## Medical students' use of caffeine for 'academic purposes' and their knowledge of its benefits, side-effects and withdrawal symptoms

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### Abstract

**Background:** Caffeine is often used for its benefits, which include increased vigilance. It does have side-effects, however, such as palpitations and withdrawal symptoms that include headaches and drowsiness. Tertiary education often requires students to study for extended hours, especially during periods of increased workload prior to tests and examinations. Medical students, who have to master a very large volume of academic work in a limited period of time, are no exception. This cross-sectional study investigated caffeine use for 'academic purposes' by first- to third-year medical students at the University of the Free State in 2006, and their knowledge of its benefits, side-effects and withdrawal symptoms.

**Methods:** Data were collected by means of an anonymous, self-administered questionnaire that was completed by students during formal class time, arranged in advance with the relevant lecturers. Questionnaires were available in Afrikaans and English. A pilot study was conducted on 20 physiotherapy students to test the questionnaire. Chi-squared and Kruskall-Wallis tests were used to compare categorical and numerical variables, respectively. Ethical approval to perform the investigation was granted by the Ethics Committee of the Faculty of Health Sciences, University of the Free State.

**Results:** A 90.5% (360/389) response rate was obtained. Ninety-four per cent of participants used caffeine, with academic purposes (62.6%) among the three most frequent reasons given for its consumption. Other reasons included social consumption (70%) and preference for the taste (72.4%). Coffee (88.2%) was the most commonly consumed caffeinated product among these students, followed by energy mixtures and tablets (37.9%), and soft drinks (36%). Third-year students were the heaviest consumers of coffee for academic purposes. An increase in caffeine consumption for academic purpose was directly related to progression from first- to third- year of the medical course. The average scores for questions on the benefits, side-effects and withdrawal symptoms were all below 1.5 out of 5. Misconceptions about caffeine were also identified. With regard to the benefits of caffeine, the most commonly cited misconception was that it could be used as a substitute for sleep (26.7% of respondents). The most common misconception regarding its side-effects was that it caused hot flushes (21.9%), while aggression (27.2%) was cited as the most common misconception regarding caffeine withdrawal.

**Conclusions:** The high percentage of caffeine usage and low scores in the caffeine knowledge test indicated that most participants were using caffeine without having sufficient knowledge of its benefits, side-effects and withdrawal symptoms. It is recommended that awareness programmes on the side-effects and symptoms of caffeine withdrawal should be implemented by the student health and counselling facilities on campus. The display of posters in strategic venues and distribution of pamphlets could assist in the dissemination of information on this extensively consumed substance.

P This article has been peer reviewed.

### Introduction

Caffeine is a central nervous system stimulant belonging to the group of xanthines.<sup>1</sup> Approximately 90% of the caffeine contained in a cup of coffee is cleared from the stomach within 20 minutes after oral ingestion, with its effects commencing within an hour and lasting for three to four hours.<sup>2</sup> The peak plasma concentration is reached after approximately 40–60 minutes,<sup>3</sup> with a half-life of approximately six hours in healthy adults.<sup>4</sup> The half-life is shorter in smokers and longer in pregnant women and women taking oral contraceptives.<sup>2</sup>

Caffeine is the most widely consumed drug in human history and is used by more than 80% of the world's population. Caffeine intake is most commonly attributed to the consumption of coffee (± 137 mg/cup of caffeinated coffee and ± 2mg/cup of decaffeinated coffee; the volume of one cup is approximately 240 ml), tea (± 47 mg/cup), caffeinated soft drinks (± 46 mg/340 ml can or bottle of cola beverage) and energy drinks (up to 80 mg/can).<sup>3,4</sup> Caffeine is also commonly found in chocolates (± 7 mg/200g) and non-beverage foodstuff, as well as some medications. Complete non-users of caffeine may therefore be close to non-existent.<sup>2,4,5</sup>

The widespread use of caffeine may be due to the fact that its habitual consumption has been significantly related to increased self-reported alertness, improved performance of vigilance tasks and fewer lapses of

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attention, improved long-term memory and faster locomotor speed.<sup>6,7</sup> It may also help to prevent several chronic diseases such as type 2 diabetes mellitus, Alzheimer's and Parkinson's disease, liver diseases (cirrhosis and hepatocellular carcinoma) and, in addition, it has antiinflammatory properties.<sup>5,8,9</sup> However, habitual caffeine consumption has not been reported to improve short-term memory, information processing, planning and attention.<sup>7</sup>

Ongoing debate currently exists with regard to the belief that caffeine can enhance psychomotor performance and mood, as different studies have revealed contradictory results. Roger et al<sup>10</sup> showed that caffeine only had reinforcing effects on mood and psychomotor performance in participants who were acutely caffeine-withdrawn and not in habitual non-consumers of caffeine. In other words, the caffeine-induced improvements in performance and mood often perceived by consumers do not represent net benefits, but rather a reversal of the performance-reducing effects of caffeine withdrawn volunteers reflected that mood and performance on a number of cognitive measures were improved after consumption of caffeine.<sup>6</sup> This study provided evidence against the argument that the behavioural changes caused by caffeine could merely be attributed to the reversal of negative withdrawal effects.

Caffeine can, however, only reliably affect cognitive performance and mood if the dosage intervals are more than eight hours apart, but not after shorter intervals.<sup>11</sup> Its use has no net restorative effects when performance and mood are decreased by sleep restriction.<sup>12</sup> Therefore, caffeine users should be advised not to consume repeated doses of caffeine within a short period of time (i.e. numerous cups of coffee within a few hours) or to neglect sleep.

The effects of caffeine on the circulatory system include direct myocardial stimulation (resulting in tachycardia, increased cardiac output, ectopic beats and palpitations), increased respiratory rate, increased gastric secretion which may lead to gastric irritation, diuresis and relaxation of the smooth muscles, all of which are regarded to be adverse side-effects of caffeine.<sup>1,2</sup> Although the effect of caffeine on blood pressure is unpredictable,<sup>1</sup> a study conducted by Shepard et al<sup>13</sup> on medical students indicated that the combination of caffeine consumption and examination stress resulted in an elevation in blood pressure of 10/6 mmHg and 9/5 mmHg in male medical students who were at high risk and low risk for hypertension, respectively.<sup>13</sup> For this reason it might be beneficial to male students at high risk of developing hypertension to refrain from caffeine use, particularly during times of stress and increased work demand.

Typically, the onset of withdrawal symptoms occurs 12 to 24 hours after abstinence, with peak intensity at 20 to 51 hours. Withdrawal symptoms, including headaches, fatigue, decreased energy/physical activity, decreased alertness, drowsiness, decreased contentedness, depressed mood, difficulty in concentrating, irritability and clouded mentality, have been reported, and may last for two to nine days.<sup>14</sup>

With regard to the effects of dosage, caffeine doses from 12.5 mg to 20 times this amount affect performance in terms of vigilance and related tasks to a similar extent, indicating a very flat dose–response relationship. Thus, increasing the dosage does not necessarily strengthen the positive effects of caffeine.<sup>11</sup> Low to moderate doses of caffeine (20–200 mg) reportedly produce increased well-being, happiness, energy, alertness,

and sociability, whereas higher doses are more likely to produce anxiety, irritability and gastric discomfort.<sup>14</sup>

Excessive ingestion (1000–1500 mg per day) leads to a state of intoxication known as caffeinism, which is characterised by restlessness, agitation, excitement, incoherent and excited thoughts and speech, and insomnia. Caffeinism is often overlooked by doctors during psychiatric assessments as these symptoms are similar to many psychiatric disorders.<sup>2</sup> Although modest acute effects may occur following initial use, tolerance to these effects appears to develop in the context of habitual use of the substance, with the occurrence of withdrawal symptoms after periods of abstinence.<sup>4</sup>

Tertiary education often necessitates students to study for extended periods of time, especially at times of increased workloads such as prior to tests or examinations. This is particularly true in the case of medical students who are expected to master large volumes of work in a limited amount of time. The use of caffeine has many benefits, such as improving alertness when experiencing fatigue. For the majority of caffeine consumers, exposure is effectively lifelong.<sup>3</sup> It should be kept in mind, however, that its continuous use, if not correctly monitored, could lead to possible dependence accompanied by disadvantageous and even harmful withdrawal symptoms and side-effects.

Consequently, a need to determine the use of caffeine by medical students, particularly for 'academic purposes', and their knowledge of its benefits, side-effects and withdrawal symptoms, was identified. Findings with regard to these issues would reflect the number of students exposed to caffeine and whether their general knowledge of caffeine needed to be addressed. Misconceptions could also be identified and corrected.

The aim of the study was to determine (i) the use of caffeine for academic and other purposes, (ii) which caffeinated products were mostly used, (iii) the frequency of caffeine use for academic purposes, and (iv) knowledge of its benefits, side-effects and withdrawal symptoms among first-, second- and third-year medical students enrolled in the Faculty of Health Sciences, University of the Free State (UFS), in 2006. Knowledge of common facts and misconceptions regarding the effects of caffeine in the target population were also investigated.

### **Methods**

A cross-sectional study was carried out on a target population that included all first- to third-year medical students. The four student researchers (then in their second academic year) conducting the study were excluded.

After an introductory presentation informing students about the rationale and implementation of the study, data were collected by means of a questionnaire available in English and Afrikaans, designed by the researchers. Participants were given the opportunity to ask questions on matters unclear to them. In addition to demographic details, information regarding different types of caffeinated products and frequency of consumption, the questionnaire included multiple-choice questions on the benefits, side-effects and withdrawal symptoms of caffeine. All participants received a consent form and information document with the questionnaire. Participation was voluntary. The signed consent forms and questionnaires were handed in separately. In order to determine participants' knowledge regarding the effects of caffeine, ten options for benefits, side-effects and withdrawal symptoms were listed from which the correct options had to be chosen. Five correct options, identified from previous studies,<sup>7,8</sup> and five incorrect options were included in each question. One mark was awarded for a correct answer, one mark was deducted for an incorrect answer, and no marks were awarded or deducted for not answering. Each question counted out of five and the marks from all three questions were added to obtain a mark out of 15. The average scores for the test, each question, and each year group, were determined and compared.

The data obtained by means of the questionnaires were analysed by the Department of Biostatistics, University of the Free State. Categorical variables were compared statistically using chi-squared tests and numerical variables using Kruskall-Wallis tests.

One of the limitations of the study was the fact that it was impossible to calculate the exact quantity of caffeine ingested by individual participants for academic purposes, as individuals prepared their coffee/ tea differently and consumed other caffeine-containing substances in fluctuating dosages. Consequently, this study compared the caffeine use of each year group by relating the percentage of use for academic purposes to the frequency of use.

Some participants might not have been aware of caffeine consumed in other products. For example, the caffeine content of Bioplus<sup>®</sup> might not have been noted. Participants could therefore mistakenly assume that they did not use caffeine-containing products. In an attempt to overcome this problem, commercial names of caffeine and non-caffeine-containing products were projected on a screen to assist participants.

Students might have been prone to guessing with regard to questions that tested their knowledge. In order to prevent this, marks were deducted for incorrect answers. Participants were informed accordingly in advance.

Another limitation of the study was that not all the benefits, side-effects and withdrawal symptoms of caffeine could be stated in the questionnaire. Only the most common benefits, side-effects and withdrawal symptoms referred to in relevant studies were included.

After approval for the investigation was obtained from the Ethics Committee of the Faculty of Health Sciences, UFS, the Vice-Rector: Academic Planning, the Dean of Student Affairs and the Head of the School of Medicine, a pilot study was conducted. Twenty (ten English- and ten Afrikaans-speaking) second-year physiotherapy students completed the questionnaire. The questionnaire was subsequently modified slightly (e.g. spelling errors were corrected and additional instructions given) to improve the legibility and to prevent participants from making errors when completing the questionnaires.

### **Results**

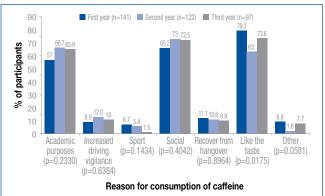
A total participation rate of 90.5% (360 out of a possible total of 398) was obtained, with the participation rate from first-, second- and third-year students being 94% (141/150), 90.4% (122/135) and 85.8% (97/113), respectively. One hundred and seventy-two participants were male (47.8%) and 186 female (51.7%), while two participants (0.5%) did not indicate their gender.

The vast majority of the participants (337/360; 93.6%) stated that they used caffeine, with no significant difference between the three academic years (p = 0.2882). Ninety-six per cent of first-years (135/141), 91% of second-years (111/122) and 93.8% of third-years (91/97) indicated that they consumed caffeine-containing products.

Preference for the taste (244/337; 72.4%), social (235/337; 70%) and academic purposes (211/337; 62.6%) were, by a large margin, the three most common purposes chosen by all the participants. Eleven per cent of the caffeine consumers indicated that they used the substance to recover from a hangover, 10.7% for increased vigilance while driving, and 4.7% to enhance performance in sport. Twenty-one (6.2%) of the participants selected the option "other" as reasons for consuming caffeine. Other reasons included routine, for warmth, with food, to stay awake, stress, to prevent withdrawal, for energy, low cost, thirst, for gastric motility, and boredom.

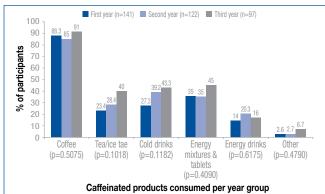
The academic year groups differed slightly with regard to the reasons selected for the consumption of caffeine. The comparison of these differences is shown in Figure 1.



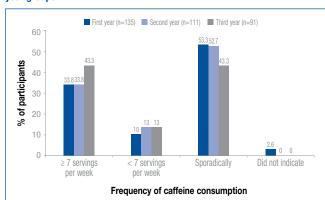


Coffee was the most commonly consumed product (88.2%), followed by energy mixtures and tablets (37.9%), and soft drinks (36%). Tea/ice tea and energy drinks were used by 29.9% and 17.1% of participants, respectively. Other products used for academic purposes, which included chocolates, such as FFWD<sup>®</sup> bars (used by six participants), and warm caffeinated drinks, e.g. hot chocolate (used by two participants), constituted the remaining 3.8%. The distribution of the type of caffeinated products consumed by each academic year group is shown in Figure 2.





As far as the frequency of caffeine usage for academic purposes is concerned, sporadic users comprised 50.2% (106/211) of the participants, while 36.5% of participants (77/211) used it more than seven times a week, and 12.3% (26/211) less than seven times a week. Two participants (0.9%) did not indicate their frequency of caffeine consumption. The frequency of caffeine consumption by participants in each academic year group is shown in Figure 3. Participants using seven or more servings of caffeine per week could be regarded as heavy users, those using less than seven servings per week as moderate users, and those using caffeine sporadically as light users.



### Figure 3: Frequency of caffeine consumption by the three academic year groups

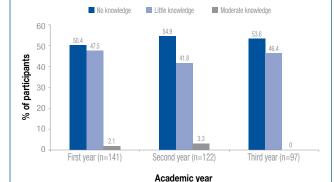
The participants' scores on the section of the questionnaire testing their knowledge were calculated and categorised (0 = without knowledge; 1 = little knowledge; 2-3 = moderate knowledge; and 4-5 = good knowledge). Average scores obtained by the different year groups are presented in Table I.

Table I: Average scores of participants on questionnaire items testing their knowledge of caffeine

	Academic year			
	First-year	Second- year	Third-year	Mean
Benefits (5)	0.5	0.5	0.5	0.5
Side-effects (5)	0.9	1.3	1.3	1.1
Withdrawal symptoms (5)	1.4	1.7	1.4	1.5
Total score (15)	2.8	3.5	3.1	3.1

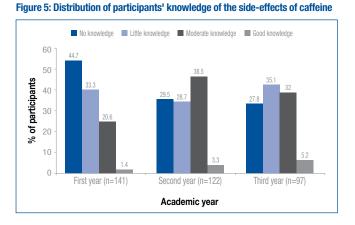
The average score obtained on their knowledge of the benefits of caffeine for the total group of participants was 0.5 out of 5. Only 1.8% of the participants were categorised as having moderate knowledge, while 45.3% had little knowledge and 52.3% had no knowledge at all. A comparison of the different categories of knowledge of the benefits of caffeine for each academic year group is shown in Figure 4. No values for the category "good knowledge" is indicated as it was zero in all the academic year groups.

The average score on the knowledge of side-effects of caffeine was 1.1 out of 5 for all three year groups. Only 3.1% of the total group of participants had good knowledge. Thirty-five per cent had no knowledge, 32.2% had little knowledge and 29.7% had moderate knowledge. Figure 5 compares the distribution of participants' knowledge of the side-effects of caffeine for each academic year group.



#### Figure 4: Distribution of participants' knowledge of the benefits of caffeine

# Academic year



The average score on the knowledge of withdrawal symptoms was 1.5 out of 5 for all three year groups. Five per cent of participants had good knowledge, while 20% had no knowledge of the withdrawal symptoms. Little and moderate knowledge was demonstrated by 35.6% and 39.4% of participants, respectively. The distribution of participants' knowledge of the withdrawal symptoms of caffeine for each of the three academic years is shown in Figure 6.

## Figure 6: Distribution of participants' knowledge of the withdrawal symptoms of caffeine

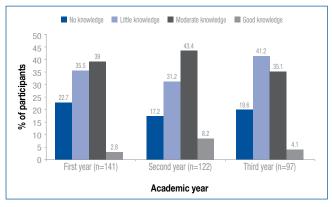


Table II indicates students' knowledge of facts and misconceptions with regard to caffeine. The correct and incorrect options in the questionnaire regarding benefits, side-effects and withdrawal symptoms are listed from most frequently to least frequently selected.

### Table II. Participants' knowledge of facts and misconceptions with regard to the benefits, side-effects and withdrawal symptoms of caffeine

Correct statements (facts)		Incorrect statements (misconceptions)				
Statement	%	Statement	%			
Benefits						
Increases vigilance	71.7	Substitute for sleep	26.7			
Increases long-term memory	3.9	Increases short-term memory	18.3			
Prevents Parkinson's disease	1.7	Slows metabolism	6.1			
Prevents Alzheimer's disease	1.4	Increases alcohol tolerance	5.3			
Prevents type 2 diabetes mellitus	0.8	Prevents impotence	1.9			
Side-effects						
Causes rapid beating of the heart	59.7	Causes hot flushes	21.9			
Increases cardiac output	39.4	Causes acne	16.4			
Increases cardiac contraction force	25.3	Causes dry eyes	8.1			
Increases respiration rate	13.6	Causes slow beating of the heart	3.9			
Increases gastric secretion	12.2	Causes impotence	3.6			
Withdrawal symptoms						
Headache	63.9	Aggression	27.2			
Fatigue	52.8	Forgetfulness	12.8			
Drowsiness	40.0	Hallucinations	4.4			
Decreased alertness	25.3	Congestion	2.8			
Constipation	11.4	Skin itching	1.4			

### **Discussion**

Participation was 90.4% for the entire target population of first- to third-year medical students. Based on the high response rate from each academic year group, it can be stated that the results obtained in this investigation are representative of the target population. The results indicated that 93.6% of the 360 participants used caffeine. This is consistent with the belief that caffeine is one of the most widely consumed substances in history.<sup>3</sup> A study by Valek et al<sup>15</sup> on high school students produced similar results, where only 10% of participants did not consume caffeine-containing products.

Academic purposes, selected by 62.6% of participants, was the third most common reason for caffeine usage in the target population (second most common in second-year students [66.7%] and third most common in first- [57%] and third-year [65.9%] students). In order to determine which year group consumed the most caffeine for academic purposes, the percentage usage of caffeine for academic purposes and the frequency of caffeine use for academic purposes were compared.

First-year students had the lowest percentage of caffeine users for academic purposes, with the lowest percentage of heavy users (33.8%) indicating that these students were the lightest consumers of caffeine. The percentage of caffeine users for academic purposes was very similar for the second- and third-year students, namely 66.7% and 65.9%, respectively. Third-year students, however, had a higher percentage of heavy users of caffeine (43.3%) compared to the first- and second-year groups (both 33.8%). Based on these findings, third-year students could therefore be regarded as the heaviest consumers of caffeine. Consumption of caffeine for academic purposes increased from the first to the third academic year. Engs and Rendell<sup>16</sup> reported similar findings

in a study on nursing students, and showed that both the quantity and frequency of caffeine use increased from the first year (245 mg) to the final (329 mg) year of the curriculum.

The average score for the caffeine knowledge test was 3.1 out of 15 for the total group of participants. From the results obtained on the individual questions it appeared that the participants had the most knowledge on the withdrawal symptoms of caffeine (average score of 1.5 out of 5), less knowledge on the side-effects (average score of 1.1 out of 5) and the least knowledge on its benefits (average score of 0.5 out of 5). These findings could be attributed to the fact that side-effects and withdrawal symptoms of caffeine are more commonly experienced than its benefits, since many of the benefits are associated with long-term use of caffeine.

With regard to common facts and myths concerning caffeine, it was evident that many students (26.7%) believed that caffeine could be used as a substitute for sleep. This perception has been proven incorrect by studies: caffeine has no net restorative effects when performance and mood are impaired by sleep deprivation.<sup>13</sup> It was also found that students were unaware of the diseases (e.g. Parkinson's, Alzheimer's and type 2 diabetes mellitus) that could possibly be prevented by caffeine, and also that caffeine usage could increase long-term, but not short-term, memory.<sup>3–10</sup> Seventy-one per cent of participants correctly identified caffeine as a vigilance enhancer, which could partially explain the consumption of caffeine.

Participants were more aware of the side-effects of caffeine, particularly with regard to its effects on the heart. Some, however, appeared to be misinformed since they considered hot flushes and acne as side-effects (21.9% and 16.4%, respectively). Headaches, fatigue and drowsiness (63.9%, 52.8% and 40%, respectively) were frequently given as withdrawal symptoms. Many students wrongly believed that aggression (27.2%) and forgetfulness (12.8%) were caffeine withdrawal symptoms.

The results of the caffeine knowledge test could have been influenced by the fact that a high percentage of the participants were caffeine consumers. They could probably have experienced the side-effects personally and therefore knew more about caffeine than non-consumers. Some participants, however, might have been heavy users of caffeine and hence were unaware of the withdrawal symptoms.

The results obtained in this study clearly showed that caffeine usage for academic purposes, especially caffeine in the form of coffee, increased as students progressed from the first to the third year of the medical course. The majority of participants were using caffeine without sufficient knowledge of its benefits, side-effects and withdrawal symptoms. Recommendations should be made to the student health and counselling service on campus to implement measures, such as displaying posters in strategic locations or distribution of information leaflets, in an attempt to improve students' knowledge of caffeine.

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### References

- 1. Ritter JM, Lewis LD, Mant TGK. A Textbook of Clinical Pharmacology. 4th ed. London: Arnold, 1999. 2. Winston AP, Hardwick E, Jaberi N. Neuropsychiatric effects of caffeine. Advances in Psychiatric
- Treatment 2005;11:432–9. 3. James JE, Critical review of dietary caffeine and blood pressure: a relationship that should be taken
- more seriously. Psychosom Med 2004;66:63–71.
- James JE, Rogers PJ. Effects of caffeine on performance and mood: withdrawal reversal is the most plausible explanation. Psychopharmacology 2005;182:1–8.
- Lopez-Garcia E, van Dam RM, Rajpathak S, et al. Changes in caffeine intake and long-term weight change in men and women. Am J Clin Nutr 2006;83:674–80.
- Christopher G, Sutherland D, Smith A. Effects of caffeine in non-withdrawn volunteers. Human Psychopharmacology 2005;20:47–53.
- Hameleers PA, Van Boxtel MP, Hogervorst E, et al. Habitual caffeine consumption and its relation to memory, attention, planning capacity and psychomotor performance across multiple age groups. Human Psychopharmacology 2000;15:573–81.
- Higdon JV, Frei B. Coffee and health: a review of recent human research. Crit Rev Food Sci Nutr 2006;46:101–23.
- Arendash GW, Schleif W, Rezai-Zadeh K, et al. Caffeine protects Alzheimer's mice against cognitive impairment and reduces beta-amyloid production. Neuroscience 2006;142:941–52.
- Roger PJ, Martin J, Smith C, et al. Absence of reinforcing, mood and psychomotor performance effects of caffeine in habitual non-consumers of caffeine. Psychopharmacology 2003;167:54–62.
- Heatherley SV, Hayward RC, Seers HE, et al. Cognitive and psychomotor performance, mood, and pressor effects of caffeine after 4, 6, 8h caffeine abstinence. Psychopharmacology 2005;178:461–70.
- James JE, Gregg ME, Kane M, et al. Dietary caffeine, performance and mood: enhancing and restorative effects after controlling for withdrawal reversal. Neuropsychobiology 2005;52:1–10.
- Shepard JD, al'Absi M, Whitsett TL, et al. Additive pressor effects of caffeine and stress in male medical students at risk for hypertension. Am J Hypertens 2000;13:475–81.
- Juliano LM, Griffiths RR. A critical review of caffeine withdrawal: empirical validation of symptoms and signs, incidence, severity, and associated features. Psychopharmacology 2004;176:1–29.
- Valek M, Laslavia B, Laslavia Z. Daily caffeine intake among Osijek high school students: questionnaire study. Croatia Medical Journal 2004;45:72–5.
- Engs RC, Rendell KH. Alcohol, tobacco, caffeine and other drug use among nursing students in the Tayside Region of Scotland: a comparison between first- and final-year students. Health Education Research 1987;2:329–36.