

MIXTURE OF IRON AND COPPER SALTS MASKING METTALIC TASTE

The present invention relates to a novel oral composition without metallic taste comprising an iron source and/or a copper source, its process for preparation and its use for balancing the provision of iron as nutritional supplement.

- 5 Iron is essential to most life forms and to normal human physiology. Iron is an integral part of many proteins and enzymes that maintain good health. In humans, iron is an essential component of proteins involved in oxygen transport (Dallman PR. *Biochemical basis for the manifestations of iron deficiency*. Annu Rev Nutr **1986**, 6, 13-40). It is also essential for the regulation of cell growth and differentiation (Andrews NC. *Disorders of iron metabolism*. N Engl J Med **1999**, 341, 1986-
10 95). A deficiency of iron limits oxygen delivery to cells, resulting in fatigue, poor work performance, and decreased immunity (Haas JD, Brownlie T 4th. *Iron deficiency and reduced work capacity: a critical review of the research to determine a causal relationship*. J Nutr **2001**, 131, 691S-6S, Bhaskaram P. *Immunobiology of mild micronutrient deficiencies*. Br J Nutr **2001**, 85, S75-80).
- 15 Several oral compositions are known for the use as nutritional or dietary supplement containing iron. Known compositions are e.g. multi-vitamin and mineral supplements or oral dosage forms containing a higher dose of iron for treating iron deficiency symptoms. However, in order to avoid a bad metallic taste the amount of iron is limited and the use of a complex and expensive taste masking technology such as coating of iron containing granules or tablets, admixing taste masking
20 flavours, use of capsules is necessary.

The object of the present invention is to provide an alternative oral composition containing an iron source and/or a copper source having no metallic bad taste and avoiding a complex and expensive taste masking technology.

- 25 Surprisingly it is found that a metallic bad taste of the composition according to the present invention can be avoided.

Subject of the present invention is an oral composition comprising an iron source, selected from the group consisting of iron polymaltose, carbonyl iron, and/or copper citrate as copper source. The oral composition according to the invention has not a metallic bad taste, in particular aftertaste.

The iron source iron polymaltose is a water soluble macromolecular complex of polynuclear iron (III) hydroxide and partially hydrolised dextrin (polymaltose). Iron polymaltose is known and described in Martindale 32nd edition, 12864-h, p 1349.

5 The iron source carbonyl iron is a form of special purified elemental iron having a mean particle size of less than 7 μm . Carbonyl iron is known under the CAS number 7439-89-6, BP73.

According to the present invention copper citrate includes any kind of solvate such as hydrates. Preferably the hemipentahydrate of copper citrate is used.

The amount of the iron source in the composition according to the invention is from 1 to 60 mg, preferably, from 2 to 20 mg based on iron.

10 The amount of the copper citrate in the composition according to the invention is from 0.1 to 2 mg, preferably 0.3 to 1.1 mg based on copper.

In particular the ratio between iron and copper in the composition is from 1:2 to 50:1, preferably from 5:1 to 25:1, most from 10:1 to 20:1. "Ratio" means for the purposes of the invention the ratio by weight of the individual components based on iron and copper.

15 The composition according to the invention can comprise further active ingredients such as vitamins and minerals. Vitamins include, but are not limited to, vitamin A, beta carotene, vitamin C (ascorbic acid), vitamin D3 (cholecalciferol), vitamin E (tocopherol acetate), vitamin B1 (thiamine), vitamin B2 (riboflavin), nicotinamide, vitamin B5 (panthothenic acid), vitamin B6 (pyridoxine), folic acid, vitamin B12 (cyanocobalamin), vitamin K1 and biotin. Minerals include,
20 but are not limited to, calcium salts such as calcium carbonate, calcium phosphate, calcium glycerophosphate; magnesium salts such as magnesium phosphate or magnesium oxide; zinc salts such as zinc citrate; selenium salts such as sodium selenate; potassium iodide; manganese salts such as manganese sulphate; molybdate salts such as sodium molybdate; chrom salts such as chromium chloride; sodium chloride and potassium chloride.

25 Furthermore the composition according to the invention can also comprise in addition iron fumarate 60% Descote. A preferred composition comprises copper citrate and iron fumarate 60% Descote.

Iron fumarate 60% Descote contents 60% iron fumarate coated with 40% mono- and di-glycerides (Merck index 12th edition, p4087, ref 4094, Martindale 32nd edition, p 1339 ref 5054).

Subject of the present invention is an oral composition comprising an iron source, selected from the group consisting of iron polymaltose and carbonyl iron, and/or copper citrate and optionally at least one further mineral and/or vitamin.

5 The composition according to the invention is administered orally one or more, preferably up to three, more preferably up to two times per day. With each administration the number of dosage forms taken in at the same time should not exceed two.

The composition according to the present invention can be used as nutritional supplement or as dietary supplement for balancing the supply of iron in a patient. A patient, for the purpose of this invention, is a mammal, including a human.

10 Nevertheless, it may in some cases be advantageous to deviate from the amounts specified, depending on body weight, individual behaviour toward the active ingredient, type of preparation and time or interval over which the administration is effected. For instance, less than the aforementioned minimum amounts may be sufficient in some cases, while the upper limit specified has to be exceeded in other cases.

15 The composition according to the invention comprises suitable administration forms which deliver the compound of the invention and which include, but are not limited to, tablets, tablets which disintegrate rapidly in the oral cavity (orodispersible tablets), powders, sachets, granules, pellets, chewable tablets, chewing gums, dispersible tablets, effervescent compositions such as for example effervescent tablets or effervescent granules, liquids, solutions, emulsions, gels, syrups or
20 drops.

Preference is given to tablets, granules, orodispersible tablets, chewable tablets, chewing gums, dispersible tablets, effervescent tablets and effervescent granules. More preferably the application forms are chewable tablets, orodispersible tablets, chewing gums, dispersible tablets, effervescent tablets and effervescent granules.

25 Ingredients of the oral dosage forms are those which are accepted for pharmaceuticals and nutritional supplements and physiologically unobjectionable, for example: as fillers cellulose derivatives (e.g. microcrystalline cellulose), sugars (e.g. lactose), sugar alcohols (e.g. mannitol, sorbitol), inorganic fillers (e.g. calcium phosphates), binders (e.g. polyvinylpyrrolidone, gelatin, starch derivatives and cellulose derivatives), and all other excipients required to produce
30 formulations of pharmaceuticals and nutritional supplements of the desired properties, e.g. lubricants (magnesium stearate), e.g. disintegrants (e.g. crosslinked polyvinylpyrrolidone, sodium carboxymethylcellulose), e.g. wetting agents (e.g. sodium lauryl sulphate), e.g. release-slowing

agents (e.g. cellulose derivatives, polyacrylic acid derivatives), e.g. stabilizers, e.g. sweeteners, e.g. antioxidants, e.g. preservatives e.g. flavourings, e.g. coloured pigments, e.g. effervescent couples preferably citric acid as acid component and sodium carbonate and/or sodium hydrogen carbonate as basic component).

- 5 Liquid formulations are likewise produced by a standard method using excipients which are usual for pharmaceuticals and nutritional supplements and contain the active ingredients either dissolved or suspended. Typical administration volumes of these pharmaceutical and nutritional supplement preparations are 1 to 10 ml. Examples of excipients in these liquid formulations are: solvents (e.g. water, alcohol, natural and synthetic oils, e.g. medium chain-link triglycerides), solubilizers (e.g. glycerol, glycol derivatives), wetting agents (e.g. polysorbate, sodium lauryl sulphate), and further
10 excipients required to produce formulations of pharmaceuticals and nutritional supplements of the desired properties, e.g. viscosity-increasing agents, e.g. pH-correcting agents, e.g. sweeteners and flavourings, e.g. antioxidants, e.g. stabilizers, e.g. preservatives.

- Excipients for pharmaceuticals and nutritional supplements familiar to the skilled person are also
15 described for example in the following handbook: "Handbook of Pharmaceutical Excipients", Wade, A. & Weller, P.J., American Pharmaceutical Association, Washington, 2nd edition 1994.

- The dosage forms mentioned herein are produced by general standard processes. E.g. Tablets or chewable tablets can be produced by mixing and/or granulating the active ingredients together with the excipients to form a blend which is finally pressed to tablets. Optionally different blends
20 containing different ingredients and excipients can be premixed and combined to a final blend which is then pressed to tablets. In the case of an effervescent formulation the acid/base couple can be add e.g. to final blend or the acid and the base are added at different times to the blend. Also the base and the acid can be added to different blends which are finally combined.

- Advantage of the composition of the present invention is that for the preparation of the
25 composition a complex and expensive taste masking technology known in the prior art such as coating of tablets or coating of granules or putting the iron component into a capsule is not needed. The composition of the present invention can be prepared by simple and well-known standard procedures. Another well-known taste masking method is the addition of flavours in order to cover and mask the bad taste. This taste masking method is normally restricted to only a few applicable
30 flavours which have to be selected in each case. However, flavouring ingredients are not needed for taste masking in the composition of the present invention.

Subject of the present invention is an oral composition comprising an iron source, selected from the group consisting of iron polymaltose and carbonyl iron, and copper citrate as copper source

which has no metallic taste in particular after taste and which is not a coated tablet, coated granule or capsule.

Subject of the present invention is an oral composition comprising an iron source, selected from the group consisting of iron polymaltose and carbonyl iron, and copper citrate as copper source
5 and optionally at least one further mineral and/or vitamin wherein the composition has no metallic taste and is not a coated tablet, coated granule or capsule.

Preference is given to a fast disintegrating orodispersible tablet. The disintegration time is less equal than 100 sec., preferably less equal than 80 sec.

Examples:**Example 1:**

Chewable tablet		Tablet weight 1.230 g	
Active ingredients	Amount based on the active ingredient [mg]	Form of the active ingredient	Amount of the form of the active ingredient [mg]
vit A	400	vitamin A palmitate 100000 iu/g	13,33
vit C	30	ascorbic acid	30
Vit D3	2,5	cholecalciferol 100000 IU/g	0,8
vit E	5	tocopherol acetate 50% CWS/S	14
thiamin (B1)	1,05	thiamin nitrate 33% Rocoat	3,9
riboflavin (B2)	1,2	riboflavine 33% Rocoat	3,6
nicotinamide (PP)	13,5	nicotinamide	13,5
pantothenic acid (B5)	3	calcium pantothenate	3,26
pyridoxine (B6)	1,5	pyridoxine hydrochloride 33% Rocoat	5,46
folic acid	150	folic acid 10% trituration	1,5
Cyanocobalamin (B12)	0,75	dry vit B12 0,1% WS	0,75
biotin	75	biotin 1% trituration	7,5
calcium	60	calcium carbonate DCCS90L	166,53
magnesium	25	magnesium oxide	41,45
phosphorus			
iron	4	Carbonyl iron	4,08
zinc	3,75	Zinc citrate trihydrate	12,02
iodine	37,5	potassium iodide 5% trituration	0,75
selenium	25	sodium selenate anhydrous 1% trituration	2,5
copper	0,45	copper citrate 2,5 H ₂ O	1,28
manganese	0,9	manganese sulfate monohydrate	2,77
molybdenum	22,5	sodium molybdate dihydrate 1% trituration	2,25
chromium	12,5	chromic chloride hexahydrate 1% trituration	1,25

Example 2:

Chewable tablet		Tablet weight 1.230 g	
Active ingredients	Amount based on the active ingredient [mg]	Form of the active ingredient	Amount of the form of the active ingredient [mg]
vit A	400	vitamin A palmitate 100000 iu/g	13,33
vit C	30	ascorbic acid	30
Vit D3	2,5	cholecalciferol 100000 IU/g	0,8
vit E	5	tocopherol acetate 50% CWS/S	14
thiamin (B1)	1,05	thiamin nitrate 33% Rocoat	3,9
riboflavin (B2)	1,2	riboflavine 33% Rocoat	3,6
nicotinamide (PP)	13,5	nicotinamide	13,5
pantothenic acid (B5)	3	calcium pantothenate	3,26
pyridoxine (B6)	1,5	pyridoxine hydrochloride 33% Rocoat	5,46
folic acid	150	folic acid 10% trituration	1,5
Cyanocobalamin (B12)	0,75	dry vit B12 0,1% WS	0,75
biotin	75	biotin 1% trituration	7,5
calcium	60	calcium carbonate DCCS90L	166,53
magnesium	25	magnesium oxide	41,45
phosphorus			
iron	4	iron polymaltose	8,8
zinc	3,75	Zinc citrate trihydrate	12,02
iodine	37,5	potassium iodide 5% trituration	0,75
selenium	25	sodium selenate anhydrous 1% trituration	2,5
copper	0,45	copper citrate 2,5 H ₂ O	1,28
manganese	0,9	manganese sulfate monohydrate	2,77
molybdenum	22,5	sodium molybdate dihydrate 1% trituration	2,25
chromium	12,5	chromic chloride hexahydrate 1% trituration	1,25

Further excipients can be added to example 1 or 2:

excipients	Amount [mg]
xylitol	75
talc	50
anhydrous citric acid	20
magnesium stearate	10
orange flavour	10
Passion fruit flavour	5
aspartam	5
sucralose	1,5
iron oxide	3

Example 3:

Effervescent tablet			
Active ingredients	Amount based on the active ingredient [mg]	Form of the active ingredient	Amount of the form of the active ingredient [mg]
vit A	595	vitamin A palmitate 100000 iu/g	13,33
beta caroten	0,63	betatab 10%E	0,63
vit C	180	ascorbic acid	30
Vit D3	5	cholecalciferol 100000 IU/g	0,8
vit E	10	tocopherol acetate 50% CWS/F	14
vit K	0,03	vitamin K1 5% SD	
thiamin (B1)	4,2	thiamin phosphate	3,9
riboflavin (B2)	4,8	riboflavine phosphate	3,6
nicotinamide (PP)	54	nicotinamide	13,5
pantothenic acid (B5)	18	calcium pantothenate	3,26
pyridoxine (B6)	6	pyridoxine hydrochloride 33% Rocoat	5,46
folic acid	600	folic acid 10% trituration	1,5
Cyanocobalamin (B12)	0,003	dry vit B12 0,1% WS	0,75
biotin	0,03	biotin 1% trituration	7,5

Effervescent tablet			
Active ingredients	Amount based on the active ingredient [mg]	Form of the active ingredient	Amount of the form of the active ingredient [mg]
calcium	120	calcium carbonate	71,7
		calcium phosphate dibasic anhydrous	151,38
		calcium glycerophosphate	259,86
magnesium	45	magnesium phosphate dibasic trihydrate	322,81
phosphorus	126,3	see Ca & Mg	
iron	18	Carbonyl iron	18,33
zinc	8	Zinc citrate trihydrate	25,63
iodine	0,075	potassium iodide	0,098
selenium	0,055	sodium selenate	0,132
copper	0,9	copper citrate	2,57
manganese	1,8	manganese sulfate monohydrate	5,54
molybdenum	0,045	sodium molybdate dihydrate	0,113
chromium	0,025	chromium chloride hexahydrate	0,128
chloride	39,8	sodium chloride	30
potassium	20,4	potassium chloride	43,51

Example 4:

Effervescent tablet			
Active ingredients	Amount based on the active ingredient [mg]	Form of the active ingredient	Amount of the form of the active ingredient [mg]
vit A	595	vitamin A palmitate 100000 iu/g	13,33
beta caroten	0,63	betatab 10%E	0,63
vit C	180	ascorbic acid	30
Vit D3	5	cholecalciferol 100000 IU/g	0,8
vit E	10	tocopherol acetate 50% CWS/F	14
vit K	0,03	vitamin K1 5% SD	
thiamin (B1)	4,2	thiamin phosphate	3,9
riboflavin (B2)	4,8	riboflavine phosphate	3,6

Effervescent tablet			
Active ingredients	Amount based on the active ingredient [mg]	Form of the active ingredient	Amount of the form of the active ingredient [mg]
nicotinamide (PP)	54	nicotinamide	13,5
pantothenic acid (B5)	18	calcium pantothenate	3,26
pyridoxine (B6)	6	pyridoxine hydrochloride 33% Rocoat	5,46
folic acid	600	folic acid 10% trituration	1,5
Cyanocobalamin (B12)	0,003	dry vit B12 0,1% WS	0,75
biotin	0,03	biotin 1% trituration	7,5
calcium	120	calcium carbonate	71,7
		calcium phosphate dibasic anhydrous	151,38
		calcium glycerophosphate	259,86
magnesium	45	magnesium phosphate dibasic trihydrate	322,81
phosphorus	126,3	see Ca & Mg	
iron	18	iron polymaltose	39,82
zinc	8	Zinc citrate trihydrate	25,63
iodine	0,075	potassium iodide	0,098
selenium	0,055	sodium selenate	0,132
copper	0,9	copper citrate 2.5 H ₂ O	2,57
manganese	1,8	manganese sulfate monohydrate	5,54
molybdenum	0,045	sodium molybdate dihydrate	0,113
chromium	0,025	chromium chloride hexahydrate	0,128
chloride	39,8	sodium chloride	30
potassium	20,4	potassium chloride	43,51

Further excipients can be added to example 3 or 4:

excipients	Amount [mg]
maltitol	qs
sorbitol	qs
sodium hydrogen carbonate	950

excipients	Amount [mg]
anhydrous citric acid	1800
sodium carbonate	65
PVP	30
crospovidone	7
sucrose ester of fatty acids	0,15
beet red	5
orange flavour	77
Passion fruit flavour	30
aspartam	35
acesulfam K	20

qs: quantum satis =quantity to add to reach the tablet weight

Example 5:

Orodispersible tablet		Tablet weight 1000 mg	
Active ingredients	Amount based on the active ingredient [mg]	Form of the active ingredient	Amount of the form of the active ingredient [mg]
vit A	400	vitamin A palmitate 100000 iu/g	13,33
vit C	30	ascorbic acid	30
Vit D3	2,5	cholecalciferol 100000 IU/g	0,8
vit E	5	tocopherol acetate 50% CWS/F	14
thiamin (B1)	1,05	thiamin nitrate 33% Rocoat	3,9
riboflavin (B2)	1,2	riboflavine 33% Rocoat	3,6
nicotinamide (PP)	13,5	nicotinamide	13,5
pantothenic acid (B5)	3	calcium pantothenate	3,26
pyridoxine (B6)	1,5	pyridoxine hydrochloride 33% Rocoat	5,46
folic acid	150	folic acid 10% trituration	1,5
Cyanocobalamin (B12)	0,75	dry vit B12 0,1% WS	0,75
biotin	75	biotin 1% trituration	7,5
calcium	60	calcium carbonate DCCS90L	166,53
magnesium	25	magnesium oxide	41,45
iron	4	iron polymaltose	8,8

Orodispersible tablet		Tablet weight 1000 mg	
Active ingredients	Amount based on the active ingredient [mg]	Form of the active ingredient	Amount of the form of the active ingredient [mg]
zinc	3,75	Zinc citrate trihydrate	12,02
iodine	37,5	potassium iodide 5% trituration	0,75
selenium	25	sodium selenate anhydrous 1% trituration	2,5
copper	0,45	copper citrate 2,5 H ₂ O	1,28
manganese	0,9	manganese sulfate monohydrate	2,77
molybdenum	22,5	sodium molybdate dihydrate 1% trituration	2,25
chromium	12,5	chromic chloride hexahydrate 1% trituration	1,25
pharmaburst C1			qs 1 tablet
anhydrous citric acid			16
magnesium stearate			25
sodium hydrogencarbonate			20
pineapple flavour			3
Passion fruit flavour			3
aspartam			13
iron oxide			2,5

Example 6:

Orodispersible tablet		Tablet weight 1000 mg	
Active ingredients	Amount based on the active ingredient [mg]	Form of the active ingredient	Amount of the form of the active ingredient [mg]
vit A	400	vitamin A palmitate 100000 iu/g	13,33
vit C	30	ascorbic acid	30
Vit D3	2,5	cholecalciferol 100000 IU/g	0,8
vit E	5	tocopherol acetate 50% CWS/F	14
thiamin (B1)	1,05	thiamin nitrate 33% Rocoat	3,9

Orodispersible tablet		Tablet weight 1000 mg	
Active ingredients	Amount based on the active ingredient [mg]	Form of the active ingredient	Amount of the form of the active ingredient [mg]
riboflavin (B2)	1,2	riboflavine 33% Rocoat	3,6
nicotinamide (PP)	13,5	nicotinamide	13,5
pantothenic acid (B5)	3	calcium pantothenate	3,26
pyridoxine (B6)	1,5	pyridoxine hydrochloride 33% Rocoat	5,46
folic acid	150	folic acid 10% trituration	1,5
Cyanocobalamin (B12)	0,75	dry vit B12 0,1% WS	0,75
biotin	75	biotin 1% trituration	7,5
calcium	60	calcium carbonate DCCS90L	166,53
magnesium	25	magnesium oxide	41,45
iron	4	iron fumarate 60% Descote	20,28
zinc	3,75	Zinc citrate trihydrate	12,02
iodine	37,5	potassium iodide 5% trituration	0,75
selenium	25	sodium selenate anhydrous 1% trituration	2,5
copper	0,45	copper citrate 2,5 H ₂ O	1,28
manganese	0,9	manganese sulfate monohydrate	2,77
molybdenum	22,5	sodium molybdate dihydrate 1% trituration	2,25
chromium	12,5	chromic chloride hexahydrate 1% trituration	1,25
pharmaburst C1			qs 1 tablet
anhydrous citric acid			16
magnesium stearate			25
sodium hydrogencarbonate			20
pineapple flavour			3
Passion fruit flavour			3
aspartam			13
iron oxide			2,5

**NOT FURNISHED
UPON FILING**

Example 7: Manufacturing process for effervescent tablets

(manufacturing process for examples 3 and 4)

Vitamin Blend :

5 In a drum thiamine monophosphoric acid ester chloride dihydrate, riboflavin sodium phosphate, pyridoxine hydrochloride, sodium chloride and sorbitol (in part) are mixed together to the premix 1. Into the tank of the blender the following ingredients are introduced and mixed: premix 1, ascorbic acid, vitamin A palmitate, vitamin E powder, nicotinamide, betatab 10% E, calcium pantothenate, orange flavour, passion fruit flavour, anhydrous sodium carbonate, acesulfame potassium, aspartame, crospovidone, sorbitol (remaining part), beet red.

10 Mineral Granule :

The following ingredients are mixed: copper citrate 2.5 H₂O, zinc citrate trihydrate, iron source, manganese sulphate monohydrate, calcium carbonate, maltitol, calcium hydrogen phosphate anhydrous (remaining part), calcium glycerophosphate, magnesium hydrogen phosphate trihydrate, sodium hydrogen carbonate and potassium chloride. Thereafter the mixture is granulated by
15 spraying a binding solution made of purified water, sodium molybdate dihydrate, sodium selenate anhydrous, potassium iodide, ethanol, sucrose esters of fatty acids, povidone K90 and chromic chloride hexahydrate. The granule is dried, cooled and sieved.

Final Blend :

20 In a drum folic acid, biotin, vitamin B12, vitamin K1, vitamin D3 and sorbitol (= premix 2) are mixed together. In the tank of the tumble mixer the mineral granule, the vitamin blend, the premix 2 and anhydrous citric acid are mixed to the final blend.

Compression :

The homogeneous final blend is compressed to tablets on a rotary tablet press.

Example 8: Manufacturing process for chewable tablets

25 Premix:

In a drum dry vitamin D3, thiamine mononitrate, riboflavin, pyridoxine hydrochloride, folic acid 1, vitamin B12, calcium pantothenate, biotin, copper citrate 2.5 H₂O, manganese sulphate monohydrate, iodine, selenium, chromium, molybdenum, orange flavour, passion fruit flavour, iron oxide yellow, aspartame, sucralose NF micronized, pearlitol SD 200 are mixed for 15 minutes.

Final blend:

Thereafter the premix, vitamin A palmitate, nicotinamide, dry vitamin E, ascorbic acid, calcium carbonate, magnesium oxide heavy, iron source, zinc citrate 3 H₂O, anhydrous citric acid, xylitol, talc, pearlitol SD 200 and sorbitol are mixed for 20 minutes. Magnesium stearate is added and the

5 blend is mixed again for 5 additional minutes.

Compression:

The homogeneous final blend is pressed to tablets on a rotary tablet press.

Example 9: Manufacturing process for orodispersible tablets

Premix:

10 In a drum dry vitamin D3, thiamine mononitrate, riboflavin, pyridoxine hydrochloride, folic acid, vitamin B12, calcium pantothenate, biotin, copper citrate 2,5 H₂O, manganese sulphate monohydrate, iodine, selenium, chromium, molybdenum, pineapple flavour, passion fruit flavour, iron oxide yellow, aspartame and pharmaburst C1 are mixed for 15 minutes.

Final blend:

15 Premix, vitamin A palmitate, nicotinamide, dry vitamin E, ascorbic acid, calcium carbonate, magnesium oxide heavy, iron source, zinc citrate 3 H₂O, anhydrous citric acid, sodium hydrogen carbonate and pharmaburst C1 are mixed for 20 minutes. Thereafter magnesium stearate is added and it is mixed again for 5 additional minutes.

Compression:

20 The homogeneous final blend is compress to tablets on a rotary tablet press.

Example 10: Tablet for children

Better taste	Tablet weight	in form of	
claim	quantitative	qualitative	quantitive
vit A	1000	vitamin A palmitate 100000 iu/g	10
vit C	22.5	Acerola extract 25% vitamin C enriched	90
Vit D3	2,5 µg	cholecalciferol 100000 IU/g	0,8
vit E	6	tocopherol acetate 50% CWS/F	17.9
thiamin (B1)	0.45	thiamin nitrate 33% Rocoat	1.60

riboflavin (B2)	0.45	riboflavine 33% Rocoat	1.27
nicotinamide (PP)	6	nicotinamide	6
pantothenic acid (B5)	2	calcium pantothenate	2.17
pyridoxine (B6)	0.45	pyridoxine hydrochloride 33% Rocoat	1.61
folic acid	75 µg	folic acid 10% trituration	0.75
Cyanocobalamin (B12)	1 µg	dry vit B12 0,1% WS	1
biotin	10 µg	biotin 1% trituration	1
Choline	25	Choline bitartrate	60.75
calcium	120	calcium carbonate DCCS90L	335.30
magnesium	25	magnesium oxide	42,89
iron	6	ferrous fumarate 60% Descote	32.41
zinc	4	Zinc citrate trihydrate	12.62
iodine	60 µg	potassium iodide 5% trituration	1.137
selenium	12.5 µg	sodium selenate anhydrous 1% trituration	1.16
copper	0,40	copper citrate 2,5 H ₂ O	1,23
manganese	1	manganese sulfate monohydrate	3.09
chromium	12,5 µg	chromic chloride hexahydrate 1% trituration	1,22
Mannitol			ca. 200
anhydrous citric acid			20
talc			50
magnesium stearate			10
xylitol			75
Sorbitol			ca. 200
cherry flavour			3
Grenadine flavour			3
aspartam			3
sucralose			0.8
iron oxide			2,5

Example 11:

Effervescent tablet		Tablet weight 4800 mg	
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Active ingredients	Amount based on the active ingredient	Form of the active ingredient	Amount of the form of the active ingredient
vit A as retinol	(2667.7 IU) 800 µg	vitamin A palmitate 100000 IU/g	(2266.7 IU) 22.67 mg
		beta carotene as betatab 10%E	(400 IU) 7.20 mg
vitamin D 3	(200 IU) 5 µg	Cholecalciferol concentrate (water dispersible powder form) 100000 IU/g	2.0 mg
Vitamin E	10 mg	D-alpha-tocopherol acetate concentrate (powder form) 50 %	29.80 mg
Vitamin K	0.03 mg	vitamin K1 5% SD	0.60 mg
Vitamin B1	4.20 mg	Thiamin monophosphoric acid ester chloride dihydrate	6.59 mg
Vitamin B2	4.80 mg	Sodium riboflavin 5'-phosphate	6.56 mg
Niacin	54.0 mg	nicotinamide	54.0 mg
Pantothenic acid	18.0 mg	Calcium D-pantothenate	19.57 mg
Vitamin B6	6.0 mg	Pyridoxine hydrochloride	7.3 mg
Folic acid	0.60 mg	Pteroylmonoglutamic acid	0.60 mg
Vitamin B12	3.0 µg	Cyanocobalamin powder 0.1 % water soluble	3.0 mg
Biotin	30 µg	D-biotin	30 µg
Vitamin C	180 mg	Ascorbic acid fine powder	180 mg
Calcium	120 mg	Calcium carbonate	295.61 mg
		(see calcium pantothenate)	
Magnesium	80 mg	Magnesium carbonate	163 mg
		Magnesium sulphate dihydrate	159 mg
Iron	14 mg	Ferric pyrophosphate	56 mg
copper	0.9 mg	Copper citrate 2.5 hydrate	2.57 mg
iodine	0.075 mg	Potassium iodine	0.098 mg
zinc	8 mg	Zinc citrate trihydrate	25.63 mg
manganese	1.8 mg	Manganese sulphate monohydrate	5.54 mg
potassium	20.4 mg	Potassium chloride	38.96 mg
selenium	50 µg	Sodium selenate anhydrous	0.12 mg
chromium	0.025 mg	Chromium chloride hexahydrate	0.128 mg
molybdenum	0.045 mg	Sodium molybdate dihydrate	0.113 mg
Coenzyme Q10	3.0 mg	Coenzyme Q10 10 %	30 mg

Further excipients can be added to example 11:

excipients	Amount [mg]
Mannitol 100 mesh ²⁾	qs
Mannitol SD 200 ¹⁾	qs
Sorbitol ¹⁾	qs
Anhydrous citric acid	1800
Sodium hydrogen carbonate	950
Orange juice flavour	77
Sodium carbonate	65
Passion fruit flavour	30
aspartam	35
Potassium acesulfam	20
crospovidone	7
beet red	5
sucrose ester of fatty acids	0.15

qs: quantum satis =quantity to add to reach the tablet weight

¹⁾ Half of mannitol SD 200 and half of sorbitol are used to obtain the theoretical tablet weight of 4800 mg.

5 ²⁾ The quantity of mannitol 100 mesh is adjusted according to mineral contents in the granule.

Manufacturing process for example 11:

Vitamin Blend :

10 In a drum vitamin D3 100 CWS, biotin, folic acid, vitamin B12 0.1% WS, vitamin K1 5% SD, coenzyme Q10 10% CWS/S, sodium molybdate dihydrate, sodium selenate anhydrous and mannitol (a part) are mixed together to the premix 1. Into the tank of the blender the following ingredients are introduced and mixed: premix 1, vitamin A palmitate, nicotinamide, calcium pantothenate, vitamin E powder, pyridoxine hydrochloride, riboflavin sodium phosphate, thiamin monophosphoric, betatab 10% E, crospovidone, beet red and mannitol (a part).

15 Mineral Granule :

The following ingredients are mixed: copper citrate 2.5 H₂O, zinc citrate trihydrate, iron source, manganese sulfate monohydrate, calcium carbonate, magnesium carbonate, magnesium sulfate dihydrate, sodium hydrogen carbonate, potassium chloride, anhydrous citric acid and mannitol (rest). Thereafter the mixture is granulated by spraying a binding solution made of ethanol, sucrose

esters of fatty acids, potassium iodide and chromium chloride hexahydrate. The granule is dried, cooled and sieved.

Final Blend :

5 In the tank of the tumble mixer the mineral granule, the vitamin blend, ascorbic acid, sodium hydrogen carbonate, sorbitol, anhydrous sodium carbonate, sodium chloride, orange flavour, passion fruit flavour, potassium acesulfame, aspartame and mannitol SD 200 are mixed to the final blend.

Tabletting :

The homogeneous final blend is compressed to tablets on a rotary tablet press.

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Results:

Examples 1 to 6, 10 and 11 do not show a metallic bad taste when administered orally.

The disintegration time for examples 5 and 6 (orodispersible tablets) is 67 sec.. The disintegration time can be measured by standard methods known to the person skilled in the art.

What is claimed is:

1. Oral composition comprising an iron source, selected from the group consisting of iron polymaltose and carbonyl iron, and/or copper citrate as copper source.
2. Composition of claim 1 without metallic taste.
- 5 3. Composition of claim 1 or 2, wherein the copper salt is a hemipentahydrate.
4. Composition of any of claims 1 to 3, wherein the amount of the iron source is from 1 to 60 mg based on iron.
5. Composition of any of claims 1 to 4, wherein the amount of copper citrate is from 0.1 to 2 mg, preferably 0.3 to 1.1 mg based on copper.
- 10 6. Composition of any of claims 1 to 5 comprising at least one further mineral and/or vitamin.
7. Composition of any of claims 1 to 6 comprising in addition iron fumarate 60% Descote.
8. Composition of claim 7 comprising copper citrate and iron fumarate 60% Descote.
9. Oral nutritional supplement comprising a composition according to any of claims 1 to 8.
10. Oral nutritional supplement of claim 9 which is a chewable tablet, an orodispersible tablet
15 or an effervescent formulation.
11. Oral nutritional supplement of claim 10 which is an fast disintegrating orodispersible tablet having a disintegration time of less equal than 100 sec..
12. Process for manufacturing of the oral nutritional supplement according to claim 9 or 11.
13. Use of a composition according to any of claims 1 to 10 for balancing the supply of iron in
20 a patient.