SERENZO™
Citrus na diminuição do estresse

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*Citrus* na diminuição do estresse

**DESCRIÇÃO**

Fitoterápico composto especificamente de D-limoneno a partir do *Citrus sinensis* que auxilia no controle da inflamação associada ao estresse.

**MECANISMO DE AÇÃO**

O estresse induz o aumento das citocinas pró-inflamatórias as quais ativam a expressão de moléculas de adesão ICAM-1 responsável pela resposta inflamatória. **Serenzo™** atua na diminuição da expressão de ICAM-1, reduzindo assim o ciclo do estresse e a resposta inflamatória, além de ser um coadjuvante na modulação do cortisol, auxiliando no controle das alterações comportamentais, ocasionando assim o equilíbrio emocional. Logo, o **Serenzo™** age tanto a nível fisiológico quanto comportamental.

**INDICAÇÕES**

- Auxiliar na diminuição da compulsão alimentar associada à ansiedade;
- Contribuir no controle das alterações comportamentais como irritabilidade, alterações de humor e sono;
- Proporcionar redução na resposta a dor inflamatória ocasionado pelo estresse e seus efeitos prejudiciais.

**DOSE USUAL**

Recomendação oral de 500mg de **Serenzo™** (*Citrus sinensis*) ao dia.

**SUGESTÕES DE FÓRMULAS**

<table>
<thead>
<tr>
<th><strong>Serenzo™</strong> (<em>Citrus sinensis</em>)</th>
<th>500mg</th>
</tr>
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<tbody>
<tr>
<td>Shake qsp.</td>
<td>1 sachê</td>
</tr>
<tr>
<td><strong>Modo de uso:</strong> Dissolver 1 sachê em 1 copo com leite, 1 vez ao dia.</td>
<td></td>
</tr>
<tr>
<td><strong>Indicação:</strong> Redução dos marcadores inflamatórios, associados ao estresse</td>
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<table>
<thead>
<tr>
<th><strong>Serenzo™</strong> (<em>Citrus sinensis</em>)</th>
<th>250mg</th>
</tr>
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<tbody>
<tr>
<td>L Optizinc®</td>
<td>12,5mg</td>
</tr>
<tr>
<td>Magnésio</td>
<td>150mg</td>
</tr>
<tr>
<td><strong>Modo de uso:</strong> 1 dose, 2 vezes ao dia</td>
<td></td>
</tr>
<tr>
<td><strong>Indicação:</strong> Promover a melhora do humor</td>
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**PRINCIPAIS REFERÊNCIAS**


Vascular response to stress in health and disease

Abstract: The body’s vasculature plays a critical role in the development of functional and structural alterations responsible for tissue and organ damage in laboratory animals and human subjects during illness and senescence, and in response to stress. Components of the vasculature, namely, major arteries such as the aorta, smaller arteries, arterioles, capillaries, post-capillary venules, and collecting central veins, all serve as conduits through which vital substrates are delivered to cellular masses and/or waste products are removed. A number of physical and neurohumoral agents known to be responsive to stress stimuli exert functional control over the vasculature. Both physical and emotional stress have been found to cause significant hemodynamic alterations. Large artery rigidity, for instance, develops rapidly following stress-induced activation of the autonomic nervous system. Associated with this process is increased release into the circulation of catecholamines and angiotensin-II. At the same time, insulin resistance develops, accompanied by nitric oxide release and changes in the immune system. The response of large arterial conduits to stress is characterized by increased pulse pressure, which in turn affects the endothelium of the arterial vessels responsible for determining total peripheral resistance. Microcirculation networks, where a large fraction of the blood volume is contained, are affected as well, and the blood in them is subject to redistribution into adjacent interstitial fluid compartments. Changes in endothelial permeability, secondary to variations in pulse pressure, can lead to interstitial edema and changes in the physicochemical properties of interstitial compartments. These changes give rise to alterations in the traffic of substrates and waste products between blood and cells. This sequence of events also takes place in the vasa vasorum microcirculation that nourishes large arteries, and likely contributes to remodeling of the vascular wall and to atherogenesis. The contribution of large artery rigidity to the morbidity and mortality associated with arterial hypertension, diabetes mellitus, heart failure, and terminal uremia, is relatively well established in human populations. In addition, it appears that aortic rigidity precedes the development of arterial hypertension in the spontaneously hypertensive rat (SHR) model, as well as in individuals with borderline hypertension. The fact that some of the functional and structural vascular alterations produced by stress are reversible reinforces the importance of developing behavioral techniques and pharmacologic agents that can successfully interrupt this pathological sequence of events.

Proinflammation: a common denominator or initiator of different pathophysiological disease processes

Abstract: Proinflammation is a widespread phenomenon. It has an association with the stress (patho)physiology and is connected with various diseases. It has been discussed if proinflammation may represent a common (pre)condition in different disease states. Evidence for a common proinflammatory pattern in a variety of diseases is analyzed. Proinflammatory (pre)conditions and immune response patterns serve as a common modality in a number of clinically separate diseases. Here, nitric oxide pathways often play a significant role as well. On molecular basis, proinflammation potentially illustrates a common denominator and/or an initiator. Like stress, proinflammation seems to be a crucial autoregulatory concept. It normally serves a positive biological goal: Proinflammatory activities, e.g., are initiated to overcome infection or invasion of potentially deleterious biological agents (bacteria, viruses, parasites etc.). While fighting invasion, proinflammation usually shortens biological ‘battles’ and therefore ameliorates disease-related detrimental or subjectively unpleasing phenomena. However, proinflammation has beneficial and deteriorating capacities and may yet exert detrimental effects. This is especially true, when the fine balance between the different immune response pathways, between anti- and proinflammatory mechanisms, can not be kept. This may occur when a challenge becomes overwhelming or when patterns of a chronic (patho)physiological activity are presented. Thus, proinflammation may represent a relatively unspecific, overlapping/ analogous state, underlying various clinical disease manifestations.
The endothelium and inflammation

Abstract: The vascular endothelium contributes to and is affected by inflammatory processes. Disturbance of the endothelium's morphologic and functional integrity in response to mechanical, immunologic, and chemical injuries reflects the first step in the pathophysiological cascade of atherosclerotic disorders. At the site of an endothelial injury, invading inflammatory cells producing numerous proinflammatory factors promote and amplify both local and systemic inflammation. These early changes on a cellular and subcellular level that precede the clinical manifestation of atherosclerosis are associated with loss of profound physiological functions of the endothelium. One pivotal function of the endothelium is nitric oxide-mediated regulation of vessel tone and blood flow according to the local requirements. The assessment of nitric oxide-mediated endothelial function by different methods revealed a close relation between inflammatory activation and endothelial dysfunction in healthy volunteers, patients at risk, and patients with established cardiovascular disease. Moreover, anti-inflammatory therapeutic interventions do not only have a positive impact on disease progression, but also on endothelial function, thus further providing an indirect line of evidence linking inflammation with endothelial dysfunction.

Interferon-gamma and tumor necrosis factor-alpha mediate the upregulation of indoleamine 2,3-dioxygenase and the induction of depressive-like behavior in mice in response to bacillus Calmette-Guerin

Abstract: Although the tryptophan-degrading enzyme, indoleamine 2,3-dioxygenase (IDO), is a pivotal mediator of inflammation-induced depression, its mechanism of regulation has not yet been investigated in this context. Here, we demonstrate an essential role for interferon (IFN)gamma and tumor necrosis factor (TNF)alpha in the induction of IDO and depressive-like behaviors in response to chronic immune activation. Wild-type (WT) control mice and IFNgammaR(-/-) mice were inoculated with an attenuated form of Mycobacterium bovis, bacille Calmette-Guérin (BCG). Infection with BCG induced an acute episode of sickness that was similar in WT and IFNgammaR(-/-) mice. Increased immobility during the forced swim and tail suspension tests occurred in WT mice 7 d after BCG inoculation but was entirely absent in IFNgammaR(-/-) mice. In WT mice, these indices of depressive-like behavior were associated with chronic upregulation of IFNgamma, interleukin(1)beta, TNFalpha, and IDO. Proinflammatory cytokine expression was elevated in BCG-infected IFNgammaR(-/-) mice as well, but upregulation of lung and brain IDO mRNA was completely abolished. This was accompanied by an attenuation of BCG-induced TNFalpha mRNA and the lack of an increase in plasma kynurenine/tryptophan ratio in the BCG-inoculated IFNgammaR(-/-) mice compared with WT controls. Pretreatment of mice with the TNFalpha antagonist, etanercept, partially blunted BCG-induced IDO activation and depressive-like behavior. In accordance with these in vivo data, IFNgamma and TNFalpha synergized to induce IDO in primary microglia. Together, these data demonstrate that IFNgamma, with TNFalpha, is necessary for induction of IDO and depressive-like behavior in mice after BCG infection.

Update on uses and properties of Citrus flavonoids: new findings in anticancer, cardiovascular, and anti-inflammatory activity

Abstract: Significantly, much of the activity of Citrus flavonoids appears to impact blood and microvascular endothelial cells, and it is not surprising that the two main areas of research on the biological actions of Citrus flavonoids have been inflammation and cancer. Epidemiological and animal studies point to a possible protective effect of flavonoids against cardiovascular diseases and some types of cancer. Although flavonoids have been studied for about 50 years, the cellular mechanisms involved in their biological action are still not completely known. Many of the pharmacological properties of Citrus flavonoids can be linked to the abilities of these compounds to inhibit enzymes involved in cell activation. Attempts to control cancer involve a variety of means, including the use of suppressing, blocking, and transforming agents. Suppressing agents prevent the formation of new cancers from procarcinogens, and blocking agents prevent carcinogenic compounds from reaching critical initiation sites, while transformation agents act to facilitate the metabolism of carcinogenic components into less toxic materials or prevent their biological actions.
Flavonoids can act as all three types of agent. Many epidemiological studies have shown that regular flavonoid intake is associated with a reduced risk of cardiovascular diseases. In coronary heart disease, the protective effects of flavonoids include mainly antithrombotic, anti-ischemic, anti-oxidant, and vasorelaxant. It is suggested that flavonoids decrease the risk of coronary heart disease by three major actions: improving coronary vasodilatation, decreasing the ability of platelets in the blood to clot, and preventing low-density lipoproteins (LDLs) from oxidizing. The anti-inflammatory properties of the Citrus flavonoids have also been studied. Several key studies have shown that the anti-inflammatory properties of Citrus flavonoids are due to its inhibition of the synthesis and biological activities of different pro-inflammatory mediators, mainly the arachidonic acid derivatives, prostaglandins E 2, F 2, and thromboxane A 2. The anti-oxidant and anti-inflammatory properties of Citrus flavonoids can play a key role in their activity against several degenerative diseases and particularly brain diseases. The most abundant Citrus flavonoids are flavanones, such as hesperidin, naringin, or neohesperidin. However, generally, the flavones, such as diosmin, apigenin, or luteolin, exhibit higher biological activity, even though they occur in much lower concentrations. Diosmin and rutin have a demonstrated activity as a venotonic agent and are present in several pharmaceutical products. Apigenin and their glucosides have been shown a good anti-inflammatory activity without the side effects of other anti-inflammatory products. In this paper, we discuss the relation between each structural factor of Citrus flavonoids and the anticancer, anti-inflammatory, and cardiovascular protection activity of Citrus flavonoids and their role in degenerative diseases.

Radical scavenging activity of various extracts and fractions of sweet orange peel (Citrus sinensis)

Seven different extracts, fractions and residues of Navel sweet orange (Citrus sinensis) peel were evaluated for their radical scavenging activity by the DPPH radical dot and luminol induced chemiluminescence methods. Also, the Folin–Ciocalteu method was used to determine the total phenolic content. High phenolic content and radical scavenging activities were found for the ethyl acetate fraction. Comparison was made with reference compounds, Trolox, ascorbic acid, quercetin, which are already known for their good antioxidant activity. The radical scavenging activity of the ethyl acetate fraction approached the activity of the standards.Total phenolic content showed a small relation with radical scavenging activity. The radical scavenging activity examined with the DPPH method correlated well to values obtained by chemiluminescence. The antioxidant activity found in the fractions of Citrus sinensis, should be attributed to the presence of flavonoids and other phenolic compounds. Among the various classes of flavonoids: flavanone glycosides, flavones and flavonols seem to prevail as indicated by two dimensional thin layer chromatography and color reactions. This information shows that ethyl acetate fraction of navel sweet orange peel can be used as antioxidant in food and medicinal preparations.

Naturally occurring anxiolytic substances from aromatic plants of genus Citrus

Currently, anxiety is one of the most common mental disorders affecting humanity and its prevalence is increasing. Anxiolytic substances occupy a prominent post in the ranking of the most utilized drugs by man. However, the anxiolytic drugs have an unfavorable risk/benefit ratio, especially benzodiazepines. Several medicinal plants have been used in traditional folk medicine for their anxiolytic or sedative properties. It is well reported in the literature that aromatic substances have the power to influence emotional states in humans. Several plants rich in essential oil have been used in the treatment of anxiety. In addition, a great number of essential oils are currently in use as aromatherapy agents to relieve stress and depression. These oils are considered a holistic complementary therapy utilized for increased comfort and reduce stress. For this reason, we performed a literature review used papers indexed in Elsevier Science Direct and PubMed a source of research. The dates were collected of reviewed studies from 2000 to 2011 using essential oils of genus citrus with anxiolytic effects in preclinical models and clinical studies. Ethnopharmacological data has confirmed the popular use of plant species of the genus Citrus with sedatives, hypnotics, tranquillizers and anti-epileptics activities to treat disorders of the central nervous system. Given these assumptions, this paper aims to describe the principal evidence in the literature about the use of essential oils of genus Citrus with anxiolytic effects in preclinical models and clinical studies.
REFERÊNCIAS


