

1. NAME OF THE MEDICINAL PRODUCT

Viva Tonic

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each 5ml contains:

Korean Ginseng Extract 40mg

Ferrous Fumarate 45.539mg

Thiamine Hydrochloride 3.5mg

Riboflavine 1mg

Pyridoxine Hydrochloride 2mg

Nicotinamide 15mg

Calcium D-Pantothenate 6mg

Cyanocobalamin 2mcg

For full list of excipients, see section 6.1.

3. Pharmaceutical form

Oral Syrup

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- Iron deficiency and vitamin deficiency states
- Low mental and physical vigour due to fatigue and stress
- Convalescence from debilitating illnesses and in anorexia

4.2 Posology and method of administration

Posology

Adults (18 years and above): 5ml to 10ml daily

Method of administration

For oral administration.

4.3 Contraindications

- Cases of known allergy to any of the ingredients including allergy to plants in the Araliaceae family, and in disturbances of iron metabolism.
- Should not be administered within one hour of administration of Antacids or Tetracyclines.
- Stomach ulcers or other intestinal diseases.
- Patients with hormone sensitive conditions, such as breast cancer, uterine cancer, or endometriosis.
- Individuals with high blood pressure should only take Viva tonic under the supervision of a qualified practitioner. Since ginseng may act as a blood thinner, discontinue use at least seven days before surgery.
- Children under 18 years of age

4.4 Special warnings and precautions for use

- Use with caution in established cases of primary (idiopathic) or secondary iron storage and in anaemias associated with ineffective erythropoieses.
- Caution is advised in patients with bleeding disorders or taking drugs that may affect the risk of bleeding or blood clotting. Dosing adjustments may be necessary.
- Caution is advised in patients with diabetes or hypoglycemia, and in those taking drugs, herbs, or supplements that affect blood sugar.

4.5 Interaction with other medicinal products and other forms of interaction

Iron

The Bioavailability of iron ingested with food is probably one half or one third of that seen in the fasting subject. Antacids also reduce the absorption of iron if given concurrently. Iron preparation may cause black discoloration of the stool, and sometimes darken the teeth with prolonged use. It should not be taken within one hour of administration of Tetracycline.

Ginseng

Do not use Ginseng without first talking to your practitioner or healthcare provider if you taking any of the following medications:

Blood Thinning Medications:

- Aspirin (Ginseng may inhibit platelet activity)
- Warfarin (Ginseng may decrease effectiveness)

Caffeine or other substances that stimulate the central nervous system

Ginseng may increase their effects possibly causing:

- irregular heartbeat
- insomnia
- nervousness
- sweating

Haloperidol (anti-psychotic medication):

Ginseng may exaggerate the effects so do not take them together

Morphine: Ginseng may block the pain killing effects of morphine.

Monoamine Oxidase Inhibitors MAOIs (antidepressant medication) especially:

Phenelzine - Interaction with Ginseng may cause symptoms such as:

- headaches
- manic-like episodes/insomnia
- tremulousness

Diabetes medications: Medication adjustments may be necessary

Heart disease medications (Including calcium channel blockers such as nifedipine):

The effects of the cardiac glycoside drug digoxin may be increased when used with ginseng in patients with heart failure

Diuretics:

Decreased effects of the diuretic drug, Furosemide in particular.

4.6 Fertility, pregnancy and lactation

Pregnancy and Breastfeeding

Ginseng has been used traditionally in pregnant and breastfeeding women. Animal studies and preliminary human research suggest possible safety, although safety has not been clearly established in humans. Therefore, ginseng use cannot be recommended during pregnancy or breastfeeding. There is a report of neonatal death and the development of male characteristics in a developing baby girl after exposure of a pregnant mother to ginseng.

4.7 Effects on ability to drive and use machines

Not relevant

4.8 Undesirable effects

Viva Tonic is well tolerated. When taken in excess amount or above the recommended dosage, gastro-intestinal disturbances such as abdominal cramp, nausea, diarrhea and vomiting are noticed. The side effects are related to the amount of elemental iron taken rather than the type of preparation.

There is preliminary evidence that formulations containing ginseng may increase the QTc interval (thus increasing the risk of abnormal heart rhythms) and decrease diastolic blood pressure two hours after ingestion in healthy adults.

All forms of iron therapy may cause temporary staining of the teeth and dark stools.

Administration of viva tonic may cause hypermenorrhoea and emmeniopathy, if bleeding persists upon cessation of therapy, consult your doctor.

Based on limited evidence, long-term use of formulations containing ginseng may be associated with skin rash or spots, itching, diarrhea, sore throat, loss of appetite, excitability, anxiety, depression, or insomnia. Less common reported side effects include headache, fever, dizziness/vertigo, blood pressure abnormalities (increases or decreases), chest pain, difficult menstruation, heart palpitations, rapid heart rate, leg swelling, nausea/vomiting, or manic episodes in people with bipolar disorder.

Based on human research, ginseng may lower blood sugar levels. This effect may be greater in patients with diabetes than in non-diabetic individuals. Caution is advised in patients with diabetes or hypoglycemia, and in those taking drugs, herbs, or supplements that affect blood sugar. Serum glucose levels may need to be monitored by a healthcare provider, and medication adjustments may be necessary.

A severe life-threatening rash known as Stevens-Johnson syndrome occurred in one patient and may have been due to contaminants in a ginseng product. A case report describes liver damage (cholestatic hepatitis) after taking a combination product containing ginseng.

Ginseng may have estrogen-like effects, and has been associated with reports of breast tenderness, loss of menstrual periods, vaginal bleeding after menopause, breast enlargement (reported in men), difficulty developing or maintaining an erection, or increased "sexual responsiveness." Ginseng may produce manic symptoms, based on a case report.

4.9 Overdose

Symptoms

Ingestion of 20 mg/kg elemental iron is potentially toxic and 200-250 mg/kg is potentially fatal.

No single method of assessment is entirely satisfactory - clinical features as well as laboratory analysis must be taken into account. The serum iron taken at about 4 hours after ingestion is the best laboratory measure of severity.

Serum Iron	Severity
< 3 mg/L (55 micromol/L)	Mild toxicity
3-5 mg/L (55-90 micromol/L)	Moderate toxicity
> 5 mg/L (90 micromol/L)	Severe toxicity

Early signs and symptoms include nausea, vomiting, abdominal pain and diarrhoea. The vomit and stools may be grey or black. In mild cases early features improve but in more serious cases there may be evidence of hypoperfusion (cool peripheries and hypotension), metabolic acidosis and systemic toxicity. In serious cases, there can be recurrence of vomiting and gastrointestinal bleeding, 12 hours after ingestion. Shock can result from hypovolaemia or direct cardiotoxicity. Evidence of hepatocellular necrosis appears at this stage with jaundice, bleeding, hypoglycaemia, encephalopathy and positive anion gap metabolic acidosis. Poor tissue perfusion may lead to renal failure. Rarely, gastric scarring causing stricture or pyloric stenosis (alone or in combination) may lead to partial or complete bowel obstruction 2-5 weeks after ingestion.

High doses of ginseng have been associated with rare cases of temporary inflammation of blood vessels in the brain (cerebral arteritis), abnormal dilation of the pupils of the eye, confusion or depression, nervousness and may lead to problems sleeping.

Management

Supportive and symptomatic measures include ensuring a clear airway, monitor cardiac rhythm, BP and urine output, establishing IV access and administering sufficient fluids to ensure adequate hydration. Consider whole bowel irrigation. If metabolic acidosis persists despite correction of hypoxia and adequate fluid resuscitation, an initial dose of 50 mmol sodium bicarbonate may be given and repeated as necessary, for adults guided by arterial blood gas monitoring (aim for a pH of 7.4). Consider the use of desferrioxamine, if /the patient is symptomatic (other than nausea), serum iron concentration is between 3-5 mg/L (55-90 micromol/L) and still rising. Haemodialysis does not remove iron effectively but should be considered on a supportive basis for acute renal failure as this will facilitate removal of the iron-desferrioxamine complex.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Iron bivalent, oral preparations

ATC code: B03AA02

Ginseng

Panax Ginseng, also known as Korean Ginseng is part of the Araliaceae plant family. Panax means "all heal" in Greek and for centuries it has been used as a cure-all in many different cultures, particularly Chinese medicine. Korean Ginseng is classified as an adaptogen. An adaptogen works to strengthen and normalize body functions.

The main active ingredients of Korean ginseng are ginsenosides. These steroid-like phytochemicals have adaptogenic properties, which give ginseng property to counter the effects of stress. The glycosides act on the adrenal glands, helping to prevent adrenal hypertrophy and excess corticosteroid production in response to stress. Ginsenosides increase protein synthesis and activity of neurotransmitters in the brain. Ginseng stimulates the formation of blood vessel and improves blood circulation in the brains, thereby improving memory and cognitive abilities. Ginseng is also used for diabetes, migraine, infections, radiation and chemotherapy protection, to aid in sleep, and to stimulate the appetite.

Korean ginseng contains steroids such as panaxtriol. The steroids are remarkably similar in structure to anabolic steroids found naturally in our body. This makes Korean ginseng ideal for athletes and body builders looking for a natural alternative to anabolic steroid. Korean ginseng is also used by women for treatment of post-menopausal symptoms.

Iron

Iron is an essential constituent of the body, being necessary for haemoglobin formation and for the oxidative process of living tissues. The body contains about 4g of iron most of which is present as haemoglobin. The remainder is present in the storage forms, ferritin or haemosiderin, in the reticuloendothelial system or as myoglobin with smaller amount occurring in haem-containing enzymes or in plasma bound to transferrin.

Iron and iron salts should only be given for the treatment of other types of anaemia except where iron deficiency is also present. Iron deficiency anaemia should be determined and treated.

Compound of iron are used in the treatment of microcytic anaemia, including simple achlorhydric anaemia, simple anaemia of pregnancy, the nutritional anaemia of infants, anaemia due to excessive haemorrhage and anaemia associated with infections and malignant disease.

Externally, some iron salts are powerfully astringent and styptic. Iron therapy should be continued after the haemoglobin concentration has returned to normal, to replenish the body stores of iron.

Vitamin B₁ (Thiamine)

Thiamine is practically devoid of pharmacodynamic actions when given in usual therapeutic doses; even large doses produce no discernible effects. Isolated clinical reports of toxic reaction to the long-term parenteral administration of Thiamine probably represent rare instances of hypersensitivity.

The only established therapeutic use of Thiamine is in the treatment or the prophylaxis of Thiamine deficiency. The syndromes of Thiamine deficiency seen clinically can range from beriberi through wernicke's encephalopathy and korsakoff's syndrome to alcoholic polyneuropathy. Thiamine, a water-soluble vitamin, is an essential coenzyme for carbohydrate metabolism. Thiamine deficiency develops when the dietary intake is inadequate; severe deficiency leads to chronic beriberi characterized by peripheral neuritis, bradycardia, muscle weakness and paralysis.

Vitamin B₂ (Riboflavin)

Riboflavin, a water-soluble vitamin, is essential for the utilization of energy from food. The active, phosphorylated forms, flavine mononucleotide and flavine adenine dinucleotide are involved as coenzymes in oxidative/reductive metabolic reactions.

Riboflavin deficiency develops when the dietary intake is inadequate. Deficiency leads to the development of a well-defined syndrome known as ariboflavinosis, characterized by cheilosis, angular stomatitis, glossitis and seborrhoeic keratosis of the nose and ano-genital region. There may be ocular symptoms including itching and burning of the eyes, photophobia and corneal vascularisation. Riboflavin deficiency may occur in association with other vitamin B complex deficiency states such as pellagra.

Riboflavin is used in the treatment and prevention of Riboflavin deficiency.

Vitamin B₆ (Pyridoxine)

Pyridoxine, a water-soluble vitamin is involved principally in amino acid metabolism, but is also involved in carbohydrate and fat metabolism. It is also required for the formation of haemoglobin.

Deficiency of Pyridoxine is rare in humans due to its wide spread distribution in foods. Pyridoxine deficiency may however be drug induced and can occur, for instance, during isoniazid therapy. Inadequate Pyridoxine deficiency in adults lead to the development of peripheral neuritis, deficiency in children also affect the CNS.

Pyridoxine is used in the treatment and prevention of Pyridoxine deficiency states. Pyridoxine has also been used to treat seizure due to hereditary syndromes of Pyridoxine deficiency or dependency in infants.

Pyridoxine has also been tried in a wide variety of other disorders, including the treatment of depression and other symptoms associated with the premenstrual syndrome and the use of oral contraceptives.

Vitamin B₁₂ (Cyanocobalamin)

Vitamin B₁₂, water-soluble vitamins occur in the body mainly as methylcobalamin and as adenosylcobalamin and hydroxycobalamin. It act as coenzyme in nucleic acid synthesis.

Vitamin B₁₂ deficiency may occur in strict vegetarians with an inadequate dietary intake, in patients with malabsorption syndromes or metabolic disorder, nitrous oxide induced megaloblastosis or following anaemias and neurological damage.

Vitamin B₁₂ preparations are used in the treatment and prevention of Vitamin B₁₂ deficiency. It is desirable to identify the cause of deficiency before commencing therapy. Treatment usually results in rapid haematological improvement and a striking clinical response.

Vitamin C (Ascorbic Acid)

Ascorbic acid, a water-soluble vitamin is essential for the synthesis of collagen and intercellular material. Ascorbic acid deficiency develops when the dietary intake is inadequate. Deficiency leads to the development of a well-defined syndrome known as scurvy characterized by capillary fragility, bleeding (especially from small blood vessel and the gum) anaemia, cartilage and bone lesions and slow healing of wounds.

Ascorbic acid is used in the treatment and prevention of Ascorbic acid deficiency. It completely reverses symptoms of deficiency. Ascorbic acid has been used to acidify urine and has also been tried in the treatment of idiopathic methaemoglobinaemia and many other disorders.

Calcium D-Pantothenate

Pantothenic acid is traditionally considered to be a vitamin B substance. It is a component of co-enzyme A which is essential in the metabolism of carbohydrate, fat and protein.

Deficiency of pantothenic acid is unlikely in man because of its wide spread distribution in food. It is administered as a nutritional supplement often as calcium salt and usually in conjunction with other vitamins of the B group.

Nicotinamide

Nicotinic acid and nicotinamide, the form that occurs naturally in the body are water-soluble vitamin B substances, which are converted to Nicotinamide Adenine Dinucleotide Phosphate (NADP). These coenzymes are involved in electron transfer reactions in the respiratory chain.

Nicotinamide deficiency develops when dietary intake is inadequate. Deficiency leads to the development of a syndrome known as pellagra characterized by skin lesions, especially on areas exposed to sunlight, with hyperpigmentation and hyperkeratinisation. Other symptoms include diarrhoea, abdominal pain, glossitis,

stomatitis, and loss of appetite, headache, lethargy and mental and neurological disturbances. Nicotinic acid deficiency may occur in association with other vitamin B complex deficiency states. Nicotinamide is used in the treatment and prevention of Nicotinic acid deficiency. Nicotinamide is preferred, as it does not cause vasodilatation.

5.2 Pharmacokinetic properties

Iron

Iron is irregularly and incompletely absorbed from the gastro-intestinal tract the main sites of absorption being the duodenum and jejunum. Absorption is usually increased in conditions of iron deficiency or when given in the fasting state. Absorption of iron may be reduced in certain disease states.

Apart from haemorrhage, iron is mainly lost from the body in the faeces, urine, skin and sweat, but the total loss is small. In healthy men and non-menstruating women the loss is replaced by the absorption of about 1mg of iron daily; about 2mg needs to be absorbed daily by menstruating women.

In childhood and adolescence, the need is proportionately greater because of growth. In pregnancy and lactation 3mg or more must be absorbed daily.

Vitamin B₁ (Thiamine)

Thiamine is well absorbed from the gastro intestinal tract following oral administration, although the absorption of large doses is limited. It is also rapidly absorbed following intra muscular administration. It is widely distributed to most body tissues and appears in breast milk. Thiamine is not stored to any appreciable extent in the body and amounts in excess of the body's requirements are excreted in the urine as unchanged Thiamine or as metabolites.

Thiamine requirements are directly related to the carbohydrate intake and the metabolic rate. A daily dietary intake of 1 to 1.3mg of Thiamine is recommended for healthy men and 0.7 to 1mg for healthy women.

Vitamin B₂ (Riboflavin)

Riboflavin is readily absorbed from the gastro intestinal tract. Although Riboflavin is widely distributed to body tissues, little is stored in the body. Riboflavin is converted in the body to the coenzyme Flavine mononucleotide and then to another coenzyme Flavine adenine dinucleotide. About 60% of FMN and FAD are bound to plasma proteins. Riboflavin is excreted in urine, mainly as metabolites. As the dose increases, larger amounts are excreted unchanged. Riboflavin crosses the placenta and is distributed in breast milk.

The Riboflavin requirement is often related to the energy intake but it appears to be more closely related to the resting metabolic requirements. A daily dietary intake of about 1.3 to 1.8mg of Riboflavin is recommended.

Vitamin B₆ (Pyridoxine)

Pyridoxine is readily absorbed from the gastro-intestinal tract following oral administration and is converted to the active forms pyridoxal phosphate and pyridoxamine phosphate. They are stored mainly in the liver where there is oxidation to 4-pyridoxic acid, which is excreted in the urine. Pyridoxine crosses the placenta and also appears in the breast milk.

For adults, the daily requirement of Pyridoxine is probably about 2mg and this amount is present in most normal diets. Meats, especially liver, cereals, eggs, fish and certain vegetables and fruits are good source of Pyridoxine.

Vitamin B₁₂ (Cyanocobalamin)

Vitamin B₁₂ substances bind to intrinsic factor and are then actively absorbed from the gastro intestinal tract. Absorption is impaired in patients with an absence of intrinsic factor, with a malabsorption syndrome or with disease or abnormality of the gut, or after gastrectomy.

Vitamin B₁₂ is extensively bound to specific plasma proteins called Transcobalamins, Transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. It is stored in the liver, excreted in the bile and undergoes enterohepatic recycling; part of a dose is excreted in the urine, most of it in the first 8 hours. Vitamin B₁₂ diffuses across the placenta and also appears in breast milk.

For adults, the daily requirement of Vitamin B₁₂ is probably about 1 to 3µg and this amount is present in most normal diets.

Vitamin C (Ascorbic Acid)

Ascorbic acid is readily absorbed from the gastro intestinal tract and is widely distributed in the body tissues. It is reported to be 25% bound to plasma proteins. The amount of ascorbic acid in the body in health is about 1.5g. The concentration is higher in leucocytes and platelets than in erythrocytes and plasma. In deficiency states the concentration in leucocytes declines later and at a slower rate, and has been considered to be a better criterion for the evaluation of deficiency than the concentration in plasma.

Ascorbic acid is reversibly oxidised to dehydroascorbic acid; some is metabolised to ascorbate – 2 – sulphate, which is inactive and oxalic acid, which are excreted in the urine. Ascorbic acid in excess of the body's needs is also rapidly eliminated in the urine. Ascorbic acid crosses the placenta and is distributed into breast milk. It is removed by haemodialysis.

A daily dietary intake of about 30 to 60mg Ascorbic acid has been recommended for adults. There is, however, wide variation in individual requirements. Humans are unable to form their own ascorbic acid and so a dietary source is necessary. Most dietary ascorbic acid is obtained from fruit and vegetable sources; only small amounts are present in milk and animal tissues.

Calcium D-Pantothenate

Pantothenic acid is readily absorbed from the gastro intestinal tract following oral administration. It is widely distributed in the body tissues and appears in breast milk. About 70% of Pantothenic acid is excreted unchanged in the urine and about 30% in the feces.

Pantothenic acid is rapidly absorbed in foods-meat, legumes and whole grain cereals are particularly rich sources. Recommended daily intakes of Pantothenic acid have not been set, but human requirements are adequately met by a daily intake of about 4 to 10mg.

Nicotinamide

Nicotinamide is absorbed readily from all portions of the intestinal tract and the vitamin is distributed to all tissues. The principal route of metabolism of Nicotinic acid and nicotinamide is by the formation of N—methylnicotinamide, which in turn is metabolized further. Small amounts of the unchanged vitamins appear in the urine following therapeutic doses of nicotinic acid and nicotinamide. The daily adult requirement is probably about 15-20mg.

5.3 Preclinical safety data

No further data.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sucrose
Methyl Hydroxybenzoate
Propyl Hydroxybenzoate
Citric Acid
Sorbitol Solution (70%)
Caramel
Ascorbic Acid
Xanthan Gum
Polysorbate 80
Deionised Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years

6.4 Special precautions for storage

Store below 30°C. Protect from light.

6.5 Nature and contents of container

200ml Amber bottle with aluminium screw cap.

6.6 Special precautions for disposal and other handling

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT/MANUFACTURER

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