

Summary of the dossier: Caesalpinia spinosa dried extract, Capsules 250 mg.

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This is an application for marketing authorization of dried extract of Caesalpinia Spinosa (hereinafter referred to as "Caesalpinia Spinosa dried extract" or "P2Et extract") for use as an ingredient in food supplements. The application has been prepared in accordance with the administrative and scientific requirements of Commission Implementing Regulation (EU) 2017/2469 laying down for applications referred to in Article 10 of Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods. It is also in line with the guidance of the European Food Safety Authority (EFSA) on the preparation and submission of an application for authorization of a novel food in the Context of Regulation (EU) 2015/2283.

Caesalpinia spinosa extract is produced by ethanol extraction, dried and purified in an approved manufacturing plant that follows Good Manufacturing Practice (GMP), established in Colombian Law through the corresponding regulatory authority (Instituto Nacional de Vigilancia de Medicamentos y Alimentos "INVIMA"). The raw material meets the criteria established for the production of this food supplement. Our strict raw material sourcing and processing protocols aim to produce a consistent and standardized Caesalpinia Spinosa extract. Quality control measures are implemented to ensure that each batch of finished product meets our stringent safety and quality standards.

The new food ingredient is intended for use only in food supplements with a maximum daily dose of 500 mg. The final product contain dried extract Caesalpinia Spinosa 250 mg per capsule. The capsules should be consumed twice a day. The product is unlikely to substitute for any other food in the diet and there is no and there is no exposure to the fruit or its extract through other food sources.

The application is also supported by a number of toxicological studies, which aim to demonstrate the safety of this novel food, with extensive data from preclinical studies in animal models of acute and chronic administration of Caesalpinia spinosa extract (180 days continuous), as well as genotoxicity and pharmacokinetic studies. The NOAEL (Level with no observable adverse effect) is defined, which for Rattus norvegicus is 2000 mg/kg/day. In addition, we conducted research in clinical studies in healthy human volunteers (continuous for 30 days). The recommended duration of use is based on previous studies in healthy volunteers and in preclinical animal models. These studies have shown that oral intake of the novel food up to 600 mg per day is well tolerated, according to the safety profile in healthy humans. Taking into account its traditional use (being rich in polyphenols derived from gallic acid) with significant antioxidant activity, and the ability to induce autophagy in tumor cells and reduce the systemic

inflammatory response in animal models, we have developed a study in patients with COVID-19 in which a daily dose of 500 mg was safe and was not associated with any adverse effects.

Plant extracts with medicinal properties are known for their ability to exert a wide variety of biological actions, where their various active molecules, acting at low concentrations and by multiple mechanisms, are able to offer health benefits much more potent than those that could be exerted by each molecule separately (synergistic effect) (Yong Y, 2014). The use of these in humans on an industrial scale must be justified by both their effectiveness and safety, as well as their sustainable production capacity. The standardized extract of P2Et meets these requirements. In the section (related to preclinical and clinical trials), we have provided scientific evidence, both our own and from other research groups, which allows us to predict that intermittent consumption of the P2Et extract, in addition to being safe at the indicated dose, thanks to its antioxidant and regenerative properties, can offer the individual protection, both at the cellular and systemic levels, by limiting the deleterious effects of free radicals generated both by unhealthy lifestyle habits, very common in a high percentage of the Western population (unbalanced diet rich in saturated fats and sugars, smoking, alcohol intake), and environmental (prolonged exposure to UV light and pollution), whose chronic and systematic exposure can lead to inflammatory diseases ranging from diabetes and cardiovascular problems, to neurodegenerative diseases and cancer. Additionally, the immunomodulatory capacity also evaluated for this extract can act as a coadjuvant in the treatment of respiratory diseases of viral origin, modulating both the innate immune response mediated by proinflammatory cytokines and viral replication. On the other hand, by enhancing the adaptive immune response mediated by T lymphocytes, or innate, through NK cells, which can be activated against pathogenic microorganisms, it can help prevent the progression of infectious diseases, resulting in an important natural alternative to the use of antibiotics, which is now of vital importance in the face of increasing resistance to antimicrobials. Intermittent consumption of the standardized P2Et extract offers an effective, safe and affordable natural alternative for the prevention/elimination of diseases of inflammatory and oxidative origin most common in modern man.