COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Scoping paper on the potential risks from energy drinks in the diet of children and adolescents.

Introduction

1 "Energy drinks" are defined by the presence of compounds, mainly caffeine, that are intended to enhance the consumer's physical performance and cognitive state, as opposed to "sports" drinks, which are formulated to replace water and electrolytes lost during exercise.

2 The term "energy drink" is used in inverted commas in this paper since this is the commonly used name for these products. The energy derived by the consumer is from their carbohydrate content, rather than the presence of caffeine and other possible stimulants. However, term is also used for the sugar-free varieties of these drinks for the sake of consistency. Proprietary names are used occasionally.

3 In 2016, more than 20 brands of "energy drink" were on sale in the UK.[1] A recorded 3.74 million people drank "Red Bull energy drink" in the UK that year, making it the most popular "energy drink" brand by its number of users. Sales of "energy drinks" constituted 13.4% of the soft drinks market in the same year [2]

4 The global market research company Mintel produced a report in 2017 on sports and "energy drinks". "Energy drinks" are reported to have had 19% volume growth since 2012 to 669 million litres in 2017, with low- or zero-sugar varieties proving popular. The company forecast a further 10% volume growth for the "energy drinks" market over 2017-22 to 739 million litres, and to 25% growth by 2022, passing the £2 billion litre mark. https://store.mintel.com/uk-sports-and-energy-drinks-market-report

5 "Energy drinks" in the UK vary in price but can be cheap, costing £0.25 per can (bought as a pack of 6 costing £1.50) (Tesco "Blue Spark").

---

[1] https://www.statista.com/statistics/308493/leading-brands-of-energy-drinks-excluding-colas-or-mixers-for-alcoholic-drinks-in-the-uk/

[2] https://www.statista.com/statistics/422739/soft-drink-market-share-by-category-in-the-united-kingdom/

6 The EU has had legislation in place since 2011 that requires all drinks (excluding tea and coffee) containing over 150 mg of added caffeine per litre, with the statement: “High caffeine content. Not recommended for children or pregnant or breast-feeding women”. In addition, the amount of caffeine in mg per 100 ml of drink must appear after this statement.

7 Some countries, such as Australia and Canada also require a maximum daily consumption limit to be stated on packaging (500 ml or 160 mg caffeine in Australia: Peacock *et al* (2016))

8 The British Soft Drink Association, the trade body for soft drink manufacturers, produced a Code of Practice in 2015, laying down rules for the labelling and the responsible marketing for “energy drinks” to the effect that consumers are aware of the potential effects of drinking these products and that the exposure of school-age children to related advertising is kept to a minimum.

9 EFSA (Zucconi *et al* , 2013) published a report on the gathering of consumption data on specific consumer groups of “energy drinks”. A total of 31,070 validated questionnaires were collected from adolescents in schools across Europe. Of the respondents, 68% had drunk at least 1 “energy drink” in the previous year and 28% had drunk one in the previous 3 days. Seventy-five percent of the 15-18 age group and 55% of the 10 – 14 age group were consumers, comprising 74% of males and 63% of females. Thirty-six percent of the total sample had consumed “energy drinks” with alcohol in the previous year.

10 Verster & Koenig (2017) reviewed the literature on caffeine consumption from all sources across the USA & Canada, Europe, including the UK, Australia, New Zealand and South Korea across all age groups. Despite the heterogeneity of the study protocols, the overall mean intake of caffeine across countries and ages was largely within the EFSA guideline of 3 mg/kg bw/day, although there were some exceedances at the 90% consumption level. The major sources of caffeine were coffee or tea, with “energy drinks” overall making a small (<= 3%) but increasing contribution.

11 The Mintel report states that a ban the sale of energy drinks to under- 16s was recommended by the Food Research Collaboration, part of the Centre for Food Policy of City University London in July 2016. This was itself part of a report suggesting that these drinks are associated with a range of health complaints and risky behaviours, although gaps in the available evidence were acknowledged.

12 The Chef Jamie Oliver’s company has made a public statement (Matthews, 2018), saying that there should be a ban on the sale of so-called “energy drinks” to consumers under the age of 16 years.

13 The UK teachers’ union the National Association of Schoolmasters and Union of Women Teachers (NASUWT) has campaigned for a ban on the sale of “energy drinks” to children under 16 years of age on the grounds of protecting their members from violent and disruptive behaviour in the classroom. The union is also concerned with an increase use of cannabis in parallel with “energy drinks”.

14 The supermarket Waitrose was the first UK retailer to restrict the sale of "energy drinks" to people over 16 years of age (Gillingham, 2018). Waitrose were followed in this by all of the major food retailers in the UK and most recently by Boots.

15 In August 2018, HM Government has produced a consultation document and impact assessment for stakeholders on banning the sale of "energy drinks" to young people. The consultation document asks for opinions on the relevant age restriction (16 or 18 years), whether and how vending machine sales should be restricted, the possible costs, whether any obstacles to implementation might be expected and the impact it may have on lower socio-economic and other groups in society. The impact assessment documents the effects that may ensue from actions other than a ban, for example, direct pricing, an industry levy, education and exclusion zones around schools. It outlines the costs and the health and monetary benefits.
https://www.gov.uk/government/consultations/ending-the-sale-of-energy-drinks-to-children
The NASUWT has praised this proposal
https://www.nasuwt.org.uk/article-listing/ban-on-energy-drink-sales-to-under-16s-welcomed.html

16 HM Government has also recently (from 1 April 2018) enacted legislation to tax industries producing or importing soft drinks with an added sugar content of greater than 5g/ 100ml. The provisions of this Soft Drinks Industry Levy are provided in Guidance on the Gov.UK website. The intention of this measure is to encourage industry to reformulate their products into healthier versions in the light of increasing rates of type 2 diabetes, tooth decay and childhood obesity and obesity related diseases. Companies thus have the choice of reformulating their products or paying the duty and thence possibly passing on the cost to the consumer or absorbing it

Sugar content of "energy drinks"

17 An internet search reveals that the sugar content of "energy drinks" varies depending upon brand and type, i. e. "diet", "light" or "regular". Diet varieties contain no sugar but contain artificial sweeteners, light varieties contain from 1 to 6 g of sugar per 8 fl.oz. serving (237 ml), in addition to artificial sweeteners, and the regular varieties contain from 13 to 33 g of sugar per 8 fl.oz. serving, some of which also contain artificial sweeteners. Moreover, the caffeine content of "energy drinks", while greater than other caffeinated soft drinks, can be much lower than that found in proprietary servings of coffee available from high street vendors. The sugar content of coffee and tea will vary with the consumers' taste, but it is unlikely to be as high as that found in most regular "energy drinks".
http://www.sugarydrinkfacts.org/resources/nutrition/Energy-Drink-Tables.pdf

18 The regular drinks above would all exceed the 5 g/100 ml legal limit described in paragraph 9 and thus would be subject to the new tax or have to be reformulated.

19 Hashem *et al* (2017) reported cross-sectional surveys of the amount of sugar, energy and caffeine in "energy drinks" in the UK and changes that had taken place

between 2015 and 2017 before the new tax came into effect. Very small changes in sugar content were noted over the reporting period (10.6% in 2015 to 9.5% in 2017) but caffeine content and serving sizes remained high (31% and up to 500 ml),

20 Leiper (2015) reviewed the factors influencing gastric emptying and the intestinal absorption of beverages in humans. Gastric volume showed a negative exponential relationship to emptying, and energy density of a solute was inversely proportional to emptying rate. Isoenergetic amounts of carbohydrates, proteins and fats appeared to be delivered to the duodenum at approximately the same rate. Initial changes in temperature affect nerve conduction and muscle motility, leading to a heat-induced increase in gastric emptying for about 10 minutes post ingestion but intragastric temperature rapidly returned to normal core levels and with it emptying rate. Beverage carbonation had little effect on emptying rate. Thus, high sugar beverages should enter the small intestine, where caffeine absorption mostly takes place, at a slower rate than their equivalent sugar-free varieties.

21 Mosca *et al* (2016) point out that “energy drinks”, like other sugary soft drinks may have a role in the currently increasing rates of childhood and adolescent obesity, which is related to type-2 diabetes, metabolic syndrome and non-alcoholic fatty liver disease.

https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-obesity-physical-activity-and-diet/statistics-on-obesity-physical-activity-and-diet-england-2018

22 Olateju *et al* (2015) studied the effects of consuming 750 ml of “Red Bull” “energy drink” (28g carbohydrate, 80mg caffeine/250 ml), “Red Bull” “energy drink” light (carbohydrate free, 80 mg caffeine/ 250 ml) or a sugary control drink (21g carbohydrate/ 250 ml, adjusted to equal carbohydrate concentration) on blood glucose and caffeine, heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mood and cognition of 16 adults, >18 years old, 11 female, with type 1 diabetes. The sugary drinks raised blood glucose immediately after consumption and this was still significant in the “energy drink” group relative to the control group at 3 hours, whereas the non-caffeinated sugary drink was not. No effects were found of any of the drinks on mood or cognition.

23 Haslam *et al* (2018) reviewed the literature evidence for the interaction between an individual’s sugar-sweetened beverage (SSB) consumption and the genes associated with the development of obesity, type-2 diabetes, cardiovascular disease, non-alcoholic fatty liver disease and gout. Overall SSB consumption was associated with type-2 diabetes independent of genetic predisposition. Obesity showed the strongest gene-SSB interaction while an interaction for the other diseases, despite the presence of feasible mechanisms, for example, the effects of fructose on liver fat and uric acid production, showed a less obvious genetic basis.

Non-sugar components of “energy drinks”

Caffeine

24 Caffeine (1,3,7-trimethylxanthine) is a secondary metabolite of a number of plant species that has been taken as a stimulant in beverages made from these plants for thousands of years. Caffeine is widely present in tea, coffee and chocolate at differing concentrations.

25 The absorption of an oral dose of caffeine varies depending upon the rate of gastric emptying, with the plasma Tmax (the time of maximal plasma concentration) ranging from 15 to 120 minutes. The volume of distribution is about 0.7 l/kg, corresponding to intracellular tissue water and elimination is by first-order kinetics. Caffeine is metabolised initially primarily by demethylation to paraxanthine, theobromine, and theophylline, which are also pharmacologically active substances (Arnaud 1985)

26 The stimulatory effects of caffeine on the central nervous system are mediated by binding to adenosine A1 and A2a receptors. Antagonism of the A1 receptor leads to the effects of caffeine on sleep and arousal whereas antagonism of A2a potentiates dopaminergic neurotransmission, leading to a “reward” -type stimulus. (review by Temple 2009) Other effects of caffeine such as cyclic AMP phosphodiesterase inhibition and effects on calcium levels only begin to be seen at doses where toxicity becomes evident McLellan *et al*, 2016), although low levels of caffeine may increase the opening frequency of ryanodine receptors, especially in cardiac muscle, leading to a greater likelihood of arrhythmias (Porta *et al* (2011).

27 Single doses of caffeine derived to be of no concern for adults (3 mg/kg bw per day for a 70-kg adult) should also apply to children, since caffeine clearance in children and adolescents is at least as great as that of adults, and that the limited studies available on the acute effects of caffeine on anxiety and behaviour in children and adolescents support this level of no concern. As with adults, caffeine doses of about 1.4 mg/kg bw may increase sleep latency and reduce sleep duration in some children and adolescents, particularly when consumed close to bedtime. (EFSA 2015)

28 Caffeine is known to promote diuresis and natriuresis by antagonising adenosine A1 receptors in the proximal tubule of the nephron. (Review by Osswald and Schnermann (2011)).

29 Caffeine intoxication is characterised by nervousness, irritability, anxiety, insomnia, tremor, tachycardia, palpitations and gastrointestinal upset. Other reported adverse effects include vomiting and abdominal pain, hypokalaemia, hallucinations, increased intracranial pressure, cerebral oedema, stroke, paralysis, rhabdomyolysis, altered consciousness, rigidity, seizures, arrhythmias, and death. (Reviewed by Seifert *et al* (2013))

30 Temple *et al* (2010) studied the effect of acute administration of caffeine at doses of 50, 100 and 200 mg to 28 male and 26 female adolescents aged 12 to 17

years from schools in Buffalo, Michigan, USA. The subjects were dosed orally in a double-blind, placebo-controlled manner with caffeine in a de-carbonated soft drink to reduce expectations of consuming caffeine and to mask its taste. Heart rate and blood pressure were measured, and food preferences, reasons for “energy drink” consumption and behavioural effects were polled. Caffeine appeared to cause a dose-dependent fall in heart rate ($p = 0.001$) and increase in diastolic blood pressure ($p = 0.0001$). Individuals habitually consuming high-caffeine (> 50 mg/day) were more disposed to eat high fat, high sugar or high-fat-and-sugar foods compared with low (< 50 mg/day) caffeine consumers. Boys gave greater importance to the feelings of increased overall energy, the immediate boost or “rush” and increase in physical performance after “energy drink” consumption than did girls.

31 Temple *et al* (2014) investigated the effects of caffeine on heart rate and blood pressure in pre- and post-pubertal children (8 – 9 and 15 – 17-year-olds respectively). Reductions in heart rate and increases in SBP and DBP were seen in both age groups, with no significant differences between boys and girls in the younger age group. Post-puberty, however, girls showed a significantly smaller fall in heart rate and rise in DBP and significantly greater rise in SBP than did the boys in the same age group ($p < 0.05$ in all cases). The authors suggested that this effect may have been caused by oestradiol inhibition of CYP450 metabolism of the caffeine but noted that changes in background patterns of caffeine could have affected the findings. However, HR was significantly decreased and the increase in SBP significantly reduced by caffeine in the luteal phase of the menstrual cycle compared with the follicular phase, suggesting some hormonal involvement in these effects.

32 Monnard *et al* (2016) also found a gender difference in the response to “energy drinks” on cerebrovascular blood flow velocity (CVBV), which was reduced more in women than in men ($p<0.05$) within 10 minutes of consumption, possibly due to the caffeine, interaction of the caffeine with sugar, or changes in insulin levels. The authors suggested that this had finding might have clinical relevance since neurocardiogenic syncope is already more prevalent in women than in men and reduction in CVBV may increase the chances of such an event.

33 Individuals differ in their response to caffeine by virtue of variability in their intrinsic rates of metabolism and acquired tolerance due to frequency of exposure. Caffeine is metabolised in the liver, largely by CYP1A2, producing the partially demethylated products theobromine, paraxanthene and theophylline . Some individuals with poor expression of CYP 1A2 or the genetic variant PDSS2 metabolise caffeine slowly, thus prolonging its pharmacological and toxicological effects (Pirastu *et al* (2016))

34 White *et al* (2016) compared the pharmacokinetics of caffeine in a group of healthy young adults (aged 18 – 30 years) when administered under different consumption conditions: as chilled (4^{o}C) “Red Bull” “energy drink” over 2 minutes or 20 minutes, as chilled coffee over 2 minutes or 20 minutes and as hot (85^{o}C) coffee. The dosage in each case was normalised to 160 mg of caffeine in 450 ml of beverage. Blood samples were taken from in-dwelling venous cannulae prior to dosing and then at intervals up to 480 minutes post-dose and plasma caffeine was

analysed by LC-MS. The highest maximum plasma caffeine concentration (C_{max}) was in the hot coffee group and the lowest in the slowly consumed “energy drink” group ($p<0.05$) but there were no significant differences in the T_{max}, area under the curve (AUC), mean absorption time or mean residence time between the groups. This study agreed with others in that clearance of caffeine was lower in women taking low-dose oral contraceptives but in general all of the dosage groups gave very similar results.

35 Robertson *et al* (1981) performed a wash-out experiment on adults who had not consumed caffeine for 21 days prior to the experiment. Test subjects were initially dosed with a placebo of isotonic salts, then a dose of 250 mg caffeine over 7 days, followed by placebo again for 4 days. Controls received placebo throughout. The caffeine raised systolic and diastolic pressure significantly relative to a placebo on the first day of dosing within 2 hours of ingestion, but, by day 7 of dosing, pressures were no longer affected. The same was true of plasma and urinary adrenaline, noradrenaline and plasma renin levels. There was no significant effect of the caffeine on heart rate in this study.

36 Chronic consumption of caffeine leads to withdrawal symptoms when it is interrupted. The major symptoms are headache and fatigue, but also may include depression, decreased cognitive performance, irritability, nausea and muscle aches (reviewed by Reissig *et al* 2009). The same review points out the possibility of caffeine dependence in some individuals.

37 Temple (2009) reviewed the effects of caffeine on children and covered effects on addiction, cross-sensitisation with other substances, brain development, sleep, behaviour, diet and obesity, and risk-taking behaviour. The conclusion was that at that time, caffeine consumption, including “energy drinks”, was increasing, with unknown consequences for health and development.

38 Caffeine contributes a bitter flavour to the taste of “energy drinks” in a dose-related manner and detracts slightly from their sweetness. (Tamamato *et al* (2010)). Some of the students in the attitude surveys (see below) felt that the difference in taste from other soft drinks made “energy drinks” attractive and “grown up” things to consume.

39 Boyle *et al* (2018) reviewed the evidence for interactions between the caffeine and the sugar in “energy drinks”. Caffeine in combination with glucose has been found to improve cognitive performance and subjective mood but there have been no dose-response studies or studies that take into account the different rates of absorption of the two compounds. Only 7 studies have looked at both components separately and in combination. There are potential mechanisms on central nervous system neurotransmitters that could account for possible interactions, but further work would be needed to investigate these.

40 Miles-Chan *et al* (2015) compared the effects of caffeine alone with sugar-free and regular “Red Bull energy drink” on young male adults and found that all three treatments increased blood pressure. The “Red Bull” “energy drink” containing sugar increased heart rate, stroke volume, cardiac output and diastolic pressure, but

decreased total peripheral resistance. Sugar-free “Red Bull energy drink” and caffeine alone, in contrast, increased total peripheral resistance. Since the SCF (2003) considered that taurine was not found to affect any of the measured parameters, the authors concluded that interactions between the sugar and the caffeine or the sugar and other components of the “energy drink” were responsible for this differential effect.

41 Shi *et al* (2016) performed a systematic review and meta-analysis on the effect of caffeine on insulin sensitivity in clinical trials on healthy subjects. Coffee is known to be associated with a protective effect against type 2 diabetes. The meta-analysis showed that acute administration of caffeine (from 3 to 6 mg/kg bw) reduced insulin sensitivity and the effect on diabetes was therefore attributed more to better control of calorie intake in coffee drinkers than to the caffeine itself. However, decaffeinated coffee was shown in some studies to be less effective in its anti-diabetic effects, suggesting that the effect may be largely attributable to caffeine. The acute impairment of glucose tolerance by caffeine may be due to an observed increase in plasma adrenaline and beta-receptor activity, since insulin signalling is not affected (Thong and Graham, 2002, Thong *et al* 2002). There is experimental evidence that chronic caffeine consumption may reverse age-related insulin resistance in skeletal muscle (Guarno *et al*, 2013). Overall, the action of caffeine on glucose homeostasis is still open to debate

42 Annex 1 compares a list of energy drinks and their caffeine and sugar content, along with serving sizes and dose received by children at two ages, with that for other caffeinated and non-caffeinated soft drinks and other, usually hot, beverages.

<u>Other components</u>

43 In addition to sugar and caffeine, “energy drinks” vary in their lesser components. For instance, the most popular brand, “Red Bull” “energy drink” also contains the compound taurine and B-group vitamins. “Red Bull” “energy drink” no longer lists D-glucurono-γ-lactone in its ingredients but other brands contain this compound as well as guarana (a tropical shrub, the berries of which contain caffeine, theophylline and theobromine), ginseng, gingko biloba, L-carnosine, inositol, or a mixture of these and other minor components, but Higgins *et al* (2010) suggest that they are all at levels too low to be of toxicological concern.

Taurine

44 Taurine (2-aminoethanesulfonic acid**)**, is widely distributed in animal tissues and a constituent of bile. It is sometimes described as an amino acid.

45 Taurine is involved in the conjugation of bile acids, antioxidation, osmoregulation, membrane stabilization, phase 2 drug metabolism and modulation of calcium signalling. It is essential for cardiovascular function, and in the development and function of skeletal muscle, the retina, and the central nervous system (Higgins *et al* (2010). Taurine appears to fulfil most of the criteria for being a

neurotransmitter in the central nervous system, although specific receptors for it have not yet been discovered and its actions in the brain have been attributed to modulation of the receptor response of other established transmitters such as GABA (at GABA A) and glycine (Ripps and Shen 2012, Kilb, 2017)a) Taurine appears to protect neurones against glutamate-induced excitotoxicity.
(Wu and Prentice, 2009)

46 Miles-Chan *et al* (2015) compared the effects of sugar-free "Red Bull" "energy drink" with those of caffeine and water on the resting energy expenditure and respiratory quotient of 8 healthy young male volunteers. The "energy drink" enhanced thermogenesis and shifted the RQ in favour of carbohydrate metabolism, and this was mimicked by the caffeine solution. The authors concluded that the other components of the "energy drink" played no part in its stimulatory effects.

47 Reisenhuber e*t al* (2006) found that with an "energy drink" containing 80 mg caffeine and 1g of taurine per 250 ml, the taurine, either alone or in combination with caffeine had no effect on urinary output, natriuresis nor urine osmolarity.

48 Giles *et al* (2012) examined the effects of caffeine (200 mg), taurine (2000 mg) and glucose (50 g) alone and in combination on mood, performance of cognitive tasks and salivary cortisol levels in undergraduate students, aged 18 – 21years. Subjects were tested for effects on their attention span, working memory and reaction time and were asked to fill in a number of questionnaires covering their consumption of caffeinated products, experience of caffeine withdrawal and subjective mood. Salivary cortisol and heart rate were measured as objective measures of arousal/ stress. The data suggested that only caffeine improved cognitive performance in a consistent way.

49 Peacock *et al* (2013) found that the presence of taurine in a caffeine-containing drink to some extent ameliorated the stimulatory effects of the caffeine. On its own, caffeine maintained the subjects'levels of wakefulness and attention for a longer time than a placebo. In the presence of taurine, these attributes degraded over time similarly to the placebo. This would be in line with the known pharmacological attenuation effects of taurine receptor activation although rat studies suggest that ingested taurine has little effect on its levels in the brain (Sved *et al*, 2007).

50 Calabro *et al* (2012) reported the case of a 20-year-old man who presented with a tonic-clonic seizure after drinking 4 – 6 cans of "Red Bull" "energy drink" daily for 5 months. The patient had no medical history of epilepsy and no other lifestyle causes could be found for the episode. His EEG was normal, but he was mildly confused in the treatment room and was given a months' treatment with levetiracetam, The authors concluded that the taurine in the drink, possibly in combination with the caffeine had had some modulatory effect on the patient's GABAergic neurotransmission, leading to neural hyperexcitability.

51 Taurine does not appear to contribute to the taste of "energy drinks" at up to approximately 4200 mg/l (Tamamato *et al* (2010)).

D-glucurono-γ-lactone

52 D-glucurono-γ-lactone is naturally present in the human body as a metabolite of glucose and may be involved in the phase 2 metabolism of drugs as a source of glucuronic acid. It appears to have few if any pharmacological or toxicological properties. In other animals, including some mammals, this compound is known to be a substrate for ascorbic acid biosynthesis. Since this pathway does not occur in primates and guinea pigs, rodents may not be ideal as toxicological models for humans. EFSA (2009).

Ginseng

53 Shah *et al* (2016) studied the ECG and blood pressure effects of "energy drinks" and ginseng on a group of 30 healthy volunteers, aged 18 – 40. Participants drank 2 cans of "energy drink" (total 320 mg caffeine, 4000 mg taurine and 800 mg ginseng, with other common components), a cherry-and-lime flavoured carbonated drink containing 800 mg ginseng or the equivalent carbonated drink without additions. Ginseng was not found to affect ECG parameters or blood pressure.

Guarana

54 Smith and Atroch (2007) document the rise of guarana (*Paullinia cupana*) from a traditional tonic and medicine of Amazonian tribes to an ingredient in global "energy drink" brands. Guarana seeds contain 2 – 7.5% caffeine, with traces of theophylline and theobromine and it is present in modern "energy drinks" but these authors found it to be in too small amounts to exert effects beyond those of the caffeine and sugar ingredients. Moustakas *et al* (2015) investigated the effects of caffeine, glucose and guarana in a model system (the planarian worm *Dugesia tigrina*). Guarana alone stimulated worm locomotion in a dose-related manner from 0.01 mM caffeine content but inhibited it at 10mM relative to a water control. Caffeine caused only a small, insignificant increase in locomotor activity of the worms across concentrations of 0.001 – 10 mM whereas locomotion was stimulated significantly after 2 minutes by a combination of caffeine and guarana, both titrated to 0.1mM caffeine. The stimulatory effect of the low-level guarana was prolonged by the presence of glucose, but glucose had no effect on the response to caffeine. The conclusion was that the effect of guarana was due to another component other than caffeine but its identity was not investigated.

B vitamins

55 Huang *et al* (2014) considered that niacin (vitamin B3, nicotinamide) in an "energy drink" might contribute to hepatic damage in the case of a 35-year-old man who regularly binge-drank beer in addition to daily consumption of 3 "Rockstar" "energy drinks", delivering 120 mg of niacin per day

56 In a letter to the editor of the Journal of Hepatology, Robin *et al* (2018) highlighted the case of a 17-year old boy who admitted consuming up to six 500 ml cans of an "energy drink" per day and presented with non-alcoholic steatohepatitis (NASH). The authors referred to the work of Harb *et al* (2016) and Vivekanandarajah *et al* (2011) and postulated that, in addition to high levels of fructose (from the sucrose in the "energy drink"), the presence of high levels of niacin, could contribute to this toxic effect. When the boy lost weight, stopped consuming "energy drinks", his blood ALT level fell from 274 U/l to 66 U/l seven months after his first referral. The effect if the boy's weight loss on his health was not discussed.

Reasons for, and patterns of, "energy drink" consumption

57 Several papers report polling young people for their reasons for consuming "energy drinks" and their choice of product. Some papers quantified the responses and these have been tabulated below (Table 1). The column titles are not exactly as stated in all of the papers tabulated but amount to the same response: for example a response like "Help me stay awake" and another like "Give me energy" have been combined in the column "Energy boost". "Other" are minor miscellaneous responses that do not have equivalents in all of the papers. In some studies, participants included several reasons for "energy drink" consumption, leading to the sum of the responses exceeding 100%

58 Although not of high caffeine content, Smit *et al* (2006) found that both "Lucazade Energy" brand drink (caffeine 121 mg/l, sugar 179 g/l) and the taste of "Lucozade Energy" both improved perceived alertness, mental energy, and mental performance (including concentration) in subjects aged 18 – 50 years, gender breakdown not reported. This suggests that anticipation of the effects of caffeine may have an influence on its perceived effects.

59 In Italy, Gallimberti *et al* (2013) used a 63-question questionnaire to poll "energy drink" use among 916 young adolescents, aged 11 – 13 years. In this study the age-and-sex group in the highest "at least one "energy drink" a week" category was 11-year-old girls, with a score of 90.3%. Seventy-five percent of boys of the same age group were in that category. Weekly consumption of "energy drinks" decreased with age, although infrequent but continuing consumption increased to 50.4% in boys and 35.6% in girls by the age of 13. Consumption of "energy drinks" was also significantly associated with smoking ($p = 0.015$) and drinking alcohol ($p = 0.009$)

60 Costa *et al* (2014) interviewed 40 Australian adolescents aged 12 – 15 years regarding their use of "energy drinks". The interviews consisted of 7 specific questions that covered knowledge, frequency, reasons for drinking, influences, psychological and physiological effects. Most participants knew what "energy drinks" were although there was some confusion with sports drinks and other beverages such as Coca Cola. "Energy drinks" were easily accessible, sometimes from parents, consumed for sport or to increase wakefulness. Taste was a positive factor, as was peer pressure and advertising. Adverse effects were also recognised and put some students off continued consumption.

61 In a later study, Costa *et al* (2016) polled 399 Australian school students aged 12 – 18 years, 64% male, on their “energy drink” use. Of consumers, 73% were male, the mean age of first consumption was 10.5 years, and the age range with the maximum number of consumers was 14 – 15 years. Participants in the survey consumed up to 7 “energy drinks” per session and 36% of consumers stated that they had exceeded the Australian government’s recommended adult daily limit of 2 “energy drinks”, 6.4% saying that they did so on a weekly basis.

62 McCrory *et al* (2017) asked 41 young Canadian people aged 12 – 18 years for their perceptions and knowledge of “energy drinks”. Participants largely recognised the correct products as “energy drinks” and although some in the younger age groups (12 – 15 years) reported shops refusing to sell these products, generally “energy drinks“ were easily available. Reasons cited for “energy drink use were for providing an energy boost for sport or study, their taste and when socialising. Warning labels were largely unrecognised but, when pointed out, they were felt to be too small, uninformative or not applicable.

63 Turton *et al (*2016) explored adolescent attitudes and beliefs on caffeine and caffeinated beverages in two schools in different areas of London, Ontario, Canada. Participants seemed well aware of the levels of caffeine in beverages and of its potential to cause adverse effects. Taste was a major deciding factor, as was availability. Some older adolescents felt that drinking caffeinated beverages made them feel more mature and believed that younger siblings should not drink them. The media and advertising were strong positive influences, as well as parental role modelling, although parents also exerted a controlling influence on consumption. Finally, adhering to what was perceived to be the social norm influenced some pupils.

64 Temple *et al* (2016) performed a study on a small group (36) of adolescents and adults 15 to < 30 years old. relating to the influence of price and labelling on “energy drink” purchase. “Consumers” (>= 2 “energy drinks” per week) were more affected in their willingness to purchase “energy drinks” by changes in the price of the product than were “non-consumers” (< 1 “energy drink”/ month) (p<0.001 v p,0.01 respectively), Adolescents, but not adults were persuaded to reduce their consumption of “energy drinks” by labelling giving the caffeine content or a warning (p = 0.007).

65 A qualitative study was performed by Visram *et al* (2017) on the perceptions of “energy drinks” in focus groups of young people in England (aged 10 – 11 years, n = 20 and 13 – 14 years, n = 17). Reasons given by the participants for consuming “energy drinks” covered taste of the product, pricing relative to other soft drinks, and ready availability and promotion. Consumption took place in public places, in relation to social and sporting activities and computer gaming (especially amongst boys). Even though the policy of a school was to not allow “energy drinks”, some children drank them on the way to and from school and clubbed together with friends to buy them. Parents and other adults had a role in facilitating or limiting consumption but some of the children themselves thought some age restrictions should be necessary.

No single dominant factor was recognised to address the consumption of “energy drinks” by young teenagers.

66 Reid *et al* (2017) polled young Canadians aged 12 – 17 years on their use of “energy drinks”. A total of1103 adolescents took part in the study. 57% of the 12 – 14 year-olds and 69% of 15 – 17 year-olds had ever consumed an “energy drink” . The main locations for consumption were at home (48 and 43%) and at school (35 and 42%). Major reasons for consumption were curiosity/novelty (33 and 42%), taste (26 and 26%) and because friends drank them (23 and 28%). 3% and 16% respectively drank “energy drinks” in conjunction with alcohol use

67 Ha *et al* (2017) found that among 833 adolescent Korean “energy drink” consumers, aged 16 - 17 years, 95% were aware of the high levels of caffeine in “energy drinks” and 35% consumed them habitually. Twenty-eight percent of users felt that the drinks posed a severe health tthreat, while 54% did not ($p < 0.05$). Thirty-six percent reported being exposed to “energy drink” advertising while 33% did not.

68 Kumar *et al* (2015) polled 779 adolescents, aged 12 to 17 years, on their perceptions and use of “energy drinks”. Of the sample, 9% drank “energy drinks”, At least once-weekly “energy drink” consumption was highest among 16 to 17-year olds who were physically active 3 or more times in the week. Nineteen percent of the sample thought that “energy drinks” were safe for teenagers, and 12.5% thought that “energy drinks” were a type of sports drink. These beliefs were positively correlated with “energy drink” consumption.

69 Aluqmany iet al (2013) found that in a group of 600 female secondary school students, aged 15 – 18 years, 55.5% consumed “energy drinks-. Most of the consumers, were irregular drinkers (45%, < 1 – 3 times per month), 48.6% maintained their choice of drink based on price, and 61% said that they would only decide to stop drinking “energy drinks” if they suffered side effects, while 8% declared they would stop if sales were restricted.

70 Sather *et al* (2016) found that in a group of US naval air force trainees, the age of their first consumption of “energy drinks” influenced their later “energy drink” consumption pattern. Those who had first drunk an “energy drink” at age 13 – 16 were approximately 5 times more likely to consume “energy drinks” in larger quantities on a single occasion in later life than those who had not started “energy drink” drinking until they were more than 20 years old. This finding suggests that adolescent “energy drink” drinking, if not immediately detrimental may lead to future behaviour that may have acute health consequences later in life. However, this study was cross sectional, retrospective and self-reported, leading to potential bias and the inability to ascribe causality

Table 1. Reasons for consuming "energy drinks.	Reason for consumption %						
Country	Physical performance	Help with study	Energy boost	Taste	Peer pressure/ advertising/availability/ price	Other	reference
Trinidad & Tobago	8.5	19.7	47.0	23.1		1.7	Babwah *et al* (2014)
Poland	51	33	10	65		56	Górnicka *et al* (2014)
Canada	33.4	48.1	72.8	30.2	37.1	70.7	Wiggins *et* al (2017)
USA	35	12	67			57	Bashir *et al* (2016)
EU countries	7		38	40		15	Zucconi *et al* (2013)
USA	29	32	61	6	28	34	Nordt *et al* (2017)
Bahrain	6.1	4.4	43.3	40	1.7	4.5	Nassaif *et al* 2015
Poland	23.6			69.4	48	10.3	Nowak & Jasionowski 2015
Poland				47	33	22	Nowak & Jasionowski 2016
Saudi Arabia (Adolescents and adults)	25.6	14.6	20.8			39	Aluqmany *et al* (2013)
Saudi Arabia	34	3.9	10	33	3	1	Faris (2013)
India (Caffeinated		23	48			65	Gera *et al 2016*

products inc.EDs)							
Taiwan (adults)		27	49	31		32	Chang *et al 2017*
Pakistan (adults)	10	15	25	9	11	22	Usman *et al* (2015)

Effects on behaviour

71 Utter *et al* (2018) found that “energy drink” consumption in 8500 New Zealand adolescents (aged <= 13 to =17 years) correlated positively and in a dose-related manner (No “energy drink” < 1-3 “energy drinks” < 4+ “energy drinks” in the previous 7 days) with unsafe behaviours such as risky motor vehicle use, violence, unsafe sex, binge drinking, smoking and disordered eating. Measures of mental health were also negatively impacted (for example depressive symptoms, $p < 0.001$) but body-mass index was unaffected by increasing “energy drink” consumption ($p < 0.26$). Once again, this study, although reasonably large was cross sectional, self-reported and may have been influenced by the drop-out rate of 32%.

72 Studies such as that of Utter *et al* (2018, above) may be confounded by the well documented propensity of adolescents to indulge in “risky” behaviour in the absence of “energy drink” consumption. For example, Arnett (1992) reviewed studies on reckless behaviour in adolescents, where the behavioural drivers were related to the normal development of cognitive function, peer pressure, parental influence and socialisation. Studies have considered the influence of puberty and brain development on adolescent behaviour, including the differential maturation of the basal ganglia (nucleus accumbens and amygdala) that are associated with emotional expression and the “cognitive” prefrontal cortex, but found such associations to be inconsistent (Smith *et a* (2013), Mills *et al* (2014)). Not all adolescents indulge in risky behaviour and Romer (2010) suggests that experiences from early childhood can lead to a life-long tendency to impulsive behaviour, leading to sensation-seeking and impatience which may then be influenced by further brain development in the teenage years.

Effects on sleep

73 Aepli *et al* (2015) found that adolescents and children (aged 10 to 16.9 years) consuming caffeine at a mean of 2.5 mg/kg bw/day showed a significant ($p<0.05$) reduction in electrical slow-wave brain activity in the first two hours of sleep, associated with deep NREM sleep, compared with controls (consuming caffeine at 0.1 mg/kg bw/day). This effect was not significant during the last two hours of sleep. This effect was associated with later bedtimes and poorer overall sleep quality.

74 Sampassa-Kanyinga *et al* (2018) found a significant reduction in sleep duration in “energy drink”-consuming students in middle-school (13 -15 years old), $p<0.016$, and high-school (16-18 years old), $p<0.001$. The effect was significant when the data were adjusted for age, sex, ethnic background, subjective socioeconomic group, substance use, physical activity and BMI z-score, but not when unadjusted. The authors recognised that the study had limitations in that it was cross sectional, which did not allow causal inferences to be drawn, self-reported and thus subject to personal bias, missed out the 8% of students in private or alternative schools and without parental supervision, leading to possible non-responders and confounding factors such as abuse of other substances.

75 Conversely, Patte *et al* (2018) found no longitudinal effect on sleep duration in grade 9 to 12 school students (aged 15 to 18) following an increase in caffeine intake by a change in consumption of “energy drinks” from < 3 days per week to 3+ days per week. Positive associations were found for cyber bullying, screen time and homework time. The effect of other substance use (alcohol, tobacco and cannabis) was inconsistent.

76 Galland *et al* (2017) surveyed the sleep hygiene practices and sleep quality of 692 New Zealand adolescents, aged 16 to 17 years, including their consumption of “energy drinks” and other caffeinated beverages. “Energy drinks” were consumed in relatively small amounts after the evening meal compared with other beverages, especially tea, coffee and Coco Cola. In general, boys drank more “energy drinks” and girls drank more of the other beverages. Evening caffeine consumption from any source did not affect sleep quality but did lead to increased odds of poor daytime functioning, as evaluated by the Pittsburgh Sleep Quality Index.

77 Carskadon and Tarokh (2014) reviewed the current knowledge of the physiology of sleep regulation and the changes in sleeping patterns in adolescents. Intrinsic changes in sleeping patterns are at odds with the requirements of the school day, leading to shorter sleeping times and greater consumption of caffeinated beverages to stave off day-time sleep.

78 Concerto *et al* (2010) polled a group of 70 Italian university students (46 female, 24 male, aged 25 – 40 years) on their use of cigarettes, and caffeinated hot, soft and “energy drinks” and concomitant sleeping parameters. Poor sleep, as indicated by the Pittsburgh Sleep Quality Index (made up of reported quality, latency, duration, efficiency, disturbances, use of medication and daytime dysfunction) was correlated with perceived daily stress and coffee consumption but no other factors. The authors recognised that the study was cross-sectional and the result might reflect the coffee-drinking culture of Southern Italy.

79 In a larger but similar study, Sanchez *et al* (2013) polled 2,458 Peruvian students (1,493 female, 965 male, aged 18 – 22 years) on their weekly consumption of cigarettes, alcohol and stimulant beverages and sleep parameters. Slightly more females than males (58 vs 52%) reported poor sleep and the odds ratio of poor sleep increased with “energy drink” consumption but decreased with cigarettes and alcohol. The authors recognised that a longitudinal study would better allow the determination of any relationship between stimulant use and sleep quality.

80 Drake *et al* (2013) looked at the sleep-disruptive effect of the same dose of caffeine (400 mg, taken in pill form), taken at different times before bedtime (0, 3 or 6 hours) on 12 healthy normal sleepers. The subjects were 6 males and 6 females, aged 21 – 36, who filled in sleep diaries as well as undergoing objective measurement of sleep parameters (e.g. latency, efficiency, % slow wave, % REM). All objective and subjective sleep parameters were negatively impacted by caffeine dosed up to and including 6 hours before bed, suggesting that evening and even afternoon consumption of caffeinated beverages could reduce sleep quality and quantity. Limitations on this study were recognised as including small group size,

narrow age range of the subjects, background caffeine tolerance of individuals and the relatively untried instrumentation used.

Adverse effects of "energy drinks".

81 A number of reviews were picked up in the PubMed search that covered the health effects of "energy drinks" on children and adolescents: Seifert *et al* (2011), Owens *et al* (2014), Arria *et al* (2014), Alhyas *et al* (2015). Harris (2015), Visram *et al* (2015), Richards and Smith (2016a), Al-Shaar *et al* (2017), Temple *et al* (2017), De Sanctis *et al* (2017).

82 The general conclusions from all of these reviews are that the consumption of "energy drinks" by adolescents has been and is a growing concern on which little research had and has been performed to address. Most research that has been performed has taken the form of cross-sectional studies and self-completed questionnaires which leave the final analysis unable to ascribe causation and are subject to user bias.

83 Lisdahl *et al* (2018) outlined the plan for an upcoming study on the effects of substance abuse on adolescent brain cognitive development that will provide prospective longitudinal assessment of the use of various substances, including caffeine, and their effects on neurocognitive, health and psychopathological outcomes in children and teenagers in the USA. The study will run over 10 years, consisting of six-monthly telephone interviews and 1-yearly personal meetings, with subjects beginning at 9 – 10 years of age.

84 The United States National Poisons Data System receives telephoned information from the public on cases of toxicity from "energy drink" consumption by children, adolescents and adults. In 2010 – 2011, the incidence of moderate – major adverse effects related to energy drinks was 15.2% of reports for "energy drinks" and 39.3% for alcoholic energy drinks. (Seifert *et al* (2013)). The total number of cases reported per month for "energy drinks" rose from just over 60 in October 2010 to around 170 in March 2011 and then fluctuated between 100 and 150 per month. Calls related to co-consumption with alcohol rose from <20 in October 2010 to Just >40 in November 2010, when a ban on the sale of pre-mixed alcoholic "energy drinks" came into force, and thereafter decline to 20/ month and fewer. Around half of the reported cases involved unintentional exposures by children < 6 years old.

85 Borron *et al* (2018) analysed the adverse incidents arising from "energy drink" consumption that had been reported to poison centres in Texas, in relation to total "energy drink" sales for 2010 – 2014. A total of 855 exposures to "energy drinks" were reported and of the effects that had been followed up, 135 were minor (transient/ minimally bothersome), 64 were moderate (more prolonged, perhaps needing treatment but not life-threatening) and 4 were major (life-threatening, disabling or disfiguring). The most frequent and highest acuity clinical effect was tachycardia, which affected 1 child (<= 12 years), 11 adolescents (13 – 19 years) and 17 adults (>20 years). Compared with total 5-year sales of "energy drinks" of approximately 1.9 billion units in Texas, moderate and major adverse outcomes were

calculated to be 0.58 and 0.053 per hundred million units respectively. The authors noted that this study relied upon phone calls from members of the public and GPs, which depended upon the judgement of the person making the call.

86 Kristjansson *et al* (2014) found a dose-response relationship between “energy drink” consumption in Icelandic children aged 10 – 12 years (none – <1 per day – 1+ per day) and the prevalence of headaches, stomach aches, sleeping problems and low appetite. This study used a well-established protocol and questionnaire, with a 90% completion rate. However, it was cross-sectional, which did not allow cause and effect to be attributed, relied on two questions, without any biochemical tests, to verify caffeine intake and did not include measurements of the respondents’ body mass index or sugar consumption, which could confound findings.

87 Schwartz *et al* (2015) found that “energy drink” consumption in middle school students was more prevalent in males than females and among black and Hispanic students than white. “Energy drink” consumption was associated with a greater risk of hyperactivity / inattention at school ($p<0.004$). Sweetened beverage consumption in general, which included “energy drinks”, was also significantly associated with the end-point of the study ($p< 0.006$). This study provides data on young age ethnic and socioeconomic factors and type of beverage consumption but is cross-sectional, self-reported and gave no indication of the psychological drivers of consumption.

88 Park *et al* (2016) studied the effects of “energy drinks” on sleep, stress and suicidality in 68,043 Korean adolescents (aged 12 – 18 years). “energy drink” consumption was significantly positively associated in a dose related manner with sleep dissatisfaction, depressive mood, and with thinking of, planning and attempting suicide. Consumption of junk food (i. e. processed food high in sugar and/or fat) also correlated with “energy drink” drinking and appeared to exacerbate the adverse effects arising from it.

89 Richards and Smith (2016b) performed cross-sectional and longitudinal studies on the effects of caffeine consumption from “energy drinks” as well as other beverages on the health of English secondary school students (12 – 16 years old). Surveys were conducted at two time-points 6 months apart. Data on demographics, diet, emotional state and total caffeine consumption were collected. At both the earlier (T1) and later (T2) time points, adverse effects on health were seen in high level (>1000 mg/week) caffeine consumers until the data were controlled for dietary, demographic and lifestyle factors, when although the effects at T2 remained, those at T1 disappeared. The surveys used the term “general health” which may have been misinterpreted by some of the respondents, 6 months may not have been an adequate time-gap and the distribution of questionnaires at the two time-points may have been uneven. These factors may have confounded the results.

90 Kim *et al* (2017) also investigated relationships between stress, lack of sleep, low school performance and “energy drink” consumption with suicide attempts of over 120,000 Korean adolescents (aged 13 – 18 years) All of the above conditions were positively related to suicide attempts. Correcting for the stress, sleep and performance factors revealed frequent “energy drink” consumption to be positively associated with suicidality on its own. The authors suggested that consumption of

“energy drinks” could exacerbate the other factors. Once more, causality could not be shown and the study, and the input relied on self-assessment.

91 Bashir *et al* (2016) reported on data from 612 questionnaires completed by adolescents aged 12 to 18 years regarding consumption of “energy drinks” and subsequent subjective experiences. Respondents recorded experiencing frequent headaches, feelings of anger, difficulty breathing, feeling weak, sleep disturbance and increased urination. This study was limited by the self-assessment nature of the data, the small size of the sample (that was also split between two locations) and being uncontrolled for the use of alcohol, tobacco and other caffeinated beverage consumption that may have modified the reported responses.

92 Hammond *et al* (2018) performed a survey of the adverse effects of caffeinated “energy drinks” on adolescents from 12 – 17 years and young adults from 18 – 24 years. Of 2058 respondents, 73.8% reported having consumed an “energy drink”, of whom 55.4% reported having had at least one adverse event (including fast heartbeat, difficulty sleeping and headache), 3.1% of “energy drink” consumers had sought or considered seeking medical assistance for the event. Of coffee drinkers, 36% had had an adverse event, of whom 1.4% had sought or considered seeking medical assistance for the event.

93 Van Batenburg-Eddes *et al* (2014) observed a potentially adverse effect of “energy drinks” on executive functions – behavioural self-reflection and control - that develop from the maturation of the prefrontal cortex of the brain, an area undergoing active development during adolescence. Self-estimation from psychological testing and parental estimation of behavioural problems were used in this study. Once again it was recognised that this study was limited by consumption being self-reported, small in group size (564 Dutch subjects aged 11 – 16 years, of whom 244 were females) and being cross-sectional in nature. It was recognised that pre-existing executive function deficiencies may have led to “energy drink” consumption and not vice versa.

94 Jain *et al* (2012) looked at the effect of a range of sports drinks and “energy drinks” on enamel dissolution. Samples of enamel taken from extracted teeth were weighed before being soaked in either a sport drink or “energy drink” for 15 minutes, followed by two hours of soaking in artificial saliva. This was repeated 4 times per day for 5 days and then the samples were dried and weighed again. Weight loss was significantly greater with “energy drinks” than with sports drinks. The titratable acidity of a drink was directly related to the weight loss in the samples: the higher the titratable acidity, the greater the weight loss. “energy drinks” had 3 – 4 times the level of titratable acidity than sports drinks, though all of the beverages had a pH low enough to lead to enamel demineralisation (< pH 5.5: pH of drinks was about 3).
.

95 Iyer *et al* (2016) reported the case of a 35-year-old man who presented with a case of rhabdomyolysis after consuming a self-reported two servings of the “energy drink” “Neon Volt” prior to a two-hour workout in the gym. No aspects of his medical history could account for his muscle inflammation, myoglobinuria.and high creatine kinase, AST and ALT levels. The patient was put on intravenous saline for 3 days and his symptom subsided. The authors were surprised at this extreme reaction to

the “energy drink” and exercise and were sceptical about the accuracy of his stated level of consumption.

Cardiovascular effects

96 A small number of recent case studies in adolescents have implied the involvement of “energy drink” consumption in their aetiology.

97 Usain and Jawaid (2012) described the case of a 16-year-old boy with a previously normal blood pressure presenting with elevated readings of 140 – 160/ 80 – 100 mm Hg. He had drunk approximately 3 cans of the “energy drink” Sting” per day for 2 weeks. He was advised to abstain from “energy drink” use and his symptoms resolved within 2 weeks.

98 Di Rocco *et al* (2013) described cases of atrial fibrillation in two boys aged 14 and 16 following ingestion of “energy drinks”. In the first case, the boypresented with an irregular heartbeat of around 130 beats per minute (bpm) two hours after a running race. He had consumed an unknown quantity of a highly caffeinated beverage the day before and a can of ““Red Bull” “energy drink”” five days earlier that had been accompanied by a “fluttering sensation” in his chest. A dose of 7.5 μg/kg bw of digoxin returned his heart to normal sinus rhythm and 70 – 80 bpm and one month later he had a normal electrocardiograph (ECG) reading. . The second patient had drunk an unknown quantity of ““Red Bull” “energy drink”” mixed with vodka and presented with a heart rate of 160 bpm and chaotic atrial tachycardia/ fibrillation. He was given 2 litres of normal saline and his heart rate fell immediately and then reverted spontaneously to normal sinus rhythm 12 hours later.

99 Polat *et al* (2013) described the case of a 13-year-old boy who suffered acute onset “crushing” mid-sternal chest pain 8 hours after consuming an “energy drink” for the first time. Coronary angiography (imaging of the coronary arteries) revealed extensive dissection of the left descending coronary artery, characterised by a separation of the layers of the artery wall, a rare condition carrying the risk of acute coronary syndrome and sudden cardiac death. The symptoms subsided after treatment with aspirin, enoxaparin (an anticoagulant), nitroglycerine, enalapril (an angiotensin converting enzyme inhibitor) and metoprolol (a β_1 noradrenaline receptor antagonist) and a month later, left ventricular function was normal.

100 Samanta (2015) reported a case of reversible cerebral vasoconstriction syndrome in a 16-year-old boy who had consumed 4 cans of an “energy drink” (total caffeine intake 320 mg) four hours earlier. Magnetic resonance imaging (MRI) scans showed intermittent narrowing of the anterior, middle and posterior cerebral arteries, leading to the symptoms of thunderclap headache, vomiting, left leg numbness and gait difficulty. The patient was given analgesics and antiemetics followed by verapamil (an L-type calcium channel inhibitor) and was discharged with a warning to avoid “energy drinks” and caffeine. When scanned again 6 months later his cerebral arteries were normal.

101 Wilson *et al* (2012) reported the case of a 17-year-old male who presented with severe left-side chest pain, radiating into the left arm. An ECG revealed elevations in the ST segment in some leads and depressions in the same segment in others. There was no evidence of illicit drug use or any family history of premature coronary artery disease, but the patient admitted to drinking 3 – 4 “Red Bull” and 2 – 3 “Monster” “energy drinks” the night before, constituting up to 800 mg caffeine. Oral nitroglycerine and the calcium channel antagonist diltiazem were administered and, by the third day, the patient’s condition was stable enough for him to be discharged with advice to abstain from caffeinated beverages. A diagnosis of caffeine intoxication was reached but with the recognition that “energy drinks also contain other possibly contributory components.

102 A number of studies have looked at the effects of “energy drinks” in the general population, which may be relevant to their effects on adolescents as well as any other age group.

103 Scott *et al* (2011) described a case of myocardial infarction in a 19-year-old man who had in the prior week consumed 2 – 3 cans of “Red Bull” “energy drink” daily. The patient had a raised blood level of troponin I (a protein involved in muscle contraction that is used as a marker for myocardial infarction) but no family or medical history that could explain the problem and the authors were left with the conclusion that the “energy drink” was the cause.

104 A case of ECG ST-segment elevation myocardial infarction (STEMI) in a 27-year-old male who habitually drank 4 – 5 “energy drinks” over a 12-hour period of evening shift work was reported by Gharacholou *et al* (2016). There was no evidence of coronary obstruction, stenosis, dissection or embolism and the effect was attributed to the “energy drink” consumption. The patient was treated with long-acting nitrates and a Ca-channel antagonist and his ECG parameters returned to normal.

105 Solomin *et al* (2015) reported the case of a 26-year-old male who presented with left-sided chest pain following consumption of his “usual” ~ 4 litres of “energy drink”. The patient’s ECG revealed STEMI and a thrombus that completely occluded one of his coronary arteries was discovered. The authors speculated that the excess of “energy drink” had caused coronary vasospasm, leading to reduced blood flow and clot formation, although the patient also smoked 20 cigarettes a day, so smoking-related vasospasm could not be ruled out. An arterial stent was inserted and the patient was discharged with an antiplatelet agent, ACE inhibitor, beta blocker, statin and an agreement to give up smoking and “energy drinks”.

106 In 2013, There was a case report of a 28-year-old Turkish man who consumed 3 cans of an “energy drink” (240 mg caffeine in total) and lost consciousness 5 1/2 hours later. He was taken to intensive care suffering from ventricular tachycardia. On being shocked back into rhythm, the patient appeared normal but on the third day after admission he died of a sudden cardiac arrest. Nothing in the patient’s medical or family history that appeared to make him prone to heart disease, so the author attributed the cause to the consumption of the “energy drink” (Avci *et al,* 2013).

107 Grant *et al* (2016) reported the case of a 44-year-old woman who habitually consumed daily five 448 ml cans of “Monster energy drink” The patient presented with a sudden-onset severe headache that was revealed to be caused by a cerebral aneurysm. She was catheterised in preparation for balloon remodelling and this caused vasospasm and a haemorrhagic stroke. Further surgery resolved the aneurysm but the patient had severe persistent right arm and hand weakness thereafter. While the “energy drink” could not be singled out as the cause of this event, the authors felt that there was sufficient indirect evidence in the literature for clinicians to routinely ask their patients about their “energy drink” use.

108 Some studies have been conducted on healthy volunteers to observe the effects of “energy drink” consumption in the absence of disease states or excessive consumption

109 Hajsadeghi *et al* (2016) gave 250 ml of an “energy drink” (80 mg caffeine, with taurine, glucuronolactone, vitamins and sugar) to 44 healthy subjects aged 15 to 30, of whom 24 were female. Cardiovascular disease, medications, substance abuse, pregnancy and lactation were controlled for. Heart rate, systolic and diastolic blood pressure (HR, SBP and DBP) and ECG parameters were measured before consumption and up to 4 hours afterward. HR was observed to decline over 2 hours (80 to 75 beats per minute) and plateau up to 4 hours without significant changes in SBP or DBP. The most common ECG change was in the ST-T (the S wave to T wave segment on the ECG and the T wave itself), beginning 30 minutes post dose ($p<0.004$), observed as T-wave inversion in various leads. This effect could reflect myocardial damage, but the authors recognised that larger and longer-lasting clinical studies would be needed to confirm this effect.

110 In 2009, Steinke *et al* studied the effects of an “energy drink” (100 mg caffeine, 1000 mg taurine, B vitamins, glucuronolactone/ can) on the ECG parameters, BP and HR of a group of healthy volunteers, aged 18 to 40 years. Test subjects drank 2 cans of the “energy drink” and measurements were taken pre-drink and at 30 minutes and 1, 2, 3 and 4 hours post drink. The subjects then drank the same amount daily for the next 6 days and were measured again on day 7. On both day 1 and day 7, an increase in HR and SBP were observed, which were maximal at 4 hours post drink and an increase in DBP that was maximal at 2 hours post drink. No change was observed in corrected QT interval on the ECG. Adverse effects were reported by 47% if the subjects over the course of the study, including jitteriness, disturbed sleep, abdominal cramping and increased urination. The authors suggested that people with cardiovascular disease should avoid consuming “energy drinks”

111 Kurtz *et al* (2013) performed a randomised double-blind controller crossover study on the blood pressure and heart rate in healthy young volunteers (aged 20 – 26 years), given either a caffeinated or decaffeinated “energy shot” (a small volume, concentrated “energy drink”). The drinks were both 57ml, sweetened with sucralose. The decaffeinated version actually contained 6 mg of caffeine and the caffeinated version was reported to contain between 138 and 215 mg caffeine per bottle. The caffeinated version contained citicoline (choline phosphoester of cytidine

diphosphate) but no niacin whereas the decaffeinated version contained choline and niacin, but the formulations of both drinks were otherwise the same. Relative to the decaffeinated drink, the caffeinated drink caused a significant increase in SBP at 1 and 3 hours after consumption ($p = 0.001$ and 0.042 respectively). DBP was similarly raised significantly, but heart rate was not significantly affected. Caffeine was held to be the cause of these effects, although both drinks caused some minor adverse effects.

112 Svatikova *et al* (2015) found that a 480 ml can of “Rockstar” “energy drink” (containing 240 mg caffeine, 2000 mg taurine and extracts of guarana, ginseng root and milk thistle) increased the mean blood pressure of a group of healthy volunteers (aged 26 – 31 years, 14 men, 11 women) by 6.4%, whereas a placebo raised mean blood pressure by 1% ($p< 0.001$). No significant difference in heart rate was noted between the drinks. Plasma noradrenaline levels were also raised significantly ($p = 0.003$) by the “energy drink” relative to the placebo.

113 Grasser *et al* (2015) found that consuming a can of “Red Bull” “energy drink”, in combination with a mental arithmetic test as a form of mental stress had a cumulative effect on a group of healthy volunteers (aged 19 to 29, 10 men, 10 women). The “energy drink” alone increased SBP by 7 mm Hg, DBP by 4 mm Hg and heart rate by 7 bpm. With the test, SBP, DBP and heart rate increased by a further, by 3 mm Hg, 3 mm Hg and 13 bpm respectively. These latter increases were also seen in the control group consuming water. On their own, both water and “Red Bull” “energy drink” decreased cerebral blood flow (water by ~3 cm/s and “Red Bull” “energy drink” by 9 mm/s) and although the test reduced the fall in both cases, the difference was still significant (~ 7 cm/s, $p < 0.005$). No improvement in the subjects’ number of mistakes or perceived stress in the mental test was seen, leaving the authors to suggest that the “energy drinks” purported increase in performance was a dubious claim.

114 Sullivent *et al* (2012) investigated the effect of a sugar-free “energy drink” or a non-caffeinated placebo on the cardiovascular responses in two groups ($n = 7$ in both cases) of students aged 18 – 30 years. Participants drank either the “energy drink” or placebo 40 minutes before an exercise test on a treadmill. Maximal oxygen uptake (VO_2max), SBP, DBP, HR, ectopic beats and Rate-Pressure Product (RPP) were determined. The only significant effects of the “energy drink” relative to the control were a reduction in exercise VO_2max and an increase on post-exercise DBP ($p < 0.05$ in both cases). The authors concluded that the “energy drink”, rather than being ergogenic, was ergolytic, reducing estimated fitness levels, and elevated heart demand and recovery BP after exercise.

115 Pommerening *et al* (2015) performed a crossover study to investigate the effect of a sugar-free “energy drink” on platelet agglutination in healthy volunteers. On two occasions, a minimum of a week apart, 32 volunteers (22 male, 10 female, median age 27 years) consumed 448 ml of either water or a sugar-free “energy drink” (140 mg caffeine plus taurine, ginseng, L-carnitine, glucuronolactone, inositol and guarana). Blood samples were taken and platelet aggregation was stimulated by several effectors: ADP, arachidonic acid, collagen, thrombin-receptor activating peptide or the antibiotic ristocetin). Energy drink consumption significantly increased

($p=0.018$) the arachidonic acid-induced agglutination but not that of the other effectors. The authors suggested that this could be a mechanism by which “energy drink” consumers had an increased risk of adverse cardiovascular events.

116 Nowak *et al* (2018) dosed 68 healthy young adults (mean age 25 years) with either 3 portions of an “energy drink” (240mg caffeine in total) or the same volume of water. After 3 hours the “energy drink” group’s diastolic BP had risen from 76 to 83 mm Hg ($p = 0.003$) but their systolic BP and heart rate were unaffected. None of the water group’s cardiovascular parameters were affected. Blood glucose in the “energy drink” group increased over the same time period from 82 to 100 mg/dL ($p < 0.001$). Adverse effects were reported in the “energy drink” consumption group, mainly of excitation, general malaise, somnolence, head ache and stomach ache. The authors discussed the possible health consequences (obesity, type 2 diabetes) of consuming high-sugar content beverages.

117 Worthley *et al* (2010) studied the effect of an “energy drink” (80 mg caffeine, 1000 mg taurine and 600 mg glucuronolactone) on blood pressure, endothelial function and platelet agglutination in a group of 50 young adults (aged 20 – 24, 34 male,16 female). Mean arterial BP, but not heart rate, increased following “energy drink” consumption relative to water control ($p <0.05$). Platelet aggregation was studied ex vivo by treatment of blood samples from the participants with adenosine diphosphate at 1 and 10 μmol/l. Platelet aggregation was increased significantly in the “energy drink” consumers at the low ADP concentration ($p <0.003$) but the effect was not significant at the high ADP concentration ($p < 0.07$). To assess endothelial function, the ratio of an arterial pulse wave amplitude was measured before and one minute after the occlusion of a peripheral vessel. The ratio was significantly reduced in the “energy drink” group ($p < 0.06$). Endothelial-independent vasodilatation induced by 400 μg sublingual nitroglycerine was unaffected by “energy drink” use. Since the latter effects were not documented for coffee use, and since taurine was regarded as being protective of the cardiovascular system, the authors speculated that glucuronolactone might have been at least partially responsible although no work was undertaken to test this possibility.

118 In contrast, Molnar and Somberg (2014) evaluated peripheral endothelial function in 19 healthy volunteers (11 men, 9 women, aged 19 – 29 years) in response to 3 different energy drinks and coffee and observed functional improvements with two of the “energy drinks”, “5-hour” and “Red Bull” “energy drink” , but not with “NOS” “energy drink” or coffee. Caffeine was once again precluded from being the functional component but it or their identity was not investigated.

Consumption of “energy drinks” relative to other substances

119 Several reports deal with co-consumption of “energy drinks” with other psychoactive substances, notably alcohol. Several reports consider the influence of this mixed consumption on “risky” behaviours such as drink driving and unsafe sex. Gallimberti *et al* (2015) suggest that energy drinks should be regulated in early adolescents since they provide a route into the taking of risks with other substances

such as alcohol, tobacco and marijuana that act as gateways to the use of more damaging drugs.

120 Reid *et al* (2015) collected longitudinal data from a cohort of Ontario secondary school pupils aged 15 – 18 years relating to their "energy drink" consumption and their use of these products concurrently with alcoholic beverages. Overall, 17.5% of the sample (4016 respondents) reported using "energy drinks" with alcohol in the previous 12 months. 71.6% reported never doing this, 6.4% said they had not done this in the previous 12 months and 3.7% said that they did not know.

121 Miyake and Marmorstein (2015) found a positive relationship between high "energy drink" consumption by young New Jersey adolescents, 12 – 13 years old, (who consumed at least one "energy drink" per week) and alcohol consumption 16 months later, that was not seen with coffee or other soft drink consumption. The most probable cause for this finding was held to be lack of parental monitoring of the consumption of both types of beverage. Consumption of alcohol by the same age group did not appear to correlate with changes in later levels of alcohol consumption.

122 Kponee *et al* (2014) found in a survey of adolescents from Boston, Mass. USA that those who consumed "caffeinate alcoholic drinks", either alcohol mixed with soft drinks, tea or coffee ("traditional CABs") or alcohol mixed with "energy drinks" , energy shots or energy pills "(non-traditional CABs"), consumed more alcohol per month ($p<0.05$) and were more prone than non-consumers to engage in binge drinking ($p<0.05$).Consumers of "non-traditional CABs" were also more likely to engage in fighting and acquire alcohol-related injuries that required medical treatment. However, while the percentage of adolescents surveyed consuming any CAB was 52,4%, those using "energy drinks", energy shots and caffeine pills totalled15.4%.

123 Scalese *et al* (2017) found that while mixing "energy drinks" with alcohol increased the probability of Italian adolescents to indulge in a wide range of risky behaviours such as binge drinking, cannabis and other drug use, unsafe sex, and fighting, the differences between the response to "energy drinks" alone and alcohol-plus-EDs were small. Perceived reduction in alcohol sedation was a motive for mixing it with "energy drinks". The authors felt that education and changes in marketing were required to address the observed behavioural effects.

124 Vieno *et al* (2018) found that of 13.725 Italian adolescents, aged 15 – 19 years, 4495 reported gambling in the previous year, of whom 62.5% were male. Of the gamblers, 5.1% reported drinking alcohol-mixed "energy drinks" (AmEDs) 6 times or more that month. 43% of these were classified as at-risk and problem gamblers (ARPG), compared with 23.6% of 6-times or-more-alcohol-alone consumers. AmED consumers were 3 times more likely to be ARPG than non-consuming adolescents.

125 In the UK, the Licencing Act 2003 (https://www.legislation.gov.uk/ukpga/2003/17/section/1) makes it illegal for children between the ages of 5 and 16 years to consume alcohol and for adolescents under the age of 18 years to purchase it. This legislation should at least reduce the

consumption of "energy drink" – alcohol mixtures by children and adolescents in the UK.

126 ED use has also been found to be associated with smoking and drug use (for example Mann *et al*, 2016, Terry-McElrath *et al* 2014, Polak *et al* 2016, Everen & Everen 2015.)

127 Williams *et all* (2017) found that recent (i.e. within the previous 7 days) consumers of energy drinks among 1570 teenagers were more likely to eat fried and high-sugar foods than those who had not consumed the drinks (foods such as cake, p<0.011; sugary cereal (p<0.001: or fried chicken, p<0.001).

<u>Other reported effects of "energy drinks"</u>

128 Seidl *et al* (2000) found that consumption of "Red Bull" "energy drink" by graduate students maintained feelings of well-being, vitality and social extravertedness for longer than was seen with a placebo control. Since half of the subjects were non-caffeine-users, the observed effect was not attributed to recovery from caffeine withdrawal.

129 Alford *et al* (2001) also found beneficial effects relative to control drinks. "Red Bull" "energy drink" consumption increased significantly ($p < 0.05$) aerobic endurance and performance of subjects on cycle ergometers, as well as reaction time, concentration and memory.

130 Smit *et al* (2004) found that "energy drinks" maintained arousal compared with a sensory-matched placebo and that caffeine was mainly responsible for this effect, with a very minor contribution from the carbohydrate content of the drink. This effect was at least partially attributed to caffeine "withdrawal reversal". The effect of carbonation on mood was variable but in some cases was consistent with reducing the uptake of caffeine and / or carbohydrates.

131 Rahnama *et al* (2010) gave 10 male athletes (aged 20 – 24 years) either one of two "energy drinks" - "Red Bull" or "Hype" – or a placebo drink 40 minutes before exercise on a treadmill. The "energy drinks" increased VO_2 (53 vs 47 ml.kg/min, p<0.05) and time to exhaustion (14.6 vs 13 minutes, p<0,05) relative to the placebo. without significant differences in pre- and post-test heart rate or blood lactate concentration between the groups. The authors suggested that the taurine content of the "energy drinks" (1000 mg/serving) may have ameliorated the effect of the caffeine on heart rate.

132 Abian-Vicen *et al* (2014) tested the effects of an "energy drink" on the physical performance of adolescent basketball players and found a small but significant ($p < 0.05$) increase in jump height 60 minutes after ingestion, but not in basketball shooting precision.

133 Prins *et al* (2014) found that ingesting “Red Bull” “energy drink” 60 minutes before completing a 5-km time trial on a treadmill led to a small but significant ($p = 0.016$) improvement in running performance in a group of 18 late teens and early adults. Subjects’ rating of perceived exertion and mood were not altered by the “energy drink”.

134 In a meta-analysis of the effects of “energy drinks” on physical performance, Souza *et al* (2017) documented the effects of a range of doses of caffeine ((40 – 325 mg) and taurine (71 – 3105 mg) in jumping, muscle strength and endurance, sport-specific actions and sprinting over 34 studies. Although some studies showed no effect on the parameter measures, across the meta-analysis, there was a significant ($p<0.001$) improvement in all parameters but sprinting ($p< 0.06$). Performance improvement was affected significantly by the taurine content of the drinks ($p< 0.04$) but not by their caffeine content.

135 Conversely, Jeffries *et al* (2017) found that ingestion of a gelatine capsule containing 80 mg caffeine and 1 g taurine, equivalent to many “energy drinks”, did not improve repeat-sprint cycling performance in a group of 11 male young adults. Greater fatigue appeared to be induced to ne induced within sprints and at the end of the trial, without affecting perceived exertion but with increased heart rate and blood lactate concentration.

<u>Expert opinions</u>

EFSA Caffeine

136 In 2015, EFSA stated that ”Single doses of caffeine up to 200 mg (about 3 mg/kg bw for a 70-kg adult) do not give rise to safety concerns. The same amount does not give rise to safety concerns when consumed < 2 hours prior to intense physical exercise under normal environmental conditions... Habitual caffeine consumption up to 400 mg per day does not give rise to safety concerns for non-pregnant adults. Habitual caffeine consumption up to 200 mg per day by pregnant women does not give rise to safety concerns for the fetus. Single doses of caffeine and habitual caffeine intakes up to 200 mg consumed by lactating women do not give rise to safety concerns for breastfed infants. For children and adolescents, the information available is insufficient to derive a safe caffeine intake. The Panel considers that caffeine intakes of no concern derived for acute caffeine consumption by adults (3 mg/kg bw per day) may serve as a basis to derive single doses of caffeine and daily caffeine intakes of no concern for these population subgroups.”

137 In 1999 the SCF stated: “*For children who do not normally consume much tea or coffee and who might substitute “energy” drinks for cola or other soft drinks, consumption of “energy” drinks might represent an increase in daily caffeine exposure compared with their previous intake. …consumption of 160 mg caffeine/day from 0.5l of “energy drink would be equivalent to 5.3 mg/kg bw/day for a 10-year-old, 30 kg child. This could result in transient behavioural changes, such as increased arousal, irritability, nervousness or anxiety.”*

138 EFSA (2011) collated the daily consumption of caffeine from “energy drinks” from different dietary surveys across the surveyed population in each study and across “energy drink” consumers in the same study. Across the whole sample, the group that consumed the most caffeine from “energy drinks” was that of adolescents, aged from 10 to < 18 years (means from 0.0 to 5.7 mg/day and 95th percentile from 0.0 to 40.0 mg/day). Across “energy drink” consumers, The mean intake of caffeine by adolescents ranged from 29.0 – 90.1 mg/day and 95th percentile of 145.6 mg/day. 41% of adolescent “energy drink” consumers drank them in relation to sport.

139 The highest contribution to caffeine intake from “energy drinks” was from the UK (11%), followed by the Netherlands (8.1%) and Belgium (5.3%)

EFSA taurine and D-glucurono-γ-lactone

140 The SCF (1999) concluded that *“Toxicological studies did not reveal any indication for a genotoxic, carcinogenic or teratogenic potential of taurine. However, there is no adequate study on chronic toxicity/carcinogenicity. Investigation of subacute/ subchronic toxicity has also been fragmentary. Overall, the available data are insufficient to establish an upper safe level for daily intake of taurine.”* https://ec.europa.eu/food/sites/food/files/safety/docs/sci-com_scf_out22_en.pdf

141 In 2003 the SCF stated: ”…*the potential for interactions between caffeine and taurine has not ruled out the possibility of stimulatory effects from both substances at the level of the central nervous system. At the cardiovascular level, if there are any interactions between caffeine and taurine, taurine might reduce the cardiovascular effects of caffeine. The main area for likely additive interactions is in the diuretic actions of caffeine and taurine, which could be further enhanced by ingestion of alcohol.”*

142 The EFSA statement on the use of taurine and D-glucurono-γ-lactone as constituents of “energy drinks” (2009) concluded that since these compounds are both natural constituents of the human body and that the NOAEL for any adverse effects for both compounds is 2 orders of magnitude above their mean exposure in “energy drink” consumers, their presence in “energy drinks” would not be a concern for health.

143 EFSA (2015) stated Other constituents of “energy drinks” at typical concentrations in such beverages (about 300–320, 4 000 and 2 400 mg/L of caffeine, taurine and D-glucurono-γ-lactone, respectively), as well as alcohol at doses up to about 0.65 g/kg bw, would not affect the safety of single doses of caffeine up to 200 mg

144 Interactions of taurine with caffeine with regard to the diuretic effect of “energy drinks” were regarded as unlikely but other potential interactions between these compounds were not investigated.

145 It was held unlikely that D-glucurono-γ-lactone would interact with caffeine, taurine, alcohol or physical exercise.

COT

146 In their Statement on the interaction of caffeine with alcohol and their combined effects on health and behaviour (2012), the COT concluded that the available evidence did not show conclusively that the two drugs interact with one another in a toxicological or behavioural manner. Evidence that caffeine ameliorated the intoxicating effects of alcohol was found to be inconsistent, and it was uncertain whether reports of increased alcohol and caffeine consumption represented a psychological interaction or the fact that such co-consumers were predisposed to consume mixtures of psychoactive agents in general.

BfR

147 The BfR conducted a survey in Germany on the consumption of “energy drinks” by 7460 people, of which 8% or 508, fulfilled the consumption criteria and completed the interview. Forty five percent, 3063 people who were initially approached, had never had an “energy drink”. Several social scenarios were highlighted as situations for “energy drink” consumption and for 15 – 20-year-old subjects, music festivals and discos/dancing/parties were the main events. Taste and energy-boosting properties were given as the main incentives to drink “energy drinks”.

Conclusions

148 This paper has concentrated on the effects of the use and abuse of “energy drinks” in adolescents, because this group has been the focus of recent interest in the media. However, data on the effects of energy drinks on mostly young adults have been included here for comparison where the nature of the effect would be relevant to any age group and may indicate a general principle of the effects observed.

149 “Energy drinks” contain variable amounts of caffeine as their main active constituent. The caffeine intake from a serving of “energy drink”, while higher than that of other caffeinated soft drinks, may be similar to that in a serving of coffee from a high-street vendor, depending upon the make of each beverage;

150 The sugar content of a serving of “regular energy drinks” is 1 – 2 times that of a serving of caffeinated and non-caffeinated soft drinks. All types of sugar-sweetened drinks may contribute to obesity, tooth decay and other diet-related diseases. New legislation should reduce the level of sugar in soft drinks and energy drinks alike.

151 The effects of caffeine consumption appear to be modified by dose, genetics, tolerance, withdrawal symptoms, expectations and social situations. Negative health related effects are seen in both adolescents and adults and largely relate to ingestion

of large quantities of “energy drinks”. However, even modest amounts seen to exert measurable effects on heart rate and ECG parameters that may be a risk to health of people with underlying conditions such as Long Q-T Syndrome.

152 The pharmacological and toxicological effects of other non-caffeine constituents are dismissed in some accounts but regarded by others as relevant to the overall effects of “energy drinks”.

153 There appears to be no difference in the pharmacokinetics of caffeine consumed slowly, quickly, hot or cold, as coffee or in sugar-free “energy drinks”.

154 Children and adolescents have until recently had full access to “energy drinks” but new voluntary restrictions by food retailers should limit this. Taste of these products is a common driver for consumption but overall, drinking energy drinks is influenced by various, sometimes conflicting, factors including perceived stimulation, availability, warnings on packaging, advertising, peer pressure and parental influence. Most surveys suggest that boys consume a greater volume of “energy drinks” than do girls.

155 Some children and adolescents are aware that “energy drinks” can cause adverse health effects, whereas others are not.

156 Use of “energy drinks” have been related to adverse effects including poor sleep, reduced school performance and acute physical effects probably related to excess caffeine consumption. “Energy drinks” are also consumed mixed with alcohol, which may lead to exacerbation of “risky” behaviours. However, any effects of “energy drinks” on adolescent behaviour overlie the already-documented behaviour patterns of this age group, arising from biological and social development, and since most of the studies are cross sectional or small-group longitudinal, it is difficult to determine how “energy drink” consumption affects or is affected by this background.

157 There is long-standing legislation in place in the UK that restricts the sale of alcoholic beverages to minors, which would be expected to reduce the exposure of children and adolescents to mixtures of alcohol and “energy drinks”.

158 Overall the consumption of “energy drinks” by children and adolescents is a complex social issue. The acute toxicological and physiological effects of the main active constituent of “energy drinks”, caffeine, are well documented, while those of other ingredients are disputed. New legislation should reduce the amount of sugar in “energy” and soft drinks. Only a small proportion of children and adolescents admit to “energy drink” use at levels likely to cause toxicity. Although the effects of low-level chronic consumption of these drinks are unknown, children and adolescents have long had chronic exposure to caffeine and its metabolites through consuming tea, coffee, cola and chocolate.

Questions for the Committee

1 Does the Committee agree with the summary of the available evidence drawn above?

2 Does the Committee consider that there are adverse physiological effects in children and adolescents caused by the consumption of energy drinks?

3 Does the Committee consider that the studies outlined in this paper provide evidence that children and adolescents may be more susceptible than adults to the effects of energy drinks?

4 Do Members consider that robust conclusions can be reached despite the uncertainties in the evidence base? If not, what suggestions would they make regarding research to reduce these uncertainties and what would be the priorities for future work?

5 Would the Committee consider it useful to compare the effects of “energy drink” consumption described in this paper with the effects of coffee consumption in the same age groups?

6 What further considerations do the Committee have regarding the consumption of energy drinks to adolescents and children?

References

Abian-Vicen J, Puente C, Salinero JJ, González-Millán C, Areces F, Muñoz G, Muñoz-Guerra J, Del Coso J. A caffeinated energy drink improves jump performance in adolescent basketball players. Amino Acids 2014. **46**(5): 1333 – 1341.

Aeple A, Kurth S, Tesler N, Jenni OG, Huber R. Caffeine consuming children and adolescents show altered sleep behaviour and deep sleep. Brain Sci. 2015 **5**: 441 – 455.

Alford C, Cox H, Wescott R. The effects of “Red Bull” “energy drink” energy drink on human performance and mood. Amino Acids 201. **21**(2):139 – 150.

Alhayas L, El Kashef A, AlGhaferi H. Energy drinks in the Gulf Cooperation Council states: a review. Journal of the Royal Society of Medicine Open. 2015. DOI 10.1177/2054270415593717.

Al-ShaarL, Vercammen K, Lu C, Richardson S, tamez M, Mattei J. Health effects and public health concerns of energy drink consumption in the United States: a mini-review. Frontiers in Public Health 2017 **5:** doi: 10.3389/fpubh.2017.00225.

Aluqmany A, Mansoor R, Saad U, Abdullah R, Ahamd A. Consumption of energy drinks among female secondary school students, Almadinah Alumawwarah, kingdom of Saudi Arabia, 2011. Journal of Taibah University medical Sciences **8**(1): 60 – 65.

Arnaud MJ. The pharmacology of caffeine. Progress in Drug Research1987. **31**: 273 – 313.

Arria AM, Bugbee BA, Caldiera KM, Vincent KB. Energy drink use and high-risk behaviors: research evidence and knowledge gaps. Nutrition Reviews 2014. **72**(1):87 – 97.

Avci S, Sarikaya R, Buyukcam F. Death of a young man after overuse of energy drink. American Journal of Emergency Medicine 2013. **31**: 1624 e1 – 1624 e4.

Bashir D, Reed-ScHRader E, Olympia RP, Brady J, Rivera R, Serra T, Weber C. Clinical symptoms and adverse effects associated with energy drink consumption in adolescents. Pediatric Emergency Care 2016 **32**(11): 751-755.

Borron SW, Watts Sh, Herrera J, Larson J, Baeza S, Kingston RI. Energy drink exposures reported to Texas poison centers: analysis of adverse incidents in relation to total sales, 2010 – 2014. Regulatory Toxicology and Pharmacology 2018 **97**: 1 – 14.

Boyle NB, Lawton CL, Dye L. The effects of carbohydrates, in isolation and combined with caffeine, on cognitive performance and mood – current evidence and future directions. Nutrients 2018. **10**: 192 – 238.

Calabro RS, Italiano D, Gervasi G, Bramanti P. Single tonic-clonic seizure after energy drink abuse. Epilepsy and Behavior 2012. **23**: 384 – 385.

Concerto C, Conti C, Muscatello MR, Signorelli MS, Zoccali R, Coira D, Aguglia E, Battaglia F. Sleep quality, perceived stress and caffeinated drinks intake in psychiatry residents: a cross-sectional study. Journal of Caffeine Research 2010. **7**(1): 18 – 22.

Carskadon MA and Tarokh L. Developmental changes in sleep biology and potential effects on adolescent behaviour and caffeine use. Nutrition Reviews2014. **72**(S1): 60 – 64.

Chang Y-J, Peng C-Y, Lan Y-C. Consumption of energy drinks among undergraduate students in Taiwan: related factors and associations with substance use. International Journal of Environmental Research and Public Health 2017. **14**: 954 – 1002.

Costa BM, Hayley A, Miller P. Young adolescents' perceptions, patterns, and contexts of energy drink use: a focus group study. Appetite 2014 **80**:183 – 189.

Costa BM, Hayley A, Miller P. .Adolescent energy drink consumption: an Australian perspective. Appetite 2016 **105**: 638 – 642.

De Sanctis V, Soliman N, Solimjan AT, Elsedfy AT, Elsedfy H, Di Maio S, EL Kholy M, Fiscina B. Caffeinated energy drink consumption among adolescents and potential health consequences associated with their use: a significant public health hazard. Acta Biomedica 2017. **88**(2): 222 – 231.

Di Rocco JR, During A, Morelli PJ, Heyden M, Biancaniello TA Atrial fibrillation in healthy adolescents after caffeinated beverage consumption: two case reports. Journal of Medical Case Reports 2011 **5**:18 – 23P.

Drake C, RoeHRs T, Shambroom J, Roth T. Caffeine effects on sleep taken 0, 3, or 6 hours before going to bed. Journal of Clinical sleep medicine 2013. **9**(11): 1195 – 1200.

EFSA 2009 The use of taurine and D-glucurono-γ-lactone as constituents of the so-called "energy" drinks 1 Scientific Opinion of the Panel on Food Additives and Nutrient Sources added to Food The EFSA Journal (2009) 935, 1-31.

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies) 2015. Scientific Opinion on the safety of caffeine. EFSA Journal 2015; **13**(5):4102, 120pp. doi:10.2903/j.efsa.2015.4102.

Evren C, Evren B. Energy-drink consumption and its relationship with substance use and sensation seeking among 10th grade students in Istanbul. Asian Journal of Psychiatry 2015. **15**:44 – 50.

Faris MA-IE. Patterns of Caffeinated Energy Drinks Consumption amog Adolescents and Adults in Hail, Saudi Arabia Food and Nutrition Sciences, 2014 5:158-168.

Galland BC, Gray AR, Penno J, Smith C, Lobb C, Taylor RW Gender differences in sleep hygiene practices and sleep quality in New Zealand adolescents aged 15 to 17 years. Sleep Health 2017 **3**:77 – 83.

Gallimberti L, Buja A, Chindamo S,Vinelli A, Lazzarin G, Terraneo A,Scafato E, Baldo V. Energy drink consumption in children and early adolescents. European Journal of Padiatrics 2013 **172**: 1335 – 1340.

Gallimberti L, Buja A, Chindamo S, Lion C, Terraneo A, Marini E, Perez LJG, Baldo V. Prevalence of substance use and abuse in late childhood and early adolescence: what are the implications? Preventive Medicine Reports 2015. **3**: 862 – 867.

Gera M, Kalra S, Gupta P. Caffeine intake among adolescents in Delhi. Indian Journal of Cpommunity Medicine 2016. **41**(2): 151 – 153.

Gharacholou SM, Ijioma N, Banwart E, Del Carpo munoz, F. ST-segment myocardial infarction and normal coronary arteries after consuming energy drinks. Case Rreports in Cardiology 2017;2017:4061205. doi: 10.1155/2017/4061205. Epub 2017 Jan 19. PMID:2820346.

Giles GE, Mahoney CR, Brunyé TT, Gardony AL, Taylor HA, Kanarek RB. Differential cognitive effects if energy drink ingredients: caffeine, taurine, and glucose. Pharmacology, Biochemistry and Behavior 2012. **102**: 569 – 577.

Gillingham E 2018 Waitrose introduces minimum age limit on sales of high caffeine energy drinks.

Górnicka M, Pierzynowska J, Kaniewska E, Kossakowska K, Wozniak A. School pupils and university students surveyed for drinking beverages containing caffeine. Rocz. Panstw Zakl Hig 2016 **65**2:113 – 117.

Grasser EK, Dulloo AG, Montani J-P. Cardiovascular and cerebrovascular effects in response to “Red Bull” “energy drink” consumption combined with mental stress. American Journal of Cardiology 2015. **115**(2): 183 – 189.

Grant RA, Cord BJ, Kuzomunhu L, Sheth K, Gilmore E, Matouk CC. Aeurysmal subarachnoid haemorrhage and severe, catheter-induced vasospasm associated with excessive consumption of a caffeinated energy drink. Interventional Neuroradiology. 2016. **22**6: 674 – 678.

Guarino MP, Ribeiro MJ, Sacramento JF, Conde SV. CHRonic caffeine intake reverses age-induced insulin resistance in the rat: effect on skeletal muscleGlut4 transporters and AMPK activity. Age 2013. **35**: 1755 – 1765.

Ha D, Song I, Jang G, Lee E-K, Shin J-Y. use pattern and predictors of use of highly caffeinated energy drinks among South Korean adolescents: a study using the health belief model. BMJ Open 2017. **7**:e017224. Doi:10.1136/bmiopen-2017-017224.

Hajsadeghi, S, Mohammadpour F, Manteghi MJ, Kordshakeri K, Tokazebani M, Rahnmani E, hassanzadeh M. Effects of energy drinks on blood pressure, heart rate, and electrocardiographic parameters: an experimental study on healthy young adults. Anatolian Journal of Cardiology 2016 **16**: 94 – 99.

Hammond D, Reid J, Zukowski S Adverse effects of caffeinated energy drinks among youth and young adults in Canada: a web-based survey. Canadian Medical Association Journal 2014 **6**(1): E19 – E25.

Harb JN, Taylor ZA, Khullar V, Sattari M. Rare cause of acute hepatitis: a common energy drink BMJ Case Rep.2006.

Harris JL. Energy drinks and adolescents: what’s the harm? Nutrition reviews 2015. **75**(4): 247 – 257.

Hashem KM, He FJ, MacGregor GA. Cross-sectional surveys on the amount of sugar, energy and caffeine in sugar-sweetened drinks marketed and consumed as energy drinks in the UK between 2015 and 2017: monitoring the reformulation progress. BMJ Open 2017, **7** e018136. Doi: 10.1136/bnjopen-2017-018136.

Haslam DE, McKeown NM, Herman MA, Lichtenstein AH, Dashti HS. Interactions between genetics and sugar-sweetened beverage consumption om health outcomes: A review of gene-diet interaction studies. Frontiers in Endocrinology 2018 **8** 9pp doi:10.3389/fendo.2017.00368.

Higgns JP, Tuttle TD, Higgins CL Energy beverages: content and safety. Mayo Clinic Proceedings 2010 **85**(11): 1033 – 1041.

Huang B, Kunkel D, El Kabany M. Acute live failure following one year of daily consumption of a sugar-free energy drink. ACG Case Reports Journal 2014 **1**(4): 214 – 216.

Iyer PS, Yelisetti R, Miriyala V, Siddiqui W, Kaji A. A remarkable case of rhabdomyolysis associated with ingestion of energy drink “neon volt”. Journal of Community Hospital Internal Medicine Perspectives 2016 **6** http://dx.doi.org/10.3402/chimp.v6.32528.

Jeffries O. Hill J, Patterson SD, WaldronM. Energy drink doses of caffeine and taurine have a null or negative effect on sprint performance. Journal of Strength and Conditioning Research2017. Doi: 10.1519/JSC.0000000000002299.

Kilb W. Putative role of taurine as a neurotransmitter during perinatal cortical development. Advances in Experimental Medical Biology 2017. **975**: 281 – 292.

Kim SY, Sim S, Choi H. High stress, lack of sleep, low school performance, and suicide attempts are associated with high energy drink intake in adolescents. PLOS One 2017 **12**(11): e0187759.

Kponee KZ, Siegal M, Jernigan DH. The use of caffeinated alcoholic beverages among underage drinkers: results of a national survey. Addictive Behaviors 201 4**39**(1):1 – 14.

Kristjansson AL, Sugfusdottir ID, Mann MJ, James JE. Caffeinated sugar-sweetened beverages and common physical complaints in Icelandic children aged 10-12 years. Preventive Medicine 2014 **58**: 40 – 44.

Kumar G, Park S, Onufrak S. Perceptions about energy drinks are associated with energy drink consumption among U.S. youth. American Journal of Health Promotion 2015. **29**(4): 238 – 244.

Kurtz AM, Leong J, Anand M, Dargush AE, Shah SA. Effects of caffeinated versus decaffeinated energy shots on blood pressure and heart rate in healthy young volunteers. Pharmacotherapy 2013. **33**(8): 779 – 786.

Leipner JB. Fate if ingested fluids: factors affecting gastric emptying and intestinal absorption of beverages in humans. Nutrition Reviews 2015 **73**(S2): 57 – 72.

Lisdahl KM, Sher KJ, Conway KP, Gonzalez R, Feldstein Ewing SW, Nixon SJ, Tapert S, Bartsch H, Goldstein RZ, Heitzeg M. Adolescent brain cognitive development (ABCD) study: overview of substance use assessment methods. Developmental Cognitive Neuroscience 2018. **32**: 80 – 96.

Mann MJ, Smith ML, Kristjansson AL. Energy drink consumption and substance use risk in middle-school students. Preventive Medicine reports 2016. **3**: 279 – 282.

Matthews L Energy drinks are #NotForChildren
http://waitrose.pressarea.com/pressrelease/details/78/NEWS_13/909
https://www.jamieoliver.com/news-and-features/features/energy-drinks-are-not-for-children.

McLellan TM, Caldwell JA, Liebermann HR. A review of caffeine's effects on cognitive, physical and occupational performance. Neuroscience and Behavioral Reviews 2016. **71** 294 – 312.

McCrory C, White CM, Bowman C, Fenton N, Reid JL, Hammond D. Perceptions and knowledge of caffeinated energy drinks: results from focus groups with

Canadian youth. Journal of Nutritional Education and Behavior **49**(4): 304 – 312 (including supplementary material).

Miles-Chan JL, Charrière N, Grasser EK, Montani J-P, Dultoo AG. The blood pressure-elevating effect of “Red Bull” “energy drink” energy drink is mimicked by caffeine but tHRough different hemodynamic mechanisms. Physiological Reports 2015 **3**(2): e12290 1 – 9.

Miles-Chan JL, Charrière N, Grasser EK, Montani J-P, Dultoo AG. The thermic effect of sugar-free “Red Bull” “energy drink” : do the non-caffeine bioactive ingredients in energy drinks play a role? Obesity 2015 **23**(1): 16 – 19.

Mills KL, Goddings A-L, Clasen LS, Giedd JN, Blakemore S-J The developmental mismatch in structural brain maturation during adolescence. Developmental Neuroscience 2014 **36**: 147 – 160.

Miyake ER and Marmorstein NR. Energy drink consumption and later alcohol use among adolescents. Addictive Behaviors 2015 **43** 60 – 65.

Molnar J, Somburg JC. Evaluation of the effects of different energy drinks and coffee on endothelial function. American Journal of Cardiology 2015. **116**: 1457 – 1460.

Monnard CR, Montani J-P, Grasser EK. Cerebro- and cardio-vascular responses to energy drink in young adults: is there a gender effect? Fronteers in Physiology 2016. **7**: Article 346, 6 pp.

Moustakas D, Mezzio M, Rodriguez BR, Constable MA, Mulligan ME, Voura EB. Guarana provides additional stimulation over caffeine alone in the planarian model. PLOS One 2015. **10**(4):e0123310. doi:10.1371/journalpone0123310.

Nassaif MM, Alobed GJJ, Alaam NAA, Alderrazi AN, Awdhalla MS, Vaithinathan AG. Energy drink consumption practices of young people in BaHRain. Central Asian Journal of Global Health 2015. **3**(2) doi: 10.5195/cajgh.2015.216/http://cajgh.pitt.edu.

Nordt SP, Claudius I, Rangan C, Armijo E, Milano P, Yanger S, Tomaszsewski C. Reasons for energy drink use and reported adverse effects among adolescent emergency department patients. Pediatric Emergency Care 2017 **33**(12): 770 – 773.

Nowak D, Jasionowski A. Analysis of the consumption of caffeinated energy drinks among Polish adolescents. International Journal of Environmental Research and Public Health 2015. **12**: 7910 – 7921.

Nowak D, Jasionowski A. Analysis of consumption of energy drinks by a group of adolescent athletes. International Journal of Environmental Research and Public Health 2016. **13**: 768 - 778.

Nowak D, Gośliński M, Nowatkowska K. The effect of acute consumption of energy drinks on blood pressure, heart rate and blood glucose in a group of healthy young adults. International Journal of Environmental Research and Public Health. 2018. **15**: 544 – 554.

Osswald H , Chnermann J. Methylxanthines and the kidney. Handbook of Experimental Pharmacology 2011; **200**: 391 – 412.

OwensJA, Mindell J, Baylor A. Effect of energy drink and caffeinated beverage consumption on sleep, mood, and performance in children and adolescents. Nutrition Reviews 2014. **72**(S1): 65 – 71.

Park S, Lee Y, Lee JH. Association between energy drink intake, sleep, stress, and suicidality in Korean adolescents: energy drink use in isolation or in combination with junk food consumption. Nutrition Journal 2016 **15**:87 – 94.

Patte KA, Qian W, Leatherdale ST. Modifiable predictors of insufficient sleep durations: A longitudinal analysis of youth in the COMPASS study. Preventive Medicine 2018 **106**: 164 – 170.

Peacock A, Martin FH, Carr A. Energy drink ingredients: contribution of caffeine and taurine to performance outcomes. Appetite 2013 **64** 1 – 4.

Peacock A, Droste N, Pemmay A, Miller P, Lubman DI, Bruno R. Awareness of energy drink intake guidelines and associated consumption practices: a cross-sectional study. BMC Public Health 2016 **16**: 6 – 16.

Pirastu N, Kooyman M, Robino A, van der Spek A, Navarini L, Amin N, Kardden LC, Van Duijn LM, Gasparini P. Non-additive genome-wide association scan reveals a new gene associated with habitual coffee consumption. Nature Scientific Reports 2016 **6**:31590; doi:10.1038/srep31590 (2016).

Polak K, Dillon P, Koch JR, Millar WG Jr, Thacker L, Svikis D. Energy drink use is associated with alcohol and substance use in eighth, tenth and twelfth graders. Preventive Medicine Reports 2016. **4** 381 – 384.

Polat N, Ardiç I, Akkoyun M, Vuruşkan E. Spontaneous coronary artery dissection in a healthy adolescent collowing consumption of caffeinated "energy drinks".Arch. Turk. Soc. Cardiol. 2013 **41**: 738 – 742.

Pommerening MJ, Cardenas JC, Radwan ZA, Wade CE, Holcomb JB, Cotton BA. Hypercoagulability after energy drink consumption. Journal of SurgicalResearch 2015. **199**: 635 – 640.

Porta M, Zima AV, Nani A, Diaz-Sylvester PL, Copello JA, Rames-Franco J, Blatter LA, Fill M. Single ryanodine receptor achnnel basis of caffeine's action on Ca^{2+} sparks. Biophysical Journal 2011. **100**: 931 - 938

Prins PJ, Goss FL, Nagle EF, Beals K, Robertson RJ, Lovelekar MT, Welton GL. Energy drinks improve five-kilometer running performance in recreational endurance runners. Journal of Strength and Conditioning Research 2016. **30**(11):2979 – 2990.

Rahnama N, Gaeini AA, Kazemi F. The effectiveness of two energy drinks on selected indices of maximal cardiorespiratory fitness and blood lactate levels in male athletes. Journal of Research in Medical Science 2010 **15**(3): 127 – 132.

Reid JL, Hammond D, McCrorey C, Dubin JA, Leatherdale ST. Use of caffeinated “energy drinks” among secondary school students in Ontario: prevalence and correlates of using “energy drinks” and mixing with alcohol. Canadian Journal of Public Health2015 **106**(3): e101 – e108.

Reid JL, , McCrorey C, White CM, Martineau C, Vanderkooy P, Fenton N, Hammond D. Consumption of caffeinated energy drinks among youth and young adults in Canada. Preventive Medicine Reports 2017. **5**: 65 – 70.

Reisenhuber A, Boehm M, Posch M, Aufricht C. Diuretic potential of energy drinks/ Amino Acids 2006. **31**: 81 – 83.

Reissig CJ, Strain EC, Griffiths RR Caffeinated energy drinks – a growing problem. Drug and Alcohol Dependence 2009 **99**:1 – 19.

Richards G and Smith AP. A review of energy drinks and mental health, with a focus on stress, anxiety, and depression. Journal of Caffeine Research 2016a. **6**(2):

Richards G and Smith AP Caffeine consumption and general health in secondary school children: a cross-sectional and longitudinal analysis. Frontiers in Nutrition 2016b **3**:52 – 62.

Ripps H, Shen W. Review: Taurine: A “very essential” amino acid. Molecular Vision 2012. **18**: 2673 – 2686.

Robertson D, Wade D, Workman R, Woosley RL, Oates JA. J. Clin. Invest 1981 **67**: 1111 – 1117.

Robin S, Buchanan R, Poole R. Energy drinks and adolescents – a hepatic health hazard? Journal of Hepatology (2018). **68**: 856 – 857.

Romer D. Adolescent risk taking, impulsivity, and brain development: implications for prevention. Developmental Psychology 2010. **52**(3): 263 – 276.

Sampassa-Kanyinga H, Hamilton HH, Chaput J-P Sleep duration and consumption of sugar-sweetened beverages and energy drinks among adolescents. Nutrition 2018 **48**: 77 – 81.

Sather TE, Woolsey CL, Williams Jr RD, Evans Jr MW, Cromartie F. Age of first use of energy beverages predicts future maximal consumption among naval pilot and flight officer candidates. Addictive Behaviors Reports 2016. **3**: 9 – 13.

Scientific Committee on Food (SCF)Opinion on caffeine, taurine and d-glucurono-g-lactone as constituents of so-called "energy" drinks, adopted on 21 January 1999. Minutes of the 115th meeting of the Scientific Committee on Food held on the 20th – 21st January 1999. European Commission DG Consumer Policy and Consumer Health Protection. Document XXIV/2146/99.

SCF Opinion of the Scientific Committee on Food on additional information on "energy drinks" (Expressed on 5 March 2003). SCF/CS/PLEN/ENDRINKS/16 Final.

Scalese M, Denoth F, Siciliano V, bastiani L, Cotochini R, Citilli A, Molinaro S. Energy drink and alcohol mixed energy drink use among high school adolescents: association with risk taking behaviour, social characteristics. Addictive Behaviors 2017. **72:**93 – 99**.**

Schwartz DL, Gilstad-Hayden K, Carroll-Scott A, Grilo SA, McCaslin C, Schwartz M Ickovics JR. Energy drink and youth self-reported hyperactivity/inattention symptoms. Acad. Pediatr. 2015 **15**(3):297 – 304.

Scott MJ, El-Hassan M, Khan AA. Myocardial infarction in a young adult following the consumption of a caffeinated energy drink. BMJ Case Reports 2011 Jun 30. doi: 10.1136/bcr.02.2011.385 .

Seidl R, Peyrl A, Nicham R, Hauser E. A taurine and caffeine-containing drink stimulates cognitive performance and well-being. Amino Acids 2000. **19**(3-4):635 – 642.

Seifert SM, Schaechter JL, Hershorin ER, Lipschulz SE. Health effects of energy drinks on children, adolescents, and young adults. Pediatrics 2011. **127**(3):511 – 528.

Seifert SM, Seifert SA, Schaechter JL, Bronstein AC, Benson BE, Hershorin ER, Arheart KL, Franco VI, Lipschulz SE. An analysis of energy drink toxicity in the National Poison Data System. Clinical Toxicology 2013 **51**: 566 – 574.

Shah SA, Occiano A, Nguyen TA, Chan A, Sky JC, Bahttachharyya M, O'Dell KM, Shek A, Nguyen NN. Electrocardiographic and blood pressure effects of energy drinks and *Panax ginseng* in healthy volunteers: a randomized clinical trial. International Journal of Cardiology **218**: 318 – 323.

Shi X, Xue W, Liang S, Zhao J, Zhang X. Acute caffeine ingestion reduces insulin sensitivity in healthy subjects: a systematic review and meta-analysis. Nutrition Journal 2016. **15**: 103 – 110.

Smith AR, Chein J, Steinberg L. Impact of socio-emotional context, brain development, and pubertal maturation on adolescent risk-taking. Hormones and Behavior 2013. **64**(2): 323 – 332.

Smith N, Atroch AL. Guarana's journey from regional tonic to aphrodisiac and global energy drink. Evidence-based complementary medicine 2007. **7**(3): 279 – 282.

Smitt HJ, Cotton JR, Hughes SC, Rodgers PJ. Mood and cognitive performance effects of "energy" drink constituents; caffeine, glucose and carbonation. Nutrition and Neuroscience 2004. **7**(3):127 – 139.

Smit HJ, Grady ML, Finnegan YE, Hughes S-AC, Cotton JR, Rogers PJ. Role of familiarity on effects of caffeine- and glucose-containing soft drinks. Psychology and Behavior. 2006. **87**: 287 – 297.

Solomin D, Borron SW, Watts SH. STEMI associated with overuse of energy drinks. Case Reports in Emergency Medicine 2015. **2015**: http://dx.doi.org/10.1155/2015/537689

Souza DB, Coso JD, Casonatto J, Polito MD. Acute effects of caffeine-containing energy drinks on physical performance: a systematic review and meta-analysis. European Journal of Nutrition **56**(1): 13 – 27.

Steinke l, Lanfear DE, Dhanapal V, Kalus JS. Effect of "energy drink" consumption on hemodynamic and electrocardiographic parameters in healthy young adults. The Annals of Pharmacotherapy 2009. **43**: 596 – 602.

Sillivent J, Blevins J, Peak K. Energy drinks: ergolytic or ergogenic? International Journal of Exercise Science 2012. **5**(3): 214 – 222.
Svatikova A, Covassin N, Somers KR. A randomized trial of cardiovascular responses to energy drink consumption in healthy adults. Journal of the American Medical Association 2015. **314** (19): 2079 – 2082.
Sved DW, Godsey JL, Ledyard SL, Mahoney AP, Stetson PL, Ho S, Myers NR, Resnis P, Renwick AG. Absorption, tissue distribution, metaboloism and elimination of taurine given orally to rats. Amino Acids "007 **32** 459 – 466.

Tamamato LC, Schmidt SJ, Lee S-Y. Sensory profile of a model energy drink with varying levels of functional ingredients – caffeine, ginseng, and taurine. Journal of Food Science 2010 **75**(6):S271 – S278.

Temple JL. Caffeine use in children: what we know, what we have left to learn, and why we should worry. Neuroscience and Behavioral Reviews 2009. **33**:793 – 806.

Temple JL, Dewey AM, Briatico LN. Effect of acute caffeine administration on adolescents. Experimental and Clinical Psychopharmacology 2010 **18(**6): 510 – 520.

Temple JL, Ziegler AM, Graczyk A, Bendlin A, Sion T, Vattana K. Cardiovascular responses to caffeine by gender and pubertal stage. Pediatrics 2014. **134**(1): e112 0 e119.

Temple JL, Ziegler AM, Epstein LH. Influence of price and labelling on energy drink purchasing in an experimental convenience store. Journal of Nutrition, "energy drink"ucation and Behavior 2016 **48**(3): 54 – 59.

Temple JL, Bernard C, Lipschultz SE, Czachor JD, Westphal JA, Mestre MA. The safety of ingested caffeine: a comprehensive review. Frontiers in Psychiatry 2017 **8**.doi: 10. 3389/fpsyt.2017.00080.

Terry-McElrath YM, O'Malley PM, Johnston LD. Energy drinks, soft drinks, and substance abuse among US secondary school students. Journal of Addiction Medicine 2014. **8**(1): 6 – 13.

Thong FSL, Graham TE. Caffeine-induced impairment of glucose tolerance is abolished by β-adrenergic receptor blockade in humans. Journal of Applied Physiology 2002. **92**: 2347 – 2352.

Thong FSL, Derave W, Kiens B, Graham TE, Ursø B, Wojtaszewski JFP, Hansen BF, Richter EA. Caffeine-induced impairment of insulin action but not insulin signalling in human skeletal muscle is reduced by exercise. Diabetes 2002. **51**: 583 – 590.

Turton P, Piché L, Battram DS. Adolescent attitudes and beliefs regarding caffeine and the consumption of caffeinated beverages. Journal of Nutrition, "energy drink"ucation and Behavior 2016 **48**(1): 181 – 189.

Usman A and Jawaid A. Hypertension in a young boy: an energy drink effect. Research Notes 2012 **5**:591- 593.

Utter J, Denny S, Teevale T, Sheridan J. Energy drink consumption among New Zealand adolescents: associations with mental health, health risk behaviours and body size. Journal of Paediatrics and Child Health 2018 **54**:279 – 283.

Van Batenburg-Eddes T, Lee NC, Weeda WD, Krabbendam L and Huizinga M. the potential adverse effect of energy drinks on executive functions in early adolescence. Frontiers in Psychology 2014 **5**:1 – 9.

Verser JC and Koenig J. Caffeine intake and its sources: a review of national representative studies. Critical reviews in Food Science and Nutrition 2018. **58**: 1250 – 1259.

Vieno A, canale N, Potente R, Scalese M, Griffiths MD, Molinaro S. The multiplicative effect of combining alcohol with energy drinks on adolescent gambling. Addictive Behaviors 2018 **82**: 7 – 13.

Visram S, Cheetham M, Riby DM, Crossley SJ, Lake A. Consumption of energy drinks by children and young people: a rapid review examining evidence of physical effects and consumer attitudes. BMJ Open 2016. **6**:e010380. Doi:10.1136/bmjopen-2015-010380.

Visram S, Crossley Sj, Cheetham M, Lake A. Children and young people's perceptions of energy drinks: a qualitative study. PLOS ONE 2017 **12**(11): e0188668. http://doi.org/10.1371/journal.pone.0188668.

Vivekanandarajah A, Ni S, Waked A. Acute hepatitis in a woman following excessive ingestion of an energy drink: a case report. Journal of Medical Case Reports 2011. **5**:227 – 229.

White JR Jr, Padowski JM, Zhong Y, Chen G, Luo S, Lazarus P, Layton ME, McPherson S. Pharmacokinetic analysis and comparison of caffeine administered rapidly or slowly in coffee chilled or hot versus chilled energy drink in healthy young adults. Clinical Toxicology 2016. **54**(4): 308 – 312.

Wiggins D, Reid J, White CM, Hammond D. Use and perceptions of caffeinated “energy drinks” and energy shots in Canada. American Journal of Preventive Medicine 2017 **53**(6): 866 – 871.

Williams RD Jr., Odum M, Housman KM. Adolescent energy drink use related to intake of fried and high-sugar foods. American Journal of Health and Behavior 2017. **41**(4): 454 – 460.

Wilson R, Kado HS, Samson R, Miller AB. A case of caffeine-induced coronary artery vasospasm in a 17-year-old male. Cardiovascular Toxicology 2012. **12**: 175 – 179.

Worthley MJ, Prabhu A, De Siscio P, Schultz C, Sanders P, Willoughby SR. Detrimental effects of energy drink consumption on platelet and endothelial function. The Australian Journal of Medicine 2010. **123**: 184 – 187.

Wu J-Y and Prentice H. Role of taurine in the central nervous system. Journal of Biomedical science 2010 **17(**Suppl.1)S1:

Zucconi S, Volpato C, Adinolfi F, Gandini E, Gentile E, Loi A, Fioriti L. Gathering consumption data on specific consumer groups of energy drinks. Supporting Punlications 2013:EN-394. www.efsa.europa.eu/publications

Literature search terms

Energy drinks AND adolescents AND toxicity
health
consumption
components
alcohol
drugs
behaviour

COMMITTEE ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PRODUCTS AND THE ENVIRONMENT

Scoping paper on the potential risks from energy drinks in the diet of children and adolescents.

Annex A

Caffeine and sugar content of "energy drinks", other s"oft" drinks and hot beverages

	Caffeine/ serving (mg)	Serving size (ml)	Caffeine/ Litre (mg/l)	Caffeine intake for children aged 10 /serving (mg/kg)	Caffeine intake for children aged 16 /serving (mg/kg)	Sugar/ serving (g)	Sugar/l (g/l)
Caffeinated soft drinks							
Cherry Coke	34	355	96	1.10	0.60	42	118
Cherry Coke Zero	34	355	96	1.10	0.60	0	0
Coca Cola Classic	34	355	96	1.10	0.60	37.6	106
Coca Cola Lite	28	355	79	0.90	0.49	17	48
Coca Cola Zero Sugar	34	355	96	1.10	0.60	0	0
Diet Cherry Coca Cola	34	355	96	1.10	0.60	0	0
Diet Coke	46	355	130	1.48	0.81	0	0
Diet Dr Pepper	41	355	115	1.32	0.72	0	0
Diet Pepsi (UK, AU, NZ)	43	355	121	1.39	0.75	0	0
Pepsi Max	43	355	121	1.39	0.75	0	0
Dr Pepper	41	355	115	1.32	0.72	41	115
Lucozade Energy	46	380	121	1.48	0.81	68	179
Energy drinks							
NOS	160	473	338	5.16	2.81	54	114
Monster	160	475	338	5.16	2.81	50	100
Monster Absolute Zero	140	473	296	4.52	2.46	0	0
"Red Bull" "energy drink"	80	250	320	2.58	1.40	27.5	110
"Red Bull" "energy drink" Sugar-free	80	250	320	2.58	1.40	0	0
"Red Bull" "energy drink" Total zero	80	250	320	2.58	1.40	0	0
Rockstar	160	473	338	5.16	2.81	60	127
Rockstar Zero Carb	240	473	507	7.74	4.21	0	0
V	109	355	307	3.52	1.91	37.1	105
Wicked	155	473	310	5.00	2.72	63.2	126
Relentless	160	473	338	5.16	2.81	50.5	107
Mountain Dew	54	355	152	1.74	0.95	46	130
Coffee							
Americano	154	355	434	4.97	2.70		

Baskin Robbins Cappachino Blast	234	710	330	7.55	4.11		
Caffe Mocha	152	355	428	4.90	2.67		
Café Nero	80	355	225	2.58	1.40		
Cappachino	154	355	434	4.97	2.70		
Brewed coffee	163	237	688	5.26	2.86		
Decaf brewed coffee	6	237	25	0.19	0.11		
Instant coffee	57	237	241	1.84	1.00		
Instant decaf coffee	3	237	13	0.10	0.05		
Espresso	77	44	1750	2.48	1.35		
Costa	277	450	616	8.94	4.86		
Maxwell House	117	237	494	3.77	2.05		
McDonalds	145	473	307	4.68	2.54		
Starbucks Grande	330	473	698	10.65	5.79		
Starbucks Bottled iced	70	325	215	2.26	1.23		
Tea							
Chai	50	237	211	1.61	0.88		
Lipton iced tea	48	592	81	1.55	0.84		
Black	42	237	177	1.35	0.74		
Decaf	5	237	21	0.16	0.09		
Green	25	237	105	0.81	0.44		
Iced	47	237	198	1.52	0.82		
Instant	40	237	169	1.29	0.70		
Jasmine	25	237	105	0.81	0.44		
Oolong	37	237	156	1.19	0.65		
White	28	237	118	0.90	0.49		
Non-caffeinated soft drinks							
Vimto		330				32.3	98
Sprite		330				23.4	71
Lucozade		330				13.5	41
Bottle Green		330				25	76
Fanta		330				24.4	74
7 Up		330				37.6	114
Irn Bru		330				37.6	114

Values calculated from data on https://www.caffeineinformer.com/