

Plant Extracts as Alternative Therapeutic Agents for Anaemia: A ReviewKm Sukh Wati¹, Mohd. Ehsan¹, A K Singh¹ and M K Nandi^{2*}¹Pharmacy Ayurveda, Faculty of Ayurveda, Institute of Medical Sciences, Rajiv Gandhi South Campus, Banaras Hindu University^{2*}Department of Medicinal Chemistry, Faculty of Ayurveda, Institute of Medical Sciences, Rajiv Gandhi South Campus, Banaras Hindu University**Abstract**

Anaemia, one of the most common blood nutrition deficiency affecting at all ages of people. In Ayurveda, according to Acharya Charak, sign and symptoms of anaemia has close resemblance to Pandu Roga as like paleness, weakness, Heart Tonic, Eye Inflammation etc. As WHO claims, Anaemia is a medical situation in which the amount of RBCs or Hb count is lower than the normal individual and it is estimated that over 40 percent of children below age five are anaemic. On the basis of reported data plant extracts have been proved to be effective alternative therapy for the management of anaemic conditions. Physicians mostly prescribe iron-rich diet and vitamin supplements for the treatment of anaemia. Iron supplements are easily available in markets, if consumed prolonged, it can cause severe problems like gastro intestinal problems, hepatic disorders and sometimes even cause cancer. Hence, scientists are looking for an alternative for these iron supplements for the management of anaemia. Plant extracts could play a great role against anaemia. In this study, extracts of 20 different plants as like- *Solanum nigrum*, *Terminalia chebula*, *Beta Vulgaris* etc. are discussed, which are experimentally proven to be effective in anaemia. Applications of these medicinal plants in anaemia is also mentioned in classical Ayurveda literature from ancient time. So, these plant extracts are may be an alternative therapy for the management of anaemia and this study could help researchers for research in anaemia and other related disorders.

Keywords: Anaemia, Haemoglobin, Pandu Roga, Iron Supplements*Corresponding author Email: manmathk.nandi1@bhu.ac.in

Introduction

According to World Health Organisation, Anaemia is a medical situation in which the amount of RBCs or Hb count is lower than the normal individual. Haemoglobin (Hb) is required to transport oxygen and if there were insufficient or unusual RBCs (red blood cells), or not sufficient Hb (haemoglobin), then the body tissues get reduced amount of oxygen. Hence the ability of circulatory system to transport oxygen get affected. This leads to biological symptoms like fatigue, paleness, giddiness and breath shortness etc. The ideal Hb count essential to meet the need of physiology differs by age, sex, altitude of house, pregnancy conditions and smoking habits and The most usual reasons of anaemia consists nutritional paucities, specifically iron insufficiency, though paucities in Vit-B₁₂, folate, and Vit- A are also significant causes for sickle cell anaemia, thalassemia's and many infectious diseases, like HIV, tuberculosis and malaria etc. Anaemia is a severe world-wide public health issue that predominantly affects young individuals and women who are pregnant. According to WHO estimations 42% children under 5-year age group are anaemic, one-third of reproductive age women are anaemic and 40 percent of all pregnant women throughout the world are anaemic. [1] One approach for Anaemia treatment is administration of iron supplements with oral iron supplements. The objective of iron supplementation is to increase the levels of iron and Hb in our body. Iron supplements can cause some adverse effects like Dark stools, Constipation, and Heartburn etc. [2] Overdosing of iron reported to cause gastro-Intestinal, cardiovascular, hepatic and CNS toxicity. This is because of a straight corrosive outcome of iron on the Gastro Intestinal mucosa and the toxicity of free unbounded iron in the blood flow. [3] Medicinal plants are reported to be a good source of help in the control of various severe diseases like anaemia in developing countries. [4] Many ayurvedic formulations, rich with medicinal plant extracts are commercially available and recommended for the management of anaemia. In this study 20 plants are thoroughly reviewed, which have been reported to be anti-anaemic in activity.

Material Methods

List of Medicinal plant extracts having potential to counter anaemia as proven by experimental model

S. No	Name of Plant Extract	Part Use	Dose	References
1.	<i>Moringa oleifera</i>	Leaf	200-300mg/kg b. w. (Rat)	[5]
2.	<i>Terminalia chebula</i>	Fruit	250-500mg/kg b. w. (Rat)	[6]
3.	<i>Beta Vulgaris</i>	Rhizome	100-400mg/kg b. w. (Rat)	[7]
4.	<i>Solanum nigrum</i>	Leaf	100-400mg/kg b. w. (Rat)	[8]
5.	<i>Theobroma cacao</i>	Stem bark	25, 50, 75mg/kg b. w. (Rat)	[9]
6.	<i>Hibiscus sabdariffa</i>	Seed	400mg/kg b. w. (Rat)	[10]
7.	<i>Brassica oleraceae</i> var <i>italica</i>	Flower	100-200 mg/kg b. w. (Rat)	[11]
8.	<i>Phyllanthus niruri</i> Linn	Whole Plant	250, 500, and 1000 mg/kg b. w. (Rat)	[12]
9.	<i>Gossypium hirsutum</i> L.	Leaf	100–400 mg/kg b. w. (Rat)	[13]
10.	<i>Justicia secunda</i>	Leaf	200mg/kg b.w. (Rat)	[14]
11.	<i>Falcaria vulgaris</i>	Leaf	25, 50, 100, and 200 mg/kg b. w. (Rat)	[15]
12.	<i>Amaranthus cruentus</i>	Leaf	200-400 mg/kg b. w. (Rat)	[16]
13.	<i>Acacia nilotica</i>	Leaf	100 mg/kg and 200 mg/kg b. w. (Rat)	[17]
14.	<i>Brillantasia nitens</i>	Leaf	400, 800, 1600, 3200 mg/kg b. w. (Rat)	[18]
15.	<i>Telfairia occidentalis</i>	Leaf	200mg/kg b. w. (Rat)	[19]

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16.	<i>Spinacia oleracea</i>	Leaf	100 mg/kg b. w. (Rat)	[20]
17.	<i>Sorghum bicolor</i>	Leaf	200-300 mg/kg b. w. (Rat)	[21]
18.	<i>Mangifera indica</i>	Stem Bark	25, 50, and 100 mg/kg b. w. (Rat)	[22]
19.	<i>Pterocarpus erinaceus</i>	Stem Bark	250 and 500 mg/kg	[23]
20.	<i>Lophira lanceolata</i>	Leaf	200, 400, and 800 mg/kg b. w. (Rat)	[24]

Moringa oleifera

Anslem O Ajugwo et al studied the extract of *Moringa oleifera* prepared from leaves of the plant by maceration process using water as a solvent to analyse the anti-anaemic potential of the plant extract. The obtained extract was used at 200, 300mg/kg dose for four weeks to analyse the anti-anaemic activity in Wistar albino rats, after inducing the anaemic condition in animals by injection of phenylhydrazine at 40 mg/kg b.w. dose for 2 days through intra-peritoneal route. This study reported that significant increase in RBC count (6.1 ± 0.66), Hb count (13.8 ± 1.12) and packed cell volume (38.8 ± 3.96 %) whereas reduction in level of WBC count (5.9 ± 1.08) in group of rats which was treated with dose 300mg/kg bodyweight as comparative to negative control group. [5]

Terminalia chebula

According to Kumari Babli et al the extract of *Terminalia chebula* prepared from dried fruits of the plant by soxhletion process and the distilled water was used as solvent. The obtained extract was used in acute toxicity study and no mortality was recorded up to 500mg/kg. The albino rat group which was treated with plant extract at dose of 250mg/kg reported increase in blood parameters like TLC (7.441 ± 0.11), eosinophil (3.293 ± 0.04), total RBC (4.383 ± 0.03), Hb (14.03 ± 0.02) when compared with positive control. [6]

Beta vulgaris

It was reported that the extract of *Beta vulgaris* prepared from rhizome of the plant by maceration process using ethanol as a solvent. The obtained extract was used to analyse the anti-anaemic activity in Wistar albino rats and induction of anaemia was done by injection of phenylhydrazine at 60 mg/kg dose bodyweight for 3 days through intra-peritoneal route and the anaemic rats were treated with rhizome extract of *Beta vulgaris* for 14 days with dose range of 100-400mg/kg. This study reported that significant increase in haematological parameter in anti-anaemia study as dose dependent manner like RBC count (9.45 ± 0.17), Hb count (17.32 ± 0.26), PCV (52.30 ± 0.96) when compared with both positive control and negative control group of rat. [7]

Solanum nigrum

Umaru H. Aduwamai et al studied and analyse the extract of *Solanum nigrum* prepared from leaves of the plant by maceration process using methanol as a solvent to analyse the anti-anaemic action in Wistar Albino rats. Induction of anaemia was induced by injection of 10 mg/kg phenylhydrazine for 8 days through intra-peritoneal route and the anaemic rats were treated with leaf extract of *Solanum nigrum* for 3 weeks with dose range of 100-400mg/kg. This study reported that an increase in HGB (14.26 ± 0.27 g/dl), RBC ($7.51 \pm 0.07 \times 10^6$), PCV ($65.60 \pm 1.03\%$), MCH (31.24 ± 0.71 g/dl), MCV (79.40 ± 0.66 fl) and PLT ($481.60 \pm 3.11 \times 10^9$) values were recorded in a dose dependent mode when comparison was done with to negative control group. The most effective dose was recorded to be 400mg/kg for anti-anaemic action of *Solanum nigrum* extract. [8]

Theobroma cacao

O. Modupe et al reported that the extract of *Theobroma cacao* prepared from leaves of the plant by method described by Oldiji [30]. The obtained extract was used for anti-anaemic activity in weanling albino rats of both sexes and by giving iron deficient diet for 4 weeks anaemia was induced and the anaemic rats were treated with leaf extract of *Theobroma cacao* for 4 weeks with dose range of 25, 50, 75mg/kg. This study reported that significantly increased in RBC (5×10^6 cells/mm³), PCV (36%), Hb (11g/dl) in the extract dosing group as compared to IDD (iron diet deficient) group and the effective dose of *Theobroma cacao* for anti-anaemic potential was 25mg/kg. [9]

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Hibiscus sabdariffa

This study, reported that the extract of *Hibiscus sabdariffa* was prepared from seeds of the plant by maceration process using distilled water as a solvent. The obtained extract was used to study and analyse the anti-anaemic activity in Wistar albino rats and anaemia was induced by bleeding off 5-7 ml from each rat which is 30 % of their blood volume through the orbital plexus. The anaemic rats were treated with 400mg/kg seed extract of *Hibiscus sabdariffa* for 4 weeks. This study reported significant increase in the level of haematological parameters like PCV (43 ± 2.13 %), Hb (13.76 ± 0.82 g/dl) and RBC count ($6.9 \pm 0.26 \times 10^6/\mu\text{L}$) as compared to control bled group. [10]

Brassica oleraceae var italica

Avula et al studied the extract of *Brassica oleraceae var italica* inflorescence was used in study for anti-anaemic activity in Sprague Dawley rats and induction of anaemia was done by injection of 60 mg/kg phenylhydrazine for 2 days through intra-peritoneal route and the anaemic rats were treated inflorescence extract of *Brassica oleraceae var italica* with dose range of 100, 200mg/kg for 14 days. This study reported that increment in level of haematological parameters like Hb (14.35 ± 0.27 g/dl), RBC (6.06 ± 0.13) and reduction in WBC (7.050 ± 0.18). *Brassica oleraceae var italica* extract at 200mg/kg dose found to be similar effective as standard drug. [11]

***Phyllanthus niruri* Linn.**

Muhammad et al reported that the extract of *Phyllanthus niruri* Linn. prepared from whole plant by maceration process using a distilled water as a solvent. The obtained extract was used for anti-anaemic activity in Wistar albino rats and induction of anaemia was done by oral intake of 2,4-DNPH (20 mg/kg b.wt) for 7 days once daily. The anaemic rats were treated with *Phyllanthus niruri* extract at dose range of 250, 500 & 1000mg/kg for 14days. This study reported that dose dependent increment in haematological parameters like Hb (11.31 ± 0.28 g/dl), RBC ($5.33 \pm 0.10 \times 10^6/\mu\text{L}$), reduction in WBC ($11.81 \pm 0.32 \times 10^3/\mu\text{L}$) and study reported that plant extract at 1000mg/kg plant extract showed similar efficacy as standard drug folic acid (75µg/kg). [12]

***Gossypium hirsutum* L.**

Midala et al studied and analysed the extract of *Gossypium hirsutum* L. prepared from leaves of the plant by maceration process using ethanol as a solvent. The obtained extract was used for anti-anaemic activity in Wistar albino rats. Induction of anaemia was done by intra-peritoneal injection of phenylhydrazine for 2 days and the anaemic rats were treated with leaf extract of *Gossypium hirsutum* L. for 4 weeks at dose range of 100, 200, 300, 400mg/kg. This study reported that significant increase in PCV (64.30 ± 0.45 %), Hb (16.43 ± 0.14 g/dL), RBC ($7.00 \pm 0.02 \times 10^6/\mu\text{L}$), PLT ($766.67 \pm 0.88 \text{mm}^3$), decrease in WBC ($19.25 \pm 0.14 \times 10^3/\mu\text{L}$) at a dose of 400mg/kg plant extract and the plant extract at 400mg/kg proved to be more effective to counter anaemia symptoms over the animals feed with standard diet. The Study is reported that up to dose of 5000mg/kg is safe for rats. The study reported that the plant extract of *Gossypium hirsutum* L. is also effective in protection against liver damage induced by phenylhydrazine. [13]

***Justicia secunda* Vahl.**

Ahimsa Yamoah et al reported that *Justicia secunda* Vahl extract prepared from leaves of the plant by maceration process using methanol and ethyl acetate as solvent system. In this study three extracts have been reported to be used i.e. water extract, methanol extract and ethyl acetate extract. The obtained extracts were used for the study of haematinic activity in Sprague Dawley rats. Induction of anaemia was done by injecting phenylhydrazine at dose of 20 mg/kg bodyweight for 3 days through intra-peritoneal route and the anaemic rats were treated with 200mg/kg aqueous leaf extract, methanolic leaf extract and ethyl acetate leaf extract of *Justicia secunda* Vahl. for 18 days. This study reported that significant increase in mean Hb (219.6) mean RBC (142.8) in group of rats which were treated with aqueous extract at a dose of 200mg/kg bodyweight as compared to negative group, methanolic extract treated, ethyl acetate extract treated group. [14]

Falcaria vulgaris

It was reported that the extract of *Falcaria vulgaris* prepared from leaves of the plant by soxhletion process using distilled water as a solvent. The obtained extract was used for anti-anemic activity in Wistar

albino rats. Anaemia was induced by injecting phenylhydrazine intra-venous at 20 mg/kg bodyweight for 5 days and the anaemic rats were cured with leaf extract of *Falcaria vulgaris* for 15 days in dose range 25, 50, 100, 200mg/kg. This study reported that significant surge in biochemical parameters like PLT, RBC, MCV and reduction hepatic parameters in group of rats which were treated with dose 200mg/kg body-weight as compared to negative group.[15]

Amaranthus cruentus

Pandey et al studied and reported that the extract of *Amaranthus cruentus* prepared from leaves of the plant by maceration process using ethanol as solvent. The obtained extract was used for anti-anaemic activity in Wistar albino rats and induction of anaemia was done by injecting phenylhydrazine at dose 60 mg/kg bodyweight for 3 days through intra-peritoneal route and the anaemic rats were cured with leaf extract of *Amaranthus cruentus* for 4 weeks with dose range of 200, 400mg/kg. This study stated that the plant extract significantly counter the anaemic parameters in experimental animals. [16]

Acacia nilotica

This study reported that the extract of *Acacia nilotica* obtained from leaves of the plant by soxhletion process using ethanol as a solvent. The plant extract was used for anti-anaemic activity in adult albino rats and anaemia was induced by injection of phenylhydrazine (PHZ) dissolved in olive oil in the ratio 1ml: 14ml, through the peritoneal route. The anaemic rats were treated with leaf extract of *Acacia nilotica* for 2 weeks in dose range of 100, 200mg/kg. This study reported that significant surge in haematological parameters like RBC ($6.98 \times 10^{12}/l$), Hb (14.85g/dl) PLT ($539 \times 10^9/l$) and reduction in WBC ($13.49 \times 10^9/l$) by treating the animal with 200mg/kg dose, when comparison was done with negative control group of rats. [17]

Brilliantasia nitens

Akah et al studied and analysed the extract of *Brilliantasia nitens* prepared from leaves of the plant by maceration process using methanol as a solvent. The obtained extract was used for anti-anaemic activity in albino rats and induction of anaemia was done by injecting phenylhydrazine at 10mg/kg for 8 days through intra-peritoneal route of drug administration. The anaemic rats were treated with leaf extract of *Brilliantasia nitens* for 4 weeks through oral dose of 400, 800, 1600, 3200mg/kg. The haematological parameters were measured and reported that increase in level of PCV (60%), RBC ($8 \times 10^6/mm^3$) and HB conc. (18) etc. in rats which were treated with dose 800mg/kg, as compared to other group of rats. [18]

Telfairia occidentalis

According to Oladele et al the extract of *Telfairia occidentalis* prepared from leaves of the plant by soxhletion process using 90% ethanol as a solvent. The obtained extract was used for anti-anaemic activity in Wistar albino rats. Induction of anaemia was done by injecting phenylhydrazine 20 mg/kg bodyweight for 2 weeks through intra-peritoneal route and the anaemic rats were treated with leaf extract of *Telfairia occidentalis* for 2 weeks at 200mg/kg. This study reported that significant increase in PCV (27%), RBC (3.87 ± 0.38) and PLT (457.59 ± 38.50) when compared with negative control group. [19]

Spinacia oleracea

It was reported that the extract of *Spinacia oleracea* prepared from leaves of the plant by maceration in distilled water for 48 hours. Then filtrate was dried. The obtained extract was used for anti-anaemic activity in Wistar albino rats and induction of anaemia was done by injecting phenylhydrazine 60 mg/kg bodyweight for two-days intra-peritoneal route and the anaemic rats were treated with 100mg/Kg leaf extract of *Spinacia oleracea* for 4 weeks. This study reported that significant increase in haematological indices in group of rats which was treated with extract dose 100mg/kg body weight. [20]

Sorghum bicolor

According to Luka et al the extract of *Sorghum bicolor* prepared from leaves of the plant by maceration process using water as a solvent. The obtained extract was used for anti-anaemic activity in Wistar albino rats. Induction of anaemia was done by injecting phenylhydrazine 40 mg / kg bodyweight for two days through intra-peritoneal route and the anaemic rats were treated with leaf extract of *Sorghum bicolor* at dose range of 200-300mg/kg for 4 weeks. This study reported that significant dose dependent

increase in haematological parameter like PCV ($36.00 \pm 1.80\%$), Hb ($12.70 \pm 0.24\text{g/dl}$) and RBC ($4.15 \pm 0.05 \times 10^6/\mu\text{l}$) when compared to negative control group. [21]

Mangifera indica

It was reported that the *Mangifera indica* stem bark extract prepared from the plant by decoction method by using water as a solvent. The obtained extract was used for anti-anaemic activity in Wistar albino rats. Induction of anaemia was done by oral intake of 2, 4-DNPH at 20mg/kg bodyweight for 7 days and the anaemic rats were treated with leaf extract of *Mangifera indica* for two weeks, with 50, 100mg/kg p.o dose. This study reported that significant increase in Hb (12g/dl) and PCV (35%) in group getting treatment with 100mg/kg leaf extract. Hence it 100mg/kg dose is experimentally proven dose for treatment of anaemia with leaf extract of *Mangifera indica*. [22]

Pterocarpus erinaceus

Nadro et al studied and analysed that the *Pterocarpus erinaceus* extract prepared from leaves of the plant by maceration process by using distilled water as solvent. The obtained extract was used for anti-anaemic activity in Wistar albino rats. Anaemia was induced by single sub-cutaneous injecting phenylhydrazine at 80mg/kg and the anaemic rats were cured with dose of $250\text{--}500\text{mg/kg}$ leaf extract of *Pterocarpus erinaceus* for 2 weeks. This study reported that significant increase in RBC (6.17 ± 0.08), Hb (13.57 ± 0.13), PCV ($54.66 \pm 0.16\%$) and reduction of WBC (8.34 ± 0.16) in 250mg/kg extract treated group. Hence it is proved that 250mg/kg dose is more effective than 500mg/kg leaf extract of *Pterocarpus erinaceus*. [23]

Lophira lanceolata

Osafanme et al reported that the extract of *Lophira lanceolata* prepared from leaves of the plant by maceration process by using distilled water as a solvent. The obtained extract was used for acute toxicity study and up to 5000mg/kg no toxicity was recorded. The anti-anaemic activity was studied in Wistar albino rats by inducing anaemia by oral incubation of 10mg/kg phenylhydrazine for eight days. The anaemic rats were cured with leaf extract of *Lophira lanceolata* for 3 weeks at dose range of 200, 400, 800mg/Kg . This study reported that major increase in Hb ($12.16 \pm 1.13\text{g/dl}$), RBC ($3.67 \pm 0.42 \times 10^6/\mu\text{l}$) and PCV ($44.21 \pm 1.32\%$) in group which was treated with extract dose at 200mg/kg . Hence it was 200mg/kg dose proved to be effective dose for treatment of anaemia by leaf extract of *Lophira lanceolata*. [24]

Discussion

Anaemia is condition develop in an individual mostly due to abnormal quantity of red blood cell. The lack of sufficient red blood cell and abnormality in other haematological parameters, leads to development of various biological symptoms like laziness, difficulty in breathing, weakness, eye Inflammation and paleness etc. In Ayurveda, Acharya Charak, described similar sign and symptoms of anaemia science ancient time under the disease as pandu rog (due to deficit of two main blood components i. e. RBC and its iron carrying pigment -haemoglobin). [25] The early diagnosis and regular medication for a period of time is necessary to counter anaemia is necessary; otherwise it may be fatal for the patient. India, one of the leading country in South-Asian continent with respect to occurrence of anaemia. Some of the common modern medication recommended for the treatment of anaemia are like ferrous ammonium citrate, carbonyl iron [26], ferrous fumarate [27], ferumoxylol, L-methylfolate, and cyanocobalamin [28] etc., but long term use of these medication is harmful to human being. So, alternative medicines designed from medicinal plant parts or its extracts are now preferable by physicians for the treatment of anaemia in long term treatment. Some of commercially available polyherbal formulations for the treatment of pandu roga are as punarnavadi mandura [29], tapyadi lauh [30], laghumalini vasanta [31] and darvyadi lauha [32] etc. In this review, we have investigated about 20 plant extracts which have been reported for its anti-anaemic activity on different strains of Rat. From the reported data, we have observed that some plant extract act on the body physiology in dose dependent manner, as the dose get increased their results get improved and some have effectiveness at moderate dose. This study also revealed about various approaches to induced anaemia as like phenylhydrazine induced anaemia, haemorrhage induced and some for diet deficient induced anaemia. It is observed that treatment of anaemia by improving/enriching the nutrient diet with plant extract or synergizing plant extract treatment with nutrient rich diet showed better results.

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Conclusion

In this review we concluded that all the 20 Plant Extracts used for anti-anaemic study were found to be effective to improve the decreased haematological parameters in Rats. It seems that the plant extracts with minimal dose could be a good alternative for anaemia remedy. These plant extracts should be tried in clinical trials and requires more advance research.

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