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A method for the management of cancer and treatment of cancer comorbidities, including but not limited to cancer-related fatigue, cachexia, anorexia, pain, anemia, asthenia, depression, muscle weakness, nausea, vomiting, skin, and skin appendages adverse reactions; said method comprising the administration by the conventional and non-conventional oral, topical, parenteral routes and intra- tumoral injection, or in combination thereof, or the administration as adjuvant potentiator in other therapies using the forenamed routes, of a composition containing as active ingredient an extract of *Allium* species, which contains querceting, an extract of *Citrus* species and an extract of *Paullinia* species and an extract of *Theobroma* species.

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METHOD FOR THE MANAGEMENT OF CANCER AND CANCER TREATMENT-RELATED COMORBIDITIES

5 TECHNICAL FIELD

The invention concerns a method for the management of cancer and treatment cancer comorbidities, including but not limited to cancer-related fatigue, cachexia, anorexia, pain, anemia, asthenia, depression, impaired cognitive function, loss of appetite, muscle weakness, nausea, vomiting, arthritis, organ
10 damage, including but not limited to radiation-induced burns, heart disorders due to cardiotoxicity by chemo- and radiotherapy, hypertension, thromboembolism, occasional chest pain, difficulty in breathing, shortness of breath, dizziness, fainting, pallor (pale skin or lips), headaches, difficulty in concentrating, insomnia, difficulty in staying warm, bleeding problems, nail damages, and skin appendages
15 adverse reactions, exemplified by irritation and dry skin, sore and dry ulcerated mouths.

BACKGROUND OF THE INVENTION

So far, the main anti-cancer therapeutic strategies have consisted in
20 inhibiting the non-controlled cell proliferation. Nonetheless, as tumour evolution has multifaceted mechanisms, more strategies should be considered in order to address the remaining gaps in cancer management, and more importantly in alleviating the side effects of cancer treatments. Previous research indicates that inflammatory cells and pro-inflammatory molecules mostly contribute to tumor
25 growth and progression. In experimental settings, reduction of inflammatory molecules (e.g. cytokines) inhibits cancer development. Based on earlier research, blockade of inflammation appears to be a relevant strategy for management of

cancer. Therefore, controlling or reducing such a process of “malignant flame” (inflammation) represents a crucial approach in the management of cancer.

Anticancer therapies have extended patients’ life expectancy; however, cancer-related and its treatment-related comorbidities have become an issue for cancer survivors. The above mentioned disorders are among the most feared side-effects of anticancer agents so that the quality of life (QoL), as well as the life expectancy might be countered by reduced QoL and increased mortality.

Asthenia fatigue syndrome (AFS) or cancer-related fatigue is a common symptom perceived during and after treatment by patients with cancer and consists of pathologic fatigue, poor endurance, and impaired motor and cognitive function. It is a symptom, difficult to define, with a set of vague sensations, different for each patient. Some studies in cancer have reported the findings about how the above-mentioned comorbidities can increase the severity of cancer related fatigue.

A growing body of research has examined the hypothesis that cancer-related fatigue is driven by activation of the pro-inflammatory cytokine network. Actually, inflammation appears to play an essential role in cancer-related fatigue before, during and after cancer therapies. Accordingly, controlling or reducing the persistent inflammatory process can be beneficial to the management of cancer related fatigue.

The persistent pathological conditions in cancer patients may favour up-regulated expressions of pro-inflammatory mediators / cytokines and cause a sustained high level of chronic inflammation in the whole body, forming an important ground for triggering the comorbidities of cancer.

In the context of cancer treatment, anti-cancer chemo-agents destroy rapidly dividing cancer cells, as well as all the fast dividing non-cancer cells, which

undergo apoptosis due to chemotherapy agents and radiotherapy attack. The massive apoptosis of so many non-cancerous cells results in a large amount of secondary necrotic cells. These necrotic cells will cause and sustain inflammation by stimulating production of pro-inflammatory molecules.

5 Many internal and external factors can contribute to unwanted prolonged inflammation. However, activated vascular endothelial cells (ECs) in the human vasculature, as they are in direct contact with blood, play pivotal roles in the development of acute and chronic inflammation. Therefore, vascular EC may represent a relevant therapeutic target for the management of cancer and
10 treatment of cancer comorbidities, including but not limited to cancer-related fatigue, cachexia, anorexia, pain, anemia, asthenia, depression, muscle weakness, nausea, vomiting, skin and skin appendages adverse reactions.

One of the possible mechanisms by which inflammation may contribute to the development of tumorigenesis includes enhanced expression of pro-
15 inflammatory mediators such as cytokines (e.g. Interleukin 8) and adhesion molecules, e.g. ICAM-1 (Intercellular Adhesion Molecule 1, also known as CD54), E-selectin/ELAM-1 (also known as CD62E). The adhesion molecules can be found in low concentrations in the membranes of endothelial cells that "line" the interior surface of blood vessels in the whole vascular system. Their expression
20 levels are essential in the inflammatory process. A lower expression of such pro-inflammatory molecules indicates lesser inflammation, while higher expression indicates augmented inflammatory status. Upon toxic or pathological insults, the produced TNF-alpha (Tumor Necrosis Factor) will greatly stimulate expression of adhesion molecules and cytokines exemplified by E-selectin, ICAM-1 and
25 Interleukin 8 (IL-8). Increased expressions of adhesion molecules and cytokines mediate immune and inflammatory responses via recruitment of leukocytes to

inflammatory sites (infiltration of inflammatory cells through local vascular endothelium).

A former study showed that, compared with controls, the levels of soluble E-selectin and ICAM-1 were significantly higher in breast cancer patients at late stage. Besides, elevated adhesion molecule levels were predictive of decreased survival.

In addition, various pro-inflammatory mediators may not only switch on the tumor-prone inflammatory angiogenesis, a process that is essentially controlled by vascular endothelial growth factor, but also promote tumor metastasis.

Hence, for reducing harmful inflammation, it is critical to limit the synthesis of these pro-inflammatory molecules so as to decrease the anomalous inflammatory response.

Our studies show that, at molecular level, a composition comprising the ingredients mentioned hereafter is an anti-inflammatory agent, capable of reducing TNF α induced expression of adhesion molecules ICAM-1 and E-selectin on HUVECs (Human Umbilical Vein Endothelial Cells), as well as the cytokine IL-8 expression. Such anti-inflammatory potential results in inhibition of tumour progression and reduction of tumor size (see in the section above and data in the examples, obtained from both *in vitro* and *in vivo* studies). Thus, a composition comprising the ingredients mentioned hereafter provides anti-inflammatory effect for the support management of cancer and treatment of cancer comorbidities.

A composition comprising the ingredients mentioned hereafter was subcutaneously injected into a mouse cancer model in a randomized experiment. It was observed that, compared to non-treated mice, the said composition inhibits tumor growth and tumor size in treated mice (see data in the example 2 obtained from both *in vitro* and *in vivo* studies).

A composition comprising the ingredients mentioned hereafter was used in a topical formulation by cancer patients in order to prevent chemotherapy induced alopecia. Some patients reported that, apart from the beneficial effect on unwanted hair loss, other symptoms, such as fatigue, which they were also suffering from, started to improve steadily.

SUMMARY OF THE INVENTION

A composition comprising the ingredients mentioned hereafter was used orally by a patient suffering from liver cancer. Based on the physicians and patient's report and pictures taken before and after the intake of the said composition, his general state turned out to improve significantly, including alleviation of cancer related fatigue.

It has been discovered that the administration by oral route, topical, or parenteral route, intra-tumoral injection, or a combination thereof, of a composition containing as active ingredient an extract of *Allium species*, which may contain quercetin, an extract of *Citrus species* and an extract of *Paullinia species* and an extract of *Theobroma species*, has a novel and previously unknown effect for the management of cancer and treatment of cancer comorbidities.

The present invention proposes a method for the management of cancer and treatment of cancer comorbidities, including but not limited to cancer-related fatigue, cachexia, anorexia, pain, anemia, asthenia, depression, muscle weakness, nausea, vomiting, skin and skin appendages adverse reactions; comprising the administration by both conventional and non-conventional routes, and or as adjuvant potentiator in cell therapies, or topical route, or parenteral route, or intra-tumoral injection, or in combination, of a composition containing as

active ingredient an extract of *Allium species*, which preferably contain quercetin, an extract of *Citrus species* and an extract of *Paullinia species* and an extract of *Theobroma species*.

5 BRIEF DESCRIPTION OF THE FIGURES

Figure 1 corresponds to the curves of the mean body weight (in grams) measured at different times.

Figure 2 corresponds to the curves of the mean tumor volume (in mm³)
10 measured at different times.

DETAILED DESCRIPTION OF THE INVENTION

In particular, the present invention concerns a method for the
15 management of cancer and treatment of cancer comorbidities, including but not limited to cancer-related fatigue, cachexia, anorexia, pain, anemia, asthenia, depression, impaired cognitive function, loss of appetite, muscle weakness, nausea, vomiting, arthritis, organ damage, including but not limited to radiation-induced burns, heart disorders due to cardiotoxicity by chemo- and radiotherapy,
20 hypertension, thromboembolism, occasional chest pain, difficulty in breathing, shortness of breath, dizziness, fainting, pallor (pale skin or lips), headaches, difficulty in concentrating, insomnia, difficulty in staying warm, bleeding problems, nail damages, and skin appendages adverse reactions, exemplified by irritation and dry skin, sore and dry ulcerated mouths; comprising the administration by oral
25 route, topical, or parenteral route, intra-tumoral injection, or a combination thereof, of a composition containing as active ingredient an extract of *Allium*

species, which may contain quercetin, an extract of *Citrus species* and an extract of *Paullinia species* and an extract of *Theobroma species*.

Among the methods for the management of t cancer and treatment of
5 cancer comorbidities, according to the invention, those which are of more particular interest are the methods in which the preferred oral composition contains from 30% to 93% by weight of an extract of *Allium species*, which contains quercetin, from 3% to 33% by weight of an extract of *Citrus species*, from 0.10% to 2.5% by weight of an extract (atomized or not) of *Paullinia species* and
10 from 0.10% to 2.5% by weight of an extract (atomized or not) of *Theobroma species*, based on the total weight of the four active ingredients.

According to an embodiment, the composition comprises from 30% to 93% by weight of an extract of *Allium species*, which contains quercetin, from 3%
15 to 33% by weight of an extract of *Citrus species*, from 0.10% to 2.5% by weight of an extract (atomized or not) of *Paullinia species*, from 0.10% to 2.5% by weight of an extract (atomized or not) of *Theobroma species*, from 0.5% to 3.0% by weight of Sodium chloride and from 25% to 50% by weight of Glycerin, based on the total weight of the composition.

20

Among the methods for the management of cancer and treatment of cancer comorbidities, those which are the more preferred interest are the methods in which the compositions are used not only as conventional oral composition, composition for injection, topical application, but also as an adjuvant potentiator in
25 for the management of cancer and its treatment-related comorbidities. The compositions contain from 30% to 93% by weight of an extract of *Allium species*,

which contains quercetin, from 3% to 33% by weight of an extract of *Citrus* species, from 0.10% to 2.5% by weight of an extract (atomized or not) of *Paullinia* species and from 0.10% to 2.5% by weight of an extract (atomized or not) of *Theobroma* species, based on the weight of the four active ingredients.

5

According to an embodiment, the compositions contain from 30% to 93% by weight of an extract of *Allium cepa*, from 3% to 33% by weight of an extract of *Citrus lemon*, from 0.10% to 2.5% by weight of an extract (atomized or not) of *Paullinia* species and from 0.10% to 2.5% by weight of an extract (atomized or not) of *Theobroma* species, based on the weight of the four active ingredients.

10

According to an embodiment, the composition contains from 30% to 93% by weight of an extract of *Allium* species, which contains quercetin, from 3% to 33% by weight of an extract of *Citrus* species, from 0.10% to 2.5% by weight of an extract (atomized or not) of *Paullinia* species, from 0.10% to 2.5% by weight of an extract (atomized or not) of *Theobroma* species, from 0.5% to 3.0% by weight of Sodium chloride and from 25% to 50% by weight of Glycerin, based on the total weight of the composition.

15

The term extract of *Allium* species refers particularly to extracts and native extracts obtained from all species of the genus *Allium* (family *Liliaceae*) and especially *Allium cepa*, which may contain quercetin. The term extract of *Citrus* species refers particularly to extracts and native extracts obtained from all species of the genus *Citrus* (family *Rutaceae*) and especially *Citrus lemon*. The term extract (atomised or not) of *Paullinia* species refers particularly to extracts and native extracts obtained from all species of the genus *Paullinia* (family

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Sapindaceae) and especially *Paullinia cupana*. The term extract (atomised or not) of *Theobroma species* refers particularly to aqueous-alcoholic extracts and native extracts obtained from all species of the genus *Theobroma* (family *Malvaceae*) and especially *Theobroma cacao*.

5

The most preferred compositions used according to the invention are: those containing approximately 87% by weight of an extract of *Allium cepa*, which contains quercetin, approximately 12% by weight of an extract of *Citrus lemon*, approximately 0.5% by weight of an extract (atomized or not) of *Paullinia cupana* and approximately 0.5% by weight of an extract (atomized or not) of *Theobroma cacao*, based on the total weight of the four active ingredients.

According to the invention, the composition is chronically administered in a mixture containing as active ingredient an extract of *Allium species*, which contains quercetin, an extract of *Citrus species* and an extract of *Paullinia species* and an extract of *Theobroma species*.

According to an embodiment of the invention the composition is administered daily during a period of several months or longer with a composition containing as active ingredient an extract of *Allium species*, which contains quercetin, an extract of *Citrus species* and an extract of *Paullinia species* and an extract of *Theobroma species*.

In order to obtain a measurable effect on the management of cancer and treatment of cancer comorbidities, it is necessary to perform the administration of the compositions chronically, preferably during at least 6 months.

When using the compositions obtained according to the invention, doses may vary within relatively wide limits and must be set according to the person being treated and the condition concerned. Pharmaceutical compositions normally contain from 0.4 to 1000 mg, preferably from 2 to 400 mg, of active ingredients as defined
5 above, in the form of dry extract.

The present invention also concerns a composition containing as active ingredient an extract of *Allium* species, which contains quercetin, an extract of Citrus species and an extract of *Paullinia* species and an extract of *Theobroma*
10 species for use in the management of cancer and for the treatment of cancer comorbidities, including but not limited to cancer-related fatigue, cachexia, anorexia, pain, anemia, asthenia, depression, muscle weakness, nausea, vomiting, skin, and skin appendages adverse reactions; by both conventional and non-conventional routes, and/or as adjuvant potentiator in cell therapies, or topical
15 route, or parenteral route, or intra-tumoral injection, or in combination thereof.

According to an embodiment of the invention the composition for use in the management of cancer and for the treatment of cancer comorbidities contains an extract of *Allium* species, which contains quercetin, an extract of Citrus species
20 and an extract (atomized or not) of *Paullinia* species and an extract (atomized or not) of *Theobroma* species.

According to a further embodiment of the invention the composition for use in the management of cancer and for the treatment of cancer comorbidities,
25 contains from 30% to 93% by weight of an extract of *Allium* species, which contains quercetin, from 3% to 33% by weight of an extract of Citrus species, from

0.10% to 2.5% by weight of an extract (atomized or not) of *Paullinia* species and from 0.10% to 2.5% by weight of an extract (atomized or not) of *Theobroma* species, based on the total weight of the four active ingredients.

The following embodiments are provided:

- 5 1. A composition containing as active ingredient an aqueous-alcoholic or native extract of *Allium species*, which contains quercetin, an aqueous-alcoholic or native extract of *Citrus species*, an aqueous-alcoholic or native extract of *Paullinia species* and an aqueous-alcoholic or native extract of *Theobroma species* for use in the
10 treatment of cancer by inhibition of tumour progression and reduction of tumour size or in the treatment of cancer comorbidities selected from the group consisting of cancer-related fatigue, cachexia, pain, anemia, asthenia, depression and muscle weakness; wherein said composition is for administration by an oral route, an injection route,
15 a topical route, a parenteral route, or an intra-tumoral injection, or a combination thereof.
2. The composition according to embodiment 1, wherein the composition contains the extract of the *Allium species*, which contains quercetin, the extract of the *Citrus species*, an atomized
20 extract of the *Paullinia species* and an atomized extract of the *Theobroma species*.
3. The composition according to embodiment 1 or 2, wherein the composition contains from 30% to 93% by weight of the extract of *Allium species*, which contains quercetin, from 3% to 33% by weight
25 of the extract of *Citrus species*, from 0.10% to 2.5% by weight of the extract of *Paullinia species* and from 0.10% to 2.5% by weight of the

extract of *Theobroma* species, based on the total weight of the four active ingredients.

4. The composition according to any one of embodiments 1 to 3, for the treatment of cancer comorbidities selected the group consisting of cancer-related fatigue, cachexia, pain, anemia, asthenia and depression.
5. The composition according to any one of embodiments 1 to 3, for the treatment of cancer-related fatigue.
6. Use of a composition containing as active ingredient an aqueous-alcoholic or native extract of *Allium species*, which contains quercetin, an aqueous-alcoholic or native extract of *Citrus species*, an aqueous-alcoholic or native extract of *Paullinia species* and an aqueous-alcoholic or native extract of *Theobroma species* for the treatment of cancer by inhibition of tumour progression and reduction of tumour size or for the treatment of selected from the group consisting of cancer-related fatigue, cachexia, pain, anemia, asthenia, depression and muscle weakness; wherein said composition is for administration by an oral route, an injection route, a topical route, a parenteral route, or an intra-tumoral injection, or a combination thereof.
7. Use of a composition containing as active ingredient an aqueous-alcoholic or native extract of *Allium species*, which contains quercetin, an aqueous-alcoholic or native extract of *Citrus species*, an aqueous-alcoholic or native extract of *Paullinia species* and an aqueous-alcoholic or native extract of *Theobroma species* for the treatment of cancer by inhibition of tumour progression and reduction

of tumour size or for the treatment of cancer comorbidities selected from the group consisting of cancer-related fatigue, cachexia, pain, anemia, asthenia, depression and muscle weakness; wherein said composition is for administration by an oral route, an injection route, a topical route, a parenteral route, or an intra-tumoral injection, or a combination thereof.

8. The use according to embodiment 6 or 7, wherein the composition contains the extract of the *Allium* species, which contains quercetin, the extract of the *Citrus* species and an atomized extract of the *Paullinia* species and an atomized extract of the *Theobroma* species.
9. The use according to any one of embodiments 6 to 8, wherein the composition contains from 30% to 93% by weight of the extract of *Allium* species, which contains quercetin, from 3% to 33% by weight of the extract of *Citrus* species, from 0.10% to 2.5% by weight of the extract of *Paullinia* species and from 0.10% to 2.5% by weight of the extract of *Theobroma* species, based on the total weight of the four active ingredients.
10. The use according to any one of embodiments 6 to 9, for the treatment of cancer comorbidities selected the group consisting of cancer-related fatigue, cachexia, pain, anemia, asthenia and depression.
11. The use according to any one of embodiments 6 to 9, for the treatment of cancer-related fatigue.

EXAMPLE OF TREATMENT

The patients have received, every day by oral, topical, parenteral routes, or intratumoral injection, alone or in combination, a treatment containing :

- an extract of *Allium cepa* (containing querceting): 87.04 %
- 5 - an extract of *Citrus lemon*: 11.96 %
- an atomised extract of *Paullinia cupana*: 0.50 %
- an atomised extract of *Theobroma cacao*: 0.50 %

(hereafter composition A).

This lotion has been prepared as indicated in example 1 of patent application WO
10 2008/113912.

Composition A which is a mixture of four natural ingredients has been reported to beneficially affect defects in abnormal cell apoptosis, as well as in inflammatory processes. This has indicated that composition A is capable of affecting positively in the management of the above-mentioned cancer and cancer
15 treatment related comorbidities.

Example 1: Study of the composition, containing as active ingredient an extract of Allium species, which contains quercetin, an extract of Citrus species and an extract of Paullinia species and an extract of Theobroma species, on its anti-inflammatory effect via inhibiting TNF alpha-induced expression of pro-inflammatory molecules: ICAM-1, E-selectin and Interleukin 8, as summarized
20 Table 2a, 2b and 2c).

Table 1. The tested compositions

Compound	Ingredient	in total %wt
A	Allium Cepa	50,0
	Citrus	50,0
B	Allium Cepa	87,5
	Citrus	12,5
C	Allium Cepa	87,0
	Citrus	12,0
	Guarana dry extract	0,5
	Cacao dry extract	0,5
Control	Medium	

Table 2a. The effects of “compositions” on the expression of adhesion molecule **ICAM-1 (CD54)** on the surface of endothelial cells (HUVECs)

Composition	Non-treated cells measured by sABC*	TNF-treated cells measured by sABC*	% Increase (+) % Reduction (-) compared to control
Medium (control)	3 172	386 181	
A	2 061	296 561	-23%
B	1 947	297 444	-23%
C	1 664	254 171	-34%

* specific Antibody Bound per Cell

Table 2b. The effects of “compositions” on the expression of adhesion molecule **E-selectin/ELAM-1 (CD62E)** on the surface of endothelial cells (HUVECs)

Composition	Non-treated cells measured by sABC*	TNF-treated cells measured by sABC*	% Increase (+) % Reduction (-) compared to control
Medium (control)	Non detectable	3 074	
A	251	4 235	+38%
B	186	3 447	+12%
C	65	1 648	-46%

* specific Antibody Bound per Cell

Table 2c. The effects of “**compositions**” on the expression of cytokine **Interleukin 8 (IL-8)** by endothelial cells (HUVECs)

Composition	Non-treated cells measured by sABC*	TNF-treated cells measured by sABC*	% Increase (+) % Reduction (-) compared to control
Medium (control)	1 164	5 406	
A	1 067	6 274	+16%
B	1 015	5 563	+3%
C	887	4 827	-11%

* specific Antibody Bound per Cell

Example 2: Study on the anti-tumor activity of a new “composition” using nude mice carrying subcutaneous human tumor of type KB.

Figure 1 illustrates the curves of the average weight of nude mice bearing subcutaneous human tumor type KB. Mice were randomized at Day 7 and received a daily injection of 100 µl composition solution (THI) of 0.3% and 1.0% respectively for five consecutive days.

In Figure 1, x-axis represents time (days); y-axis represents average weight of nude mice (g). Blue (curve 2): control vehicle; Pink (curve 3): composition (THI) of 0.3%; Yellow (curve 1): composition (THI) of 1%. No significant weight changes were observed.

Figure 2 illustrates the curves of the mean tumor volume of nude mice bearing subcutaneous human tumor type KB. Mice were randomized at Day 7 and received a daily injection of 100 µl composition solution (THI) of 0.3% and 1.0% respectively for five consecutive days.

In Figure 2, x-axis represents time (days); y-axis represents average tumor volume of nude mice (mm³). Blue (curve 2): control vehicle; Pink (curve 3): composition (THI) of 0.3%; Yellow (curve 1): composition (THI) of 1%. No

significant weight changes were observed. Composition (THI) 0.3% show anti-tumor effect compared to control.

In some aspects, embodiments of the present invention as described herein
5 include the following items:

Item 1. A composition containing as active ingredient an aqueous-alcoholic extract of *Allium species*, which contains quercetin, an aqueous-alcoholic extract of *Citrus species*, an aqueous-alcoholic extract of *Paullinia species* and an aqueous-alcoholic extract of *Theobroma species* for use in the treatment of cancer
10 by inhibition of tumour progression and reduction of tumour size and in the treatment of cancer comorbidities selected from the group consisting of cancer-related fatigue, cachexia, pain, anemia, asthenia, depression and muscle weakness; wherein said composition is for administration by an oral route, an injection route, a topical route, a parenteral route, or an intra-tumoral injection, or a
15 combination thereof.

Item 2. The composition according to item 1, wherein the extract of the *Paullinia species* and the extract of the *Theobroma species* are atomized.

Item 3. The composition according to item 1 or 2, wherein the composition contains from 30% to 93% by weight of the extract of *Allium species*, which
20 contains quercetin, from 3% to 33% by weight of the extract of *Citrus species*, from 0.10% to 2.5% by weight of the extract of *Paullinia species* and from 0.10% to 2.5% by weight of the extract of *Theobroma species*, based on the total weight of the four active ingredients.

Item 4. The composition according to any one of items 1 to 3, for use in the
25 treatment of cancer comorbidities selected the group consisting of cancer-related fatigue and asthenia.

Item 5. The composition according to any one of items 1 to 3, for the treatment of cancer-related fatigue.

Item 6. Use of a composition containing as active ingredient an aqueous-alcoholic extract of *Allium species*, which contains quercetin, an aqueous-alcoholic
 5 extract of *Citrus species*, an aqueous-alcoholic extract of *Paullinia species* and an aqueous-alcoholic extract of *Theobroma species* for the preparation of a medicament for the treatment of cancer by inhibition of tumour progression and reduction of tumour size and for the treatment of cancer comorbidities selected from the group consisting of cancer-related fatigue, cachexia, pain, anemia,
 10 asthenia, depression and muscle weakness; wherein said composition is for administration by an oral route, an injection route, a topical route, a parenteral route, or an intra-tumoral injection, or a combination thereof.

Item 7. Use of a composition containing as active ingredient an aqueous-alcoholic extract of *Allium species*, which contains quercetin, an aqueous-alcoholic
 15 extract of *Citrus species*, an aqueous-alcoholic extract of *Paullinia species* and an aqueous-alcoholic extract of *Theobroma species* for the treatment of cancer by inhibition of tumour progression and reduction of tumour size and for the treatment of cancer comorbidities selected from the group consisting of cancer-related fatigue, cachexia, pain, anemia, asthenia, depression and muscle weakness;
 20 wherein said composition is for administration by an oral route, an injection route, a topical route, a parenteral route, or an intra-tumoral injection, or a combination thereof.

Item 8. The use according to item 6 or 7, wherein the extract of the *Paullinia species* and the extract of the *Theobroma species* are atomized.

25 Item 9. The use according to any one of items 6 to 8, wherein the composition contains from 30% to 93% by weight of the extract of *Allium species*,

which contains quercetin, from 3% to 33% by weight of the extract of *Citrus* species, from 0.10% to 2.5% by weight of the extract of *Paullinia* species and from 0.10% to 2.5% by weight of the extract of *Theobroma* species, based on the total weight of the four active ingredients.

- 5 Item 10. The use according to any one of items 6 to 9, for use in the treatment of cancer comorbidities selected the group consisting of cancer-related fatigue and asthenia.

 Item 11. The use according to any one of items 6 to 9, for the treatment of cancer-related fatigue.

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CLAIMS

1. A composition containing as active ingredient an aqueous-alcoholic
extract of *Allium species*, which contains quercetin, an aqueous-
5 alcoholic extract of *Citrus species*, an aqueous-alcoholic extract of
Paullinia species and an aqueous-alcoholic extract of *Theobroma*
species for use in the treatment of cancer by inhibition of tumour
progression and reduction of tumour size and in the treatment of cancer
comorbidities selected from the group consisting of cancer-related
10 fatigue, cachexia, pain, anemia, asthenia, depression and muscle
weakness; wherein said composition is for administration by an oral
route, an injection route, a topical route, a parenteral route, or an intra-
tumoral injection, or a combination thereof.
2. The composition according to claim 1, wherein the extract of the
15 *Paullinia species* and the extract of the *Theobroma species* are
atomized.
3. The composition according to claim 1 or 2, wherein the composition
contains from 30% to 93% by weight of the extract of *Allium species*,
which contains quercetin, from 3% to 33% by weight of the extract of
20 *Citrus species*, from 0.10% to 2.5% by weight of the extract of *Paullinia*
species and from 0.10% to 2.5% by weight of the extract of *Theobroma*
species, based on the total weight of the four active ingredients.
4. The composition according to any one of claims 1 to 3, for use in the
treatment of cancer comorbidities selected the group consisting of
25 cancer-related fatigue and asthenia.

5. The composition according to any one of claims 1 to 3, for the treatment of cancer-related fatigue.
6. Use of a composition containing as active ingredient an aqueous-alcoholic extract of *Allium species*, which contains quercetin, an aqueous-alcoholic extract of *Citrus species*, an aqueous-alcoholic extract of *Paullinia species* and an aqueous-alcoholic extract of *Theobroma species* for the preparation of a medicament for the treatment of cancer by inhibition of tumour progression and reduction of tumour size and for the treatment of cancer comorbidities selected from the group consisting of cancer-related fatigue, cachexia, pain, anemia, asthenia, depression and muscle weakness; wherein said composition is for administration by an oral route, an injection route, a topical route, a parenteral route, or an intra-tumoral injection, or a combination thereof.
7. Use of a composition containing as active ingredient an aqueous-alcoholic extract of *Allium species*, which contains quercetin, an aqueous-alcoholic extract of *Citrus species*, an aqueous-alcoholic extract of *Paullinia species* and an aqueous-alcoholic extract of *Theobroma species* for the treatment of cancer by inhibition of tumour progression and reduction of tumour size and for the treatment of cancer comorbidities selected from the group consisting of cancer-related fatigue, cachexia, pain, anemia, asthenia, depression and muscle weakness; wherein said composition is for administration by an oral route, an injection route, a topical route, a parenteral route, or an intra-tumoral injection, or a combination thereof.

8. The use according to claim 6 or 7, wherein the extract of the *Paullinia* species and the extract of the *Theobroma* species are atomized.
9. The use according to any one of claims 6 to 8, wherein the composition contains from 30% to 93% by weight of the extract of *Allium* species,
5 which contains quercetin, from 3% to 33% by weight of the extract of *Citrus* species, from 0.10% to 2.5% by weight of the extract of *Paullinia* species and from 0.10% to 2.5% by weight of the extract of *Theobroma* species, based on the total weight of the four active ingredients.
10. The use according to any one of claims 6 to 9, for use in the treatment
10 of cancer comorbidities selected the group consisting of cancer-related fatigue and asthenia.
11. The use according to any one of claims 6 to 9, for the treatment of cancer-related fatigue.

Figure 1

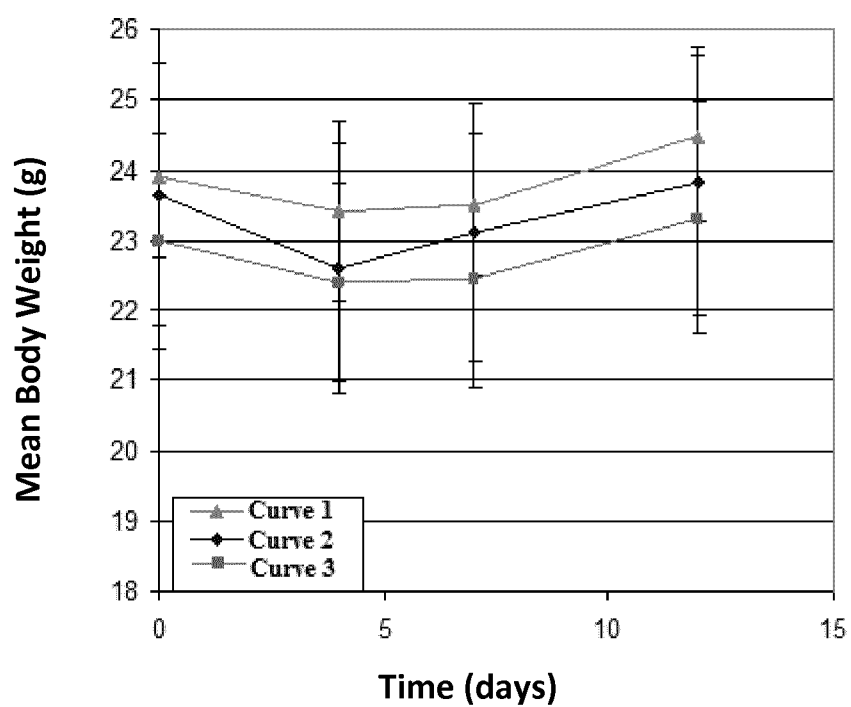


Figure 2

