Management of stress levels in healthcare professionals with standardized dry extract of *Rhodiola rosea*

ABSTRACT

Aims: The objective was to evaluate the effect of using a standardized dry extract of Rhodiola rosea in stress management.
Study design: The study was a randomized, placebo-controlled clinical trial.

Place and Duration of Study: It was conducted at a hospital in Palmas, Tocantins, and lasted 15 days.
Methodology: It was conducted with 25 healthcare professionals, divided into control and placebo groups, where a dose of 210mg of Rhodiola rosea was used for 15 days in the control group. A perceived stress scale was applied, anthropometric measurements were taken, and laboratory samples were collected.
Results: The sample, predominantly female (88%), was composed of professionals in various healthcare roles, most working in a 12-hour shift system. The findings indicated that a significant portion of participants (52%) felt dissatisfied with their body weight, with 36% categorized as overweight or obese based on BMI. Additionally, 48% had waist circumference values indicating an increased risk for chronic diseases. The stress level assessment using the Perceived Stress Scale showed no statistical difference between those using Rhodiola rosea extract and the placebo, despite previous studies suggesting Rhodiola's efficacy in stress reduction. The lack of significant results in this study contrasts with other research that demonstrated the effectiveness of Rhodiola rosea in improving stress-related symptoms.**Conclusion:**The results showed no significant difference between the use of the herbal medicine and the placebo in improving stress.

Keywords: Rhodiola rosea, Herbal Medicine, stress.

1. INTRODUCTION

Stress has been considered an occupational disease by Brazilian social security legislation since 1999 (Law No. 3048, 06/05/1999). It is defined as a process in which the individual perceives demands in the work environment as stress-inducing factors that exceed their coping abilities, thereby triggering negative reactions (BANDEIRA, 2017). It mainly affects healthcare professionals such as nurses, nursing technicians, doctors, and others (ALMEIDA et al., 2016; SANTOS et al., 2017; ZORZAL, 2020).

According to the "Quarterly Bulletin on Disability Benefits" of 2017, produced by the Social Security Secretariat of the Ministry of Finance in conjunction with the Ministry of Labor regarding mental illness and work between 2010 and 2016, reactions to severe stress and adjustment disorders play an important role in work-related leave, being considered the main reason for leave related to mental disorders, both for accident-related sickness benefits and disability retirement of the same nature (BRAZIL, 2017).

Stress management strategies can be pharmacological, with an emphasis on antidepressants, selective serotonin reuptake inhibitors, anxiolytics, mood stabilizers, and others (BERNIK et al., 2003). The use of medicinal plants such as *Rhodiola rosea* L. can assist in supporting the prevention and relief of stress reactions (STOJCHEVA & QUINTELA, 2022). Non-pharmacological strategies include psychotherapy and integrative and complementary therapies for treatment (NASCIMENTO et al., 2022).

Nutrition plays an important role in stress management, as consuming healthy foods can positively influence mental health (GLABSKA et al., 2020). Moreover, chronic stress can threaten the balance of the immune system (DEAK et al., 2015), and this imbalance can trigger or worsen various diseases and contribute to weight gain and obesity (ABESO, 2016; LIU et al., 2017). Therefore, the aim was to evaluate the effect of using a standardized dry extract of *R. rosea* in stress management.

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2. MATERIAL AND METHODS

2.1 Study Design

A double-blind, randomized, controlled clinical trial that evaluated the effect of nutritional support combined with standardized dry extract of *R. rosea* compared to a placebo control in 24 healthcare professionals.

2.2Study Participants

The healthcare professionals were of both sexes, with 21 working in a shift system of 12 hours of work followed by 36 hours of rest, and 4 working regular office hours of 8 hours daily, at a hospital in Palmas, TO. They used the product as part of their normal routine, without hospitalization, in order to investigate the efficacy of *R. rosea* extract and nutritional support in managing stress among these volunteers.

2.3 Study Location

The study was conducted at a private hospital located in the central region of Palmas, Tocantins. This hospital employs approximately 400 staff members, including doctors, nurses, nursing technicians, physiotherapists, nutritionists, psychologists, speech therapists, as well as administrative staff, cleaning personnel, and kitchen workers.

2.4 Plant Sample and Placebo

The *R. rosea* extract samples were obtained from a compounding pharmacy in the city of Palmas, Tocantins, which is properly registered with health authorities. The *R. rosea* extract and the placebo were both prepared at the same pharmacy and placed in identical gelatin capsules, labeled with the letters A and B. Neither the researchers nor the participants knew which treatment was being administered initially (double-blind test).

The capsules were given to each individual, who used them during the treatment period in the morning at home.

2.5 Data Collection

2.5.1Volunteer Selection

Healthcare professionals were invited to participate in the study. After the invitation, those who showed interest completed an online questionnaire. Subsequently, a screening process was conducted to meet the inclusion and exclusion criteria.

All the enrolled participants met the criteria, and initially, 40 healthcare professionals of both sexes were selected.

After the screening, the 40 volunteers were invited to a first meeting, but 25 attended. These individuals were informed about the experimental protocol and the need to sign the informed consent form (Figure 1).

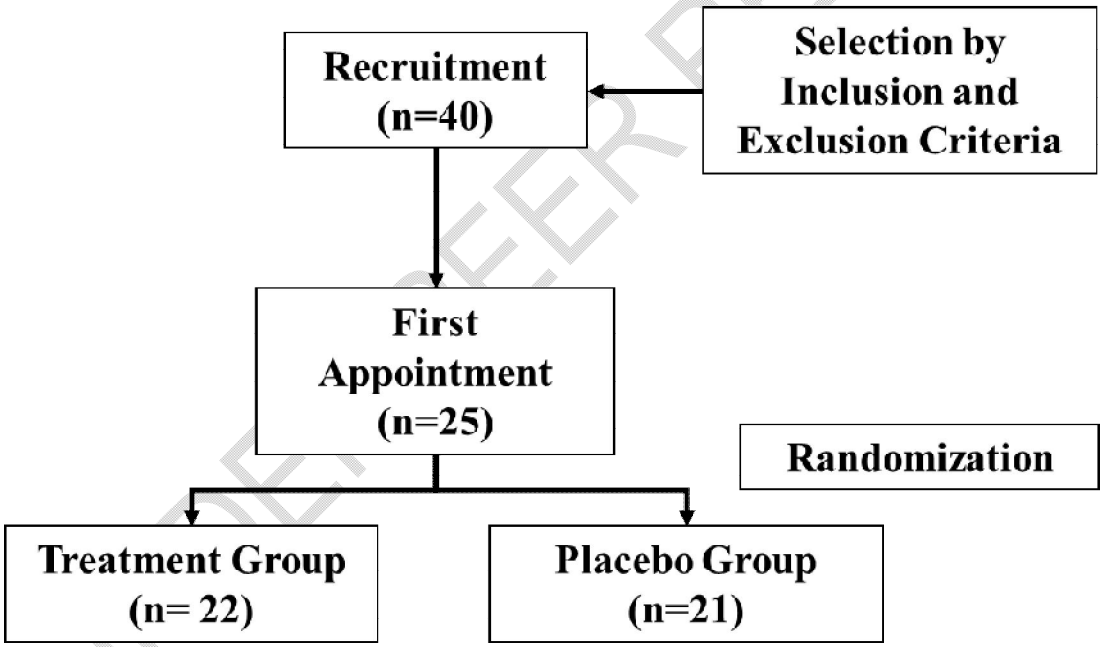

Figure 1. Volunteer Selection.

5.5.2 Inclusion and Exclusion Criteria

The study included men and women aged between 20 and 40 years, who worked in a 12-hour shift system (12x36) and in regular office hours of 8 hours per day.

Participants who were smokers and pregnant women were excluded from the study. Chronic smoking, in itself, can lead to the development of adverse psychological symptoms and is

associated with increased release of the stress hormone cortisol (COHEN et al., 2019). The use of medicinal plants for therapeutic purposes requires caution, as their active ingredients may cause disorders during pregnancy, with embryotoxic, teratogenic, or even abortive effects (PIRES et al., 2021).

5.5.3 Experimental Protocol

The experimental protocol was adapted from the studies by Noreen et al. (2013) and according to the Technical Manual of the Ministry of Health (BRASIL, 2008) "Operational Instructions: Necessary Information for Conducting Clinical Trials with Phytotherapeutics," as shown in the table below (Table 1).

Table1. Experimental Protocol.

Group	Phase 1 (15 Days)		Phase 2 (15 Days)
1	Sample A (Rhodiola rosea)	**Interval (7 Days)**	Sample B (Placebo)
2	Sample B (Placebo)		Sample A (Rhodiola rosea)

Each group was evaluated for the use of the placebo and treatment (Rhodiola rosea) over a period of 15 days for each treatment, with a minimum seven-day interval between treatments. The administered dose followed the dosage used by Noreen et al. (2013), which was one 210 mg capsule/day of Rhodiola rosea. Sample A was Rhodiola rosea (210 mg) and Sample B was the placebo (50 mg of boldo).

For the experimental protocol, a total of four consultations were conducted, which are described in Figure 1.

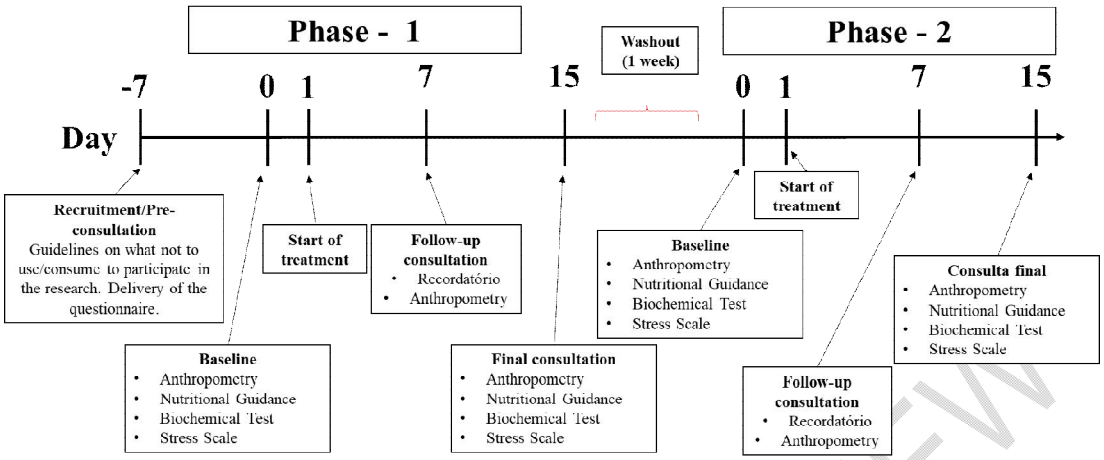

Figure2. Description of the Consultations Conducted.

5.5.4 Evaluation of Stress Levels

To evaluate stress symptoms, the **Perceived Stress Scale – PSS-10** was used (Cohen et al., 1983; Reis et al., 2010), in the version validated and translated into Portuguese (Figure 2). The PSS is a general scale and can be used across various age groups, as it does not contain questions specific to any particular context. It consists of 10 items designed to assess how unpredictable, uncontrollable, and overloaded the participant perceives their life to be.

Each question has response options that range from zero to four:

- 0 = Never
- 1 = Almost never
- 2 = Sometimes
- 3 = Almost always
- 4 = Always

The total score of the scale is the sum of the responses to these 10 items, with scores ranging from 0 (minimum) to 40 (maximum).

This scale allows for an overall assessment of perceived stress, providing a simple but reliable measure of how individuals evaluate the level of stress in their lives. It is widely used in clinical and research settings due to its ease of use and validity across different populations.

5.6 Ethical Aspects

The research project and the informed consent form (ICF) were approved by the Ethics Committee in Research with Human Beings of the Federal University of Tocantins, with the CAAE number 50427521.9.0000.5519.

This project follows the Technical Manual of the Ministry of Health (Brazil, 2008), titled "Operational Instructions: Necessary Information for Conducting Clinical Trials with Phytotherapies".

5.7Statistical Analysis

The data were stored in spreadsheets and validated using **GraphPad Prism 8.0** software. The following statistical tests were conducted to assess the data:

1. **Normality Test**:
    - **Shapiro-Wilk test** and **Kolmogorov-Smirnov test** were used to check the normality of the data. Both tests were performed with a significance level of **0.01**. The results indicated that there was no significant deviation from normality, suggesting that the data followed a normal distribution.
2. **Comparison Between Groups**:
    - Initially, **ANOVA** (Analysis of Variance) was conducted to compare the means between the treatment group (*Rhodiola rosea*) and the placebo group. The significance level was set at **0.05**.
    - After ANOVA, a **Tukey post-hoc test** was performed to compare the means of the different groups and identify where the differences occurred. However, no significant differences were found between the groups at the **0.05** level.

In summary, the statistical analysis indicated no significant differences in the perceived stress scores between the *Rhodiola rosea* and placebo groups, based on both the normality tests and the ANOVA results.

3. RESULTS AND DISCUSSION

3.1 Participants' Profile

The table 2 characterizes the sociodemographic profile of the sample, including data on gender, age, income, and body mass index (BMI). The sample consisted of a total of 25 participants, with a predominance of females (88%). The most common age range among participants was 30 to 34 years (52%). Regarding family income, 76% earned less than four minimum wages.

Table2. Descriptive Table of Sociodemographic Characteristics of Healthcare Professionals from a Private Hospital in Palmas, Tocantins (n=25).

Variables	**Participants (n)**	**%**
Gender		
Male	3	12
Female	22	88

Age		
20 - 24	2	8
25 - 29	2	8
30 - 34	13	52
35 - 39	8	32
40	0	0
Income		
1 – 2 Minimum wages	7	28
2 – 4 Minimum wages	12	48
4 – 10 Minimum wages	6	24

Artuzu et al. (2017) also found a higher participation of female healthcare professionals (72.5%) and an average age of 33.21 years when analyzing the clinical and nutritional profile of 80 workers from a hospital unit according to their work shifts. Silva et al. (2020) identified that 68% of nursing professionals had an income of less than 4 minimum wages.

In Table 3, participants were asked about their professional occupation, work shift, and whether they held more than one job. The highest participation was from healthcare professionals, with nurses (44%) and nursing technicians (32%) representing the largest groups, while 24% were made up of physiotherapists, nutritionists, pharmacy assistants, and occupational safety technicians. 84% of professionals worked in a 12-hour shift system, with 36 hours of rest. Of these, 44% worked the day shift, 24% worked the night shift, and 16% worked a double shift (both day and night). Thus, 7 (28%) professionals held more than one job, with the majority being nursing technicians and nurses.

Table3. Descriptive Table of the Careers of Healthcare Professionals from a Private Hospital in Palmas, Tocantins (n=25).

Variables	**Participants (n)**	**%**
Professional Occupation		
Nursing Technician	8	32
Occupational Safety Technician	1	4
Nurse	11	44
Physiotherapist	2	8

Pharmacy Assistant	1	4
Nutritionist	2	8
Work Shift		
Business hours(8h)	4	16
Day shift(12h)	11	44
Night shift(12h)	6	24
Day and night shift(12h)	4	16
Has more than one job?		
No	18	72
Yes	7	28

Regarding professional occupation, Lin et al. (2021) also found higher participation among nurses (46.8%), followed by doctors (17.7%), nursing technicians (18.8%), and administrators (16.7%) when observing employees at a Medical University Hospital in China.

The work shifts corroborated with the study by Dalri (2013), which observed that 53% of nursing professionals in an emergency hospital unit worked the day shift, and 42% worked the night shift. The night shift work rhythm was positively associated with work-related personal wear and tear (LIN et al., 2021).

Regarding the existence of additional employment, Bohrer (2020), when observing nursing professionals at a hospital in the interior of Rio Grande do Sul, found that 75% of the professionals held only one employment contract, findings similar to those in the present study.

The dual work shift among healthcare professionals is more commonly associated with nurses, who work uninterrupted hours to ensure higher pay (BALDOINO & SANTOS, 2020). This routine can lead to health issues such as stress, sleep disorders, pain, physical and psychological wear and tear, fatigue, and nutritional damage, producing a negative impact on the quality of life of these professionals and influencing the quality and safety of care provided to the patients under their care (COELHO et al., 2014).

3.2 Nutritional status of the participants

Table 4 represents body perception and nutritional status according to body mass index and waist-to-hip ratio. Regarding body perception, participants were asked about how they felt about their current weight and their body satisfaction. Concerning body perception, 52% of the participants felt overweight and, consequently, were dissatisfied with their bodies.

With body mass index (BMI) calculated from weight and height, it was observed that approximately 15 participants (60%) had a classification of normal weight, while 9 (36%) participants had a BMI equal to or greater than 25 kg/m², classified as overweight and obesity, with 7 of them working in a 12X36 shift system.

To complement the BMI assessment, waist circumference was measured, and the waist-to-hip ratio was calculated. It was observed that a total of 48% of participants had values above the reference for waist circumference and 36% for the waist-to-hip ratio, indicating an increased risk for chronic diseases (WHO, 1998).

Blake et al. (2021) identified body dissatisfaction in more than half (58.4%) of 310 nursing professionals in the United Kingdom. This dissatisfaction with weight was also negatively correlated with BMI, where participants with higher BMIs were less satisfied with their weight.

Obesity is considered a global health problem, and due to the risk of developing associated comorbidities such as type 2 diabetes, coronary artery disease, hypertension, pulmonary embolism, stroke, asthma, joint problems, and various types of cancer, it increases mortality rates among individuals (ROFF & JAPPY, 2017; NIMPTSCH et al., 2019).

Table4. Body perception and nutritional status of healthcare professionals from a private hospital in Palmas, Tocantins State. (n = 25).

Variables	**Participants (n)**	**%**
feelings about current weight		
Thin	3	12
Normal	9	36
Slightly overweight	5	20
Overweight	5	20
Obese	3	12
body satisfaction		
Yes	12	48
No	13	52
BMI*		
Underweight	1	4
Healthy weight	15	60

Overweight but not obese	5	20
Obese class I	4	16
WC**		
Increased risk	6	24
Greatly increased risk	6	24
WHR***		
No risk	16	64
Greatly increased risk	9	36

*BMI: Body Mass Index**WC: Waist circumference***WHR: Waist-to-hip ratio

According to IBGE data, in Brazil, the percentage of adults (≥18 years of age) with excess weight in 2019 was 62.6% for women and 57.5% for men (IBGE, 2019). Fracalossi & Antunes (2020) observed an average BMI compatible with overweight, 26.9 ± 4.6 kg/m², when observing 446 hospital staff members. The prevalence of overweight and obesity is high among nursing professionals due to their exposure to various risk factors for nutritional disorders, such as poor sleep quality (COELHO et al., 2014).

Working in shifts can increase the risk of overweight and obesity due to changes in eating habits, such as the intake of high-calorie diets, along with physical inactivity and sleep deprivation. These findings were observed by Liu et al. (2018) in a systematic review and meta-analysis involving a total of 27 independent studies with 311,334 participants, where 10,473 cases of overweight and 51,024 cases of obesity were identified in shift workers.

Pazza et al. (2014), when observing the waist circumference of nursing technicians working the night shift in a public hospital, found that 36% had an increased risk for cardiovascular diseases. Almeida et al. (2006) found an increased waist-to-hip ratio in 27% of healthcare workers employed at a hospital in the city of Fortaleza.

3.3 Stress level of participants with the use of Rhodiola rosea L. and placebo.

Figure 3 represents the stress level of participants obtained through the perceived stress scale at the beginning and end of the treatment with the use of Rhodiola rosea L. at a dose of 210 mg and placebo boldo 50 mg. It was observed that there was no statistical difference between the treatments.

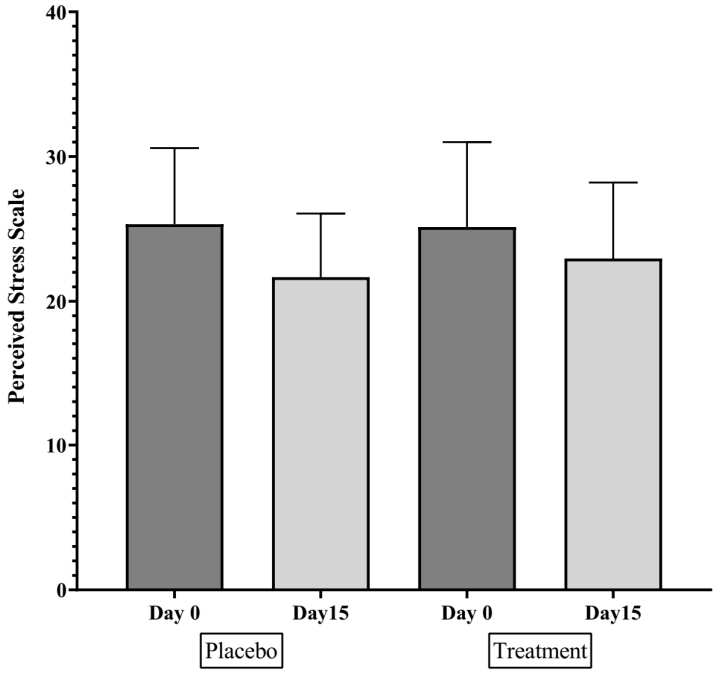

Figure3. Stress level with the use of Rhodiola rosea L. and placebo based on the Perceived Stress Scale of healthcare professionals from a private hospital in Palmas, Tocantins State. (n = 22).

Contrary to the findings of the present study, Edwards et al. (2012), when investigating the therapeutic effects and safety of 200 mg twice a day for 4 weeks of Rhodiola rosea extract in 101 participants, observed that the medication is safe and effective in improving life stress symptoms to a clinically relevant degree. Lekomtseva et al. (2017) also observed the therapeutic effect, safety, and tolerability in 10 individuals with the administration of 2 × 200 mg for 8 weeks. At the end of the study, a significant improvement in chronic or prolonged fatigue symptoms was observed, along with a favorable safety and tolerability profile. Kasper and Dienel (2017) also observed relief from stress and burnout symptoms in a multicenter study of 118 patients with burnout, who used a daily dose of 400 mg of Rhodiola rosea extract administered over 12 weeks.

4. CONCLUSION

Therefore, despite the exhausting work routine, most of the healthcare professionals in the present study had an adequate nutritional status based on body mass index, waist circumference, and waist-to-hip ratio, but most felt overweight and consequently dissatisfied with their bodies.

Although the participants' reports indicated improvement in work activity and sleep, the use of the herbal medicine Rhodiola rosea for 15 days at a dose of 210 mg did not achieve anxiolytic effects, suggesting a higher dose and longer exposure to the medication for effects on stress levels.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

ETHICAL APPROVAL

The research project and the informed consent form (ICF) were approved by the Ethics Committee in Research with Human Beings of the Federal University of Tocantins, with the CAAE number 50427521.9.0000.5519.

REFERENCES

1. ABESO - Brazilian Association for the Study of Obesity and Metabolic Syndrome. Brazilian guidelines on obesity. 4th ed. p. 188, São Paulo, 2016.

2. ALMEIDA, L. A. et al. Factors that generate Burnout Syndrome in health professionals. Care is Fundamental Online. Rio de Janeiro, v. 8 n. 3 p. 4623-8. 2016.

3. ALMEIDA, V. C. F. et al. Anthropometric analysis of health workers: an alternative to predict risks for chronic diseases. Rev. RENE, v. 7, n. 2, p. 39-47. Fortaleza, 2006.

4. ARTUZO, I. P. et al. Clinical and nutritional profile of workers in a hospital unit according to work shift. Health and Research Journal. v. 10, n. 2, p. 347-356, 2017.

5. BANDEIRA, M. A. D. Occupational stress in physicians: a literature review. Revista Amazônia Science & Health, Gurupi, v. 5, n. 2, p. 25-32. 2017.

6. BALDOINO, E. S.; SANTOS, M. C. QUALITY OF LIFE OF NURSING PROFESSIONALS WITH DOUBLE WORK DAYS: a literature review. GOIÂNIA, 2020.

7. BERNIK, M. et al. Pharmacological treatment of posttraumatic stress disorder. Braz. J. Psychiatry 25 (suppl 1), 2003.

8. BOHRER, C. Z. Night work: possible impacts on the lives of nursing professionals at a hospital in the interior of Rio Grande do Sul. Santa Cruz do Sul, 2020.

9. BLAKE, H. et al. Obesity and Diet Predict Attitudes towards Health Promotion in Pre-Registered Nurses and Midwives. Int J Environ Res Public Health. 2021.

10. BRAZIL. Decree No. 3048 of May 6, 1999. Social Security Regulation. PE - Federal Executive Branch, Brasília, 1999.

11. BRAZIL. Ministry of Health. World Health Organization - WHO. Operational instructions: information necessary for conducting clinical trials with herbal medicines. Brasília, 2008. 19

p. (Series A. Standards and Technical Manuals). Translation of: "Operational guidance: information needed to support clinical trials of herbal products".

12. BRAZIL. Ministry of Finance. 1st Quarterly Bulletin on Disability Benefits. Mental Illness and Work. The granting of disability benefits related to Mental and Behavioral Disorders between 2010 and 2016. Brasília, 2017.

13. COELHO, M. P. et al. Nutritional impairments and sleep pattern disorders of nursing workers. Rev Bras Enferm 67 (5), 2014.

14. COHEN, A. et al. The Relationship Between Tobacco Smoking, Cortisol Secretion, and Sleep Continuity. Subst Use Misuse. 2019.

15. COHEN, S. et al. A global measure of perceived stress. Journal of Health and Social Behavior, v. 24, p. 385-396. 1983.

16. BRAZILIAN INSTITUTE OF GEOGRAPHY AND STATISTICS FOUNDATION - IBGE. One in four adults in the country was obese in 2019; Primary Care was well evaluated. Rio de Janeiro: IBGE, 2019.

17. FRACALOSSI, M. G.; ANTUNES, M. T. Relationship between nutritional status, food consumption and length of service in hospital workers in Porto Alegre. Porto Alegre, 2020.

18. DALRI, R. C. M. B. Workload of emergency nurses and its relationship with stress and salivary cortisol. Thesis (Doctorate). University of São Paulo. Ribeirão Preto, 2013.

19. DEAK, T. et al. Neuroimmune mechanisms of stress: sex differences, developmental plasticity, and implications for pharmacotherapy of stress-related disease. Stress, Amsterdam, v. 18 n. 4, p. 367-380. 2015.

20. EDWARDS, D. et al. Therapeutic effects and safety of Rhodiola rosea extract WS® 1375 in subjects with life-stress symptoms--results of an open-label study. Phytother Res. 2012.

21. GLABSKA, D. et al. Fruit and Vegetable Intake and Mental Health in Adults: A Systematic Review. Nutrients. 2020.

22. KASPER, S.; DIENEL, A. Multicenter, open-label, exploratory clinical trial with Rhodiola rosea extract in patients suffering from burnout symptoms. Neuropsychiatr Dis Treat. 2017.

23. LEKOMTSEVA, Y.; ZHUKOVA, I.; WACKER, A. Rhodiola rosea in subjects with Prolonged or Chronic Fatigue Symptoms: Results of an Open-Label Clinical Trial. Complementary Medicine Research. v.24, p. 46-52, 2017.

24. LIN R. T. et al. Long working hours and burnout in health care workers: Non-linear dose-response relationship and the effect mediated by sleeping hours-A cross-sectional study. J Occup Health. 2021.

25. LIN R. T. et al. Long working hours and burnout in health care workers: Non-linear dose-response relationship and the effect mediated by sleeping hours-A cross-sectional study. J Occup Health. 2021.

26. LIU, Y. et al. Inflammation: The Common Pathway of Stress-Related Diseases. Frontiers in Human Neuroscience, Shanghai, v. 11, p. 1-11. 2017.

27. LIU, Q. et al. Is shift work associated with a higher risk of overweight or obesity? A systematic review of observational studies with meta-analysis. Int J Epidemiol. 2018.

28. NASCIMENTO, M. C. et al. Mental health of accounting science teachers: the use of stress coping strategies. R. Cont. Fin. – USP, São Paulo, v. 33, n. 88, p. 150-166. 2022.

29. NOREEN, E. E. J. et al. The effects of an acute dose of rhodiola rosea on endurance exercise performance. Journal of Strength and Conditioning Research, v. 27, n.3, p. 839–847, 2013.

30. NIMPTSCH, K. et al. Diagnosis of obesity and use of obesity biomarkers in science and clinical medicine. Metabolism. 2019.

31. PAZZA, S. et al. Nutritional assessment of night-shift nursing technicians at a public hospital in northern Rio Grande do Sul. Nursing Journal. FW, v. 8, n. 8, p. Rio Grande do Sul, 2012.

32. PIRES C. A. et al. The use of herbal medicines and medicinal plants by pregnant women. Rev. Fitos. Rio de Janeiro. 2021.

33. REIS, R. S. et al. Validation article of the Brazilian version (in press). Perceived Stress Scale: Reliability and Validity Study in Brazil. Journal of Health Psychology. v. 15, n. 1, p.107-14. 2010.

34. SANTOS, S. V. M. et al. Socioeconomic, epidemiological and labor characteristics of hospital nursing professionals. Recom, v. 7, 2017. Available at: http://seer.ufsj.edu.br/index.php/recom/article/view/1391/1567 . Accessed on: 06/15/2021.

35. ROFF, H.; JAPPY C. Adiposity and the Role of Neuroendocrine Hormones in Energy Balance. AACN Adv Crit Care. 2017.

36. STOJCHEVA, I. E.; QUINTELA, J. C. The Effectiveness of Rhodiola rosea L. Preparations in Alleviating Various Aspects of Life-Stress Symptoms and Stress-Induced Conditions-Encouraging Clinical Evidence. Molecules. 2022.

37. WHO, World Health Organization. Physical status: The use and interpretation of anthropometry. Report of a WHO expert committee. World Health Organization technical report series. Geneva. 1998.

38. ZORZAL, L. G. C. Stress levels among nurses in risk classification in state hospitals in Espírito Santo. Enferm. Foco, Espirito Santo, v. 11 n. 1 p. 131-135. 2020