

LAMIRIDOSIN

1. PRODUCT NAME

Lamiridosin Dietary Supplement.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1. Overview

The active ingredients contained in this food supplement are Flavonoids, Catechins and Lamiridosin. Flavonoids are plant polyphenols that have shown many beneficial effects due to their properties as antioxidants, chelating free radicals. Flavonoids in turn have given positive responses about his ability antiallergic, and immunomodulatory and antiproliferative. Catechins are flavonoids whose main properties include that of acting as an antiinflammatory, immunoregulatory and hepatoprotective. The Lamiridosin is aglicano of iridoid, which has shown in in vitro and in vivo hepatoprotective and antiviral some capacity against hepatitis C.

2. Qualitative and quantitative

Each capsule contains 240mg Calendula (0,48-1,2 mg flavonoids), 140 mg Agrimonia (0.7 mg catechins) and 140 mg Nettle (0.7 mg Lamiridosin).

3. PHARMACEUTICAL FORM

Soft gelatin capsules.

4. CLINICAL

1. Therapeutic indications

It helps eliminate toxins, strengthens the natural defenses and helps cleanse the body.

2. Dosage and method of administration

Dosage:

Adults: 1 capsule every twelve hours.

Method of administration:

Oral use

3. Contraindications

Hypersensitivity to Flavonoids, Catechins or Lamiridosin or any of the excipients.

4. Warnings and precautions for use

Pediatric Population

No information is available about the effect of this food supplement in pediatric populations.

5. Drug interactions and other forms of interaction

You can reduce the effect of cytochrome P450 1A2 substrate, such as Clorozapina (Clozaril), cyclobenzaprine (Flexexil), Haloperidol (Haldol).

May potentiate the action of UDP-glucuronosyltransferase 1A1 and therefore may increase the action of drugs dependent on this enzyme, such as acetaminophen (Tyenol), estrogens and oral contraceptives.

Can inhibit Aromatase metabolism by enhancing the effects of drugs that are metabolized as Aminoglutamida (Cytroden), anastrozole (Arimidex), exemestane (Aromasin), letrozole (Femara).

Cyclosporine prolongs its plasma levels and extends its lifespan.

It inhibits the cytochrome P450 2C8, increasing serum levels of its metabolites such as paclitaxel

It inhibits the cytochrome P450 2D6, increased serum levels of metabolites and thus increased their effects these substrates are codeine, flecainide or Haroperidol.

Warning excipients

Must not exceed the recommended daily dose (2 capsules).

6. Fertility, Pregnancy and Lactation

No evidence exists that any of the ingredients may cause fetal harm, despite this, the supplement must be used during pregnancy only if necessary.

Components can pass into breast milk should be administered with caution during lactation.

7. **Effects on ability to drive and use machines**

There have been no evidence that food supplement Lamiridosin can negatively influence the ability to drive or operate dangerous machinery.

8. **Adverse Reactions**

Not described in literature.

5. **PROPERTIES**

1. **Lamiridosin**

Under the heading of iridoids are grouped a series of bicyclic monoterpenes (C₁₀) derived biosynthetically the monoterpene geraniol, which have as common a basic structure ciclopentapirano called iridano, for the first time been detected in ants of the genus *Iridomirmex*. These compounds may like structures found open (Secoiridoid) or closed (iridoids) heterosídica usually in the form, mainly as glycosides.

There are a number of plants used for their pharmacological properties precisely because some of its active principles in nature iridoids. Among the most important of these devil's claw, gentian and valerian, which are used in underground organs and olive leaf.

The name refers to Lamiridosin the active form of iridoid Lamiridoside a aglicano of Lamiridoside, obtained from it, either by natural means or synthetically.

The iridoids are a group of monoterpene compounds found routinely in nature as glycosides, when subjected to enzymatic hydrolysis, being the type of enzymes used as sugar hydrolase β -glucosidase. In this case you lose one molecule of glucose and aglicano is obtained as a result of hydrolysis. These compounds appear to show greater biological activity than the original glycosides.

The Lamiridosin is obtained from the aqueous extract of *Lamium album*, more specifically of the flowering tops. The extract obtained by maceration of the plant dry for 24 hours in deionized water. This process leads to the isolation of two inseparable epimers including chromatographic techniques like HPLC (High Performance Liquid Chromatography), found in a 1:1 ratio. These compounds have not been previously

referenced as isolated compounds, chemically or enzymatically prepared entities, are regarded as new compounds.

It has been observed that, if the alcoholic extract the compound obtained is not obtainable Lamalbid when extraction is performed in water. This phenomenon may be that when extraction is carried out in water, hydrolysis occurs glucoside by enzymes present in the matrix of the plant, while the methanol inactivates these enzymes.

2. Flavonoids and catechins

Flavonoids are phenolic constituents of the non-energy part of the human diet are natural pigments present in vegetables, seeds, fruits and beverages such as wine and beer. At first no action substances were considered beneficial to human health, but later shown to have multiple positive effects due to its antioxidant and free radical scavengers.

They were discovered in 1930 by Nobel Laureate Szent-György. At first they were assimilated soluble vitamins, but this fact could not be confirmed and in the 1950s this term was abandoned.

Flavonoids contained in its structure a variable number of phenolic hydroxyl groups and have excellent properties of chelating iron and other transition metals, giving them a high antioxidant capacity, which is directed fundamentally to hydroxyl radicals and superoxide species highly reactive involved in the initiation of lipid peroxidation.

They are low molecular weight compounds that share a common skeleton diphenyl-pyran (C6-C3-C6), consisting of two phenyl rings (A and B) linked through a pyran ring C (heterocyclic). This basic structure allows for a multitude of substitution patterns and changes in the ring C. Depending on their structural features can be classified into:

- Flavonoid content, as catechin, a group-OH in position 3 of C ring
- Flavonols, represented by quercetin, which possesses a carbonyl group in position 4 of ring C and a hydroxyl group at C3 position.
- Flavones, such as diosmetina, which possess a carbonyl group in position 4 of ring C and lack the hydroxyl group in position 3.
- Anthocyanidins, have the hydroxyl group in position 3 but also have a double bond between carbons 3 and 4 of ring C.

The three most important characteristics for its function include the presence in ring B of the structure or O-dihydroxy catechol, the presence of a double bond in position 2,3 and finally the presence of hydroxyl groups in positions 3 and 5. You can submit them all as quercetin or only one of them as catechin. Usually they are attached to a glycoside posing as an O-glycoside, while the non-carbohydrate called aglycone. The glycosides are more soluble in water and less reactive toward free radicals than the respective aglycones or flavonoids.

The flavonoids can bind to biological polymers, such as enzymes, hormones, transporters, and DNA, chelate metal ions from the transition zone such as Fe^{2+} , Cu^{2+} , Zn^{2+} , catalyze electron transport, debug free radicals. Because of this protective effects have been reported in various pathologies such as diabetes mellitus, heart disease, viral infections, stomach and duodenal ulcer and inflammation. Among other notable properties are its ability to act as antiviral, and anti-allergic and their properties, immunomodulatory, antithrombotic and antiinflammatory.

Were carried out studies to determine its ability to alleviate the allergic processes pair, determining that quercetin and catechin are able to prevent allergic reactions induced by histamine, inhibiting the release of this to basophils and mast cells, it also presents the ability to increase circulation time in blood and steroids.

Marigold extracts have shown immunomodulating capacities in the sense of favoring the regulatory balance and the final integrated response of the immune system or help to prevent a malfunction of the.

About flavonoids have conducted studies on the antiproliferative ability of tumor cells in vitro studies for a long time ago, in this sense apigenin turned out to be active in cell lines of colon, ovarian and breast cancer, other flavonoids have been shown to inhibit the growth HL60 promyelocytic cells (Middleton et al, 1994)

6. CLINICAL STUDIES

Were carried out studies on the antiviral capacity of the iridoid aglicanos, noting that these possess antiviral activity than the glycosides are not they come from. And numerous studies on the different activities of different flavonoids.

1. STUDIES *IN VITRO*

In vitro studies in liver cells HUG-7, showed that Lamiridosin is capable of carrying out a strong antiviral activity specific for hepatitis C, dose-dependent (IC_{50} concentration of ca. $20 \mu\text{g} / \text{ml}$).

Regarding its toxicity was evaluated in Hep 62 2.2.15 and found that, at concentrations of 50 micrograms / ml was not cytotoxic response, indicating that Lamiridosin not induce toxicity at doses of effective concentration.

Regarding flavonoids have been numerous in vitro studies demonstrating the antiviral capacity Influenza A virus, herpes simplex virus, Arenovirus. The hesperidin was evaluated in Madin-Darby canine kidney (MDCK) in its antiviral activity against viru Human Influenza A, The study was carried out by treating the cells before, after and while they were inoculated with influenza virions. The pre-inoculation treatment produced no results antivirals, while those treated at once and after inoculation induced a reduction in viral replication, being more effective in reducing post-treatment

replication inoculation. Also turned out that hesperidin showed no cytotoxicity in a dose range of 0-25 mM.

In another study showed in vitro epigallocatechin exert antiviral activity, against herpes simplex virus.

Also the (-)-epigallocatechin 3-gallate, has antiproliferative effects in various human cell lines querantocitos, implying some capacity chemotherapy in the skin by radiation damage (Barthelmes et al, 1998).

Friedman et al (2002) studied the antifungal and antibacterial capacity of calendula, proving to be effective against *Campylobacter jejuni*.

The immunomodulatory activity has been highlighted in several studies in vitro, such as those carried out by Wagner et al (1985) and Amirghofan (2000), both show the proliferative activity of Pals.

Regarding its antiproliferative capacity of tumor cells, extracts of calendula has demonstrated cytotoxic activity in three tumor cell lines (MRc5, HEP2 and Ehrlich), where the marigold extract was effective in inhibiting cell proliferation compared with control.

The immunomodulatory response of marigold extract has been studied in vitro in human lymphocytes, resulting in an increase in the proliferation of human Plus two to five times higher than control. He also saw a decrease in tumor cell proliferation over control.

2. **STUDIES *IN VIVO***

In a study carried out on 14 humans who were administered the product for 45 days and were evaluated in which clinical, biological and virological, found that 100% of the patients improved the clinical manifestations of the disease themselves . Regarding the biochemical manifestations in 85% of patients showed a decrease in levels of transaminases and transaminase in 15% decreased levels of AST. As for ALT levels, there were no variations. When we studied the effect of the product on viral load, we found that in 31% of patients this parameter decreased.

Regarding the flaonoides, studies carried out in vivo animal models in mice, pigs, etc, have demonstrated their ability antiviral against herpes simplex virus and arenovirus.

We have tried to view the antibacterial capacity of the polyphenols, in this sense has carried out a study with mice, which were inoculated trophozoites of *G lamblia* (protozoitos), and assessed the ability of two plant extracts rich in flavonoids (including the (-)-epicatechin. the treatment was initiated six days after infection, and both extracts were effective against bacteria with IC₅₀ of 0.125 mg / kg and 0.506 mg / kg

He has made several clinical studies to see the influence of flavonoids on cholesterol, resulting in all cases that are capable of lowering LDL, in situations of hypercholesterolemia.

Another study carried out by dentists, will study the ability of the catechins contained in green tea, the activity against oral bacteria. For this purpose the saliva collected from 32 individuals, using water as a control and as a mouthwash product based on green tea, catechins worth. The mouthwash was effective in reducing the number of bacteria, particularly against streptococcus mutans, the principal cause of dental caries.

A trial was conducted in mice, which measured the ability of a marigold extract to study the antiproliferative and immunostimulatory capacity of tumor, the study was carried out in male mice aged 6-8 weeks, ascites was measured and the survival after two weeks of inoculation of murine Ehrlich carcinoma (10^6 cells) and administered 25 mg / kg of marigold extract in different concentrations, administered orally or parenterally, the study showed that there was a higher survival rate in mice receiving the extract, and of these, the effectiveness was greater when the extract was administered orally.

The immunostimulatory capacity was carried out in male mice was studied in these different subpopulations lymphocytes, the mice that received the extract of marigold increased cells CD 23, CD 24, PANNK and PANKT in relation to the control group significantly the increase of these cells indicate a lymphocyte proliferation, particularly of B cells, CD4⁺ T cells and NKT cells.

7. **PHARMACEUTICAL PARTICULARS**

1. **List of excipients**

Maltodextrin

Magnesium stearate.

Silicon Dioxide

2. **Incompatibilities**

Not applicable

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