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EXPLORATIVE HEMATINIC POTENTIAL OF MEDICINAL PLANTS: A COMPHRENSIVE REVIEW

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Abstract

Anaemia is a prevalent malnutrition-related illness that is a global health concern impacting both developed and developing nations. It can pose an expanded risk to health and generate significant issues for the advancement of social and economic development. According to the WHO (2023), a third of the world's population suffers from anemia as a result of illnesses and a low diet of nutrients. Natural plants should be used in the treatment of anemia and anaemic patients in order to refill their iron and restore their iron content. This will aid in raising oxyhemoglobin levels and benefit quality of life, morbidity, and prognosis in the chronic conditions. It also raises oxyhemoglobin levels, primarily in pregnant women and adolescents. Anemia can be found in many long-term inflammatory conditions, such as congestive heart failure and chronic kidney disease. This study aims to provide an understanding of anemia, risk factors, symptoms, prevalence, and etiology. It also provides an updated summary of diagnosis, pathophysiology, types of anemia, and treatment. Additionally, it includes a screening model for anemia and need for herbal plants that are used for treating anemia.

Key words **-** Anaemia, Malnutrition, Natural plants, Oxyhemoglobin, Iron deficiency anemia Inflammatory conditions.

I. INTRODUCTION

People of any age group might be affected by the hazardous public health condition of anemia. It is characterized by a decrease in hemoglobin levels and a decline in the blood's capacity to carry oxygen (Marks Peter W 2019).

It causes reduced oxygenation of the tissue and can accelerate the course of numerous concomitant conditions. (Lin TF, Huang JN *et al*., 2018)

Iron is an essential component of the blood protein hemoglobin (Hb), which makes iron deficiency the most common cause of anemia. Aside from these abnormalities, prolonged inflammation, parasite infections, hereditary disorders, and deficits in vitamins B12 and A have also been connected to anemia. (Marks Peter W 2019)

There are variations in anemia levels among age groups, sex groupings, altitudes, smoking habits, and gestational periods. (Premkumar, S. Ramanan, *et al*., 2019)

Anemia can also result from other dietary deficits, such as those involving the vitamins B12, B6, A, C, D, and E, as well as folate, riboflavin, copper, and zinc.(F. Wieringa *et al.*, 2016)

Anemia is associated with expanded rates of morbidity and mortality in women and children(Black RE *et al*.,(2013), impaired children's behavioral and cognitive development and decreased productivity at work, (Walker SP., *et al*.,(2007). Preschool-aged children (PSC) and women of reproductive age (WRA) are the groups most affected.

1.1 Risk Factors

It includes poor absorption, low intake of iron, bacterial infections, and different degrees of long-term blood loss. Women with iron deficiency or anemia frequently experience premature birth and low birth weight. (B. De Benoist, *et al*.,(2008).

1.2 Symptom

It includes fatigue, intolerance to exercise, pale or yellowish skin, tinnitus, weakness, agitation, dyspnea, and chest pain. weariness, headaches, leg cramps, fingernails, and commissural cheilitis (mouth cracks). (Goldman L, Schafer AI *et al*., 2011)

1.3 Prevalence

It was shown that anemia was prevalent in 37.32% of the patients. 19.91% of people had mild anemia, 16.3% had moderate anemia, and 1% had severe anemia, according to the WHO classification. 5.6% of adolescents nationwide between the ages of 12 and 19 had anemia, with women predominating. (T. Shamah-Levy, *et al.*, 2013) .

The WHO categorization indicates that anemia is more common among pregnant women (17.9%) and in women of reproductive age overall (11.6%). Anemia resulting from iron deficiency often affects 1 in 6 expectant mothers. The frequency of anemia is 16.5% among people 60 years of age and older. (Marcela O' Farrill- cadena *et al*., 2013)

II. AETIOLOGY

The primary reason for anemia is the imbalance between the body's storage of iron and its need for iron in tissues as a result of blood loss-related illnesses. (Gysell Ibanez, *et al*., 2013)

The main causes are:

1. <u>Inadequate consumption of iron</u>: This is primarily observed in the pediatric population, in children during growth spurts, especially in low-weight babies, early-weaned newborns, and during adolescent spurts.
2. <u>Enhanced Iron Requirement</u>: The elevated need for Iron during Pregnancy and Lactation.
3. <u>Impaired iron absorption</u>: Increased iron loss in the body results from malabsorption, which can be brought on by digestive issues, celiac disease, and restricted HCl secretion (from using proton pump inhibitors excessively). (Miller JL., 2013)
4. <u>Abnormal iron loss (chronic bleeding)</u>: The main causes of chronic disorders, including gastro-intense bleeding, erosive gastritis, bowel polyps, and colon cancer, are linked to vaginal bleeding in adolescents and adults, as well as dysfunctional uterine bleeding in adults of both sexes.
5. A recessive germline mutation in the TMPRSS6 gene causes familial iron deficiency. This mutation encodes a type II serine protease in the liver that controls the expression of hepcidin. It causes abnormalities in the DMT-iron transport protein, which is linked to a decrease in the body's iron intake and metabolism. (Pasricha S-RS *et al*., 2010)

III. PATHOPHYSIOLOGY

A biological imbalance between erythrocyte production and loss is the cause of anemia. The reasons for this imbalance can include hemolysis, blood loss, or both. It can also be brought on by excessive or inadequate erythropoiesis (induced by conditions like inflammation, dietary inadequacies, or hereditary abnormalities involving Hb). (Camilo M Chapparao, *et al*., 2019)

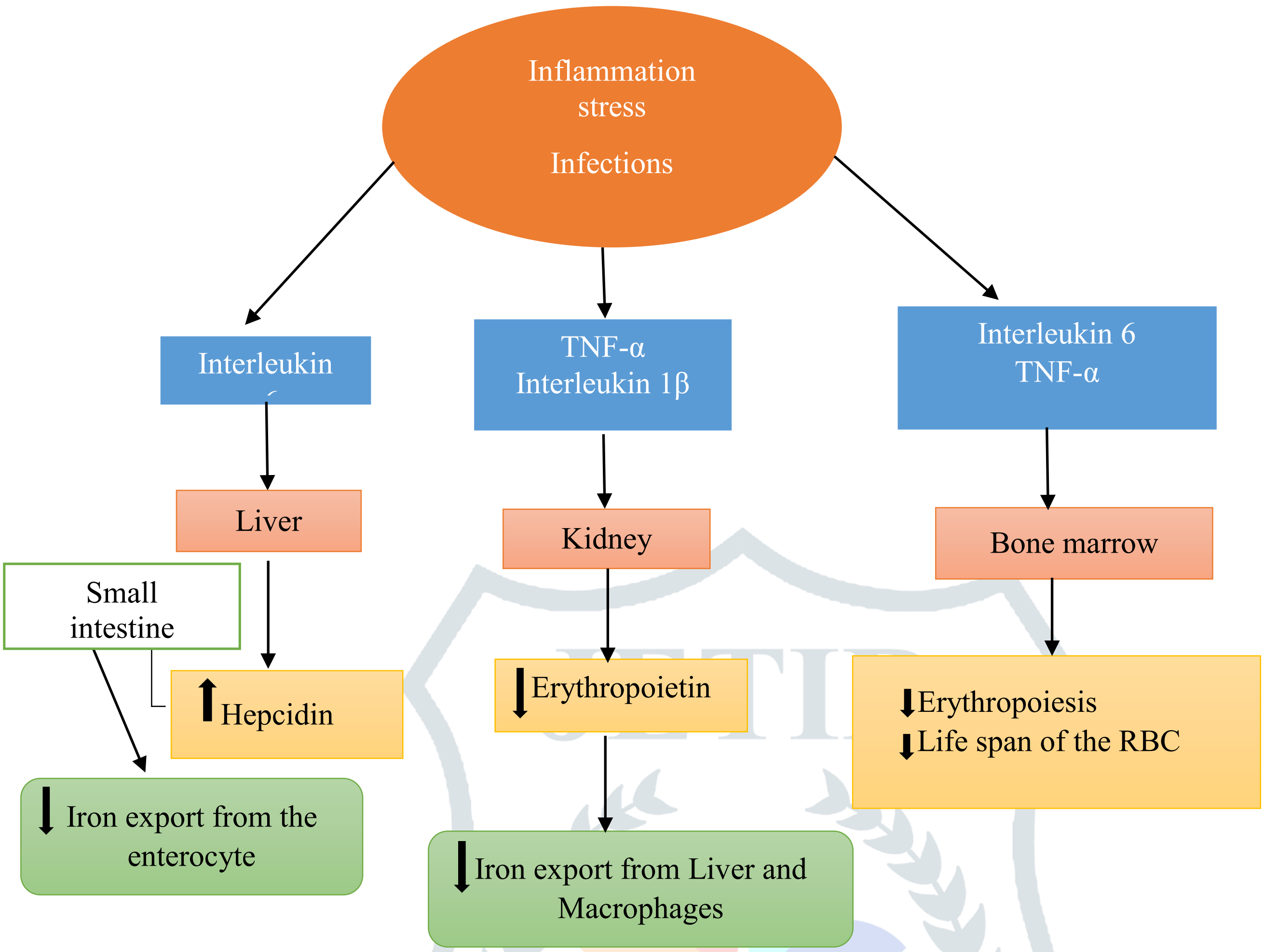

Figure 1: Schematic representation of pathophysiology of anaemia

IV. DIAGNOSIS

As per WHO anemia is defined as having less than 12 g/dL of oxyhemoglobin (Hb) in women and less than 13 g/dL in males. Serum ferritin, the molecule that stores iron, should be at or below 30 µg/L in an isolated iron deficiency. (Stein J, *et al.,* 2013). Conversely, ferritin is an acute-phase protein that can increase in the presence of inflammation. Therefore, if there is concurrent inflammation, such as elevated C-reactive protein, ferritin less than 100 µg/L is indicative of Iron Deficiency Anaemia (IDA).(Weiss G, 2015)

Various laboratory tests and imaging modalities may be relevant in the assessment of anemia. These include:

1. Reticulocyte count: Indicates the amount of red blood cells produced by the bone marrow.
2. Complete blood count(CBC): This comprises hemoglobin, hematocrit, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC).
3. Iron profile: consists of ferritin, serum iron, and total iron-binding content (TIBC).
4. Serum creatinine: Aids in assessing kidney function
5. Peripheral blood smear: microscopic examination of red blood cell morphology
6. Thyroid function tests: These include measuring levels of thyroid-stimulating hormone (TSH) and thyroxine (T4).
7. Coagulation screen: It includes activated partial thromboplastin time (APTT), prothrombin time/international normalized ratio (PT/INR), and thrombin time (TT).
8. Hemolysis profile: Includes indirect bilirubin, lactate dehydrogenase (LDH), and haptoglobin.
9. Hemoglobin electrophoresis: Assesses the amino acid chains of hemoglobin.(Zuniga C. P, *et al.*, 2018) (Karakochuk CD, et al., 20)

V. TYPES OF ANAEMIA

Erythrocyte morphology was used to categorize anemia into two categories. They are as follows:
1. Microcytic anemia: Iron deficiency anemia (IDA) caused by insufficient iron.
2. Macrocytic anemia: Hemolytic anemia, aplastic anemia, and vitamin B12-deficient anemia

1. Microcytic anaemia:

It is characterized by a low MCV (less than 83 microns) and is defined as the presence of tiny, frequently hypochromic red blood cells in a peripheral blood smear. Microcytic anemia is most frequently caused by an iron shortage. (A C Massey,1992)

a. Iron deficiency anemia(IDA) :

This is the most prevalent kind of anemia, when the body produces fewer red blood cells as a result of low iron levels. This causes weakness, heavy menstruation, and an increased risk of chronic illnesses. (Mukherjee, K.L., *et al*., 2012), (Scheinberg, P *et al*., 2011)

Drugs which are used to treat IDA:

Iron-rich diets and supplements can be used to treat (johnson-wimbley TD *et al*., 2011),(Baker RD *et al*., 2010)

Iron supplements:

Table 1: Drugs and type of formulation for iron supplements

Drugs	Formulation
Sodium Ferric gluconate	Aqueous or injection (12.5mg per mL)
Iron sucrose	Aqueous or injection (20mg per mL)
Iron dextrose	Aqueous or injection (50mg per mL)
Ferrous sulfate	oral (65mg)
Ferrous fumarate	oral (106mg)
Ferrous gluconate	oral (38mg)
Iron polymaltose	Oral (100 mg)

Iron-rich foods : Cereals, fortified bread, red meat, kidney beans and green vegetables.

2. Normocytic/Macrocytic anaemia:

Adult macrocytosis is characterized by a mean corpuscular volume (MCV) of red blood cells (RBCs) greater than 100 femtoliters (fL). (Takayo Nagao, *et al*., 2017)

a. Aplastic anaemia:

This rare blood disorder occurs when the bone marrow is unable to generate enough red blood cells (RBCs).

It frequently results in autoimmune illnesses that harm stem cells and change the body's iron levels. (Tuba Karagul Yıldız *et al*., 2021)

Drugs which are used to treat Aplastic anaemia

Table 2: Drugs for aplastic anaemia

Immunosuppressive drugs	Cyclosporin
Corticosteroids	Methylprednisolone
Hematopoietic stem cell transplantation	–
Bone Marrow transplant	HLA matched sibiling
Specific anti-bodies	ALG(anti-Lymphocyte globulin), ATG (anti-thymocyte globulin)

b. Hemolytic anaemia:

When red blood cells are being destroyed more quickly than they are being created. It could be bought or inherited. (Alberto Zanella and Wilma Barcellini,2014)

VI. SCREENING MODEL FOR ANTI ANAEMIA ACTIVITY IN RODENTS

Phenylhydrazine-induced anaemia in rats: (Aboudoulatif Diallo *et al*.,2008)

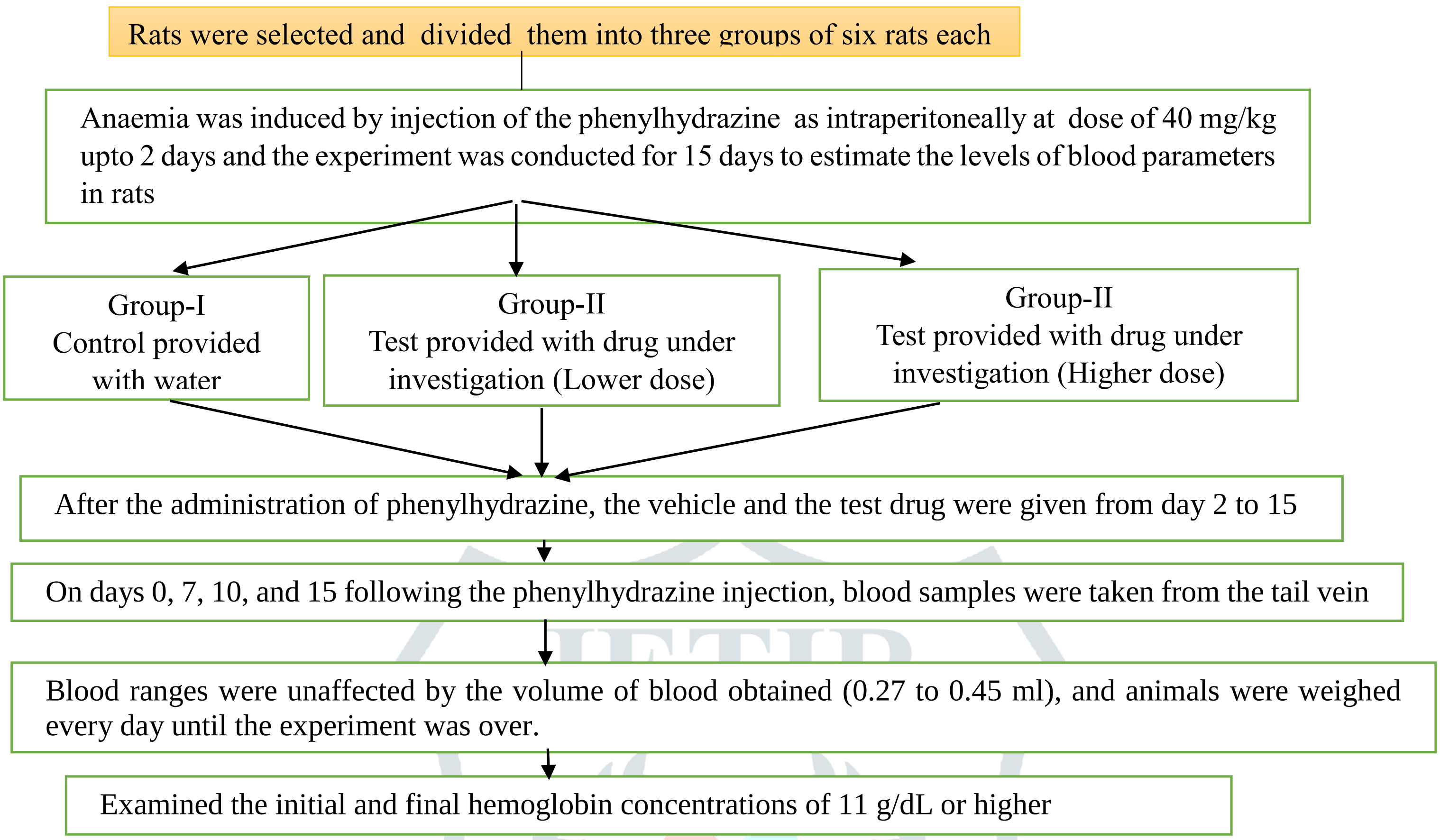

Figure 2: Flow chart for phenylhydrazine induced anaemia in rats

VII. VARIOUS HERBAL PLANTS WHICH ARE USED TO TREAT ANAEMIA

1. Allium ascalonicum:

Owoyele *et al*., (2004) used the phenylhydrazine-induced anemia paradigm in mice to determine the hematological effect of an EtOH extract of *Allium ascalonicum*. Different doses of 50, 100, and 200 mg/kg body weight were administered orally to the male albino rats over a period of 21 days, which predicted the blood parameters, like red blood cell and white cell counts, as well as serum lipid levels. The outcomes demonstrated that there was a consequential rise in white blood corpuscle parameters and a decline in red blood corpuscle parameters at 200 mg/kg of extract. With no discernible impact on triglyceride levels, it also lowers the levels of high-density lipoprotein (LDL), low-density lipoprotein (LDL), and total cholesterol (TCH) in rats.

2. Amaranthus cruentus:

Pandey *et al*.,(2016) conducted research on the hematopoietic effect of *Amaranthus cruentus* extract using rats-induced toxicity with phenyl hydrazine. In the plant study, test animals were given varying amounts of *Amaranthus cruentus* extract together with phenylhydrazone, which causes anaemia in animals. This activity made it very evident that the numbers of oxyhaemoglobin and red blood corpuscle had dramatically increased. mostly a plant with high levels of calcium, protein, folic acid, and vitamins. For investigation purposes, the leaves were utilized. Rats and mice were used for the screening model. The test group received phenyl hydrazine intraperitoneally for three days in a row, along with a 200, 400 mg/kg leaf extract, and the results were compared to the standardized medication Ferritop-Z. After 25 days, the data showed drastic rises ($P < 0.001$) in oxyhemoglobin and red blood cells. Interestingly, the 400 mg/kg leaf extract dose showed similar efficacy to the standardized medication Ferritop-Z for traditional anemia. These results imply that *Amaranthus cruentus* is an alternate anemia treatment, offering a possibly affordable and natural remedy for this common health issue.

3. Asparagus racemosus:

Chaudhary *et.al*., (2016) done an activity on the potential effect of *Asparagus racemosus* root extract on experimental anemic and thrombocytopenic conditions by employing rats. Comparing the root extract of 750 mg/kg to the illness group (anemia), there is a drastic rise in the red blood corpuscle, oxyhemoglobin, and a dropoff in MCH ranges and white cells. The investigation made use of roots.The dosages of the extracts were 250, 500, and 750 mg/kg. It was evaluated that by giving the 250 mg/kg BB dose of asparagus racemosus extract, the phenylhydrazine group was able to raise their oxyhaemoglobin (8.57 g/dL) and red blood cell corpuscle range (4.46 x 1012).

4. Cnidosculus aconitifolius:

Atata *et al*., (2020) investigated the anti-anaemic effects of *Cnidosculus aconitifolius* ethanol leaf extract on rodents that had been induced to become anemic in mice with the help of cyclophosphomide. In this investigation, leaves were used, which were extracted and administered at a different doses of 100–500 mg/kg BB. This resulted in a high restoration effect on hematological parameters. Each mouse had a two-week course of treatment, during which time blood samples were taken for hematological examination. The findings demonstrated that the hematological parameters rose in the groups of 2, 3, and 5 mice that received EtOH extracts of Cnidoscolus aconitifolius and chemiron at doses of 100 mg/kg and 500 mg/kg, respectively. A significant ($P < 0.05$) rise in the red blood corpuscle count (8 x 1012/L) and oxyhemoglobin levels (14 g/dL) was seen and compared with the hematological data in the standardized group. The only two elements of group 5 were red blood corpuscle (5 x 1012/L) and oxyhemoglobin levels (12 g/dL). Consequently, cyclophosphamide-induced anemia in mice was treated with an extract from the leaves of *Cnidoscolus aconitifolius.*

5. Curcuma Longa Linn:

Prihardini *et al*.,(2019) evaluated the results of raising the levels of red blood corpuscle and oxyhaemoglobin in rats when $NaNO_2$ was employed as an inducer and examined the antianaemic effects of *Curcuma longa* Linn. ethanolic extract and juice. Turmeric juice has an additional benefit due to its polar group. In this investigation, turmeric rhizome juice was used. The experiment, which employed 200 mg/kg BB of turmeric extract in EtOH, revealed that the Wistar rat had significantly higher quantities of red blood corpuscle and oxyhaemoglobin than the other rats. As compared to previous turmeric ratios (13.92 g/dL and 7,842 x106), test results indicated that oxyhemoglobin and erythrocytes responded consequentially better to a 200 mg/Kg BB dose of turmeric squeezing. This effect was greater than the initial levels.

6. Falcaria Vulgaris:

Goorani *et al*., (2019) According to research, the activity of the aqueous extract of *Falcaria vulgaris* leaves in rats indicates that the extract has anti-anaemic properties. This experiment used the soxhletation method with leaves, and SPSS-21 software was used for data analysis. Weight, leukocytes, neutrophils, platelets, red blood corpuscle, oxyhemoglobin, PCV, MCV, and MCHC were all significantly ($p < 0.05$) higher in the group that received 200 mg/kg BB of *F. vulgaris* leaf water extract than in the untreated rat group. The final evaluation's red blood corpuscle value at 200 mg/kg BB was 7.4 x 1012, but it fell short of the control group's red blood corpuscle value (8.1 x 1012). In comparison to the unidentified group, the administration of *Falcaria vulgaris* water extract at multiple dosages resulted in a substantially ($p < 0.05$) higher number of erythrocytes.

7. Glycyrrhiza glabra:

Zangeneh *et al*., (2017) assessing the activity of the anti-anemic effects of a *Glycyrrhiza glabra* aqueous extract in rats given phenylhydrazine treatment. *Glycyrrhiza glabra* has been shown to have protective effects against anemia. An experiment was conducted by using leaves. The mice with phenylhydrazine-induced anemia were studied. Mice were divided into five subgroups: three groups got different dosages of *Glycyrrhiza glabra* (30, 60, and 120 mg/kg), one group received phenylhydrazine for one day, and one group remained untreated. Animals from every group were slaughtered on the fifteenth day of treatment, and blood samples were collected for analysis of their immunological, hematological, and biochemical characteristics. At a dosage of 120 mg/kg, *Glycyrrhiza glabra* dramatically raised oxyhemoglobin (13 g/dL) and red blood corpuscle (7.4 x 1012) levels. The levels of red blood corpuscle, oxyhemoglobin, PVC, and MCV in untreated controls can rise with all three dosages of Glycyrrhiza glabra, but they still fall short of those in the control group. In conclusion, the outcomes showed that utilizing Glycyrrhiza glabra aqueous extract may have an anemic effect.

8. Justicia carnea Vahl:

Desna Amelliya *et al*., (2021) conducted an antianaemic action with *Justica carnea* valh leaves. It is a medicinal plant with a broad range of pharmacological properties that may improve blood flow. This study suggests that *Justicia carnea* leaves have both antianemic properties and the potential to be toxic to vital organs, including the kidney and liver, at large doses. In addition to organ analysis for the histopathological study, serums were used for biochemical analysis. The quantitative phytochemical examination reveals the presence of alkaloids (1.88 mg), tannins (2.16 mg), and saponins (2.50 mg) as secondary metabolites. The oxyhemoglobin values for doses of 500 mg (15.10 g/dL) and 1000 mg/kgBB (14.30 g/dL) showed remarkable ($p<0.05$) raise in hemoglobin levels, and the hematological component rose in relation to the four distinct dosages.

9. Limonia acidissima:

Anacletus *et al.,* (2018) investigated the anti-anaemic effects of Limonia acidissima leaf aqueous extract on phenylhydrazine-induced anemia in Wistar rats and ascertained the folic acid and vitamin B12 potentials. For four

(4) weeks, rats were given an aqueous extract of *Limonia acidissima* leaves, utilizing leaves as the source material. Comparing the groups treated with an aqueous extract of Limonia acidissima at doses of 100, 200, and 300 mg/kgbw to the anemic non-treated rats, the groups showed consequential (P<0.05) elevated levels of Hb, MCV, WBC, and RBC in the first two weeks of the study. A further remarkable (P<0.05) rise in these parameters was observed in the fourth week. Aggregates derived from the plant Limonia acidissima exhibit high levels of antioxidant properties and have been shown to have wound-healing properties by scavenging free radicals.

10. Syzygium polyanthum (Wight) Walp:

Kartika Adyani *et al*., (2018) conducted activity on the Iron Deficiency Anaemia Model Rats by introduce Bay Leaf Extract (*Syzygium Polyanthum (Wight) Walp*). Oxyhemoglobin levels in the group of mice was evulated and given bay leaf extract at different doses were similar to the anemic tablets. It can be argued that administering bay leaf produces a result that is similar to that of traditional therapy, namely blood-added pills. This is a one-month course of treatment. Oxyhemoglobin levels were measured using a Sysmex auto-hematological analyzer. A statistically significant increase in different oxyhemoglobin levels was seen in P1, P2, and P3 (p<0.05), according to the analysis of the median test. The LSD test results showed that all treatment groups (mice given varying dose ranges of bay leaf extract; 2.2, 4.4, and 6.6 mg) had oxyhemoglobin levels that were significantly different from the control group (-ve). All treatment groups that received varying dosages of extract had oxyhemoglobin levels that were not remarkably different from those of the control (+ve), which is the group that took the blood-added tablets and was not given any additional treatment. At a dose of 6.6 grams of bay leaf extract, treatment group 3 experienced the highest increase in oxyhemoglobin (2.65 g%), followed by treatment group 1 (2.2 g% and 1.55 g%). oxyhemoglobin levels increased by 0.7 g% in the control group (+ve).

11. Trigonella foenum-graecum:

Chourasiya *et al*., (2019) concluded the study on the hemopoietic and anti-anemia properties of Trigonella foenum-graecum in a rat model. In this investigation, seeds were used. plant, proving that Trigonella foenum-graecum seeds are the primary ingredient in the treatment of anemia. The phytonutritional components of seed extract are displayed, including flavonoids, sterols, carbohydrates, and saponins. Mice were used in this model, and phenylhydrazine was added. Soxhelation was used to prepare the hydroalcoholic extract from seeds. All test groups received phenylhydrazine, with the exception of the control group, which was given seed extract. Hematological indicators, such as oxyhemoglobin, white cell count, and red blood cell corpuscle, were assessed over a period of two to thirteen days. Red blood cell (51.0%), white blood cell (54.8%), and oxyhemoglobin (52.5%) percentages all drop off. (Dr. Ruchita Shrivastastava *et al*., 2019).The amount of white blood cells, oxyhemoglobin, and red corpuscles at a dose of 400 mg/kg significantly increased when the hematological parameters were re-examined on day 13. Significant improvement in anemia control is recommended by this study.

12. Wrightia tinctoria:

Bigoniya P *et al*., (2013) demonstrated the use of W. tinctoria bark in the treatment of anemia in albino mice and assessed TIBC, ferritin, and iron levels in the blood. Following a 60-day fraction of *W. tinctoria* (FWT) treatment, there was a substantial rise (P < 0.05) in the levels of PCV, oxyhaemoglobin, red blood cell corpuscle, and white blood cells. Following the FWT treatment, MCV and ferritin levels (P<0.001) rose while the TIBC range, iron levels, and MCV levels drastically dropped. Additionally, FWT revealed a considerable drop in ferritin and iron levels in the serum and a rise in PCV, oxyhaemoglobin, and red blood corpuscle. Following FWT therapy with butadiene and phenylhydrazine, anemic rats showed a minor number of blood cells with inconsequential morphologies and a slight dropoff in red blood cell corpuscle. The plant extract demonstrated its ability to preserve the integrity of the red blood erythrocyte membrane, and the results suggest a significant (P<0.05) increase in the ability to cure mice's anemia.

(Shilpa V *et al*.,2019)

VIII. CONCLUSION

It is abundantly evident from the above explanation that plants have a significant impact on human health in a variety of ways. They also give humans nutritional and medical assistance, which helps to either directly or indirectly treat a variety of illnesses. Among these, anemia is one that can be treated with dietary supplements and herbal remedies. Anemia is more prevalent in underdeveloped countries due to a variety of contributing factors. Due to the limited resources and complex socioeconomic circumstances in developing countries, combating anemia is a global public health priority. Numerous studies have shown that anemia is quite common in adolescent boys and girls. Adolescent health is the most important indicator of a nation's level of development. Therefore, this needs immediate attention. Research indicates that combining preventative supplements with nutrition education could be a more successful tactic for improving compliance and nutrition status. Nonetheless, it is feasible to achieve an anemia-free community if the general public-especially the rural population-is educated on the causes of anemia and its preventive and curative measures. This well-documented and carefully cited review will definitely help the researcher when designing experimental study protocols, selecting the best antianaemic drug, and cross-referencing published methods.

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CONFLICT OF INTEREST

Authors does not have conflict of interest in the publication of this manuscript.

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