)-7-(1alpha-hydroxy-2alpha-ethoxy-6alpha-acetyloxy-3-oxocyclohex-4-enoyl)-benzyl alcohol (Flacourtacin), 2-(4,6-dibenzoyl-beta-glucopyranosyl)-5-hydroxy benzyl alcohol (4-benzoylpoliothryoside),

		(2E)-heptyl-3-(3,4-dihydroxyphenyl) acrylate (3), (+)-catechin (4) and sitosterol-beta-D-glucoside. anti-inflammatory, analgesic, antispasmodic, activity, antibacterial activity, antioxidant activity, Hepatoprotective, memory enhancer
Dhanayak		5–1% volatile oil, consisting mainly of delta-linalool (55–74%), alpha-pinene, and terpinene. It also contains flavonoids, coumarins, phthalides, and phenolic acids (including caffeic and chlorogenic).
Amalaki		ellagic acid, lupeol, oleanolic aldehyde etc. Bark: leucodelphinidin, procyanidin, tannin etc. Fruit: vitamin C, phyllembin, linolic acid, indole acetic acid, ellagic acid, phyllemblic acid Spasmolytic, mild CNS depressant, hypolipidaemic, antiatherosclerotic, antimutagenic, antimicrobial, antioxidant, immunomodulatory, antifungal, antitumor, hypoglycaemic, anti-inflammatory, antibacterial, antiulcer, adrenergic potentiating, HIV-1 reverse transcriptase inhibitory action. - Drug interaction- <i>Emblica Officinalis</i> may help to enhance absorption of iron salts due to its high contents of Vitamin C
Bhumi amalaka		lignans, flavonoids, glycosides, alkaloids, ellagitans, phenylpropanoids, gernanin, amaritin and corilagin. It also contains kaempferol, niranthin components derived from the leaves. This drug is useful in diseases which cause debility like <i>Rakta pitta Kshaya</i> etc. It has an action on <i>Raktadhatu</i> and <i>Pittadosha</i> Anti-anaemic, Hepatoprotective, Antioxidant, Anti spasmodic pain reliver, anti-inflammatory, Hepatoprotective, antioxidant, Anti-oxidant, immune modulator, Anti-viral (hepatitis B), Lipid lowering activity, Anti-microbial activity, Anti-malarial, Anti-ulcer.
Guduchi		alkaloids, diterpenoid lactones, glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds and polysaccharides. <i>Guduchi</i> possess properties like <i>Rasayan</i> (Immuno-modulator) <i>Balya</i> (tonic), <i>Agni Deepana</i> , and pacifies all the three dosha. Also, it is useful in conditions like Pain (indicated in <i>Vata rakta</i> where <i>Parvasandhi shoola</i> is a cardinal symptom), Jaundice and Anaemia which are the three main symptoms of Sickle cell Disease. It is Immunomodulatory, anti-inflammatory, antioxidant. Benefits: <i>Guduchi</i> reducing the frequency of infections and inflammatory episodes in SCA patients, thereby improving their quality of life. Antioxidant, Haematinic, Antipyretic Digestive, Analgesic, Appetizer, Antistress, Antimicrobial Antiendotoxic
Jivanti		tannin, terpinod/sterols, alkaloids, saponins, flavonoids, carbohydrates, and glycosides
Satavari		steroidal saponins, mucilage, and alkaloids.
Jaiphal		macelignan, carvacrol, myristicin, β - caryophyllene, β -pinene, α -pinene, p-cymene, and eugenol.
Shunthi		Shogaols, Paradols, Gingerdiols, Gingerdiacetates, Gingerdiones, 6-gingersulfonic acid, Gingerenones and a number of Diarylheptanoids, Diterpenes, Gingerglycolipids A, B & C.

Chitraka		Chitranone, plumhagin, 3-chlorplumbagin, zeylanone & zeylinone, isozeylinone, plumbagic acid, plubazeylanone Antihelmenthic, digestive, carminative, chronic intermittent fever, inflammation, hepato-splenomegaly, rejuvenating, anemias, piles .
Bringhraj		This drug is having properties like Rasayana, Balya, Shothahara and indicated in Pandu which is the common and cardinal symptom of SCD.
Gorakh mundi		Spaeranthine, sphaeranthanolid, sesquiterpenoids, Eudesmanoids, methyl chavicol, d-cadinene, α -ionone, p-methoxycinnamaldehyde, α terpinene, citral, geraniol, geranyl acetate, β -ionone, oscimene, eugenol, sphaeranthene, sphaeranthol, estragole, Indicusene. Hepatoprotective, Anti-inflammatory, Analgesic, antipyretic, Anxiolytic, Neuroleptic, Sedative, Immunomodulatory, Antioxidant,
		mast cell stabilization, Antimicrobial, Anti- fungal, Antiviral.
Ikshu		chlorogenic acid, cinnamic acid, flavones, hydroxycinnamic acid, sinapic acid, caffeic acid, apigenin, luteolin, triclin. Anti-thrombotic activity, Analgesic activity, Anti-inflammatory effect, antihepatotoxic activity, antioxidant activity, cholesterol lowering properties.
Pippali		The fruit contain several aristolactams and dioxoaporphines, also contains the long chain isobutylamide, longamide, besides guineensine and the lignans, pluviatilol, methyl pulviatilol, sesamin and asarinine. Piperine is the major alkaloid of peppers. Piperine is anti-pyretic, hypotensive, CNS stimulant, exert significant protection against hepato toxicity, and enhanced bioavailability of hexobarbitol, phenytoin, propranolol and theophylline. N-isobutyl-deca- trans-2-4-dienamide, isolated from fruits, exhibited anti-tubercular property. Milk extract of fruit effectively reduced passive cutaneous anaphylaxis. The root powder exhibits anti-fertility activity.

CONCLUSION

We have attempted to provide an overview of the many Ayurvedic herbs used in the treatment of sickle cell anaemia in this paper. The target specificity of certain Ayurvedic plants, including garlic, Cabanus cujan plant, F. xanthoxyloides root, Khayasenegalenis, Cissus populnea, *dadima*, *Punarnava* and many more, should be investigated in relation to sickle cell anaemia.

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