

As a library, NLM provides access to scientific literature. Inclusion in an NLM database does not imply endorsement of, or agreement with, the contents by NLM or the National Institutes of Health.

Learn more: [PMC Disclaimer](#) | [PMC Copyright Notice](#)



[Int J Health Sci \(Qassim\)](#). 2014 Oct; 8(4): 393–401.

PMCID: PMC4350893

PMID: [25780358](#)

## Effects of chocolate intake on Perceived Stress; a Controlled Clinical Study

[Ahmed Al Sunni](#) and [Rabia Latif](#)

### Abstract

---

#### Background

Cocoa polyphenols have been shown to reduce stress in highly stressed, as well as normal healthy individuals, we wondered whether commercially available chocolate could reduce perceived stress in medical students or not, so we decided to conduct this study.

#### Methods

Sixty students were divided into 3 groups (10 males + 10 females/group): i) Dark chocolate (DC) ii) Milk chocolate (MC) iii) White chocolate (WC). Subjects answered a PSS-10 (Perceived Stress Scale) questionnaire at baseline and after consumption of chocolate (40 g/day) for 2 weeks. Data were analyzed by using Microsoft Excel and SPSS version 20. Descriptive analyses were conducted. Means were compared across the study groups by One-Way ANOVA and within the same group by paired 't' test.

#### Results

Mean stress scores compared between the groups by ANOVA revealed statistically not significant differences before ( $F = 0.505$ ;  $P = 0.606$ ) and after chocolate consumption ( $F = 0.188$ ;  $P = 0.829$ ). Paired 't' test compared stress scores means before and after chocolate supplementation within the same group and exhibited statistically significant decrease in DC ( $t = 2.341$ ;  $p \text{ value} = 0.03$ ) and MC ( $t = 3.302$ ;  $p \text{ value} =$



0.004) groups. Mean stress scores decreased, on average, by approximately 2 and 3 points in DC and MC groups, respectively, at 95% Confidence Interval. The difference was more evident and statistically significant in female students as compared to the males.

## Conclusion

Consumption of 40 g of Dark and Milk chocolate daily during a period of 2 weeks appear to be an effective way to reduce perceived stress in females.

**Keywords:** Perceived Stress, Medical Students, Chocolate, Controlled Clinical Study

## Introduction

---

Stress is defined as “the non-specific response of the body to any demand for change.” The effects of stress on public health are profound. Researchers have related stress to a number of diseases ranging from cardiovascular disease to diabetes and even various cancers. <sup>(1-4)</sup>

The stress associated with medical students while undergoing medical education is an accepted model of stress and produces consistent findings. Nearly all medical colleges have an authoritarian and rigid atmosphere that encourages competition instead of cooperation among learners. <sup>(5)</sup> Fairly high levels of stress among medical students have been documented worldwide. <sup>(6-10)</sup> A study conducted in three British medical universities found the prevalence of stress to be 31.2%. <sup>(11)</sup> In Malaysia and Thai medical colleges, stress prevalence was 41.9% <sup>(12)</sup> and 61.4% <sup>(13)</sup> respectively. In Saudi Arabia, local epidemiological data about stress among medical undergraduate students are scarce. Results of two recent studies from Saudi Arabia have suggested high rates of stress (63 % and 71 %) among medical students. <sup>(14, 15)</sup>

The study of medicine is extensive, laborious and very stressful especially during preclinical study period. Students are subjected to endless working hours, and examinations. Peers, teachers or parental pressures add an extra burden. Students often have to work beyond their threshold strength to get an outstanding grade-point-average. Hence, medical students experience considerable stress that may result in negative academic, emotional and health outcomes. <sup>(16)</sup> Attention must be directed to reduce the stress in undergraduate medical education if we are to maintain the commitment and enthusiasm in the students.

Recent evidence showed that nutritional interventions exert a beneficial effect on many of the biological risk factors produced by stress, <sup>(17)</sup> cocoa products being one of them. Chocolate has been shown to reduce stress in highly stressed, <sup>(18)</sup> as well as normal healthy individuals <sup>(19)</sup> in two randomized controlled studies. Since cocoa polyphenols could reduce stress in highly stressed, as well as normal healthy individuals, we wondered whether commercially available chocolate could reduce perceived stress in medical students or not.

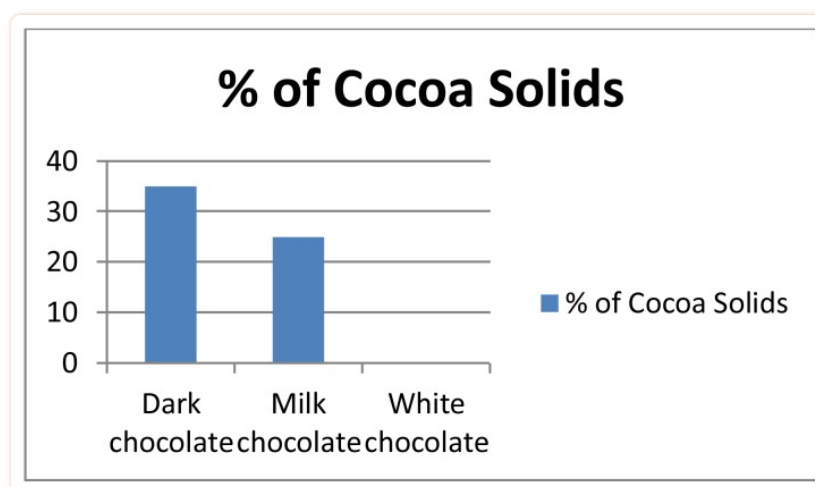
## Material and Methods

It was a non-randomized, parallel controlled clinical study (CCS). Permission and ethical approval to conduct the study was sought and granted by the University Deanship of Scientific Research. Since stress perception by medical students is linked with their academic year, <sup>(14)</sup> we targeted students from the same academic year, positioned in the main university campus, to be able to be contacted easily as a group.

Participants were drawn by non-probability convenience sampling from 2<sup>nd</sup> year Medicine class in our University. Participation into the study was solely on a voluntary basis and students who volunteered were reassured that all information obtained will be kept confidential and secure. Our inclusion criteria were (i) non-smoker (ii) no known chronic diseases such as diabetes, coronary heart disease, or other major illnesses (iii) willing to consume 40 g of the chocolate daily for 2 weeks. Our exclusion criteria included (i) use of any medication (ii) known history of any illness (endocrinal, metabolic, psychiatric) at recruitment (iii) Pregnancy (iv) females who were expected to undergo menstrual phase of uterine cycle during chocolate eating phase, and (iv) inaccessibility to follow up.

Sixty students (30 males, 30 females) from 2<sup>nd</sup> year medical class were recruited to participate in the study. The subjects were advised that the intake of cocoa and chocolate other than the study chocolate be discontinued 1 week prior to the study and that this restriction should be maintained throughout the study period. Based on the type of chocolate given, subjects were divided equally into 3 groups (10 males + 10 females/group) as follows: i) Dark chocolate group (DC) ii) Milk chocolate group (MC) and iii) White chocolate group (WC).

The protocol of the study visit was as follows: During the first visit before the commencement of the study, subjects were given information about the study, and, if the consent was given, more specific instructions were provided. At the first study visit, subjects were divided into DC, MC and WC groups, based on their own preference, and study chocolates were given. The subjects were instructed to consume the daily amount of chocolate in a single portion. The composition, nutrient content and calories per bar were identical in DC, MC and WC except the amount of cocoa solids ([Table 1](#) and [Figure 1](#)).



[Figure 1](#)

Amount of cocoa solids per bar

**Table 1**

Ingredients present in study chocolates

| S. No | Ingredients                 | Dark Chocolate | Milk Chocolate | White Chocolate |
|-------|-----------------------------|----------------|----------------|-----------------|
| 1     | Cocoa solids                | Present        | Present        | Absent          |
| 2     | Cocoa butter                | Present        | Absent         | Present         |
| 3     | Cocoa processed with alkali | Absent         | Absent         | Present         |
| 4     | Milk solids                 | Absent         | Present        | Present         |
| 5     | Milk fat                    | Present        | Absent         | Absent          |
| 6     | Lactose                     | Absent         | Absent         | Present         |
| 7     | Sugar                       | Present        | Present        | Present         |
| 8     | Emulsifier (Soya Lecithin)  | Present        | Present        | Present         |
| 9     | Flavouring agent (Vanilla)  | Present        | Present        | Present         |

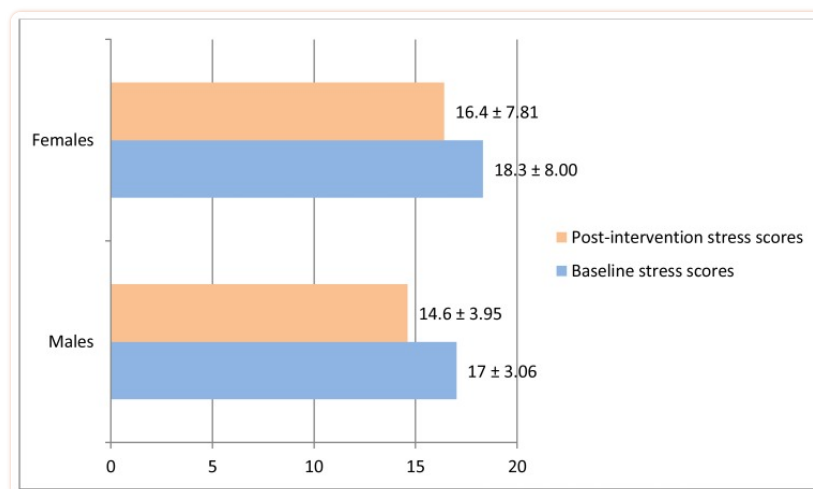
Subjects were studied at baseline and after consumption of chocolate (40 g/day) for 2 weeks. Data collection was accomplished by using a questionnaire PSS-10 (Perceived stress scale) which is the most widely used psychological instrument for measuring the perception of stress. It consisted of 10 items that measured perceived stressful experiences over the previous month with a 5-point Likert scale ranging from never (=0), almost never (=1), sometimes (=2), fairly often (=3) and very often (=4).<sup>(20)</sup> The PSS-10 has a possible range of scores from 0 to 40. We used Arabic version whose internal consistency reliability assessed using Cronbach's  $\alpha$ , was reported to be 0.74.<sup>(21)</sup> Students answered the questionnaire in direct supervision of either of the two authors. Test-retest technique was adopted to check the reliability and validity of the questionnaire. Ten students asked to solve the same questionnaire with a two weeks lag to see if they answered in the same manner.

### Statistical Analysis

The collected data was entered in Microsoft Excel spreadsheet; coding of the variables was done. PSS scores were obtained by reversing responses (e.g., 0 = 4, 1 = 3, 2 = 2, 3 = 1 and 4 = 0) to the four positively stated items (items 4, 5, 7 and 8)<sup>(22)</sup> and then summing across all scale items. The scale yielded a single score, with high scores indicating higher levels of stress and low scores indicating lower levels of stress. Statistical analysis of the coded data was done by using SPSS version 20 and the results were expressed as (Means  $\pm$  standard deviation). Difference between baseline and end-point values within the pooled groups were tested by paired 't' test. Means were compared across the study groups by One-Way ANOVA. Differences with *p* values of 0.05 or less were considered significant.

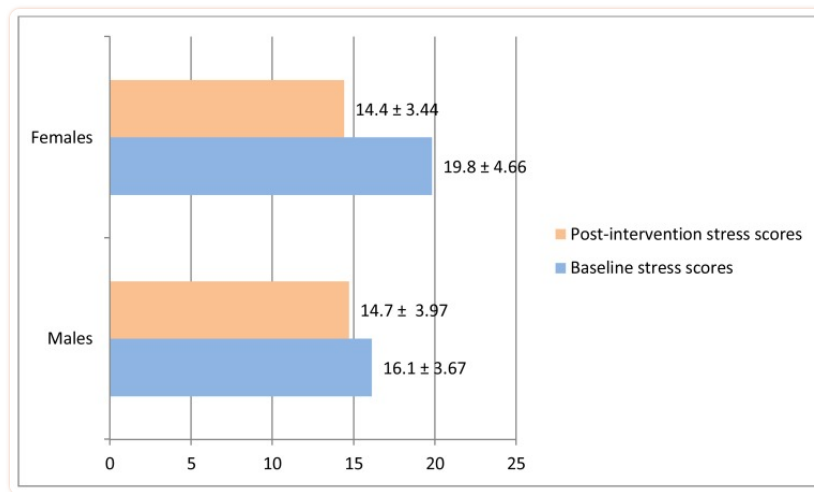
### Results

Pre- and Post-chocolate consumption perceived stress as reported by the students has been shown in [Table 2](#). Baseline stress scores between the groups compared by ANOVA revealed statistically insignificant differences ( $F = 0.505$ ;  $P = 0.606$ ) ([Table 3](#)), meaning that our groups were not different from one another. Overall, compliance with the nutritional instructions and restriction was good, as none of the subjects reported consumption of the restricted foods (cocoa and chocolate products other than the study chocolate). Mean stress scores among the groups also did not differ significantly from one another at the end of treatment; as revealed by ANOVA ( $F = 0.188$ ;  $P = 0.829$ ) ([Table 3](#)). Paired 't' test was used to compare the means of stress scores before and after chocolate supplementation within the same group and it exhibited statistically significant differences in DC ( $t = 2.341$ ;  $p \text{ value} = 0.03$ ) and MC ( $t = 3.302$ ;  $p \text{ value} = 0.004$ ) groups ([Table 3](#)). In DC and MC groups, mean stress scores decreased, on average, by approximately 2 and 3 points respectively at the 95% Confidence Interval (95% CI). Thorough probing of the results showed that the difference was more evident and statistically significant in female students as compared to the males in DC and MC groups ([Figure 2](#) and [3](#)). In WC group, there were statistically insignificant differences among pre- and post-chocolate consumption mean stress scores in males and females ([Figure 4](#)).



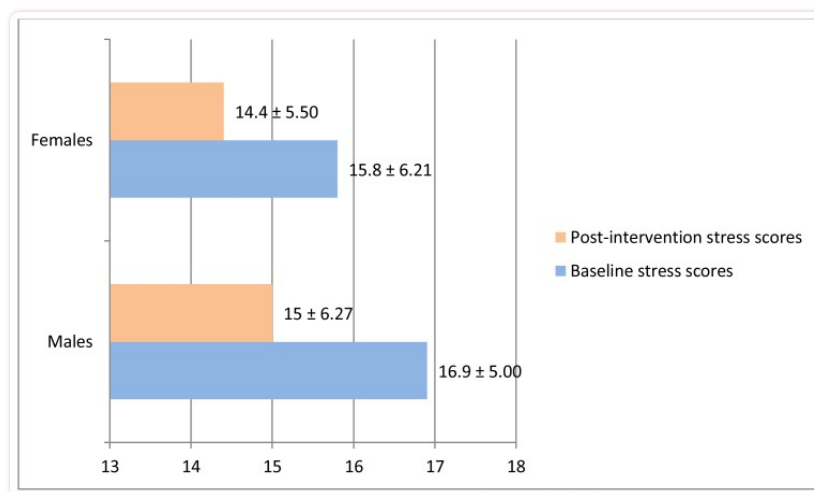
[Figure 2](#)

Dark Chocolate Group Mean stress scores (Mean  $\pm$  SD) pre and post intervention.



[Figure 3](#)

Milk Chocolate Group Mean stress scores (Mean ± SD) pre- and post-intervention.



[Figure 4](#)

White Chocolate Group Mean stress scores (Mean ± SD) pre- and post-intervention.

Table 2

Perceived stress as reported by the students Pre and Post-chocolate consumption

|   | Questions   |      | 0        | 1            | 2         | 3         | 4          |
|---|---|------|----------|--------------|-----------|-----------|------------|
|   |   |      | Never    | Almost never | Sometimes | Often     | Very often |
|   |   |      | No. (%)  | No. (%)      | No. (%)   | No. (%)   | No. (%)    |
| 1 | In the last month, how often have you been upset because of something that happened unexpectedly?             | Pre  | 5 (8.3)  | 22 (36.7)    | 23 (38.3) | 8 (13.3)  | 2 (3.3)    |
|   |   | Post | 8 (13.3) | 21 (35)      | 22 (36.7) | 7 (11.7)  | 2 (3.3)    |
| 2 | In the last month, how often have you felt that you were unable to control the important things in your life? | Pre  | 8 (13.3) | 18 (30)      | 26 (43.3) | 5 (8.3)   | 3 (5)      |
|   |   | Post | 8 (13.3) | 28 (46.7)    | 16 (26.7) | 7 (11.7)  | 1 (1.7)    |
| 3 | In the last month, how often have you felt nervous and “stressed”?  | Pre  | 1 (1.7)  | 11 (18.3)    | 19 (31.7) | 22 (36.7) | 7 (11.7)   |
|   |   | Post | 3 (5)    | 14 (23.3)    | 27 (45)   | 13 (21.7) | 3 (5)      |
| 4 | In the last month, how often have you felt confident about your ability to handle your personal problems?     | Pre  | 0        | 5 (8.3)      | 25 (41.7) | 27 (45)   | 3 (5)      |
|   |   | Post | 0        | 0            | 12 (20)   | 37 (61.7) | 11 (18.3)  |
| 5 | In the last month, how often have you felt that things were going your way?                                   | Pre  | 1 (1.7)  | 7 (11.7)     | 24 (40)   | 22 (36.7) | 6 (10)     |
|   |   | Post | 1 (1.7)  | 6 (10)       | 22 (36.7) | 29 (48.3) | 2 (3.3)    |
| 6 | In the last month, how often have you found that you could not cope with all the things that you had to do?   | Pre  | 6 (10)   | 20 (33.3)    | 27 (45)   | 5 (8.3)   | 2 (3.3)    |
|   |   | Post | 5 (8.3)  | 28 (46.7)    | 21 (35)   | 6 (10)    | 0          |
| 7 | In the last month, how often have you been able to control irritations in your life?                          | Pre  | 1 (1.7)  | 5 (8.3)      | 23 (38.3) | 28 (46.7) | 3 (5)      |
|   |   | Post | 0        | 5 (8.3)      | 20 (33.3) | 31 (51.7) | 4 (6.7)    |
| 8 | In the last month, how often have you felt that you were on top of things?                                    | Pre  | 0        | 7 (11.7)     | 26 (43.3) | 26 (43.3) | 1 (1.7)    |
|   |   | Post | 0        | 6 (10)       | 18 (30)   | 33 (55)   | 3 (5)      |

Table 3

Mean stress scores in all three groups.

| Groups*         | Perceived Stress Scores (Mean $\pm$ SD) |                   | T value | p-value (Paired t test) |
|-----------------|---|-------------------|---------|-------------------------|
|                 | Baseline                                | Post-intervention |         |                         |
| Dark Chocolate  | 17.65 $\pm$ 5.93                        | 15.5 $\pm$ 6.09   | 2.341   | 0.03                    |
| Milk Chocolate  | 17.95 $\pm$ 4.50                        | 14.55 $\pm$ 3.62  | 3.302   | 0.004                   |
| White Chocolate | 16.35 $\pm$ 5.52                        | 14.70 $\pm$ 5.75  | 0.930   | 0.364                   |
| p-value (ANOVA) | 0.61                                    | 0.83              |         |                         |

\*(Number of subjects/group = 20)

## Discussion

Dark chocolate and other cocoa products have received lot of attention all over the world as dietary supplements to improve cardiovascular health. However the scientific evidence those cocoa products may alleviate stress as well is a relatively novel finding. Stress and our body reaction to it is one of the risks of coronary artery disease. In this regard, if chocolate can buffer our response to stress, this would be a novel cardio protective effect of chocolate.

To the best of our knowledge, this is the first study focusing on the effects of chocolate supplementation on perceived stress in medical students. The results of our study demonstrate significant reduction in perceived stress score after consuming dark and milk chocolate for 2 weeks, more so in females than in male students. Our results are in conformity with a clinical trial <sup>(19)</sup> which provided strong evidence that a daily consumption of 40 grams of dark chocolate for two weeks reduced levels of stress hormones in highly stressed people. Our study results are also in agreement with a recent randomized, placebo-controlled trial that reported that those men who consume dark chocolate had significantly lower levels of cortisol and epinephrine (peripheral stress hormones) compared to control subjects after a mock psychosocial stress test. <sup>(18)</sup> However the ACTH levels (central stress hormone) were identical in both groups. The researches concluded that dark chocolate intake blunted the body's response to the brain signals of stress. In particular, the response of the adrenal gland, which produces cortisol, was much less. Wirtz et al., <sup>(18)</sup> also assessed cognitive stress appraisal by using the Primary Appraisal Secondary Appraisal (PASA) questionnaire. It was noticed that, since the body stress response was less significant, men consuming dark chocolate reported having less feelings of stress during the process as compared to the control subjects. The decrease in the mean stress scores after consumption of white chocolate was statistically not significant.

This shows that the blunting of the perceived stress was not due to sweet nature of dark or milk chocolates but due to cocoa solids which were present in dark and milk chocolate but were absent in white chocolate. Cocoa solids are one of the richest sources of flavanol antioxidants. <sup>(23)</sup> The link between stress and oxidative status in human body is now well-established. It has been demonstrated that stress increases lipid peroxidation and an imbalance between antioxidant enzyme activities. <sup>(24)</sup> In this perspective, antioxidants



supplementation is considered as a beneficial strategy for improving stress. <sup>(25,26)</sup> There is a strong possibility that flavonoid rich chocolate supplementation might have acted through a modulation of oxidative status, that is the enhancement of endogenous antioxidant defense and the subsequent reduction of oxidative stress. Nevertheless, further studies are needed to confirm this hypothesis, and the exact mechanism of action remains to be explored.

The observed gender-specific difference in perceived stress scores following chocolate intake may be partly attributed to effects of sex hormones. <sup>(27, 28)</sup> Scientific evidence shows that hypothalamic-pituitary-adrenal axis response during the stress differs markedly between males and females and there is an increased sensitivity of the adrenal cortex in women as compared to men. <sup>(29)</sup> Future studies are warranted in post-menopausal women to see whether these gender differences persist or diminish after menopause. Last but not the least, the benefits of chocolate need to be carefully considered with the calories consumed.

## Conclusions

---

Dark and Milk chocolate appear to be an effective way to reduce perceived stress in females.

## Limitation

---

Our study was based on self-reported information provided by students. Therefore, there is some probability for reporting bias. To ensure treatment compliance, the study was non-randomized. The students chose whether they preferred Dark, Milk or White Chocolate. This non-randomization means failure of the blinding of the identity of treatments from participants, investigators and assessors. Therefore, one should be cautious in drawing cause and effect hypothesis from our results. Last but not the least; small sample size in each group was also one of the limitations.

## Acknowledgement

---

The authors acknowledge the financial support provided by the Deanship of Scientific Research, University of Dammam for this study.

## References

---

1. Veen G, Giltay EJ, DeRijk RH, van Vliet IM, van Pelt J, Zitman FG. Salivary cortisol, serum lipids, and adiposity in patients with depressive and anxiety disorders. *Metabolism*. 2009;58(6):821–7. [[PubMed](#)] [[Google Scholar](#)]
2. Thayer JF, Yamamoto SS, Brosschot JF. The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. *Int J Cardiol*. 2010;141(2):122–31. [[PubMed](#)] [[Google Scholar](#)]
3. Heraclides A, Chandola T, Witte DR, Brunner EJ. Psychosocial stress at work doubles the risk of type 2 diabetes in middle-aged women: evidence from the Whitehall II study. *Diabetes Care*. 2009;32(12):2230–5. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
4. Kruk J. Self-reported psychological stress and the risk of breast cancer: A case-control study. *Stress*. 2012;15(2):162–71. [[PubMed](#)] [[Google Scholar](#)]

5. Blache G. Doctors, Despite it All: Stresses in Medical Training. *Holistic Med.* 1988;3(3):151–60. [[Google Scholar](#)]
6. Wilkinsos TJ, Gill DJ, Fitzjohn J, Palmer CL, Mulder RT. The impact on students of adverse experiences during medical school. *Med Teach.* 2006;28:129–35. [[PubMed](#)] [[Google Scholar](#)]
7. Ross S, Cleland J, Macleod MJ. Stress, debt and undergraduate medical performance. *Med Educ.* 2006;40:584–9. [[PubMed](#)] [[Google Scholar](#)]
8. Dahlin M, Joneborg N, Runeson B. Stress and depression among medical students: a cross-sectional study. *Med Educ.* 2005;39:594–604. [[PubMed](#)] [[Google Scholar](#)]
9. Singh G, Hankins M, Weinman JA. Does medical school cause health anxiety and worry in medical students? *Med Educ.* 2004;38:479–81. [[PubMed](#)] [[Google Scholar](#)]
10. Styles WM. Stress in undergraduate medical education: ‘the mask of relaxed brilliance’ *Br J Gen Pract.* 1993;43:46–7. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
11. Firth J. Levels and sources in medical students. *BMJ.* 1986;292:1177–80. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
12. Sherina MS, Rampal L, Kaneson N. Psychological stress among undergraduate medical students. *Med J Malaysia.* 2004;59:207–11. [[PubMed](#)] [[Google Scholar](#)]
13. Saipanish R. Stress among medical students in a Thai medical school. *Med Teach.* 2003;25:502–6. [[PubMed](#)] [[Google Scholar](#)]
14. Abdulghani HM, AlKanhal AA, Mahmoud ES, Ponnampereuma GG, Alfari EA. Stress and Its Effects on Medical Students: A Cross-sectional Study at a College of Medicine in Saudi Arabia. *J Health PopulNutr.* 2011;29(5):516–22. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
15. Al-Sunni A, Latif R. Perceived stress among medical students in preclinical years: A Saudi Arabian Perspective. *Saudi Journal for Health Sciences.* 2014;3(3):155–9. [[Google Scholar](#)]
16. Willcock S, Daly MG, Tennant CC, Allard BJ. Burnout and psychiatric morbidity in new medical graduates. *Med J Aust.* 2004;181:357–60. [[PubMed](#)] [[Google Scholar](#)]
17. Kimura K, Ozeki M, Juneja LR, Ohira H. L-Theanine reduces psychological and physiological stress responses. *Biol Psychol.* 2007;74(1):39–45. [[PubMed](#)] [[Google Scholar](#)]
18. Wirtz PH, von Känel R, Meister RE, Arpagaus A, Treichler S, Kuebler U, et al. Dark Chocolate Intake Buffers Stress Reactivity in Humans. *J Am CollCardiol.* 2014;63(21):2297–9. [[PubMed](#)] [[Google Scholar](#)]
19. Martin FP, Rezzi S, Peré-Trepat E, Kamlage B, Collino S, Leibold E, et al. Gut Microbiota, and Stress-Related Metabolism in Free-Living Subjects. *J Proteome Res.* 2009;8(12):5568–79. [[PubMed](#)] [[Google Scholar](#)]
20. Oman D, Shapiro S, Thoresen C, Plante T, Flinders T. Meditation lowers stress and supports forgiveness among college students: A randomized controlled trial. *J Am Coll Health.* 2008;56(5):569–78. [[PubMed](#)] [[Google Scholar](#)]
21. Chaaya M, Osman H, Naassan G, Mahfoud Z. Validation of the Arabic version of the Cohen Perceived Stress Scale (PSS-10) among pregnant and postpartum women. *BMC Psychiatry.* 2010;10:111. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
22. Tavoracci MP, Ladner J, Grigioni S, Richard L, Villet H, Dechelotte P. Prevalence and association of perceived stress, substance use and behavioral addictions: a cross-sectional study among university students in France, 2009–2011. *BMC Public Health.* 2013;13:724. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]

23. Miller KB, Hurst WJ, Payne MJ, Stuart DA, Apgar J, Sweigart DS, et al. Impact of Alkalization on the Antioxidant and Flavanol Content of Commercial Cocoa Powders. *J Agric Food Chem*. 2008;56(18):8527–33. [[PubMed](#)] [[Google Scholar](#)]
24. Lucca G, Comim CM, Valvassori SS, Réus GZ, Vuolo F, Petronilho F, et al. Effects of chronic mild stress on the oxidative parameters in the rat brain. *Neurochem Int*. 2009;54:358–62. [[PubMed](#)] [[Google Scholar](#)]
25. Milesi MA, Lacan D, Brosse H, Desor D, Notin C. Effect of an oral supplementation with a proprietary melon juice concentrate (Extramel®) on stress and fatigue in healthy people: a pilot, double-blind, placebo-controlled clinical trial. *Nutrition Journal*. 2009;8:40. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
26. Carillon J, Notin C, Schmitt K, Simoneau G, Lacan D. Dietary Supplementation with a Superoxide Dismutase-Melon Concentrate Reduces Stress, Physical and Mental Fatigue in Healthy People: A Randomised, Double-Blind, Placebo-Controlled Trial. *Nutrients*. 2014;6:2348–59. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
27. Kajantie E, Phillips DI. The effects of sex and hormonal status on the physiological response to acute psychosocial stress. *Psychoneuroendocrinology*. 2006;31:151–78. [[PubMed](#)] [[Google Scholar](#)]
28. Goldstein JM, Jerram M, Poldrack R, Ahern T, Kennedy DN, Seidman LJ, et al. Hormonal cycle modulates arousal circuitry in women using functional magnetic resonance imaging. *J Neurosci*. 2005;25:9309–16. [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
29. Roelfsema F, van den Berg G, Frölich M, Veldhuis JD, van Eijk A, Buurman MM, et al. Sex-dependent alteration in cortisol response to endogenous adrenocorticotropin. *J Clin Endocrinol Metab*. 1993;77:234–40. [[PubMed](#)] [[Google Scholar](#)]