1. NAME OF THE MEDICINALPRODUCT

JAWAVITE SYRUP

2. QUALITATIVE AND QUANTITATIVECOMPOSITION

Each 5ml contains:

VIT A 3000IU, VIT B1 3MG, VIT B2 2MG, VIT B6 1MG, VIT C 60MG,

VIT D3 600IU, NICOTINAMIDE 20MG

3. PHARMACEUTICALFORM

Jawavite is a yellow coloured and viscous syrup packed in amber coloured bottles of 100ml

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

For vitamins and minerals deficiency

4.2 Posology and method of administration

Jawavite is available in form of flavored syrup for children in following
Dosage:
For Children under 6years: One teaspoon (5ml) daily
Children above 6 years: One teaspoonful, (5ml) twice daily or as directed by the physician.

4.3 Contraindications:

None.

4.4 Special warnings and precautions for use:

None

4.5 Interaction with other medicinal products and other forms of interaction

None

4.6 Fertility, Pregnancy and lactation

None

4.7 Effects on ability to drive and use machines

None known.

4.8 Undesirable effects

No side effects will arise with the use of Jawavite formulation as it is a dietary supplement.

4.9 Overdose

All symptoms due to over dose of vitamin are disappeared on withdrawal of the administration of the vitamin.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

The common ingredients in multivitamins include ascorbic acid (vitamin C), cyanocobalamin (vitamin B12), thiamine (vitamin B1), riboflavin (vitamin B2), niacin (vitamin B3), Methyl Paraben,

Propyl Paraben, Sodium Bicarbonate, Sodium Benzoate, Liquid Glucose, Xanthan Gum, Sodium Hydroxide, Oil Orange Concentrate, Mixed Fruit Flavour, Sodium Saccharin and vitamin A, D and E. Among these ingredients vitamin A and D may cause significant systemic signs. Acute ingestion of other listed ingredients in companion animals can result in self limiting GI upset (e.g. vomiting, diarrhea, anorexia, lethargy). However, toxicity is typically rare in pets.

Multivitamin preparations contain varying amounts of iron. Unless otherwise listed, iron should be assumed to be elemental iron. Various iron salts may contain 12-48% elemental iron. Iron has direct caustic or irritant effects on the GI Mucosa. It can also be a direct mitochondrial poison. Once the iron carrying capacity of serum has been exceeded, free iron is deposited in the liver where it damages mitochondria, leading to necrosis of periportal hepatocytes. Signs of iron toxicosis usually develop within 6hrs. Initial vomiting and diarrhea, with or without blood, may be followed by hypovolemic shock, depression, fever, acidosis and liver failure 12-24 hours later, often with a period of apparent recovery in between. Oliguria and anuria secondary to shock induced renal failure may also occur. Ingestion of > 20mg/kg of elemental iron generally warrants decontamination and administration of GI protectants. Additional treatment and monitoring will be necessary for patients that have ingested >60mg/kg of elemental iron. Milk of magnesia can complex with iron to decrease its absorption from the GI tract. Serum iron levels and the total iron binding capacity should be checked at 3 hr and again at 8-10hours post exposure. If serum iron is .300mg/Dl., or greater than the total iron binding capacity, chelation therapy may be needed. Desferroxamine 940mg/kg, IM, every 4-8hr) is a specific iron chelator and is most effective within the first 24ouhrs post ingestion, before iron has been distributed from blood to tissues. Other signs should be treated symptomatically. Even though vitamin A toxicity following consumption of large amounts of fish oil or bear's liver has been well documented, it is less likely to occur following acute ingestion of multivitamins. The amount of vitamin A needed to cause toxic effects is 10-1,000 times the dietary requirements for most species. The vitamin A requirement for cats is 10,000 IU/kg of diet fed, with levels up to 100,000IU/kg of diet

considered to be safe. For dogs, the requirements is 3,333IU/kg of diet fed, with up to 333,300 IU /kg of diet considered to be safe. Signs associated with acute vitamin A toxicity include general malaise, anorexia, nausea, peeling skin, weakness, tremors, convulsions, paralysis and death.

Vitamin D is included in many calcium supplements to aid the absorption of the calcium. Most vitamins contain cholecalciferol (vitamin D3). After consumption, cholecalciferol is converted into 25-hydroxycholecalciferol (calcifediol) in the liver, which is subsequently converted to the active metabolite 1,25- di-hydroxycholecalciferol (calcitriol) in the kidneys. One IU of vitamin D3 is equivalent to 0.025ug of cholecalciferol. Even though the oral LD50 of cholecalciferol in dogs has been reported as 88mg/kg, signs have been seen at dosages as low as 0.5mg/kg. Vomiting, depression, polyuria, polydipsia, and hyperphosphatemia may be seen within 12hr of a significant vitamin D exposure, following by hypercalcemia and acute renal failure 24-48hrs post exposure. In addition to renal failure, the kidneys, heart and GI tract may show signs of necrosis and mineralization. Initial treatment should include decontamination and assessment of baseline calcium, phosphorus, BUN and creatinine. Multiple doses of activated charcoal with a cathartic should be administered. If clinical signs of toxicosis develop, treatment consists of saline dieresis and the use of furosemide, corticosteroids and phosphate binders.

Specific agents such as (salmon) calcitonin or pamidronate may be needed for patients that remain hypercalcemic despite symptomatic treatment. Stabilization of serum calcium may require days of treatment due to the long half-life of calcifediol (16-30days).

5.2 Pharmacokinetic properties

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5.3 Preclinical safety data

Vitamin A

Is one of the few vitamins that have toxic manifestations, this has caused sporadic problems. Toxicity has been either acute or chronic.

Vitamin A is readily available in high concentrations and the rational of if a little bit helps, give a lot will undoubtedly continue to be followed and result in problems, especially in companion animals. The toxic dose is quite large compared to prophylactic or therapeutic requirements.

Carnivores have a greater margin of safety than other species. However toxicity will occur if more than four times the storage capacity of the liver is administered. In many aspects,

signs of vitamin A toxicity resemble signs of deficiency and include lethargy, colic, bone and joint pain, restlessness, brittle hoofs and nails, alopecia, and dry scaly skin.

Vitamin D3

Overdose of vitamin D decrease bone mineralization and cause calcification of some soft tissues as a result of excessive blood levels of Ca and PO4.Toxicity tends to be chronic in nature since vitamin D is slowly metabolized. However, acute toxicosis caused by errors in formulation has been seen in swine and horses. Toxicity is often more of a problem than vitamin D deficiency in over supplemented pets.

Haschet et al.(1978) reported that vitamin D toxicity causes an initial necrosis in active bone cells. They were dealing with a very acute toxicity syndrome, and hypervitaminosis that is more chronic may not be analogous.

Two different genera of plants have been found to contain active 1,25-(OH)2D combined with a glycoside. Ingestion of either cestrum diunum (Sweet jasmine), common in southern Florida, or Solanum spp., native to Argentina, can result in uncontrolled levels of active vitamin D and toxicity. Grazing animals, particularly horses, have been affected.

Vitamin B1 (Thiamine Hydrochloride)

There are no reports of teratogenic, mutagenic or carcinogenic effects of Vitamin B1 and no adverse effects have been seen, but hypersensitivity reactions have occurred, mainly after parenteral administration. These reactions have ranged in severity from very mild to, very rarely, fatal anaphylactic shock, depending on the frequency of administration of the drug by the parenteral route.

Vitamin B2 (Riboflavin)

Riboflavin has been found to be practically non-toxic.LD50 in mice and rats are 340-560 mg /kg $^{-1}$ intraperitonecally.

Daily administration of riboflavin (10-25mg/kg^{-1} body weight to rats and dogs for up to 4 months produced no toxic effect. Large doses of riboflavin result in a bright yellow discoloration of the urine which may interfere with certain laboratory tests.

Vitamin B6 (Pyridoxine Hydrochloride)

Beagles receiving a daily dose of 300mg/ kg^{-1} of pyridoxine hydrochloride developed a swaying gait with 9 days. They eventually became unable to walk, but were not weak. Long term administration of large doses of pyridoxine is associated with the development of severe peripheral neuropathies; it has been stated that this occur with doses in excess of about 2gm daily.

Vitamin B12

Allergic hypersensitivity reactions have occurred rarely following the administration of the vitamin b12 compounds cyanocobalamin.

Nicotinamide

In acute toxicity testing, the estimated LD50 for subcutaneous administration was 1.7g kg^{-1} in rat. In rats fed a choline- deficient diet, large doses of nicotinamide resulted in growth inhibition, decreased food intake and weight gain per food intake, liver and kidney hypertrophy, and fatty liver.

Nicotinamide toxicity may also impair RNAA and DNA synthesis due to ATP and 5-phosphoribosyl-1 pyrophosphate depletion.

Vitamin C (Ascorbic Acid)

Ascorbic acid is usually well tolerated. Large doses are reported to cause diarrhea and other gastro-intestinal disturbances. It has also been stated that large dose may result in hyperoxaluria and the formation of renal calcium oxalate calculi and ascorbic acid should therefore be given with care to animals with hyperoxaluria. Tolerance may be induced with prolonged use of large doses. Also renal impairment associated with excessive oxalate excretion has been produced. Dental enamel erosion has been attributed, because of daily ingestion of chewable ascorbic acid tablet over a period of 3 years; the pH of saliva had changed so that calcium was lost from the tooth enamel.

6. PHARMACEUTICALPARTICULARS

6.1 List of excipients

Sugar
Methyl Paraben
Propyl Paraben
Sodium Bicarbonate
Sodium Benzoate
Liquid Glucose
Xanthan Gum
Sodium Hydroxide
Oil Orange Concentrate