PROFESSIONAL INFORMATION

Scheduling Status: S0

1. Proprietary Name

Burnout

2. Qualitative and Quantitative Composition

Each capsule contains the composition as per table 2.1 below.

2.1 Composition

Each white capsule contains	
Beta-carotene (providing elemental vitamin A)	75 ug
Lynside® Forte B100 EU (S. cerevisiae enriched with B vitamins) of which Vitamin B1 (Thiamine) of which Vitamin B2 (Riboflavin) of which Vitamin B3 (Nicotinamide) of which Vitamin B5 (D-Calcium pantothenate) of which Vitamin B6 (Pyridoxine HCl) of which Vitamin B8 (Biotin) of which Vitamin B9 (Folic acid) of which Vitamin B12 (Cyanocobalamin)	56.3 mg 0.3 mg 0.3 mg 3.8 mg 1.4 mg 0.4 mg 12.4 ug 50.7 ug 0.6 ug
Malpighia glabra (Acerola cherry) [fruit extract standardised to 25% Vitamin C]	50 mg
Ascophyllum nodosum (Kelp) (providing elemental iodine)	15 ug
S. cerevisiae enriched with Magnesium oxide (Providing elemental Magnesium)	10 mg
Selenomethionine (as Selenium SeLECT™) (providing elemental selenium)	2.5 mg
Lynside® Forte ZN100K (Zinc) (S. cerevisiae enriched with Zinc, providing elemental Zinc)	2.5 mg
Ocimum sanctum (Holy basil) [herb, 10 mg of a 10:1 extract providing 100 mg dried herb equivalent]	250 mg
Withania somnifera (Ashwagandha) [root, 10 mg of a 15:1 extract providing 150 mg dried herb equivalent]	150 mg
N-Acetyl-L-Cysteine (NAC)	50 mg
Phosphatidyl serine	50 mg
Vitis vinifera (Grape) [seed extract standardised to 95% proanthocyanidins]	25 mg
Rhodiola rosea, root powder	25 mg
Pterostilbene	15 mg

2.2 Sugar Free.

2.3 For full list of excipients see section 7.1.

3. Pharmaceutical Form

60 white size 0 capsules containing light brown coloured, free-flowing powder.

4. Clinical Information

4.1 Indications for Use

Where a deficiency in the active ingredients may exist. Where improvement in sleep is needed.

4.2 Method of Administration and Posology

4.2.1 Administration

Orally.

4.2.2 Posology

Adults and children over 18 only.

Take 2 capsules daily.

Take capsules with a sufficient quantity of water.

Do not chew the capsules swallow whole.

Take capsules at approximately the same time every day.

4.3 Contraindications

Not recommended for individuals who are hypersensitive (allergic) to soy or any of the ingredients contained in the product.

4.4 Special Warnings and Precautions

Not recommended for individuals who are under the age of 18. Not recommended for individuals who are pregnant or breastfeeding. Do not exceed the recommended daily dose.

4.5 Interactions

S. cerevisiae: Major risk of interactions with MAOIs. Moderate risk of interactions with antidiabetic drugs and lithium.

Magnesium: Moderate risk of interactions with aminoglycoside antibiotics, antacids, bisphosphonates, calcium channel blockers, digoxin, ketamine, quinolone antibiotics, skeletal muscle relaxants, sulfonylureas, and tetracycline antibiotics. Major risk of interactions with levodopa/carbidopa.

Zinc: Moderate risk of interactions cephalexin, cisplatin, integrase inhibitors, penicillamine, quinolone antibiotics, ritonavir, and tetracycline antibiotics.

Ashwagandha: Moderate risk of interactions with antidiabetic drugs, antihypertensive drugs, benzodiazepines, CNS depressants, immunosuppressants and thyroid hormone.

Holy basil: Moderate risk of interactions with anticoagulant drugs, antidiabetic drugs and pentobarbital.

Acerola cherry: Moderate risk of interactions with alkylating agents and antitumour antibiotics.

Rhodiola: Moderate risk of interactions with antidiabetic drugs, antihypertensive drugs, cytochrome P450 2C9 substrates, immunosuppressants, losartan and p-glycoprotein substrates.

Grapeseed: Moderate risk of interactions with anticoagulant drugs, cyclosporine, cytochrome P450 1A2, cytochrome P450 2D6, cytochrome P450 2E1, cytochrome P450 3A4, midazolam and phenacetin.

N-Acetyl Cysteine: Major risk of interactions with nitro-glycerine. Moderate risk of interactions with activated charcoal, anticoagulant drugs, antihypertensive drugs, and chloroquine.

Phosphatidyl serine: Moderate risk of interaction with anticholinergic and cholinergic drugs.

4.6 Pregnancy and Lactation

Not recommended for individuals who are pregnant or breastfeeding.

4.7 Effects on ability to drive and use machinery.

No known effect.

4.8 Side Effects

Mild gastrointestinal disturbances, such as nausea, diarrhoea, constipation, indigestion, bloating, metallic taste in the mouth, and flatulence.

5 Pharmacological Classification

Category D: 33.7 Combination Product.

Complementary Medicine.

6 Pharmacokinetic Properties

Beta Carotene

Absorption: Absorption of beta-carotene is variable. The intestine has a limited capacity to absorb intact beta-carotene. Beta-carotene appears to be absorbed better from supplements than food. The amount of beta-carotene absorbed from food is only about 5% to 30% of that from synthetic supplements due to complexes it forms with proteins and fibre. Heating food may break down these complexes. Beta-carotene requires some dietary fat for absorption, but supplemental beta-carotene is similarly absorbed when taken with high-fat (36 grams fat) or low-fat (3 grams fat) meals The amount of beta-carotene absorbed and converted to vitamin A also depends upon the individual's vitamin A status, beta-carotene body stores, and the amount of beta-carotene ingested.
There is more than one isomer of beta-carotene and there may be differences in their absorption. The 9-cis-beta-carotene isomer is poorly absorbed, and most of it is converted to all-trans-beta-carotene in the intestine.
Beta-carotene supplements are available in both oil matrix gelatine capsules and water-miscible forms. Some clinical trials have used water-miscible beta-carotene (10%) beadlets. The water miscible form seems to produce a 47% to 50% higher plasma beta-carotene level than oil matrix gelatine capsules.
Metabolism: Some ingested beta-carotene is converted to vitamin A in the intestinal mucosa while some is converted to vitamin A in the liver. Although beta-carotene is partly metabolized to vitamin A, high intake of beta-carotene does not result in vitamin A toxicity because the proportion converted to vitamin A decreases as beta-carotene intake increases.
Distribution: The cis isomers of beta-carotene account for less than 5% of carotenoids in plasma, but 10% to 25% of carotenoids in the tissues are beta-carotene cis isomers. Carotenoids are mainly carried in the blood on low-density lipoproteins (LDLs).
Excretion: Beta-carotene is excreted in the faeces.

Thiamine

Absorption: Orally, thiamine is absorbed at the proximal part of the small intestine. At smaller doses it is absorbed by active transport, and at higher doses it is absorbed by passive diffusion.
Distribution: Thiamine is distributed into the skeletal muscle, the heart, the liver, the kidneys, and the brain.
Metabolism: Thiamine is phosphorylated during intestinal uptake. Most of thiamine in the adult human body occurs as the metabolically active form thiamine diphosphate (thiamine pyrophosphate or TDP).
Excretion: Thiamine and its metabolites are excreted in the urine, and urinary thiamine is used as a biomarker for the assessment of thiamine intake.

Biotin

Absorption: After oral administration, biotin is completely absorbed and reaches peak concentration after 1-2 hours. However, dietary biotin is bound to lysine residues of protein. Before it can become bioactive, it must be cleaved by biotinidase from food proteins. After being cleaved, biotin is transported across the intestinal lumen enterocytes by the sodium-dependent multivitamin transporter (SMVT) and into the liver and peripheral tissues. Biotin can be absorbed by passive diffusion when extracellular levels of biotin exceed 25 mcM/L.
Distribution: Following oral absorption, SMVT mediates biotin uptake into liver and peripheral tissues; SMVT also mediates renal reabsorption of biotin. When administered intravenously, a large fraction of biotin is stored in the liver, where mitochondrial acetyl-CoA carboxylase serves as a biotin reservoir. In contrast to the kidney and liver, the central nervous system retains most of its biotin during phases of depletion.
Metabolism: Biotin metabolites are formed by beta-oxidation, sulphur oxidation, or both.
Excretion: About half of the dose of biotin is excreted within 24 hours. Biotin is excreted in the urine as unmetabolized biotin or as the biotin metabolites bisnorbiotin, biotind,l-sulfoxides, bisnorbiotin methyl ketone, biotin sulfone, and tetranorbiotin-l-sulfoxide Animal research suggests that biliary excretion is relatively minor. Biotin is recycled endogenously. This may be the reason why deficiency symptoms take a long time to develop and are rarely seen in humans.

Nicotinamide

Absorption: Nicotinamide riboside is a precursor in the biosynthetic pathway of nicotinamide adenine dinucleotide (NAD+). Oral administration or nicotinamide riboside leads to notable, dose-dependent increases in blood NAD+ levels, suggesting that nicotinamide riboside is bioavailable when taken orally The time to maximum serum concentration (Tmax) of nicotinamide riboside taken orally is 3 hours
Metabolism: Nicotinamide riboside is converted to nicotinamide mononucleotide (NMN) by the nicotinamide ribose kinases NRK1 and NRK2. These enzymes phosphorylate nicotinamide riboside Nicotinamide riboside is also converted to niacinamide (nicotinamide) by purine nucleoside phosphorylase (PNP). Both pathways contribute to the NAD+ metabolome Nicotinamide riboside is also converted to niacinamide by intestinal bacteria
Elimination: Nicotinamide riboside has a half-life of 2.7 hours.

Folic Acid

Absorption: Folate in food is about 20% to 50% less bioavailable than synthetic folic acid, which is almost 100% bioavailable. Before folate from food can be absorbed, the polyglutamate side chain must undergo enzymatic deconjugation in the small intestine to form the absorbable monoglutamate form Folate deconjugation occurs maximally at a pH of 6-7). Folate levels in the blood increase approximately 30 minutes following consumption in foods and levels remain elevated for up to 5 hours with no difference in the area under the curve (AUC) for monoglutamyl vs. polyglutamyl folates The bioavailability of polyglutamyl forms of folic acid appears to be approximately 50% to 78% of monoglutamyl folic acid.
Some vitamin manufacturers claim that supplements containing L-methylfolate are better than folic acid-containing supplements. There is some evidence that L-methylfolate is slightly more bioavailable than folic acid. However, with continuing use of the supplements there is no difference in blood levels. Some manufacturers claim that L-methylfolate is a better alternative to folic acid because some people lack the enzymes to convert folic acid to L-methylfolate. But so far, there is no reliable evidence that this makes a meaningful difference. For example, equivalent doses of folic acid and L-methylfolate raise folate levels in pregnant women equally well
There is also interest in the reduced form of synthetic folate, L-5-methyltetra-hydrofolate (L-5-MTHF), which is dependent on vitamin B12 for metabolism. A single dose of L-5-MTHF seems to result in faster and greater absorption when compared with folic acid, both in those with the homozygous (TT) MTHFR and the wild-type (CC) MTHFR genotypes During longer supplementation periods of up to 16 weeks, this increased bioavailability seems to be less pronounced but maintained. Two small clinical studies in females show that taking L-5-MTHF (Metafolin, Eprova) 1.3 mg or L-5-MTHF 416 mcg daily for 12-16 weeks resulted in slightly higher folate concentration in red blood cells when compared with taking the molar equivalent of folate 1 mg or 400 mcg daily for 12-16 weeks
Distribution: In patients with coronary artery disease, plasma 5-methyltetrahydrofolate increases proportionately with treatment dose of folic acid, whereas vascular tissue 5-methyltetrahydrofolate does not.
Metabolism: After folic acid is absorbed, it is reduced to tetrahydrofolate and then enters a methylation cycle (Tetrahydrofolate is then converted to L-methyl folate. In patients with coronary artery disease, plasma 5-methyltetrahydrofolate increases proportionately with treatment dose of folic acid However, unmetabolized folic acid is also found in both plasma and breast milk when folic acid is consumed.
Excretion: Folic acid is excreted mainly in the urine.

Cyanocobalamin

Absorption: Vitamin B12 is primarily absorbed (60%) by binding with intrinsic factor to be actively transported in the terminal ileum. In addition to active absorption, it is estimated that about 1.2% of vitamin B12 is absorbed by passive diffusion. Dietary vitamin B12 is cleaved from proteins at normal gastric pH. Conditions involving increased gastric pH such as atrophic gastritis, use of acid-suppressing drugs, or partial gastrectomy, reduce vitamin B12 absorption. Loss of intrinsic factor in pernicious anaemia and total gastrectomy also reduce absorption. Intramuscular administration is often used to avoid these absorption problems. More recently, high oral doses of vitamin B12 (300 to 1000 mcg) have been used to capitalize on absorption by passive diffusion and treat pernicious anaemia and malabsorption from food A fasting state seems to increase vitamin B12 absorption when compared with a

postprandial state, and a maximum concentration seems to occur about three hours after oral supplementation
Elimination: Orally, vitamin B12 as cyanocobalamin and cyanocobalamin-SNAC has a half-life of about 25-30 hours. Intravenously, vitamin B12 as cyanocobalamin has a half-life of about 15 hours.

Acerola Cherry:

Absorption: There is some evidence that vitamin C is more bioavailable when ingested in acerola than when taken as an ascorbic acid dietary supplement. When healthy Japanese males 22-26 years of age ingested vitamin C 50 mg as diluted acerola juice or as a supplement dissolved in water, acerola juice produced a higher area under the concentration/time curve (AUC) for vitamin C and a lower amount of vitamin C excreted in the urine over the following 6 hours.

Zinc

Absorption: About 15% to 40% of the zinc in foods is absorbed. Bioavailability is influenced by zinc status. Absorption increases in states of zinc deficiency and if zinc intakes are low (Zinc is mostly absorbed in the small intestine, particularly the jejunum In human research, zinc oxide absorption is best in an acidic environment Zinc acetate is absorbed over a wide pH range and might be a better choice in people with reduced stomach acid In laboratory research, zinc uptake in human intestinal epithelial cells is similar for zinc chloride, zinc methionine, and zinc propionate
Zinc absorption may be influenced by dietary factors. In humans, diets high in phytate result in a reduced bioavailability of zinc, even during fortification Vegetarian diets also result in a decrease in the total amount of zinc absorbed, but these diets are without effect on fractional absorption However, although zinc absorption may be increased with some protein sources, others, such as bovine serum albumin and soy protein, may reduce its absorption
Distribution: More than 85% of the total zinc in the body is in skeletal muscle and bone

Metabolism: In human research, zinc given intravenously or orally resulted in zinc going rapidly to the liver, followed by two component exponential loss patterns .Plasma levels following intravenous administration decreased to <2% of that injected by 24 hours; following oral administration levels decreased from a maximum of 1.2% of that ingested 3 hours after intake to 0.7% by 24 hours .

Excretion: Most zinc is excreted in the faeces, with a small amount eliminated in the urine However, urinary zinc levels appear to increase in patients with type 2 diabetes and congestive heart failure During lactation, zinc excretion increases via breast milk. The body seems to compensate for this increased demand by increasing zinc absorption and conserving endogenous zinc.

N-acetyl cysteine:

Absorption: The bioavailability of oral N-acetyl cysteine is low, ranging from 4% to 10%. The low bioavailability may be attributed to deacetylation of N-acetyl cysteine in the intestinal mucosa and lumen. In pharmacokinetic research, the area under the curve (AUC) in humans after a single oral 600 mg N-acetyl cysteine dose was 32.87 mcM/L, while the Tmax was about 0.7-1 hour for both 200 mg and 600 mg doses Other research suggests that the Tmax is closer to 1.5 hours In patients receiving standard intravenous N-acetyl cysteine treatment for acetaminophen poisoning, the average plasma concentration of N-acetyl cysteine was 554 mg/L after the initial loading dose (150 mg/kg over 15 minutes). At steady-state, an N-acetyl cysteine level of 35 mg/L was maintained after 12 hours, and the AUC was 1748 mg/hr/L The AUC of N-acetyl cysteine is elevated in patients with cirrhosis
Distribution: Assessing the pharmacokinetics of N-acetyl cysteine is difficult because it binds to cysteine and other sulfhydryl molecules. Because these compounds are widely available in tissues, N-acetyl cysteine is rapidly removed from plasma N-acetyl cysteine is highly protein-bound Some pharmacokinetic research shows that oral N-acetyl cysteine is approximately 50-64% protein-bound (with a volume of distribution of 0.33-0.59 L/kg At high concentrations, oral N-acetyl cysteine remains active in the human lung for approximately five hours
Metabolism: Animal research suggests that N-acetyl cysteine is rapidly metabolized to disulphides via deacetylation and oxidation
Excretion: The plasma clearance of N-acetyl cysteine was found to be 0.84 L/hr/kg after a 400 mg oral dose and 0.11 L/hr/kg after a 200 mg intravenous dose After intravenous treatment for acetaminophen poisoning, total clearance

of N-acetyl cysteine was 3.18 mL/min/kg in one study N-acetyl cysteine has a renal clearance of approximately 30% In other research, the fraction of an oral dose of 600 mg excreted in the urine in 36 hours is 3.7%. The major excretory product of N-acetyl cysteine appears to be sulphate The half-life of intravenous N-acetyl cysteine has been reported to be less than 30 minutes in some pharmacokinetic research The terminal half-life of intravenous N-acetyl cysteine is around 5.6-5.7 hours while the terminal half-life of oral N-acetyl cysteine is around 6.25 hours both oral and intravenous N-acetyl cysteine range from 5.6-6.25 hours In other research, the half-life of oral N-acetyl cysteine after taking 600 mg orally twice daily for 3 days is 15.4 hours in Chinese individuals and 18.7 hours in Caucasians Patients with cirrhosis appear to have a slower plasma clearance and prolonged half-life

Phosphatidyl serine

Absorption: The peak concentration of D-serine in the blood seems to occur about an hour after oral administration.
Metabolism: The enzyme serine racemase (SR) converts L-serine to D-serine and vice versa. D-amino acid oxidase (DAAO) quickly catabolizes and deaminates D-serine into pyruvic acid. DAAO controls the level of serine in the brain and decreases bioavailability of orally administered serine. When NMDA receptors are overstimulated, nitric oxide is produced, which activates DAAO and suppresses SR activity.

Vitis vinifera

Absorption: In humans, the aglycone forms of resveratrol and quercetin in grape juice appear to be absorbed more readily than the glycoside derivatives (Proanthocyanidins and flavonoids from grape seed extract and grape juice are absorbed and distributed into serum within two to three hours of ingestion Oligomeric proanthocyanidins (OPCs) are poorly absorbed in the human small intestine When applied topically, (-)-epicatechin, a constituent of grape seed extract (GSE), penetrates the skin and is retained in the upper part of the skin for approximately 1% and 3% of the dose in formulations containing butylated hydroxytoluene and alpha-tocopherol, respectively.
Distribution: Proanthocyanidins and flavonoids from grape seed extract and grape juice can be detected in serum within two to three hours of ingestion.
Metabolism: Polyphenols from grape juice are metabolized to phenolic acids by colonic microbiota The most common phenolic acids produced include syringic acid, 3- and 4-hydroxyhippuric acid, 4-hydroxymandelic acid, 3-hydroxyphenylpropionic acid, and 3-hydroxyphenylacetic acid.
Elimination: Anthocyanins and phenolic acids formed from polyphenols in grape juice extract are excreted in the urine.

Ascophyllum Nodosum

Absorption: After oral consumption of Ascophyllum nodosum extract, phlorotannin's and phlorotannin metabolites are detectable in plasma. Iodine levels are also increased after taking Ascophyllum nodosum powder However, the iodine from Ascophyllum nodosum is not absorbed as well as with potassium iodide supplementation.
Metabolism: Phlorotannin's from Ascophyllum nodosum are conjugated as glucuronides and/or sulphates. Most phlorotannin metabolites are detected in plasma between 6 hours and 24 hours after intake, suggesting that metabolism by gut microbes occurs in the large intestine prior to absorption.
Excretion: In humans, both conjugated and unconjugated phlorotannin's were excreted in the urine between 8 and 24 hours after taking Ascophyllum nodosum Iodine absorbed from Ascophyllum nodosum powder is excreted in the urine.

7. Pharmaceutical Information

7.1 List of Excipients

Vegetarian capsules, milled rice flour.

7.2 Incompatibilities

None.

7.3 Shelf Life

24 months from date of manufacture.

7.4 Storage

Store in a cool dry place, between 15°C -25°C. Store in original container.

7.5 Presentation

60 white capsules packed in a 300 ml cylindrical white container with a lid and packaged in a single carton.

7.6 Disposal and handling of product

All unused medication should be disposed of in accordance with local regulatory authority.

8. Holder of certificate of registration

FoodGrown™©
371 Angus Crescent
Northlands Business Park
North Riding
Gauteng
South Africa

9. Registration Number

Still to be allocated

10. Date of first authorisation

Still to be allocated

11. Date of review

New

12. Reference: https://naturalmedicines.therapeuticresearch.com/

APPLICANT DETAILS:

FoodGrown™©
371 Angus Crescent
Northlands Business Park
North Riding
Gauteng
South Africa
+27(0)87 265 4789

DATE OF PUBLICATION:

16 May 2023