

Gentle Cleanse 1

ADVANCED Naturals PRODUCT MONOGRAPH

Product composition

Medicinal Ingredients:

Each capsule contains:

Milk Thistle seed (<i>Silybum marianum</i>) 70% silymarin	200 mg
Artichoke leaf (<i>Cynara scolymus</i>)	75 mg
Burdock root, organic (<i>Arctium lappa</i>)	50 mg
Beet root, organic (<i>Beta vulgaris</i>)	25 mg
Blessed Thistle aerial parts, organic (<i>Cnicus benedictus</i>)	25 mg
Dandelion root, organic (<i>Taraxacum officinale</i>)	25 mg
Garlic bulb, organic (<i>Allium sativum</i>)	25 mg
Green Tea leaf (<i>Camellia sinensis</i> L. Kuntze)	25 mg
Hawthorn berry (<i>Crataegus laevigata</i>)	25 mg
Kelp thallus, organic (<i>Ascophyllum nodosum</i>)	25 mg
Mullein leaf (<i>Verbascum thapsus</i>)	25 mg
Nettle leaf, organic (<i>Urtica dioica</i>)	25 mg
Oregano Leaf, organic (<i>Origanum vulgare</i>)	25 mg
Parsley leaf, organic (<i>Petroselinum crispum</i>)	25 mg
Red Clover flower (<i>Trifolium pratense</i>)	25 mg
Turmeric root (rhizome), organic (<i>Curcuma longa</i>)	25 mg
Yarrow flower (<i>Achillea millefolium</i>)	25 mg
Yellowdock root, organic (<i>Rumex crispus</i>)	25 mg
Ginger root (rhizome), organic (<i>Zingiber officinale</i>)	40 mg
Fennel seed, organic (<i>Foeniculum vulgare</i>)	25 mg
Peppermint leaf, organic (<i>Mentha piperita</i>)	10 mg
Cayenne pepper fruit, organic (<i>Capsicum annuum</i>)	5 mg
Coriander seed, organic (<i>Coriandrum sativum</i>)	5 mg
Gentian root (<i>Gentiana lutea</i>)	5 mg
Black Pepper fruit, organic (<i>Piper nigrum</i>)	5 mg
Cellulase (<i>Trichoderma longibrachiatum</i>)	750 CU / 5 mg

Non-medicinal ingredients: Hypromellose (vegetable capsule), water

Recommended dose: Adults: Take two capsules per day, in the morning.

Duration of use: Use for a minimum of 3 weeks to see beneficial effects and for longer use consult a health care practitioner.

Indication: Used in Herbal Medicine to promote a healthy liver.

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

Warnings: Keep out of reach of children. Consult a health care practitioner prior to use if you have a liver disease, diabetes, gallstones, are taking blood thinners, protease inhibitors, antiplatelet medication, have iron deficiency or anaemia, excess stomach acid, stomach or duodenal ulcers and/or inflammation. Consult a health care practitioner if symptoms persist or worsen.

Precautions: None. Not to be used by children.

Adverse Effects: Hypersensitivity/allergy is known to occur, in which case, discontinue use. Some people may experience headaches.

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

Milk Thistle seed (*Silybum marianum*) 70% 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 flavanone 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).

Pharmacologically, Silymarin 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 systematic review by Tamayo and Diamond (2007) examined several randomized clinical studies that assessed 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. The article suggested 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 to 14.5 g dried seed, standardized to 140-600 mg silymarin (calculated as silibinin/silybin) per day.

Artichoke leaf (*Cynara scolymus*)

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. 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 may confer liver protection by scavenging free radicals. The NHPD (2008) recognizes artichoke leaf as an effective agent to help increase bile secretion and confer liver protection. The herb has demonstrated a good safety profile when taken at recommended doses of 4.5 to 10 g dried leaf equivalent per day (NHPD, 2008).

Burdock root, organic (*Arctium lappa*)

Traditional Chinese herbalists have used burdock root to treat various ailments. The herb acts as a diaphoretic which is thought to be beneficial in treating gallbladder or liver disorders (Bensky et al., 2004). The recommended daily dosage for Burdock root is 1.2 to 18 g dried root per day (NHPD, 2008). Its chemical constituents include phenylpropane derivatives, biophenols, sesquiterpenes, triterpenes, organic acids and polysaccharides (Bensky et al., 2004).

Beet root, organic (*Beta vulgaris*)

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. This phytochemical is also thought to exhibit beneficial antioxidant properties and confer liver protection by preventing the deposition of fat in the liver. 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 treatment with hepatoprotectants on chemically induced-hepatic injury in rats. The effects of *B. vulgaris* to silymarin, the latter a traditional hepatoprotectant, were compared; *B. vulgaris* extract was found to be as effective as silymarin in improving liver function. Abdelmalek et al. (2001) conducted a pilot study to assess the effects of betaine on liver function in humans. Patient with non-alcoholic steatohepatitis were treated with betaine daily for 12 months. Following treatment with betaine, a reduction in liver necro-inflammation was observed; liver enzyme activity returned to physiologically normal ranges. Results suggested that *B. vulgaris* may contribute to overall liver protection.

Blessed Thistle aerial parts, organic (*Cnicus benedictus*)

Blessed thistle is traditionally used in Herbal Medicine as a digestive tonic and bitter, to increase appetite and aid digestion (stomachic). Blessed thistle is a very minor ingredient in the product, a digestive tonic to support digestive processes and the assimilation of food. (NHPD, 2008)

Dandelion root, organic (*Taraxacum officinale*)

Dandelion root is used traditionally in the treatment of various health conditions, specifically hepatobiliary problems. It is commonly used as a coffee substitute and is ingested as a food in Europe (Newall et al., 1996; Bradley, 2006). The main physiological action of the herb is to increase bile

secretion in order to promote liver health (Bradley, 2006). Active constituents of dandelion root include taraxoside, sesquiterpene lactones, triterpenes, phenolic acids, as well as carbohydrates, vitamins and minerals (Bradley, 2006). Dandelion root has an established safety profile at the recommended daily dosage of 1.5-24 g daily (NHPD, 2008).

Garlic bulb, organic (*Allium sativum*)

Garlic bulb is used traditionally in Herbal Medicine to help relieve the symptoms associated with upper respiratory tract infections and catarrhal conditions, to help reduce elevated blood lipid levels/hyperlipidaemia in adults, and to help maintain cardiovascular health in adults (NHPD, 2008). Stajner (2008) reported that garlic bulb provides antioxidant enzyme activities (superoxide dismutase, catalase, guaiacol peroxidase, glutathione peroxidase), activities closely tied with hepatic systems. Antioxidant activity is one of mechanisms of action that may support liver health.

Green Tea leaf (*Camellia sinensis* L. Kuntze)

Green tea extract is made using the leaves from *Camellia sinensis*. The leaves have been traditionally used in Herbal Medicine as an antioxidant, which may help to maintain liver health. The active phytochemicals in green tea extract include caffeine, theobromine, and to a small extent, theophylline (Hoffman, 2003). In order to obtain antioxidant benefits, the NHPD (2008) recommends consumption of green tea extract that provides up to 690 mg total catechins and no more than 150 mg caffeine daily. Studies have been conducted to assess the effects of green tea extract as an antioxidant and hepatoprotectant in various liver damage models. Bruno et al. (2008) investigated the effects of a green tea extract on liver function in leptin-deficient mice. Mice were fed 1% green tea extract daily. Results showed decreases in lipid levels (compared to control animals) and improvements in obesity-induced hepatic injury, suggesting a role for green tea extract as a hepatoprotectant. Hamden et al. (2008) evaluated the effects green tea extract on cadmium-induced liver damage in mice. Mice were fed cadmium and green tea extract daily for 6 months. Significant improvement in liver function was observed when compared with control animals.

Hawthorn berry (*Crataegus laevigata*)

Hawthorn berry has been traditionally used in Herbal Medicine for its antioxidant properties. Its phytochemicals include procyanidins, flavonoids, hydroxycinnamic acid derivatives, and pentacyclic terpenes; its flavonoids confer antioxidant properties. Recommended doses of 1.5 to 3.5 g per day have been shown to be safe (Bradley, 2006). Possible hepatoprotective effects from hawthorn berry were studied in a rat model of myocardial infarction. Rats were subjected to chemically-induced myocardial infarction which are associated with liver damage, followed by treatment with hawthorn berry extract. Improved liver function was observed; the results suggested that antioxidant properties from hawthorn berry may contribute to liver health (Thirupurasundari et al., 2005).

Kelp thallus, organic (*Ascophyllum nodosum*)

Fucus is traditionally used as an herbal, stated to possess antihypothyroid, anti-obesic and antirheumatic properties. Traditionally, fucus has been used for lymphadenoid goitre, myxoedema, obesity, arthritis, and rheumatism. (Newall et al., 1996) Brown seaweed refers to species of *Ascophyllum* using the thallus part, and taken at 5 to 10 g daily, is very well tolerated. Any side effects are typically associated with iodine content (Newall et al., 1996; Bradley, 2006)

Mullein leaf (*Verbascum thapsus*)

Mullein leaf has been used in Traditional Chinese Medicine for its phytochemicals present in the leaf, mainly saponins and mucopolysaccharides. The active chemical is aucubin (Blumenthal et al., 1998) and several animal studies investigating the role of aucubin on liver biochemistry have been performed. Using various chemically-induced liver damage murine models, Chang (1998) observed improved hepatic physiology following treatment with aucubin, including reduction of hepatitis B viral DNA replication *in vitro*. Results suggested that mullein leaf may be beneficial as a hepatoprotectant. Mullein leaf has shown a good safety profile when taken at doses of 3 to 4 g per day (Blumenthal et al., 1998).

Nettle leaf, organic (*Urtica dioica*)

Both the leaves and/or the whole herb of the stinging nettle have been used in traditional herbalism as a nutritive tonic (Blumenthal et al., 1998). Chemical constituents present in the herb include various acids, amines, flavonoids, choline acetyltransferase, β -sitosterol, coumarin and tannins (Newall, 1996). The NHPD (2008) recognizes stinging nettle as a traditional nutritive tonic, with a good safety profile when taken in recommended doses of 1.2-18 g daily.

Evidence from induced liver damage models suggests that stinging nettle may have antioxidant effects and may serve as a hepatoprotectant. Yener et al. (2008) studied the effects of nettle as an antioxidant and hepatoprotective in rats. Rats were fed 2 mL stinging nettle seed oil together with aflatoxin; aflatoxin induced hepatic insult. Control animals received no stinging nettle seed. Oxidative stress in the liver tissue was measured and higher levels of free radical scavenging enzymes were observed in the seed oil-treated group when compared to the control group. In a study by Celik and Tuluce (2007), rats were fed 2.5 g dried leaves from the stinging nettle and *Camellia sinensis* (also an herbal antioxidant) and exposed to trichloroacetic acid (TCA) to induce liver toxicity. Results suggested that treatment with nettle leaf helped to maintain liver function. Turkdoan et al. (2003) studied the effects of stinging nettle seed extract on liver function following hepatic insult with carbon tetrachloride. Rats were fed decoction extracts derived from 50 g ground nettle seed. Researchers observed prevention of carbon tetrachloride-induced cirrhosis and fibrosis in the animals fed decoction extracts of ground nettle seed.

Oregano Leaf, organic (*Origanum vulgare*)

Oregano has been shown to possess antioxidant capacity in various *in vitro* models.

In a study by Nurmi et al. (2006), phenolic acids recovered in human urine following single ingestion of *Origanum onites* extract were analyzed. Excretion was increased 4- and 2-fold during 0 to 24-hour and 24 to 48-hour follow-up, respectively. Mean increases in excreted phenolic compounds exceeded ingested amounts of identified phenolic acids; result were partly explained by rosmarinic acid content (the main identified phenolic constituent in the extract) and flavonoid content (present in minor amounts). Rosmarinic acid and flavonoids were possibly metabolized into a double amount of simple phenolic metabolites. Further, unidentified phenolic constituents in the extract partly contributed to the excretory increase. Results showed that constituents of oregano extract, and in particular their metabolites, may contribute to the dietary intake of phenolic antioxidants.

Kulisic et al. (2007) studied antioxidative effects of essential oils and aqueous tea infusions (obtained from oregano, thyme and wild thyme) on oxidative susceptibility of low-density lipoproteins (LDL) have been studied. Dose-dependent protective effects on copper-induced LDL oxidation were observed. These protective effects are thought to be related to the phenolic monoterpenes, thymol and carvacrol, the dominant compounds in these essential oils. The strong protective effect of aqueous tea infusions is considered to be related to the large amounts of polyphenols, namely rosmarinic acid and flavonoids (quercetin, eriocitrin, luteolin-7-O-glucoside, apigenin-7-O-glucoside, luteolin, apigenin) present. The most pronounced effect found with use of oregano. Findings may have implications for the effect of these compounds on LDL *in vivo*.

Parsley leaf, organic (*Petroselinum crispum*)

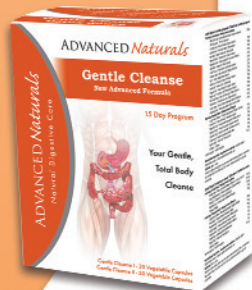
Parsley possesses carminative, antispasmodic, diuretic, emmenagogue, expectorant, antirheumatic, and antimicrobial properties. Traditionally, it has been used for flatulent dyspepsia, colic, cystitis, dysuria, bronchitic cough in the elderly, dysmenorrhoea, functional amenorrhoea, myalgia, and specifically for flatulent dyspepsia with intestinal colic. Parsley seed oil has been reported to stimulate hepatic regeneration.

Commonly consumed as part of the diet, its pharmacological and toxicological properties are associated primarily with the volatile oil, particularly the apiole, myristicin, and furocoumarin components. Most of the reported uses for parsley are likely due to the volatile oil. (Newall et al., 1996) Parsley is included in the formulation as a minor supportive ingredient.

Red Clover flower (*Trifolium pratense*)

Red clover flower has been used as a traditional medicine. The flower contains many phytochemicals including the flavonoid formononetin, phenolic acids, and volatile oils, which function to enhance antioxidant properties (Bradley, 2006).

Red clover flower has been investigated *in vitro*. Rufer et al. (2006) suggested that its flavonoids, biochanin A and formononetin, may be the main antioxidant chemicals. Mu et al. (2009) assessed the effects of formononetin as an antioxidant; increases in liver enzyme activity and decreases in lipid peroxidation in both the liver and serum were associated with ingestion of red clover flower treatment. The study results suggested a role for red clover flower as an antioxidant, which may help confer liver protection. Red clover flower has been generally regarded as safe (GRAS) in the U.S. and is recognized as a food by the Council of Europe (Bradley, 2006)



Turmeric root (rhizome), organic (*Curcuma longa*)

Turmeric root has traditionally been used as a choleric (Blumenthal *et al.* 1998). The constituent in turmeric root responsible for its choleric properties is curcumin, which acts on the gallbladder to increase bile secretion. The herb root also contains chemicals such as volatile oils and other dicyanometane derivatives (Blumenthal *et al.* 1998). Turmeric root may be an effective agent for liver protection with a good safety profile when taken at recommended doses of 1.5 to 3 g of daily (Blumenthal *et al.* 1998).

In an *in vivo* study conducted to evaluate the antioxidant effects of turmeric root on chemically-induced liver injury, rats received either curcumin, saikosaponin (the active phytochemical found in bupleurum root) or a combination of the two phytochemicals. Positive effects on liver function and cholesterol levels were observed with ingestion of curcumin and with ingestion of saikosaponin; decreases in liver fibrosis, inflammation and necrosis were observed following treatment with curcumin and saikosaponin. The greatest effects on the liver were observed when the phytochemicals were ingested in combination, suggesting an additive effect. (Wu *et al.* 2008). In an *in vitro* study, curcumin was found to stimulate an increase in liver detoxification enzymes, an effect found with many known antioxidants (Nishinaka *et al.* 2007).

Yarrow flower (*Achillea millefolium*)

Yarrow, the dried aerial parts of *Achillea millefolium*, has diaphoretic, antipyretic, anti-inflammatory, spasmolytic, aromatic bitter, haemostatic, hypertensive, and emmenagogue properties. The plant has been used for digestive complaints, loss of appetite, feverish conditions, the common cold, hypertension, and for menstrual irregularities. (Bradley, 1992)

Yellowdock root, organic (*Rumex crispus*)

Yellow dock contains anthraquinone glycosides (approximately 3% to 4%; nepodin, physcion, and emodin), tannins and oxalates. While anthraquinones usually have a strong cathartic action on the bowel, in this herb they act mildly, possibly tempered by the tannin content. Yellow dock promotes the flow of bile and has the somewhat obscure action of blood cleansing. Its influence on the gallbladder gives it a role in the treatment of jaundice due to congestion. (Hoffman, 2003; Newall *et al.*, 1996)

Ginger root (rhizome), organic (*Zingiber officinale*)

Ginger root rhizome has been shown clinically to help prevent nausea and vomiting associated with motion sickness and/or seasickness; and has been used in Western herbalism to relieve digestive upsets/disturbances including flatulence, dyspepsia, spasm indigestion and nausea, and to relieve coughs and colds (NHPD Monograph).

Mallikarjuna *et al.* (2008) investigated the effect of ginger on hepatic antioxidant enzymes in ethanol-treated rats. Ethanol treatment served to decrease superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase and glutathione levels, with estimated increases in malondialdehyde (MDA) levels. Following treatment with 1% dietary ginger for 4 weeks, ethanol-induced effects were reversed. Results suggested that ginger may have protective role against the ethanol induced hepatotoxicity.

Fennel seed, organic (*Foeniculum vulgare*)

Fennel seed (*Foeniculum vulgare*) has been used traditionally for digestive disturbances, including bloating and flatulence. (NHPD, 2009; Blumenthal, 1998) Individuals requiring laxative action may commonly experience such symptoms, which may be ameliorated by sweet fennel.

Peppermint leaf, organic (*Mentha piperita*)

Peppermint leaf (*Mentha piperita*) has been used traditionally to aid digestion and for the relief of flatulence and dyspepsia. (NHPD, 2008). The daily dose of the ingredient provided by the product is well within safety limits of the NHPD Monograph.

Cayenne pepper fruit, organic (*Capsicum annuum*)

Cayenne pepper (*Capsicum annuum*) has been used traditionally to aid digestion (NHPD, 2009). This property further supports digestive health. The ingredient is minor supportive in the formula and proven to be safe based on the monograph.

Coriander seed, organic (*Coriandrum sativum*)

Coriander seed (*Coriandrum sativum*) has been used traditionally for dyspeptic complaints and for stimulating the digestion. (Blumenthal, 1998; Bradley, 2006) In Germany, coriander is used as a medicinal tea and a component of carminative and laxative remedies (Blumenthal, 2000). This further supports its use in digestive health. Its safety is very well established in doses up to 3 g daily.

Gentian root (*Gentiana lutea*)

Gentian root (*Gentiana lutea*) has been used traditionally to help relieve digestive disturbances and dyspepsia (NHPD, 2008). This ingredient may therefore be of benefit in individuals using laxative products. Doses of 0.1 to 6 g per day of the dried root have been proven safe.

Black Pepper fruit, organic (*Piper nigrum*)

Black pepper (*Piper nigrum*) has been used traditionally for stomach and digestive disorders. (Williamson, 2002) Evidence of safety is presented below.

In a study to examine the effects of red and black pepper on small intestinal peristalsis, 16 healthy subjects were given either powdered red pepper (2 g) or black pepper (1.5 g) in gelatin capsules, followed by measurements of orocecal transit time (OCTT) using the lactulose hydrogen breath test. Increases in OCTT were observed after red pepper and black pepper consumption, which was attributed to the known effects of capsaicin, a potent stimulator of many biologically active peptides. Although the effect of spices on OCTT is likely to vary depending upon the dose and nature of the product, it is of clinical importance in the management of various gastrointestinal tract disorders. (Vazquez-Olivencia *et al.* 1992)

In a 6-week randomized, double-blind study to assess the effects of red and black pepper on the gastric mucosa, 8 healthy subjects received meals containing red pepper (0.1 g, 0.5g, and 1.5 g), black pepper (1.5 g), aspirin (655 mg; positive control) and distilled water (negative control). Each subject received 6 spice preparations, separated by a 1-week interval. Serial gastric washes were performed after test meal administration and gastric contents were analyzed for DNA, pepsin, blood, sodium, potassium, parietal cell secretion, and nonparietal cell secretion. Both red pepper and black pepper caused significant increases in parietal secretion, pepsin secretion, and potassium loss. Gastric cell exfoliation was also increased. Effects of both red and black pepper were comparable to aspirin in all parameters studied. The only adverse reaction reported was mucosal microbleeding, which was possibly dose-related. (Myers *et al.* 1987)

Cellulase (*Trichoderma longibrachiatum*)

Cellulase enzyme has been included in the formula to support digestive function. Evidence of safety is provided in studies by Bonilla, 1999, Heiwinkel, 1960, and in case reports provided by Wortzel, 1977. No significant adverse reactions were observed in any of these studies.

In a 1-year prospective study to analyze the efficacy of cellulase in gastric phytoezoars, 7 patients diagnosed with gastric phytoezoars by gastroscopy were treated with cellulase. Complete dissolution of the gastric phytoezoars was observed in all 7 patients after 1 year. No side effects or recurrence was reported in follow-up. Researchers concluded that cellulase should be regarded as the treatment of choice for gastric phytoezoars. (Bonilla *et al.* 1999)

Cellulase activity was examined following oral administration of different cellulase preparations isolated from *Penicillium notatum*. The enzyme concentration necessary for significant breakdown of vegetable foodstuffs was determined; and subsequently, each tablet was formulated as 200 units (enzyme activity was 5 units per mg). Each patient took 2 to 3 tablets three times per day; total 1200 to 1800 cellulase units per day. Patients were asked to record any adverse effects throughout the trial. One of the 50 patients complained of nausea and one patient elected to withdraw from the study. No toxic effects were observed based on the dosages studied. (Heiwinkel *et al.* 1960)

Ingredient Summary:

Milk Thistle seed (*Silybum marianum*) 70% silymarin

- Used in Herbal Medicine to promote a healthy liver.
- Artichoke leaf (*Cynara scolymus*)**
 - Traditionally used to increase bile secretion and confer liver protection.
- Burdock root, organic (*Atractium lappa*)**
 - Traditionally used as a diaphoretic to expel liver-harming toxins.
- Beet root, organic (*Beta vulgaris*)**
 - Contains active chemicals which may contribute to liver protection.

Blessed Thistle aerial parts, organic (*Chicus benedictus*)

- Blessed thistle is traditionally used in Herbal Medicine as a digestive tonic and bitter.

Dandelion root, organic (*Taraxacum officinale*)

- Helps stimulate bile secretion to promote healthy liver function.

Garlic bulb, organic (*Allium sativum*)

- Garlic bulb confers antioxidant activity, one of mechanisms of action that may support liver health.

Green Tea leaf (*Camellia sinensis* L. Kuntze)

- Provides antioxidant properties and traditionally used to support liver health.

Hawthorn berry (*Crataegus laevigata*)

- Demonstrates antioxidant properties which may help to improve liver health.

Kelp thallus, organic (*Ascophyllum nodosum*)

- Fucus is traditionally used as an herbal, stated to possess antihypothyroid, anti-obesic and antirheumatic properties.

Mullein leaf (*Verbascum thapsus*)

- Contributes to liver health.

Nettle leaf, organic (*Urtica dioica*)

- Traditionally used as a nutritive tonic which may confer liver protection.

Oregano Leaf, organic (*Origanum vulgare*)

- Oregano has been shown to possess antioxidant capacity.

Parsley leaf, organic (*Petroselinum crispum*)

- Parsley seed oil has been reported to stimulate hepatic regeneration.

Red Clover flower (*Trifolium pratense*)

- Demonstrates antioxidant properties which may help to improve liver health.

Turmeric root (rhizome), organic (*Curcuma longa*)

- Traditionally used to help stimulate bile secretion to promote healthy liver function.

Yarrow flower (*Achillea millefolium*)

- Traditionally used for digestive complaints.

Yellowdock root, organic (*Rumex crispus*)

- Yellow dock promotes the flow of bile.

Ginger root (rhizome), organic (*Zingiber officinale*)

- Ginger rhizome has been used traditionally to help relieve digestive upset/disturbances including lack of appetite, nausea, digestive spasms, indigestion, dyspepsia and flatulent colic (carminative).

Fennel seed, organic (*Foeniculum vulgare*)

- Fennel seed has been used traditionally to help relieve digestive disturbances including bloating and flatulence.

Peppermint leaf, organic (*Mentha piperita*)

- Peppermint Leaf has been used traditionally to aid digestion (stomachic) and to help relieve flatulent dyspepsia.

Cayenne pepper fruit, organic (*Capsicum annuum*)

- Cayenne pepper has been used traditionally to aid digestion.

Coriander seed, organic (*Coriandrum sativum*)

- Coriander seed has been used traditionally for dyspeptic complaints and loss of appetite.
- Coriander seed has been used traditionally as a carminative (flatulence), weakly spasmolytic, and as a stimulant to the digestion.

Gentian root (*Gentiana lutea*)

- Gentian Root has been used traditionally to help relieve digestive disturbances/dyspepsia.

Black Pepper fruit, organic (*Piper nigrum*)

- Black Pepper has been used traditionally for stomach and digestive disorders and colds and bronchitis.

Cellulase (*Trichoderma longibrachiatum*)

- Cellulase has been included in the formula to support digestive function.

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Gentle Cleanse 2

ADVANCED Naturals PRODUCT MONOGRAPH

Product composition

Medicinal Ingredients:

Each capsule contains:

Rhubarb root (<i>Rheum palmatum</i>) 4:1 extract, equivalent to 500 mg.....	125 mg
Ginger root (rhizome), organic (<i>Zingiber officinale</i>).....	225 mg
Flax seed, organic (<i>Linum usitatissimum</i>).....	150 mg
Buckthorn bark (<i>Rhamnus frangula</i>).....	75 mg
Triphala Blend.....	75 mg
Chebulic myrobalan fruit (<i>Terminalia chebula</i>).....	25 mg
Indian gooseberry fruit (<i>Emblica officinalis</i>).....	25 mg
Belleric myrobalan fruit (<i>Terminalia bellirica</i>).....	25 mg
Ginger root (rhizome), organic (<i>Zingiber officinale</i>).....	40 mg
Fennel seed, organic (<i>Foeniculum vulgare</i>).....	25 mg
Peppermint leaf, organic (<i>Mentha piperita</i>).....	10 mg
Cayenne fruit, organic (<i>Capsicum annuum</i>).....	5 mg
Coriander seed, organic (<i>Coriandrum sativum</i>).....	5 mg
Gentian root (<i>Gentiana lutea</i>).....	5 mg
Black Pepper fruit, organic (<i>Piper nigrum</i>).....	5 mg
Cellulase (<i>Trichoderma longibrachiatum</i>).....	750 CU / 5mg

Non-medicinal ingredients: Hypromellose (vegetable capsule), water

Recommended dose: Adults: Take two capsules per day, in the evening.

Duration of use: Consult a health care practitioner for use beyond 2 weeks..

Indication: Gentle Cleanse provides Ginger, Rhubarb and Buckthorn which have been traditionally used in Herbal Medicine to help relieve digestive upset/disturbances including lack of appetite, nausea, digestive spasms, indigestion, dyspepsia and flatulent colic (carminative).

Gentle Cleanse provides Rhubarb which has been traditionally used in Herbal Medicine as a laxative.

Gentle Cleanse provides Buckthorn and Flaxseed which have been traditionally used in Herbal Medicine as stool softeners.

Contraindications: Do not use if you are pregnant, breastfeeding, have abdominal pain, nausea, fever or vomiting or if you have a chronic gastrointestinal disorder, acute stomach irritation, inflammation, and stomach or duodenal ulcers. Do not use if you are allergic to anethole or plants of the Apiaceae/Carrot family.

Warnings: Keep out of reach of children.

Consult a health care practitioner prior to use if you are taking blood thinners, have gallstones, and/or anaemia.

Consult a health care practitioner if constipation persists after one week of use and/or if symptoms persist or worsen.

Precautions: None.

Not to be used by children.

Adverse Effects: Some people may experience headaches.

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

Rhubarb root (*Rheum palmatum*) 4:1 extract, equivalent to 500 mg

Rhubarb root (*Rheum officinalis*) has been used traditionally for occasional constipation where soft stool is desirable (laxative properties) and as an antidiarrhoeal agent. (Newall *et al.*, 1996) Doses up to 4 g daily have been shown to be safe and effective. (Bradley, 1992; Newall, 1996) The ingredient is supportive to the flaxseed in this product and provides complementary effect to the formula.

Chinese herbalists have relied on rhubarb rhizomes and roots for thousands of years. The rhizomes and roots contain powerful anthraquinones and tannins that act as stimulant laxatives and astringents, respectively. In traditional Chinese medicine, rhubarb root is also used to treat gastric ulcers.

Ginger root (rhizome), organic (*Zingiber officinale*)

Ginger root has been used traditionally in Herbal Medicine to help relieve digestive upset/disturbances including lack of appetite, nausea, digestive spasms, indigestion, dyspepsia and flatulent colic (carminative). Ginger has also been investigated for the prevention of motion sickness. (NHPD Monograph; Newall *et al.*, 1996)

Flax seed, organic (*Linum usitatissimum*)

Flax seed has been used traditionally in Herbal Medicine as a bulk-forming laxative, for gentle relief of occasional constipation. The herb promotes bowel movement by increasing bulk volume and water content. (NHPD Monograph) Flax seed has been used traditionally for its laxative effects by increasing volume and initiating intestinal peristalsis, and for its protective effects on the intestinal mucosa (Blumenthal *et al.*, 2000; Willoughby *et al.*, 1996; ESCOP, 2003).

The usual cause of chronic constipation is a lack of adequate dietary fiber. In people who eat too little of fiber-containing foods, the stool becomes hard, dry and small. Whereas the soft, bulky stool can move easily along the passage of the colon, the hard, dry stool sticks to the dry wall of the colon and requires that the colon develop high-pressure waves to be moved. This straining produces pressure on all of the abdominal wall, forcing the development of hernias, varicose veins (due to pressure on the long veins of the legs), hiatus hernia (upward pressure forcing the stomach into the chest), diverticulitis and diverticulosis (weakening and infection of the colon wall), hemorrhoids, anal fissures and fistulae. Colorectal cancers may also be more common in patients with lifelong habit constipation. This may be due to the concentrated exposure of carcinogens to the colonic surface, as a result of the

hard dry stool and its slow movement or evacuation. The primary focus of a bowel cleansing program is to promote mucosal detoxification to rid toxins from bowel bacteria and excretion through feces. This is mainly accomplished through increasing fiber which absorbs toxins for elimination, stimulates natural muscular movement in the colon, and reduces inflammation and soothes the bowel/colon.

Buckthorn bark (*Rhamnus frangula*)

Buckthorn bark has been used traditionally for constipation. Other conditions for use include conditions in which soft feces are desirable, haemorrhoids and post-rectal-anal operations. Buckthorn bark consists of the dried branches of the trunks and branches of *R. Frangula*, as well as its preparations in effective dosage. (Blumenthal, 1998)

The main constituents of the dried bark are the anthraquinone glycosides A and B and frangulins A and B; the anthraquinone derivatives provide the laxative effect. These compounds increase the motility of the colon by inhibiting stationary and stimulating propulsive contractions. This results in accelerated intestinal passage and, because of the shortened contraction time, a reduction in liquid absorption through the lumen.

Triphala Blend

Chebulic myrobalan fruit (*Terminalia chebula*)

Indian gooseberry fruit (*Emblica officinalis*)

Belleric myrobalan fruit (*Terminalia bellirica*)

Chebulic myrobalan fruit (*Terminalia chebula*)

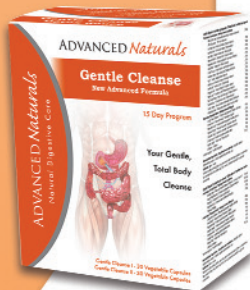
T. chebula has been used in traditionally Ayurvedic medicine in combination with *T. Bellerica* and *E. Officinalis* as Triphala. Various parts of the plant have been used in traditional medicine, including the fruit, leaves and stem. The fruits of the plants have been recognized as natural laxatives (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.

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 increased 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 or 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 (Dhanao, 2001).

Belleric myrobalan fruit (*Terminalia bellirica*)

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, 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. bellirica* was found to be the second most potent antioxidant, second only to *Averrhoa carambola*, commonly known as starfruit. The blend of *T. bellirica*, *E. officinalis* and *T. catappa* is known in Ayurvedic medicine as *Triphala*. *T. bellirica* 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**).

Ginger root (rhizome), organic (*Zingiber officinale*)

Ginger root rhizome has been shown clinically to help prevent nausea and vomiting associated with motion sickness and/or seasickness; and has been used in Western herbalism to relieve digestive upsets/disturbances including flatulence, dyspepsia, spasm indigestion and nausea, and to relieve coughs and colds (**NHPD Monograph**).

Fennel seed, organic (*Foeniculum vulgare*)

Fennel seed (*Foeniculum vulgare*) has been used traditionally for digestive disturbances, including bloating and flatulence. (**NHPD, 2009; Blumenthal, 1998**) Individuals requiring laxative action may commonly experience such symptoms, which may be ameliorated by sweet fennel.

Peppermint leaf, organic (*Mentha piperita*)

Peppermint leaf (*Mentha piperita*) has been used traditionally to aid digestion and for the relief of flatulence and dyspepsia. (**NHPD**). The daily dose of the ingredient provided by the product is well within safety limits of the NHPD Monograph.

Cayenne fruit, organic (*Capsicum annuum*)

Cayenne pepper (*Capsicum annuum*) has been used traditionally to aid digestion (**NHPD, 2009**). This property further supports digestive health. The ingredient is minor supportive in the formula and proven to be safe based on the monograph.

Coriander seed, organic (*Coriandrum sativum*)

Coriander seed (*Coriandrum sativum*) has been used traditionally for dyspeptic complaints and for stimulating the digestion. (**Blumenthal, 1998; Bradley, 2006**) In Germany, coriander is used as a medicinal tea and a component of carminative and laxative remedies (**Blumenthal, 2000**). This further supports its use in digestive health. Its safety is very well established in doses up to 3 g daily.

Gentian root (*Gentiana lutea*)

Gentian root (*Gentiana lutea*) has been used traditionally to help relieve digestive disturbances and dyspepsia (**NHPD, 2008**). This ingredient may therefore be of benefit in individuals using laxative products. Doses of 0.1 to 6 g per day of the dried root have been proven safe.

Black Pepper fruit, organic (*Piper nigrum*)

Black pepper (*Piper nigrum*) has been used traditionally for stomach and digestive disorders. (**Williamson, 2002**) Evidence of safety is presented below.

In a study to examine the effects of red and black pepper on small intestinal peristalsis, 16 healthy subjects were given either powdered red pepper (2 g) or black pepper (1.5 g) in gelatin capsules, followed by measurements of orocecal transit time (OCTT) using the lactulose hydrogen breath test. Increases in OCTT were observed after red pepper and black pepper consumption, which was attributed to the known effects of capsaicin, a potent stimulator of many biologically active peptides. Although the effect of spices on OCTT is likely to vary depending upon the dose and nature of the product, it is of clinical importance in the management of various gastrointestinal tract disorders. (**Vazquez-Olivencia et al, 1992**)

In a 6-week randomized, double-blind study to assess the effects of red and black pepper on the gastric mucosa, 8 healthy subjects received meals containing red pepper (0.1g, 0.5g, and 1.5 g), black pepper (1.5 g), aspirin (655 mg; positive control) and distilled water (negative control). Each subject received 6 spice preparations, separated by a 1-week interval. Serial gastric washes were performed after test meal administration and gastric contents were analyzed for DNA, pepsin, blood, sodium, potassium, parietal cell secretion, and nonparietal cell secretion. Both red pepper and black pepper caused significant increases in parietal secretion, pepsin secretion, and potassium loss. Gastric cell exfoliation was also increased. Effects of both red and black pepper were comparable to aspirin in all parameters studied. The only adverse reaction reported was mucosal microbleeding, which was possibly dose-related. (**Myers et al, 1987**)

Cellulase (*Trichoderma longibrachiatum*)

Cellulase enzyme has been included in the formula to support digestive function. Evidence of safety is provided in studies by **Bonilla, 1999, Heiwinkel, 1960**, and in case reports provided by **Wortzel, 1977**. No significant adverse reactions were observed in any of these studies.

In a 1-year prospective study to analyze the efficacy of cellulase in gastric phytobezoars, 7 patients diagnosed with gastric phytobezoars by gastroscopy were treated with cellulase. Complete dissolution of the gastric phytobezoars was observed in all 7 patients after 1 year. No side effects or recurrence was reported in follow-up. Researchers concluded that cellulase should be regarded as the treatment of choice for gastric phytobezoars. (**Bonilla et al, 1999**)

Cellulase activity was examined following oral administration of different cellulose preparations isolated from *Penicillium notatum*. The enzyme concentration necessary for significant breakdown of vegetable foodstuffs was determined; and subsequently, each tablet was formulated as 200 units (enzyme activity was 5 units per mg). Each patient took 2 to 3 tablets three times per day; total 1200 to 1800 cellulase units per day. Patients were asked to record any adverse effects throughout the trial. One of the 50 patients complained of nausea and one patient elected to withdraw from the study. No toxic effects were observed based on the dosages studied. (**Heiwinkel et al, 1960**)

Ingredient Summary:

Rhubarb root (*Rheum palmatum*) 4:1 extract, equivalent to 500 mg

- Rhubarb has been used traditionally both as a laxative and an antidiarrhoeal agent.

Ginger root (rhizome), organic (*Zingiber officinale*)

- Ginger rhizome has been used traditionally to help relieve digestive upset/disturbances including lack of appetite, nausea, digestive spasms, indigestion, dyspepsia and flatulent colic (carminative).

Flax seed, organic (*Linum usitatissimum*)

- Bulk-forming laxative.
- Promotes bowel movement by increasing bulk volume and water content.
- Gentle relief of occasional constipation (irregularity).

Buckthorn bark (*Rhamnus frangula*)

- Buckthorn bark has been used traditionally for constipation.

Triphala Blend

Chebulic myrobalan fruit (*Terminalia chebula*)

- Provides antioxidant properties and traditionally used to support gastrointestinal health

Indian gooseberry fruit (*Emblica officinalis*)

- Provides antioxidant properties and traditionally used to support gastrointestinal health

Belleric myrobalan fruit (*Terminalia bellirica*)

- Provides antioxidant properties and traditionally used to support gastrointestinal health

Fennel seed, organic (*Foeniculum vulgare*)

- Fennel seed has been used traditionally to help relieve digestive disturbances including bloating and flatulence.

Peppermint leaf, organic (*Mentha piperita*)

- Peppermint Leaf has been used traditionally to aid digestion (stomachic) and to help relieve flatulent dyspepsia.

Cayenne fruit, organic (*Capsicum annuum*)

- Cayenne pepper has been used traditionally to aid digestion.

Coriander seed, organic (*Coriandrum sativum*)

- Coriander seed has been used traditionally for dyspeptic complaints and loss of appetite.
- Coriander seed has been used traditionally as a carminative (flatulence), weakly spasmolytic, and as a stimulant to the digestion.

Gentian root (*Gentiana lutea*)

- Gentian Root has been used traditionally to help relieve digestive disturbances/dyspepsia.

Black Pepper fruit, organic (*Piper nigrum*)

- Black Pepper has been used traditionally for stomach and digestive disorders and colds and bronchitis.

Cellulase (*Trichoderma longibrachiatum*)

- Cellulase has been included in the formula to support digestive function.

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