HERBIEVITE ANTI-STRESS ADULTS (softgels)
Western Herbal Complementary Medicine and Health Supplement.

HERBIEVITE ANTI-STRESS ADULTS is unregistered and has not been evaluated by SAHPRA for its quality, safety or intended use. This medicine is not intended to diagnose, treat, cure or prevent any disease.

SCHEDULING STATUS
Not scheduled

1. NAME OF THE MEDICINE
HERBIEVITE ANTI-STRESS ADULTS (softgels)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Active Substance:
Each softgel contains:
Fish Oil 200 mg
Vitamin C (Ascorbic Acid) 30 mg
Vitamin E (D-a-Tocopherol Acetate) 1,5 mg
Vitamin A 40 µg
Vitamin D3 Oil2,5 µg

3. PHARMACEUTICAL FORM
Chewable soft capsules.HERBIEVITE ANTI-STRESS ADULTS is an off-white, opaque softgel.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
HERBIEVITE ANTI-STRESS ADULTS plays a factor in the maintenance of good health.
HERBIEVITE ANTI-STRESS ADULTS is a multi-vitamin/fish oil supplement.

4.2 Posology and method of administration
Take 6 chewable soft gel capsules for persons 18 years and older.

4.3 Contraindications
HERBIEVITE ANTI-STRESS ADULTS CONTAINS SOYABEAN OIL AND FISH OIL.
IF YOU ARE ALLERGIC TO PEANUTS, SOYA, FISH OR FISH DERIVATIVES, DO NOT USE THIS MEDICAL PRODUCT. HERBIEVITE ANTI-STRESS ADULTS must not be used in patients with:
- Hypersensitivity to the active substances (Fish Oil, Vitamin A, C, E or D3) or to any of the excipients listed in section 6.1

Fish Oil
Fish oil is contraindicated with the following allergic conditions:
- Vitamin E Analogues.
- Omega-3(N-3) Polyunsaturated Fatty Acids.
- Docosahexanoic Acid (DHA).
- Fish containing product.
- Linoleic Acid.
- Linolenic Acid.

Vitamin A
Vitamin A is contraindicated in pregnancy and breastfeeding patients (see Fertility, pregnancy and lactation). It should be prescribed with caution to patients with hepatic disease, renal disease, alcoholism, and acne vulgaris.

Vitamin D3
Vitamin D3 must not be used in patients with:
- Hypercalcaemia and/or hypercalciuria.
- Nephrolithiasis (Renal calculi).
- Hypervitaminosis.
- Severe renal impairment.

Vitamin E
The following conditions are contraindicated with this medicine:
A Vitamin K deficiency.
- An eye condition in which the retina is damaged (retinitis pigmentosa).
- Bleeding disorders.
- Diabetes.
- A history of a previous heart attack or stroke.
- Head and neck cancer.
- Liver disease.

4.4 Special warnings and precautions for use
Fish Oil
HERBIEVITE ANTI-STRESS ADULTS should be used with caution in patients with known sensitivity or allergy to fish. Some people who are allergic to seafood such as fish might also be allergic to fish oil supplements.
- Taking fish oil might increase some of the symptoms of bipolar disorder.
- Fish oil might increase the risk of bleeding in people with liver scarring due to liver disease.
- Taking fish oil might increase some of the symptoms of depression.
- Fish oil can lower blood pressure and might cause blood pressure to drop too low in people who are being treated with blood pressure-lowering medications.
- Higher doses of fish oil can lower the body's immune system response. This could be a problem for people whose immune system is already weak.

Vitamin A
- People with conditions that affect fat absorption, such as celiac disease, short gut syndrome, jaundice, cystic fibrosis, pancreatic disease, and cirrhosis of the liver, are not able to absorb vitamin A properly. To improve vitamin A absorption, these people should use vitamin A preparations that are water-soluble.
- A type of high cholesterol called "Type V hyperlipoproteinemia" - this condition might increase the chance of vitamin A poisoning. Do not take vitamin A if you have this condition.
- Intestinal infections such as hookworm can reduce how much vitamin A the body absorbs.
- Iron deficiency might affect the body's ability to breakdown and use vitamin A.
- Too much vitamin A might make liver disease worse. Do not take vitamin A if you have liver disease.

Vitamin C
- Diabetics, patients prone to recurrent renal calculi, those undergoing stool occult blood tests, and those on sodium-restricted diets or anticoagulant therapy should not take excessive doses of vitamin C over an extended period of time.
- Vitamin C may interfere with tests and assays for urinary glucose, giving false-negative results with methods utilising glucose oxidase with indicator (e.g. Labstix, Tes-Tape) and false-positive results with neocuproine methods.
- Estimation of uric acid by phosphotungstate or uricase with copper reduction and measurement of creatinine in non-deproteinised serum may also be affected.
- High doses of vitamin C may give false-negative readings in faecal occult blood tests.
- Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take HERBIEVITE ANTI-STRESS ADULTS.

Vitamin D3
- HERBIEVITE ANTI-STRESS ADULTS should be used with caution in patients with impairment of renal function and the effect on calcium and phosphate levels should be monitored. The risk of soft tissue calcification should be taken into account. In patients with severe renal insufficiency, vitamin D in the form of Cholecalciferol is not metabolised normally and other forms of vitamin D should be used.
- HERBIEVITE ANTI-STRESS ADULTS should not be taken by patients with a tendency to form calcium-containing renal calculi.
- Caution is required in patients receiving treatment for cardiovascular disease (see section 4.5 – Interaction with other medicines and other forms of interaction).
- HERBIEVITE ANTI-STRESS ADULTS should be prescribed with caution to patients suffering from sarcoidosis because of the risk of increased metabolism of vitamin D to its active form. These patients should be monitored with regard to the calcium content in serum and urine.
- Allowances should be made for vitamin D supplements, other vitamin D containing medicines or from other sources.
- The need for additional calcium supplementation should be considered for individual patients. Calcium supplements should be given under close medical supervision.
- Medical supervision is required whilst on treatment to prevent hypercalcaemia.

Vitamin E
- Avoid taking supplements containing vitamin E or other antioxidant vitamins (beta-carotene, vitamin C) immediately before and following angioplasty without the supervision of a health care professional. These vitamins seem to interfere with proper healing.
- Vitamin E might make bleeding disorders worse. If you have a bleeding disorder, avoid taking vitamin E supplements.
- Vitamin E taken for 2 years or more can worsen insulin resistance when given with a liver disease called non-alcoholic fatty liver disease (NAFLD).
- Exercise is sometimes used by people with osteoporosis to improve bone strength. Exercising and taking high doses of vitamin E and vitamin C might lessen the benefits of exercise on bone strength.
- Vitamin E might increase the risk of bleeding during and after surgery. Stop using vitamin E at least 2 weeks before a scheduled surgery.
- Vitamin E might worsen clotting problems in people whose levels of vitamin K are too low.

4.5 Interaction with other medicines and other forms of interaction
Fish Oil
- Fish oils seem to help reduce some fat levels in the blood. These fats are called triglycerides. Birth control pills might decrease the effectiveness of fish oils by reducing these fat levels in the blood. Some birth control pills include ethinyl estradiol and levonorgestrel (Triphasil), ethinyl estradiol and norethindrone (Ortho-Novum 1/35, Ortho-Novum 7/7/7), and others.
- Fish oils seem to decrease blood pressure. Taking fish oils along with medications for high blood pressure might cause your blood pressure to go too low. Some medications for high blood pressure include captopril (Capoten), enalapril (Vasotec), losartan (Cozaar), valsartan (Diovan), diltiazem (Cardizem), Amlodipine (Norvasc), hydrochlorothiazide (HydroDiuril), furosemide (Lasix), and many others.
- Fish oils might slow blood clotting. Taking fish oils along with medications that also slow clotting might increase the chances of bruising and bleeding. Some medications that slow blood clotting include aspirin, clopidogrel (Plavix), diclofenac (Voltaren, Cataflam, others), ibuprofen (Advil, Motrin, others), naproxen (Anaprox, Naprosyn, others), dalteparin (Fragmin), enoxaparin (Lovenox), heparin, warfarin (Coumadin), and others.

Vitamin A
- There is an increased risk of hypervitaminosis A if vitamin A is given with synthetic retinoids such as acitretin, isotretinoin, and tretinoin.
- Vitamin A can interact with some antibiotics. Taking very large amounts of vitamin A along with some antibiotics can increase the chance of a serious side effect called intracranial hypertension. But taking normal doses of vitamin A along with tetracyclines doesn't seem to cause this problem. But taking normal doses of vitamin A along with tetracyclines doesn't seem to cause this problem. Do not take large amounts of vitamin A if you are taking antibiotics.Some of these antibiotics include demeclocycline (Declomycin), minocycline (Minocin), and tetracycline (Achromycin).
- Taking large amounts of vitamin A might harm the liver. Taking large amounts of vitamin A along with medications that might also harm the liver can increase the risk of liver damage. Do not take large amounts of vitamin A if you are taking a medication that can harm the liver.Some medications that can harm the liver include acetaminophen (Tylenol and others), amiodarone (Cordarone), carbamazepine (Tegretol), isoniazid (INH), methotrexate (Rheumatrex), methyldopa (Aldomet), fluconazole (Diflucan), itraconazole (Sporanox), erythromycin (Erythrocin, Ilosone, others), phenytoin (Dilantin), lovastatin (Mevacor), pravastatin (Pravachol), simvastatin (Zocor), and many others.
- Warfarin (Coumadin) is used to slow blood clotting. Large amounts of Vitamin A can also slow blood clotting. Taking vitamin A along with warfarin (Coumadin) can increase the chances of bruising and bleeding. Be sure to have your blood checked regularly. The dose of your warfarin (Coumadin) might need to be changed.

Vitamin C
- Ascorbic acid increases the renal excretion of amphetamine. The plasma concentration of ascorbate is decreased by smoking and oral contraceptives.
- The body breaks down estrogens to get rid of them. Vitamin C might decrease how quickly the body gets rid of estrogens. Taking vitamin C along with estrogens might increase the effects and side effects of estrogens.
- Large amounts of vitamin C might decrease how much fluphenazine (Prolixin) is in the body. Taking vitamin C along with fluphenazine (Prolixin) might decrease the effectiveness of fluphenazine (Prolixin).
- Vitamin C is an antioxidant and might decrease the effectiveness of some medications used for cancers.
- Taking large doses of vitamin C might reduce how much of some medications used for HIV/AIDS stays in the body. This could decrease the effectiveness of some medications used for HIV/AIDS. Some of these medications used for HIV/AIDS include amprenavir (Agenerase), nelfinavir (Viracept), ritonavir (Norvir), and saquinavir (Fortovase, Invirase).
- Concurrent administration of ascorbic acid with desferrioxamine enhances urinary iron excretion. Ascorbic acid should be used with caution in patients with idiopathic haemochromatosis and thalassaemias and their cardiac function should be monitored.
- Taking vitamin C, beta-carotene, selenium, and vitamin E together might decrease the effectiveness of some medications used for lowering cholesterol. Some medications used for lowering cholesterol include atorvastatin (Lipitor), fluvastatin (Lescol), lovastatin (Mevacor), and pravastatin (Pravachol).
- Taking vitamin C along with vitamin E, beta-carotene, and selenium might decrease some of the helpful effects of niacin. Niacin can increase the good cholesterol. Taking vitamin C along with these other vitamins might decrease the effectiveness of niacin for increasing good cholesterol.
- Warfarin (Coumadin) is used to slow blood clotting. Large amounts of vitamin C might decrease the effectiveness of warfarin (Coumadin). The dose of your warfarin (Coumadin) might need to be changed.
- Concomitant administration of aluminium-containing antacids may increase urinary aluminium elimination. Concurrent administration of antacids and ascorbic acid is not recommended, especially in patients with renal insufficiency.
- Co-administration with amygdalin (a complementary medicine) can cause cyanide toxicity.
- The body breaks down acetaminophen (Tylenol, others) to get rid of it. Large amounts of vitamin C can decrease how quickly the body breaks down acetaminophen.
- The body breaks down aspirin to get rid of it. Large amounts of vitamin C might decrease the breakdown of aspirin. Decreasing the breakdown of aspirin might increase the effects and side effects of aspirin. Do not take large amounts of vitamin C if you take large amounts of aspirin.
- Vitamin C is taken up by cells. Taking nicardipine (Cardene) or nifedipine (Adalat, Procardia) along with vitamin C might decrease how much vitamin C is taken in by cells.
- Vitamin C might decrease how quickly the body gets rid of salsalate (Disalcid). Taking vitamin C along with salsalate (Disalcid) might cause too much salsalate (Disalcid) in the body and increase the effects and side effects of salsalate.

Vitamin D3
Phosphate infusions should not be administered to lower hypercalcaemia of hypervitaminosis D because of the dangers of metastatic calcification.
- Patients treated with cardiac glycosides may be susceptible to high calcium levels and should have ECG parameters and calcium levels monitored. It is recommended to reduce the dose or interrupt treatment if the calcium content in the urine exceeds 7.5 mmol/24 hours (300 mg/24 hours).
- Simultaneous administration of benzothiadiazine derivatives (thiazide diuretics) increases the risk of hypercalcaemia because they decrease the calcium excretion in the urine. The calcium levels in plasma and urine should therefore be monitored for patients undergoing long-term treatment.
- If Cholecalciferol is combined with metabolites or analogues of vitamin D careful monitoring of serum calcium levels is recommended.
- Anti-convulsants e.g. phenytoin, phenobarbital, primidone may diminish the effect of Cholecalciferol due to hepatic enzyme induction.
- Rifampicin may reduce the effectiveness of Cholecalciferol due to hepatic enzyme induction.
- Isoniazid may reduce the effectiveness of Cholecalciferol due to inhibition of the metabolic activation of Cholecalciferol.
- Drugs leading to fat malabsorption, e.g. orlistat, liquid paraffin, cholestyramine, may impair the absorption of Cholecalciferol.
- The cytotoxic agent actinomycin and imidazole antifungal agents interfere with vitamin D activity by inhibiting the conversion of 25-hydroxyvitamin D to 1,25-dihydroxyvitamin D by the kidney enzyme, 25-hydroxyvitamin D-1-hydroxylase.
- Concomitant use of glucocorticoids can decrease the effect of vitamin D.

Vitamin E
Various drugs may interfere with the absorption of vitamin E including cholestyramine, colestipol, and orlistat. High doses of vitamin E may increase the effects of oral anticoagulants.
- Taking large amounts of vitamin E along with cyclosporine (Neoral, Sandimmune) might increase how much cyclosporine (Neoral, Sandimmune) the body absorbs. By increasing how much cyclosporine the body absorbs, vitamin E might increase the effects and side effects of cyclosporine (Neoral, Sandimmune).
- Some medications are changed and broken down by the liver. Vitamin E might increase how quickly the liver breaks down some medications. Taking vitamin E along with some medications that are broken down by the liver can decrease the effectiveness of some medications. Before taking vitamin E talk to your healthcare provider if you are taking any medications that are changed by the liver. Some medications changed by the liver include lovastatin (Mevacor), ketoconazole (Nizoral), itraconazole (Sporanox), fexofenadine (Allegra), triazolam (Halcion), and many others.
- Vitamin E might slow blood clotting. Taking vitamin E along with medications that also slow clotting might increase the chances of bruising and bleeding. Some medications that slow blood clotting include aspirin, clopidogrel (Plavix), diclofenac (Voltaren, Cataflam, others), ibuprofen (Advil, Motrin, others), naproxen (Anaprox, Naprosyn, others), dalteparin (Fragmin), enoxaparin (Lovenox), heparin, warfarin (Coumadin), and others.
- Taking vitamin E, beta-carotene, vitamin C, and selenium together might decrease the effectiveness of some medications used for lowering cholesterol. It is not known if taking vitamin E alone decreases the effectiveness of some medications used for lowering cholesterol. Some medications used for lowering cholesterol include atorvastatin (Lipitor), fluvastatin (Lescol), lovastatin (Mevacor), and pravastatin (Pravachol).
- Taking vitamin E along with beta-carotene, vitamin C, and selenium might decrease some of the beneficial effects of niacin. Niacin can increase the good cholesterol. Taking vitamin E along with these other vitamins might decrease the good cholesterol.
- Warfarin (Coumadin) is used to slow blood clotting. Vitamin E can also slow blood clotting. Taking vitamin E along with warfarin (Coumadin) can increase the chances of bruising and bleeding. Be sure to have your blood checked regularly. The dose of your warfarin (Coumadin) might need to be changed.

Fertility, pregnancy and lactation
Vitamin A
Vitamin A does not readily diffuse across the placenta, but is present in breast milk.
Vitamin A can cause birth defects. It is especially important for pregnant women to monitor their intake of vitamin A from all sources during the first three months of pregnancy.

Vitamin D3
Pregnancy
The cholecalciferol metabolite, 25(OH)D, crosses the placenta; maternal serum concentrations correlate with fetal concentrations at birth.
Maternal hypercalcemia, possibly caused by excessive vitamin D intake during pregnancy, has been associated with hypercalcemia in neonates, which may lead to supravalvular aortic stenosis syndrome, the features of which may include retinopathy, mental or growth retardation, strabismus, and other effects. Hypercalcemia during pregnancy may also lead to suppression of parathyroid hormone release in the neonate, resulting in hypocalcemia, tetany, and seizures.
Breastfeeding
Vitamin D3 (Cholecalciferol) and its metabolites are excreted in breast milk.
Overdose in infants induced by nursing mothers has not been observed.
However, when prescribing additional vitamin D to a breast-fed child the practitioner should consider the dose of any additional vitamin D given to the mother.
Caution should be exercised when taking HERBIEVITE VITAMIN D3 while pregnant or breast-feeding. Please consult your healthcare practitioner first if your pregnant or lactating.

Vitamin E

Vitamin E appears in breast milk but is poorly transferred across the placenta.

4.7 Effects on ability to drive and use machines
HERBIEVITE ANTI-STRESS ADULTS has no effect on your ability to drive vehicles or operate machinery.

4.8 Undesirable Effects
Fish Oil
Most people do not commonly experience side effects with fish oil at normal doses.
Fish oil can cause side effects including:
- belching
- bad breath
- heartburn
- nausea
- loose stools
- rash
- and nosebleeds

Vitamin A
Most people do not commonly experience side effects with vitamin A at normal doses.
High doses might increase the risk of osteoporosis and hip fracture, particularly in older people.
Long-term use of large amounts of vitamin A might cause serious side effects including:
- fatigue
- irritability
- mental changes
- anorexia
- stomach discomfort
- nausea
- vomiting
- mild fever
- excessive sweating
- and many other side effects.

In women who have passed menopause, taking too much vitamin A can increase the risk of osteoporosis and hip fracture.Drinking alcohol may increase vitamin A's potentially harmful effects on the liver.
Vitamin A might be unsafe for children when taken high doses. When amounts greater than those recommended are taken, side effects can include:
- irritability
- sleepiness
- vomiting
- diarrhea
- loss of consciousness
- headache
- vision problems
- peeling skin
- increased risk of pneumonia and diarrhea
- and other problems

Vitamin C
- Nervous system disorders: headache.
- Vascular disorders: flushing.
- Gastrointestinal disorders: nausea, vomiting and stomach cramps. Large doses of ascorbic acid may cause diarrhoea.
- Skin and subcutaneous tissue disorders: redness of skin.
- Renal and urinary disorders: Patients known to be at risk of hyperoxaluria should not ingest ascorbic acid doses exceeding 1g daily as there may be increased urinary oxalate excretion. Ascorbic acid has been implicated in precipitating haemolytic anaemia in certain individuals deficient of glucose-6-phosphate dehydrogenase.
- Increased intake of ascorbic acid over a prolonged period may result in increased renal clearance of ascorbic acid, and deficiency may result if the intake is reduced or withdrawn rapidly. Doses of more than 600mg daily have a diuretic effect.

Vitamin D3
Most people do not commonly experience side effects with vitamin D at normal doses.
Along with its needed effects, Vitamin D3 (cholecalciferol) may cause some unwanted effects.
Incidence not known
- Cough
- Difficulty swallowing
- Dizziness
- Fast heartbeat
- Hives or itching
- Puffiness or swelling of the eyelids or around the eyes, face, lips or tongue
- Skin rash
- Tightness in the chest
- Unusual tiredness in the chest
- Unusual tiredness or weakness

Metabolic: Metabolic side effects have included Hypercalcemia
Renal: Uncommon: Hypercalciuria
Dermatologic: Rare: Pruritus, rash, urticaria
Hypersensitivity: Frequency not reported: Hypersensitivity reactions such as angioedema or laryngeal edema
Gastrointestinal: Frequency not reported: Nausea, vomiting
Vitamin E
Most people do not commonly experience side effects with vitamin E at normal doses.
Side effects can include:
- nausea
- diarrhea
- stomach cramps
- fatigue
- weakness
- headache
- blurred vision
- rash
- and bruising and bleeding

Reporting of suspected adverse reactions.
Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to:
- SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8
- CONTEGO PHARMACEUTICALS (Pty) Ltd | 250 Nadine Street, Robertville, Roodepoort | Gauteng, South Africa

4.9 Overdose
Vitamin C
Large doses of ascorbic acid may cause diarrhoea and the formation of renal oxalate calculi. Symptomatic treatment may be required.
Ascorbic acid may cause acidosis or haemolytic anaemia in certain individuals with a deficiency of glucose 6-phosphate dehydrogenase. Renal failure can occur with massive ascorbic acid overdosage. Gastric lavage may be given if ingestion is recent otherwise general supportive measure should be employed as required.
Vitamin D3
Acute or chronic overdose of Cholecalciferol can cause hypercalcaemia, an increase in the serum and urinary concentrations of calcium.
The symptoms of hypercalcaemia are not very specific and consist of nausea, vomiting, diarrhoea often in the early stages and later constipation, anorexia, fatigue, headache, muscle and joint pain, muscle weakness, polydipsia, polyuria formation of renal calculi, nephrocalcinosis, kidney failure, calcification of soft tissues, changes in ECG measurements, arrhythmias and pancreatitis. In rare and isolated cases there are reports that hypercalcaemia is fatal.
A very serious allergic reaction to this medicine is rare. However, get medical help right away if you notice any symptoms of a serious allergic reaction, including: rash, itching/swelling (especially of the face/tongue/throat), severe dizziness, trouble breathing.

Treatment of overdose
A normalisation of hypercalcaemia due to vitamin D intoxication lasts several weeks. The recommendation for the treatment of hypercalcaemia is the avoidance of any further administration of vitamin D, including supplements, dietary intakes and the avoidance of sunlight. A low calcium or calcium-free diet can also be considered.
Rehydration and the treatment with diuretics e.g. furosemide to ensure adequate diuresis should be considered. Additional treatment with calcitonin or corticosteroids can also be considered.
Phosphate infusions should not be administered to lower hypercalcaemia of hypervitaminosis D because of the dangers of metastatic calcification.
Vitamin E
Relatively large amounts of vitamin E usually cause no harm but occasionally muscle weakness, fatigue, nausea, and diarrhea occur. The most significant risk is bleeding, mainly with doses > 1000 mg a day.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacological classification: D 32.16 Other – Western Herbal Complementary Medicine.
Fish Oil
Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA), are essential fatty acids.
EPA and DHA are poor substrates for the enzymes responsible for triglyceride synthesis and they inhibit esterification of other fatty acids.
Vitamin A
Vitamin A is a fat-soluble vitamin.
It is essential for growth, for the development and maintenance of epithelial tissue, and for vision, particularly in dim light.
Vitamin C
Ascorbic acid, coupled with dehydroascorbic acid to which it is reversibly oxidised, has a variety of functions in cellular oxidation processes. Ascorbic acid is required in several important hydroxylations, including the conversion of proline to hydroxyproline (and thus collagen formation e.g. for intercellular substances and during wound healing); the formation of the neurotransmitters 5-hydroxytryptamine from tryptophan and noradrenaline from dopamine, and the biosynthesis of carnitine from lysine and methionine. Ascorbic acid appears to have an important role in metal ion metabolism, including the gastrointestinal absorption of iron and its transport between plasma and storage organs. There is evidence that ascorbic acid is required for normal leucocyte functions and that it participates in the detoxification of numerous foreign substances by the hepatic microsomal system. Deficiency of ascorbic acid leads to scurvy, which may be manifested by weakness, fatigue, dyspnoea, aching bones, perifollicular hyperkeratosis, petechia and ecchymosis, swelling and bleeding of the gums, hypochromic anaemia and other haematopoietic disorders, together with reduced resistance to infections and impaired wound healing.
Vitamin D3
Vitamin D (ergocalciferol-D2, cholecalciferol-D3, alfacalcidol) are fat-soluble sterols, sometimes considered to be hormones or hormone precursors, which are essential for the proper regulation of calcium and phosphate homoeostasis and bone mineralization.
Cholecalciferol (vitamin D) is a provitamin. The active metabolite, 1,25-dihydroxyvitamin D calcitriol), stimulates calcium and phosphate absorption from the small intestine, promotes secretion of calcium from bone to blood; promotes renal tubule phosphate resorption. Cholecalciferol is the naturally occurring form of vitamin D. It is produced from 7-dehydrocholesterol, a sterol present in mammalian skin, by ultraviolet irradiation.
Vitamin E
Vitamin E, a fat-soluble vitamin, prevents the oxidation of polyunsaturated fatty acids. It reacts with free radicals, which are the cause of oxidative damage to cell membranes, without the formation of another free radical in the process.

5.2 Pharmacokinetic properties
Fish Oil
During and after absorption, there are three main pathways for the metabolism of the omega-3 fatty acids:
- the fatty acids are first transported to the liver where they are incorporated into various categories of lipoproteins and then channelled to the peripheral lipid stores
- the cell membrane phospholipids are replaced by lipoprotein phospholipids and the fatty acids can then act as precursors for various eicosanoids
- the majority is oxidised to meet energy requirements

The concentration of EPA and DHA, in the plasma phospholipids corresponds to the EPA and DHA incorporated into the cell membranes.Animal pharmacokinetic studies have shown that there is a complete hydrolysis of the ethyl ester accompanied by satisfactory absorption and incorporation of EPA and DHA into the plasma phospholipids and cholesterol esters.
Vitamin A
Vitamin A substances are readily absorbed from the gastrointestinal tract but absorption may be reduced in the presence of fat malabsorption, low protein intake, or impaired liver or pancreatic function.
Vitamin A esters are hydrolysed by pancreatic enzymes to retinol, which is then absorbed and re-esterified.
Some retinol is stored in the liver. It is released from the liver bound to a specific a 1 - globulin (retinol-binding protein) in the blood.
The retinol not stored in the liver undergoes glucuronide conjugation and subsequent oxidation to retinal and retinoic acid; these and other metabolites are excreted in urine and faeces.
Vitamin A does not readily diffuse across the placenta, but is present in breast milk.
Vitamin C
Absorption
Ascorbic acid is well absorbed from the gastrointestinal tract.
Distribution
Ascorbic acid is widely distributed to all tissues. Body stores of ascorbic acid normally are about 1.5g. The concentration is higher in leucocytes and platelets than in erythrocytes and plasma.

Elimination
Ascorbic acid additional to the body's needs, generally amounts above 200mg daily, is rapidly eliminated; unmetabolized ascorbic acid and its inactive metabolic products are chiefly excreted in the urine. The amount of ascorbic acid excreted unchanged in the urine is dose-dependent and may be accompanied by mild diuresis.
Vitamin D3
Absorption
Vitamin D substances are well absorbed from the gastrointestinal tract. The presence of bile is essential for adequate intestinal absorption; absorption may be decreased in patients with decreased fat absorption.
Distribution
Absorbed vitamin D circulates in the blood in association with vitamin D–binding protein. Vitamin D and its metabolites circulate in the blood bound to a specific μ-globulin. Vitamin D can be stored in adipose and muscle tissue for long periods of time. It is slowly released from such storage sites and from the skin where it is formed in the presence of sunlight or ultraviolet light. Ergocalciferol and cholecalciferol have a slow onset and a long duration of action.
Cholecalciferol and ergocalciferol are hydroxylated in the liver by the enzyme vitamin D 25-hydroxylase to form 25-hydroxycholecalciferol (calcifediol) and 25-hydroxyergocalciferol respectively. These compounds undergo further hydroxylation in the kidneys by the enzyme vitamin D 1hydroxylase to form the active metabolites 1,25-dihydroxycholecalciferol (calcitriol) and 1,25-dihydroxyergocalciferol respectively.
Further metabolism also occurs in the kidneys, including the formation of the 1,24,25-trihydroxy derivatives. Of the synthetic analogues, alfacalcidol, dihydrotachysterol, and doxercalciferol are converted directly in the liver to their active metabolites (calcitriol, 25-hydroxydihydrotachysterol, and 1,25-dihydroxyergocalciferol respectively).
Elimination
Vitamin D compounds and their metabolites are excreted mainly in the bile and faeces with only small amounts appearing in urine; there is some enterohepatic recycling but it is considered to have a negligible contribution to vitamin D status. Certain vitamin D substances may be distributed into breast milk.
Vitamin E
Absorption of vitamin E from the gastrointestinal tract is dependent on the presence of bile and on normal pancreatic function.
The amount of vitamin E absorbed varies widely between about 20% and 80% and appears to decrease as the dose is increased.
It enters the blood via the chylomicrons in the lymph and is bound to beta lipoproteins. It is widely distributed to all tissues, and stored in adipose tissue.
Some vitamin E is metabolised in the liver to glucuronides of tocopheronic acid and its y-lactone. Some is excreted in the urine, but most of a dose is slowly excreted in the bile.
Vitamin E appears in breast milk but is poorly transferred across the placenta.

PHARMACEUTICAL PARTICULARS
List of excipients
Mannitol 180mg / per softgel(E421)
Gelatin (E441)
Glycerol (E422)
Soyabean oil
Purified Water
Mono- and diglycerides of fatty acids (E471)
Lecithin (E322)
Flavouring
Titanium dioxide (E171)
Aspartame 2.35mg / per softgel (E962)
Citric acid (E300)
Acesulfame K1.39mg / per softgel (E950)
Rosemary Extract (E392)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years.

6.4 Special precautions for storage
Store at or below 25 °C. Protect from heat and light.
KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and contents of container
HERBIEVITE ANTI-STRESS ADULTS are packed in white HDPE containers with white cap, containing a desiccant in pack size of 30 Softgels.

6.6 Special precautions for disposal and other handling
No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Contego Pharmaceuticals (Pty) Ltd
250 Nadine Street
Robertville, Roodepoort
Gauteng, South Africa
+27 87 150 7529

8. REGISTRATION NUMBER
To be allocated.

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION
To be allocated.