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Eleutherococcus, Schisandra, Rhodiola and Ginseng, for stress and fatigue - a review

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Abstract

Introduction. Eleutherococcus senticosus (ES), Schisandra chinensis (SC), Rhodiola rosea (RR) and Panax ginseng GSG are well known for their adaptive role.

Objectives. The objective was to highlight the interest for the research of ES, SC, RR and GSG adaptogens in relation to stress, mental stress, oxidative stress, fatigue, mental fatigue.

Results. Of the four adaptogens, the greatest interest in research was for GSG and the lowest for ES. For each adaptogen, relative to N, the interest in research related to keyword combinations was reduced. For all four adaptogens, keyword combinations were most studied for S. For all keyword combinations, the greatest interest in research was shown for RR and GSG respectively. For all keyword combinations, the greatest interest in research was for studies: a) on animals, in the case of S, OS and GSG+MS; on human subjects, for MS (except GSG+MS), F and MF; b) with subjects of both genders; c) with subjects aged between 19-44 years, excepting GSG+S, GSG+OS and GSG+F.

Instead of conclusions. ES, SC, RR and GSG are described as adaptogens, having important effects in stress modulation and in reducing oxidative stress and fatigue, including mental fatigue.

Key words: Eleutherococcus senticosus, Schisandra chinensis, Rhodiola Rosea, Ginseng, adaptogens, stress, oxidative stress, fatigue

Introduction

The adaptogen concept is examined from a historical, biological, chemical, pharmacological and medical perspective using a wide variety of primary and secondary literature (Davydov & Krikorian, 2000). The term adaptogen was introduced into scientific literature in 1958 to denote substances that increase the "state of non-specific resistance" during stress, based on Hans Selye's theory of stress and the general adaptation syndrome (Panossian, 2013). An adaptogen increases body resistance to physically, chemically or biologically noxious factors, thereby having a normalizing effect on body functions and inflicting no harm (Levin, 2015). The plants with adaptogenic properties cited in the literature include Eleutherococcus senticosus, Schisandra chinensis, Rhodiola rosea and Panax ginseng (Panossian, 2017).

The root of Acanthopanax senticosus (also called Eleutherococcus senticosus or Siberian ginseng) has been used extensively in China, Russia and Japan as an adaptogen to fight stress and fatigue (Huang et al., 2011).

Schisandra chinensis is often referred to as an example of medicinal plant used in modern Chinese medicine; it first gained recognition as an adaptogen in the official medicine of the USSR in the early 1960s, principally as a result of the large number of pharmacological and clinical studies carried out by Russian scientists in the preceding two decades; it increases the physical working capacity and confers a stress-protective effect against a broad spectrum of harmful factors (Panossian & Wikman, 2008).

Rhodiola is a genus of medicinal plants that originated in Asia and Europe and are used traditionally as adaptogens, antidepressants, and anti-inflammatory remedies; these

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plants are rich in polyphenols, and salidroside and tyrosol are the primary bioactive marker compounds in the standardized extracts of Rhodiola rosea (Chiang et al., 2015).

Panax ginseng (also known as ginseng and Korean ginseng) is one of the best known and most studied adaptogens; it is the most studied among plants belonging to the *Panax* genus; it is grown in China, Korea, Japan, and Russia while having a long-time (some thousands years) history of administration in oriental medicine and is available in many forms (Oliynyk & Oh, 2013).

Hypothesis

Eleutherococcus senticosus (ES), Schisandra chinensis (SC), Rhodiola rosea (RR) and Panax ginseng GSG are well known for their adaptive role. Less has been explored their comparative influence on some features related to stress, mental stress, oxidative stress, fatigue, mental fatigue, by referring to PubMed publications.

Objectives

The objective was to highlight the interest of research in ES, SC, RR and GSG adaptogens in relation to stress, mental stress, oxidative stress, fatigue, mental fatigue.

Material and methods

Analysis of PubMed publications was made for the four selected adaptogens: ES, SC, RR, GSG.

To evaluate the relationship of the four chosen adaptogens with sport, we selected the following areas of analysis, which are frequently approached in relation to stress and fatigue: stress (S), mental stress (MS), oxidative stress (OS), fatigue (F), mental fatigue (MF).

The adaptogens - stress and fatigue relationship was analyzed in two types of investigations:

A. Analysis for the keyword combinations. The same keyword combinations were selected for the four adaptogens. They are presented with their abbreviations (Abb) in Table I.

B. Analysis for all keyword combinations, for some filters, with their corresponding subfilters:

- *Species:* other animals (A), humans (H)
- *Sex:* human male (HM), human female (HF), human male and female (HM+HF)
- *Age:* birth-18 years (0-18), 19-44 years (19-44), 45-64 years (45-64), 65+ years (>65), 80+ years (>80)

Results

Data collection was performed during October 2018. For all groups, data distribution was normal, according to the Kolmogorov-Smirnov test. The analysis was made on the chosen time periods.

A. Analysis for the keyword combinations

In Tables II, III, IV and V, the following are presented: periods of time during which articles containing these keyword combinations were published on PubMed site; duration of these periods (No years); total number of publications for the entire period (N); and number of publications per year (N/year). The presentation compares the total number of publications for the four chosen adaptogens.

Table II

Analysis for the chosen keywords, regarding ES

Keyword combinations	Period	No years	N	N/year
ES	1965-2018	**53**	586	11.06
ES+S	1967-2018	51	**74**	**1.45**
ES+MS	1990-2015	25	16	0.64
ES+OS	2001-2018	17	19	1.12
ES+F	1969-2016	47	30	0.64
ES+MF	2004-2014	*10*	*4*	*0.4*

Table III

Analysis for the chosen keywords, regarding SC

Keyword combinations	Period	No years	N	N/year
SC	1945-2018	**73**	989	13.55
SC+S	1995-2018	23	**110**	**4.7**
SC+MS	2005-2016	11	14	1.3
SC+OS	1995-2018	23	79	3.43
SC+F	1956-2016	60	15	0.25
SC+MF	1956-2014	58	4	*0.07*

Table IV

Analysis for the chosen keywords, regarding RR

Keyword combinations	Period	No years	N	N/year
RR	1963-2018	**55**	814	14.8
RR+S	1986-2018	32	**191**	5.94
RR+MS	1986-2016	30	46	1.53
RR+OS	2000-2008	*8*	95	**11.9**
RR+F	2000-2018	18	66	3.67
RR+MF	2000-2018	18	20	1.12

Table V

Analysis for the chosen keywords, regarding GSG

Keyword combinations	Period	No years	N	N/year
GSG	1940-2018	**78**	8823	113.1
GSG+S	1964-2018	54	**810**	15
GSG+MS	1979-2016	37	76	2.06
GSG+OS	1998-2017	*19*	465	**24.4**
GSG+F	1964-2018	54	174	3.23
GSG+MF	1992-2017	25	15	*0.6*

Table I

Keyword combinations for the four adaptogens

Keyword combinations	Abb	Keyword combinations	Abb	Keyword combinations	Abb	Keyword combinations	Abb
ES	ES	SC	SC	RR	RR	GSG	GSG
ES and stress	ES+S	SC and stress	SC+S	RR and stress	RR+S	GSG and stress	GSG+S
ES and mental stress	ES+MS	SC and mental stress	SC+MS	RR and mental stress	RR+MS	GSG and mental stress	GSG+MS
ES and oxidative stress	ES+OS	SC and oxidative stress	SC+OS	RR and oxidative stress	RR+OS	GSG and oxidative stress	GSG+OS
ES and fatigue	ES+F	SC and fatigue	SC+F	RR and fatigue	RR+F	GSG and fatigue	GSG+F
ES and mental fatigue	ES+MF	SC and mental fatigue	SC+MF	RR and mental fatigue	RR+MF	GSG and mental fatigue	GSG+MF

The comparison for ES, SC, RR and GSG shows that: the longest period of publication (78), the highest N (8823) and the highest N/years (113.1) were all for GSG.

The publication periods for the keyword combinations were the longest (in bold) for ES+S (53), SC+S (73), RR+S (55), GSG+S (78), and the shortest (*in italics*) for ES+MF (10), RR+OS (9\8), GSG+OS (19).

N for the keyword combinations was the highest (in bold) for ES+S (74), SC+S (110), RR+S (191), GSG+S (810), and the lowest (*in italics*) for ES+MF (4).

N/year for the keyword combinations was the highest (in bold) for ES+S (1.45), SC+S (4.7), RR+OS (11.9), GSG+OS (24.4), and the lowest (*in italics*) for SC+MF (0.07), GSG+MF (0.6).

B. Analysis for all keyword combinations, for some filters, with their corresponding subfilters (Figs. 6, 7, 8, 9)

a. Analysis for ES

Regarding *filters,* the number of publications for the keyword combinations was: a) the highest (in bold) for subfilters: A, for ES+S (50); HM+HF, for ES+S (12); 19-44, for ES+SP (11), and b) zero (*in italics*) regarding A, for ES+AT; 0-18, for ES+OS; 45-64 and >65, for ES+AT; >80, for ES+OS, ES+SP, ES+AT.

b. Analysis for SC (Fig. 7)

Regarding *filters,* the number of publications for the keyword combinations was: a) the highest (in bold) for subfilters: A, for SC+S (76); HM+HF, for SC+S (13); 19-44, for SC+S (6), and b) zero (*in italics*) for subfilters: all subfilters, for SC+AT; regarding sex and age subfilters, for SC+SP; regarding HM, for SC+PF and SC+E; regarding HF, for SC+MF, SC+PF and SC+E.

c. Analysis for RR (Fig. 8)

Regarding *filters,* the number of publications for the keyword combinations was: a) the highest (in bold) for subfilters: A, for RR+S (84); HM+HF, for RR+S (24); 19-44, for RR+S (18), and b) zero (*in italics*) for subfilters: A, HF, 0-18, 45-64, >65 and >80, for RR+AT; for 0-18 and >80, for RR+OS.

d. Analysis for SC (Fig. 9)

Regarding *filters,* the number of publications for the keyword combinations was: a) the highest (in bold) for subfilters: A, for GSG+S (457); HM+HF, for GSG+S (71); 45-64, for GSG+S (24), and b) zero (*in italics*) for subfilters: 0-18, for GSG+MF; for >65, for GSG+AT; >80, for GSG+MS; GSG+PS; GSG+AT; GSG+MF; GSG+PF.

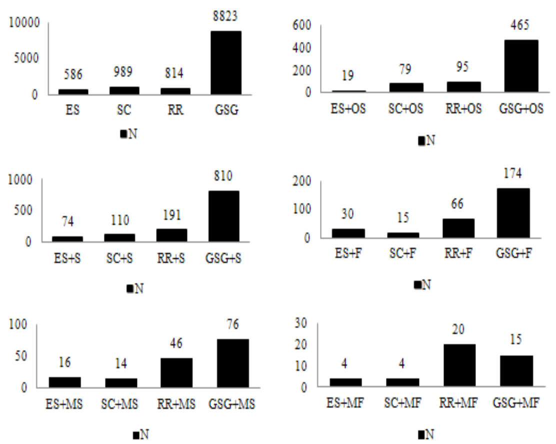

Fig. 6 – Analysis for ES, SC, RR and GSG, regarding N

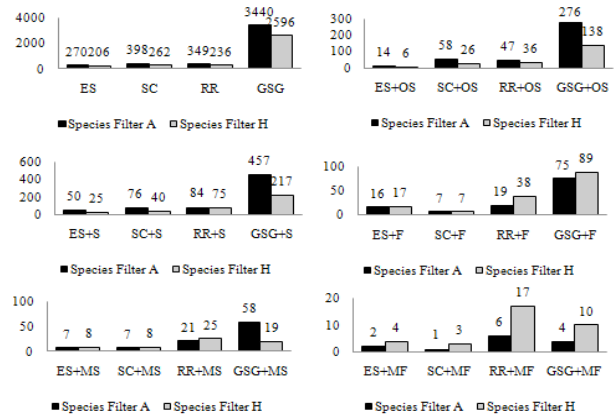

Fig. 7 – Analysis for ES, SC, RR and GSG, regarding the species filter

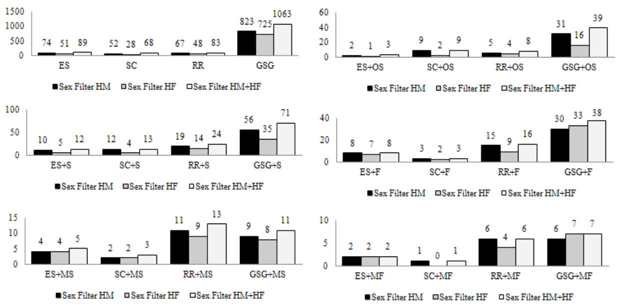

Fig. 8 – Analysis for ES, SC, RR and GSG, regarding the sex filter

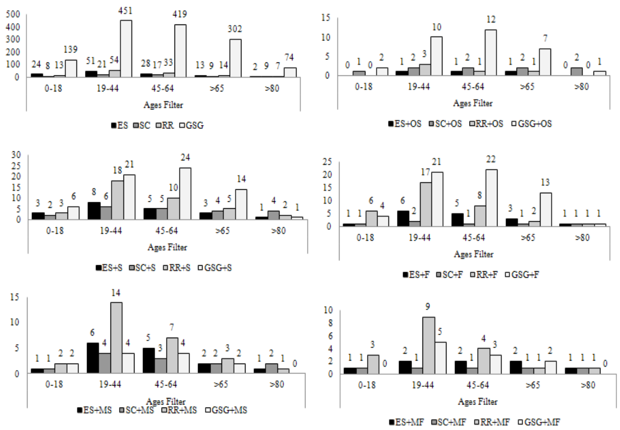

Fig. 9 – Analysis for ES, SC, RR and GSG, regarding the age filter

Discussion

1) Specifications

This article is a continuation of previous research of the authors, regarding the topic of adaptogens (Jurcău et al., 2018a): Schizandra chinensis (Jurcău et al., 2013), Rhodiola Rosea (Jurcău et al., 2017), Ginseng (Jurcău et al., 2018b).

2) Analysis of the results of the present study

Of the four adaptogens, the greatest interest of research was in GSG (8823), with an average of 113.1 publications per year, while the lowest interest was in ES (586), with an average of 11.06 publications per year. For each adaptogen, relatively to N, the interest of research in keyword combinations was reduced. For all four adaptogens, keyword combinations were most studied for S and least studied for MF (for ES). Regarding all keyword combinations, the greatest interest of research was in N for RR and GSG, respectively: S - RR=191 and GSG=810; MS - RR=46 and GSG=76; OS - RR=93 and GSG=465; F - RR=66 and GSG=174; MF - RR=20 and GSG=15. For all keyword combinations, the greatest interest of research was in studies: on animals, in the case of S, OS and GSG+MS; on human subjects, for MS (except GSG+MS), F and MF. For all keyword combinations, the greatest interest of research was in studies with subjects of both genders; and the lowest interest of research was in studies with female subjects. For all keyword combinations, the greatest interest of research was in subjects aged between 19-44 years, excepting GSG+S, GSG+OS and GSG+F, where most of the publications were conducted on subjects aged 45-64 years; and the lowest interest of research was in studies with subjects aged >80 years.

Exemplification of actions of the selected adaptogens. Pubmed quote evidence

It concerned four areas related to sports, namely: stress (S), mental stress (MS), oxidative stress (OS), mental fatigue (MF). For the authenticity of the information, we preserved the original form, in the quotations made.

Eleutherococcus senticosus (ES)

"ES is often referred to as 'Siberian ginseng' and its extensive use probably dates back only to the mid-1950s and early 1960s" (Davydov & Krikorian, 2000). "It has been used as a tonic and anti-fatigue agent in northeastern Asia and eastern Russia from ancient time" (Zhu et al., 2011).

"ES exhibits anti-fatigue, anti-stress, immuno-enhancing effect, CNS activity, and anti-depressive effect; its pharmacological activities were mainly due to lignans and iridoid glycosides" (Deyama et al., 2001).

"The content of eleutheroside E of ES root cortex may partly contribute to the anti-fatigue action, the recovery of the reduction of NK activity and the inhibition of corticosterone elevation induced by swimming stress" (Kimura & Sumiyoshi, 2004). For example, "fatigue among subjects with chronic fatigue syndrome assigned to ES was substantially reduced during the study" (Hartz et al., 2004). "ES may enhance recovery from physical fatigue induced by forced swimming by accelerating energy changes through fatty acid β-oxidation in skeletal muscle" (Sumiyoshi & Kimura, 2016).

Schisandra chinensis (SC)

"SC fruits are a famous traditional Chinese medicine to treat all kinds of fatigue" (Chi et al., 2016). "SC and ES increased endurance and mental performance in patients with mild fatigue and weakness" (Panossian & Wikman, 2009).

"Schisandrin A, a class of active lignans of SC, has protective effects on DNA damage and apoptosis induced by hydrogen peroxide (H_2O_2) in C2C12 cells, effectively attenuates H_2O_2-induced cytotoxicity and DNA damage; so, it maintains energy metabolism through the preservation of mitochondrial function while eliminating reactive oxygen species generated by H_2O_2 in C2C12 cells; therefore, it may have a beneficial effect on the prevention and treatment of diseases associated with apoptosis induced by oxidative stress" (Choi, 2018). "α-cubebenoate isolated from an extract of SC fruits inhibited lipopolysaccharide (LPS)-induced expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 (COX-2) in a concentration-dependent manner, thereby suppressing productions of nitric oxide (NO) and prostaglandin E2 (PGE2) in vitro in peritoneal macrophages; α-cubebenoate also inhibited LPS-induced accumulation of polymorphonuclear lymphocytes in LPS-induced peritonitis model in vivo; so, α-cubebenoate may act as an anti-fatigue constituent of SC through anti-inflammation and could be of therapeutic use as a treatment for inflammatory diseases" (Chen et al., 2008).

"SC polysaccharide (SCP) composition consisted of 12 amino acids, of which alanine, aspartate and glutamate were identified as involved; the growth and the behaviors of the rats in the chronic fatigue syndrome model group improved after SCP treatment, and the therapeutic mechanism was partially due to the restoration of the disturbed pathways" (Chi et al., 2016). "Extracts of SC fruits and seeds have been used to reduce symptoms of stress such as fatigue and weakness, to enhance physical performance, and to promote endurance; they produced central nervous system (CNS) stimulation, increased energy, improved mood, remission of fatigue, and normalization of sleep" (Panossian, 2013).

Rhodiola Rosea (RR)

"RR, also known as "golden root" or "roseroot", has been used in the traditional medicine of Russia, Scandinavia and other countries, and has been extensively studied as an adaptogen with various health-promoting effects" (Brown et al., 2002). "RR is a plant that lives at high altitude in Europe and Asia, widely used for its high capacity to increase the organism resistance to different stress conditions. RR extract has a significant protection in presence of the oxidative agent" (Battistelli et al., 2005).

"RR exhibited excellent potential in singlet oxygen and hypochlorite scavenging as well as FRAP potential, iron chelating ability and protection of protein thiol groups due to the high percentage of polyphenols, capable of neutralizing oxidative and chain reactions induced by free radicals because they are excellent donors of protons (Frei et al., 2003) and electrons" (Chen et al., 2008). "RR extract administration for 4 weeks could reduce swimming-enhanced oxidative stress possibly via the reactive oxygen species scavenging capability and the enhancement of the antioxidant defense mechanisms" (Huang et al., 2009).

"Treatment with RR standardized extract of rhizome significantly improved the perceptive and cognitive cerebral functions in young, healthy physicians, during night duty, so RR can reduce general fatigue under certain stressful conditions" (Darbinyan et al., 2000). "Approximately 140 compounds were isolated from roots and rhizome of RR and a number of clinical trials demonstrate that repeated administration of RR extract SHR-5 exerts an anti-fatigue effect that increases mental performance (particularly the ability to concentrate in healthy subjects), and reduces burnout in patients with fatigue syndrome; several mechanisms of action are possible contributors: interactions with HPA-system (cortisol-reducing), protein kinases p-JNK, nitric oxide, and defense mechanism proteins" (Panossian et al., 2010).

Ginseng (GSG)

"GSG has been traditionally used for several millennia in Asian countries, including Korea, China, and Japan, not only as a nourishing and tonifying agent but also as a therapeutic agent for a variety of diseases, immunity improvement, fatigue relief, memory improvement, antioxidation" (So et al., 2018).

"GSG exhibits antioxidant properties with increasing concentrations: a very good ability to scavenge superoxide and hydroxyl radicals" (Vaško et al., 2014). "The underlying molecular mechanisms in the hepatoprotection of ginsenoside Rk1 in APAP-induced hepatotoxicity may be due to its antioxidation, antiapoptosis, anti-inflammation, and antinitrative effects" (Hu et al., 2019). "Ginsenoside Rg1 reduced the excessive ROS and the occurrence of cell apoptosis" (Gao et al., 2019).

"Panax GSG administration, compared to placebo: decreased the total self-rating numeric scale score (NRS); improved mental NRS score; reduced the visual analogue scale (VAS) score; lowered the reactive oxygen species (ROS) and malondialdehyde (MDA) levels; increased total glutathione (GSH) concentration and glutathione reductase (GSH-Rd) activity; so, PGSG has antifatigue effects in patients with ICF, and the changes in antioxidant properties contribute in part to its mechanism" (Kim et al., 2013). "Ginsenoside Rg3 (Rg3) is one of the key components of a frequently used herbal tonic panax ginseng for fatigue treatment that could improve exercise performance and resist fatigue possibly through elevating silent information regulator of transcription 1 deacetylase activity" (Yang et al., 2018). "Panax GSG, consumed by healthy young adults, enhanced performance of a mental arithmetic task and ameliorated the increase in subjective feelings of mental fatigue experienced by participants during the later stages of the sustained, cognitively demanding task performance" (Reay et al., 2006). "GSG is one of the most widely used in fatigue, because it is believed to improve energy, physical and emotional health, and well-being; both American and Asian ginseng may be viable treatments for fatigue in people with chronic illness" (Arring et al., 2018).

Instead of conclusions

ES, SC, RR and GSG are described as adaptogens, having important effects in stress modulation and in reducing oxidative stress and fatigue, including mental fatigue.

Conflicts of interest

Nothing to declare.

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