



INFLUENCE OF A ROMANIAN PHYTOTHERAPIC PRODUCE CALLED „ANTISTRES”, CONTAINING GINSENG, ON ANXIETY AND SALIVARY CORTISOL, IN ONE EXAM OF EXAMS STUDENT SESSION

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Abstract

Ginseng (GSG) is one of the most popular herbs in oriental countries and has, among other effects, an anti-stress activity. We assess the impact of a phytotherapeutic product (PP), on anxiety and salivary cortisol, in stress caused by a difficult exam of exams students session. Chosen subjects were students, selected according to the requirements of the study. Stress has been represented by a difficult exam of session students exams. Anxiety and salivary cortisol were analyzed. The PP used contains GSG root. Statistical evaluation was made on the basis of Student test. Anxiety and salivary cortisol were significantly reduced immediately pre- and poststress in subjects who were administered the PP containing GSG, compared with subjects who did not follow the phytotherapeutic treatment. In stress caused by a difficult students session exam, increasing anxiety was anticipatory, pre-stress, and increasing salivary cortisol was more intense post-stress. Under PP containing GSG influence, anxiety and salivary cortisol were significantly reduced immediately pre - and post exam. Between GSG treated group and untreated group, there were differences on dynamic

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developments for anxiety and salivary cortisol, and the influence of used PP containing GSG was significantly more intense on anxiety than on salivary cortisol. The use of PP containing GSG, may be an effective, safe and accessible modulation path for stress caused by a difficult students session exam.

Keywords: stress, students exams, anxiety, salivary cortisol, Ginseng, phytotherapy

Introduction

Student stress. It is known that a student under optimal stress does bring out his or her best, but extremes can result in stress induced disorders and deteriorating performance (Malathi & Damodaran, 1999). In 2010, it has been said that most students experience some level of anxiety during the exam (Latas, Pantić, & Obradović, 2010). Later, it has been proven that there is high levels of exam anxiety among the medical students and there is a need for anxiety-reduction programmes (Afzal, Afzal, Siddique, & Naqvi, 2012).

One of the possibilities to reduce stress is to use natural sources extracts such as Ginseng.

Ginseng (*Panax ginseng*, C. A. Meyer, Araliaceae) (GSG) is one of the most popular herbs in oriental countries such as China, Japan and Korea (Kitaoka, Uchida, Okamoto, Chikahisa, Miyazaki, Takeda, & Séi, 2009) and has an anti-anxiety and anti-depressant activity. (Chatterjee, Verma, & Palit, 2010). *G common classification* by Wikipedia (3): *a) Panax quinquefolius*, is the American ginseng (root). *b) Panax vietnamensis*, *Panax ginseng* is the Asian ginseng (root), discovered in Vietnam, the southernmost ginseng known, available in four forms: fresh, red, white and sun ginsengs. Wild ginseng is used where available. *Fresh ginseng* is the raw product. *White ginseng* is fresh ginseng which has been dried without being heated. *Red ginseng* is more common as herbal medicine than white ginseng. *Sun ginseng* is created from a heat processing method which increases ginsenoside components such as ginsenoside, Rg.sub.3, Rk.sub.1 and Rg.sub.5, by steaming white ginseng at a higher temperature than red ginseng. The increased steaming temperature produces an optimal amount of biological activity due to its ability to amplify specific ginsenosides. *c) Wild ginseng* can be processed to be red ginseng. *Panax ginsengs*, which are the adaptogenic herbs, principally *Panax ginseng*

and *P. quinquefolius*. Ginseng is characterized by the presence of ginsenosides. *d) Siberian ginseng* (*Eleutherococcus senticosus*) is in the same family, but not genus, as true ginseng and has a woody root. It is considered to be an adaptogenic herb. The active compounds in Siberian ginseng are eleutherosides, not ginsenosides. Also, it is known that white and red varieties of ginseng have positive results on experimental anxiety (Bhattacharya & Mitra, 1991) and can be used as a potent therapeutic agent in treating mixed anxiety-depressive disorder (MAD) (Chatterjee et al., 2010).

Previous author's results on stress field (Jurcău, Jurcău, & Bodescu, 2011, 2012a, 2012b, Jurcău & Jurcău, 2012c, 2013), justify the authors interest for further assessment of this type of stress, the exam student stress.

Working hypothesis. The stress of exams students session represents a subject that has spawned much research. On the other hand, studies with the theme of Ginseng are numerous, especially relating to long-term stress. The GSG influence on stress caused by exams session is less investigated. The present paper has as a premise the evaluation of stress modulation, induced by a difficult exam in session, by the help of a phytotherapeutic produce (PP) that contains GSG, assessed on the basis of some emotional and hormonal changes.

Objective

We assess the impact of PP containing GSG root, on anxiety and salivary cortisol, in stress caused by a difficult exam of exams students session.

Methods

Study and measurements have been carried out in January 2011, in the 122 Medical Family Cabinet in Cluj-Napoca.

Participants

Participation of all subjects in the study was anonymous and voluntary. The selection of subjects was made on the basis of the questionnaire for detecting the state of anxiety STAY X 1. From the trials were excluded persons with mental disorders, cortisonic therapies and toxic addiction - alcohol,

tobacco, drugs, coffee. Two groups were explored: the control group (C), that has not been given any therapy and the experimental GSG group (G) which has been administered PP. Both groups have been subjected to the same type of stress caused by intense and short term physical effort.

The number of subjects from a group was 12 (6 men, 6 women), both for G and C. Average age was $20,1 \pm 3$ for G and $19,3 \pm 4$ for C (Table 1). Participants were asked to not consume alcohol, coffee, do not smoke and not to use any medication and no antioxidant in on the day before physical stress. All participants were sedentary subjects.

Table 1. The number and type of subjects to groups

Group	Experimental stress (G)	Control (C)
Nr. of subjects	12	12
Average age	$20,1 \pm 3$	$19,3 \pm 4$
Gender	Women (6), Men (6)	Women (6), Men (6)

Explorations - Instruments

The examinations consisted of measuring anxiety and salivary cortisol. As reference were considered to be the values of the group has not been administered PP, C.

Psychological assessment

Self-assessment questionnaire, S.T.A.I. X1, X2 (Inventory of trait- state anxiety) has been used for anxiety (A) (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983). S. T. A.I. scores range from a minimum score of 20 to a maximum score of 80 in both A - State and A - Trait scales. Subjects respond to each item of S. T. A. I., by assessing themselves on a scale with 4 points (Tables 2 and 3). A - State scala is balanced with 10 directly quoted items and 10 vice versa quoted items; vice versa quoted items in A - State scala are: 1, 2, 5, 8, 10, 11, 15, 16, 19, 20. A Trait - Scala has 13 directly quoted items and 7 vice versa quoted items, in which case it is not possible to effect the balanced scale; vice versa quoted items in A - Trait scala are: 1, 6, 7, 10, 13, 16, 19. The psychometric properties of the STAI are good, with a Crombach α (Crombach, 1951, 2004) of 0,83, higher than the conventional cut-off value of 0,71.

Table 2. A - Stats scala categories

1	Not at all
2	Little
3	Pretty
4	Very much

Table 3. A - Trait scala categories

1	Almost never
2	Sometimes
3	Often
4	Almost always

Hormonal evaluation

Assessment of salivary cortisol was made from Synevo laboratory in Cluj-Napoca, by immuno-detection by electrochemiluminiscence (straps) (Carrozza, Corsello, Paragliola, Ingraudo, Palumbo, Locantore, Sferrazza, Pontecorvi, & Zuppi, 2010).

Procedure

The indicators determination program was the same for C and G, being carried out as follows: time 1 = first time-determination (Pre Stress 1 = T₁) - the day before the test, at 8.00 in the morning; time 2 = second determination (Pre Stress 2 = T₂) - 30 min before the start of the sample; time 3 = third determination (Post Stress 3 = T₃) and time 4 = fourth determination (Post Stress 4 = T₄) - 15 min and respectively 24 hours after the effort.

Design

For stress it was chosen as a model a difficult exam of exams students session.

Phytotherapic produce (PP) „*Antistres*” containing GSG, was administered only to group G, for 21 days pre-stress period of, 2 capsules, 3 times a day at 6 hour intervals (6.00-12.00-18.00), until the day before the test. PP is recommended for its anti-stress protective effects (1).

Statistical evaluation:

- The results obtained were analysed using SPSS 13.0 application.
- For continuous examination of data, Student's t test has been used.
- The data were considered significant at a $p < 0,05$.

Results

Note that the *reference values* were those of C and the *reference time* was considered to be T₂.

Anxiety for C was significantly increased at time T₂, both compared with T₁ ($p < 0,001$), T₃ ($p < 0,02$) and T₄ ($p < 0,005$). At all peri-stress times, anxiety values in C were higher than in G, significant differences being at times T₂ ($p < 0,003$), T₃ ($p < 0,01$) and T₄ ($p < 0,04$) (Figure 1). There were no significant gender differences, for anxiety values.

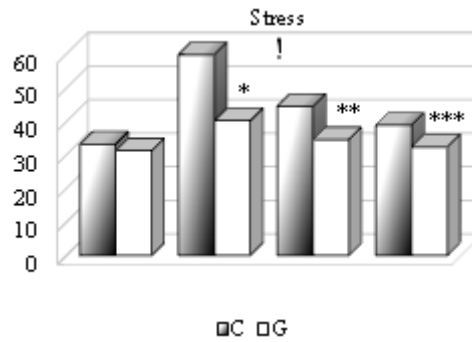


Figure 1. Anxiety score changes, under G influence, in exam student stress
 C = control group, G = experimental GSG group, "stress" = time of exam
 * $p < 0,003 = T_2C - T_2G$, ** $p < 0,01 = T_3C - T_3G$, *** $p < 0,04 = T_4C - T_4G$

Salivary cortisol for C was significantly increased at time T₃, both compared with T₁ ($p < 0,001$), T₂ ($p < 0,01$) and T₄ ($p < 0,04$). At all peri-stress times, salivary cortisol values for C were higher than for G, significant differences being at times T₂ ($p < 0,01$), T₃ ($p < 0,002$) and T₄ ($p < 0,003$) (Figure 2). There were no significant gender differences, for salivary cortisol values.

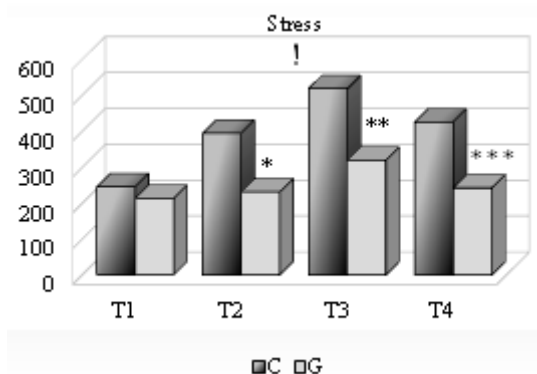


Figure 2. Salivary cortisol changes, under G influence, in exam student stress
 C = control group, G = experimental GSG group, "stress" = time of exam
 * $p < 0,01 = T_2C-T_2G$, ** $p < 0,002 = T_3C-T_3G$, *** $p < 0,003 = T_4C-T_4G$

Comparison of peristress evolution of anxiety and salivary cortisol show the PP result on the parameters dynamic values in C compared to G. Thus, the G stress impact is reduced, G-C compared differences being significant at T_2 , T_3 and T_4 , both for anxiety ($p < 0,003 = T_2C-T_2G$, $p < 0,01 = T_3C-T_3G$, $p < 0,04 = T_4C-T_4G$), and salivary cortisol ($p < 0,01 = T_2C-T_2G$, $p < 0,002 = T_3C-T_3G$, $p < 0,003 = T_4C-T_4G$) (Figure 3).

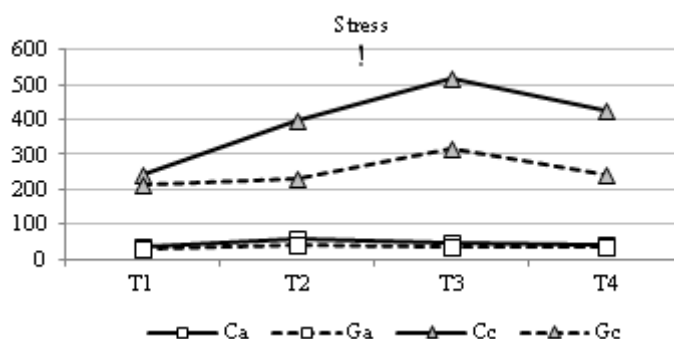


Figure 3. Comparison of studied parameters variations.
 Groups: Ca = Control - anxiety, Cc = Control - salivary cortisol,
 Ga = experimental - anxiety, Gc = Experimental - salivary cortisol
 "stress" = time of intense and short term physical effort

Percentage differences between times T_2 and T_3 for C and G. PP has the most intense impact at T_2 for anxiety ($p < 0,005$) and at T_3 for salivary cortisol ($p < 0,01$). The PP impact is significantly greater on anxiety ($p < 0,05$) than on salivary cortisol (Figure 4).

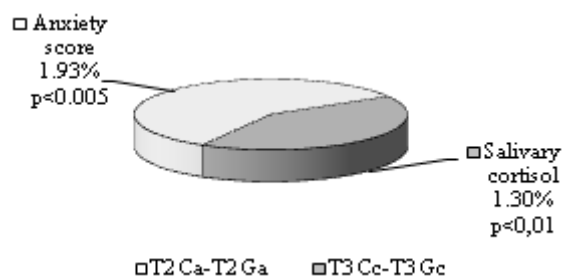


Figure 4. Percentage differences between C and G at times T_2 and T_3 , for anxiety (Ca and Ga) and salivary cortisol (Cc and Gc)

Discussion

Ginseng is an herbal plant reputed to increase resistance to stress and improve immune function (Biondo, Robbins, Walsh, McCargar, Harber, & Field, 2008). Pharmacological study has proved ginsenoside-Re to be the chief active constituent of *Panax ginseng* (Dou, Wen, Pei, Chen, & Ma, 1997). It has been proven that the anxiolytic effect of GSG is due to decrease pentylentetrazole-induced in rat brain MAO activity (Bhattacharya & Mitra, 1991). In the case of *Panax ginseng*, some of its complex known effects are related to affective and anxiety disorders, including the enhancement of neuroprotection, cellular resilience and plasticity (Wang, Flaisher-Grinberg, Li, Liu, Sun, Zhou, & Einat, 2010). *Panax quinquefolium* (PQ) has significant adaptogenic properties and that's why, can be used as a potent therapeutic agent in treating mixed anxiety-depressive disorder (MAD) (Chatterjee et al., 2010).

PubMed evidence of G anti-stress action

Ginsenosides had an anti-stress property (Lee, Jung, Kim, Lee, & Chung, 2006). Anxiolytic activity of components of ginseng root, Rb₁ has been demonstrated (Carr, Bekku, & Yoshimura, 2006, Lee et al., 2006) and Rg₃ (Lee et al., 2006). It has been proven that RG and its constituents, Rg₃ and Rh₂, may exert anxiolytic effects by antagonizing GABA/benzodiazepines (Kim, Choi, Kim, & Kim, 2009). Among the GSG constituents are included saponins. Ginseng total saponin (GTS) administration lead to an anti-stress effect (Lee et al., 2006). It was found that total saponins extracted from the caudexes and leaves of *Panax notoginseng* (SCLPN) determine improving mental function, treating insomnia, and alleviating anxiety (Xiang et al., 2011). There is assumption that wild ginseng (WG) extract would modulate the hypothalamus CRF and NPY systems what would lead to inhibition of anxiety and depression responses due to morphine withdrawal (Lee, Kim, Shim, Lee, & Hahm, 2011).

Anxiety

Chronologically PubMed evidence of G anxiolytics and anti-stress action. Among the earliest studies regarding G is included one in which the putative anxiolytic activity of the white and red varieties of ginseng, the root of *Panax ginseng*, was investigated in rats and mice using a number of experimental paradigms of anxiety and compared with that of diazepam (Bhattacharya & Mitra, 1991). In another study it was observed heightened anxiety before exam (Spangler, 1997). In another study, postmenopausal women with climacteric syndromes were treated with daily oral administration of 6 g RG for 30 days, the result being Cornell Medical Index (CMI) and the State-Trait Anxiety Inventory (STAI) A-state scores decreased within normal range (Tode, Kikuchi, Hirata, Kita, Nakata, & Nagata, 1999). It was found that the anxiolytic potential of SG is stronger than that of RG in the elevated plus-maze model (Park, Cha, Seo, Hong, Han, & Oh, 2005). Ginseng root has been widely used for the management of anxiety and emotional instability (Carr et al., 2006). In a study on male mice by using a number of experimental paradigms of anxiety, It was concluded that the PQS might be a potential candidate for use as an anxiolytic drug (Wei, Yang, Wang, & Wu, 2007). It was found also that, the STAI score was significantly reduced after using G (Kitaoka et al., 2009). *Panax quinquefolium* (PQ) at 100 mg/kg (po) were

effective as an anti-anxiety as well anti-depressant activity and had no motor in-coordination in mice (Chatterjee et al., 2010). Also, altered Korean red ginseng has been used as a treatment for patients suffering from anxiety (Kim, Kim, Jeong, & Kim, 2011).

Cited studies present the GSG generally effect on anxiety. Results obtained by testing anxiety, under the action of a PP containing GSG, are consistent with the recent data provided by studies related to this parameter changes under the GSG action. Unlike them, our study has proven the PP containing GSG diminishing effect on anxiety induced by stress caused by intense and short term physical effort on sedentary persons.

Salivary cortisol

Chronologically PubMed evidence of G action on cortisol. It was proven higher cortisol level, under the exam condition (Spangler, 1997). That Korean red ginseng decrease cortisol/ dehydroepiandrosterone (DHEA) (C/D) ratio (Tode, 1999). James M. Howard said that cortisol evolved as the natural antagonist of DHEA activity and is the basis of the “fight or flight mechanism” (Howard, 2006). G appeared to normalize corticotrophinreleasing factor (CRF) system balance in the hypothalamus by influencing the HPA axis, resulting in the increased negative feedback and reduced the anxiety- and depression-like symptoms strongly associated with morphine discontinuation, probably by modulating CRF and neuropeptide Y (NPY) expressions in the hypothalamus. Then, CRF and NPY might be a biological target or a mechanistic rationale for developing alternative medications in the treatment of anxiety and depression (Lee et al., 2011). It was found that protopanaxatriol saponins in Ginseng produces inhibitory activity of corticosteroid production in the adrenal fasciculata cells in vivo (Hasegawa, Nakagawa, Miyate, Takahashi, Ohta, Tachikawa, & Yamato, 2013).

Cited studies show the GSG general action on cortisol. The results obtained by testing that we have done on salivary cortisol, under the action of PP containing GSG, are consistent with the provided data by the latest studies related to cortisol changes, under GSG action. Difference to them is that, , our study has proven the PP containing GSG effect of reducing the salivary cortisol, on sedentary persons subjected to stress caused by intense and short term physical effort.

Conclusions

In stress caused by a difficult students session exam, increasing anxiety was anticipatory, pre-stress, and increasing salivary cortisol was more intense post-stress.

Under PP containing GSG influence, anxiety and salivary cortisol were significantly reduced immediately pre - and post- exam.

Between GSG treated group and untreated group, there were differences on dynamic developments for anxiety and salivary cortisol, and the influence of used PP containing GSG was significantly more intense on anxiety than on salivary cortisol.

The use of PP containing GSG, may be an effective, safe and accessible modulation path for stress caused by a difficult students session exam.

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