A SYNERGISTIC COMPOSITION FOR TREATING ANEMIA

BACKGROUND OF THE INVENTION

FIELD OF THE INVENTION

[0001] The present invention relates to a synergistic composition for treating anemia or supplementing iron. Particularly, the present invention relates to a synergistic composition that provides preferable efficacy in improving iron absorption, hemoglobin formation, and treatment of anemia, and further alleviates dysmenorrhea.

DESCRIPTION OF THE PRIOR ART

[0002] Anemia can be roughly classified into three categories: (1) those due to bone marrow production abnormality, such as aplastic anemia, and those due to bone marrow invasion by malignant tumors, such as leukemia; (2) those due to failure of red blood cell maturation, such as pernicious anemia of vitamin B12 deficiency and iron-deficiency anemia; and (3) those due to blood loss or destruction, such as bleeding from injury, iron-deficiency anemia, or destruction of red blood cells caused by all reasons.

[0003] Iron-deficiency anemia is one of the most common sorts of anemia among patients. It is resulted from depletion of iron stored in human bodies. Patients with iron-deficiency anemia usually have decreasing number or volume of red blood cells or increasing number of platelets and low concentration of globulin. Since iron is an important element of globulin, iron deficiency in bodies will eventually lead to anemia. Iron deficiency affects red blood cell maturation.

In addition, patients with symptoms of bleeding lose iron because of loss of blood. Generally, females are more prone to iron deficiency than males, and the main reasons include physical and dietary factors. Since the onset of puberty, each female loses 0.5 mg iron daily in average during menstrual periods, and that is 50% higher than the amount of iron a male would have been losing.

[0004] No matter whether a person has anemia or not, iron deficiency by itself affects the person's learning and working performances. The Third National Health and Nutrition Examination Survey (NHANES III) of the United States shows that among children within 6 to 16 years old, those with iron deficiency had lower math test scores than those who are healthy do, and odd ratio of those with iron deficiency is 2.3 times greater than that of those who are healthy. The data shows that both iron deficiency and anemia in children and teenagers affect their cognitive and learning abilities.

[0005] Supply of iron from daily diet is usually higher than the actual required iron amount for human bodies. However, due to the effects of iron's chemical forms, food composition, and physical conditions, the rate of iron absorption in human bodies are usually low. The rate of iron utilization of a group whose diet rich in red meat and animal source foods can reach 18%. However, the rate of dietary iron utilization of people in Asia is about 10% because people in this region live primarily on a white meat-based diet. Without nutrients fortification policies, it is more common that people in Asia show signs of iron deficiency. Therefore, people in Asia should carefully choose foods that lead to high rate of iron utilization or moderately take iron supplements to solve the problems of iron deficiency or anemia.

[0006] Chalybeate is the major drug for treating iron-deficiency anemia or supplementing iron. Ferrous sulfate, iron gluconate, and ferric pyrophosphate are commonly used as commercial chalybeate. However, chalybeate may cause side effects. Mild side effects of chalybeate include stomach upsets such as nausea, stomachache, constipation, or diarrhea, whereas severe side effects include intestinal hemorrhage, hypoxemia, metabolic acidosis, and renal failure.

[0007] In the prior art, ferrous sulfate is a widely used chalybeate because its active ingredient is divalent iron, which has a higher absorption rate and a lower price. Ferrous sulfate is internationally used as an index of bioavailability of iron. However, ferrous sulfate may cause side effects, such as stomach upset.

[0008] Siwu decoction is a commonly used traditional Chinese herbal formula, mainly containing four Chinese herbal medicinal materials *Angelica sinensis*, *Ligusticum wallichii*, *Paeonia lactiflora*, and *Rehmannia glutinosa*. It is commonly believed that Siwu decoction can relieve menstrual discomfort, and scientific data show that Siwu decoction can indeed alleviate dysmenorrhea (Yeh *et al.*, A randomised placebo-controlled trial of a traditional Chinese herbal formula in the treatment of primary dysmenorrhea. PLoS One. 2 (8), e719, 2007). However, no scientific reports have described that Siwu decoction can improve iron absorption or facilitate hemoglobin formation. In Fact, scientific data show that Siwu decoction or a Siwu extract cannot improve hemoglobin formation. Although there are products containing combinations of *Angelica sinensis*, *Ligusticum wallichii*, *Paeonia lactiflora*, and *Rehmannia glutinosa, Dimocarpus longan, Diospyros lotus* L., other Chinese herbs, and chalybeate, there is no references or scientific reports revealing the correlation between Siwu and iron absorption.

[0009] So far, there are still demands for developing more efficient medicines for treating anemia or food composition as an iron supplement that does not have side effects.

SUMMARY OF THE INVENTION

[0010] In view of the above mentioned, the purpose of the present invention is to provide a synergistic composition for treating anemia or supplementing iron, which does not have side effects or has side effects in a minor level. Particularly, the composition has preferable effects in hemoglobin formation and has synergistic effects compared to a single components used alone.

[0011] In one aspect, the present invention provides a synergistic composition for treating anemia or supplementing iron, comprising a combination of the following components: (A) an extract of Siwu, the Siwu comprising *Angelica sinensis, Ligusticum wallichii, Paeonia lactiflora*, and *Rehmannia glutinosa*; and (B) ferrochel.

[0012] According to certain embodiments of the present invention, the Siwu comprises *Angelica sinensis, Ligusticum wallichii, Paeonia lactiflora,* and *Rehmannia glutinosa* in an amount of weight ratio of 1-10:1-10:0.3-3:0.3-3, preferably in a weight ratio of 1-6:1-6:0.3-2:0.3-2. In one embodiment, the weight ratio of *Angelica sinensis, Ligusticum wallichii, Paeonia lactiflora,* and *Rehmannia glutinosa* is 3:3:1:1.

[0013] According to the present invention, the extract of Siwu and ferrochel are contained in a synergistic composition in a quantity being effective in a synergistic manner in treating anemia or supplementing iron. For example, the amount of ferrochel may be 1% or more by total weight of the synergistic composition to

achieve synergistic effects. In certain embodiments of the present invention, the amount of ferrochel by total weight of the synergistic composition is 1-50%, preferably 1-30%, more preferably 1-20%, and in a specific embodiment 1-10%, for example, about 5-10%.

[0014] In another aspect, the present invention provides a medicament for treating anemia or supplementing iron, comprising a therapeutically effective amount of a synergistic composition of the present invention, and a pharmaceutically acceptable carrier.

[0015] In further aspect, the present invention provides use of a synergistic composition of the present invention in the manufacture of a medicament for treating anemia or supplementing iron.

[0016] According to certain embodiments of the invention, the synergistic composition can be used for treating iron-deficiency anemia, especially for female patients, because the efficacy of treatment is found that after being administered with the synergistic composition of the invention the concentration of hemoglobin, volume of red blood cells, concentration of serum ferritin, concentration of serum iron, and hematocrit are increased and transferrin/ferritin ratio is decreased so to be of treatment efficacy. It is also found that symptoms of dysmenorrhea are alleviated.

[0017] These and other aspects of the present invention can be more clearly illustrated by the following description of preferred embodiments and drawings. Even though there might be variations or modifications, they do not depart from the novel concepts and scope disclosed in the present invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0018] FIG. 1 shows the effects of the composition of the present invention in patients with iron-deficiency anemia. FIG. 1(A) shows the average hemoglobin concentration of the subjects in stages of pre-administration, administration (weeks 2, 4, 8, and 12), and post-administration (week 16) respectively. FIG. 1(B) shows the changes of the average hemoglobin concentration of the subjects in stages of pre-administration, administration (weeks 2, 4, 8, and 12), and post-administration (week 16) relative to that of pre-administration respectively.

DETAILED DESCRIPTION OF THE EMBODIMENTS

[0019] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by a person skilled in the art to which this invention belongs.

[0020] As used herein, the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise. Thus, for example, reference to "a component" includes a plurality of such components and equivalents thereof known to those skilled in the art.

[0021] In one aspect, the present invention provides a synergistic composition for treating anemia or supplementing iron, comprising a combination of the following components: (A) an extract of Siwu, the Siwu comprising *Angelica sinensis, Ligusticum wallichii, Paeonia lactiflora*, and *Rehmannia glutinosa*; and (B) ferrochel.

[0022] According to the present invention, components A and B of the synergistic composition are contained in a quantity being effective in a synergistic

manner in treating anemia or supplementing iron. It goes without saying that components A and B are the active ingredient or the sole active ingredient of the synergistic composition of the present invention. In certain embodiments of the present invention, the synergistic composition consisting essentially of components A and B, i.e. an extract of Siwu and ferrochel. The synergistic compositions according to the invention preferably contain components A and B in the ratio of 1:1 to 99:1, and particularly preferably in the ratio 2:1 to 9:1.

[0023] The term "Siwu" used herein refers to a traditional Chinese herbal formula comprising or consisting essentially of four Chinese herbs, which are *Angelica sinensis, Ligusticum wallichii, Paeonia lactiflora,* and *Rehmannia glutinosa*. An extract of Siwu may be obtained by extracting the four herbs in one pot, or by extracting the individual herbs separately and then mix the respective extracts. Any known formula of Siwu decoction or Siwu may be used in the present invention and is extracted by commonly known or conventional methods. For example, *Angelica sinensis, Ligusticum wallichii, Paeonia lactiflora,* and *Rehmannia glutinosa* with a weight ratio of 1-10:1-10:0.3-3:0.3-3, preferably 1-6:1-6: 0.3-2:0.3-2 may be used in the preparation of an Siwu extract. In one embodiment of the present invention, the weight ratio of *Angelica sinensis, Ligusticum wallichii, Paeonia lactiflora,* and *Rehmannia glutinosa* is 3:3:1:1.

[0024] The term "ferrochel" used herein means a heterocyclic structural complex formed by two molecules of glycine and a ferrous ion. The structure and properties of ferrochel is different from other forms of iron. Many researches prove that the bioavailability of ferrochel is better than that of ferrous sulfate, and thus ferrochel can improve nutritional efficacy of iron. Ferrochel used in the

present invention can be commercially purchased or prepared by known standard methods.

[0025] As shown in Example 1, administering an extract of Siwu alone does not improve hemoglobin formation. However, comparing with the Siwu extract or ferrochel that is used alone, administering a composition containing a Siwu extract and ferrochel shows an unexpected synergistic effect in increasing iron absorption and improving hemoglobin formation, and further effectively treating anemia and acting as an iron supplement.

[0026] According to the present invention, the Siwu extract and ferrochel of a synergistic composition are contained in a quantity being effective in a synergistic manner in treating anemia or supplementing iron. For example, the amount of ferrochel may be 1% or more by total weight of the synergistic composition to achieve synergistic effects. In certain embodiments of the present invention, the amount of ferrochel by total weight of the synergistic composition is 1-50%, preferably 1-30%, more preferably 1-20%, and in a specific embodiment 1-10%, for example, about 5-10%.

[0027] The composition of the present invention can be prepared in forms of foods or drugs. By any known skill, the composition can be made as food or drug products along with excipients, fillers or pharmaceutically acceptable carriers, and mixed with additives if necessary. In certain embodiments of the present invention, the synergistic composition is prepared as a liquid formulation. In certain other embodiments, the synergistic composition is prepared as a food composition.

[0028] The synergistic composition may also be prepared as a pharmaceutical composition for treating anemia or supplementing iron, comprising a

therapeutically effective amount of a synergistic composition of the present invention and a pharmaceutically acceptable carrier. It can be prepared from a synergistic composition of present invention in a therapeutically effective amount by adding a suitable pharmaceutically acceptable carrier based on well-known or conventional technologies or methods in medicine.

[0029] The term "therapeutically effective amount" used herein means an amount of medicine that can effectively treat or prevent anemia or be used as an iron supplement. The amount can be adjusted based on methods of administration and the results of treatment, including age, body weights, symptoms, effects of treatment, methods of administration, and treatment periods.

[0030] In one embodiment of the present invention, the synergistic effects of the composition are demonstrated by the synergistic efficacy of hemoglobin formation improvement. By measuring the change of hemoglobin concentration before or after administration, one can acknowledge the composition's synergistic efficacy in improving hemoglobin formation. As shown in the results of clinic trials of the synergistic composition of the present invention, the composition can be used for treating female patients suffering from anemia. It is found that after administration, the concentration of hemoglobin, volume of red blood cells, concentration of ferritin, concentration of serum iron, and hematocrit are increased and transferrin/ferritin ratio is also decreased. The synergistic composition also alleviates dysmenorrhea. Thus, in another aspect, the invention provides use of a synergistic composition of the present invention in the manufacture of a medicament for treating anemia or supplementing iron. In further aspect, the present invention provides a medicament for treating anemia or supplementing iron, comprising a therapeutically effective amount of a

synergistic composition of the present invention, and a pharmaceutically acceptable carrier. As to the test of dysmenorrhea alleviation, the Visual Analog Scale, a self-descriptive tool, is used to evaluate a subject's feeling of pain. The scale is presented in an either horizontal or vertical continued line in length of 10 centimeters. The left or lower end (0^{th} centimeter) is denoted "not painful" and the right or upper end (10^{th} centimeter) is denoted "extremely painful." Each centimeter in the scale signifies one score in level of pain. When being evaluated, the subject is requested to note the score to his/her own feeling of pain.

[0031] According to the present invention, the anemia includes but is not limited to iron-deficiency anemia. According to certain embodiments of the present invention, the medicament is effective in increasing blood hemoglobin concentration.

[0032] The descriptions above and the following examples should be understood as of demonstrative purpose instead of limiting in any way to the scope of the present invention.

[0033] **Example 1:** Animal Experiments

[0034] A. Laboratory animals: male Wistar rats.

[0035] B. Biochemical and chemical agents:

[0036] 1. AIN93G diet (the components of AIN93G diet are shown in Table 1):

Table 1 The components of iron-deficient AIN93G diet

Component	Weight (g)
Casein from Bovine Milk	200
Corn starch	132

Dextrinized cornstarch	497.5
Soybean oil	70
Alphacel non-nutritive bulk	50
Custom AIN93G mineral mix without ferric citrate	35
AIN93 vitamin mix	10
DL methionine	3
Choline Bitartrate	2.5
Total	1000

[0037] 2. Siwu extract powder:

[0038] Siwu extract in this example is prepared from *Angelica sinensis*, *Ligusticum wallichii*, *Paeonia lactiflora*, and *Rehmannia glutinosa* in a weight ratio of 3:3:1:1. The extract is then dried into powder.

[0039] 3. Ferrochel powder:

[0040] Grind ferrochel into powder.

[0041] C. Animal experiment design:

[0042] The animal experiment is divided into two stages, the iron deficiency stage and the regeneration stage.

[0043] 1. Iron deficiency stage

[0044] All of the rats were fed on AIN93G diet without iron for 2 to 4 weeks to the extent where the rats are in anemia of iron-requiring. All of the rats ate the diet freely, and their diet intake amounts were recorded. During the experiment, blood samples were collected from tail vein in order to monitor the reduction of rats' hemoglobin concentration.

[0045] 2. Regeneration stage

[0046] The rats having anemia were evenly assigned to 3 groups, 6 rats per group. The rats in Group 1 (ferrochel and Siwu extract) were fed on diet having the composition of ferrochel and the Siwu extract. The rats in Group 2 were fed on diet with ferrochel. The rats in Groups 3 were fed on diet with Siwu extract. The diet is primarily based on AIN93G formulation along with ferrochel powder + Siwu extract powder, ferrochel powder, or Siwu extract powder in different iron form respectively as the iron source (called iron source) according to demand of each group. The iron sources and contents of each group are shown in Table 2.

Table 2. The iron sources and contents of the fodder in the regeneration stage

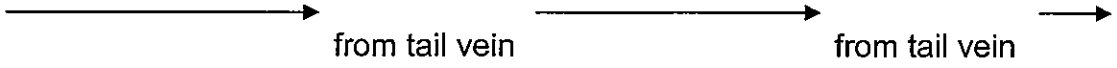
Group	Iron source	Iron content (ppm)
Group 1	composition of ferrochel and Siwu extract	12
Group 2	ferrochel	12
Group 3	Siwu extract	0.04 ≅ 0

[0047] The iron contents of Group 1 (ferrochel and Siwu extract) and Group 2 (ferrochel) were both 12 ppm. In Group 1 (ferrochel and Siwu extract), the amount of ferrochel is 5% - 10% by total weight of the composition. Group 3 (Siwu extract) almost does not contain iron. Group 1 (ferrochel and Siwu extract) and Group 3 (Siwu extract) contains the same amount of the Siwu extract powder.

[0048] The regeneration stage lasted for 2 weeks. All of the rats ate the diet freely, and their diet intake amounts were recorded. The rats are weighted and their growth status is observed. At the end of the regeneration stage, blood samples were collected from tail vein to measure the rats' hemoglobin concentration, and then the rats are sacrificed with carbon dioxide. The experiment design is shown as follow.

Iron deficiency stage Collect blood Regeneration Collect blood

for 2 to 4 weeks samples stage for 2 weeks samples Sacrifice



[0049] D. Analysis of hemoglobin concentration

[0050] Cyano-methemoglobin method was used to measure hemoglobin concentration. Mix evenly 2.5 ml of Drabkin's reagent and 10 μl of a blood sample, and then incubate the mixture for 10 minutes at room temperature. After that, measure absorbance at 540 nm. According to Beer's Law, absorbance is proportional to the medium concentration and the light path length of absorbing species. The relation can be written as $A = \epsilon bc$, wherein A is absorbance, ϵ is molar absorptivity, c is concentration, and b is the light path length of the absorbing species. Concentration of hemoglobin was quantified by with the following information: the molar absorptivity of Hb-CN is 11.0 $cm^{-1}mM^{-1}$Hb subunit, the equivalent weight of hemoglobin is 16114, and the blood samples in this example were diluted 251-fold.

[0051] E. Results: Changes of the average concentration of hemoglobin of the rats in every group are shown in Table 3.

Table 3 The effects of diet with different iron sources on rats' hemoglobin concentration at the regeneration stage

Group	Iron source	Additional iron content (ppm)	N	Hemoglobin concentration (g/dL)		Changes inhemoglobin concentration (g/dL)
				Beginning	End	
Group 1	ferrochel and Siwu extract	12	6	6.21±1.38	8.89±1.33[a]	2.68±0.57[a]
Group 2	ferrochel	12	6	5.87±0.86	8.02±0.81[a]	2.14±0.35[b]

Group 3	Siwu extract	0	6	6.20±0.86	6.14±1.59[b]	-0.07±0.46[c]

* The numbers in Table 3 stand for "mean ± standard deviation." Students' t test was used to statistically analyze the data, where $p < 0.05$ means there are significant differences. Where the letters marked in the same column differ, there are significant differences.

[0052] As shown in Table 3, hemoglobin concentration of rats with iron-deficiency anemia is about 6g/dL, and there are no significant differences among 3 groups. However, after taking different iron sources for two weeks, there are significant differences in hemoglobin concentrations of rats among different groups. The data show that taking Siwu extract alone (Group 3) does not improve hemoglobin formation. Although taking ferrochel alone (Group 2) can improve hemoglobin formation, the improvement of hemoglobin formation after taking the composition of ferrochel and Siwu extract (Group 1) has significant differences ($p<0.05$) compared to both taking ferrochel alone (Group 2) and taking Siwu extract alone (Group 3). The results show that the combination of ferrochel and the non-effective Siwu extract has an unexpected synergistic effect.

[0053] **Example 2:** Human Clinical Trial

[0054] A. Subjects:

[0055] The subjects in this example were females over 12 years old and were not menopausal. The subjects suffered from iron-deficiency anemia, where their hemoglobin concentrations were 8 - 12 g/dL and the concentrations of serum iron were lower than 12 μg/L. All of the subjects were not pregnant during the clinical trial.

[0056] B. Medicine:

[0057] The 50 ml aqueous solution of ferrochel and Siwu extract of the present invention (the composition of the present invention) used in this example was made by the following process. Dissolve Siwu extract powder and 50 mg of ferrochel powder in 50 ml water, in which the Siwu extract powder was made from 393.75 mg of *Angelica sinensis*, 393.75 mg of *Ligusticum wallichii*, 131.25 mg of *Paeonia lactiflora*, and 131.25 mg of *Rehmannia glutinos* (meaning that the four herbs were in a weight ratio of 3 : 3 : 1 : 1). Relative to the total weight of the composition of ferrochel and Siwu extract, the amount of ferrochel is about 5% - 10% by weight of the composition, for example, about 10%.

[0058] C. Experiment Design:

[0059] 1. Administration stage

[0060] All of the subjects took the abovementioned medicine for 12 weeks. Each subject drank 50 ml/bottle of the aqueous solution of the composition of the present invention, two bottles every day. Collect subjects' blood samples before and during administration stage (week 2, 4, 8, and 12) to check hemoglobin concentration, hemoglobin volume, ferritin concentration, concentration of serum iron, hematocrit, and the ratio of transferrin to ferritin.

[0061] 2. Post- administration stage

[0062] All of the subjects stopped taking the medicine after administration stage. Collect subjects' blood samples 4 weeks post-administration (week 16) to check hemoglobin concentration, hemoglobin volume, ferritin concentration, concentration of serum iron, hematocrit, and the ratio of transferrin to ferritin.

[0063] D. Results

[0064] As shown in FIG. 1, during the administration stage, hemoglobin concentration of subjects increased as the period of medicine intake increased. FIG. 1(A) shows that comparing with the average hemoglobin concentration before the medication stage, the average hemoglobin concentrations of the subjects measured every 2 weeks during the administration stage have statistically significant differences. Even though the subjects stopped taking the medicine after 12 weeks of the administration stage, the average hemoglobin concentrations of the subjects maintained in a high level. FIG. 1(B) shows the comparisons of the average hemoglobin concentration measured every 2 weeks during the medication stage compared to that of pre-administration. The differences are more obviously significant. (* means $p<0.05$, ** means $p<0.001$, and *** means $p<0.0001$). In addition, as checked other items in Table 4, hemoglobin volume, ferritin concentration, concentration of serum iron, and hematocrit at the end of the administration stage (week 12) and those at the end of the post-administration stage (week 16) all increased compared to those in pre-administration stage. Moreover, the ratio of transferrin to ferritin at the end of the administration stage (week 12) and the ratio at the end of the post-administration stage (week 16) both decreased compared to the ratio in pre-administration stage. The values of these factors all have significant differences ($p<0.0001$). The results above demonstrate that the composition of the present invention is effective in treating anemia, especially iron-deficiency anemia. On the other hand, as shown in VAS item of Table 4, the visual analogue score of pain at the end of the administration stage (week 12) is significantly improved compared to that in pre-administration stage, and the values have significant difference ($p=0.0004$).

Table 4 Results of human clinical trials

Items (normal range)	Value in pre-administration stage (SD)	Value at the end of the administration stage (week 12) (SD)		Value at the end of the post-administration medication stage (week 16) (SD)	
Hemoglobin concentration (12.0-16.0 g/dl)	9.81 (1.02)	12.14 (1.17)	P<0.0001	11.70 (1.45)	P<0.0001
Hemoglobin volume (81-99 fl)	72.81 (7.39)	82.48 (6.33)	P<0.0001	82.12 (6.93)	P<0.0001
Ferritin concentration (13-150 ng/dl)	4.85 (1.72)	13.75 (1.72)	P<0.0001	8.01 (1.88)	P<0.0001
Concentration of serum iron (50-175 ug/dl)	22.08 (1.82)	70.55 (2.33)	P<0.0001	34.76 (1.88)	P<0.0001
Hematocrit (37-47 %)	30.96 (2.61)	36.61 (3.09)	P<0.0001	35.17 (3.67)	P<0.0001
The ratio of transferrin to ferritin	5.12 (1.45)	2.57 (1.36)	P<0.0001	3.54 (1.50)	P<0.0001
Visual Analog Score of Pain	3.30 (2.98)	2.36 (2.57)	P=0.0004	2.23 (2.35)	P<0.0001

[0065] Based on the description herein, without further explanations, a person having ordinary skill in the art can apply the present invention to the broadest scope. Accordingly, the detailed description, the embodiments, and the claims of the present invention should be understood as for the purposes of demonstration instead of limitation in any way to the scope of the present invention.

CLAIMS

What is claimed is:

1. A synergistic composition for treating anemia or supplementing iron, comprising a combination of the following components:

(A) an extract of Siwu, the Siwu comprising *Angelica sinensis, Ligusticum wallichii, Paeonia lactiflora*, and *Rehmannia glutinosa*; and

(B) Ferrochel.

2. The synergistic composition of claim 1, wherein the Siwu comprises *Angelica sinensis, Ligusticum wallichii, Paeonia lactiflora,*and *Rehmannia glutinosa* in a weight ratio of 1-10:1-10:0.3-3:0.3-3.

3. The composition of claim 2, wherein the Siwu extract is made from *Angelica sinensis, Ligusticum wallichii, Paeonia lactiflora,* and *Rehmannia glutinosa* in a weight ratio of 3:3:1:1.

4. The synergistic composition of claim 1, wherein the Ferrochel is contained in an amount of 1% or more by total weight of the synergistic composition.

5. The synergistic composition of claim 4, wherein the Ferrochel is contained in an amount of 1% - 30% by total weight of the synergistic composition.

6. The synergistic composition of claim 5, wherein the Ferrochel is contained in an amount of 1% - 10% by total weight of the synergistic composition.

7. The synergistic composition of claim 1, which is a liquid formulation.

8. A medicament for treating anemia or supplementing iron, comprising:

a therapeutically effective amount of a synergistic composition according to any of claims 1 to 7; and

a pharmaceutically acceptable carrier.

9. The medicament of claim 8, wherein the anemia is iron-deficiency anemia.

10. The medicament of claim 8, which is effective in increasing blood hemoglobin concentration.

11. Use of a synergistic composition according to any of claims 1 to 7 in the manufacture of a medicament for treating anemia or supplementing iron.

12. The use of claim 11, wherein the anemia is iron-deficiency anemia.

13. The use of claim 11, wherein the medicament is effective in increasing blood hemoglobin concentration.