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Tonic, fortifier and aphrodisiac: adaptogens in the Brazilian folk medicine

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Review

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Abstract: In Brazil, many plants are used as tonic, fortifier, aphrodisiac, anti-stress, among other uses that are similar to the indications of an adaptogen. In general, such plants are used unspecifically, in situations of stress and fatigue, in the recovery after a previous pathological or debilitating state, or simply aiming at the maintenance of a healthy state. This article discusses the popular terms employed in the Brazilian folk medicine for the plants with this profile, their particularities and limitations. The article also discusses the possible mechanisms of action of an adaptogen and compares the main Brazilian plants used for that purpose: guarana (*Paullinia cupana* Kunth, family Sapindaceae), muirapuama (*Ptychopetalum olacoides* Benth., Olacaceae), catuaba (*Anemopaegma arvense* (Vell.) Stellfeld & J.F. Souza, Bignoniaceae, and *Trichilia catigua* A. Juss., Meliaceae), nó-de-cachorro (*Heteropterys aphrodisiaca* O. Mach, Malpighiaceae), damiana (*Turnera diffusa* Willd. ex Schult., Turneraceae) and pfaffia or Brazilian ginseng (*Pfaffia* sp, Amaranthaceae).

Introduction

The term adaptogen, or resistogen, as it is usually called, was created by Nikolai Lazarev in the former Soviet Union to classify a group of substances that can improve the body's nonspecific resistance after being exposed to various stressing factors, promoting a state of adaptation to the exceptional situation (Brekhman & Dardymov, 1969). Israel Brekhman, his successor, established that a plant should meet three requirements in order to be considered an adaptogen (Brekhman & Dardymov, 1969): i) to be innocuous and not to disturb the body functions more than necessary. This means that an adaptogen should not produce effect on a healthy individual not submitted to stress; ii) to show a nonspecific activity, that is, to increase the body resistance in relation to harmful agents such as physical (heat, cold, variations of pressure, etc.), chemical (poisons and toxic substances) and biological (infections by viruses and bacteria); iii) to have a normalizing influence on a pathological state, independently of the nature of that state and the change in the previous pathological state (for instance, increase resistance to both heat and cold, aiming at balancing the body in adverse situations).

Even though these criteria are still mentioned, they are now being questioned, since the advances regarding this issue demonstrate, among other things, that adaptogens might indeed promote biochemical alterations in healthy individuals. Moreover, the way they are formulated, such concepts are considered vague and imprecise, therefore making it difficult to define whether the plants considered adaptogens today actually meet the three criteria.

In the 90's, a group of scientists interested in the theme, comprised by Hildebert Wagner (Germany), George Wikman (Sweden) and Alexander Panossian (Armenia), proposed as a definition that "adaptogens are natural bioregulators that increase the body's ability to adapt to environmental factors and avoid damage caused by those factors" (Panossian et al., 1999). In fact, the great merit of adaptogens is to minimize the body response to stress, reducing the negative reactions in the alarm phase and eliminating, or at least decreasing, the onset of the exhaustion phase that is part of the so-called syndrome of general adaptation (Wagner et al., 1994; Wagner, 1995; Rege et al., 1999).

However, adaptogens are indicated not only to counteract stress and its resulting damage. They are often used chronically to elicit a healthy state, or to improve or reduce some disorders and illnesses that result from aging, such as memory and attention deficits, tiredness

and general weakness, sexual impotence, among others (Wahlström, 1987; Russo, 2001). According to this line of thought, one can classify a plant as being potentially adaptogenic when it is used popularly for prophylactic rather than healing purposes; as a tonic, a fortifier, etc. This kind of use is common in countries of Eastern Asia such as China, India, Korea and Japan as part of their traditional medicine, in which many plants are used to help individuals keep a physical and psychic well-being (Fulder, 1980; Wahlström, 1987; Davydov & Krikorian, 2000; Chan, 2005; ven Murthy et al., 2010). Even though it is a millenary practice, the principles of traditional Asian medicine are still unknown to most part of the Western population, including the medical and scientific communities (Dahanukar & Thatte, 1997; Chan, 2005).

Adaptogens are essentially prescribed for prophylactic purposes. However, they can also be used by healthy individuals to improve their cognitive and physical performance, in which case their efficacy is questionable.

Chart 1 brings a relation of the main adaptogen plants all over the world, indicating the family and the part used. In this list we can observe a higher incidence of plants of the Araliaceae family, being the root the medicinal part commonly employed. The Korean ginseng (*Panax ginseng* C.A. Meyer, Araliaceae), whose roots are used for various purposes, is the best known example of adaptogen plant.

The Brazilian flora has countless plants that are used as adaptogens, that is, instead of being used for a specific ailment, they are employed for the same purposes of adaptogen plants, generally referred to as tonics, fortifiers, revigorating, among so many other popular terms (Carlini, 1991; Mendes & Carlini, 2007). This article will discuss the meaning of those popular terms and some of the plants best characterized as Brazilian adaptogens: guarana (*Paullinia cupana* Kunth, Sapindaceae), muirapuama (*Ptychopetalum olacoides* Benth., Olacaceae), fáfia or Brazilian ginseng (*Pfaffia glomerat*a Spreng., among other species, Amaranthaceae), damiana (*Turnera diffusa* Willd. ex Schult.,Turneraceae), nó-de-cachorro [*Heteropterys aphrodisiaca* O. Mach, Malpighiaceae) and catuaba (*Anemopaegma arvense* (Vell.) Stellfeld ex de Souza (Bignoniaceae) and *Trichilia catigua* A. Juss. (Meliaceae) species].

Data search

The folk terms related to the adaptogenic effect that are discussed in this review were obtained from a survey in dozens of books about medicinal plants and folk medicine published in Brazil. The complete list of these books is available in Mendes (2005) and Mendes & Carlini (2007). It was used the databanks Scopus and PubMed to access the main studies carried out with possible Brazilian adaptogen plants.

The "adaptogen" in the Brazilian popular culture

The diversity of popular terms to explain the uses and effects of medicinal plants, along with the way different populations see illnesses and their manifestations, often make it hard to understand the exact meaning of their indications. The variety of designations used in the Brazilian popular medicine is compatible with the dimensions of the country and its cultural diversity. Therefore, it is important to highlight the fact that the same popular term might have different meanings depending on the region and community investigated.

Although there are several plants used in the country for the same purposes of adaptogens, this term is not often used in the Brazilian popular culture. Chart 2 is an attempt to classify the plants regarding popular uses related to adaptogenic effect (PURAE), as well as their possible terms in English.

Out of the terms used generically (listed in Chart 2), the most commonly used and also one of the least precise is probably the word "tonic". Elisabetsky & Siqueira (1998) report that tonics are found in several

Chart 1. Some of the best-known adaptogen plants over the world.

Scientific name	Folk name	Family	Part used
Bryonia alba L.	loshtak	Curcubitaceae	root
Eleutherococcus senticosus (Rupr. & Maxim.) Maxim.	Siberian ginseng, taiga	Araliaceae	root
Ocimum sanctum L.	tulsi	Lamiaceae	whole plant
Panax ginseng C.A. Meyer	Korean ginseng	Araliaceae	root
Panax quinquefolius L.	American ginseng	Araliaceae	root
Rhodiola rosea L.	Artic root, golden root	Crassulaceae	root
Schisandra chinensis (Turcz.) Baill.	Chinese magnolia vine	Schisandraceae	fruits
Withania somnifera Dunal	Indian ginseng, ashwagandha, winter cherry	Solanaceae	root

traditional medical systems, regarding substances used by elderly individuals; those who are convalescing; to face periods of physical or mental stress, or simply to keep a good health. In another context, the word tonic may refer to isolated organs or parts of the body, as in cardiac tonic, capillary tonic, etc, and therefore are not within the range of action of a typical adaptogen, whose action extends to the body as a whole. Other terms used in the Brazilian popular medicine, and with the same purpose, are energetic, fortifier, regenerator, and restorative, among others. Plants that present those properties are also referred to as stimulants. However, the term stimulant was not included in Chart 2, since it represents an acute effect, characteristic of psychoactive drugs. Even though an adaptogen may also present a stimulant effect, it is different from that induced by stimulants of the central nervous system (Panossian & Wagner, 2005), being more closely associated with the idea of an energy drink, and its adaptative actions are the result of chronic use and slow adaptation mechanisms of the body, as this article will discuss later.

"Depurative", another common term not included in Chart 2, does not mean much alone, since it is often observed along with the tonic and fortifying properties. According to popular medical dictionaries, depurative is a substance that has the property to purify the blood, being also used to mean substances that "thin the blood". It is widely recognized that blood viscosity interferes in the blood flow, and therefore in the distribution of oxygen and glucose to the whole body. The aging process leads to a reduction in the blood flow, especially because of the reduction in the plasticity of the capillaries and of the red blood cell walls, which impairs the irrigation of the brain tissue. In this sense, *Ginkgo biloba* L. (Ginkgoaceae) can be mentioned as an example of a plant recognized by its capacity to reduce blood viscosity, increasing the brain blood flow, which may, in turn, contribute to its beneficial effect on memory (Santos et al., 2003). Nootropic drugs, such as piracetam, increase the blood flow in the capillaries and improve the brain irrigation by acting as vasodilators with activity in the brain. Substances with this property are known as revulsive, that is, they increase blood flow.

It is important to consider the understanding of "illness" in popular medicine. We frequently observe the concept that illness manifests as a response to blood impurities, therefore demanding an intervention in the sense of cleansing or purifying the blood. Depurative drugs, along with laxatives, emetic, diuretic and diaphoretic drugs could help in the process of cleansing the body as a whole.

An important indication of adaptogens is as a geriatric agent, preventing or minimizing the physical and cognitive deficits that result from aging. In fact, the elderly population is the main therapeutic target of several phytotherapic medications available in the market.

Chart 2. Portuguese terms and expressions related to the adaptogenic action and possible corresponding in English.

Properties	Indication
Afrodisíaco - aphrodisiac Analéptico - analeptic Anti-estresse - anti-stress Ativador da memória - memory booster Aumenta a libido - increases libido Dinamogênico - dynamogenic Energético - energetic Estimulante sexual - sexual stimulant Excitante das funções cerebrais - excitatory of brain functions Excitante dos órgãos genitais - excitatory of genital organs Fortificante - fortifier Fortificante dos nervos e sistema nervoso - fortifier of the nerves and nervous system Neurotônico - neurotonic Panacéia - Panacea Reconstituinte - restoring Reduz cansaço - reduce tiredness Regenerador - regenerator Rejuvenescedor - rejuvenator Restaurador das forças - restorer of strength Restaurativo - restorative Revigorante - revigorating Revulsivo - revulsive Tônico, tonificante – tonic (general, muscular, of the nervous system) Vitalizante / revitalizante - vitalizing / revitalizing	Abatimento - discouragement Adinamia - adynamia Astenia (geral ou psíquica) – Aesthenia, weakness (general or psychological) Atonia muscular - atonia Cansaço - tiredness (physical or intellectual) Caquexia - cachexia Convalescença - convalescence Debilidade (física, orgânica, sexual) - debility (physical, organic, sexual) Depauperamento do organismo - depletion of the body's reserves Desânimo - despondency Doenças causadas por esgotamento nervoso - illnesses caused by nervous breakdown Enfraquecimento da memória - memory weakness Envelhecimento - aging Esgotamento - exhaustion (physical, nervous, mental) Estafa, fadiga - fatigue Esterilidade / infecundidade - sterility / infertility Estresse - stress Exaustão (física, mental e intelectual) - exhaustion (physical, mental and intellectual) Falta de atenção ou memória - lack of attention or memory Fraqueza geral / orgânica- general / organic weakness Fraqueza infantil - child weakness Impotência sexual - sexual impotence Indisposição - indisposition Lassitude - lassitude Letargia - lethargy Mal de altitude - altitude sickness Marasmo - boredom Memória fraca - weak memory Neurastenia - neurasthenia Neurastenia genital ou sexual - genital or sexual neurasthenia Preguiça - laziness Raciocínio dificultado - impaired reasoning Senilidade - senility Velhice - aging age

With aging, there is a gradual decline in the body functioning as a whole, leading to constant tiredness; physical indisposition; reduction of motivation; learning and memory difficulties; impotence and disinterest in sex, among other deficits (Albert & Knoefel, 1994). Plants prescribed as aphrodisiacs, sexual stimulants, energetic, rejuvenating, or those indicated to fight feebleness, weakness and impaired memory would hence be useful to counterbalance the harm that arises from aging.

Other terms, such as restoring, normalizing and revigorating, regard the property of this class of substance

to help in the recovery from pathological processes and previous debilitation, whether it is in the elderly or the young. Consequently, they are indicated for convalescence; asthenia (general debility); cachexia (state of severe undernourishment); depletion of the body's reserves; fatigue; mental or physical exhaustion, among others.

Sometimes the description of the medical virtues of an adaptogen plant in the popular literature uses expressions as "heightens mental faculties", "beats weakness", "gives the nervous system a boost", or "awakens dormant vital forces". Similar popular terms are used in the traditional medicine of many countries, sometimes within well established "systems", as the *rasayana* (Ayurvedic medicine) and the *jamu* (traditional medical system of Malaysia and India) (Davydov & Krikorian, 2000). Other times, an adaptogen plant receives the reputation of panacea, as in the case of *Panax ginseng* (pan=all; axos=cure). In Brazil, the *Pfaffia paniculata* (Mart.) Kuntze (Amaranthaceae) and other species of Pfaffia are sometimes called "para-tudo" (for-everything, a reference to its broad use), as well as the species *Gomphrena arborescens* L. f. (Amaranthaceae), *Drimys winteri* J.R. Forst. & G. Forst. (Winteraceae) and *Tabebuia aurea* (Silva Manso) Benth. & Hook. f. ex S. Moore (Bignoniaceae) (Lorenzi & Matos, 2002; Mendes & Carlini, 2007).

It is interesting to observe that the commercial names of some ginseng-based phytotherapic medications registered in the Brazilian Ministry of Health mention its alleged usefulness, conveying the idea of a tonic, geriatric or aphrodisiac product. In the middle of the last century there was in Brazil a product commercialized by a laboratory that was in the market at the time, Silva Araújo, called Energil®. Its formula was a combination of phosphate salts and strychnine, testicular extracts and vegetable extracts of muirapuama and catuaba. In the advertisements of the product it was announced as dynamogenic and neurotonic in convalescence; to treat asthenia, emotional exhaustion, insufficiency of genital functions and senility, and it showed the picture of an elderly man in a happy disposition. Another traditional product, Viriliflora® (Figure 1), was commercialized by the laboratory Flora Medicinal. It was composed by the tinctures of *Ptychopetalum olacoides, Tynanthus fasciculatus* Miers (Bignoniaceae) and *Anemopaegma mirandum* (Cham.) Mart. ex DC. (Bignoniaceae) (current botanical names), all of them Brazilian plants popularly used as aphrodisiacs.

Chemical constituents of adaptogen plants

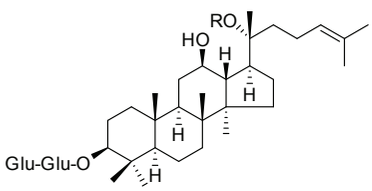
It was initially believed that for a plant to be considered an adaptogen it should be rich in saponins and should not contain alkaloids (Brekhman & Dadymov, 1969; Carlini, 1991). However, it is clear that adaptogen plants are distinctly different as regards their chemical composition; hence their effect cannot be attributed to one single class of substances (Wagner, 1995; Davydov & Krikorian, 2000).

Generally speaking, a set of active principles of one or more classes have a synergic interaction to produce the beneficial effect of adaptogen plants. Therefore, we should highlight the ginsenosides (triterpene glycosides) present in *P. ginseng*, the eleutherosides (phenylpropanoid or coumarin derivatives) in *Eleutherococcus senticosos* (Rupr. & Maxim.) Maxim., Araliaceae, the ginkgolides and bilobalide (terpenoids) of *Ginkgo biloba,* among others (Wagner, 1995; Pang et al., 1996). On basis of their secondary metabolites, Panossian et al. (2007) classified some adaptogen plants as stress-protectors [*P. ginseng, Bryonia alba* L.,Cucurbitaceae, and *Withania somnifera* (L.) Dunal, Solanaceae, and typical adaptogens [*Rhodiola rosea* L., Crassulaceae, and *Schisandra chinensis* (Turcz.) Baill., Schisandraceae].

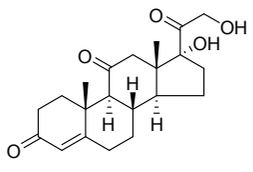
Davydov & Krikorian (2000) suggest that many of the regulatory effects are due to the capacity of the constituents present in those plants to mimetize hormones and endogenous molecules structurally similar. Some saponins and other triterpenic constituents have a chemical structure quite similar to that of steroid hormones, such as ginsenoside Rb_1 (**1**) and ginsenoside Rg_3 (**2**), hence their acting mechanisms are partially attributed to this similarity – see cortisol for comparison (**3**). On the other hand, some phenolic constituents, as lignans and phenylpropanoids, such as eleutheroside B (also called syringin) (**4**), are structurally similar to catecholamines, like noradrenaline (**5**), important mediators of the activation of the sympathetic nervous system (Panossian & Wikman, 2005).

Mechanisms of action of adaptogen plants

While most of the drug classes have specific sites or well established mechanisms of action, adaptogens seem to act through different systems, with the combination



1 R = O-Glu-Glu
2 R = H



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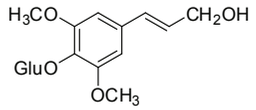

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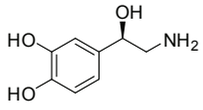

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Figure 1. Flask of Viriliflora®, composed by the tinctures of *Ptychopetalum olacoides, Tynanthus fasciculatus* and *Anemopaegma mirandum.*

of those actions being responsible for their beneficial and protective effects (Wagner et al., 1994; Panossian & Wikman, 2009). It is a known fact that adaptogens might act enhancing the capacity of the body to respond to stressing stimuli by activating/deactivating mediators of response to stress, as corticosteroids, catecholamines and nitric oxide (Panossian et al., 1999; 2007; Rege et al., 1999; Panossian & Wikman, 2005; 2009). Adaptogens may also act in an unspecific way, through its antioxidant and immunomodulating activities, and others (Rege et al., 1999; Davydov & Krikorian, 2000; Chen et al., 2008).

Among the several activities mentioned, the modulation of the hypothalamic-pituitary-adrenal axis (HPA) is probably the most studied, and seems to be one of the main mechanisms of action of adaptogens. Apparently, they do not only modulate the functioning of the axis under stressful conditions, but act on their own as well, acutely stimulating the production of adrenocorticotropic hormone and corticosteroid, slightly changing the basal levels of these hormones that stabilize some time after administration (Wagner, 1995; Panossian et al., 1997; 1999, Panossian & Wikman, 2009). In this case, the adaptogen is described as a mild stressor (stress mimetic) that would have a beneficial effect, increasing the mobilization of energy sources and preventing the need for a more abrupt reaction to stress (Wagner et al., 1994; Panossian et al., 1999, Kimura & Sumiyoshi, 2004). Under situations of chronic stress, adaptogens would act by reestablishing the functioning of the axis, stopping the liberation of stress hormone by the negative feedback mechanism (Figure 2). The role of adaptogens in the HPA would take place mainly by promoting a positive regulation of certain stress modulators, especially the heat shock protein HSP70, which plays a key role in the apoptosis and cell lifespan (Chowdhuri et al., 2002; Panossian et al., 2009; Panossian & Wikman, 2009).

A second system that seems to play an important role in the set of positive actions of adaptogens is the immune system. A number of plants considered adaptogens are immunostimulants: *Eleutherococcus senticosus, Withania somnifera, Bryonia alba, Ocimum sanctum* L. Lamiaceae, and the *Panax ginseng*, as well (Wagner, 1995; Panossian et al., 1997; Davydov & Krikorian, 2000; Davis & Kuttan, 2000; Mediratta et al., 2002; Kimura & Sumiyoshi, 2004). Evidence shows that the immune, sympathoadrenal systems and the HPA axis (stress system) share several mediators, with effects on target organs in common (Brown et al., 1990; Kvetnansky et al., 1995; Carrasco & van de Kar, 2003).

Another effect that certainly contributes to the set of actions of adaptogens is its antioxidant activity, even though this activity is not clearly observed in all plants considered adaptogens. The role of antioxidants in the prevention of neurodegenerative diseases and those related to aging is well known (Harman, 1994; Moosmann & Behl, 2002; Di Matteo & Esposito, 2003), which reinforces the importance of this activity by the plants commonly used to decrease the deficits resulting from aging. Some examples are *Ginkgo biloba* (Bridi et al., 2001), *Schisandra chinensis* (Hancke et al., 1999), *Rhodiola rosea* (Chen et al., 2008) and *Eleutherococcus senticosus* (Lin & Huang, 2000; Chen et al., 2008), plants with a considerable antioxidant action.

Since they act by improving cognitive performance, it is believed that adaptogens can also modulate the cholinergic system and other neurotransmission systems. Some studies corroborate this hypothesis, suggesting that *P. ginseng* and *G. biloba* interfere in the cholinergic and monoaminergic neurotransmission (Petkov et al., 2003; Liu et al., 2004). Elisabetsky & Siqueira (1998) also state that the modulation of the dopaminergic, monoaminergic and serotonergic systems are important targets for plants and preparations used in conditions of nervous weakness, depression and sexual impotence.

Other mechanisms that seem to contribute to the action of adaptogens include the modulation of genic transcription and protein synthesis, and the modulation of the several glycolysis phases. For more details on the molecular mechanisms of adaptogens, please see Panossian & Wikman (2009).

Brazilian plants with an adaptogen profile

In Brazil, many plants used to improve memory, sexual and physical performance, or to preserve a healthy state (Chart 3), are generically called tonics or fortifiers. Several parts of those plants can be used, and sometimes the plant is used as food or drink, as in the case of buriti (*Mauritia flexuosa* L. f., Arecaceae), cocoa (*Theobroma cacao* L., Sterculiaceae), mate (*Ilex paraguariensis* A. St.-Hil., Aquifoliaceae) and guarana (*Paullinia cupana*). Table 1 compares the popular uses of the main Brazilian plants presented in Chart 3 with the classic adaptogens well established in the literature. One can observe that the Brazilian plants are used mainly as aphrodisiacs, while

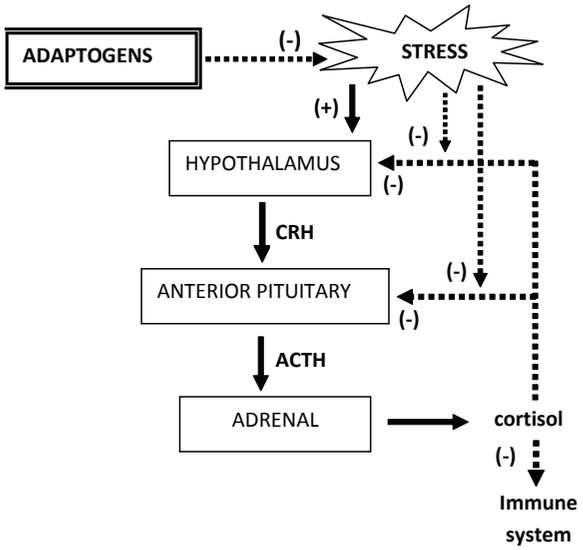

Figure 2. Response to stress by the hypothalamic-pituitary-adrenal axis. In situations of chronic stress, the mechanism of negative feed back is lost. Adaptogens restore the functioning of the axis. Thick lines: stimulation; dotted lines: inhibition.

classic adaptogens are indicated mainly for their anti-stress property. Among the Brazilian plants, guarana is the best known internationally, being indicated as tonic, stimulant, to improve memory, among other uses (Mendes & Carlini, 2007).

Native of the Amazon region, guarana was already used by the native Indians as tonic and stimulant before Brazil was discovered. The *in vitro* evaluation of the antioxidant effect of guarana seeds showed a powerful action, possibly as a result of the large concentration of tannins (Mattei et al., 1998). The administration of guarana extract to mice, both acutely and chronically, partially reversed the scopolamine-induced amnesia, and the addition of the extract to their drinking water prolonged the swimming time of the animals, in some evaluation intervals (Espínola et al., 1997).

In a study carried out with young volunteers, Kennedy et al. (2004) observed an increase in their cognitive performance in parameters of attention, working memory and accuracy after treatment with guarana, ginseng or a combination of the two plants. A later study showed that a multivitamin supplement containing guarana reduced the mental fatigue of volunteers after tests of mental effort (Kennedy et al., 2008).

The effects of *Pfaffia glomerata*, one of the species known as Brazilian ginseng, were also evaluated as to its adaptogenic effects. Aging mice showed improvement in learning and memory after chronic treatment with *P. glomerata* extract (Marques et al., 2004). Another study detected a protective effect against ulcerogenesis, such action being attributed to the effect of the plant in increasing the secretion of nitric oxide (Freitas et al., 2004). Elderly volunteers submitted to ergospyrometric and cognitive tests after the use of *P. glomerata* showed improvement in some cognitive tests and no toxic effects (Marques, 1998; Marques et al., 2002). However, no improvement was detected in the parameters analyzed in the test of effort. Even though scientific studies have focused mainly on the *P. glomerata*, other species of *Pfaffia* are commonly used by the population and sold generically as Brazilian ginsengs (also known outside Brazil as "suma"), being the *Pfaffia paniculat*a and the *Pfaffia iresinoides* (Kunth) Spreng (Amaranthaceae) the most common (Marques, 1998; Davydov & Krikorian, 2000).

Another Brazilian plant that has been extensively studied, with results that corroborate its use as an adaptogen, is muirapuama (*Ptychopetalum olacoides*). Muirapuama is used in the North of Brazil as a nerve tonic and to increase physical and sexual performance. Studies with standardized extracts of its roots showed antioxidant, neuroprotective, anti-stress properties, and reversal in states of induced amnesia (da Silva et al., 2004; Siqueira et al., 2004; 2007; Piato et al., 2010).

With fewer studies on their properties but the same popularity of muirapuama, several species designated as catuaba in different regions of Brazil stand out. There is great confusion as to the identification of which species are actually used by the population for medical purposes and those available in the market (Ducke, 1966; Lorenzi & Matos, 2002). In the state of Minas Gerais and in the Middle-West of Brazil, *garrafadas* (bottled brew) are made with the bark and the roots of the species *Anemopaegma arvense* (synonym: *A. mirandum*), while in other regions the bark of the species *Trichilia catigua* is used. Other species also described as catuaba are *Erythroxylum vacciniifolium* Mart., Erythroxylaceae, and *Tetragastris catuaba* Soares da Cunha, Burseraceae, to mention a few (Lorenzi & Matos, 2002). Some studies suggest a possible analgesic and antidepressant effect for the *Trichilia catigua* mediated by dopaminergic mechanisms (Campos et al., 2005; Viana et al., 2009), while rare are the studies on *Anemopaegma arvense* reported in the literature.

As in the case of catuaba, the roots of nó-de-cachorro (*Heteropterys aphrodisiaca*) are often prepared as *garrafadas*, and employed against physical debility and as a sexual stimulant. The chronic treatment of aging rats with hydroalcoholic extract of nó-de-cachorro reversed the memory impairment observed in the passive avoidance and in the T maze (Galvão et al., 2002). Later studies showed that the treatment time and the dose could be reduced, and suggest the involvement of the dopaminergic system among the mechanisms of action of *H. aphrodisiaca* (Galvão, 2003; Galvão et al., 2004/2005).

Damiana (*Turnera diffusa*, synonym *Turnera*

Chart 3. Main Brazilian plants used for purposes similar to those of an adaptogen.

Plant	Region where it is found	Popular uses
Buriti - *Mauritia flexuosa* L. f., Arecaceae	Cerrado, marshy regions and riparian forests	The oil and the pulp are used as energetic and fortifier
Cacau - *Theobroma cacao* L., Sterculiaceae	Native of the tropical forests of Central America and South America; also grown in Bahia	Raw material of chocolate, the seeds (and sometimes the pulp) are used as a powerful energetic and to supply more resistance against low temperatures
Catuaba - *Anemopaegma arvense* (Vell.) Stellfeld ex de Souza, Bignoniaceae	Cerrado, in central Brazil	The root is considered a powerful tonic, aphrodisiac, used to treat neurasthenia and difficulty to concentrate
Catuaba - *Trichilia catigua* A. Juss., Meliaceae	Brazilian Cerrado, mainly in Bahia	The part used of this species of catuaba is the bark, and it is indicated for the same medicinal uses mentioned above
Cipó-caboclo - *Davilla rugosa* Poiret., Dilleniaceae	Present mainly in the Atlantic Forest, but scattered all over tropical Brazil	The whole plant is used as stimulant and aphrodisiac, but each part has its own use
Cipó-cravo - *Tynanthus elegans* Miers, Bignoniaceae	Broad geographic distribution, including the Southeast of Brazil and Bolivia	The whole plant is used as infusion or decoction (roots) against weakness, exhaustion and impotence
Damiana - *Turnera diffusa* Willd. ex Schult., Turneraceae	From the Southern of California to Argentina. In Brazil it is found mainly in the agreste and the Northeastern sertão (backcountry)	Leaves and aerial parts are used as tonic and aphrodisiac
Fáfia/Brazilian ginseng - *Pfaffia glomer*ata (Spreng.) Pedersen, Amaranthaceae, and other species	Regions of tropical climate, can be found all over Brazil and abundantly in Paraná	The roots of several species of fáfia are used as tonic and aphrodisiac, as a substitute of the Korean ginseng, sometimes being part of adulterations of products sold as *P. ginseng*
Guarana - *Paullinia cupana* Kunth, Sapindaceae	Amazon region; grown in many other areas	The seed powder is used as general tonic, stimulant, and to fight physical and mental exhaustion.
Mate - *Ilex paraguariensis* A. St.-Hil., Aquifoliaceae	Pampas (South American lowlands), in the South of Brazil and South America, mainly in high areas	The leaves are used to provide improvement of general disposition. Usually used as chimarrão (a kind of infusion) or tereré (as a cold tea)
Muirapuama - *Ptychopetalum olacoides* Benth., Olacaceae	Amazon forest	Roots and bark are considered powerful neuromuscular tonic and are also used as aphrodisiac
Nó-de-cachorro - *Heteropterys aphrodisiaca* O. Mach, Malpiguiaceae	Pantanal (wetland) and Cerrado	Roots are prepared in garrafadas as sexual tonic and to fight weakness

Source: Corrêa (1984), Lorenzi & Matos (2002) and Mendes & Carlini (2007).

aphrodisiaca Ward) is a bush that can be largely found in the Americas. In Brazil, it is most easily found in the Northeast region. The plant is used as an aphrodisiac and against neurasthenia, and has a history of use that dates back to the ancient Maya civilization. In fact, the largest production and commercialization of damiana is in Mexico, where the plant is included in the official pharmacopeia. Studies with rodents support the use of the plant as a sexual stimulant (Arletti et al., 1999; Estrada-Reyes et al., 2009) and also present evidence of its anxiolytic action (Kumar & Sharma, 2005). On the other hand, a recent study did not detect any positive effects on rodents evaluated in tests of memory and stress after treatment with hydroalcoholic extract of de *T. diffusa* (Bezerra et al., 2011).

Other Brazilian plants with popular uses similar to those of a typical adaptogen were identified by means of a survey in books on the Brazilian flora and its popular medicine (Mendes, 2005; Mendes & Carlini, 2007).

Final considerations

As this article discussed, adaptogens comprise a particular class of pharmacological agents with multiple actions and some peculiarities. However, the diversity of indications and alleged miracles for this type of drugs led them to be disdained by the medical community.

The biomedical model has always postulated that each drug would be useful for one single illness, acting on receptors or other targets specific to that pathology (Capra, 1993). Nowadays we can observe a change in this paradigm, with the treatment of the body as a whole being valued, and a special emphasis placed on the drugs known as multi-target, that is, drugs that act through different mechanisms. Many phytotherapeutic drugs largely accepted seem to act in that way, possibly by the synergic action of their active principles (Spinella, 2002; Ulrich-Merzenich et al., 2007). Adaptogen plants are characterized by their diffuse and

Table 1. (+) Popular uses described for the main adaptogen plants and for some Brazilian plants with the same profile. Double-plus (++) indicates the main uses. The circles (o) indicate that the plant is not used for that purpose or that the use is very limited.

Plant	Folk use				
	anti-stress	enhancement of mental capacity	↑ physical performance and endurance	aphrodisiac	anti-aging
Panax ginseng C.A. Meyer, Araliaceae	++	+	++	+	+
Eleutherococcus senticosus (Rupr. & Maxim.) Maxim., Araliaceae	++	+	++	+	+
Rodiola rosea L. (Crassulaceae)	++	+	+	o	o
Ginkgo biloba L., Ginkgoaceae[1]	+	++	+	o	++
Guaraná *Paulinia cupana* Kunth, Sapindaceae	+	++	++	+	+
Fáfia *Pfaffia* sp., Amaranthaceae	+	+	+	++	+
Muirapuama *Ptychopetalum olacoides* Benth., Olacaceae	+	+	+	++	+
Catuaba[2]	+	+	+	++	+
Damiana *Turnera diffusa* Willd. ex Schult., Turneraceae	o	o	+	++	o
Nó-de-cachorro *Heteropterys aphrodisiaca* O. Mach, Malpiguiaceae	+	+	+	++	+

[1]*Ginkgo biloba* is not considered a classical adaptogen, but it is included here due its similar effects.
[2]The species *Anemopaegma arvense* (Vell.) Stellfeld ex de Souza (Bignoniaceae) and *Trichilia catigua* A. Juss. (Meliaceae) are popularly used for the same purposes.

unspecific action on the body (Wahlström, 1987; Davydov & Krikorian, 2000).

Another reason why the scientific community does not accept adaptogens is the difficulty to obtain results that could verify their alleged effects using classical pharmacological methods (Ramachandran et al., 1990; Carlini, 1991; Rege et al., 1999). Another problem is that the beneficial actions of adaptogens can be better observed after chronic treatment. One should not forget that, within this type of use, an adaptogen is ingested mainly for the individual to remain healthy, that is, preventively. Therefore, the models most often employed in the evaluation of an adaptogen are those in which animals are submitted to stress, hence the capacity of the plant to protect against that type of damage can be evaluated, in other words, its prophylactic use (Wagner et al., 1994; Rege et al., 1999; Panossian & Wikman, 2005). Animal models of memory and learning are also commonly used, since the property of adaptogens to improve cognitive processes is another key point among their multiplicity of actions. Nevertheless, these different aspects (physical resistance, cognition and anti-stress effect) can not be easily evaluated in humans, a reason why many adaptogens come up against scientific corroboration. The evaluation of biochemical markers of response to stress, such as the hormones of the HPA axis, nitric oxide, arachidonic acid, heat shock proteins, eicosanoids, among others, have proved quite useful to support the physiological and behavioral data routinely evaluated, and may be a good way to help identify adaptogen plants.

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References

Albert MS, Knoefel JE 1994. *Clinical neurology of aging.* 2 ed. New York: Oxford University Press.

Arletti R, Benelli A, Cavazzuti E, Scarpetta G, Bertolini A 1999. Stimulating property of *Turnera diffusa* and *Pfaffia paniculata* extracts on the sexual behavior of male rats. *Psychopharmacology 143*: 15-19.

Bezerra AG, Mendes FR, Tabach R, Carlini EA 2011. Effects of a hydroalcoholic extract of *Turnera diffusa* Willd. ex Schult., Turneraceae, in tests for adaptogenic activity. *Rev Bras Farmacogn 21*: 121-127.

Brekhman II, Dardymov IV 1969. New substances of plants origin which increase nonspecific resistence. *Annu Rev Pharmacol 9*: 419-430.

Bridi R, Crossetti FP, Steffen VM, Henriques AT 2001. The antioxidant activity of standardized extract of *Ginkgo biloba* (EGB 761) in rats. *Phytother Res 15*: 449-451.

Brown MR, Koob GF, Rivier C 1990. *Stress: neurobiology and neuroendocrinology.* New York: Marcel Dekker Inc.

Campos MM, Fernandes ES, Ferreira J, Santos AR, Calixto JB 2005. Antidepressant-like effects of *Trichilia catigua* (catuaba) extract: evidence for dopaminergic-mediated mechanisms. *Psychopharmacology (Berl) 182*: 45-53.

Capra F 1993. O modelo biomédico. In Capra F (ed.) *O ponto de mutação.* São Paulo: Editora Cultrix, p. 116-155.

Carlini EA 1991. Efeito adaptógeno ou resistógeno de algumas plantas. In Buchillet D (ed) *Medicinas tradicionais e medicina ocidental na Amazônia.* Belém: Edições Cejup, p. 45-59.

Carrasco GA, van de Kar LD 2003. Neuroendocrine pharmacology of stress. *Eur J Pharmacol 463*: 235-272.

Chan K 2005. Chinese medicinal materials and their interface with Western medical concepts. *J Ethnopharmacol 96*: 1-18.

Chen TS, Liou SY, Chang YL 2008. Antioxidant evaluation of three adaptogen extracts. *Am J Chin Med 36*: 1209-1217.

Chowdhuri DK, Parmar D, Kakkar P, Shukla R, Seth PK, Srimal RC 2002. Antistress effects of bacosides of *Bacopa monnieri:* modulation of Hsp_{70} expression, superoxide dismutase and cytochrome P_{450} activity in rat brain. *Phytother Res 16*: 639-645.

Corrêa MP 1984. *Dicionário das plantas úteis do Brasil e das exóticas cultivadas.* Brasília: Ministério da agricultura/ Instituto brasileiro de desenvolvimento florestal.

da Silva AL, Piato ALS, Bardini S, Netto CA, Nunes DS, Elisabetsky E 2004. Memory retrieval improvement by *Ptychopetalum olacoides* in young and aging mice. *J Ethnopharmacol 95*: 199-203.

Dahanukar SA, Thatte UM 1997. Current status of Ayurveda in phytomedicine. *Phytomedicine 4*: 359-368.

Davis L, Kuttan G 2000. Immunomodulatory activity of *Withania somnifera. J Ethnopharmacol 71*: 193-200.

Davydov M, Krikorian AD 2000. *Eleutherococcus senticosus* (Rupr. & Maxim.) Maxim. (Araliaceae) as an adaptogen: a closer look. *J Ethnopharmacol 72*: 345-393.

Di Matteo V, Esposito E 2003. Biochemical and therapeutic effects of antioxidants in the treatment of Alzheimer's disease, Parkinson's disease, and amyotrophic lateral sclerosis. *Curr Drug Targets CNS Neurol Disord 2*: 95-107.

Ducke A 1966. A catuaba na botânica sistemática científica e pseudo-científica. *Rev Bras Farm 47*: 267-271.

Elisabetsky E, Siqueira IR 1998. Is there a psychopharmacological meaning for traditional tonics? In Prendergast HDV, Etkin NL, Harris DR, Houghton PJ (eds.) *Plants for food and medicine.* London: Royal Botanical Gardens, p. 373-385.

Espínola EB, Dias RF, Mattei R, Carlini EA 1997. Pharmacological activity of guarana (*Paullinia cupana* Mart.) in laboratory animals. *J Ethnopharmacol 55*: 223-229.

Estrada-Reyes R, Ortiz-López P, Gutiérrez-Ortíz J, Martínez-Mota L 2009. *Turnera diffusa* Wild (Turneraceae) recovers sexual behavior in sexually exhausted males. *J Ethnopharmacol 123*: 423-429.

Freitas CS, Baggio CH, Da Silva-Santos JE, Rieck L, Santos CAM, Júnior CC, Ming LX, Cortez DAG, Marques MCA 2004. Involvement of nitric oxide in the gastroprotective effects of an aqueous extract of *Pfaffia glomerata* (Spreng) Pedersen, Amaranthaceae, in rats. *Life Sci 74*: 1167-1179.

Fulder S 1980. *The root of being. Ginseng and the pharmacology of harmony.* London: Huchinson and Co.

Galvão SMP 2003. *Heteropterys aphrodisiaca* O. Mach. *(extrato BST 0298): estudos pré-clínicos farmacológicos e toxicológicos.* São Paulo, 163p. Tese de Doutorado, Universidade Federal de São Paulo.

Galvão SMP, Marques LC, Oliveira MGM, Carlini EA 2002. *Heteropterys aphrodisiaca* (extract BST0298): a Brazilian plant that improves memory in aged rats. *J Ethnopharmacol 79*: 305-311.

Galvão SMP, Mendes FR, Oliveira GM, Mattei R, Carlini ELA 2004/2005. Possíveis efeitos adaptógenos da *Heteropterys aphrodisiaca* O. Mach. - extrato BST 0298: uma planta da área do pantanal brasileiro. *Arq Bras Fitomed Cient 2*: 41-55.

Hancke JL, Burgos RA, Ahumada F 1999. *Schisandra chinensis* (Turcz.) Baill. *Fitoterapia 70*: 451-471.

Harman D 1994. Free-radical theory of aging. Increasing the functional life span. *Ann NY Acad Sci 717*: 1-15.

Kennedy DO, Haskell CF, Robertson B, Reay J, Brewster-Maund C, Luedemann J, Maggini S, Ruf M, Zangara A, Scholey AB 2008. Improved cognitive performance and mental fatigue following a multi-vitamin and mineral supplement with added guarana (*Paullinia cupana*). *Appetite 50*: 506-513.

Kennedy DO, Haskell CF, Wesnes KA, Scholey AB 2004. Improved cognitive performance in human volunteers following administration of guarana (*Paullinia cupana*) extract: comparison and interaction with *Panax ginseng. Pharmacol Biochem Behav 79*: 401-411.

Kimura Y, Sumiyoshi M 2004. Effects of various *Eleutherococcus senticosus* cortex on swimming time, natural killer activity and corticosterone level in forced swimming stressed mice. *J Ethnopharmacol 95*: 447-453.

Kumar S, Sharma A 2005. Anti-anxiety activity studies of various extracts of *Turnera aphrodisiaca* Ward. *J Herb Pharmacother 5*: 13-21.

Kvetnansky R, Pacak K, Fukuhara K, Viskupic E, Hiremagalur B, Nankova B, Goldstein DS, Sabban EL, Kopin IJ 1995. Sympathoadrenal system in stress; interaction with the hypothalamic-pituitary-adrenocortical system. *Ann NY Acad Sci 771*: 131-158.

Lin CC, Huang PC 2000. Antioxidant and hepatoprotective effects of *Acathopanax senticosus. Phytother Res 14*: 489-494.

Liu JX, Cong WH, Xu L, Wang JN 2004. Effect of combination of extracts of ginseng and *Ginkgo biloba* on acetylcholine in amyloid beta-protein-treated rats determined by an improved HPLC. *Acta Pharmacol Sin 25*: 1118-1123.

Lorenzi H, Matos FJA 2002. *Plantas medicinais no Brasil: nativas e exóticas cultivadas.* Nova Odessa: Instituto Plantarum.

Marques LC 1998. *Avaliação da ação adaptógena das raízes de Pfaffia glomerata* (Sprengel) Pedersen - *Amaranthaceae.* São Paulo, 145p. Tese de Doutorado, Universidade Federal de São Paulo.

Marques LC, Danucalov MA, Torres F, Galduróz JCF, Carlini ELA, Silva AC 2002. Estudo clínico duplo-cego de extrato padronizado (BNT-08) das raízes de *Pfaffia*

glomerata (Spreng.) Pedersen: avaliação do efeito tônico em atividade física. *Rev Bras Farmacogn 12*: 44-47.

Marques LC, Galvão SMP, Espínola E, Dias RF, Menezes MGM, Carlini ELA 2004. Psychopharmacological assessment of *Pfaffia glomerata* roots (extract BNT-08) in rodents. *Phytother Res 18*: 566-572.

Mattei R, Dias RF, Espínola EB, Carlini EA, Barros SBM 1998. Guarana (*Paullinia cupana*): toxic behavioral effects in laboratory animals and antioxidant activity *in vitro. J Ethnopharmacol 60*: 111-116.

Mediratta PK, Sharma KK, Singh S 2002. Evaluation of immunomodulatory potential of *Ocimum sanctum* seed oil and its possible mechanism of action. *J Ethnopharmacol 80*: 15-20.

Mendes FR 2005. *Avaliação farmacológica da carqueja (Baccharis trimera) e do cipó-caboclo (Davilla rugosa), duas plantas brasileiras utilizadas popularmente como tônicas, em testes para ação adaptógena.* São Paulo, 156p. Tese de doutorado, Universidade Federal de São Paulo.

Mendes FR, Carlini EA 2007. Brazilian plants as possible adaptogens: an ethnopharmacological survey of books edited in Brazil. *J Ethnopharmacol 109*: 493-500.

Moosmann B, Behl C 2002. Antioxidants as treatment for neurodegenerative disorders. *Expert Opin Investig Drugs 11*: 1407-1435.

Pang Z, Pan F, He S 1996. Ginkgo biloba L.: history, current status and future prospects. *J Altern Complement Med 2*: 359-363.

Panossian A, Wagner H 2005. Stimulating effect of adaptogens: an overview with particular reference to their efficacy following single dose administration. *Phytother Res 19*: 819-838.

Panossian A, Gabrielian E, Wagner H 1997. Plant adaptogens. II. *Bryonia* as an adaptogen. *Phytomedicine 4*: 85-99.

Panossian A, Hambardzumyan M, Hovhanissyan A, Wikman G 2007. The adaptogens Rhodiola and Schizandra modify the response to immobilization stress in rabbits by suppressing the increase of phosphorylated stress-activated protein kinase, nitric oxide and cortisol. *Drug Target Insights 1*: 39-54.

Panossian A, Wikman G 2005. Effect of adaptogens on the central nervous system. *Arq Bras Fitomed Cient 2*: 109-131.

Panossian A, Wikman G 2009. Evidence-based efficacy of adaptogens in fatigue, and molecular mechanisms related to their stress-protective activity. *Curr Clin Pharmacol 4*: 198-219.

Panossian A, Wikman G, Kaur G, Asea A 2009. Adaptogens exert a stress-protective effect by modulation of expression of molecular chaperones. *Phytomedicine 16*: 617-622.

Panossian A, Wikman G, Wagner H 1999. Plant adaptogens. III. Earlier and more recent aspects and concepts on their mode of action. *Phytomedicine 6*: 287-300.

Petkov VD, Belcheva S, Petkov VV 2003. Behavioral effects of *Ginkgo biloba* L., *Panax ginseng* C.A. Mey. and Gincosan®. *Am J Chin Med 31*: 841-855.

Piato AL, Detanico BC, Linck VM, Herrmann AP, Nunes DS, Elisabetsky E 2010. Anti-stress effects of the "tonic" *Ptychopetalum olacoides* (Marapuama) in mice. *Phytomedicine 17*: 248-253.

Ramachandran U, Divekar HM, Grover SK, Srivastava KK 1990. New experimental model for the evaluation of adaptogenic products. *J Ethnopharmacol 29*: 275-281.

Rege NN, Thatte UM, Dahanukar SA 1999. Adaptogenic properties of six *Rasayana* herbs used in Ayurvedic medicine. *Phytother Res 13*: 275-291.

Russo E 2001. Adaptogens. In Russo E (ed.) *Handbook of psychotropic herbs. A scientific analysis of herbal remedies for psychiatric conditions.* New York: The Haworth Press, Inc., p. 181-198.

Santos RF, Galduróz JCF, Balbieri A, Castiglioni MLV, Ytaya LY, Bueno OFA 2003. Cognitive performance, SPECT, and blood viscosity in elderly non-demented people using *Ginkgo biloba. Pharmacopsychiatry 36*: 127-133.

Siqueira IR, Cimarosti H, Fochesatto C, Nunes DS, Salbego C, Elisabetsky E, Netto CA 2004. Neuroprotective effects of *Ptychopetalum olacoides* Bentham (Olacaceae) on oxygen and glucose deprivation induced damage in rat hippocampal slices. *Life Sci 75*: 1897-1906.

Siqueira IR, Fochesatto C, Torres IL, da Silva AL, Nunes DS, Elisabetsky E, Netto CA 2007. Antioxidant activities of *Ptychopetalum olacoides* ("muirapuama") in mice brain. *Phytomedicine 14*: 763-769.

Spinella M 2002. The importance of pharmacological synergy in psychoactive herbal medicines. *Altern Med Rev 7*: 130-137.

Ulrich-Merzenich G, Zeitler H, Jobst D, Panek D, Vetter H, Wagner H 2007. Application of the "-omic-" technologies" in phytomedicine. *Phytomedicine 14*: 70-82.

Ven Murthy MR, Ranjekar PK, Ramassamy C, Deshpande M 2010. Scientific basis for the use of Indian ayurvedic medicinal plants in the treatment of neurodegenerative disorders: ashwagandha. *Cent Nerv Syst Agents Med Chem 10*: 238-246.

Viana AF, Maciel IS, Motta EM, Leal PC, Pianowski L, Campos MM, Calixto JB 2009. Antinociceptive activity of *Trichilia catigua* hydroalcoholic extract: new evidence on its dopaminergic effects. *Evid Based Complement Alternat Med*: (doi:10.1093/ecam/nep144).

Wagner H, Nörr H, Winterhoff H 1994. Plant adaptogens. *Phytomedicine 1*: 63-76.

Wagner HKM 1995. Immunostimulants and adaptogens from plants. In Arnason JT, Mata R, Romeo JT (eds.) *Phytochemistry of medicinal plants*. New York: Plenum Press, p. 1-18.

Wahlström M 1987. *Adaptogens. Nature's key to well-being.* Gotemburg: Utgivare Publisher.

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