The liver (from the Latin *ficiatu*), is the largest gland and the second largest organ of the human body. It works both as exocrine gland, releasing secretions in a system of channels which open onto an external surface, and endocrine gland, when release substances into the blood or lymphatic vessels.

The hepato- prefix and the hepatic adjective come from the *hepar* Greek term, which in turn comes from *hepaomai* that means to repair, to set, in respect of the regenerative capacity of this organ.

**WHAT ARE THE FUNCTIONS OF THIS ORGAN?**

- Cholesterol production
- Methylation process
- Vitamin B storage
- Bile production
- Steroid hormones production
- Transformation of T4 into T3
- Hepcidin production and iron regulation in the small bowel
- Temporary nutrient storage (glucose-glycogen)
- Removal of toxins from blood
- Regulation of nutrient and metabolite levels, maintaining a constant supply of sugars, fatty acids, amino acids, nucleotides and cholesterol.

**CONCEPT OF DETOXIFICATION**

Detoxification has always followed the medical art, the notion of purification of foreign or harmful substances was very clear for traditional doctors and was accompanied by purification rites with implications that went beyond the purely physical aspect. In modern functional medicine, the theoretical hypotheses are reviewed in the light of scientific and biochemical discoveries, we speak of “toxins” or “xenobiotics”, chemically defined substances whose metabolic damage, which have their paths, are studied based on the possibilities of entry and exit through them, the eliminating organs, particularly the liver and kidneys. It has been discovered that toxins are not only external but also internal and therefore, in addition to xenobiotics, we speak of “endobiotics”, molecules that, once used, must be discarded by the same enzyme systems of external toxins. Detoxification is an important element of the therapeutic approach as it helps biological tissues to function optimally and effectively prevents the disease without waiting for the symptom to appear.
THE WORLD OF TOXINS

The nature surrounds us with biological substances, some of which have a toxic effect, so industries create thousands of new chemicals substances every year, and even our modern life produces many substances harmful to health. Many of these substances have mutagenic, carcinogenic effects or interfere with the metabolism of enzymes in our body and are considered toxic. Foods are also sources of toxins from contaminants of general pollution or from the use of pesticides and fertilizers, not to mention the dyes and preservatives that are introduced in food preparation. Furthermore, cooking methods are a source of toxins: fry with oil that releases highly oxidizing peroxides and cook at high temperatures on the grill or on the spit than causes the formation of mutants such as benzopyrene and acrolein. Similary, smoked foods contain smoke-causing carcinogens.

Beyond the diet, the respiratory exposure to volatile organic compounds (VOCs) becomes a frequent risk associated with numerous adverse effects, including kidney damage, immune problems, hormonal imbalances, blood disorders and increased cases of asthma and bronchitis. Another very common cause is the domestic (internal) pollution due to the fact that wall dyes, wood coatings, furniture and carpets are often impregnated with pesticides.

Attention should be paid to new apartments and furniture that release harmful substances and other substances used in the building, and rooms must be well ventilated. It is not possible to completely eliminate toxic exposure from all possible sources, but there are ways to minimize it.

Here are some simple tips: use stainless steel, clay or glass cookware, limit fried, smoked and spit-roasted foods, cook over low heat, do not cook in plastic containers.

Eat organic food with few contaminants, avoid foods with preservatives. Avoid plastic cutlery and dishes, plastic containers with bisphenol A (BPA) and phthalates. Use natural detergents to wash dishes.

THE DIFFERENT METHODS OF DETOXIFICATION

From the perspective of functional phytotherapy, we talk about three levels of detoxification:

A. Biochemical or hepatic detoxification, acts at the level of detoxifying enzymes ad occurs mainly in the liver;
B. The detoxification of the tissue or matrix acts on the connective tissue of each tissue (or matrix) and is free of typical residues which accumulates, depending on personal trends and habits.
C. A detox diet cleans the body from residues accumulates through the usual diet, substances that predispose to specific disorders.
DETOXIFICATION PROCESS IN THE BODY
It consists of a biochemical process that solubilizes toxins in water, usually of a lipidic nature, in order to expel them from the kidneys or through the biliary fluid. From a biochemical perspective, three detoxification phases are distinguished, each followed by specific enzymes with different metabolic needs, but which must work in a coordinated way to carry out their work. The three phases are:

TRANSFORMATION PHASE I
The toxins are oxidized by the cytochrome by the addition of water-soluble molecules at specific points of attack. If the toxin does not have these attachment points, a separate group of enzymes is first added, that will chemically transform it in order to include these molecular support points.

CONJUGATION PHASE II
The modified toxins are bound to the molecular group to make them soluble. The most common groups are the glucuronic acid, sulfate, methyl, acetyl and some amino acids such as glycine and taurine.

ACTIVE TRANSPORT PHASE III
It occurs in the cell walls through the actively present protein, or with energy consumption that requires ATP. Proteins are found in the liver, kidneys, intestines and brain. Detoxifying enzymes have the characteristic of acting on many different molecules and of being inducible in the presence of toxin.

They are found in the organ more exposed to toxins like the liver, but also in the lungs and intestines. The hepatic cells has the largest amount of cytochrome because, through the portal vein, it plays as a venous filter on the whole intestine, thus acting as a safety ring, identifying and preventing the entry of food toxins into the general blood flow and their elimination through the bile.

**Figure 01**

### PHASE I
Cytochrome enzyme

- **Reactions**
  - Oxidation
  - Reduction
  - Hydration
  - Halogenation

- **Nutrients Used**
  - Riboflavin (vit B2)
  - Niacin (vit B3)
  - Pyridoxine (vit B5)
  - Folic acid
  - B12 vitamin
  - Glutathione
  - Branched chain amino acids
  - Phospholipids

- **Fat-soluble (non polar) toxins** are phospholipids

### PHASE II
Conjugation ways

- **Reactions**
  - Sulfation
  - Glucuronidation
  - Glutathione conjugation
  - Acetylation
  - Amino acid conjugation
  - Methylation

- **Nutrient used**
  - Glycine
  - Taurine
  - Glutamine
  - Methionine

- **INTERMEDIARY METABOLITES**

- **REACTIVE oxygen intermediates**

- **FREE radicals**

- **Antioxidant protective nutrients and plant derivatives**
  - Carotenes (Vit A)
  - Ascorbic acid (vit C)
  - Tocopherols (Vit E)
  - Selenium
  - Copper
  - Zinc
  - Manganese
  - Coenzyme Q10
  - Thios (found in garlic, onions and cruciferous derivatives)
  - Bioflavonoids

- **EXTRACTION DERIVATIVES**
  - Polar hydrophilic
  - Feces
  - Stool
  - Kidneys
  - Urine

- **Secondary tissue damage**

- **Endotoxins**
  - Metabolism end products
  - Bacterial endotoxins

- **Ethotoxins**
  - Medicines
  - Pesticides
  - Food Additives
  - Household chemicals
  - Pollutants / contaminants
  - microbes

- **Superoxide**
IS THERE A PHASE III?

Recently, the Antiporter activity (p-glycoprotein or multidrug resistance) has been defined as the Phase III detoxification system. The Antiporter activity is an important factor in the metabolism of the first passage of pharmaceutical and other xenobiotic products. The Antiporter is an efflux pump dependent on the energy pumped out from a cell by xenobiotics, decreasing the intracellular concentration of xenobiotics. The Antiporter activity in the intestine seems to be co-regulated with the intestinal enzyme Cyp3A4 of the Phase I.

This observation suggests that the Antiporter can support and promote detoxification. Probably, its pumping function of non-metabolized xenobiotics out of the cell and returning to the intestinal lumen may allow more opportunities for the Phase I to metabolize xenobiotics before they are put in circulation (Figure 2).

Two genes encoding the Antiporter activity have been described: the multidrug resistance gene 1 (MDR1) and the multidrug resistance gene 2 (MDR2). The product of MDR1 gene is responsible for the drug resistance of many tumor cells and is usually found in epithelial cells of the liver, kidneys, pancreas, small and large intestine, brain and in testicular epithelial cells. MDR2 activity is mainly expressed in the liver and may play a similar role to intestinal MDR1 for liver detoxification enzymes; its function is not currently defined.

In the toxin removal process, the most important fact is the coordination of the three phases; otherwise dangerous accumulations could occur. The biggest problem is between Phase I and II.

In the first phase, many oxidized compounds with high reactive capacity are produced, which act as free radicals and must be immediately blocked by the Phase II results. If it doesn’t happen, due to inactivation of enzymes or insufficient quantity, a great cellular damage is created. We should not disturb this balance with a wrong diet (as we will say later), with cigarette smoke, alcohol and many drugs, including some antibiotics, antidepressants, antifungals and anti-arrhythmic. In order to improve detoxification, it’s not a question of increasing the activity of Phase I, which can cause damage, but is to have an antioxidant action. In cells there is a protein called nuclear factor, derived from erythroid (NrF2), found in the cytoplasm, when free radicals grow, NRF2 moves into the nucleus and activates genes that produce enzymes that can act as antioxidants. Therefore, in case of heavy metal poisoning (lead, arsenic, chromium, mercury, etc.) which activates many free radicals, NRF2 stimulates the synthesis of metal-proteins that chelate and block these metals.

* Antiporter A cell membrane protein that moves two substances in opposite directions across the membrane

Figure 02
ASSESSMENT OF THE HEPATIC SYSTEM

The liver is a silent organ, we do not clearly notice when it is slightly damaged. The evaluation of transaminases and jaundice are signs of liver alteration, necrosis or stasis are very advanced signs of obvious damage. But there are mild and sometimes vague signs and symptoms that, by carefully observing, signal liver dysfunction and the need for detoxification.

MOST FREQUENT SUBJECT SYMPTOMS:

Frequent unexplained fatigue, difficulty to recover the effort, headache especially in the frontal area, tinnitus, blepharitis and conjunctivitis, drowsiness after meals, bitter taste in the mouth, halitosis, increased thirst, frequent rashes, high sensitivity to strong odors (smell and scent), itching and burning, sensitivity to garlic or onion

FREQUENT SYMPTOMS:

Erythema, redness of the face and eyes, and slight yellowing of the skin, especially with fasting, presence of dark spots. Other signs: reactions to penicillin, aspirin, alcohol, immune weakness with frequent inflammatory diseases, sore throat, cough. Finally, even unexplained anxiety, mood swings, depressive thoughts.

LIVER AND HORMONES

The liver plays a importante role in the degradation of hormones by Phase I or Phase II enzymes, which eliminates altered or excess molecules. If detoxification is delayed, the hormones will only be partially metabolized or eliminated. These partially metabolized molecules do not activate hormonal response processes, such as fully active ones, while they compete with active hormones for receptor binding sites and inactivate normal hormonal return pathways. Therefore, they are somewhat similar to “abnormal” hormones, which do not work properly, but are as effective as normal hormones that interfere with hormone receptors and feed back pathways. The end result will be a patient with symptoms of hormonal imbalance, but with laboratory tests that may seem really normal due to abnormal hormones that are not sufficiently degraded due to a partial detoxifying liver.

DESMOVIT®: SYNERGY OF TWO DRUGS

1. **DESMODIO ADSCENDENS**
   Desmodium adscendens is a plant of the fabaceae family, native to the Peruvian Amazon rainforest, which is also found in South America and the west coast of Africa. In traditional Brazilian medicine, the leaves of this plant treat leucorrhoea, muscle pain, pain, ovarian inflammation, excessive urination, gonorrhea and diarrhea (Heard O., 1994).

The plant Desmodium adscendens is widely used as juice or tea in various parts of the world. In its composition there are: polyphenols, flavonoids, anthocyanins and tannins that confer antioxidant properties.

This biennial herbaceous plant of the Fabaceae family (Leguminosae), native to the humid equatorial zones, has recently been used in occidental phytotherapy for its peculiar characteristics:

1. Absence of cholagogue action,
2. No interference in enzymes of Phase I and II,
3. Enhanced antiallergic action.

**ACTIVE INGREDIENTS:**

Triterpenes saponosides: soyasaponin I and III, dihydroxy saponin I.

Flavonoids: 11,2 mg / g of weight on dry isoflavones aromatic compounds. Activity: hepatoprotective, antioxidant, anti-inflammatory.
MODE OF ACTION

- Inhibits lipid peroxidation of hepatocytes;
- Inhibits hepatic monooxygenase, which reduces the oxygenation of arachidonic acid and the release of inflammatory substances. The hepatoprotective action is performed though an antioxidant and anti-inflammatory action,
- Immune modulation with stimulating effect on monocytes/macrophages, starting from 1-3 weeks and transient depressive (modified after a week) in IgG and IgA, and depression sustained in IgE.
- Smooth muscle of the whole body due to the activation of cellular cyclo-oxygenases, the production of prostaglandins with muscle relaxant action (PGE2) and the modulation of leukotriene synthesis of bronchoconstrictors. In vivo and in vitro action: activates cyclooxygenases, increases prostaglandin synthase, inhibits contraction of smooth muscle, acts on arachidonic acid.

RESEARCH ARTICLE

Desmovit® clinical trial in patients with cancer, receiving chemotherapy.
CLINICAL INDICATIONS:
Liver diseases (liver failure, viral hepatitis, toxic hepatitis), hepatoprotective and depurative, allergies and asthma, autoimmune disorders, adjuvant in oncology. Useful in detoxifying from drugs and alcohol. Toxicity: in rats, negative tests for genotoxicity and carcinogenicity.

ANTIOXIDANT COMPOSITION:
Flavonoides -12.8 mg / g of dry weight catechin
Polyphenols - 11.1 mg / g of dry weight gallic acid
Anthocyanin - 0.182 mg / g of dry weight Tannin - 0.39 mg / g of dry weight

Its antioxidant functions bring benefits such as antimutagenicity, anti-carcinogenicity and anti aging (Yang CS, 2011).

According to Muanda, François Nsemi et al. study, 2010, the higher the concentration of the Desmodium adscendens extract, the greater the reduction of reactive oxygen species.

Figure 03: Concentration-response curve for reduction of ROS generated by exogenous H$_2$O$_2$. R (%) ROS exo H$_2$O$_2$, reduction (%) os ROS generated by exogenous H$_2$O$_2$; CCE: Concentration of extract.
Besides its antioxidant function, Desmodium adscendens is a hepatoprotective able to reduce the oxidative stress of liver cells, especially at low doses of the active ingredient according to the François, Celine et al. study (2014), thus improving the detoxification capacity of the liver.

In this study, oxidative stress was induced by glucose, so we can associate Desmodium adscendens with Glycoxil®.
The calcareous algae consists mainly of calcium carbonate which occurs in three different structures of calcium, calcite 65%, aragonite 23%, and vaterite 12%.

Other minerals include magnesium (55 g / kg), potassium (7 g / kg), iron (800 mg / kg), phosphorus (500 mg / kg), manganese (50 mg / kg), iodine (30 mg / kg), copper (10 mg / kg), zinc (10 mg / kg), boron (10 mg / kg), molybdenum (0.2 mg / kg), selenium (1.8 mg / kg) and cobalt (0.1 mg / kg).

The integration of lithothamnium calcareum was able to increase bone density and mineralization in female animal models subjected to different treatments with a diet low in nutrients. At the end of 15 months a difference in bone mineral density was detected in animals fed a low-nutrient diet plus algae. Animals with supplementation showed an increase in bone mineral (C) compared to animals treated without integration (B) ASLAN et al. 2011 (Figure 4)

**WE CAN ASSOCIATE LITHOTHAMNIIUM CALCAREUM WITH SILICIUM (ORTHO SILICIC ACID – OSA E MONOMETHYL SILANE TRIOL – MMST) IN ORDER TO INCREASE BONE MINERALIZATION**

A clinical study in humans using Lithothamnium calcareum and its combinations demonstrated the possibility of reducing pain during exercise (walking) in patients with osteoarthritis at the end of 12 weeks (FRESTEDT et al., 2008).
GASTROINTESTINAL PROTECTION

A study conducted by Schiavo et al. 2012, using animal models, showed the gastroprotective effect of Lithothamnium calcareum following a gastric lesion. The proposed mechanism, according to the authors, is the property of calcium to regenerate the gastric mucosa.

Figure A

![Graph A]

Figure B

![Graph B]

In a study conducted by Aslam et al, 2009, the use of Lithothamnium calcareum has been shown to inhibit the proliferation and differentiation of different intestinal carcinoma cell lines. The authors underline the importance of calcium as a powerful inhibitor of the growth and differentiation of these cells.

Influence of alga extract (Figures A and B) on growth inhibition and on the differentiation of intestinal colon cancer cell lines. Source: Aslam et al, 2009.
**Desmovit benefits:** Desmovit mainly acts on inflammation. When the liver is affected by a subclinical inflammation, it does not detoxify properly anymore. It has anti-histaminic and antileukotriene effect, inhibiting arachidonic acid monoxidase. Therefore, Desmovit prevents the inflammatory process in hepatocytes by allowing hepatocytes to act in phases I, II and III.

- It acts in Phase I as an antioxidant and helps in detoxification by reducing inflammation (not by acting directly on the cytochrome)
- Reduces inflammation of the liver as a whole (it does not stimulate the cytochrome or glycoprotein)
- Why can Desmovit be used with medicines?
- It does not stimulate cytochrome P450 or glycoprotein block, which can cause hepatotoxic effects on the liver
- Desmovit indirectly restores the detoxification capacity of the liver, thanks to its anti-inflammatory and antioxidant activity, making the Phases I, II and III work correctly

**INDICATIONS**

Antioxidant activity (increase in glutathione, superoxide dismutase and catalase)

Hepatitis

Cirrhosis,

Alterations in hepatic metabolism and

Alterations in the production of bile salts

Cancer patients

**REFERENCES**


