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Review of herbal plant associated with anti-anemic property and mechanism of action

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Abstract

Anemia is a global public health problem affecting both developing and developed countries, it occurs at all stages of life but is more prevalent in pregnant women and young children. It is one of the commonest associations in patients of heart failure and has been shown to be associated with increased mortality in both acute and chronic heart failure. Conventional drugs (Vitamin B_{12}, Ferrous preparations) used in the management of anemia are either unaffordable or unavailable and may still have undesirable side effects (abdominal discomfort, dry mouth, nausea, constipation). While herbal medicines that are in use are cheap and are thought to be readily available and less toxic. The need for less expensive, and safe management options has stimulated a surge in continuous research towards the use of herbal medicine for the treatment of anaemia. Most of herbal resources used in anaemia management have not been scientifically validated for their claim, and there is paucity of literature on the phytochemial constituents and Mechanism of action. The goal of this review is to expound various plants used for the treatment of anaemia with their phytochemical properties and mechanisms of action in experimental animal models. Twenty one plant with antianaemic activity were thoroughly sought and their findings reviewed. This information will create a center of attention for scientists and consequently play a major role in future research and documentation of herbal resources in the treatment of anaemia. However, Scientists are therefore encouraged to isolate and characterize these medicinal plant.

Keywords: Herbal plant; Anaemia; Haematology; Phenylhydrazine; Antioxidant

1. Introduction

According to WHO anaemia is a condition that develops when blood lacks enough healthy RBC or haemoglobin. It is characterized by a decrease in Haemoglobin concentration (Hb), Red Blood Cells Count (RBC) and Packed Cell Volume (PCV) [1,2]. Anaemia could also be defined as a condition in which the number of red blood cells (RBCs) is insufficient to meet the body's physiologic needs. World Health Organization report Specific physiologic needs vary with a person's age, gender, altitude, smoking behavior, and different stages of pregnancy [3]. Based on the level of hemoglobin (Hb), (WHO) cut-off points for anaemia varies by age, sex, pregnancy status and altitude [3]. It affects people of all ages, although the people at greater risk are the elderly, young women of child-bearing age and the infants. Based on recommended hemoglobin concentrations thresholds (<10.5 g/dl in second trimester of pregnancy, <11 g/dl in first and third trimester of pregnancy, and under-5 children, <11.5 g/dl in pre-school children, <12 g/dl in adolescents, and non-pregnant women and <13 g/dl in men), the WHO estimates that 2 billion people are anemic [4]. There are over 400 types of anaemia, with haemolytic anaemia being the most frequent [5]. Haemoglobin is contained in red blood cells which are the most abundant visible components in the blood system. Reduced number of erythrocytes can cause anemia and lack of oxygen for body tissues [6]. Several studies have shown that hemolytic anemia is associated with

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oxidative stress within erythrocytes. Anaemia is a serious global public health problem that particularly affects young children and pregnant women. WHO estimates that 42% of children less than 5 years of age and 40% of pregnant women worldwide are anaemic [3].

Defining anemia in countries with a significant population living at high altitude is not a straightforward task. The Andes mountains are the world's longest mountain range and boast some of the highest peaks. Stretching over 4,500 miles, the Andes cover seven countries—Venezuela, Colombia, Ecuador, Peru, Bolivia, Chile, and Argentina. In Peru, e.g., 27.3% of children under five years old reside at 2500 meters. These inhabitants have responded to chronic hypoxic conditions with increased levels of hemoglobin. Thus, a correction formula has been implemented to more precisely assess hemoglobin levels for children residing at high altitude as compared with those living at sea level. Intended to establish an easy and unique way to diagnose anemia while avoiding the altitude variability factor, this correction factor has also been adopted by the Peruvian guidelines which follow the World Health Organization (WHO) standards. This correction factor has never been critically evaluated. It is surprising, since all prevention strategies and measures of success ultimately rely on this factor [7,8].

The use of herbal drugs in the treatment of anaemia is a common practice in many countries of Africa. These plants, which abound in the environment, enjoy wide acceptability by the population and serve as cheaper alternatives to orthodox medicines. In view of this, there is a need to search for plants with antianaemic properties and adequately document them, hence this review. The review therefore addresses the scientific identification of the plant including, the geographical location or cultural/ethno-medicinal use of the plant for anaemia (and other possible ethno-medicinal uses), as well the ascribed mechanism(s) of action of the plant are all presented in this review.

2. Pathophysiology of haemolytic anaemia

The spleen is the primary organ of RBC destruction. The red pulp of the spleen consists of a branching system of cords and venous sinuses. The primary function of this meshwork is phagocytosis, specifically the destruction of old or damaged RBCs. The spleen separates the RBCs from the plasma and temporarily retains them in the red pulp. Young and viable RBCs pass through the spleen rapidly, and defective and older RBCs are culled out and destroyed. Passage from cord to sinus is the ultimate test of size, shape, compliance, and stretch [9]. For example, aging RBCs are targeted for destruction through exposure of galactose moieties in the membrane. Rigid cells that cannot squeeze through, such as sickled cells, are caught in the interendothelial slits of the vascular meshwork. In pliant RBCs with rigid inclusions, such as malarial parasites, the inclusion may be pitted out.

2.1. Scientific proof and mechanism of action of medicinal plant possessing antianaemic effect of the extract are as follows;

2.1.1. Limonia acidissima

Limonia acidissima is the only species within the monotypic genus *Limonia*. It is native to the Indomalaya ecozone to Bangladesh, India, Pakistan, Sri Lanka, and in Indochinese eco-region east to Java and the Malesia eco-region. Common names for the species in English include wood-apple and elephant-apple [10]. The people from the Eastern part of Nigeria, Enugu people to be precise have its local name to be “Akpuru”. It is reputed for its medicinal properties. *Limonia acidissima* is a large tree growing to 9 metres (30 ft) tall, with rough, spiny bark. The leaves are pinnate, with 5-7 leaflets, each leaflet 25–35 mm long and 10–20 mm broad, with a citrus-scent when crushed [11]. The fruit is a berry 5–9 cm diameter, and may be sweet or sour. It has a very hard rind which can be difficult to crack open, and contains sticky brown pulp and small white seeds.

[12] reported: aqueous extract of *Limonia acidissima* leaves was administered to the rats for four (4) weeks period. In the groups treated with aqueous extract of *Limonia acidissima* at the doses of 100mg/kgbw, 200mg/kgbw and 300mg/kgbw, Hb, MCV,WBC and RBC were significantly ($p<0.05$) elevated in the first two weeks of the investigation, while a further significant ($p<0.05$) increase occurred in the fourth week in comparison to the Phenylhydrazine-induced anemic non- treated rats. *Limonia acidissima* plant derivative aggregates acquire extreme levels of antioxidant characteristics and also exposed wound healing actions through scavenging of these free radicals [13].

2.1.2. Tectona grandi

Teak is a tropical deciduous forest tree species. The species is a member of the family "Verbenaceae" order "Laminales". The natural distribution of teak is limited to the Southeast Asian region. The species occurs naturally only in the Indian Peninsular, Burma, Northern Thailand and Northwestern Laos along the northern Thai border [14]. It has a distribution range from the longitude of 73"E in India to 104" 30 in Thailand [15]. The northern boundary limit of teak is about 25"

30' N lat. in the Kachin State of Burma [14] and its southern boundary limit lies from 9"N lat. in India through 15"-16"N lat. In Burma to 16"30' lat. in Thailand [15]. *T. grandis* known commonly is reported to treat malaria, anaemia associated diseases. The leaves of *T. grandis* only or in association with *Jatropha curcas* and *Flacourtia flavenscens* are used as decoction to alleviate anaemia [16].

Oral administration of *T. grandis* extract at 1 g/kg/day and 2 g/kg/day, to the rats previously treated with Phenylhydrazine, increased the concentration of haemoglobin, red blood cells number, haematocrit and reticulocytes rate. Moreover, the extract of *T. grandis* enhanced the osmotic resistance of the red blood cells that confirm the important presence of young red blood cells [17]. The antioxidant activity of *T. grandis* Linn. with its crude ethanol extracts by H_2O_2 scavenging activity, DPPH and FRAP assay proved its potential [18]. Another study examined the antioxidant activity of *T. grandis* Linn. leaf extracts employed four in vitro assay systems, i.e., Total phenolic content, reducing power, Super oxide radical scavenging activity, inhibition of H_2O_2 induced erythrocyte haemolysis method. The plant reversed anaemia indices [19].

2.1.3. Piper betle

Piper betle (Family: Piperaceae) (Vedic name: saptasira) is one such widely growing tropical plant. Its leaves contain strong pungent and aromatic flavour. It is widely consumed as a post meal mouth freshener and is traditionally credited with wound healing and digestive and pancreatic lipase stimulant activities [20]. It relieves head ache, scanty or obstructed urination as diuretic, weakness of nerves, sore throat, anti-ulcer activity. It evaluated the anti-ulcer activity of hydro- alcoholic extract of *piper betle* (HEPB) in rats [21].

[22] Lavanya *et al*., opined that anaemic rats were orally treated with aqueous extract of *Piper betel* at doses of 250, 1000 & 2000 mg/kg/day. The aqueous extract significantly increased the RBC, Hb, Hematocrit levels which conclude that it exhibits anti-anaemic activity. This study revealed antianemic activity of aqueous extract of *Piper betle*, thus confirming the traditional use of this plant in anemia treatment. *Piper betle* extract act by preventing or repair the damage done to the cells by free radicals or highly reactive oxygen species [22].

2.1.4. Justicia Secunda

Justicia Secunda is an evergreen perennial plant with stems that sometimes become more or less woody, growing up to 90–200 cm tall. The plant comprises almost 250 genera, with 2500 species, and is harvested from the wild bush for local use as medicine. The plant species are widespread in tropical regions and are poorly represented in temperate regions. The leaf decoction of *J. Secunda* is used for the treatment of various ailments including anemia, fever, malaria, cough, and cold [23].

[24] Irinmwinuwa *et al*., reported the haemopoietic effects of *Justicia secunda* leaf ethanol, the ethanol leaf extract of *J. secunda* significantly increased the hematological parameters of mice compared to the positive and negative controls ($p<0.05$). However, the n-hexane, ethyl acetate, and n- butanol extracts showed hemopoietic effects ($p<0.001$) along with the ethanol extract and standard antianemic. In the same vein [25] Yamoah and his team also investigated the effect of extracts of *Justicia secunda* leaves on red blood cells (RBC) count and haemoglobin (Hb) concentration in adult Sprague-Dawley rats to establish haematinic activity. Rats administered with water extract exhibited significant increase ($P < 0.001$) in the number of RBCs and Hb concentration compared with the vehicle-treated PHZ-induced anaemic rats. Rats administered the methanol extract followed with significant increase ($P < 0.01$) in RBC counts and Hb concentration (<0.05). A possible mechanism of action of anthocyanins lies in their effect on RBC membrane stability. Indeed, pharmacological agents that enhance SS RBC re-hydration rate may be promising drugs for the effective management of SCD. Cell re-hydration can be evaluated by the osmotic fragility test [26].

2.1.5. Triticum aestivum

Unlike trees and herbaceous dicotyledons, grasses belong to a single family (Poaceae), of uncertain origin, perhaps the Middle East or Armenia. This annual grass forms either solitary or tufted leafy culms about 2 to 3 and a half inches tall. The culms are light green, erect, terete, glabrous, and sometimes glaucous. Along the length of each culm, alternate leaves grow. The leaf blades are 6–18 mm across and 5–12 inches long. The leaves appear bluish or grayish-green, glabrous, and sometimes glaucous. These blades are ascending, arching, or rather floppy. The bases of these blades often have rounded auricles with scar-like wavy margins. The open leaf sheaths have the same characteristics as the leaves. The ligules are short-membranous and are about 1–2 mm in length; meanwhile, the nodes are swollen and glabrous [27]. *Triticum aestivum* is mentioned in Ayurveda as a herbal system of medicine and described as an immune-modulator, antioxidant, astringent, laxative, diuretics, antibacteria, antiulcer, kidney diseases [27].

Experiment has it that *Triticum aestivum* grass in a rat model was used to increase blood indices. Anaemic rats were treated orally with butanolic extract of *Piper betel* leaves, *Triticum aestivum* grass and combination of these two extracts at the doses of 20mg/kg body weight/ day for 20 days. Haematological parameters such as RBCs, haemoglobin, HCT showed significant increase ($p<0.05$). The present study revealed that combination therapy showed high anti-anaemic potential followed by *Piper betel* leaves and *Triticum aestivum* grass respectively [28]. Chlorophyll content found in wheat grass act by can repairing damaged cells and inhibit the metabolic activity of carcinogens. The number of male leukocytes increased during sodium nitrite given in the form of chemicals and carcinogens for the body, so wheat grass chlorophyll was able to reduce the number of male mice leukocytes in anemic condition [29].

2.1.6. Beta vulgaris

B. vulgaris (also known as beet) is a plant belonging to the Amaranthaceae family (formerly placed in Cheno- podiaceae). It is distributed worldwide including subtropical and tropical countries in Africa and in Asia [30]. The leaf, leaf stalks, and roots of beet plants are edible and may grow to 0.5–0.75 meters. And is useful in the functioning of the nervous and immune systems and in hematopoiesis [31]**.** *B. vulgaris* has been used in folk medicine including; vasodilating, antihypertensive**,** anti-diabetic**,** hepatoprotective and anti-cancer [32-37].

Gheith and El-Mahmoudy provided laboratory evidence supporting the hematopoietic effect of *Beta vulgaris* (beet) leaf aqueous extract in phenylhydrazine-induced anemia model in albino rats. Beet leaf extract significantly restored the levels of red blood cells, white blood cells, hemoglobin, and hematocrit in dose- and time-dependent manners. Blood indices were significantly corrected. Erythropoietin level was maintained at higher levels. Erythrocytic membrane oxidation biomarker (malondialdehyde) level was significantly reduced compared to the anemic untreated group. The extract exhibited potent, concentration (4–512 mg/mL)- dependent antioxidant activity indicated by the 2,2-diphenyl-1-picryl-hydrazyl (DPPH) assay, with IC50 value of 37.91 mg/mL [38]. *Beta vulgaris* significantly acted by protecting against the oxidative effect on erythrocytic membranes [38].

2.1.7. Ficus exasperata and *Telfeira occidentalis*

Ficus exasperata Vahl (Moraceae) is an important medicinal plant with a wide geographical distribution in Africa particularly in Nigeria [35,36]. The leaves are oval, it has elliptic leaves with a very rough surface and are alternately arranged making them look like sand paper. *Ficus exasperata* (Vahl) is commonly known as sand paper tree ("Ewe Ipin") in Yoruba. Other various local names include; Anwerenwa (Igbo), Erepin (Yoruba), Kawusa (Nupe), Ameme (Edo) [39]. The leaf extract from *Ficu`s exasperata* is reported to have diverse uses such as treating hypertensive patients, coughs and heamorrhoid [40,41]. Numerous pharmacological actions such as lipid lowering, anti-diabetic and antifungal activities have been reported for *Ficus exasperata* [42], difficult child birth, bleeding and diarrhoea in traditional medicine has been reported [43]. *Telfairia occidentalis* known as fluted pumpkin occurs in the forest zone of West and Central Africa; they are found more in Benin, Nigeria and Cameroon [44]. It is a well-known vegetable all over Nigeria. It was found first in South-east Nigeria and was distributed by the Igbos', who have cultivated this crop for a very long time. It is possible that fluted pumpkin was originally wild throughout its current range, but that wild plants have been harvested to local extinction and are now replaced by cultivation forms [45-47]. *Telfairia occidentalis* has been used in the treatment of anaemia, chronic fatigue and diabetes [48-50].

[51] examined the haematinic potentials of the aqueous leaf extracts of *Ficus exasperata* (FEAE) and *Telfeira occidentalis* (TOAE) administered separately and to establish a possible synergistic interaction when administered concurrently to chloramphenicol-induced anaemic rats. Treatment was carried out once daily for 7 days after which the rats were bled for determination of PCV, Hb and WBC count. Results of the study thus showed that Chloramphenicol induced a significant decrease PVC and Hb indicating anaemia and also resulted to a significant increase in WBC count. Aqueous leaves extracts of *Ficus exasperata* and *Telfeira occidentalis* produced significant increase in PCV and Hb with a corresponding decrease in WBC after 7 days of oral administration to anaemic rats. The plant act by increased erythropoiesis.

2.1.8. Justicia. insularis.

Justicia insularis T. Andeson (family, Acanthaceae) is an herbaceous and perennial plant 30 - 75cm high with opposite ascending branches. Its leaves are simple, opposite, and the flower white, pink or purple [52]. It can be found in variety of habitats from moist forest to dry savannah region. *J. insularis* is cultivated in home gardens in west and central African, especially in Guinea, Sierra leone, Ghana, Togo, Benin, Nigeria, Cameroon and DR Congo [53]. They are edible leaves that are gathered from the wild for local use. The leaves are used traditionally in Edo State, South South, Nigeria to treat and prevent anaemia. In Akwa Ibom State, also in South South, Nigeria, the people uses the leaves to cook soup and it is

known there as isepe- akera. J. insularis is used as a laxative, to aid digestion and as weaning agent [54]. To induce ovarian steroidogenesis and folliculogenesis in female rats [55].

Akuodor et al., investigated the effect of oral administration of ethanol leaf extract of *Justicia insularis* in Phenylhydrazine induced anaemia in Wistar rats. Rats were orally treated with distilled water and ethanol extract of *Justicia insularis* at doses of 200 mg/kg, 400 mg/kg and 600 mg/kg respectively for three weeks. The haematological parameters including the red blood cell and white blood cells and their functional indices were investigated in anaemic treated rats compared with the control rats. Administration of the ethanol leaf extract of *J. insularis* daily for three weeks significantly increased the haematological parameters which conclude that it exhibits antianaemic activity [56].

2.1.9. Wrightia tinctoria

Wrightia tinctoria which is commonly known as "Mitha indrajao", belongs to the Apocynaceae family is widely found in central India, Burma, and Timor. Bark and seeds of *W. tinctoria* are used as anti-dysenteric, carminative, astringent, aphrodisiac and diuretic, and in flatulence, stomach pain, and bilious affection [57]. [58] revealed *W. tinctoria* bark was used to treat anaemic mice albino mice, haematological parameters; iron, total iron binding capacity (TIBC), and ferritin were measured. fraction of *W. tinctoria* (FWT). FWT 60 days treatment resulted in significant rise in RBC, WBC ($P < 0.05$), along with Hb and PCV ($P < 0.001$). FWT treatment showed significant decrease in MCV, iron and TIBC, and increase in MCHC and ferritin ($P< 0.001$) level. Furthermore FWT showed significant rise in RBC, Hb, and PCV and decrease in serum iron and ferritin level significantly ($P< 0.001$) FWT treatment on PHZ and butadione induced anemic rat showed slightly hypochromic RBCs with very few irregularly-shaped cells. The plant extract act by protecting the integrity of the erythrocyte membrane and by increasing its resistance to osmotic stress/lysis, and thus reducing membrane fragility [59].

2.1.10. Solanum nigrum

Solanum nigrum is a species in the *Solanum genus*, native to Eurasia and introduced in the America, Australia, and South Africa. The plant has a long history of medicinal usage, dating back to ancient Greece. Plant parts are used in traditional medicine. The juice of the plant is used on ulcers and other skin diseases. The fruits are used as a tonic, laxative, appetite stimulant, and for treating asthma and "excessive thirst." The plant *Solanum nigrum* (black night-shade) commonly known as kumbi in Hausa is a widely used plant in oriental medicine where it is considered to be antitumor, antioxidant, anti-inflammatory, hepatoprotective, diuretic, and antipyretic and anemia[60].

The effect of *Solanum nigrum* methanol leaf extract on phenyl hydrazine induced anemia in rats was investigated using an automatic counter. Methanol extract of *Solanum nigrum* was administered to the anaemic mice at 100, 200, 300 and 400 mg/kg/body weight to groups 4, 5, 6 and 7 for three weeks orally by gastric intubation. Result obtained revealed that oral administration of *S. nigrum* methanol leaf extract to rats previously treated with phenylhydrazine significantly ($p<0.05$) increased the packed cell volume, haemoglobin, red blood cells, mean corpuscular volume, mean capsulated haemoglobin, and platelets in a dose dependent manner but decreased the white blood cells, lymphocytes and neutrophils within three weeks [61]. *Solanum nigrum* act by preventing or repairing damage done to red cells by free radicals or highly reactive oxygen species.

2.1.11. Mangifera indica

Mangifera indica is a tender Fruits Seed Kernel (MITFSK) commonly known as mango, is a species of flowering plant in the family Anacardiaceae. It is a large fruit tree, capable of growing to a height of 30 metres (100 feet). There are two distinct genetic populations in modern mangoes – the "Indian type" and the "Southeast Asian type". It is a large green tree, valued mainly for its fruits, both green and ripe. Approximately 500 varieties have been reported in India. It can grow up to 15–30 metres (50–100 feet) tall with a similar crown width and a trunk circumference of more than 3.7 m (12 ft). The leaves are simple, shiny and dark green. Mango is one of the most popular of all tropical fruits. It has strong antioxidant, immunomodulation, cardiotonic, hypotensive, wound healing, antidegenerative and antidiabetic activities [62,63]. Various parts of plant are used as a dentrifrice, antiseptic, astringent, diaphoretic, stomachic, vermifuge, tonic, laxative and diuretic and to treat diarrhea, dysentery, anaemia, asthma, bronchitis, cough, hypertension, insomnia, rheumatism, toothache, leucorrhoea, haemorrhage and piles, abscesses, broken horn, rabid dog or jackal bite, tumour, snakebite, stings, datura poisoning, heat stroke, miscarriage, anthrax, blisters, wounds in the mouth, tympanitis, colic, diarrhea, glossitis, indigestion, bacillosis, bloody dysentery, liver disorders, excessive urination, tetanus and asthma [64-66].

[67] Oluwasegun et al., investigated the effects of aqueous extract of *M. indica* stem bark on iron deficiency anaemia and disaccharidases' activities in iron deficient rat. The aqueous extract were administered to weanling albino rats induced

with iron deficiency through diet. After four weeks of feeding the rats, the Packed Cell Volume, Haemoglobin concentration and Red Blood Cell count of the iron deficient rats were significantly reduced ($P<0.05$) compared to those of healthy rats fed with iron sufficient feed. These iron status indicators were significantly increased ($P<0.05$) in rats treated with the extract when compared with untreated rats. It act by oxidation, it has been shown to improve Fe2+/Fe3+ ratio, hence facilitating the conversion of met-hemoglobin to hemoglobin [68].

2.1.12. Lophira lanceolata

Lophira lanceolata is a tree of the tropical and sub- tropical regions. It is a common tree in Cameroun, Nigeria and Sudan. It often grows gregariously on fallow land at the edge of forests. It is a tree of 8 to 10 m tall, straight or twisted, with leaves alternate, clustered at the end of short straight branches, glabrous, bright and blade *oblong-lanceolate.* The bark surface is corky grey [69]. *Lophira lanceolata* is used in traditional medicine to treat several illnesses. The decoction of the fresh leaves is administered orally against headaches, dysentery, diarrhoea, cough, abdominal pains and cardiovascular diseases. It is also used on skin to cure wounds [69].

[70] sought the haematinic activity of the aqueous extract of *Lophira lanceolata* leaves using rat model of phenylhydrazine-induced anaemia. Red Blood Cell (RBC) count, Haemoglobin (Hb) concentration and Packed Cell Volume (PCV) were analysed as indices of anaemia, treatment with graded doses (200, 400 and 800 mg/kg) of the aqueous extract of *Lophira lanceolata* leaves produced a significant ($P<0.05$) increase in the RBC count, Hb concentration and PCV time- and dose- dependently.

2.1.13. Moringa oleifera

Moringa oleifera Lam plant species belonging the family of *Moringaceae* which contains about 13 species [71]. It is a tree that can reach 7 to 12 meters in height. This plant, native to India and Arabia, is widely cultivated in tropical and subtropical regions [72]. *Moringa oleifera* is used in traditional medicine for the treatment of metabolic, inflammatory, infectious, parasitic diseases, cancer and also for the purification of water [73,74].

[75] estimated the effect of *M. oleifera* leaves diets against anemia in Wistar rats. Three groups of six rats each were formed, and two régimes food P50% and P100% contained respectively 50% and 100% of sheet *Moringa oleifera* from day 2 (D2) until the end of the experiment to day 28 (D28). Diets made from leaves of *Moringa oleifera* (P50% and P100%) have significantly restored the red blood cell parameters changed by phenylhydrazine. In addition, P50% provided better values of erythrocyte parameters than P100%. This study revealed that these diets based on *Moringa oleifera* leaves has excellent therapeutic efficacy. The mode of action of the extract could be connected with binding to the erythrocyte membranes with subsequent alteration of the surface charges of the cells thereby preventing physical interaction with aggregating agents or promote dispersal by mutual repulsion of like charges, which are involved in the haemolysis of red blood cells [76].

2.1.14. Azadirachta indica

Azadirachta indica is commonly known as neem belongs to family Meliaceae and all parts of the tree have medicinal properties known since ancient times and have been extensively used in ayurveda. Studies have shown that neem possesses anti-inflammatory, antiarthritic, antipyretic, hypoglycemic, antiulcer, antifungal, antianemic, antibacterial, and antitumor activities [77-81].

2.1.15. Emblica officinalis

Emblica officinalis is commonly called as amla and it belongs to Euphorbiaceae. Amla fruits are acrid, cooling, refrigerant, astringent, diuretic and laxative. The fermented liquor prepared from fruits is used in jaundice, dyspepsia and cough [77].

[82] Vamsee *et al.,* reported *Azadirachta indica* (neem leaves) and its combination with *Emblica officinalis* (amla) were evaluated for their antianemic activity in phenylhydrazine induced anaemic animals. hematological parameters such as haemoglobin (Hb) concentration, RBC count and WBC count were estimated. Results showed that both *Azadirachta indica* leaves and its combination with *Emblica officinalis* fruit showed significant antianemic activity but compared to *Azadirachta indica* leaf extract alone, its combination with amla showed better activity. This synergistic action of plants may be due to increase in absorption of iron from neem leaves, due to vitamin C in amla fruit and this combination may be an alternative to synthetic iron therapy in anemia. *Azadirachta indica contains* Flavanoids and liminoids which are antioxidants that act by preventing the damage caused by ROS formed in phenylhydrazine treatment [82].

2.1.16. Solanum americanum, Pterocarpus santalinoides and Vitex doniana

Solanum americanum is a member of the *Solanaceae* family and is sometimes referred to as American black nightshade and glossy nightshade. Locally, it is known as Gautan kad or Gautan kaaj in Hausa, Oju ologbo in Yoruba, and Anya nwona in Igbo [83]. In some areas of northeastern Nigeria, the plant has been used to cure diarrhea and dysentery. *Pterocarpus santalinoides* belongs to the Fabacea family of legumes. The family *Leguminosae* includes the genus *Pterocarpus,* which is widespread across the tropics and subtropics. In the South Eastern region of Nigeria, "*Uturukpa*" (Ibo) leaves from the *Pterocarpus santalinoides* tree are used to make soup. Some tribes in Eastern and Southern Nigeria employ the leaf extracts as antibacterial agents, respiratory issues, convulsions, fever, and headaches, as has also been described for *Sansevieria trifasciata* [84]. *Vitex doniana* a member of the *Verbenaceae* family popularly known as the black plum. Southern Nigeria is home to "*Uchakiri*". It is the most common species of the genus and is helpful in the treatment of ailments since it is frequently found in savannah regions. In Nigeria, *V. doniana* is known by the Hausa, Fulani, Yoruba, and Igbo names "*dinyar," "ori nla," "uchakiri*," and "*galbihi*" [85].

[86] Umerah et al., assessed the effect of "*ewa", "uturukpa"* and "*uchakiri*" on iron status of rat. The results obtained were 2.67-3.52mg iron, 0.52-0.89mg copper, 1.56-7.43mg zinc, 2.42-120.70 mg calcium 10.16-39.10mg magnesium, and 68.80-90.40 mg potassium. The mean serum ferritin, haemoglobin, packed cell volume and RBC all increased gradually after consumption of leaves extract. *V. doniana, "ewa,"* and "*Uturukpa*" *(Pterocarpus santalinoides)* "*uturukpa*" increased their levels of hemoglobin. From day 7 to day 22, all of the rats fed the vegetable extract had significantly higher heamoglobin levels. The amount of red blood cells in the experimental groups increased significantly ($p < 0.05$) after the administration of the plant extracts of *V. doniana,* "ewa," and *Pterocarpus santalinoides*." Particularly in the rats that ingested "*ewa*" extract, a considerable rise in erythrocyte levels was seen. At day 22, the rats' levels of PCV were significantly higher. The above plant extracts contain anthraquinones that could act by stimulating the production of iron.

2.1.17. Glycyrrhiza glabra

Glycyrrhiza glabra from Fabales order, Fabaceae family. *G. glabra* is found in South Europe (Spain, Italy), Turkey, Iran, Iraq, Central Asia and the north-western part of China, while *G. uralensis* is found in Central Asia, Mongolia and north-western and north-eastern parts of China. *G. glabra* has been utilized in folk medicine as an antioxidant, anti-inflammatory, antispasmodic, antipyretic, antiparasitic, antibacterial, antifungal, and antiviral agent and for curing diarrhea, gastrointestinal ulcers, and infection [89-90].

Zangeneh et al., in his experiment, evaluated the anti-anemia potential of aqueous extract of *G. glabra* on Phenylhydrazine-induced anemic rats. Several doses of *G. glabra* significantly ($p \leq 0.05$) enhanced the reduced levels of high-density lipoprotein, total protein, albumin, white blood cell, platelet, red blood cell, hemoglobin, packed cell volume, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, interleukin 4, interleukin 5, interleukin 10, interleukin 13, and interferon alpha and decreased the increased levels of alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, gamma-glutamyltransferase, ferrous, ferritin, erythropoietin, cholesterol, low-density lipoprotein, triglyceride, total and conjugated bilirubin, urea, creatinine, interleukin 1, interleukin 6, interleukin 12, interleukin 18, interferon gamma, and tumor necrosis factor alpha, as compared to the untreated group, the obtained results revealed the anti-anemia potential of aqueous extract of *G. glabra.* [91]. Antioxidants can play the main role in the destruction of free radicals and toxic materials and maintenance of hemostasis because free radicals intervene with biological cell membrane such as red blood cells through peroxidation of unsaturated fatty acids and bring about pathological changes [91].

2.1.18. Jatropha tanjorensis

Jatropha tanjorensis Ellis & Saroja belong to the family of Euphorbiaceae, is a common weed of field crops, bush re-growth, road sides and disturbed places in the higher rainfall forest zones of West Africa. It is commonly called 'hospital too far', catholic vegetable, '*Iyana-Ipaja'* or '*lapalapa*' [92]. The leaf is a commonly consumed vegetable in many parts of Southern Nigeria. It is also popular as a natural remedy against diabetes in this region [93].

[94] Idu et al., evaluated the antianaemic, acute toxicity and proximate analysis of *J. tanjorensis*. There were also significant decrease in Packed Cell Volume in groups B, C and D by day 3 of the experiment and subsequent increase by day 14 of the experiment after treatment with aqueous suspension of *J. tanjorensis* leaves. Treatment with the plant sample significantly ($P<0.05$) improved the PCV, Hb, RBC, MCV and MCHC levels of the animals that were treated with phenylhydrazine in these groups and also significantly ($P<0.05$) reduced the WBC level by day 14 of the experiment bringing it back to acceptable normal value. The extract act as powerful antioxidants which prevent or repair damage

done to red cells by free radicals or highly reactive oxygen species. Thus, it appears that the presence of these antioxidants in the plant sample reverse the damaging effect of phenyl hydrazine.

Table 1 Herbal plants possessing anti-anaemic activity

Scientific name	Common name	Family name	Anaemia induction model	Mechanism of action	Reference
Limonia acidissima	Wood apple, elephant apple	*Rutaceae*	Phenylhydrazine	Antioxidant; through scavenging of free radicals	[12, 13]
Tecona grandi	Teak	*Verbenaceae*	Phenylhydrazine	_____	[18]
Piper betle	Saptasira	*Piperaceae*	Phenyhydrazine	Acts by anti-oxidation	[22]
Justicia secunda	St John's bush / blood root	*Acarthaceae*	Phenyhydrazine	RBC membrane stability and Cell re-hydration.	[24, 26]
Triticum aestivum	Bread wheat	*Poaceae*	Phenylhydrazine	act by can repairing damaged cells.	[28,29]
Beta Vulgaris	Beef	*Amaranthaceae*	Phenylhydrazine	Antioxidation	[38]
Ficus exasperata and telfeira occidentalis	Sand paper tree and fluted pumpkin	*Moraceae*	Chloramphenicol	The plant act by increased erythropoiesis	[51]
Justicia Insularis	T. Anderson	*Acanthaceae*	Phenylhydrazine	____	[56]
Writhia tinctoria	Mitha indrajao	*Apocynaceae*	Phenylhydrazine and Butadione	The plant extract act by protecting the integrity of the erythrocyte membrane	[58,59]
Solanum nigrum	Black night shade	*Solanaceae*	Phenylhydrazine	Act by preventing or repairing damage done to red cells by highly reactive oxygen species	[61]
Magnifera lndica	Mango	*Anacardiaceae*	Diet	It act by anti-oxidation,	[67,68]
Lophira lanceolata	Dwarf red iron wood	*Ochnaceae*	Phenylhydrazine	_____	[70]
Moringa oleifera	Drumstick tree	*Moringaceae*	Phenylhydrazine	It act by binding to the erythrocyte membranes	[75,76]
Azadirachta indica and emblica officinalis	Neem and Amla	*Meliaceae and euphorbiaceae*	Phenylhydrazine	Anti-oxidantion	[82]
Solanum americanum and vitex doniana	Glossy night shade and black plum	*Solanaceae and verbanaceae*	_____	The plant act by stimulating the production of iron	[86]
Glycyrrhiza glabra	Licorice and sweet wood	*Fubaceae*	Phenylhydrazine	Anti-oxidation	[91]

Jatropha tanjorensis	Hospital too far or catholic vegetable	*Euphorbiaceae*	Phenylhydrazine	Anti-oxidation	[94]

3. Conclusion

The increasing prevalence of worldwide anaemia and its complication are alarming to all and actionable alternative may include deployment of herbal plant. However, before their use, safety and curability in animal models should be scientifically justified. There is therefore the need to search for a better alternative than synthetic drug with diverse shortcomings. Medicinal plants harbor enormous secondary metabolites which are the mainstay of herbal therapy. In that case, it is imperative that Scientists should further investigate on the different herbs in order to validate haematinic activities.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to disclosed.

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