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Plant extracts with antisickling propensities: a feasible succour towards sickle cell disease management- a mini review

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Abstract
Sickle cell disease (SCD) is known to be one of the diseases wrecking most parts of the globe without any discrimination of ethnic or racial standards. It is characterized by a variety of symptoms including, shortness of breath, heart palpitations, abdominal pains, aches and pains in the muscle. The crisis stage is characterized by severe pain in the head and whole body. In the stage of crises if the percentage of sickled erythrocytes can be some how lowered we can expect a great relief to the patient. This could also serve a major step to-words management of the SCD. Phytochemicals in the plant extracts have the therapeutic activity and is used in traditional practice by the traditional healers. Many plant extracts have been used to bring about reversal of the sickled erythrocytes *in vitro.* The present communication reviews the available literature reporting anti-sickling properties of a number of plants extracts on human blood samples.

Keywords: Sickle cell disease, Medicinal plants, Disease management

INTRODUCTION

Since the beginning of time plants have been recognized for their several lifesaving and therapeutic properties [1]. Lifestyle and eating habitsalterations among thepeople makes it vital to refer to herbal medicine as an alternative or complimentary therapeutic measure. Nearly 70% world population (mainly in the developing countries) rely entirely on such traditional medical therapies as their primary form of health care [2, 3]. Various herbs are also a part of socio-cultural and socio-economic heritage. Even in the present times rural populations turn to herbal medicine as the most preferred therapeutic source.

Phytochemicals in the plant extracts have the therapeutic activity and is used in traditional practice by the traditional healers. A substance found in medicinal plants, containing the healing property of plants [4] is known as the active principle. It differs from plant to plant and examples of active principles include: anthraquinones, flavonoids, glycosides, saponins, tannins etc. Plants also contain other compounds such as morphine, atropine, codeine, steroids, lactones and volatile oils, which possess medical values for the treatment of different diseases. In recent years, these active principles have been extracted and used in different forms such as infusions, syrups, concoctions, decoctions, infused oils, essential oils, ointments and creams [5, 6].Since most plants have medicinal properties, it is of utmost importance that their efficacy and toxicity risks are evaluated [1].

Sickle cell disease (SCD) is known to be one of the diseases wrecking most parts of the globewithout any discrimination of ethnic or racial standards.The initial record of the disease id from a medical studentwho complained of shortness of breath, heart palpitations, abdominal pains, aches and pains in the muscle. Theshape of the red blood cells was then used to describe his observations [7]. According to reports, Africa is believed to be the origin of sickle cell disease, and those afflicted with the disease are huge [8, 9]. The crisis part of the sickle cell patients is characterized by severe pain and breathlessness making it one of the most dreaded of all genetic diseases [8, 9, 10 & 11].

Sickle cell crises have been investigated in top priority by researchers all around the world in order to explore effective therapy towards solving the sickle cell disease problem. Consequent upon this, anti-sickling effects of different substances have been investigated. The potential of dried fish and shrimp extractsto inhibit polymerization of sickle cell haemoglobin (HbS), improve the iron status and lower the activity of lactate dehydrogenase (LDH) in the blood plasma. LDH is a sensitive indicator of haemolysis and its level in sickle cell blood determines the severity of crises [9]. Various chemicals such as Hydroxyurea and erythropoietin concoctions have been found to reduce LDH enzyme activity and bilirubin level in serum, with an increase in the level of foetal hemoglobin (HbF) [10, 11]. There have also been reports on effective management of SCD patients during pregnancy [12, 13].

In developing countries, medicinal plants have been used in the treatment of sickle cellcrises associated morbidiesamong the less privileged classes of the society. Traditional healers and local folks are known to possess knowledge of the traditional and healing properties of various herbs common to their locality. There is also an immense need to gather such knowledge from different geographical parts in order to compile all information in the form of a database which could be utilized by researchers all over the world.

Sickle Cell Disease

Sickle cell disease (SCD) is the result of the insertion of a glutamic acid with valine at the sixth position of the beta-globin chain of haemoglobin S (HbS) [14] with the possibility for various amino-acids to be get transposed simultaneously [15]. Sickle cell disease

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include those that produce protuberantmedicalexpressions as seen during sickle cell anaemia, sickle cell disease, sickle cell trait and an array of other related haemoglobinopathies[14, 15]. Pathophysiology of sickle cell anaemia, sickle cell disease, sickle cell trait and an array of other related haemoglobinopathies are now known to the scientific community. This in turn causes the deformation of the normal disc biconcave RBC [16]. Due to polymerization of the sickled cells, the red cell membrane loses its functional abilities which results in loss of potassium and water and a corresponding gain of sodium ion. Increased intracellular free calcium occurs during sickling [17], resulting in a loss of potassium with accompanying movements of chloride and water. Small blood vessels are blocked by the clumping of sickled erythrocytes, averting blood supply to various organs. The process of de-oxygenation in tissue capillaries causes damage to its endothelium, leading to exudation of plasma into the surrounding soft tissue. This is characteristic of the soft tissue swelling seen in most sickle cell disease patients [18].

The outermembrane of the erythrocytes possesses a compact identity which is preserved by the hydration and case of outer membrane de-hydration;it loses its identity and acquires the shape of a sickle. Nitric oxideis also believed to play a part in sickle cell disease. It was reported that it may be beneficial to SCD patients if endogenous nitrous oxideproduction is boosted, in turn, boosting the nitrous oxide response or loweringit demolition [19]. This is to prevent haemoglobin released as a result of haemolysis using the nitrous oxide and activating a flow of events that finally hinder blood supply.

Clinical Manifestations

Sickle cell disease has a variety of phenotypes which makes it quite confusing to make an diagnosis. Phenotypic expression is strikingly different among different patients [20]. Symptoms of sickle cell disease are assorted and wide-ranging and can be recognized into the following categories- a) Anaemia b) Pain consequences, andc) Organ failure. Choking of blood and injured organs results inthe experience of painful occurrences or “crises”. Sickle cell crises may be caused by blood vessel occlusion, triggered by membrane deformation [21]. SCD patients suffer from a variety of ailments which includes acute chest syndrome (ACS) which is one of the reasons for hospital admissions [22], stroke [23], and acute splenic sequestration [24-26]. Other clinical manifestations of this condition are hyposthenuria, priapism, vascular necrosis, proliferative retinopathy, aplastic crises, cholelithiasis, delayed growth and sexual maturation, chronic pulmonary disease and chronic nephropathy [27].However all these clinical features of the sickle cell disease do not appear until after the first sixth months of life, at which time most of the HbF has been replaced by HbS.

Plant Extracts used as Therapeutic Measures

Plant extracts are found to possess properties which prevent the erythrocytes from deforming and losing its integrity. In the treatment of SCD, it is required that one focuses on the ways of inhibiting sickle cell haemoglobin polymerisation, prevention or repair of red cell dehydration and interrupting the interaction of sickle cells with the endothelium[17, 28-31]. Lower drug response in SCD patients is also seen as a major factor which hinders in the discovery of an effective therapy [14]. Hydroxyurea is a known inhibitor of sickle cell polymerization and various drugs containing it has an ability to increase foetal haemoglobin concentration [32, 33].

Recent therapy focuses on the erythrocytic rehydration [33, 34]. Management of sickle cell disease (SCD) hence, involves substances which has an ability to rehydrate the erythrocytes and furthermore, preventing it from losing its shape. The anti-sickling properties of certain amino acids such as phenylalanine, alanine, lysine, arginine etc., have also been reported [35, 36].Many plant extracts were reported to lower the painful episodes and related complications of SCD[37-39].In another report, the importance of thiocyanate, hydroxyurea, and telluriteaspotentantisickling agents possessing immene potential to inhibit erythrocytic deformations.Blood transfusion is also used in the management of sickle cell disease and can help the process to a great extent [40&41]. One of the drawbacks of blood transfusion was it lowered the macrophage count in patients[42-45]. Phytochemicals found in extracts of*Piper guineensis*, *Pterocarpaosun*, *Eugenia caryophyllala* and*Sorghum bicolor*can serve as potential antisickling agents [46].*Pterocarpussantolinoides* and *Aloe vera*extracts werefound to be useful in crisis managementand extracts of Fagara*zanthoxylo ides* and *Terminalia catappa*extractswere reported to possess potential reversal properties [47-49], *Solariadulcis*[50-51] was also used in SCD management. They therefore, used *Trypanosome brucei* to investigate the effect of the plant on haematological and biochemical indices due to lack of animal models for assessing the effectiveness of the plant extract in sickle cell disease monitoring.The following plants were also found to possess potential antisickling properties - *Alchorneacordifolia, Afromomumalboviolace um, Annonasenegalensis, Cymbopogondensiflorus, Bridelia ferru ginea, Ceibapentandra, Morindalucida, Hymenocardiaacida, Coleus kilimandcharis, Dacryodesedulis, Caloncobawelwithsii*, *Vignaungui culata* and *Adansoniadigitata* L (Bambacacae) [52]. The root extracts of Zanthoxylum*macrophylla*was also reported to possess antisickling properties [53].

The potential of *Cajanus cajan*in the management of sickle cell anaemia was also reported [54, 55]. Likewise, garlicwas also suggested possessing the same properties [56, 57].

Potential of the fruits of *Carica papaya*for the sickle cell reversal was shown by [58, 59]. Furthermore, extracts from *Piperguineenses* seeds, *Pterocapusosum*stem, *Eugenia caryophyllum* fruit, and *Sorghum bicolor* leaves were found to possess properties for reversal of sickling of erythrocytes [14, 16].

Phytochemicals responsible for the Anti-sickling properties

Following reports on the antisickling potentials of plantextracts, efforts to identify the causative agent behind it was initiated. There ae an array of reports on the varios phytochemical constituents of different plant extracts. The plants*Cssuspopulnea* L., *Khayasenegalensis; Scopariadulcis;* was reported possessing anthraquinones, steroidal glycosides and cardiac glycosides along withalkaloids and tannins[58-65]

Among the role of various phytochemicals in the management of SCD the potential of various chemicals have been validated. Among the important ones are the divanilloylquinic acids and 2-dihyroxymethyl benzoic acid isolated and identified from *Fagara* [66, 67].The potential of garlic fermented extracts in the treatment and management of SCD was also demonstrated [68]. Phytohemicals such as thiocyanatewere also studied and reported it to possess potential antisickling properties [68-71].

Various plants were also found to possess an array of

phytochemicals responsible for the reversal of sickled erythrocytes. Some of them are M. *charantia;Cymbropogoncitratus*; *Camelliasinensis; Scopariadulcis;* and *Picrorhizakurroa*[72-78].

CURRENT STATUS OF RESEARCH IN THE FIELD

Works on the reversal of sickling activity has been done by – [1, 3-9, 10, 12, 13, 16-26, 28, 30-36, 38-44, 46-52, 56-63, 66-88 and 90-97]Apart from these works, there are no available reports on the antisickling properties of plant extracts in our country. Furthermore, there are absolutely no reports from Chhattisgarh or Central India. Hence, we see that the prospects of further research in this area in our country need to be assessed and promoted for the management of sickle cell anaemia.

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