CleanseMAX I

ADVANCED Naturals

PRODUCT MONOGRAPH

Product composition
Medicinal Ingredients:
Each capsule contains:

Artichoke leaf (Cynara scolymus) 4:1 extract (equivalent to 100 mg)	25 mg
Ashwagandha root (Withania somnifera) 5:1 extract (equivalent to 125 mg)	25 mg
Beet leaf (Beta vulgaris) 4:1 extract (equivalent to 80 mg)	20 mg
Bupleurum root (Bupleurum chinense) 4:1 extract (equivalent to 80 mg)	20 mg
Burdock Root (Arctium lappa) 5:1 extract (equivalent to 125 mg)	25 mg
Corn stigma and style (Zea mays)	20 mg
Dandelion root (Taraxacum officinale) 4:1 extract (equivalent to 80 mg)	20 mg
Hawthorn Berry (Crataegus laevigata) 4:1 extract (equivalent to 100 mg)	25 mg
Milk thistle seed (Silybum marianum) 161.5 mg silymarin	262.5 mg
Mullein leaf (Verbascum thapsus)	20 mg
Red clover flower (Trifolium pratense)	20 mg
Turmeric root (Curcuma longa) 4:1 extracts (equivalent to 80 mg)	20 mg

Non-medicinal ingredients: Hypromellose, water

Recommended dose: Adults: Take 2 capsules in the morning on an empty stomach (3 hours before eating).

Duration of use: For best results, use for 30 days. Consult a health care practitioner for prolonged use.

Indication: For liver protection.

Contraindications: Do not take if pregnant or breastfeeding. Do not use if you have liver or gall bladder disorders, bile duct obstruction and/or bowel obstruction. Do not use if you are allergic to plants of the Asteraceae/Compositae/Daisy family.

Warnings: Keep out of reach of children.

Precautions: Discontinue use if you develop symptoms of liver trouble. Consult a health care practitioner prior to use if you have diabetes, are taking antiplatelet medication or blood thinners, have stomach ulcers or excess stomach acid, have any cardiac disorder or are taking heart medication. Consumption with alcohol, other drugs or natural health products with sedative properties is not recommended.

Adverse Effects: Hypersensitivity, such as allergy, has been known to occur; in which case, discontinue use.

Overdose: For management of suspected product overdose it is recommended to contact your physician.

Symptoms of Overdose: Has not been investigated nor any reports have been filed.

Supporting Research and Traditional Evidence

Artichoke leaf (*Cynara scolymus*) 4:1 extract
The artichoke has been used in traditional medicine to increase liver health (Blumenthal *et al.*1998; Hoffman, 2003). The main phytochemical constituents found in the leaf include caffeoylquinic acids, sesquiterpene, aliphatic acids and flavonoids (Gruenwald *et al*. 2007). The caffeoylquinic acid derivative cynarin is thought to elicit pharmacological activity and stimulate liver function in the form of bile secretion (Bradley, 2006). The liver contains various scavenging enzymes which function in neutralizing toxic metabolites. Studies have suggested that the artichoke leaf has an antioxidant effect and can confer liver protection by scavenging free radicals. A study by Mehmetcik *et al.* (2008) assessed the antioxidant effects of artichoke leaf extract in a hepatic necrosis model in rats. The rats were pretreated with 1.5/g artichoke extract per kg daily, following which hepatic insult was chemically induced. Liver enzymes levels were assessed and observed to be decreased in the artichoke-treatment group when compared to control levels. Endogenous antioxidants remained unchanged in the artichoke pretreatment group suggesting that the artichoke leaf extract was responsible for the antioxidant effect (Mehmetcik *et al.* 2008). Scientific evidence in accordance with the NHPD (2008) recognize artichoke leaf as an effective agent to help increase bile secretion to confer liver protection and has demonstrated a good safety profile when taken at recommended doses of 4.5 -10 g dried leaf equivalent/day.

Ashwagandha root (*Withania somnifera*) 5:1 extract
Various parts of the ashwagandha plant have been used in traditional Ayurvedic medicine. It is the root of this plant which elicits pharmacological activity as a hepatoprotectant. The main phytochemical substances present in the root include steroid lactones, phytosterols and alkaloids such as withanine (Williamson, 2002). Studies have been performed to assess the effects of the ashwaganda root as an antioxidant and its effect on liver function. An *in vivo* study was performed by Bhattacharya *et al.* (2000) in which rats underwent a heavy metal load and were subsequently treated with an extract of ashwagandha root. The study assessed the antioxidant properties of the root as amount of lipid peroxidation present in the liver tissue, and liver function was based on the activities of liver enzymes. An increase in dose of root extract correlated with 1) a reduction in lipid peroxidation of the liver tissue and 2) a reversal of injury-induced effects of the heavy metal insult as the hepatic enzyme levels returned to control levels. The results of the study suggest that ashwagandha root confers healthy liver functioning through its antioxidant effect. A second study was conducted to evaluate the role of ashwagandha root as an antioxidant liver-protectant. Mice underwent lead-induced hepatic damage then were treated with a solution of root powder and assessed for lipid peroxidation in the liver and liver function. The researchers observed a correlation between antioxidant effect, as determined by a reduction in lipid peroxidation, and liver function, as determined by detoxification enzyme activity in the liver (Chaurasia *et al.*2000). The results of the study suggest that ashwagandha root elicits antioxidant properties which helps to improve overall liver health. The NHPD (2007) recognizes ashwagandha root as an effective agent which has demonstrated a good safety profile when taken at recommended doses of 6 g of dried root/day.

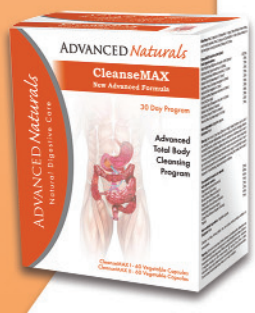
Beet leaf (*Beta vulgaris*) 4:1 extract
B. vulgaris contains chemical ingredients such as oligo- and polysaccharides, fruit acids, triterpene saponins and betaine, the pharmacologically active phytochemical. Betaine is deep red in colour and is the component which gives the roots and leaf stems their vibrant colour. Betaine is also thought to exhibit beneficial antioxidant properties and confer liver protection by preventing the deposition of fat in the liver (Gruenwald *et al.* 2007). Studies have been conducted to assess the effects of betaine on liver health and function. A study by Agarwal *et al.* (2006) assessed the effects of chemically induced-hepatic injury in rats following treatment with *B. vulgaris* extract. The study compared the effects of *B. vulgaris* with that of a known traditional hepatoprotectant, silymarin. Under the same experimental conditions, *B. vulgaris* extract was suggested to be as effective as silymarin in improving liver function. Furthermore, a pilot study was conducted to assess the effects of betaine on liver function in humans. Patient suffering from nonalcoholic steatohepatitis were treated with betaine daily for 12 months. Over time, treatment with betaine reduced the necroinflammitory state of the liver and liver enzyme activities returned to physiologically normal ranges (Abdelmalek *et al.* 2001) suggesting that *B. vulgaris* may contribute to overall liver protection. The suggested dose is 10 g daily, but it is recommended that the dose be reduced to 5 g daily for long term use. Beets are listed as a common culinary ingredient and the leaves and roots are commonly present in soups and salads, or can be eaten on their own (Facciola, 1998). Beet leaf may be an effective agent demonstrating a good safety profile for liver protection when taken at recommended doses.

Bupleurum root (*Bupleurum chinense*) 4:1 extract
Bupleurum root is a traditional Chinese medicine known as chai hu. In traditional Chinese medicine qi is thought of as energy within the body which promotes health and well being. The goal for good health is to keep qi in equilibrium, and the disease state is represented by a change in qi. In traditional Chinese medicine bupleurum root is believed to relieve "liver qi restraint," or thought to promote normal liver function by acting as a pathogen-expellant (Bensky *et al.* 2004). The main pytochemical constituents of bupleurum root include volatile oils and triterpene saponines. The active constituent is saikosaponin and is thought to confer liver protection through its antioxidant properties (Bensky *et al.* 2004). An *in vivo* study was conducted to evaluate the antioxidant effects of bupleurum root on chemically-induced liver injury in Sprague-Dawley rats. Following liver injury, the rats were dosed with saikosaponin, curcumin (the active phytochemical in turmeric which is also present in this formulation of CleanseMAX), or a combination of the two phytochemicals. Following treatment duration, the liver and serum were assayed for enzyme activity and lipid content. The researchers observed that curcumin and saikosaponin both had positive effects on liver function and cholesterol levels, as determined by a decrease in liver fibrosis, inflammation and necrosis. Moreover, a combination of the herbal constituents elicited the greatest effects on liver protection (Wu *et al.* 2008) suggesting that bupleurum root and turmeric root each contribute to liver health, and demonstrate an additive effect when taken together. Bupleurum root may be an effective agent for liver protection and with a good safety profile when taken at recommended doses of 3 – 9 g daily (Bensky *et al.* 2004).

Burdock Root (*Arctium lappa*) 5:1 extract
Traditional Chinese herbalists have used Burdock root to treat various ailments. The herb acts as a diaphoretic which is thought to be beneficial to treating gallbladder or liver disorders (Bensky *et al.* 2004). The recommended daily dosage for Burdock root is 1.2-18 g dried root per day (NHPD, 2008) and the chemical constituents include phenylpropane derivatives, bithiophenes, sesquiterpenes, triterpenes, organic acids and polysaccharides (Bensky *et al.* 2004). An *in vivo* study was conducted to assess the effects of a crude water extract of A. lappa on liver function in Wistar rats. Liver injury was induced chemically with either alcohol or carbon tetrachloride plus alcohol and the rats were given either burdock root or placebo. The burdock-treated group showed improvements in liver function, based on improvements in enzyme activity and a decrease in lipid levels (Lin *et al.* 2002). This evidence suggests that burdock root elicits antioxidant properties which may contribute to its use as a hepatoprotectant. Burdock root has been traditionally eaten as a food, in addition to being used as a medicine in traditional Chinese preparations. The NHPD (2008) recognizes that burdock root has demonstrated a good safety profile when taken at recommended doses.

Corn stigma and style (*Zea mays*)
Zea mays has been used traditionally for the treatment of certain ailments. The chemical constituents found in corn silk include flavonoids, chlorogenic acid, maysin, volatile oils, minerals and alkaloids (Bradley, 2006). An *in vivo* study was conducted to assess the role of corn peptides on lipid levels and liver function in mice with alcohol-induced liver damage. Treatment with peptides isolated from corn was associated with increased antioxidant activity in the liver tissue of the mice, as determined by the dose-dependent changes in free radical scavenging enzymes (Li *et al.* 2007). A second study was performed which observed similar results for antioxidant activity and prevalence of lipid peroxidation in an acute chemically-induced hepatitis model (Katikova *et al.* 2002). Together these studies suggest corn peptides possess antioxidant properties which may contribute to overall liver health. Recommended doses are 2 - 8 g taken 2 times daily (Bradley, 2006; Newall *et al.* 1996). *Zea mays* is commonly used as a food ingredient and is listed as GRAS (Generally Regarded as Safe) in the US and Europe (Newall *et al.* 1996; Bradley, 2006).

Dandelion root (*Taraxacum officinale*) 4:1 extract
Traditionally, dandelion root has been used in the treatment of various health conditions, specifically hepatobiliary problems. The main physiological action of the herb is to increase bile secretion from the gallbladder which is thought to promote liver health (Bradley, 2006). Active constituents of dandelion root include taraxcoside, sesquiterpene lactones, tripterpenes, phenolic acids, as well as carbohydrates, vitamins and minerals (Bradley, 2006). *In vivo* and *in vitro* studies have been performed to assess the antioxidant effects of dandelion root. One *in*



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vitro study investigated the effects of dandelion root extract and the activities of several rat liver enzymes involved in the scavenging of free radicals. A dose-dependent antioxidant effect was observed following the treatment of liver microsomes with increasing doses of root extract (Hagymasi *et al.* 2000), suggesting that dandelion root functions as an antioxidant to promote liver health. A second study assessed the effects of a water extract of dandelion root on the activities of hepatic antioxidant enzymes and lipid deposition in diabetic Sprague-Dawley rats. Treatment with dandelion root resulted in a reduction in the amount of cholesterol observed in liver tissue with a corresponding increase in liver antioxidizing enzymes, such as superoxide dismutase (Cho *et al.* 2002). Scientific evidence suggests that dandelion root functions as an antioxidant to contribute to liver health. Recommended daily dosage is 1.5-24 g daily (NHPD, 2008). Dandelion root is commonly used as a coffee substitute and is ingested as a food in Europe (Newall *et al.* 1996; Bradley, 2006). The NHPD recognizes dandelion root as effective to help stimulate bile flow with an established safety profile in when taken in recommended doses.

Hawthorn Berry (*Crataegus laevigata*) 4:1 extract

The hawthorn berry has been used in traditional herbalism. Phytochemicals include procyandins, flavonoids, hydroxycinnaminic acid derivatives and pentacyclic terpenes (Bradley, 2006). The abundance of flavonoids is responsible for the antioxidant properties of the hawthrorn berry. Studies in rats have been conducted to assess the role of these antioxidant properties in providing protection to the liver following myocardial infarction. Liver dysfunction is generally associated with myocardial infarction. All rats received an extract of hawthorn berry. The experimental group underwent chemically-induced myocardial infarcts in addition to the hawthorn treatment. Following the herbal treatment, liver biochemistry and histochemistry were assessed and the results suggested treatment with hawthorn berry increased antioxidant properties to increase liver function in following myocardial infarction-induced liver dysfunction (Thirupurasundari *et al.* 2005). Overall, studies have suggested an implication for hawthorn berry as an antioxidant which may contribute to overall liver health. Recommended doses of 1.5-3.5 g/day have demonstrated a good safety profile (Bradley, 2006).

Milk thistle seed (*Silybum marianum*) 80% silymarin

The seed of the milk thistle plant has traditionally been used to confer liver protection. Many phytochemicals are present in the seed such as flavonoids, fatty oils and sterols. The active ingredient for liver protection is the mixture of flavanonol derivatives called silymarin. Silymarin is present in the casing of the seed and is mainly composed of the active constituent silybin, making up 60-80% of the flavonoid mixture (Bradley, 2006; WHO, 2002; Gruenwald *et al.* 2007). Pharmacologically, Sylmarin contributes to liver protection by 4 main mechanisms: 1) preventing the entry of liver-damaging substances into the cell by reducing the membrane permeability of the hepatocytes, 2) eliciting antioxidant activity and scavenging free radicals, 3) stimulating ribosomal function to facilitate regeneration of the liver cells and liver tissue, and 4) as an anti-fibrotic to inhibit hepatocyte transformation and deposition of collagen associated with cirrhosis (Bradley, 2006; Blumenthal *et al.* 1998). A systemic review by Tamayo and diamond (2007) compiled several randomized clinical studies assess the effects of milk thistle, standardized to silymarin content, on liver protection. Various types of liver disorders were included in the report, including hepatitis, chronic alcohol liver disease and cirrhosis. Overall the article suggests that milk thistle is effective in conferring liver protection to patients with liver diseases, in particular for alcohol-associated liver diseases. The NHPD (2009) recognizes milk thistle seed as effective for liver protection with a good safety profile when taken at doses up to 3 - 14.5 g dried seed, standardized to140-600 mg silymarin (calculated as silibinin/silybin), per day.

Mullein leaf (*Verbascum thapsus*)

Mullein leaf has been implicated in traditional Chinese medicine. The phytochemicals present in the leaf are mainly saponins and mucopolysaccharides with the active chemical being aucubin (Blumenthal *et al.* 1998). Several *in vivo* or *in vitro* studies were conducted by Chang (1998) to investigate the role of aucubin on liver biochemistry in animals. Using various forms of chemically-induced liver damage, aucubin treatment was observed to have an effect on improving hepatic physiology in all liver damage models, including reduction of hepatitis B viral DNA replication *in vitro*. Scientific evidence suggests that mullein leaf may be beneficial as a hepatoprotectant. Mullein leaf has demonstrated a good safety profile when taken at doses of 3-4 g of herb/day (Blumenthal *et al.* 1998).

Red clover flower (*Trifolium pratense*)

Red clover flower has been used as a traditional medicine. The flower contains many plytochemicals such as flavonoids such as formononetin, phenolic acids and volatile oils which function to enhance antioxidant properties (Bradley, 2006). The function of red clover flower has been experimentally investigated *in vitro*. A study by Rufer *et al.* (2006) observed that the flower extract contains flavonoids, such as biochanin A and formononetin, which has been suggested to be the main antioxidant chemicals. A second study assessed the effects of formononetin as an antioxidant. The results indicated that an increase in liver enzyme activity and a decrease in lipid peroxidation in both the liver and serum was associated with red clover flower treatment (Mu *et al.* 2009). Overall the study suggests strong evidence for a role as an antioxidant which may help confer liver protection. Red clover flower as been regarded as safe (GRAS) in the US and is recognized as a food by the Council of Europe (Bradley, 2006).

Turmeric root (*Curcuma longa*) 4:1 extracts

Turmeric root has traditionally been used as a choleretic (Blumenthal *et al.* 1998). The constituent in turmeric root responsible for its choleretic properties is curcumin which acts on the gallbladder to increase bile secretion. The herb root also contains chemicals such as volatile oils and other dicinnamoylmethane derivatives (Blumenthal *et al.* 1998). An *in vivo* study was conducted to evaluate the antioxidant effects of turmeric root on chemically-induced liver injury in Sprague-Dawley rats. Following liver injury, the rats were dosed with curcumin, saikosaponin (the active phytochemical found in bupleurum root which is also present in this formulation of CleanseMAX), or a combination of the two phytochemicals. Following treatment, the liver and serum were assayed for enzyme activity and lipid content. The researchers observed that curcumin and saikosaponin both had positive effects on liver function and cholesterol levels, as determined by a decrease in liver fibrosis, inflammation and necrosis following treatment with the phytochemicals. Moreover, a combination of the herbal constituents elicited the greatest effects on liver protection (Wu *et al.* 2008) suggesting that bupleurum root and turmeric root each contribute to liver health, and demonstrate an additive effect when taken together. Studies have also been conducted to assess the antioxidant properties of turmeric root and how they contribute to liver health and function. In an *in vitro* study, curcumin was observed to stimulate an increase in liver detoxification enzymes which can also be induced by known antioxidants. The study investigated the transcriptional regulation of these liver detoxification enzymes, and the results indicate that like known antioxidants, curcumin works in a similar manner to increase the levels of detoxification enzymes within the liver (Nishinaka *et al.* 2007). Turmeric root may be an effective agent for liver protection with a good safety profile when taken at recommended doses of 1.5 – 3 g of daily (Blumenthal *et al.* 1998).

Ingredient Summary:

Artichoke leaf (*Cynara scolymus*) 4:1 extract
- Traditionally used to increase bile secretion and confer liver protection

Ashwagandha root (*Withania somnifera*) 5:1 extract
- Demonstrates antioxidant properties which may help to improve liver health

Beet leaf (*Beta vulgaris*) 4:1 extract
- Contains active chemicals which may contribute to liver protection

Bupleurum root (*Bupleurum chinense*) 4:1 extract
- A traditional Chinese medicine used to expel harmful substances and confer liver health

Burdock Root (*Arctium lappa*) 5:1 extract
- Traditionally used as a diaphoretic to expel liver-harming toxins

Corn stigma and style (*Zea mays*)
- Demonstrates antioxidant properties which may help to improve liver health

Dandelion root (*Taraxacum officinale*) 4:1 extract
- Helps stimulate bile secretion to promote healthy liver function

Hawthorn Berry (*Crataegus laevigata*) 4:1 extract
- Demonstrates antioxidant properties which may help to improve liver health

Milk thistle seed (*Silybum marianum*) 80% silymarin
- Confers liver protection

Mullein leaf (*Verbascum thapsus*)
- Contributes to liver health

Red clover flower (*Trifolium pratense*)
- Demonstrates antioxidant properties which may help to improve liver health

Turmeric root (*Curcuma longa*) 4:1 extracts
- Traditionally used to help stimulate bile secretion to promote healthy liver function

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NHPD Globe Artichocke Monograph. http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/prodnatur/mono_artichoke-artichaut-eng.pdf.

NHPD Milk Thistle Monograph. http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/prodnatur/applications/licen-prod/monograph/mono_thistle-chardon-eng.pdf.

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PRODUCT MONOGRAPH

Product composition

Medicinal Ingredients:

Each capsule contains:

Magnesium (Magnesium hydroxide)	125 mg
Cape Aloe leaf latex (Aloe ferox)	125 mg
Chinese Rhubarb root (Rheum palmatum)	175 mg
Slippery Elm bark (Ulmus rubra)	25 mg
Marshmallow root (Althaea officinalis)	25 mg
Fennel seed (Foeniculum vulgare)	25 mg
Ginger root, rhizome (Zingiber officinale)	25 mg
Triphala: a blend of:	
Indian gooseberry fruit (Emblica officinalis)	8.33 mg
Belleric myrobalan fruit (Terminalia bellerica)	8.33 mg
Chebulic myrobalan fruit (Terminalia chebula)	8.33 mg

Non-medicinal ingredients: Hypromellose, water

Recommended dose: Adult: Take two capsules in the evening on an empty stomach (3 hours after eating)

Duration of use: Consult a health care practitioner if constipated for more than 7 days. Allow 6-12 hours for laxative effect to occur.

Indication:Provides Aloe which has been traditionally used in herbal medicine to support the process of a colon cleanse by relieving occasional constipation through laxative action.

Contraindications: Do not use if you are pregnant or breastfeeding or are allergic to anethole or plants of the Apiaceae/Carrot family. Do not use if you currently have abdominal pain, nausea, fever, vomiting, hemorrhoids, or chronic gastrointestinal disorders. Do not use if you are taking licorice root, thiazide diuretics, corticosteroids, or drugs that may aggravate electrolyte imbalance. Do not use within 2 hours of other medicines. Do not exceed recommended dose. Do not use prior to, or after recent surgery. Keep out of reach of children.

Warnings: Keep out of reach of children.

Precautions: Consult a health care practitioner prior to use if you have a kidney disorder, or any cardiac disorder or if you are taking heart medications.

Adverse Effects: Reduce dose or discontinue use if abdominal cramps, spasms, and/or pain occur. Overuse or extended use may cause dependence for bowel function. Hypersensitivity (eg. allergy) has been known to occur (rare cases); in which case, discontinue use.

Overdose: For management of suspected product overdose it is recommended to contact your physician.

Symptoms of Overdose: Has not been investigated nor any reports have been filed.

Supporting Research and Traditional Evidence

Magnesium (Magnesium hydroxide)

Magnesium is the fourth most abundant cation in the body and is stored mainly intracellularly or in the bones (Rude and Singer, 1981). Physiologically, magnesium is absorbed along the entire length of the small intestine and to some extent within the large intestine (Brannan *et al.* 1976). Magnesium can be taken safely in doses up to 500 mg/day for healthy adults (NHPD, 2007). Gastrointestinal effects associated with magnesium deficiency include dysphagia, or a difficulty swallowing. The magnesium deficiency associated with dysphagia was found to be reversible upon magnesium supplementation (Flink, 1978). Clinical studies have been performed to assess the impact of a combination laxative treatment consisting of magnesium hydroxide and senna syrup, a traditionally used laxative. One hundred and nineteen constipated children were treated with either a bulk laxative or a combination of magnesium hydroxide/senna syrup at an average dose of approximately 4 teaspoons/day for 2 months. Following the completion of the study, 63% of the children taking the Mg/senna combination were no longer constipated suggesting that treatment with magnesium hydroxide in addition to herbal laxative remedies may contribute to increased bowel movements (Borowitz *et al.* 2005). A randomized, placebo-controlled, double-blind, crossover pilot study was conducted to evaluate the effects of magnesium hydroxide as a laxative in a dose dependent-manner. Six patients were given either placebo or magnesium hydroxide at doses of 1200, 2400 or 3600 mg/day for 5 days. The patients' stool output was monitored and the results suggested that magnesium hydroxide is effective as a laxative in a dose-dependent manner (Donowitz and Rood, 1992).The NHPD (2007) recognizes magnesium as a dietary supplement which contributes to the maintenance of good health, and scientific studies have demonstrated a good safety profile and a potential role for magnesium hydroxide as a laxative when taken at doses up to 500 mg/day.

Cape Aloe leaf latex (*Aloe ferox*)

Aloe leaf has been traditionally used as a laxative when taken orally, as well as a treatment for certain skin conditions when applied topically (NHPD, 2006; Newall *et al.* 1996). Aloe contains anthrone-C-glycosides (Van Wyk *et al.* 1995) which are metabolized to yield 1,8-dihydroxy-anthracene, a pharmacologically active metabolite. 1,8-dihydroxy-anthracene has a stimulatory influence on the colon resulting in colonic motility. Propulsive contractions increase the rate of passage of material through the intestine. Alongside the increase in colon contractions, aloe also promotes chloride secretion into the intestinal lumen which thereby increases water secretion and electrolyte diffusion into the lumen (Blumenthal *et al.* 1998). The anthraquinones present in aloe have stool-softening properties but do not disrupt the normal pattern of fecal excretion (Gruenwald *et al.* 2007). The recommended dose for aloe leaf is standardized to 20-30 mg hydroxyanthracene derivatives/day, or the smallest dosage needed to produce a laxative (Blumenthal *et al.*1998). The NHPD (2007) has recognized the dried leaf gel of *Aloe ferox* and effective as a natural laxative with a good safety profile at doses of 50-250 mg per day. Clinical evidence also suggests a role for *Aloe ferox* as a laxative. One placebo-controlled, double-blind clinical trial assessed the effects of a combination laxative therapy consisting of aloe, psyllium and celandine in 35 chronically constipated patients. The ingredients in the study preparation have similar effects on the gastrointestinal tract as the herbs present in this formulation of CleanseMAX. Psyllium has high mucilage content, similar to slippery elm bark, and celandine is a traditional herb used to soothe gastric irritation (Blumenthal *et al.* 1998). The study confirmed the effects of herbal combination therapy as an effective laxative for the treatment of constipation (Odes and Madar, 1991).

Chinese Rhubarb root (*Rheum palmatum*)

Various parts of the rhubarb plant have been used traditionally for the treatment of certain ailments and as foods. Rhubarb stem has been classified as a food by the Council of Europe, and the root has been traditionally used to treat gastrointestinal irregularities, such as constipation (Newall *et al.* 1996). Rhubarb root, like *Aloe ferox*, contains β-glycosides, including 1,8-dihydroxy-anthracene. 1,8-dihydroxy-anthracene is the active constituent and is responsible for the laxative properties of rhubarb (Bradley, 2006). This anthraquinone has a stimulatory influence on the colon resulting in colonic motility through propulsive contractions to increase the rate of passage of material through the intestine and reduce liquid absorption (Blumenthal *et al.* 1998). The recommended dose for Rhubarb root is 200 mg - 1000 mg/day to be efficacious as a laxative with a good safety profile (Newall *et al.* 1996). A recent review article summarized a few clinical studies which were not published in English. These studies focused on rhubarb root as a traditional Asian medicine. The article suggested that rhubarb root helped alleviate the symptoms associated with the treatment of various gastrointestinal conditions in a clinical setting, specifically gastric bleeding and enteroparalysis as well as contributing to the natural pH of the gastric mucosa (Chen and Wong, 2009).

Slippery Elm bark (*Ulmus rubra*)

Slippery elm bark has been used traditionally to treat certain ailments such as constipation. The inner rind of the bark contains large amounts of mucilage. When ingested this mucilage mixture of polysaccharides coats the enteric lining. The ability of the mucilage to coat the gastrointestinal tract makes the herb useful as a traditional treatment for gastric inflammation by acting as a demulcent (Gruenwald *et al.* 2007; Bradley, 2006). The effective recommended dose for slippery elm is a decoction made with ethanol in a ratio of 1:8 and a daily dose of 4 -16 ml of the decoction (Gruenwald *et al.* 2007). A study by Langmead *et al.* (2002) evaluated the antioxidant properties of a slippery elm water extract in the treatment of irritable bowel syndrome. A dose-dependent scavenging of superoxide was observed suggesting that slippery elm may be implicated in the treatment of irritable bowel syndrome by reducing colonic inflammation-associated oxidative stress.

Marshmallow root (*Althaea officinalis*)

Marshmallow has been traditionally for the treatment of certain ailments and has also been classified as a food in Europe and the United States (Newall *et al.* 1996). The medicinal parts of the plant include the leaves, roots, syrup and flowers. Marshmallow root, in particular has been traditionally used in treatment of mild inflammation of the gastric mucosa. Constituents of the root include various mucilage polysaccharides, pectin, few tannins and asparginines. Marshmallow root works in a similar manner as slippery elm bark. High levels of polysaccharide mucilage help reduce gastric inflammation by coating and soothing irritation of the enteric lining (Hoffman, 2003). The recommended effective dose of Marshmallow root is 6 -15 g of root/day with a good safety profile (Blumenthal *et al.* 1998).

Fennel seed (*Foeniculum vulgare*)

Fennel seed has been used in traditional medicine and has been implicated in the treatment of many gastrointestinal problems. Fennel seed works on the gastrointestinal tract to induce motility within the gastrointestinal lumen. High concentrations have been observed to exhibit an antispasmodic effect on the colon (Blumenthal *et al.* 1998). The seed is chemically composed of fixed oils, phenylpropanoids, flavonoids, coumarins, various glycosides and essential oils, mainly anethone, fenchone and estragone (Blumenthal *et al.* 1998; Bradley, 2006). Researchers have assessed the effects of fennel seed as part of a combination laxative for the treatment of constipation. A randomized, double-blind, placebo-controlled, single center study was conducted in which 92 elderly patients living in a nursing home were administered a daily tea concoction containing a combination of herbal constipation therapy, including fennel seed. The treatment duration lasted 28 days and herbal treatment resulted in an increase in the number of bowel movements when compared to placebo-control (Bub *et al.* 2006). The recommended dose of fennel is 0.4 g of dried seed, 3 times per day for durations up to 2 weeks (NHPD, 2008). Scientific evaluation along with traditional evidence suggests that fennel seed, as part of a combination herbal therapy, may be effective as a laxative with a good safety profile when taken at recommended doses.

Ginger root, rhizome (*Zingiber officinale*)

Traditionally ginger root has been used to treat gastrointestinal ailments such as dyspepsia and nausea (Blumenthal *et al.* 1998). Ginger helps alleviate gastrointestinal discomfort by increasing peristalsis and gastric tone (Bradley,

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2006). The root chemistry is comprised of various phytochemicals including starch, lipids, oleo-resins, such as gingerol, and volatile oils, such as zingiberene, ar-curcumene, β-sesqiuphellandrene and β-bisabolene. Studies have been conducted to assess the pharmacological properties and clinical effects of ginger. The effects on gastric motility have been evaluated in healthy volunteers. Subjects were given either 1200 mg of ginger root/day or placebo. The results indicated an increase in the frequency of antral contractions within the upper intestinal tract suggesting that ginger may be effective as a laxative in healthy subjects (Wu *et al.* 2008). Furthermore, researchers have also assessed the effects of ginger root as part of a combination laxative for the treatment of constipation. A randomized, double-blind, placebo-controlled, single center study was conducted in which 92 elderly patients living in a nursing home were administered a daily tea concoction containing a combination of herbal constipation therapy, including ginger root. The treatment duration lasted 28 days and resulted in an increase in the number of bowel movements over the treatment duration when compared to placebo-control (Bub *et al.* 2006). Scientific and traditional evidence suggest that ginger root may be effective as a laxative. The Council of Europe and the US have classified ginger as a GRAS (Generally Recognised as Safe) food and states it is generally used as a spice with an established safety profile at doses of 0.5-2 g dried rhizome, per day (Newall *et al.* 1996; NPHD 2008).

Triphala: a blend of:

Indian gooseberry fruit (*Emblica officinalis*)

Various parts of the Indian gooseberry plant have been traditionally used in Ayurvedic medicine. The leaves of the plant traditionally are used to treat respiratory ailments, while the fruits have been used to alleviate gastrointestinal discomfort, such as constipation and vomiting. The fruits are also a good source of nutrition (Williamson, 2002). The major constituents of *E. officinalis* are polyphenols, ascorbic acid, cytokinins and fatty acids. The fruit exhibits antioxidant activity in the presence of tannins to maintain gastrointestinal health. Studies have been conducted to assess the antioxidant properties of *E. officinalis*. A study by Pozharitskaya *et al.* (2007) quantified the free-radical scavenging activity and found it to be similar to that of ascorbic acid. A study by Bandyopadhyay *et al.* (2000) assessed the impact of seeds from *E. officinalis* as an antioxidant for the treatment of gastric ulcers in Sprague-Dawley rats. Prior to gastric injury, the rats were treated with dried gooseberry seed in increasing doses for 10 days. The antioxidant effect was measured by determining the abundance of superoxide dismutase, a free-radical scavenger in serum, abundance of lipid peroxidation and mucous secretion/ulcer formation of the gastric tissue. The results indicated that an increase in antioxidant activity correlated with a reduction in the formation of ulcers in the pre-treatment group. Lastly, a study by Scartezzini *et al.* (2006) suggests that 45-70% of the antioxidant activity of *E. officinalis* is derived from the high levels of vitamin C which it contains. In traditional Ayurvedic medicine, the recommended doses of Gooseberry fruit are 3-6 g of powder/day (Williamson, 2002). *E. officinalis* has demonstrated a good safety profile has been effectively used for the treatment of gastrointestinal discomfort as an ingredient in Triphala (Dhanoa, 2001).

Belleric myrobalan fruit (*Terminalia bellerica*)

In traditional Ayurvedic medicine, Belleric myrobalan fruit has been used as a "health-harmoniser". The fruit of *T. bellerica* has been used in the treatment of various conditions affecting the liver, vasculature system, respiratory system, skin and gastrointestinal tract. The active constituents are mainly triterpenoids, such as β- sitosterol, and polyphenols (Williamson, 2002). Studies have been conducted to assess the role of *T. bellerica* in the treatment of gastric ulcers and obesity. Studies have implicated an antioxidant activity of Belleric myrobalan fruit in the presence of tannins which are present in many of the additional herbs in this formula. A study by Soubir (2007) evaluated the antioxidant activities of a number of ethanolic plant extracts. Of the plant extracts assessed, *T. bellerica* was found to be the second most potent antioxidant, second only to Averrhoea carambola, commonly known as starfruit. The blend of *T. bellerica*, *E. officinalis* and *T. chebula* is known in Ayurvedic medicine as Triphala. *T. bellerica* has been traditionally used for the treatment of gastrointestinal problems in doses from 3 – 6 g of powder/day with an established good safety profile (Dhanoa, 2001).

Chebulic myrobalan fruit (*Terminalia chebula*)

T. chebula has been used in traditionally Ayurvedic medicine in combination with *T. Bellerica* and *E. Officinalis* as Triphala. Various parts of the plant have been used in traditional medicine, including the fruit, leaves and stem. The fruits of the plants have been recognized as natural laxatives (Williamson, 2002). Major pharmacologically-contributing phytochemicals include triterpene glycosides, tannins and polyphenols. Antioxidant effects associated with *T. chebula* may help contribute to a healthy gastrointestinal system by reducing gastric inflammation. A study by Chalise *et al.* (2010) investigated the effects of 15 traditionally used fruits and determined their corresponding polyphenol content and antioxidant properties. *T. chebula* was one of the 15 fruits assessed and it was observed that *T. chebula* contained the highest levels of polyphenols of any of the fruits. The level of antioxidant activity of *T. chebula* was also found to be one of the highest when compared with the antioxidant effects of vitamin C, a potent antioxidant. The only fruits to generate similar antioxidant effects were *E. officinalis* and *T. bellerica* which are also present in Triphala. This study suggests that high levels of polyphenols contained in the fruits of Triphala promote antioxidant activity which may contribute to good intestinal health. A second study assessed the role of various medicinal plants and their effects in treating gastric ulcers. Rats were treated with increasing doses of *T. chebula* fruit, *T. bellerica* fruit or *E. officinalis* fruit extract. Chemical ulceration was induced prior to treatment and treatment duration lasted 7 days. Following treatment, gastric tissue was isolated from the rats and assessed for free radical scavenging enzyme activities in the presence or absence of treatment. The mucin content in the stomach tissue was assessed to determine the effects of the herbal extracts on gastric ulcers. The results indicate that extract from the fruits of *T. bellerica*, *T. chebula* and *E. officinalis* all exhibited antioxidant activity and increased the rate of gastric healing similar to a positive control for ulcer treatment (Bhattacharya *et al.* 2007). Traditional and scientific evidence has suggested the use of *T. chebula* as a potent herbal antioxidant with a good safety profile which helps promote gastrointestinal health.

Ingredient Summary:

Magnesium (Magnesium hydroxide)
- Contributes to the maintenance of good health with a potential role for use as a laxative

Cape Aloe leaf latex (*Aloe ferox*)
- Traditionally used as a laxative

Chinese Rhubarb root (*Rheum palmatum*)
- Traditionally used as a laxative

Slippery Elm bark (*Ulmus rubra*)
- Traditionally used to reduce mild inflammation of the gastric mucosa

Marshmallow root (*Althaea officinalis*)
- Traditionally used to reduce mild inflammation of the gastric mucosa

Fennel seed (*Foeniculum vulgare*)
- Traditionally used to increase gastric motility

Ginger root, rhizome (*Zingiber officinale*)
- Traditionally used to increase gastric motility

Triphala: a blend of:

Indian gooseberry fruit (*Emblica officinalis*)
- Provides antioxidant properties and traditionally used to support gastrointestinal health

Belleric myrobalan fruit (*Terminalia bellerica*)
- Provides antioxidant properties and traditionally used to support gastrointestinal health

Chebulic myrobalan fruit (*Terminalia chebula*)
- Provides antioxidant properties and traditionally used to support gastrointestinal health

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