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ABSTRACT

The present invention relates to a food supplement composition for oral ingestion, comprising a chromium compound, a cinnamon extract, and a natural dietary fiber with antioxidant properties.

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CLAIMS

1. A food supplement composition for oral ingestion, comprising:
a chromium compound,
a cinnamon extract, and
a natural dietary fiber with antioxidant properties.

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2. The composition according to claim 1, comprising chromium (III) picolinate.
3. The composition according to claim 1 or 2, wherein the cinnamon extract derived from *Cinnamomum zeylanicum*.

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4. The composition according to any one of claims 1 to 3, wherein the natural dietary fiber comprises *Opuntia ficus indica* extract.

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5. The composition according to any one of claims 1 to 4, wherein the natural dietary fiber comprises *Opuntia ficus indica* extract derived from plants of genus *Opuntia*.

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6. The composition according to any one of claims 1 to 5, wherein the natural dietary fiber comprises *Opuntia ficus indica* extract derived from *Opuntia ficus indica* plant.

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7. The composition according to any one of claims 1 to 6, comprising from 25 mcg to 150 mcg of chromium picolinate, from 25 to 500 mg of *Cinnamomum zeylanicum*, and from 250 mg to 750 mg of *Opuntia ficus indica* is present between 250 mg to 750 mg.

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8. A tablet, capsule or sachet containing a composition according to anyone of claims 1 to 7.
9. The tablet, capsule or sachet according to claim 8, further comprising an emulsifier and/or lubricant as an excipient.

- 5 10. The food supplement composition according to anyone of claims 1 to 7 for use in
a method of assisting the normal macronutrient metabolism of a human subject.

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DESCRIPTION**FOOD SUPPLEMENT COMPOSITION FOR ASSISTING TO NORMAL MACRONUTRIENT METABOLISM**10 **TECHNICAL FIELD**

The present invention relates to a food supplement composition for assisting with macronutrient metabolism of humans.

15 **BACKGROUND OF THE INVENTION**

The increased incidences of conditions that have been attributed to diets are characterized by high fat intake and repeated ingestion of refined foods and sugars, coupled with low fiber and vegetable intake.

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Diet, along with the natural aging process, causes deterioration in the way in which the body metabolizes blood glucose. When the body cannot properly metabolize blood glucose, a tendency to store glucose as fat typically occurs. This is one reason levels of body fat increase with age. There is also a known link with these conditions to a variety of ailments including heart disease and hypertension. Similarly, there is a known link between insulin resistance and increased visceral adiposity. Therefore, when glucose regulation is out of balance, a greater propensity for adiposity exists.

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It has long been known that natural and/or synthetic substances may aid in controlling blood glucose. Such substances act by a variety of mechanisms. For example, some substances act by mimicking the effects of endogenous insulin and are therefore capable of replacing endogenous insulin. Such substances include synthetic insulin injections such as those which are routinely prescribed to individuals with Type I diabetes. Other commonly prescribed substances known to mimic the effects of insulin include the naturally occurring compounds taurine, 4-hydroxyisoleucine, arginine, and vanadium. Although these compounds have been shown to work as insulin mimetics by acting in

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5 the body to decrease serum blood glucose levels, they have not been successfully developed into viable food supplements to assist in normal macronutrient metabolism.

A common feature in all cases of chromium depletion reported in humans is an impaired glucose tolerance and glucose utilization probably resulting from an increased resistance to the action of insulin. These lead to elevated plasma concentrations of fatty acids, increased utilization of fatty acids as a source of energy, and possibly to abnormalities in nitrogen metabolism, as nitrogen retention increased with the administration of chromium chloride. Although there is no consensus about the mechanism by which chromium could exert these effects, consensus opinions from authoritative bodies are generally in agreement that chromium facilitates the action of insulin, thus contributing to macronutrient metabolism.

Chromium is part of enzymes of the carbohydrate and lipid metabolism, promotes carbohydrates catabolism by potentiating insulin action and thereby influencing carbohydrates metabolism, promotes fat catabolism by potentiating insulin action and thereby influencing lipid metabolism, and glucose metabolism.

20 Natural products are often prone to deterioration, especially during storage, leading to loss of active component, production of metabolites with no activity and, in extreme cases, production of toxic metabolites. Phytoformulations often suffer degradation during storage by oxidation, hydrolysis, crystallization, emulsion breakdown, enzymatic deterioration and chemical reactions with the additives and excipients. Temperature and moisture are the two major factors that affect quality and stability of a herbal product. A chemical reaction increases by a factor of between two- and three fold for every 10°C rise in temperature. Moisture absorbed on to the surface of solid drug often increases the rate of decomposition if it is susceptible to hydrolysis.

WO 2006/127779 A2 relates to dietary supplement compositions and method of use thereof for enhancing insulin sensitivity of a person, comprising chromium and cinnamon bark extract in addition to several other ingredients like thiamin, alpha-lipoic acid and vanadium etc. and other natural extracts like sylvestre leaf extract.

5 US 2016/03600776 A1 relates to dietary supplement compositions as well as methods for using dietary supplement compositions to control glucose levels, comprising chromium (e.g. Chromium Oligofructose Complex), a cinnamon extract etc.

CN105658093 A relates to dietary supplements zinc, chromium, Ginseng extract, cinnamon extract etc.

10 GB 2507254 A relates to a composition for use in inhibiting the breakdown of carbohydrates passing through the gastrointestinal tract and thereby preventing or reducing absorption of sugar. The composition comprises white kidney bean extract, fenugreek, cinnamon and chromium picolinate as a chromium compound.

15 The problems related to the low intake of dietary fibers and the benefits of using antioxidants to maintain a healthy metabolism have been known in the state of the art.

Individuals with high intakes of dietary fiber appear to be at significantly lower risk for developing coronary heart disease, stroke, hypertension, diabetes, obesity, and certain gastrointestinal diseases. Increasing fiber intake lowers blood pressure and serum cholesterol levels. Increased intake of soluble fiber improves glycemia and insulin
20 sensitivity in non-diabetic and diabetic individuals. Fiber supplementation in obese individuals significantly enhances weight loss. Increased fiber intake benefits a number of gastrointestinal disorders including the following: gastroesophageal reflux disease, duodenal ulcer, diverticulitis, constipation, and hemorrhoids. Prebiotic fibers appear to enhance immune function. Dietary fiber intake provides similar benefits for children as
25 for adults. The recommended dietary fiber intakes for children and adults are 14 g/1000 kcal. [1]

The aim of the present invention is to provide a food supplement composition which assists the macronutrient metabolism in a human subject.

BRIEF DESCRIPTION OF THE INVENTION

30 The present invention provides an alternative or improved food supplement composition for assisting the macronutrient metabolism in a human subject.

5 One object of the present invention is to provide a stable food supplement composition with natural ingredients.

Another object of the present invention is to provide a food supplement composition regulating blood sugar.

One another object of the present invention is to provide a food supplement
10 composition with dietary fiber with antioxidant property.

Accordingly, in a first aspect, the present invention provides a composition for oral ingestion comprising a cinnamon extract, a chromium compound and a dietary fiber with antioxidant properties.

In another aspect, the present invention provides a tablet, capsule or sachet containing a
15 chromium compound, a cinnamon extract, and a natural dietary fiber with antioxidant properties.

In another aspect, the present invention provides a food supplement composition containing a chromium compound, a cinnamon extract, and a natural dietary fiber with antioxidant properties, for use in a method of assisting the normal macronutrient
20 metabolism of a human subject.

DETAILED DESCRIPTION OF THE INVENTION

As used herein, the term “extract” refers to an active ingredient or fraction isolated from a plant by using a solvent or a solvent system. Also as used herein, the term “extract solution” refers to the solution of the extract solvated in the solvent.

25 The extraction procedure for obtaining any of the plant extracts employed in accordance with the invention, unless otherwise indicated, may be carried out in various ways. For example, an herbal extract solution can be one of an infusion, a decoction, maceration, or a product from another extraction technique performed on a subject plant by man. In yet another example, the plant parts can be crushed and/or milled and optionally dried
30 before being contacted with the extraction solvent; the extraction can be assisted with shaking, agitating, and/or heating; the extraction can be microwave and/or ultrasound

5 assisted; the solvent can be filtered and reduced under reduced pressure evaporation; the filtered solids may be re-extracted to yield a second crop; and so forth.

As used herein, the term “food supplement” refers to a food or food product that provides health benefits in a human.

10 The present invention provides a food supplement composition that advantageously includes several components that work in tandem for macronutrient metabolism in a human.

The present invention provides a synergistic combination for assisting normal macronutrient metabolism especially in individuals who consume high amounts of carbohydrates (including sugar) and/or fat.

15 The synergistic oral compositions of the present invention increases energy metabolism rate by contributing to normal macronutrient metabolism when administered orally to humans.

20 The food supplement compositions of the present invention contain effective amounts of minerals and natural extracts and do not contain dangerous/unhealthy pharmaceutical stimulants or any other stimulants that would have serious side effects.

Accordingly, in a first aspect, the invention provides a food supplement composition for oral ingestion comprising a cinnamon extract, a chromium compound and a dietary fiber with antioxidant properties.

25 The novel food supplement composition of the present invention facilitates the action of insulin together with a dietary fiber with antioxidant properties. Having three components in combination the food supplement composition of the present invention counteracts a high fat and/or carbohydrate diet or at least helps minimize it's negative effects on the human subject's metabolic system by assisting macronutrient metabolism.

30 The chromium is preferably in the form of a chromium compound, preferably a chromium (III) compound such as chromium (III) salt or coordination complex. More preferably the chromium compound is chromium (III) picolinate. Chromium (III)

- 5 picolinate may be prepared by aqueous reaction of chromium (III) chloride with three equivalents of picolinic acid.

As used herein, the term “cinnamon” refers to the inner bark of trees of the genus *Cinnamomum*.

- 10 Cinnamon extract is derived from plants of the genus *Cinnamomum*. Sri Lanka in the South Asian region produces the largest quantity of *Cinnamomum zeylanicum* and the best quality cinnamon, also known as Ceylon cinnamon (the source of its Latin name, *zeylanicum*) or ‘true cinnamon’, is indigenous to Sri Lanka.

In one embodiment of the present invention, the food supplement composition comprises cinnamon extract derived from *Cinnamomum zeylanicum*.

- 15 The active ingredient in cinnamon is a water-soluble polyphenol compound and methylhydroxychalcone polymer (MHCP). It has been found in vitro study that MHCP mimics insulin, activates its receptor, and works synergistically with insulin in cells. It has been reported in a recent human subject study that cinnamon significantly reduces blood sugar levels in diabetes type II patients. Recent studies emerging from western
20 countries have shown many potentially beneficial health effects of cinnamon such as anti-inflammatory properties, anti-microbial activity, blood glucose control, reducing cardiovascular disease, boosting cognitive function, and reducing risk of colonic cancer.

- Opuntia ficus-*indica* (cactus pear) is a cactus well adapted to extreme climate and edaphic conditions. The semiarid regions of the central part of Mexico host the greatest
25 diversity of this cactus in the world [2]. In Mexico, the cultivated area for human consumption is around 10,000Ha. Under optimal conditions annual production can reach 50 tons of dry matter per hectare. The genus *Opuntia* embraces about 1,500 species of cactus and many of them produce edible tender stems and fruits [3]. The tender young part of the cactus stem, or cladode, is frequently consumed as a vegetable
30 in salads, while the cactus pear fruit is consumed as a fresh fruit. This cactus is a common item of consumption in Mexico (10–17 g/person/day) [4]. Chemical composition depends on variety, maturation stage and environmental conditions [5–7]. Previous studies on the chemical composition of the edible portion of cladodes and fruits from *Opuntia ficus-indica* show that these foods have a high nutritional value, mainly

5 due to their mineral, protein, dietary fiber and phytochemical contents [5,6,8,9].
Interestingly, antioxidant activity has also been reported [10, 11]

In an embodiment of the invention, natural dietary fiber composition comprises *Opuntia ficus-indica* extract.

10 In another embodiment of the invention, *Opuntia ficus-indica* extract is derived from
plants of genus *Opuntia*.

In one another embodiment of the invention, *Opuntia ficus-indica* extract is derived
from *Opuntia ficus indica* plant.

The cinnamon extract and *Opuntia ficus-indica* extract may be presented in the form of a
a powder. The cinnamon may be presented in comminuted form, for example in the
15 form of a powder such that produced by grinding cinnamon inner bark.

In the compositions of the present invention, the chromium compound may be
presented in powder form.

The compositions of the invention are typically administered orally.

The composition may contain from 25 mcg to 150 mcg of chromium picolinate, from 25
20 to 500 mg of *Cinnamomum zeylanicum*, and from 250 mg to 750 mg of *Opuntia ficus*
indica is present between 250 mg to 750 mg.

It has also been surprisingly found that the food composition of the present invention
comprising two natural extracts is stable thanks to the presence of a chromium
compound in the composition as shown by examples.

25 **Examples**

Example 1

5 Composition and list of ingredients

Ingredients	Function	mg/capsule	% per total mass
<i>Opuntia ficus indica</i> extract	Active ingredient	370	77,58
Hydroxypropyl-methylcellulose	Capsule	76	15,94
<i>Cinnamomum zeylanicum</i> bark extract 1:10*	Active ingredient	25	5,24
<i>Magnesium stearate</i>	Emulsifier	5,50	1,15
Chromium <i>picolinate</i> -Chromium	Active ingredient	0,40 - 0,05	0,08
Total		476,9	100

Due to high volume of the material and extremely low bulk and tapped density, Opuntia, Zinc and Cinnamon extract are homogenized and dry compacted using Roller Compactor equipment to form hard compacted laminates. The obtained laminates are milled to obtain suitable granulate size and the remaining material of improper size is segregated using cyclone separation procedure and re-compacted. Granules so-obtained are of increased particle size and bulk density better flowability and this process provide better fill weight control. Final mixture is shortly mixed with magnesium stearate and capsule filled.

15 Example 2

5 1. Stability Data

The aim of the study was to assess the stability of the formulation of the present invention comprising a chromium supplement, a cinnamon extract and a natural dietary fiber under temperature and humidity conditions representative of Zone II.

2. Methodology

- 10 The formulations of the present invention were used for stability testing in conditions reflective of Zone II conditions.

Samples were placed in conditions reflective of “real time” conditions $25\pm 2^{\circ}\text{C}$ / 60 ± 5 %Relative Humidity (RH).

The following procedures were carried out:

- 15 Zone II, Long Term, $25\pm 2^{\circ}\text{C}$ / 60 ± 5 % (RH)

At each time point:

- Appearance
- Chromium content Assay
- Moisture content

- 20 At 0, 12 months and 24 months

- Assessment of microbial safety was done.
- Capsule fill weight was checked

Type of the study	Test	Term (months)
	Appearance	0,3,6,9,12,18,24
	Chromium content Assay	0,3,6,9,12,18,24
	Moisture content	0,3,6,9,12,18,24

Zone II, Long Term) 25±2°C/ 60±5 % (RH).	Microbiological requirements	0,12,24
	Capsule fill weight	0,12,24

5 Stability specifications

Tests	Requirements		Method
Appearance	White, well sealed capsule		Visual
Assay Chromium content Assay	50 $\pm$ g $\pm$ 20 %		EP 6.0.
Moisture content	max 10 %		EP 6.0.
Microbiological requirements	Salmonella spp.	Absent in 25 g	SRPS EN ISO 6579: 2008
	Escherichia coli	<10 cfu/g	SRPS EN ISO 16649-1,2: 2008
	Coagulase positive stafilokokus	10 ² cfu/g	SRPS EN ISO 6888-1,2: 2009
	Enterobacteriaceae	10 ² / cfu/g	SRPS EN ISO 21528-1:2009
	Aerobic bacteria plate Count	2 x 10 ² cfu/g	SRPS EN ISO 4833:2008
	Yeasts and mold	2 x 10 ² cfu/g	SRPS EN ISO 21527-1: 2011
Capsule fill weight	476 mg $\pm$ 20%		EP 6.0.

Timeline

Test term	Date (Zone II, Long Term)
0	1.04.2016.
3 m	1.07.2016.
6 m	1.10.2016.

9 m	1.01.2017.
12 m	1.04.2017.
18 m	1.10.2017.
24 m	1.04.2018.

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Stability study results

<i>Tests/time</i>	<i>Appearance</i>	<i>Assay (mg/cps)</i>	<i>Moisture content (%)</i>	<i>Microb. req.</i>	<i>Cps. fill wgh. (mg/cps)</i>
t0	comply	50,40	4,96	comply	480,1 mg
3m	comply	49,60	4,98		
6m	comply	49,03	5,01		
9m	comply	48,90	4,99		
12m	comply	49,20	5,03	comply	480,5
18m					
24m					

3. Conclusion

- 10 All the parameters accepted by international regulatory bodies related to the stability of an oral formulation were checked during the stability study and surprisingly they were all within acceptable limits, the stability data attained as a result of the study is very important from a safety and efficacy point of view and is paramount to have an efficient food supplement that can effectively assist the macronutrient metabolism in a human
- 15 subject. Because food supplements are perishable items and natural extracts are even more so as a sub-category, their reactions to outside elements such as humidity and heat over time can decrease their efficacy and increase the risk of microbiological contamination, therefore the surprising results of this study has proven that the formulation of the present invention has demonstrated an exceptional stability at least
- 20 for a year.

- 5 This specification and examples are to be construed as illustrative only and is for the purpose of teaching those skilled in the art the manner of carrying out the invention. It is to be understood that the forms of the invention herein shown and described are to be taken as the presently preferred embodiments. As already stated, various changes may be made in the shape, size and arrangement of components or adjustments made in the
- 10 steps of the method without departing from the scope of this invention. For example, equivalent elements may be substituted for those illustrated and described herein and certain features of the invention maybe utilized independently of the use of other features, all as would be apparent to one skilled in the art after having the benefit of this description of the invention.
- 15 While specific embodiments have been illustrated and described, numerous modifications are possible without departing from the spirit of the invention, and the scope of protection is only limited by the scope of the accompanying claims.

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