

For the use of a Registered Medical Practitioner or Hospital or a Laboratory only

COLONISE MV

(Pre and Probiotic, Vitamins and Minerals Capsules)

COMPOSITION:

Each Hard cellulose Capsule in Capsule contains:

Methylcobalamin I.P.....500 mcg
Folic Acid I.P.....1.5 mg
Zinc Sulphate I.P.....25 mg
Chromium Polynicotinate.....200mcg
Selenium as Sodium selenite USP... 65mcg
Pyridoxine Hydrochloride IP 1.5 mg
Inositol B.P..... 100 mg
Alpha Lipoic Acid USP..... 50 mg

Each Inner Hard cellulose Capsule contains:

Streptococcus faecalis T-110 JPC.... 30 Million
Clostridium butyricum TO-A..... 2 Million
Bacillus mesentericus TO-A JPC.... 1 Million
Lactic acid bacillus..... 50 Million
(Lactobacillus sporogenes)

Approved colours used in capsule shell :

Overages of vitamins added to compensate loss on storage.

DOSAGE FORM

HPMC Capsules

Advantages of HPMC capsules is as follows: -

HPMC Capsules functions as controlled release agent to delay the release of a medicinal compound into the digestive tract. It is made from non-animal materials, chemically stable, low moisture content and less brittle even in more humidity.

INDICATION

It is used to correct vitamins and minerals deficiency and also helps to replace the lost beneficial bacteria in adult patients. It is for Therapeutic use only.

DESCRIPTION

Vitamins and Minerals

Mecobalamin

Methylcobalamin or Mecobalamin is having molecular weight of 1344.38gram/mol with molecular formula of $C_{63}H_{91}CoN_{13}O_{14}$.

Folic acid

Folic acid, N-[p-[[[2-amino-4-hydroxy-6-pteridiny] methyl]-amino]benzoyl]-L-glutamic acid, is a B complex vitamin containing a pteridine moiety linked by a methylene bridge to para-aminobenzoic acid, which is joined by a peptide linkage to glutamic acid.

Conjugates of folic acid are present in a wide variety of foods, particularly liver, kidneys, yeast, and leafy green vegetables. Commercially available folic acid is prepared synthetically. Folic acid occurs as a yellow or yellowish-orange crystalline powder and is very slightly soluble in water and insoluble in alcohol. Folic acid is readily soluble in dilute solutions of alkali hydroxides and carbonates and solutions of the drug may be prepared with the aid of sodium hydroxide or sodium carbonate, thereby forming the soluble sodium salt of folic acid (sodium folate). Aqueous solutions of folic acid are heat sensitive and rapidly decompose in the presence of light and/or riboflavin; solutions should be stored in a cool place protected from light.

Zinc

Zinc is an element. Its molecular weight is 65.38.

Chromium

Chromium is an element. Its molecular weight is 51.99.

Selenium

It is an element. Its molecular weight is 78.96

Pyridoxine hydrochloride

Pyridoxine hydrochloride is a vitamin B6 analog. The chemical name for pyridoxine hydrochloride is 3, 4-pyridinedimethanol, 5-hydroxy-6-methyl-, hydrochloride. The empirical formula is $C_8H_{11}NO_3 \cdot HCl$ and the molecular mass is 205.64.

Inositol

Inositol is an isomer of glucose having an empirical formula of $C_6H_{12}O_6$ and molecular weight of 180.2.

Alpha lipoic acid

Alpha lipoic acid or thioctic acid is a vitamin-like antioxidant and valeric acid derivative having the following structural formula with chemical name of 5-(1,2-Dithiolan-3-yl)valeric acid. The molecular weight is 206.3. The empirical formula is $C_6H_{14}O_2S_2$.

Pre and Probiotic

It contains a pre & probiotic combination which restores the gastrointestinal microflora, thus minimizes gastrointestinal infection, regulates bowel movements and supports gastrointestinal health.

About Pre and Probiotics

Poor eating habits, illness and some medications deplete the body's probiotics, which are necessary for maintaining a healthy digestive tract and promoting a healthy immune system. Probiotics are good microorganisms that offer many beneficial effects to the humans. Probiotic facilitates the digestion of food materials including milk products, strengthen the immune function and also improves the nutritional status by producing Vitamin B complex and K. Prebiotics are the natural food source for the probiotics (beneficial bacteria) present in the intestine. Prebiotics enable the probiotics to proliferate exponentially.

Uniqueness of Colonise MV

Colonise MV is a pre & probiotic supplement made with a combination of unique prebiotics Streptococcus faecalis T-110, Clostridium butyricum TO-A, Bacillus mesentericus TO-A and a probiotic Lactic acid bacillus (Lactobacillus sporogenes). Colonise MV is designed to replenish gastrointestinal microflora and decreasing the duration of infection and discomfort contributing to good Gastrointestinal health. Also the probiotic strengthens the immune function and also improves the nutritional status by producing Vitamin B complex and K.

The uniqueness of Colonise MV as compared to other Probiotics can be summarised as follows

- Resistant to gastric acidity and bile salts
- Survives transit through the gastrointestinal tract
- Resistant to antibiotics
- Proliferates the beneficial bacteria
- Significantly inhibits enteric pathogens
- Normalizes the altered microflora
- Has anti-inflammatory properties
- Regulates bowel movements
- Aids in digestion

Benefits of taking Colonise MV

- Replenishes the disturbed gut microflora
- Protects against enteric pathogens
- Regulates bowel movements
- Decreases the duration and severity of infection
- Aids in digestion

Three live bacteria that act as prebiotic and probiotic agents.

- a. Streptococcus faecalis T-110 (lactic acid bacteria)
- b. Clostridium butyricum TO-A (butyric acid bacteria)
- c. Bacillus mesentericus TO-A (amylolytic bacteria)

Streptococcus faecalis T-110 are live gram-positive, aerobic, non-spore forming cocci. They proliferate actively through the symbiotic action with B. mesentericus TOA and C. butyricum TO-A to yield lactic acid with inhibition of growth of harmful bacteria. This lactic acid bacteria is found in the region from the upper to lower part of small intestine.

Clostridium butyricum TO-A are live gram-positive, anaerobic, spore forming bacilli. They proliferate actively through the symbiotic action with streptococcus faecalis T-110 to yield short chain fatty acids such as butyric acid and acetic acid with a resultant decrease in intestinal pH and inhibition of growth of harmful bacteria. The short chain fatty acids, in addition, help to regularize abnormal bowel movements. The short chain fatty acids also help in adjustment of water and electrolyte concentration of the intestinal tract. They also serve as source of nutrient for intestinal mucosal cells. It is found predominantly in the region from the upper small intestine to the colon.

Bacillus mesentericus TO-A are live gram-positive, aerobic, spore forming bacilli. They proliferate actively through the symbiotic action with streptococcus faecalis T-110. It is a spore forming bacteria and produces an amylolytic enzyme (amylase) and protease to activate proliferation of streptococcus TO-A. It is also responsible for production of a nutrient which helps in increasing the count of bifidobacteria. It is found predominantly in the small intestine.

Important properties of the three live bacteria

The three bacteria proliferate actively throughout the intestinal tract through symbiosis, which is defined as the biological association of two or more species to their mutual benefit.

The three activated bacteria strongly inhibit the growth of potentially pathogenic bacteria in the gastrointestinal tract (probiotic effect). *In vitro* studies using bacterial cultures have shown that when the three live bacteria are grown together with potentially pathogenic bacteria like enterotoxigenic *Escherichia coli*, *Clostridium perfringens*, *Salmonella Typhi*, *Vibrio parahaemolyticus*, *Campylobacter*, *Yersinia enterocolitica*, the three live bacteria significantly inhibited the growth of the above mentioned potentially pathogenic organisms.

The three bacteria facilitate the proliferation of bifidobacterium, thereby increasing their count significantly in the intestine. To a lesser extent they also facilitate proliferation of lactobacilli in the intestine (prebiotic effect). The growth acceleration of bifidobacteria in the intestine by the three live bacteria is through the production of a growth factor by the bacteria *Bacillus mesentericus* TO-A.

The three bacteria normalize the intestinal flora, prevent colonization of the gastrointestinal tract by potentially pathogenic organisms and help regulate abnormal bowel movements.

Intestinal flora is normalized through its prebiotic action that helps in the proliferation of bifidobacteria and lactobacillus.

Prevention of colonization of the gastrointestinal tract by potentially pathogenic organisms is by lowering of intestinal pH by production of lactic acid (by *Streptococcus faecalis* T-110), butyric acid and acetic acid (by *Clostridium butyricum* TO-A).

Regulation of abnormal bowel movements is done by the action of short chain fatty acids such as butyric acid and acetic acid, produced by *Clostridium butyricum* TO-A, on the bowel wall.

Additionally, acetic acid and butyric acid, produced by *Clostridium butyricum*, help in adjustment of water and electrolyte concentration of the intestinal fluid and also serve as a source of nutrient for the intestinal mucosal cells.

The three live bacteria have been shown to be resistant to the action of gastric juice and intestinal juice including bile. They can therefore pass unaffected through the upper GI tract (stomach and duodenum) and colonize in the lower GI tract (upper and small intestine and colon), when taken orally.

It has been shown that these live bacteria help in normalizing the intestinal flora by promoting the growth of beneficial bacteria and preventing the growth of harmful bacteria. In cases of intestinal infection with pathogenic bacteria, intake of these three live bacteria can lower the counts of the pathogenic bacteria, while simultaneously increasing the count of beneficial bacteria. This is shown by a reversal of ratio of predominant aerobic:anaerobic bacteria to a predominant anaerobic : aerobic bacterial ratio. Here the aerobic bacteria signify the potentially pathogenic organisms whereas; the anaerobic bacteria signify the beneficial resident bacteria in the intestine. The increased count of bifidobacteria, generated in the intestine

through the action of the three live bacteria, produces Glutamine from NH_4^+ and glutamic acid in the intestine.

Glutamine is the fuel for the intestinal cells and helps in maintaining the integrity of the intestinal mucosal barrier. In this manner, the colonization by potentially pathogenic microorganisms in the intestine is inhibited.

DOSE AND METHOD OF ADMINISTRATION**Recommended Dose:**

One Capsule twice a day or as directed by the physician for optimum gastrointestinal health as it restores intestinal microflora and corrects vitamin and mineral deficiency.

Directions for Use:

Capsule to be taken with a glass of water after food.

PREGNANCY, FERTILITY AND LACTATION**Pregnancy**

There are no known hazards to the use of colonise MV in pregnancy; supplements during pregnancy are often beneficial. But it should be used under physician's concern only.

Breast Feeding Related Information

Use with caution and according to physician's advice.

CONTRAINDICATION

It is contraindicated in the patients who are having hypersensitivity to active constituents or any of the formulation ingredients.

WARNINGS AND PRECAUTIONS

If symptoms persist or worsen, seek medical advice. Do not exceed the stated dose.

It should be given with caution in patients suffering from folate deficiency.
The treatment of vitamin B12 (parent compound of methylcobalamin) deficiency can unmask the symptoms of polycythemia vera.
Don't attempt vitamin therapy without close supervision by your healthcare provider.
Do not take vitamin B12 containing supplements if Leber's disease, a hereditary eye disease as it can seriously harm the optic nerve, which might lead to blindness. Caution should be exercised when administering folic acid containing supplements to patients who may have folate dependent tumours.
No data are available for other constituents but this supplement should be taken under medical advice only.

DRUG INTERACTIONS

Absorption from the gastrointestinal tract may be reduced by neomycin, aminosalicylic acid, histamine H₂-antagonists, omeprazole, and colchicine. Serum concentrations may be decreased by use of oral contraceptives, chloramphenicol and co-trimoxazole may interfere with folate metabolism, Sulfasalazine - can reduce the absorption of folic acid. Folic acid may interfere with the toxic and therapeutic effects of Methotrexate. The absorption of zinc may be reduced by iron supplements, penicillamine, phosphorus containing preparations, and tetracyclines. Zinc supplements reduce the absorption of copper, fluoroquinolones, iron, penicillamine and tetracyclines.

UNDESIRABLE EFFECTS

Mild transient diarrhea, rarely itching, transitory exanthema.
Gastrointestinal disorders: Anorexia, nausea, abdominal distention and flatulence, constipation.
Immune system disorders: Allergic reactions, comprising erythema, rash, pruritus, urticaria, dyspnea, and anaphylactic reactions (including shock).

OVERDOSE

No data for overdose are available.

PHARMACODYNAMIC AND PHARMACOKINETIC PROPERTIES

The clinical pharmacology data for the combination constituents are not available. The individual constituent's properties are enumerated below:

Vitamins and Minerals

Pharmacodynamics

Mecobalamin

Mecobalamin is one of the biologically active form of vitamin B12. It acts as coenzymes in nucleic acid synthesis. Mecobalamin is also closely involved with folic acid in several important metabolic pathways. Methylcobalamin supports the methionine synthetase reaction, which is essential for normal metabolism of folate.

Folic acid

Folic acid is a member of the vitamin B group. Folic acid is reduced in the body to tetrahydrofolate, which is a coenzyme for various metabolic processes including the synthesis of purine and pyrimidine nucleotides, and hence in the synthesis of DNA; it is also involved in some amino-acid conversions, and in the formation and utilisation of formate.

Zinc

It is a constituent of many enzyme systems and is present in all tissues.

Chromium

Chromium is an essential trace element that potentiates insulin action and thus influences carbohydrate, lipid, and protein metabolism.

Selenium

Selenium is an essential trace element. It is an integral part of the enzyme system glutathione peroxidase, which protects intracellular structures against oxidative damage.

Pyridoxone hydrochloride

Pyridoxine hydrochloride is Vitamin B6. It is converted to pyridoxal phosphate which is the co-enzyme for a variety of metabolic transformations. It is essential for human nutrition.

Inositol

Inositol appears to be involved physiologically in lipid metabolism.

Alpha lipoic acid

Lipoic acid is used for its antioxidant effects in the treatment of diabetic neuropathy. It has been tried in the treatment of liver dysfunction and in subacute necrotizing encephalopathy. Beneficial results have been claimed in amanitin poisoning after ingestion of the mushroom *Amanita phalloides*, but such use is controversial.

Pharmacokinetic

Mecobalamin

It binds to intrinsic factor; a glycoprotein secreted by the gastric mucosa, and is then actively absorbed from the gastrointestinal 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. Absorption from the gastrointestinal tract can also occur by passive diffusion; little of the vitamin present in food is absorbed in this manner although the process becomes increasingly important with larger amounts such as those used

therapeutically. After intranasal dosage, peak plasma concentrations of cyanocobalamin have been reached in 1 to 2 hours. The bioavailability of the intranasal preparation is about 7 to 11% of that by intramuscular injection.

Folic acid

Folic acid is rapidly absorbed from the gastrointestinal tract, mainly from the duodenum and jejunum. Dietary folates are stated to have about half the bioavailability of crystalline folic acid. The naturally occurring folate polyglutamates are largely deconjugated, and then reduced by dihydrofolate reductase in the intestines to form 5- methyltetrahydrofolate, which appears in the portal circulation, where it is extensively bound to plasma proteins. Folic acid given therapeutically enters the portal circulation largely unchanged, since it is a poor substrate for reduction by dihydrofolate reductase. It is converted to the metabolically active form 5- methyltetrahydrofolate in the plasma and liver. The principal storage site of folate is the liver; it is also actively concentrated in the CSF. Folate undergoes enterohepatic circulation. Folate metabolites are eliminated in the urine and folate in excess of body requirements is excreted unchanged in the urine. Folate is distributed into breast milk. Folic acid is removed by haemodialysis.

Zinc

Absorption of zinc from the gastrointestinal tract is incomplete, and is reduced in the presence of some dietary constituents such as phytates. Bioavailability of dietary zinc varies widely between different sources, but is about 20 to 30%. Zinc is distributed throughout the body with the highest concentrations found in muscle, bone, skin, eye, and prostatic fluids. It is primarily excreted in the faeces, and regulation of faecal losses is important in zinc homeostasis. Small amounts are lost in urine and perspiration.

Chromium

Chromium is an essential trace element that potentiates insulin action and thus influences carbohydrate, lipid, and protein metabolism.

Selenium

Selenium compounds are generally readily absorbed from the gastrointestinal tract. Selenium is stored in red blood cells, the liver, spleen, heart, and nails. It is converted in tissues to its metabolically active forms. Selenium is excreted in the urine, and to a lesser extent in the faeces.

Pyridoxine hydrochloride

Pyridoxine readily absorbed from the gastrointestinal tract after oral dose and 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 and other inactive metabolites which are excreted in the urine. As the dose increases, proportionally greater amounts are excreted unchanged in the urine. Pyridoxal crosses the placenta and is distributed into breast milk.

It is extensively bound to specific plasma proteins called transcobalamins; transcobalamin II appears to be involved in the rapid transport of the cobalamins to tissues. A parent form -vitamin B12 is stored in the liver, excreted in the bile, and undergoes extensive enterohepatic recycling; part of a dose is excreted in the urine, most of it in the first 8 hours; urinary excretion, however, accounts for only a small fraction in the reduction of total body stores acquired by dietary means. Vitamin B12 diffuses across the placenta and also appears in breast milk.

Inositol

Inositol phospholipids are important in signal transduction.

Alpha lipoic acid

It is reported that alpha-lipoic acid 600 mg was administered orally once daily for 4 days, and the pharmacokinetic parameters were measured on days 1 and 4 revealed the mean percentage of the administered dose excreted in urine as parent compound was 0.2 (which is 0.67% with assumption of 30% bioavailability).

Pre and Probiotic

Pharmacodynamics

Streptococcus faecalis, *Clostridium butyricum* and *Bacillus mesentericus* are a probiotic. Probiotics are defined as live microorganisms, including *Lactobacillus* species, *Bifidobacterium* species and yeasts that may beneficially affect the host upon ingestion by improving the balance of the intestinal microflora.

Pharmacokinetics

The effectiveness of probiotics is related to their ability to survive in the acidic stomach environment and the alkaline conditions in the duodenum, as well as their ability to adhere to the intestinal mucosa of the colon and to colonize the colon. After passage through the stomach and the small intestine, those probiotics that do survive become established transiently in the colon.

EXPIRY DATE

Do not use later than the date of expiry

STORAGE

Store in a dry place at a temperature not exceeding 30°C. Protect from light.

PRESENTATION

Strip (ALU-ALU) of 10 Capsules.

MARKETED BY:



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IN/COLONISE MV/FEB-2019/02/PI

