

[54] **METHOD FOR ADMINISTERING IRON AND OTHER METALS**

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[57] **ABSTRACT**

The basic objective here is to administer alpha iron crystals rectally to accomplish dramatic results like those obtainable by administering these crystals sublingually. In this way there may be accomplished more than is possible with iron preparations given parenterally, either because blood vessels are difficult to penetrate, or because of side effects, etc. Alpha iron crystals, particularly of small or sub micron size give superior results at a more rapid rate of absorption and result in a quicker rate of absorption resulting in clinical improvement much sooner. The rectal path is one way of administration where sublingual action may not be practical.

10 Claims, No Drawings

METHOD FOR ADMINISTERING IRON AND OTHER METALS

This invention relates to the administration of iron crystals rectally and to compositions for such purposes in view of the dramatic results that have been obtained in the utilization of such crystals sublingually. The rectal route is one way of internal administration of metals, particularly iron, when administration parenterally or under the tongue is not practical, or when the latter utilization is to be supplemented. Iron will be referred to as a preferred illustrative material.

Initially it should be kept in mind that rectal mucosa are physiologically different from that of the mouth mucosa and from the standpoint of the cleanliness of the rectal space. In emergency, the iron, for example, may be given without prior preparation, but in such cases much may be partially lost or rendered useless in the presence of the foreign matter present in the rectum.

Where the passage is to be cleansed, a simple enema until the fluid appears clear is desirable, though even here, too, solid or fluid may react with the crystals. If possible, following the enema, or series of appropriate enemas, there may be used a hydrogen peroxide enema. Such treatments are illustrative below.

Either before the peroxide or thereafter, the rectum may be treated with other agents, such as selected proteolytic enzymes to facilitate the removal of undesirable tissue present, such as dead or necrotic tissues from the mucosa layer. Thus, one may mix the crystals of iron when used, with a dry powder of, for example, a proteolytic enzyme, like trypsin, or chymotrypsin, or other enzyme obtained from other sources. Briefly, when the mucosa of the rectum is clean and free from debris, the effectiveness of the alpha iron crystals, for example, are by that much more adapted to use for the desired purposes and with increased effectiveness. It may be desirable first to illustrate types of compositions before considering their manners of utilization.

Composition and articles including metallic microparticles treated to be non-pyrophoric and methods of making and using the same are first described below. Because of the unique properties exhibited by such submicron size particles they may be used in and of themselves without admixture of other metals or non-metals but may be used desirably in admixture with other particles of larger size to which they will transmit unique properties carried over into articles made from such mixed compositions.

The metal powders set forth below are used in the present invention and are most desirably superfine powders of particle size of the order of particles of tobacco smoke, in that they are submicron in size, desirably of a range of from 0.01 to 0.1 microns, but sizes of about 0.01 to about 3 microns are useful for many purposes including particularly the range from about 0.05 to 1.0 micron.

While a wide variety of metal powders are included in the present invention most desirably they are solid metals of the transition element groups (e.g. whose inner electron shield is filled) and include manganese, chromium, cobalt, nickel, copper, iron, tungsten, molybdenum, zinc, tin and zirconium and mixtures thereof with one another or with larger particle pow-

ders of larger particle size heretofore available in the art, particularly macro size particles to which latter unique properties are communicated in such mixtures. Beryllium is also included.

In accordance with this invention, compositions for use as diagnostic and therapeutic agents are produced by using alpha iron crystals preferably of submicron size, particularly in size from 50 to 500 A.U. (angstrom units). These crystals may be injected into the blood circulatory system and they have the ability to pass through the smallest capillaries of the body, which are about 50,000 A.U. in diameter. Such fine crystals may thus be transported through the vascular system and concentrated at a particular point in any of the body organs by the aid of a magnetic field. The alpha iron crystals may thus be used to transport isotopic radiation or some adsorbed healing chemical to a particular place in the body. For example, these crystals may be alloyed with a radioactive element such as cobalt or uranium, or they may be coated with an adsorbed layer of a therapeutic agent, or such alpha iron crystals of sub-micron size may be used as such, for effects produced directly by the iron crystals which interact with specific constituents of the blood, for several reasons: the local magnetic fields surrounding a single-domain crystals may be substantially greater than heretofore obtainable with large iron particles; biocatalytic or enzymic activity may be increased due to the large specific surface and geometry of the submicron crystals; and because iron plays an essential role in the blood cycle and as such in the cellular metabolism of the entire body, these submicron iron crystals influence the iron kinetics and exhibit biocatalytic activity with an effect on tumor tissue and metabolism in brain tissues.

While the alpha iron particles of submicron size may be substituted for iron in any of the utilizations that have been employed with iron particles of substantially greater size, the submicron size particles lend themselves to new techniques of administering and utilizing them. For example, patients have been given up to 120 and more milligrams of the alpha iron by placing a composition containing such alpha iron particles of submicron size under the tongue or in a fecal passage. It was found that by this technique, not heretofore employed, a new phenomenon was exhibited in that an element in its metallic state may be transported from under the tongue into the blood and its effect found in the serum in a relatively short time or from the fecal passage in a somewhat longer time. Not only is this transport of iron effected in this way, but transport of other metals such as cobalt and copper in similar submicron size may be effected in the same way and simultaneously from a composition containing them. Similarly, alpha iron crystals of Fe⁵⁹ may be transported.

The following example will illustrate composition and technique of application as well as effects obtained. The composition consisted of the following components in parts by weight:

COMPOSITION I

10,000	granulated sugar (sucrose)
1,000	alpha iron crystals of sub-micron size
10	cobalt crystals of sub-micron size
1	copper crystals of sub-micron size

These materials were mixed together in the absence of air and filled into gelatin capsules, commonly used pharmaceutically, the dose being enough of the composition to contain about 40 milligrams of iron.

TREATMENT I

The patient was a six and a half year old boy suffering from a blood disease causing hemorrhages (Idiopathic Thrombocytopenic Purpura), the content of the capsule being placed under the tongue. After each administration within ten minutes, and more significantly, after one hour, there was a manifestation in the patient's blood. The serum iron increased by 70 percent. The course of recovery was remarkable.

The following chart summarizes a number of cases in each of which the treatment was carried out under clinical conditions exactly as described in Treatment No. 1 above with the identical composition of Example No. 1 administered under the tongue by the identical procedure as given in Par. 1 above; the tests being carried out by regular hospital personnel under the supervision and control of applicant, the composition having been made and completed by applicant:

No.	Patient	Sex	Age, yrs.	Fasting serum iron (pg./100 ml.), µg. percent	Time following dose						Total serum iron ×100	Case Dx	Remarks
					10 min.	20 min.	30 min.	60 min.	90 min.	180 min.			
1.....	R.W.	M.	6½	77	79	-----	-----	137	-----	-----	178	ITP	Same patient after treatment Hb increased by 1.5 g.
2.....	R.W.	M.	6½	166	-----	-----	-----	211	-----	-----	127	ITP	
3.....	LaM.	M.	70	95	102	108	-----	146	-----	-----	153.5	Cardiac	Muscular degenerative disease.
4.....	S.S.	M.	51	101	106	117	-----	142	-----	-----	140.5	Hypothyroid	
5.....	L.R.	F.	49	140	140	-----	-----	-----	159	133	113.5	Muscular degenerative disease.	
6.....	P.G.	F.	31	69	-----	-----	192	-----	204	-----	296	M.S.	Hb increased by 1.5 grams.
7.....	D.McC.	F.	40	67	-----	-----	118	-----	138	-----	206	Arth. degen. process	
8.....	K.	M.	50	112	-----	-----	-----	231	-----	-----	206	Pulm. pathology	

¹ Note fall.

NOTE.—Peripheral blood studies are given and each identified by the reference number of this chart.

General note how one may calculate the following:
The iron-porohyrin is 4 percent of the hemoglobin (hematin—C₃₄H₃₂N₄O₄Fe).
The globin portion of the hemoglobin is 96 percent.

By direct analysis there is 0.33 percent of iron in hemoglobin.

The average amount of hemoglobin in a human is 15 Grams per 100cc, hence

15 Gms × 0.336 equals 50 milligrams of iron per 100cc, or a total of about 3 grams of iron in the body.

Now in our data an increase of 1.5 grams of hemoglobin would amount to 5 milligrams increase of iron per 100cc of the total blood, or a total of entire blood about 300 milligrams. Each test consists of giving the patient the content of twice four capsules, each capsule containing about 40 milligrams of the alpha iron crystals, or a total of about 320 milligrams. Unless this is tested with tagged iron crystals it cannot be stated that complete absorption of the crystals takes place. But this is not an essential premise to explain the increase of 1.5 Grams of hemoglobin in about one hour. For if the crystals initiate or stimulate an immediate effect of erythropoiesis, then the total iron kinetics is improved and this might reflect in the final results. Again at this point clinical data is presented, and all the mechanisms proposed is only as a guide. The final step by step mechanism will have to wait until specific studies will be conducted. The data given are

taken from hospital records, the mechanism proposed is not mandatory, but serves a useful purpose to translate the results for more complex problems in the medical research program.

TABLE II

Oral Alpha Iron

Patient No.	Age	Dx	F.S.I.	280-400		After alpha Iron given 400 mg.					Time elapsed, hours
				TIBC µg. percent	A, per- cent SI/ TIBC	S.I.	TIBC	B, per- cent SI/ TIBC	B/A ratio		
1.....			58	425	13.647	142	280	50.714	3.718	4	
2.....			53	421	12.589	338	338	100	7.943	4	
3a.....			57	406	14.039	167	268	62.313	4.439	4	
3b.....			58	426	13.615	83	363	22.885	1.679	4	
4.....			50	583	8.5763	400	418	95.693	11.1578	4	
5.....			60	473	12.684	360	378	95.238	7.508	4	
6.....			50	524	9.541	269	361	74.5152	7.8092	4	
7.....			50	546	9.1575	280	417	91.127	9.951	4	
8.....			133	657	20.243	242	426	56.807	2.806	3	
9.....			33	474	6.96202	75	442	16.96	2.436	3	
10.....			25	425	5.88235	117	439	26.6514	4.5307	3	

TABLE III
Oral Alpha Iron

Patient	$\mu\text{g./100 ml.}$ fasting normal 70-180	$\mu\text{g./100 ml.}$ normal value 280-400	After alpha iron	
	Serum iron	UIBC	Serum iron	UIBC* (400 mg.)
1.----- A.D.	$58 \frac{58}{425} = 13.647\%$	367	$\left\{ \begin{array}{l} 1. 108 \quad 142 \\ 2. 142 \quad 280 \end{array} \right. = 50.714 \text{ (3.718)}$	$\left\{ \begin{array}{l} 220 \quad 1\frac{1}{2} \text{ hr.} \\ 138 \quad 4 \text{ hr.} \end{array} \right.$
2.----- E.R.	$53 \frac{53}{421} = 12.589\%$	368	$\left\{ \begin{array}{l} 1. 115 \quad 338 \\ 2. 338 \quad 338 \end{array} \right. = 100\% \text{ (7.943)}$	$\left\{ \begin{array}{l} 294 \quad 1\frac{1}{2} \text{ hr.} \\ 0 \quad 4 \text{ hr.} \end{array} \right.$
3 ^a ----- C.P.	$57 \frac{57}{406} = 14.039\%$	349	$\left\{ \begin{array}{l} 1. 167 \quad 167 \\ 2. 167 \quad 268 \end{array} \right. = 62.313 \text{ (4.439)}$	$\left\{ \begin{array}{l} 294 \quad 1\frac{1}{2} \text{ hr.} \\ 101 \quad 4 \text{ hr.} \end{array} \right.$
3 ^b ----- C.P.	$58 \frac{58}{426} = 13.615\%$	368	$\left\{ \begin{array}{l} 1. 83 \quad 83 \\ 2. 83 \quad 363 \end{array} \right. = 22.865\% \text{ (1.679)}$	$\left\{ \begin{array}{l} 211 \quad 1\frac{1}{2} \text{ hr.}^2 \\ 280 \quad 4 \text{ hr.}^3 \\ 92 \quad 2 \text{ hr.} \end{array} \right.$
4.----- F.K.	$50 \frac{50}{583} = 8.5763\%$	533	$\left\{ \begin{array}{l} 1. 400 \quad 400 \\ 2. 400 \quad 418 \end{array} \right. = 95.693\% \text{ (11.1578)}$	$\left\{ \begin{array}{l} 18 \quad 4 \text{ hr.} \\ 180 \quad 2 \text{ hr.} \end{array} \right.$
5.----- C.M.	$60 \frac{60}{473} = 12.684\%$	413	$\left\{ \begin{array}{l} 1. 210 \quad 360 \\ 2. 360 \quad 378 \end{array} \right. = 95.238\% \text{ (7.508)}$	$\left\{ \begin{array}{l} 18 \quad 4 \text{ hr.} \\ 276 \quad 2 \text{ hr.} \end{array} \right.$
6.----- M.H.	$50 \frac{50}{524} = 9.5419\%$	474	$\left\{ \begin{array}{l} 1. 200 \quad 269 \\ 2. 269 \quad 361 \end{array} \right. = 74.5152 \text{ (7.8902)}$	$\left\{ \begin{array}{l} 92 \quad 4 \text{ hr.} \\ 92 \quad 2 \text{ hr.} \end{array} \right.$
7.----- M.F.	$50 \frac{50}{546} = 9.1575\%$	496	$\left\{ \begin{array}{l} 1. 300 \quad 380 \\ 2. 380 \quad 417 \end{array} \right. = 91.127\% \text{ (9.951)}$	$\left\{ \begin{array}{l} 37 \quad 4 \text{ hr.} \\ 377 \quad 1 \text{ hr.} \end{array} \right.$
8.----- B.	$133 \frac{133}{657} = 20.243\%$ (sample hemolyzed)	524	$\left\{ \begin{array}{l} 1. 133 \quad 242 \\ 2. 242 \quad 426 \end{array} \right. = 56.807 \text{ (2.806)}$	$\left\{ \begin{array}{l} 184 \quad 3 \text{ hr.} \\ 404 \quad 1 \text{ hr.} \end{array} \right.$
9.----- S.	$33 \frac{33}{474} = 6.96202\%$	441	$\left\{ \begin{array}{l} 1. 58 \quad 75 \\ 2. 75 \quad 442 \end{array} \right. = 16.96\% \text{ (2.936)}$	$\left\{ \begin{array}{l} 367 \quad 3 \text{ hr.} \\ 349 \quad 1 \text{ hr.} \end{array} \right.$
10.----- P.	$25 \frac{25}{425} = 5.88235$	400	$\left\{ \begin{array}{l} 1. 117 \quad 117 \\ 2. 117 \quad 439 \end{array} \right. = 26.6514 \text{ (4.5307)}$	$\left\{ \begin{array}{l} 622 \quad 3 \text{ hr.} \end{array} \right.$

¹ + = 280. ² Saliva collected. ³ Total Fe = 215 mg.

TABLE IV
Rectal Alpha Iron

Patient No.	Age	Dx	F.S.I.	After alpha iron given 400 mg.						Time elapsed, hours
				280-400 TIBC $\mu\text{g.}$ percent	A, percent SI/ TIBC	F.S.I.	TIBC	B, percent SI/ TIBC	B/A ratio	
1.-----			31	481	6.44	108	476	22.689	3.5231	3
2.-----			31	441	7.029	54	434	12.442	1.77	3
3.-----			54	523	10.325	138	488	28.278	2.738	5
4.-----			69	483	14.285	130	440	29.54	2.0679	5
5.-----						50	399	12.531		5

That in no case at any time during or as a result of the treatments reported was any adverse effect noted with respect to the treatment, that in all cases a marked increase in serum iron was noted, and in all cases the rapid increase in serum iron was noteworthy.

Desirably the alpha iron crystals of sub-micron size are mixed with a pharmaceutically acceptable non-toxic carrier, either solid or liquid. Sugar (sucrose) finely powdered may thus be used but other sugars as well as starches and any other pharmaceutically used carrier materials may be employed, solid or liquid, depending on the manner of utilization and the purposes for which employed. Proportions of the components may vary widely. In the illustrative composition given about, the cobalt and copper are exemplary of pharmaceutically acceptable adjuvants for the iron. While encapsulation has been illustrated with gelatine capsules, any other type of pharmaceutically acceptable capsule may be used provided it is inert to the composition and its components, and compositions may be tableted or formed into other forms. The compositions may be formulated for topical application and in other

types and forms of vehicles such as in liquid vehicles such as pharmaceutically acceptable petroleum fractions such as the white oils.

The metal powders of the present invention are most desirably superfine powders of particle size of tobacco smoke in that they are sub-micron in size, desirably of a range of from 0.01 to 0.1 microns, but sizes of about 0.01 to about 3 microns are useful for many purposes including particularly the range from about 0.05 to 1.0 "strong dendrites" with thick branches; "filled in dendrites" where the branches are even thicker, and finally, there is a form of the iron referred to as "platelets," which are useful for making magnetic cores.

As illustrative, reference may be made to colloidal copper crystals in the form of an aggregate of tiny cubes about one-third micron on a side plus a distribution of smaller copper particles about one-tenth micron on a side. There may also be a needle-like, or nodular, rod, generally a distribution of copper needles, rods, and particles is present. Such morphologically different forms of copper crystals have not been reported heretofore.

The crystalline architecture of the single dendritic iron particles has an important bearing on the ultimate physical properties and applications of the powder. The basic crystallite building unit appears to be a rhombic dodecahedron. The dodecahedron crystal is made up, in situ, of unit cubic cells each about 2.88° A per side. The ultimate crystallites may be single 100 to 500 A.U. rhombic dodecahedrons. The crystallites develop corner to corner along their diagonals to form a needle or rod growing in the direction perpendicular to the (111) planes of the cube. They form a single monolithic crystal. Under certain conditions nodular rods are formed when small crystallites begin to develop at the corners. Under other conditions these side-arms or secondaries develop even further, and a dendrite is formed. There are three secondaries at any node, separated by 120°, and all grow toward the growing tip at an angle of 70.5° to the direction of primary growth.

those of bulk materials. At the same time, of course, compacts of the particles have properties which are a function of the particles of which the compacts are composed. The particles of this invention in many cases measure less than 50 atoms across, approaching in this case atomic dimensions.

While many of the properties of the superfine powders of the present invention are characteristics of the various metals, other properties, such as magnetic properties, may be those of only one, or a limited class of metals. Magnetic properties may be illustrated by iron powders here. The unusually good magnetic properties are directly associated with the shape and size of the individual particles. As an exemplary illustration of magnetic properties of iron samples of the present invention the following results of an areal analysis of the particles of fine iron samples of the present invention, is summarized in Table I below.

TABLE I
Areal Analysis of Alpha Iron Particles

Sample	LCF				HCF				Relative coercive force (1033=1/100)			
	FID	DEN	WD	PL	P	NR	N	HCF/LCF	(l)/(μ)	(d)/(μ)	(l)/(d)	
5401-----	24	17	156	0	0	317	77	2.0	0.36	0.09	4.0	163
1033-1-----	59	188	94	0	10	189	69	0.7	0.39	0.16	2.5	100
1042-----	94	46	64	0	0	182	60	1.2	0.74	0.23	3.2	82
1078-----	132	24	93	6	5	124	29	0.6	1.27	0.39	3.2	38
1431-1-----	75	4	11	112	78	55	7	0.2	0.91	0.28	3.2	24

Another form of the alpha iron crystals has been referred to as a "platelet." Many of these hexagonal sheets, instead of appearing smooth and structureless, are dendritic in two dimensions, with a skeleton of growth along directions parallel to their six sides. These platelet crystals are identifiable as alpha iron by selected area diffraction. They may demonstrate the Kikuchi N pattern with Kikuchi lines for a platelet 80° A. (0.008 μ) or thinner.

The surface area per unit mass (or specific surface) is very large for metal crystals of this invention. It ranges from about 16 square meters to more than 200 square meters per gram of iron powder. This means that any process which affects the bulk of the material whose rate depends on the exposed surface area will be markedly increased as the particle size decreases. This has been shown in alloying, compacting, and coreacting the elemental powder of this invention with non-metallic materials such as nylon, butyl rubber, natural rubber, or with other metals. Its rate of oxidation is rapid and it is therefore highly pyrophoric. For active elements of sizes smaller than a micron — such as the iron powder here — the energy associated with the surface becomes an important part of the total.

The finer the powder, the greater its chemical reactivity. This is an important factor in the physio-chemical reaction between the iron powder here and other metallic and non-metallic reacting matrices, such as copper.

The microscopic dimensions of these particles make for great differences in their properties when compared with macroscopic, large particles of the same element. As a solid metal behaves very differently from the atoms of which it is composed, so these fine particles have characteristics which are very different from

Where L.C.F. = Lower Coercive Force; H.C.F. = Higher Coercive Force; F.I.D. = Filled-in Dendrites; DEN = Dendrites; W.D. = weak dendrites; PL = Platelets; P = Discrete Particles; N.R. = Nodular Rods; N = Needles.

Here it is apparent that in samples of higher coercive force the (LCF) class of particles are relatively less abundant than the (HCF) particles, and the agreement is direct, except for sample 1042 where particle size itself has entered to depress the coercive force. Sample 5401 is excellent in both aspects of morphology and has a high coercive force as well. In the areal analysis it should be emphasized that the results are quoted for the type of mounting and sample.

The following results illustrate certain properties of metals of the present invention concerning tensile strength and ductility after sintering for some iron powders of the present invention.

TABLE II

Iron Powder Type	Sintered Density gm/cc	Tensile Strength psi	Elongation % in 1 inch
Freeman No. 1	7.27	42,200	29
Freeman No. 13	7.22	80,000	4
Freeman No. 13A	7.89	116,000	3

Formulas 1, 13, and 13A refer respectively to pure iron, iron with 5 percent copper, and iron with 15 percent copper. Attention is called to the unusual densities, tensile strength, and elongations exhibited by the powders of this invention.

Data on the density versus the compacting pressure for these fine iron crystals is supplied. At 30 tsi, the green density is about 4.08 g/cc; at 40 tsi, about 4.4 g/cc; at 50, 4.6 g/cc; and at 60 tsi, 4.78 g/cc.

In general uses for the powders of this invention are inspired by the extremely fine particle size, high specific surface, free energy and apparently high diffusion potentials. These powders may be utilized most profitably to permit material compositions and structures which are unavailable or of poor quality from other metals.

The method of administering the alpha iron crystals to the sublingual mucosa may be as follows. Thus a patient may be given the content of four capsules of alpha iron crystals, each containing 40 milligrams, or a total of 160 milligrams were given at zero times. Serum iron was taken every ten, twenty, or thirty minutes. At the end of the first hour, another 160 milligrams of alpha iron were given and serum iron studies were determined every half hour as indicated. Two patients of this group were studied for their hemoglobin and in each case there was an increase of 1.5 grams of hemoglobin within three hours from zero time. (This accounts for 93.75 percent of the alpha iron given.)

In a second group consisting of ten patients, each was given 400 milligrams of alpha iron crystals at zero time, at which time serum iron and unsaturated iron binding capacity were determined, the serum iron and unsaturated iron binding capacity were taken as indicated on Table II and III. In this second group, patients had difficulty in keeping the alpha iron crystals under the tongue, and 215 milligrams were recovered from the saliva out of the 400 given, or 53.75 percent. In the table, the iron saturation factor was determined at zero time and at the indicated time lapse of four hours in seven cases and of three hours in the remaining three cases. It is usually accepted that the normal iron saturation factor is about 30 percent but all the cases were far below this normal value, except in one case (No. 8) where the blood sample was hemolyzed and the fasting serum iron and UIBC not accepted as valid. In each case the iron saturation factor rose manifold except in case 10, where the UIBC was still high. One can only conjecture that this patient had an intervening factor. By giving the iron crystals rectally, better study purposes are achieved.

The results of the first experiment with rectal administration were:

	1 hr.	2 hrs.	3 hrs.	4 hrs.
Serum Iron	40 ug%	40 ug%	40 ug%	50 ug%
FeBC	423 ug%	423 ug%	423 ug%	377 ug%

The rate of adsorption was found to be much slower rectally; after 4 hours an effect of about 15 percent was noted.

TABLE 2
RECTAL ALPHA IRON

Pat- ients	Fasting		After Alpha Iron (400Mg) given		
	Serum Iron	UIBC	Serum Iron	UIBC	
1. P.H.	31	450	77 92 108	423 395 368	1 hr. 2 hrs. 3 hrs.
2. C.M.	31	410	31 54 54	370 390 380	1 hr. 2 hrs. 3 hrs.

3. R.	54	469	50 46 138	561 505 350	1 hr. 3 hrs. 5 hrs.
4. C.	69	414	92 131 130	368 312 310	1 hr. 3 hrs. 5 hrs.
5. B.			31 46 50	441 404 349	1 hr. 3 hrs. 5 hrs.

UIBC = unsaturated iron binding capacity

all units above are in micrograms %, example 31=31ug%

Comment: fasting serum iron in ug% after given alpha iron increases, as seen in the above chart. The unsaturated iron binding capacity after giving alpha iron reduces in quantity, indicating that there was an increase in the binding of iron by the betaglobulin, this means that the carrier globulin of the iron is capable of feeding the bone marrow where the red cells are manufactured, and on the occasions tested it appears that the hemoglobin also increases. This is really phenomenal, to produce results in such short a period of time.

The results were tabulated in Table 2. Iron saturation factors of the fasting examples were very low and in each case this factor was increased by a factor of two or better. It is thus suggested that the rectal route in cases where the oral route is not satisfactory, offers a good, useful alternative.

What has been set forth above presents a new hematonic agent for iron deficient anemias, an elemental iron in the form of alpha iron crystals, possessing very high volume energy as compared with similar iron particles of the same size. This is attributed to the unique crystalline structure of these iron crystals, as it is composed of crystallites 2.8 angstrom units in diameter and fashioned as rhombic dodecahedrons which impart the unusual surface and volume energy, and because of its many geometric structures, has many declivities, crevices, points, corners, and planes all contributing to its volume energy and high adsorptive properties, which is basis for their bio-chemical and biomagnetic activities. It must have the correct geometric spacial relationship to the B₁ globulin, its chelating substrate. Because of the higher magnetic interaction of the alpha iron crystals in the transferrin a more efficient coordinating bonding is anticipated and with all the subsequent steps in the ferrokinesis. It is believed that it should lead to many useful applications in medicine. Otherwise, the data of the cases and the results are self-explanatory with an additional comment that the alpha iron crystals are utilized selectively by the B₁ globulin and the system need not be overloaded as is the case with many other iron preparations. In addition, there are no toxic effects as is the case with injectable iron, often when given in doses as low as 8 milligrams of intravenous iron salt (inducing toxic reaction in the blood).

The metal powder as obtained commercially may be washed with any of various solvents or combinations. Most frequently the powder is first washed with deionized or distilled water, followed by an alcohol and/or acetone wash to remove water and finally washed with benzene in which the powder may be stored without appreciable oxidation especially if it is kept under an inert atmosphere.

For some purposes, the powder may be washed with a dilute solution of a sequestering agent prior to the

water wash. Such sequestering agents are sold commercially under the trade name of "Versene" by Bersworth Chemical Co., and exemplified by sodium ethylenediamine tetracetate. Another suitable sequestering agent is sold commercially under the trade name "Permaclear 80." Other materials which can be used are ammonium chloride, sodium tetrphosphate and the like. Sequestering agents can also be employed at other stages in the washing procedure using solvents other than water, such as alkylene diamines, amides, ketones, e.g., acetone, and the like. A particularly preferred solution of this type is a dilute solution of "Permaclear 80" in water. Washing the powders with these solutions increases their purity from 25 percent to over 50 percent. Sequestering agents can be used in other stages in the washing procedure, and when non-solvents are used such as diamine, amides, ketones and the like.

The metallic particles of sub-micron size have wide utilization medically and diagnostically. Thus the alpha iron crystals may be introduced into the body and magnetic field applied to direct the particles to a point in the body for clinical purposes and other purposes as, for example, a tool in biochemistry, both with techniques that have been used with larger iron particles but more ready control and manipulation is possible with the very fine particles and also entirely new functions and results are obtainable that were not heretofore obtainable with larger particles or other crystalline configurations. As illustrative of such functions and results, Treatment I given above may be noted. As indicative of old methods applied to the alpha iron particles of sub-micron size the following is noted.

The magnetism may be used for separation of white blood cells by a method whereby the alpha iron particles of submicron size are coated (dusted), for example, with starch; the coated particles are injected into the blood; the white blood cells will absorb such coated iron particle; and they then can be separated in a highly inhomogeneous magnetic field of about 20,000 gauss maximum intensity at the center.

Magnetic resonance may be utilized so that the alpha iron particles or sub-micron size become available as a tool in biochemical and medical analysis, for example, in the study of the recombination rate of free radicals which have been induced by radiation in living cells.

Also these alpha iron crystals of sub-micron size may be used with a superimposed magnetic field, such field being a known device for use with other procedures, to facilitate the separation of amino-acids and proteins; also in electro-phoretic methods. By the latter it has been possible to identify a large number of hemoglobins.

In some cases it has been possible to relate a specific abnormal hemoglobin to a specific blood disease. Such investigations suggest a means of obtaining remissions in some of the blood dyscrasias.

Biological effects by magnetic fields upon living organs and animals employing the high magnetic properties of the alpha iron crystals of sub-micron size particles are manifested. Several groups of mice were selected for magnetic experiments. One group were presumed to be normal in all known respects. Another group were chosen to represent those which develop cancer spontaneously. A third group were inoculated with known cancer agents. A fourth group were used to

study the effect of magnetic treatment upon animals which were later to be irradiated by X-rays or Cobalt — 60.

All of the above groups were kept from one to four weeks in a magnetic field of 3,000 to 6,000 gauss. Each group was compared for statistical significance with controlled groups. Effects noted include: body temperature drop persisting after removal of the field for one year; substantially lesser food consumption particularly after removal from field; greater activity and younger appearance after the magnetic treatment; disappearance of estrus cycle in field; resorption of embryos in pregnant mice; decrease in white blood cell count in the magnetic field, but after removal from the field a large increase above normal values; etc.

There is therefore the aspect of increased activity of magnetism in medicinal application by utilization of the alpha iron crystals of sub-micron size as centers for magnetism, in investigations in basic biochemical problems, and in magnetic analysis in diagnosis. The treatment examples given above are indicative of the new techniques of application that thus become possible as well as the wholly unique results obtainable in the treatment of disease. Such applications include the ability to use much higher magnetic fields than have heretofore been possible.

Having set forth the invention what is claimed is:

1. A method of treating a human iron deficiency comprising administering rectally or sublingually an effective amount of alpha-iron particles of from about 0.01 to about 1 micron so that the alpha-iron particles are rapidly adsorbed and transported via the blood stream to the iron deficient blood-forming system of the human body.

2. The method of claim 1 wherein the alpha-iron particles are in a palatable non-toxic vehicle and the administering is done sublingually.

3. The method of claim 1 wherein alpha-iron particles are in a non-toxic vehicle and the administering is done rectally.

4. The method of claim 1 wherein a portion of the alpha-iron particles is replaced with a minor amount of polyvalent metal particles selected from the group consisting of copper and cobalt and mixtures thereof each of said particles being from about 0.01 to about 1 micron and the administering is done sublingually.

5. The method of claim 1 wherein a portion of the alpha-iron particles is replaced with a minor amount of polyvalent metal particles selected from the group consisting of copper and cobalt and mixtures thereof each of said particles being from about 0.01 to about 1 micron and the administering is done rectally.

6. The method of claim 4 wherein the mixture is a mixture of alpha-iron and cobalt with alpha-iron being in the predominant amount.

7. The method of claim 4 wherein the mixture is a mixture of alpha-iron and copper.

8. The method of claim 5 wherein the mixture is a mixture of alpha-iron and cobalt.

9. The method of claim 5 wherein the mixture is a mixture of alpha-iron and copper.

10. The method of claim 1 wherein the administering is done rectally the metal particles are a mixture of alpha-iron, cobalt and copper with the iron being in predominant amounts each having particle size of from about 0.01 to about 1 micron and the location of the metal mixture in the internal systems organs and areas is controlled and located magnetically.