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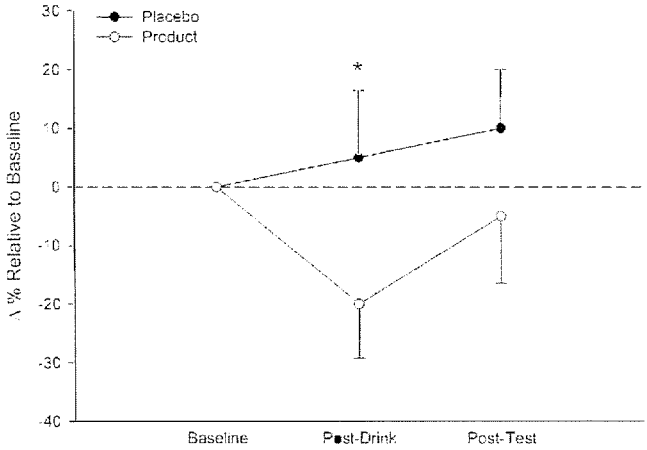
FIGURE 6



(57) Abstract: The present invention relates to compositions including L-theanine, proanthocyanidin(s); and a catechin selected from the group consisting of epigallocatechin gallate, epigallocatechin, epicatechin gallate, epicatechin and combinations thereof. The compositions may be used to treat, prevent, or provide mental clarity following a period of time after consumption. The present invention also relates to methods of treatment, and methods of manufacture and use of said composition.

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COMPOSITIONS COMPRISING L-THEANINE, PROANTHOCYANIDIN/S AND A CATECHIN AND USES THEREOF

TECHNICAL FIELD

The present invention relates to a functional composition and uses thereof, and in particular towards a composition that maintains or improves mental clarity.

BACKGROUND ART

There is a growing need for humans to maintain or improve optimal mental clarity (as a component of a larger sub-set of attributes of overall cognitive performance), and/or deal with stress, in order to meet the demands of the ever-changing expectations of society. For example, there is increased social pressure and an expectation to deliver more efficiencies in the work environment, home environment, in the education system, and so forth.

In the context of the present invention, mental clarity should be considered the absence or suppression of distracting thoughts and feelings (i.e. internal distractions potentially caused by nervousness or uncertainty), the suppression of distracting or irrelevant sensory input (i.e. external distractions), together with reasonable level of vigour. This is compared to improved attention or cognitive performance, with the differentiation that a person may be attentive or have an improved level of "cognitive performance" but also be highly nervous or uncertain. Thus a person can be still very attentive but may not have mental clarity. Mental clarity is sought after because it allows people to remain calm and unstressed, but still be able to make rational decisions, remain concentrated and determined at a job at hand.

There is a huge and growing consumer demand for any medicament, functional food, herbal extract or supplement that helps individuals to achieve a high level of mental performance, but these can not necessarily achieve mental clarity. For example, many products include the likes of caffeine, which can often lead to a sense of jitteriness or nervousness, despite leading an apparent increase in cognitive function.

For example, Bayer markets a range of Berocca® products to support mental alertness.

Many foods or food supplements are also now heavily marketed towards improving or maintaining cognitive function, including various nuts, fruits and vegetables, fish oils, just to name a few. However, the downside with many of these foods is that they only provide a desirable effect after a sustained period of consumption, for example weeks or months, normally together with an overall healthy diet

and lifestyle. Furthermore, it is often inconvenience or unpleasant to consume some food products in their unprocessed state. Supplements like fish oil capsules help to remedy this, but again such supplements are not seen by the public as having a desirable sensory perception profile.

The energy drink sector has enjoyed huge growth over recent years, based on health claims and marketing towards improving cognitive performance for a period of time after consuming the beverage, which also must taste good for commercial success. Most of these energy drinks rely on high levels of caffeine, and/or often have many unhealthy, or potentially harmful, ingredients in order to enhance the desired stimulatory effect or provide a beneficial taste. Furthermore, caffeine based energy drinks arguably may improve alertness to some extent, but as a side effect they can lead to a sense of hyper-activity, a loss of calmness, increased feeling of stress, a racing heart or a general uncomfortable jittery feeling, similar to the effects of having too much coffee. Furthermore, consuming too many of these energy drinks, either in a short time frame, or over an extended period, is a potential health concern.

Overall, there is a need to develop new functional foods/ beverages that maintain or improve mental clarity without the need for caffeine, and to do so while also providing an associated calmness and lack of nervousness, rather than hyper-activity. Like-wise, there is a need to provide consumers functional foods / beverages that provide immediate effects on mental clarity soon after consumption, have a desirable taste and mouthfeel, offer convenience, and are generally healthy to consume.

Besides caffeine, there are a wide number of compounds and natural extracts that are thought to have some form of link to cognitive performance and/or mood/stress. For example, lemonbalm, Passionflower, Valerian, Sage, Guarana, Chamomile, Ashwagandha, Brahmi, roseroot, skullcap, iranin borage, gotu kola, ginkgo and milk thistle are believed to provide some promising attributes or felt cognitive effects.

Yet, it is unclear how such active ingredients or extracts might be able to work together to achieve desirable effects towards mental clarity.

To better understand and perhaps harness the potential effects associated with these ingredients, there has been significant research into a number of these chemical compounds or extracts as alternatives to caffeine.

However, success has been hampered either by a lack of Western based scientific assessment or human trials which are costly and time consuming, contradictory results between studies, poor flavour or stability profiles, and/or high cost of the active ingredients/manufacturing. Furthermore, some compounds or extracts may only provide no, or only a very slight, improvement, and therefore can often

be viewed as not worth pursuing commercially.

It is also very difficult to predict or test results of altering the concentration / dosage of active ingredients to provide a desirable therapeutic effect. Also, research suggests that the associated effects of most compounds / extracts on cognitive performance, with mental clarity being only one aspect, appear to work through a variety of different complex modes of action, so it is very difficult to predict how different compounds may potentially work together if combined in attempt to provide a desired effect on improved mental clarity, if any.

Alternatively, the active agents may unintentionally negate one another, or provide unwanted results. Furthermore, combining different compounds together in attempt to provide synergies also can lead to potential issues with incompatibility/instability, or can negatively affect the sensory perception profile of a given composition. In summary, there is a significant hurdle of being able to study the effects of these different components, and it is impractical to test, and impossible to predict, different combinations of active agents for desirable health outcomes.

All references, including any patents or patent applications cited in this specification are hereby incorporated by reference. No admission is made that any reference constitutes prior art. The discussion of the references states what their authors assert, and the applicants reserve the right to challenge the accuracy and pertinency of the cited documents. It will be clearly understood that, although a number of prior art publications are referred to herein, this reference does not constitute an admission that any of these documents form part of the common general knowledge in the art, in New Zealand or in any other country.

Unless the context clearly requires otherwise, throughout the description and the claims, the words "comprise", "comprising", and the like, are to be construed in an inclusive sense as opposed to an exclusive or exhaustive sense, that is to say, in the sense of "including, but not limited to".

It is an object of the present invention to address the foregoing problems or at least to provide the public with a useful choice.

Further aspects and advantages of the present invention will become apparent from the ensuing description which is given by way of example only.

DISCLOSURE OF THE INVENTION

According to a first aspect of the present invention there is provided a composition including:

a) L-theanine;

b) proanthocyanidin(s); and

c) a catechin selected from the group consisting of epigallocatechin gallate, epigallocatechin, epicatechin gallate, epicatechin and combinations thereof.

According to a further aspect of the present invention there is provided a composition including:

a) L-theanine;

b) an extract from pine bark; and

c) an extract from *Camellia sinensis* or a green tea.

According to a further aspect of the present invention there is provided a use of a composition as herein described for the manufacture of a medicament for maintaining or improving mental clarity in a healthy individual.

According to a further aspect of the present invention there is provided a method of manufacturing a composition as herein described wherein the method includes the steps of mixing:

a) L-theanine or a source thereof;

b) proanthocyanidin(s) of a source thereof; and

c) a catechin selected from the group consisting of epigallocatechin gallate, epigallocatechin, epicatechin gallate, epicatechin and combinations thereof.

A method of supporting or improving mental clarity by administering to a person in need thereof with an effective amount of the composition as described herein.

Brief summary of the invention and its advantages

In a double-blind placebo-controlled randomized cross-over design in human subjects, the Applicant has surprisingly discovered that a trial composition according to the present invention led to an overall improvement in mental clarity after consumption, including:

- a better ability to quickly dispense with distracting or misleading information;
- a reduction of a sense of nervousness / tension / anxiety;
- a reduction of a sense uncertainty / confusion / bewilderment;
- an improved sense of vigour / liveliness / activity;
- no feeling of increased fatigue.

These specific traits, in combination or even individually, are highly desirable and could not have been readily predicted based on the individual components used in the composition. First, there is a very wide number of potential active ingredients or extracts that could have been used in combination for trials, and it would have been impractical to do such testing to determine the effectiveness in a suitable double-blind cross over trial as provided. Furthermore, there was every likelihood that unexpected, unwanted effects could have been observed with the combination as trialed, including potentially cancelling out effects given the individual components themselves have a complex modes of action, which are yet to be fully understood.

Instead, the composition tested showed remarkable and unexpected results in terms of improved mental clarity. If fact, the inventors were actually expecting a different result in relation to improved cognitive performance, specifically around heightened memory, processing speeds, attention, and so forth. Such effects was not observed, but the unexpected mental clarity outcome seen was subsequently actually considered a more commercially important result.

Additionally, the composition has a good sensory perception, despite difficulties with poor taste or mouth feel of some individual components. Additionally, the product has good storage stability, which again was unpredictable given the significant number of active ingredients in the composition and the potential for incompatibility / interaction with the active agents. These advantages will be discussed further throughout the specification.

Definitions and Preferred Embodiments

The inventive composition may be formulated into a range of potential products. For example, the composition may be formulated as a liquid or semi-liquid beverage or as a food supplement such as a pill, capsule or powder. Alternatively, the composition may be formulated into a food item, such as a chocolate bar, or other similar snack. Most preferably, the composition is formulated as a beverage.

Throughout the specification, the term mental clarity should be understood to include the absence, suppression or reduction of distracting thoughts and feelings (i.e. internal distractions potentially caused by tension or anxiety (e.g. nervousness) and/or confusion and bewilderment (e.g. uncertainty), the suppression or quicker identification of distracting, incorrect or irrelevant sensory input (i.e. external distractions), and/or an improved level of vigour. Mental clarity is a specific subset of overall mental performance, the latter which includes other factors such as composite memory, verbal memory, visual memory, processing speed, executive function, psychomotor speed, reaction time, complex attention, cognitive flexibility domains and overall neurocognitive index.

Preliminary tests (not shown) have indicated that the composition provides a significantly improved mental clarity for a period of about four hours after consumption compared to the control group. Further studies are being performed to assess these preliminary findings in more detail. The apparent synergistic effects as observed were also unexpected, given a potential contradiction with the actives, or inactivity when combined together. Furthermore, the heightened effects observed opens up opportunity to lower the dosage of one or more of the active agents to achieve a desirable result, which could help with lowering manufacturing costs, avoiding unwanted taste profiles of certain actives, and so forth.

L-theanine

Throughout the specification, the term L-theanine should be understood to mean γ-glutamylethylamide, or a suitable source of L-theanine, such as a green tea extract (*Camellia sinensis*, or other species of Camellia) or the edible mushroom *Xerocomus badius*. Notably, the invention does not cover D-theanine. Synthetically derived L-theanine may also be used, or even L-theanine derivatives thereof, if shown to also provide the same functionality as described herein.

L-theanine is water soluble, known to cross the blood-brain barrier, and reaches peak concentrations about one hour after consumption. There is some scientific literature to support that L-theanine can have a relaxant effect, but can have some negative effects on other aspects of cognitive performance, especially if combined with other psychoactive agents. The inventors found that when L-theanine was combined with both proanthocyanidin and at least one catechin, a beneficial synergy was observed where trial participants developed a sense of improved overall mental clarity (e.g. including faster processing of incorrect cues, improved vigour, decreased nervousness and uncertainty) but without negative effects on overall cognitive performance.

Preferably, the composition includes at least 50 mg L-theanine.

Previous studies suggest that effects of L-theanine are observed at as little as 50 mg dosage; however the Applicant expects the beneficial effects will be seen between about 50 to 500 mg per dosage.

Most preferably, the composition includes about 50-200 mg L-theanine.

Preferably, the concentration of L-theanine is above 0.005% w/v, more preferably between 0.015 to 0.17 % w/v, and most preferably about 0.08% w/v.

As described further below in the best modes section, these dosage amounts / concentration of L-theanine appeared to show the most promising results when in combination with the other components of the composition.

Of particular interest and surprise, the potential negative cognitive effects previously reported with L-theanine were not observed when combined with the other components of the composition. Equally, the calming effects of the L-theanine do not appear to have been diminished, and potentially have actually been amplified by the other components in combination.

Proanthocyanidin

Throughout the specification, the term proanthocyanidin should be understood to mean a class of polyphenols typically found in plants which are known to have powerful antioxidant properties. Proanthocyanidins are found in grapes, cranberry, apples, blueberries, and many other sources. A good source of proanthocyanidins is from pine bark extracts, from *Pinus radiata* (which is grown predominately in New Zealand) and *Pinus pinaster*, or Martime, pink bark (found predominantly in the Mediterranean region). Commercially available pine bark extracts (e.g. Enzogenol® or Pycnogenol®) which contain proanthocyanidins together with other condensed flavonoids have been shown to have therapeutic effects due to their powerful antioxidant activities.

Some preliminary studies have suggested beneficial links of proanthocyanidin to some factors associated with cognitive function, but it remains unclear whether the reported effects are due to increased blood flow, antioxidant action or other mechanisms. There is very little understanding of how these extracts may work if combined with other bioactives, or the potential effects on mood.

Here, the Applicant has shown that when pine bark extract is combined with L-theanine and EGCG, the test individuals showed a marked increase in mental clarity as previously discussed.

Preferably, the proanthocyanidin is provided within the composition as a pine bark extract.

More preferably, the proanthocyanidin is provided within the composition as *Pinus radiata* pine bark extract.

Preferably, the composition includes between 10 to 300 mg of proanthocyanidin or pine bark extract per dosage.

More preferably, the composition includes about 25 to 150 mg proanthocyanidin or pine bark extract per dosage. Most preferably the composition includes about 75 mg proanthocyanidin or pine bark extract per dosage

Preferably, the concentration of proanthocyanidin or pine bark extract in the composition is above 0.005% w/v, more preferably between 0.01 to 0.1 % w/v, and most preferably about 0.06% w/v.

Although it is possible to exceed these amounts without any likely detrimental therapeutic effects, the pine bark extract can cause problems with the taste profile of the composition. However, the Applicant points out this can often be overcome by using masking agents, if required.

Catechin(s)

The four types of catechins found in green tea (from *Camellia sinensis*) are epigallocatechin gallate (EGCG), epigallocatechin (EGC), epicatechin gallate (ECG), and epicatechin (EC). EGCG accounts for about 50-80% of the catechins in green tea. Catechins may also be found from other sources such as cocoa.

Green tea and/or its bioactives (including L-theanine, caffeine and catechins as its major components) have been associated with many therapeutic effects, including cancer treatment, improved kidney function, diabetes, reducing hyperglycemia, reduction of cortisol production, reduction in inflammation, and cardiovascular health. However, further research needs to be conducted to clearly establish the modes of action and how they may potentially be used to therapeutically treat patients with these diseases. There is also some recent evidence to suggest catechins may impart some improvements in cognitive performance, but more understanding is required to establish a definitive mode of action or correlation.

Yet, the Applicant's research has found that when a green tea extract (and in particular, EGCG or other catechins) is combined specifically with L-theanine and proanthocyanidins, preliminary experiments suggest remarkable results in terms of improved mental clarity beyond which might have been expected from the individual components alone or when combined.

Preferably, the composition includes between 50 to 600 mg of EGCG or green tea extract per dosage.

More preferably, the composition includes about 100 - 300 mg EGCG or green tea extract per dosage.

Most preferably, the composition includes about 160 mg EGCG or green tea extract per dosage.

Preferably, the concentration of EGCG or green tea extract is above 0.005% w/v, more preferably between 0.01 to 0.5 % w/v, and most preferably about 0.12 % w/v.

Therefore, in one particularly preferred embodiment, the composition includes:

a) L-theanine between 0.015 to 0.17 % w/v, and most preferably about 0.08% w/v;

b) a pine bark extract between 0.01 to 0.1 % w/v, and most preferably about 0.06% w/v; and

c) a green tea extract between 0.01 to 0.5 % w/v, and most preferably about 0.12 % w/v.

In preliminary informal tests, working within these ratios and concentration was found to be particularly beneficial in providing the desired effects. Further trials are being performed to confirm the results seen.

Preferably, the composition also includes anthocyanin.

Anthocyanins are members of the flavonoid group of phytochemicals often present in berryfruit (amongst other foods), and are most often responsible for imparting a deep red/purple/blue pigment to the fruit.

The Applicant has also seen in preliminary trials that incorporation of berryfruit extracts, such as blackcurrant extract, appears to improve results even further. The Applicant envisages that the likely active ingredients is the anthocyanins; however it is unclear how these actives may be working synergistically with the other components in the composition. Interestingly, the Applicant has encountered negative flavour issues when the berryfruit is combined with the pine bark extract in particular. Although masking agents may be used to help address this issue, further work is being conducted to assess whether the undesirable flavour profile may be addressed through other avenues.

Preferably, the composition includes between about 100 mg to 500 mg berryfruit extract per dosage, or most preferably about 500 mg per dosage.

Preferably, the composition includes about 0.2 % w/v berryfruit extract.

Preferably, the composition is caffeine free.

A significant advantage of the composition is that it does not rely on any need for a caffeine to provide the beneficial mental clarity effects, and avoids the jitteriness or anxiety associated with caffeine.

Preferably, the composition includes no added sugar.

In the context of a beverage, the composition may include a variety of excipients including natural flavours or fruit juice or concentrates; however a commercial advantage of the compositions developed is the lack of any need for added sugar to impart a pleasant tasting beverage.

Additionally, the developers also had to face self-imposed commercial goals to achieve target health ratings (including FSANZ regulations around the nutritional profiling scoring criterion) and also preferential Health Star ratings. Whilst this may seem trivial, it must be acknowledged that developing compositions with active ingredients such as these pose technical difficulty in achieving desirable shelf-life and active ingredient stability, important sensory perception profiles, health ratings, as well as achieving a functional cognitive benefit, namely mental clarity. The identification of the specific combination of active agents that not only is showing mental clarity, but also has a very good health profile (compliant with FSANZ Nutrient Profile Scoring Criterion), and allows commercially important stability and flavour profiles.

Uses / treatments

Preferably, the composition is used to treat, prevent, maintain or improve mental clarity for a period of time after consumption. For instance, as illustrated by the preliminary data, the composition may be used to:

- lower levels of tension / anxiety (or sub-sets of that such as nervousness); or
- lower levels of confusion / bewilderment (or sub-sets of that such as uncertainty); or
- improve levels of vigor activity (or sub-sets of that such as feeling lively, but without the jittery feeling often attributed from caffeine or other stimulants); or
- prevent feelings of depression or fatigue;
- or combinations thereof.

Alternatively the composition is used to treat, prevent, maintain or improve a healthy person's level of stress, mood, or sense of calmness.

BEST MODES FOR CARRYING OUT THE INVENTION

BRIEF DESCRIPTION OF THE DRAWINGS

Further aspects of the present invention will become apparent from the ensuing description which is given by way of example only and with reference to the accompanying drawings in which:

Fig 1. A schematic representation of the experimental timeline

Fig 2. Effects of Placebo and Product on the Fatigue domain (composite of words Worn Out, Exhausted, *Bushed*, *Weary* and *Fatigued*). Error bars denote ± SE.

Fig 3. Effects of Placebo and Product on all POMS Domains (sub---scores). Error bars denote ± SE.

Fig 4. Effects of Placebo and Product on the word Lively (included in the Vigor---Activity domain). Error bars denote ± SE.

Fig 5. Effects of Placebo and Product on the word Nervous (included in the Tension---Anxiety domain). Error bars denote ± SE.

Fig 6. Effects of Placebo and Product on the word Uncertain (included in the Confusion---Bewilderment domain). Error bars denote ± SE.

Fig 7. Mean effect of Placebo and Product on reaction time to Endogenous cues. Error bars denote ± SE. Panel A – Product*Cue Interaction.

Example 1- Base composition

Component	Preferred dosage range per 250 ml serving (and ratios derived therefrom)	Preferred dosage amount per 250 ml serving	Preferred concentration
L-theanine	50 mg to 500 mg	200 mg	0.08 % w/v
Pine bark extract, Pinus Radiata	50 mg to 300 mg	150 mg	0.06 % w/v
EGCG	100 mg to 700 mg	300 mg	0.12 % w/v

Example 2 - Functional beverage containing base composition

Name	Quantity	UOM
Organic Apple Juice Conc	134.82	Grams
Blackcurrant Juice Conc	8.81	Grams
Citric Acid	1	Grams
Xanthan Gum	1	Grams
Green tea extract (98% EGCG)	1.2	Grams
L-theanine	0.8	Grams
Pinus radiata bark extract (Enzogenol®)	0.6	Grams
Flavouring	4.9	Millilitres
Water to volume	1	Litre

Example 3 - Functional beverage containing base composition and blackcurrant extract

Name	Quantity	UOM
Organic Apple Juice Conc	134.82	Grams
Blackcurrant Juice Conc	8.81	Grams
Citric Acid	1	Grams
Xanthan Gum	1	Grams
Blackcurrant Extract	2	Grams
Green tea extract (98% EGCG)	1.2	Grams
L-theanine	0.8	Grams

Pinus radiata bark extract (Enzogenol®)	0.6	Grams
Flavouring	4.9	Millilitres
Water to volume	1	Litre

EXAMPLE 4: DOUBLE-BLIND PLACEBO CONTOLLED CROSS OVER STUDY IN HUMANS

Summary

The aim of this project was to explore effects of a plant extract beverage on cognitive performance. Functional ingredients within the formulation included extracts of pine bark, L-theanine and a green tea leaf extract. Several small human trials have reported acute changes in cognition following ingestion of other extracts, but the unique combination and dose used in the current studies are untested.

The plant extracts (or a cellulose placebo) were ingested in capsule form because the distinctive taste qualities of these extracts made it challenging to formulate a taste-matched placebo solution. Each treatment was ingested alongside 250ml of the product's juice base. Participants underwent a mood assessment three times per trial, visual tests twice, and neurocognitive testing 30 minutes after consuming each test drink + capsules.

Unexpectedly, the test beverage had no detectable improvement effects on overall cognitive performance measured via the cognitive test battery. Yet, beneficially, there was no decrease in cognitive performance. However, also unexpectedly, there was a dramatic effect on mental clarity, and in particular an ability to process invalid ques, an increase in the vigour-activity domain, a decrease in anxiety domain, and/or a decrease in the confusion-bewilderment domain, particularly in the post- drink and extending somewhat after post-test time-points. These unexpected attributes are seen to be a major commercially important outcome. For example, consumers may feel a sense of vigour without the nervous / jitteriness feelings associated with other drinks such as those containing caffeine. Similarly, with the lack of nervousness and uncertainty, decision making and clear-headedness is what may be contributing to the faster ability to process invalid cues.

Interestingly, higher levels of fatigue were observed post-test in the product vs placebo groups when using the POMS-SF inventory. However, no differences were observed between test drinks with visual

analogue fatigue response scale, which generally is given greater weighting than the POMS-SF for fatigue assessment.

Method

A Product and Placebo treatment were administered within a double-blind placebo-controlled randomised crossover design. Healthy adults visited the laboratory on two occasions, each visit was separated by 7 days. The trial order was block randomised with participants has equal probability of receiving both treatment orders. A fixed block size was used for stratification of participant sex.

20 healthy volunteers took part in the study (11 Female, 9 Male), with a mean age of 24 years (range 31-19), mass of 73 kg ± 14 and height of 1.8 m ± 0.1. The occupational distribution of the participants was 55% professionals and 45% students. Testing sessions were separated by a mean of 7 days (range 5-9 days).

On each visit to the laboratory participants ingested 2 capsules with 250ml of the product juice base packaged in the product bottle. Capsules contained either plant extracts or cellulose. This approach was taken because the distinctive taste qualities of the plant extracts made it challenging for the funder to formulate a taste-matched placebo solution within appropriate sensory discrimination thresholds.

The Product capsules contained 75mg of pine bark extract (Enzogenol) and 160mg of green tea extracts; min. 94% EGCG) and 100 mg L-theanine. The Placebo capsules contained 335mg of a cellulose filler. All ingredients were licensed by NZ Food Safety authorities and will be combined and packaged in a licensed commercial facility (ENZO Nutraceuticals Quality Control Laboratory). Capsules and the fruit juice base were stored at 4°C and consumed within a research kitchen (University of Auckland, Building 731.120, Tamaki Campus).

Thirty minutes after consuming the drink participants performed a standardised computer-based assessment of cognition and vision. A schematic representation of the experimental timeline is shown in Figure 1.

The cognitive test battery comprised seven tests: verbal and visual memory, finger tapping, symbol digit coding, the Stroop test, a test of shifting attention, and a continuous performance test. A detailed description of each test is given by Gualtieri and Johnson (2006). Standardised computer instructions on how to complete each test were given before the test along with practice sessions when necessary. Tests were conducted in an environmentally-controlled and sound-proofed chamber. Tests were

initiated and supervised (via a viewing window) by an experimenter and delivered unassisted and uninterrupted.

Test scoring was generated from 17 primary scores based on correct responses, error responses, number of responses, and reaction times. Primary scores were used to generate nine neurocognitive domain scores to reflect basic mental functions (composite memory, verbal memory, visual memory, processing speed, executive function, psychomotor speed, reaction time, complex attention, and cognitive flexibility) and an overall neurocognitive index score. Domain scores were generated as raw scores, calculated from composite primary scores of relevant tests, and then computed to standard scores and percentiles that represent the participants' raw score relative to an age-matched normative data set of healthy individuals. Standardized domain scores and the 17 primary scores were used for statistical analysis.

Upon completion of the test battery, a six-point Likert-type rating scale was presented on the computer screen prompting the participant to rate their current level of alertness ranging from 1 (exhausted, unable to function effectively) to 6 (fully awake and excellent alertness).

The POMS-SF is inventory that measures psychological distress via mood disturbance scores using a 30 word list of words. Each adjective is rated from 0-4 in terms of how the participant feels in the present moment; 0 – not at all, 1 – a little, 2 – moderately, 3 – quite a bit, and 4 – extremely. Each word falls under one of five domains; Depression, Vigor-Activity, Tension-Anxiety, Confusion-Bewilderment, or Fatigue. The scores given to the words that fall within each domain are then combined for an overall score. The POMS-SF was administered three times during the protocol, at Baseline, 30 min Post-Drink, and Post-Test, along with the perceptual scales.

Covert spatial attention was assessed using a visual cueing task. The initial baseline display consisted of a central fixation cross and two peripheral boxes. The instruction was to maintain fixated on the central cross at all times while responding as quickly and accurately as possible upon perception of a circular target appearing within one of the peripheral boxes. Participants responded using the left or right arrow keys on the keyboard. Before the appearance of the target, a cue was presented for 200 ms. The cue was either Endogenous (an arrow pointing to the right or left box), or Exogenous (an increase in the line width of the left or right box). Valid trials consisted of the target appearing in the cued direction, whereas for Invalid trials the target appeared opposite to the cued location. Neutral trials gave no indication as to where the target may appear, and were presented as a double-ended arrow in the endogenous trials, and an increase in the line width for both boxes in the exogenous trials. In total, 180 trials were collected, split evenly between endogenous and exogenous cues. Valid, invalid and neutral

trials were then randomised within the endogenous and exogenous blocks. Keyboard responses were collected using customised Matlab software (MathWorks R2010b, Massachusettes, USA). To ensure that participants maintained fixation on the central cross, eye movements were monitored with a head-fixed eye tracking system (ViewPoint Eye Tracker, Arrington Research Systems, Scottsdale, USA). Any trials in which the eyes deviated were rejected from analysis. Participants completed the covert attention task at baseline and again Post-Test, after the cognitive test battery.

Analysis

All self-assessments and perceptual scales were converted into a percentage along the continuum on which they were rated. Motivation, diet and stress were compared between the two sessions using a Student's paired t-test. A 2 Treatment x 3 Time Repeated Measures ANOVA with SPSS was used to assess changes in the perceptual scales, as well as the POMS questionnaire. Analysis was conducted for the five POMS domains, as well as on each individual word that contributed to the domain scores. Whilst the raw data was used for statistical analysis, the Post-Drink and Post-Test results have been normalised relative to the baseline measure for graphical representation.

Paired t-tests were used to compare the time taken to complete the cognitive test battery, alertness rating score, and all results for each individual test and subsequent domains. A missing data analysis was required for one missing data point in the alertness rating score for a participant in their Product trial. This took the mean value for the rest of the group, rounded to the nearest whole number.

Reaction Time and Percentage of Correct responses in the Covert Attention task were split into Endogenous or Exogenous categories, and each analysed using a 2 Treatment x 2 Time x 3 Cue Type RM ANOVA. Validity scores were then calculated by subtracting the Valid RT from the Invalid, and compared using a 2 Treatment x 2 Time RM ANOVA. Statistical significance was set at $p \leq 0.05$ and all means are reported ± SE.

Results

Readiness to Participate

Participants rated their motivation to participate in the trials as 76 % ± 1.7 on a scale from *very bad* to *very good*. They evaluated their diet over the 24 hours prior to each trial as 61 % ± 2.8 on a scale from *very bad* to *very good*, and their stress levels over the last 24 hours as 48 % ± 3.2 on a scale from *very bad* to *very good* in relation to normal. There were no differences between treatments or effects of trial order on these variables.

Perceptual Ratings

There was a significant effect of time (p = 0.001) across both treatments for "Feeling"; when asked what type of mood they were in, on a scale from *very bad* to *very good*. Evaluations of Feeling tended to increase Post-Drink (although this change was not significant) and then decreased below baseline values Post-Test. There was no difference between the treatments. When evaluating Arousal from *low* to *high*, and Fatigue from *not fatigued* to *highly fatigued*, there were no effects of treatment, time or trial order.

Mood Disturbance Ratings (POMS---SF)

There was a significant interaction between treatment and time for the POMS domain of Fatigue (p = 0.01) (Figure 2), as well as a main effect of time (p = 0.003).

Both drinks resulted in a decrease in ratings of fatigue, however this decrease was only maintained in the placebo trial, whereas the product resulted in an increase above baseline values (post-test). We believe this effect may merely because the product group was exerting more effort during the test. Of the 20 participants, 13 expressed higher levels of fatigue in the product treatment, compared with the placebo. Further investigation into the specific words used in the POMS questionnaire showed that this result was driven by significant interactions for the words Exhausted (p = 0.026) and Bushed (p = 0.022). We also note that other tests (visual analogue psychometric response scale) for fatigue showed no difference between the test groups.

Looking at Figure 3, post-drink results showed significant improvement in vigor-activity domains in the product group, lower tension-anxiety and confusion-bewilderment in the product group compared to the placebo. There were interactions between treatment and time for the words Lively, from the Vigor-Activity domain (p = 0.025) (Figure 3), and Nervous, from the Tension-Anxiety domain (p = 0.034) (Figure 4) and a main effect of treatment for Uncertain, from the Confusion-Bewilderment domain (p = 0.045) (Figure 5).

Cognitive Performance

Participants spent on average 28 min 11 s ± 46.5 s completing the cognitive test battery, with no differences across treatment or trial order. There were no effects of treatment on any cognitive domains (Table 1), or individual test results. Alertness was rated on a scale with the associated labels; 1 – Exhausted, unable to function effectively, 2 – Sleepy but able to function, 3 – Tired but able to function, 4 – Awake, able to function effectively, 5 – Awake and mentally alert, 6 – Fully awake and excellent alertness. A mean of 3.4 ± 0.14 was reported, with no differences with treatment or trial.

	Placebo		Product		Effect of Product
	Mean	SE	Mean	SE	p
Neurocognitive index	115.95	3.22	115.60	2.47	0.87
Composite memory	111.70	2.86	110.40	2.76	0.70
Verbal memory	110.45	3.11	108.00	3.73	0.51
Visual memory	109.00	3.26	109.20	2.51	0.96
Processing speed	169.10	7.15	175.45	6.07	0.38
Executive function	118.15	4.39	115.35	4.77	0.45
Psychomotor speed	142.60	4.93	145.65	3.76	0.41
Reaction time	114.30	2.96	113.65	3.02	0.72
Complex attention	96.20	5.73	96.30	4.22	0.99
Cognitive flexibility	120.55	6.07	113.30	5.10	0.32

Table 1. Effects of the treatments on cognitive domain scores. Data show the group mean ± SE. Note: Standard scores have a normative mean of 100 and SD of 10. Qualitative labels associated with performance levels include "very low" (<70), "low" (70---79), "low---average" (80---89), "average (90---109) and "above average" (>109). Data were compared between treatments using a paired t---test, and statistical significance was set at $p \leq 0.05$.

Covert Attention Task

For the Endogenous trials, there was a significant effect in that the product group was able to process and identify invalid cues significantly quicker than the placebo group. Additionally, overall there was a smaller difference in reaction times between valid and invalid cues for the product compared to the placebo. This may possibly indicate that in the product trials it was easier to disengage covert attention from the invalid cues and direct to the target, hence pointing to a more even decision making progress during the product trial. We believe this is a beneficial outcome providing more balanced decision making, aligned with the calming, lower nervousness effects provided by the product.

Interpretation

Overall, the trial unexpectedly did not result in an improved overall cognitive performance. However, it did substantially improve a key aspect of cognitive performance, including mental clarity / mood, and/or being able to process invalid cues quicker. These were very unexpected results, and which have considerable commercial implications.

The trial showed that the product group had significant improvements in key domains post-drink (vigour-activity, tension-anxiety, and confusion-bewilderment), and these results were particularly emphasized at the post-drink time point. At the same time, no negative effects were observed for

depression or fatigue POMS Domains. Commercially speaking, post-drink outcomes are considered to be more important than post-test outcomes as the post-drink is considered to be what primes the consumer to perform their daily tasks after consumption and act with mental clarity. Furthermore, the product group also importantly showed greater ability to quickly dispense with invalid cues, and be more balanced in terms of time taken to assess valid and invalid cues, both considered to be attributes of mental clarity.

The mechanisms of actions for each herbal ingredient is not fully understood, including any interactions or synergies between extracts, or components of the juice base.

The entire disclosures of all applications, patents and publications cited above and below, if any, are herein incorporated by reference.

Reference to any prior art in this specification is not, and should not be taken as, an acknowledgement or any form of suggestion that that prior art forms part of the common general knowledge in the field of endeavour in any country in the world.

The invention may also be said broadly to consist in the parts, elements and features referred to or indicated in the specification of the application, individually or collectively, in any or all combinations of two or more of said parts, elements or features.

Where in the foregoing description reference has been made to integers or components having known equivalents thereof, those integers are herein incorporated as if individually set forth.

It should be noted that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications may be made without departing from the spirit and scope of the invention and without diminishing its attendant advantages. It is therefore intended that such changes and modifications be included within the present invention.

WHAT I/WE CLAIM IS:

1. A composition including:
   a) L-theanine;
   b) proanthocyanidin(s); and
   c) a catechin selected from the group consisting of epigallocatechin gallate, epigallocatechin, epicatechin gallate, epicatechin and combinations thereof.

2. A composition including:
   a) L-theanine;
   b) an extract from pine bark containing proanthocyanidin(s); and
   c) an extract from Camellia sinensis or a green tea containing a catechin selected from the group consisting of epigallocatechin gallate, epigallocatechin, epicatechin gallate, epicatechin and combinations thereof.

3. The composition as claimed in any one of the above claims wherein the composition includes between about 50 mg to 200 mg L-theanine.
4. The composition as claimed in any one of the above claims wherein the concentration of L-theanine is between about 0.015 to 0.17 % w/v.
5. The composition as claimed in any one of the above claims wherein the proanthocyanidin or extract from pine bark in the composition is between about 10 to 300 mg.
6. The composition as claimed in any one of the above claims wherein the concentration of proanthocyanidin or pine bark extract in the composition is between about 0.01 to 0.1 % w/v.
7. The composition as claimed in any one of the above claims wherein the proanthocyanidin in the composition is an extract from *Pinus radiata* pine bark.
8. The composition as claimed in any one of the above claims wherein the composition includes between about 50 to 600 mg of EGCG or green tea extract.
9. The composition as claimed in any one of the above claims wherein the concentration of EGCG or green tea extract is between about 0.01 to 0.5 % w/v.
10. The composition as claimed in any one of the above claims wherein the composition also includes an anthocyanin, or a berryfruit extract containing anthocyanin.
11. The composition as claimed in claim 10 wherein the berryfruit extract is a blackcurrant extract.
12. The composition as claimed in claim 10 or 11 wherein the composition includes between about 100 mg to 500 mg or anthocyanin or berryfruit extract containing anthocyanin.

13. The composition as claimed in claim 10 to 12 wherein the composition includes about 0.2 % w/v berryfruit extract.
14. The composition as claimed in any one of the above claims wherein the composition is caffeine-free and/or sugar-free.
15. The composition as claimed in any one of the above claims wherein the composition is formulated as a liquid or semi-liquid beverage, a food or food supplement, a pill, capsule or powder.
16. A method of treatment to support, maintain, prevent or improve
    a) mental clarity,
    b) tension / anxiety,
    c) confusion / bewilderment,
    d) vigor activity,
    e) depression or fatigue
    f) or combinations thereof

    by administering to a person in need thereof with an effective amount of the composition as claimed in any of claims 1 to 14.

17. A use of a composition as claimed in any one of claims 1 to 14 in the manufacture of a medicament for supporting, maintaining, preventing or improving

    a) mental clarity,
    b) tension / anxiety,
    c) confusion / bewilderment,
    d) vigor activity,
    e) depression or fatigue
    f) or combinations thereof.

18. A method of manufacturing a composition as herein described wherein the method includes the steps of mixing:

    a) L-theanine or a source thereof;
    b) proanthocyanidin(s) or a source thereof; and
    c) a catechin selected from the group consisting of epigallocatechin gallate, epigallocatechin, epicatechin gallate, epicatechin and combinations thereof.

FIGURE 1

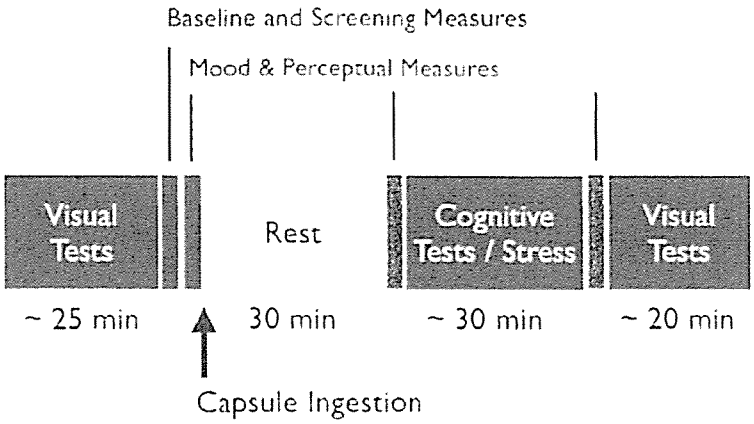

Baseline and Screening Measures
Mood & Perceptual Measures
Visual Tests
Rest
Cognitive Tests / Stress
Visual Tests
~ 25 min
30 min
~ 30 min
~ 20 min
Capsule Ingestion

FIGURE 2

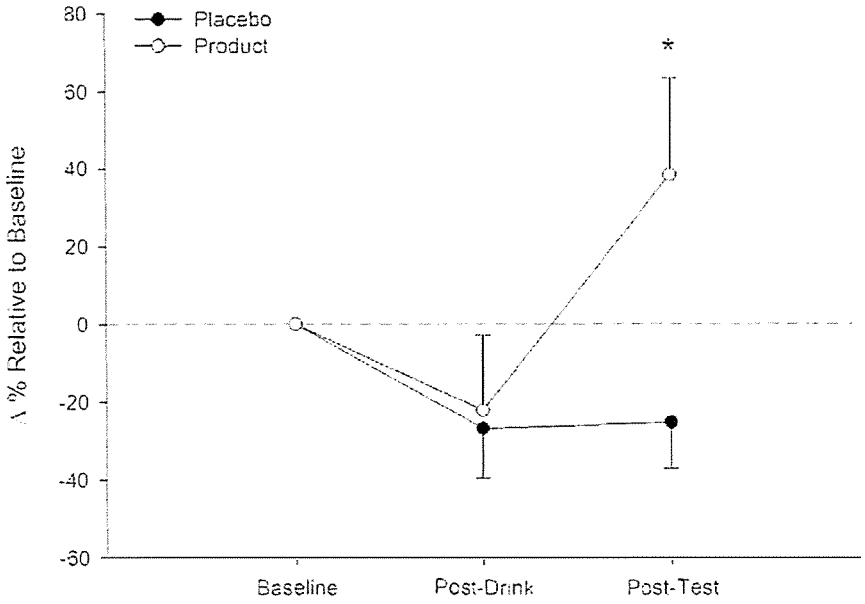

Placebo
Product
*
60
40
20
0
-20
-40
-60
Δ % Relative to Baseline
Baseline
Post-Drink
Post-Test

FIGURE 3

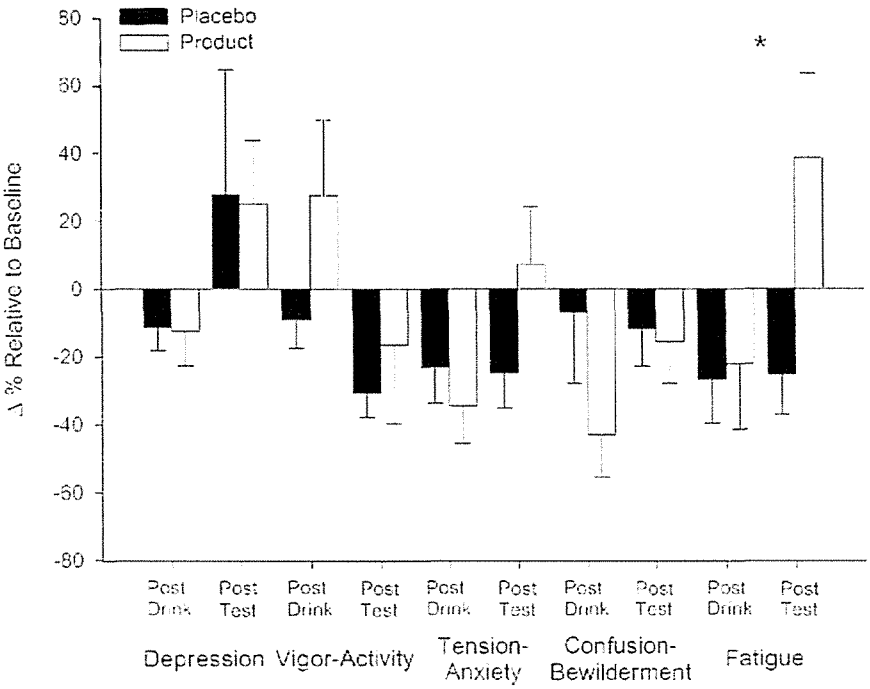

Placebo
Product
*
Δ % Relative to Baseline
80
60
40
20
0
-20
-40
-60
-80
Post Drink
Post Test
Depression
Vigor-Activity
Tension-Anxiety
Confusion-Bewilderment
Fatigue

FIGURE 4

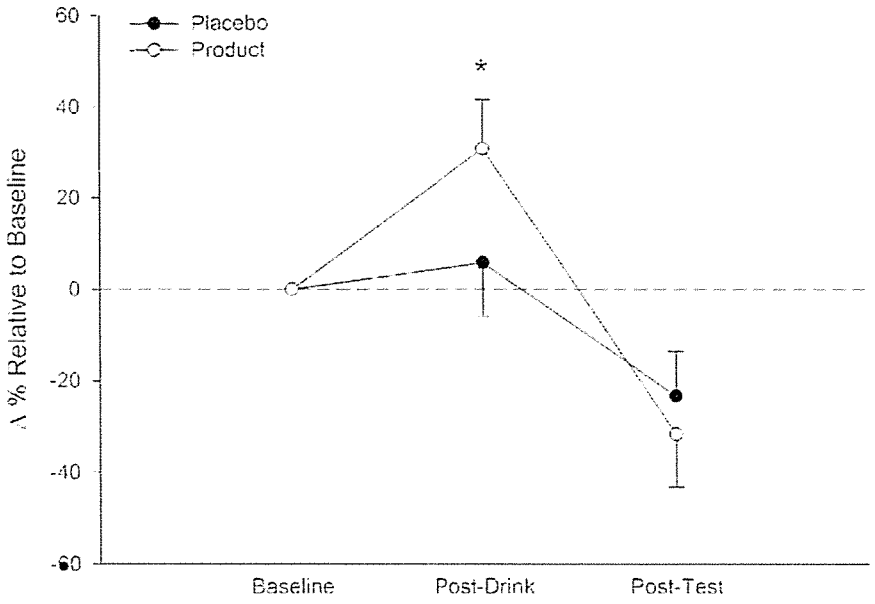

Placebo
Product
*
60
40
20
0
-20
-40
-60
Δ % Relative to Baseline
Baseline
Post-Drink
Post-Test

FIGURE 5

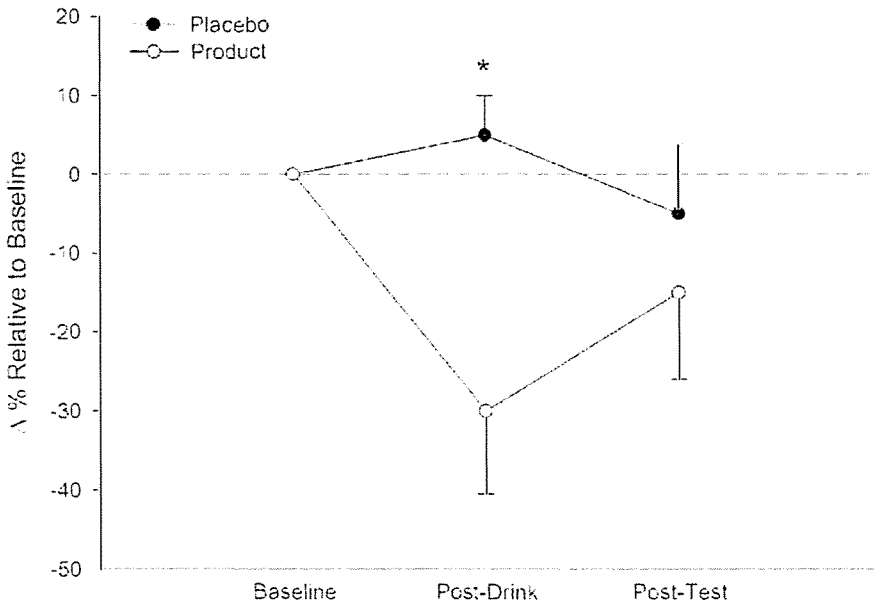

Placebo
Product
*
20
10
0
-10
-20
-30
-40
-50
Δ % Relative to Baseline
Baseline
Post-Drink
Post-Test

FIGURE 6

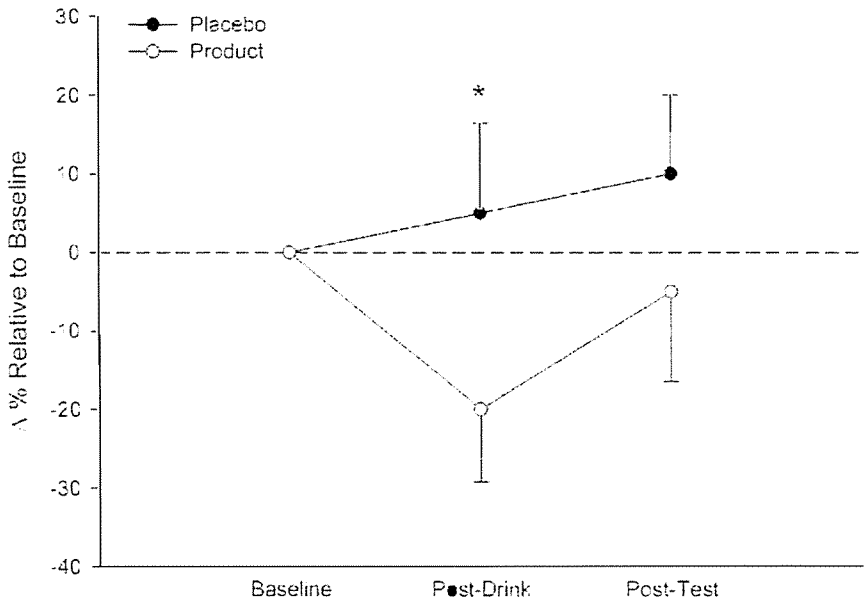
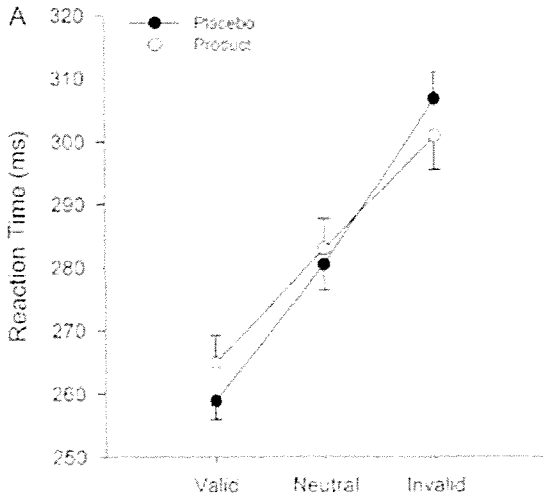

Placebo
Product
*
30
20
10
0
-10
-20
-30
-40
Δ % Relative to Baseline
Baseline
Post-Drink
Post-Test

FIGURE 7


A
320
310
300
290
280
270
260
250
Reaction Time (ms)
Placebo
Product
Valid
Neutral
Invalid

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ2017/050058

A. CLASSIFICATION OF SUBJECT MATTER

A61K 36/82 (2006.01) ***A61K 36/15 (2006.01)*** ***A61K 36/45 (2006.01)*** ***A61K 36/87 (2006.01)*** ***A61K 31/353 (2006.01)*** ***A61P 25/22 (2006.01)*** ***A61P 25/24 (2006.01)***

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

PATENW, MEDLINE, CAPLUS, BIOSIS, EMBASE, FSTA, AGRICOLA: Camellia sinensis, green tea, L-theanine, proanthocyanidin, pine bark, Pinus radiata, catechin, epigallocatechin gallate, epigallocatechin, epicatechin gallate, epicatechin, cognition, anxiety, vigor, depression, fatigue and similar terms. **Internal databases provided by IP Australia, PubMed, Espacenet, Traditional Knowledge Digital Library, Mintel GNPD, Google:** Applicant/Inventors and keywords search.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Documents are listed in the continuation of Box C	

[X] Further documents are listed in the continuation of Box C [X] See patent family annex

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
24 August 2017	24 August 2017
Name and mailing address of the ISA/AU	**Authorised officer**
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA Email address: pct@ipaustralia.gov.au	Lauren Howitt AUSTRALIAN PATENT OFFICE (ISO 9001 Quality Certified Service) Telephone No. +61262256130

INTERNATIONAL SEARCH REPORT C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		International application No. **PCT/NZ2017/050058**
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HILAL, Y. et al., 'Characterisation of white tea – Comparison to green and black tea', Journal of Consumer Protection and Food Safety. 2007, Vol. 2, pages 414-421 See '3. The key players – Phenolics in tea', '4. Flavanol related compounds', '5. Methods of Analysis'	1, 14 and 15
X	GRAHAM, H.N., 'Green Tea Composition, Consumption, and Polyphenol Chemistry', Preventive Medicine. 1992, Vol. 21, pages 334-350 See abstract, 'Tea composition', Tables 5-7	1, 14 and 15
X	US 2010/0021533 A1 (MAZED et al.) 28 January 2010 See [0109], [0121], [0122], Example 4 Mixture D, Example 5, [0214], [0215], [0229]-[0231], [0338]	1, 2, 7, 10, 11 and 14-17
X	KARHANOVA, M. et al., 'ProVens® in the Therapy of Glaucoma and Ocular Hypertension', Ceska A Slovenska Oftalmologie. 2015, Vol. 71, No. 6, pages 288-292 See abstract	1, 2, 5, 7, 8, 10, 11 and 15
X	'New Nordic Clear Brain Mental Performance & Memory Tablets (Record ID 3358877)' [retrieved from internet on 24 July 2017], <URL: http://www.gnpd.com/sinatra/recordpage/3358877/from_search/gYCHYxSV0Z/?page=1>, Published August 2015 according to Mintel GNPD See 'Product Description', 'Ingredients (Standard form)', 'Ingredients (On Pack)', 'Nutrition'	1, 2, 5, 7, 8 and 15-17
X	'New Nordic Clear Brain Mental Performance & Memory Dietary Supplement (Record ID 3756273)' [retrieved from internet on 24 July 2017], <URL: http://www.gnpd.com/sinatra/recordpage/3756273/from_search/bCTXTf849c/?page=1>, Published February 2016 according to Mintel GNPD See 'Product Description', 'Ingredients (Standard form)', 'Ingredients (On Pack)', 'Nutrition'	1, 2, 5, 7, 8 and 15-17
X	'Veritee Light Wellness Drink (Record ID 1166737)' [retrieved from internet on 24 July 2017], <URL: http://www.gnpd.com/sinatra/recordpage/1166737/from_search/3TJ3SbDVjZ/?page=1>, Published August 2009 according to Mintel GNPD See 'Product Description', 'Ingredients (Standard form)', Ingredients (On Pack)', 'Nutrition'	1, 8, 9, 14 and 15
X	WO 2008/006082 A2 (BARRON) 10 January 2008 See page 2, page 8, paragraph 4 – page 15, page 17, paragraph 2	1, 3, 8 and 14-17
X	WO 2007/131106 A2 (SILVER PALATE KITCHENS, INC.) 15 November 2007 See page 40, paragraph 3, Examples 11 and 15	1, 10 and 15
A	CAMFIELD, D.A. et al., 'Acute effects of tea constituents L-theanine, caffeine, and epigallocatechin gallate on cognitive function and mood: A systematic review and meta-analysis', Nutrition Reviews. 2014, Vol. 72, No. 8, pages 507–522 See whole document, especially 'Methods', 'Discussion'	1, 16 and 17

INTERNATIONAL SEARCH REPORT

International application No.
PCT/NZ2017/050058

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:

because they relate to subject matter not required to be searched by this Authority, namely:

the subject matter listed in Rule 39 on which, under Article 17(2)(a)(i), an international search is not required to be carried out, including

2. ☒ Claims Nos.: **18**

because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

See Supplemental Box

3. ☐ Claims Nos:

because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.

Supplemental Box

Continuation of **Box II**

The claim does not comply with Rule 6.2(a) because it relies on references to the description and/or drawings.

INTERNATIONAL SEARCH REPORT Information on patent family members	International application No. **PCT/NZ2017/050058**

This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document/s Cited in Search Report		**Patent Family Member/s**	
Publication Number	**Publication Date**	**Publication Number**	**Publication Date**
US 2010/0021533 A1	28 January 2010	US 2010021533 A1	28 Jan 2010
		US 8017147 B2	13 Sep 2011
		US 2011293278 A1	01 Dec 2011
		US 8073331 B1	06 Dec 2011
		US 2011158653 A1	30 Jun 2011
		US 8548334 B2	01 Oct 2013
		US 2015382089 A1	31 Dec 2015
		US 9426545 B2	23 Aug 2016
		US 2013338039 A1	19 Dec 2013
		US 9557271 B2	31 Jan 2017
		US 2012265596 A1	18 Oct 2012
		US 9697556 B2	04 Jul 2017
		US 2017006363 A1	05 Jan 2017
		US 9723388 B2	01 Aug 2017
		US 2009252758 A1	08 Oct 2009
		US 2009252796 A1	08 Oct 2009
		US 2010073202 A1	25 Mar 2010
		US 2011274680 A1	10 Nov 2011
		US 2016004298 A1	07 Jan 2016
		US 2017018688 A1	19 Jan 2017
		US 2017221032 A1	03 Aug 2017
WO 2008/006082 A2	10 January 2008	WO 2008006082 A2	10 Jan 2008
WO 2007/131106 A2	15 November 2007	WO 2007131106 A2	15 Nov 2007
		US 2008044539 A1	21 Feb 2008

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

INTERNATIONAL SEARCH REPORT Information on patent family members	International application No. **PCT/NZ2017/050058**

This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document/s Cited in Search Report		**Patent Family Member/s**	
Publication Number	**Publication Date**	**Publication Number**	**Publication Date**

End of Annex

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.