



Ginseng, Hypothalamo-Pituitary-Adrenal Axis and Cortisol, a Short Pubmed Approach of their Relationship

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Abstract: Introduction. Ginseng (G) is an Asian plant used as an adaptogen that has the ability to normalize bodily functions compromised by stress. Hypothalamic-pituitary-adrenal axis (HPA) is the main effectors of the stress response and cortisol (C) is the most used marker of stress. **Materials and method.** In order to highlight the relationship between G and stress, the keywords selected for analysis were G+HPA and G+C. The time periods analyzed were from 1970 to 2021. The Pubmed filters selected were: Species and Sex. **Results.** For G+HPA: publications with An were the most numerous and had the greatest numerical rise; reserch dynamic for the sex filter had a lower increase in time. For G+C: publications with H were the most numerous and had the greatest numerical rise; dynamic researches with HF had the lowest increase in time. **Conclusions.** 1) The research on the combination of the keywords G+HPA and G+C falls under the theme of the relationship between G and stress. 2) Research on animals predominated, compared to those on human subjects. 3) Research with subjects from both genders was preferred. 4) The research related to Ginseng and HPA, respectively to Ginseng and Cortisol, although numerically reduced, proves a continuously growing interest of researchers for this subject.

Keywords: cocoa; chocolate; antioxidant actions; neuro-psycho-emotional actions

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1. Introduction

The main effectors of the stress response form a set of structures which is commonly referred to as the hypothalamic-pituitary-adrenal axis (HPA) (Smith & Vale, 2006). Glucocorticoids (especially cortisol) are the downstream effectors of the HPA axis and regulate physiological changes through intracellular receptors distributed throughout the systems (Ru et al., 2015).

Ginseng is a plant used in Asia for over 4000 years (Brekhman & Dardymov, 1969). The name “Ginseng” in Chinese comes from the shape of the root. The root was then used as a tonic to invigorate weakened people and make them strong and strong (Hu, 1977; Yun, 2001; Jia & Zhao, 2009). *Panax ginseng* administration in oriental medicine and is available in many forms (Oliynyk & Oh, 2013).

Panax Ginseng is one of the plants framed as a natural adaptogen (Todorova et al., 2021). Adaptogens are defined as substances that cause non-specific resistance in living organisms, during stress (Panossian, 2013) and can produce positive stress response and the associated hormone expression (Liao et al., 2018). Ginseng root is traditionally used as an adaptogen as it is said to has the ability to normalize bodily functions and strengthen systems compromised by stress (Lee et al., 2015). Thus, ginsenoside Rb1 can block the stress response at a very early stage and therefore prevent the harmful effects of stress (Choi, 2008). Korean red ginseng vs placebo, also reduced fatigue (Bhattacharjee & Bandyopadhyay, 2020; Kim et al., 2013) in patients older than 50 years (Sung et al., 2020).

Studies on the anti-stress and adaptogen role of ginseng prove that there is research interest in this direction (Jurcău et al., 2018; Jurcău et al., 2018; Jurcău et al., 2018; Jurcău et al., 2019).

2. Hypothesis

Although studies so far prove interest in the relationship between Ginseng (G) and stress, in general, the relationship between Ginseng and the Hypothalamic-Pituitary-Adrenal Axis (HPA), and cortisol (C) respectively, is still little investigated.

3. Objectives

The objective of this study was to evaluate the interest in the relationship between G and HPA, G and cortisol (C) respectively, through an assessment of PubMed studies.

4. Material and Methods

The obtained information was from the database of the research PubMed site. The analysis was done for the time period until the 2021.

Keywords

In order to highlight the relationship between Ginseng (G) and stress, the keywords selected for analysis were: G and HPA (G+HPA), G and cortisol (G+C).

Periods of research

The periods of time analyzed were the following: 1970-1979, 1980-1989, 1990-1999, 2000-2009 and 2010-2019, 2020, 2021. The beginning of the selected time period was given by the year of the first posting of a publication corresponding to the chosen keywords.

PubMed filters

The PubMed filters I chose for analysis were: *Species* and *Sex*. Within each verified filter, a few sub-filters were analyzed:

- a) For the “Species” filter, the selected sub-filters were: animals (An), humans (H)
- b) For the “Sex” filter, the selected sub-filters were: human male (HM), human female (HF), human male+female (HM+F).

Study design

The organization was carried out on the following criteria: analysis of the chosen keywords, in relation to the sub-filters and the average number of publications per year (N/Y).

Statistical evaluation

- The results obtained were analysed using SPSS 19.0. statistical package.
- For continuous data examination, Student’s t test has been used.
- The differences were considered significant at a $p < 0,05$.

5. Results

A. Analysis of N/Y, for the keyword's combination G+HPA, G+C (Table 1, Figure 1, Figure 2)

Table 1. N/Y for the keyword's combination G+HPA, G+C

Period for G+HPA	N/Y	Species			Sex	
		An	H	HM	HF	HM+F
2000-2009	0,2	0,2	0	0	0	0
2010-2019	1,1	0,4	0,4	0,1	0,1	0,1
2020	3	3	1	1	1	1
2021	1	0	1	1	1	1
Period for G+C	N/Y	Species			Sex	
		An	H	HM	HF	HM+F
1970-1979	0,2	0,1	0,1	0,1	0,1	0,1
1980-1989	0,3	0,1	0,2	0	0	0
1990-1999	0,3	0,2	0,1	0,1	0,1	0,1
2000-2009	0,8	0,1	0,7	0,6	0,2	0,6
2010-2019	1,4	0,5	0,8	0,4	0,6	0,7
2020	2	1	1	1	1	1
2021	1	1	0	0	0	0

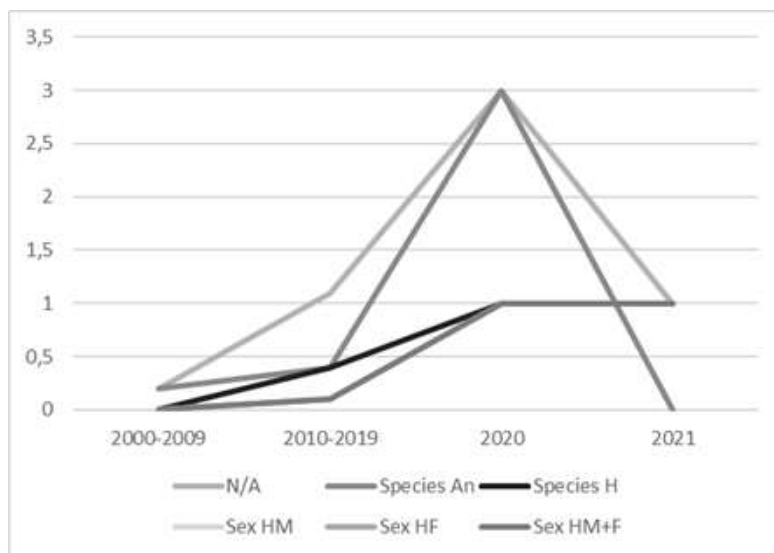


Figure 1. N/Y for G+HPA, for the Species and Sex filters

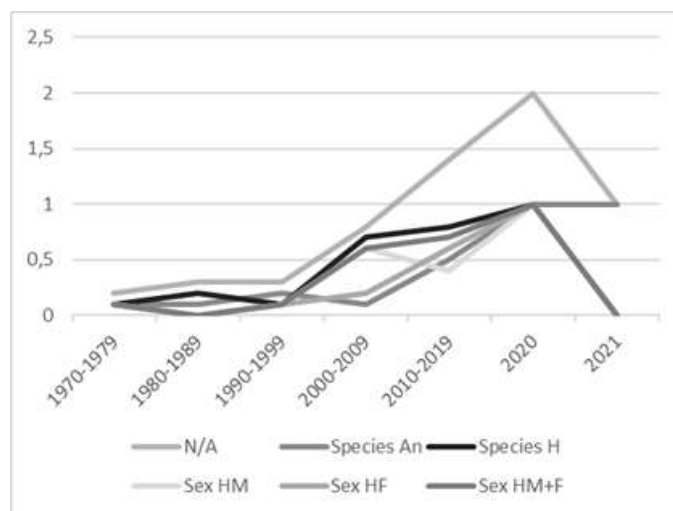


Figure 2. N/Y per year for G+C, for the Species and Sex filters

From the analysis of Table 1, Figure 1 and Figure 2, we can see:

a) For G+HPA: 1) N/Y for G+HPA were: the most numerous in 2020 for An (3); the fewest for the decade 2000-2009 (0.2); no publications were found for H for decade 2000-2009. 2) From the date of the first publication until 2021, an increase number of publications have been observed after the 2000s with a peak in 2020, for all the sub-filters of the two chosen filters. 3) The dynamics of publication in time show that publications with an were the most numerous and had the greatest numerical rise; research dynamic for the sex filter had a lower increase in time.

b) For G+C: 1) N/Y for G+C: were the most numerous in 2020 (2), has the same value (1) for all the chosen sub-filters; were the fewest for decade 1970-1979 (0.2); no publications were found for HM, HF, HM+F for the 1980-1989, 2021 periods. 2) From the date of the first publication until 2021, an increase in the number of publications has been observed after the 1990s, with a peak in 2020, for all the sub-filters of the two filters chosen. 3) The dynamics of publication in time show that publications with H were the most numerous and had the greatest numerical rise; dynamic researches with HF had the lowest increase in time.

B. Statistical analysis for the filter Species (Table 2)

There is no statistical difference between N/Y and An and between N/Y and H, both for G+HPA and G+C.

Table 2. Statistical Analysis for G+HPA and G+C, for the Filter Species

Statistical analysis	G+HPA			G+C		
	N/Y	Species		N/Y	Species	
		An	H		An	H
Mean	1,3250	0,9000	0,6000	0,8571	0,4286	0,4143
Standard derivation	1,1871	1,4095	0,4899	0,6680	0,4152	0,4059
p value related to N/A		0,3307	0,1610		0,0899	0,0825

C. Statistical analysis for the filter Sex (Table 3)

a) *For G+HTA*. There is no statistical difference between N/Y and HM, HF and respectively HM+F. There is no statistical difference between N/Y and HM+F; HM+F and HM, HM+F and HF.

b) *For G+C*. There is a significant difference between N/Y and HM (0.0461) and respectively HF (0.0393). There is no statistical difference between N/Y and HM+F; HM+F and HM, HM+F and HF.

Table 3. Statistical Analysis for G+HPA and G+C, for the Filter Sex

Statistical analysis	G+HPA				G+C			
	N/Y	Sex			N/Y	Sex		
		HM	HF	HM+F		HM	HF	HM+F
Mean	1,3250	0,5250	0,5250	0,5250	0,8571	0,3143	0,2857	0,3571
Standard derivation	1,1871	0,5500	0,5500	0,5500	0,6680	0,3761	0,3761	0,4036
p value related to N/A		0,1425	0,1425	0,1425		0,0461	0,0393	0,0607
p value related to HM+F		0,5000	0,5000			0,4203	0,3689	

6. Discussion*A. Analysis for keywords*

An analysis was performed for the number of publications displayed on the PubMed site for a period of about 21 years, for G+HPA, and 51 years, for G+C. The rhythm of researches has been progressive from the beginning of the first publication, proving that there is an increasing interest in time for the chosen combination of keywords, especially after 2000 for G+C and after 2010 for G+HPA. The N/Y for G+HPA was comparable to N/Y for G+C. Research on G+C was much earlier compared to G+HPA, thus proving that the relationship of G with a marker of stress was a topic of greater interest.

B. Analysis for Filters

Species filter. In the case of G+HPA, studies with an were more numerous compared to those with H. In the G+C case, studies that included H were more numerous in the periods 2000-2009, 2010-2019. The predominant use of animals could be explained by the greater accessibility of animal research.

Sex filter. For G+HPA: because there were no differences between the number of publications, it can be understood that the research was carried out with both M and F. For G+C: the number of publications that mentioned both genders subjects was generally higher than the one in which male or female were mentioned, so, proving the interest of those publications.

7. Conclusion

1. The research on the combination of the keywords G+HPA and G+C falls under the theme of the relationship between G and stress.
2. Research on animals predominated, compared to those on human subjects.
3. Research with subjects from both genders was preferred.
4. The research related to Ginseng and HPA, respectively to Ginseng and Cortisol, although numerically reduced, proves a continuously growing interest of researchers for this subject.

7.1. Conflict of Interests

Nothing to declare.

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