Committee on TOXICITY

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

Statement 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 at high levels, 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, but this does not necessarily describe their effects. Energy derived by the consumer is from their carbohydrate content. Any energy obtained from the presence of caffeine and other possible stimulants is equivocal at best, despite what is implied by their marketing. However, sugar-free varieties of these drinks are also available, and the term is used here 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" showed 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, to pass the £2 billion mark. https://store.mintel.com/uk-sports-and-energy-drinks-market-report

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[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/

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

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, to carry 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 Drinks 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 of “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 consumption data for 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 one “energy drink” in the previous year and 28% had drunk one in the previous 3 days. Seventy-five percent of the 15-18-year age group and 55% of the 10-14-year 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 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 the major food retailers in the UK and most recently by Boots.

12 In August 2018, HM Government produced a consultation document and impact assessment for stakeholders on banning the sale of “energy drinks” to young people. The consultation document asked 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 documented 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 outlined the costs and the health and monetary benefits.
https://www.gov.uk/government/consultations/ending-the-sale-of-energy-drinks-to-children
The National Association of Schoolmasters Union of Women Teachers (NASUWT) praised this proposal
https://www.nasuwt.org.uk/article-listing/ban-on-energy-drink-sales-to-under-16s-welcomed.html

13 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”

14 An internet search revealed 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 fluid ounce (fl. oz). serving (237 ml), in addition to non-sugar sweeteners, and the regular varieties contain from 13 to 33 g of sugar per 8 fl. oz. serving, some of which also contain non-sugar sweeteners.
http://www.sugarydrinkfacts.org/resources/nutrition/Energy-Drink-Tables.pdf

15 The regular drinks above would all exceed the 5 g/100 ml legal limit for added sugar described in paragraph 13 and thus would either be subject to the new tax or have to be reformulated.

16 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 g/100 ml in 2015 to 9.5 g/100 ml in 2017) but caffeine content and serving sizes remained high (31 mg/100 ml and up to 500 ml, respectively),

17 Leiper (2015) reviewed the factors influencing gastric emptying and the intestinal absorption of beverages in humans. Gastric emptying showed a negative exponential relationship with volume, and emptying rate was inversely proportional to the energy density of a solute. Isoenergetic amounts of carbohydrates, proteins and fats appeared to be delivered to the duodenum at approximately the same rate. Initial changes in temperature affected 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.

18 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

19 Olateju *et al* (2015) studied the effects of consuming 750 ml of “Red Bull” “energy drink” (28 g carbohydrate, 80 mg caffeine/250 ml), “Red Bull” “energy drink” light (carbohydrate free, 80 mg caffeine/ 250 ml) or a non-caffeinated sugary control drink (21 g carbohydrate/ 250 ml, adjusted to equal carbohydrate concentration, although it is not clear how this was achieved). Effects on blood glucose and caffeine, heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), mood and cognition were determined. The subjects in this study were 16 adults, aged >18 years, with type 1 diabetes, 11 of whom were female. Both of the sugary drinks raised blood glucose within 30 min of consumption. After 3 hours the blood glucose concentration remained significantly elevated in the “energy drink” group relative to the control group In No effects were found of any of the drinks on mood or cognition.

20 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. No mention is made of whether other sources of sugar intake were assessed in the literature retreived. 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

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

22 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 this difference in

taste from other soft drinks made “energy drinks” attractive and “grown up” things to consume.

23 The caffeine content of “energy drinks”, while greater than in other caffeinated soft drinks, can be lower than that found in proprietary servings of coffee available from high street vendors (Appendix A).

24 The absorption of an oral dose of caffeine varies depending upon the rate of gastric emptying, with the plasma T_{max} (the time of maximal plasma concentration) ranging from 15 to 120 minutes. The volume of distribution is about 0.7 l/kg, corresponding to total body water. Elimination is by first-order kinetics, although the process is saturable at high but achievable concentrations. Caffeine is initially metabolised, mainly by hepatic CYP1A2, primarily by demethylation to paraxanthine, theobromine, and theophylline, which are also pharmacologically active substances (Arnaud 1985)

25 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 (Fredholm 1995, review by Temple 2009). Other effects of caffeine such as cyclic AMP phosphodiesterase inhibition and effects on calcium levels begin to be seen only at doses where toxicity becomes evident (McLellan *et al*, 2016), although lower 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).

26 Single doses of caffeine estimated to be of no concern for adults (3 mg/kg bw) should also apply to children, since caffeine clearance in children and adolescents is at least as great as that of adults, and 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 in 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).

27 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). The dose of caffeine that leads to significant acute diuresis is in the order of 300 mg, or about 4–5 cups of regular coffee. Caffeine-induced diuresis appears to be modulated by increasing age and by habituation, both of which decrease the diuretic effect.

28 Most cases of caffeine intoxication are characterised by nervousness, irritability, anxiety, and insomnia and, at higher doses, tremor, tachycardia, palpitations and gastrointestinal upset. Reported adverse effects at extreme doses 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).

29 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 caused a dose-dependent fall in heart rate ($p = 0.001$) and increase in diastolic blood pressure ($p = 0.0001$). Individuals habitually consuming > 50 mg caffeine/day were more disposed to eat high fat, high sugar or high-fat-and-sugar foods compared with consumers of < 50 mg caffeine/day. 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.

30 Temple *et al* (2014) investigated the effects of caffeine at doses of 1 and 2 mg/kg bw on heart rate and blood pressure in groups of approx. 25 pre- and post-pubertal children (8 – 9 and 15 – 17-year-olds respectively). The effects of the two doses were similar. 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 CYP metabolism of the caffeine but noted that changes in background patterns of caffeine intake could have affected the findings and thus oestradiol, whatever its involvement, was unlikely to be the sole cause of the effect observed. However, HR was significantly decreased and the increase in SBP by caffeine was significantly reduced in the luteal phase of the menstrual cycle compared with the follicular phase, suggesting some hormonal involvement in these effects.

31 Monnard *et al* (2016) also found a gender difference in the response to “energy drink” (“Red Bull” or water) in groups of 22-23 years old, 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. Data for the negative control were reported in earlier papers. The authors suggested that their finding might have clinical relevance since neurocardiogenic syncope is more prevalent in women than in men and reduction in CVBV may increase the chances of such an event.

32 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 CYP1A2 or the genetic variant PDSS2 show a prolongation of the pharmacological and toxicological effects of caffeine (Pirastu *et al,* 2016).

33 The pharmacokinetics of caffeine (at least in young adults aged 18 – 30 years) do not appear to vary significantly with the characteristics of consumption: there were no significant differences in the time to maximum plasma concentration (T_{max}), area under the curve (AUC), mean absorption time or mean residence time between groups drinking chilled (4°C) “Red Bull” “energy drink” over 2 minutes or 20 minutes, chilled coffee over 2 minutes or 20 minutes or hot (85°C) coffee. (White *et al* 2016). The results of 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.

34 Repeated intake of caffeine leads to a diminution of its cardiovascular effects. Robertson *et al* (1981) found that a daily dose of 250 mg caffeine significantly raised systolic and diastolic blood pressure, relative to a placebo, within 2 hours of ingestion on the first day of dosing, but this effect was no longer evident by day 7 of dosing. The same was true of the effects of caffeine on plasma and urinary adrenaline, noradrenaline and plasma renin levels. There was no significant effect of caffeine on heart rate in this study.

35 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.

36 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 from “energy drinks”, was increasing, with unknown consequences for health and development.

37 Caffeine in combination with glucose has been reported 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 involving effects on central nervous system neurotransmitters that could account for possible interactions, but further work would be needed to confirm their involvement (Boyle *et al* 2018).

38 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 preparations increased blood pressure. The “Red Bull” “energy drink” containing sugar increased heart rate, stroke volume, cardiac output and diastolic blood 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 did not 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.

39 The difference in the effects reported on heart rate may reflect the decline in the sensitivity of baroreceptors in the aortic arch. In young people, the baroreceptors are sufficiently sensitive to cause a rebound decrease in heart rate in response to the caffeine-induced increase in diastolic blood pressure. The sensitivity of the baroreceptors decreases with age and although there is inter-individual variation, this may explain the absence of a caffeine-related effect or increase in heart rate in older age groups.(Pfeiffer *et al* 1983)

40 Coffee has been reported to be associated with a protective effect against type 2 diabetes (Bhupathiraju *et al,* 2017, Sanjtos and Lima, 2016), although the strength of this relationship has been questioned (Nordestgaard *et al*.2016, Kwok *et al* 2016) A meta-analysis (Shi *et al* 2016) 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 caffeine itself. However, in some studies decaffeinated coffee was 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

41 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.

Other components

42 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 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 L-carnosine, inositol, extracts from guarana (a tropical shrub, the berries of which contain caffeine, theophylline and theobromine), ginseng, ginkgo biloba, or a mixture of these and other minor components.

43 Few studies are available that have investigated the effects of the minor components of “energy drinks”. 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 is a constituent of bile. It is sometimes described as an amino acid (although, more properly, it is an amino sulfonic acid).

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 found 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, 2017a). Taurine appears to protect neurones against glutamate-induced excitotoxicity (Wu and Prentice, 2009).

45 Studies in rats suggest that ingested taurine has little effect on its levels in the brain, but it rapidly equilibrates with endogenous body pools and any excess is rapidly eliminated by the kidneys (Sved *et al*, 2007).

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

47 Some studies have suggested an influence of taurine on the effects of “energy drinks” on GABAergic neurotransmission (Calabro *et al* 2012) and in attenuating the effects of caffeine (Peacock *et al* 2013), but others have found no evidence of such interactions (Miles-Chan *et al* 2015; Reisenhuber e*t al* 2006; Giles *et al* 2012).

D-glucurono-γ-lactone

48 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 a number of non-human species, 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 this compound for humans (EFSA, 2009).

Ginseng

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

Guarana

50 Guarana seeds contain 2 – 7.5% caffeine, with traces of theophylline and theobromine and extracts are present in some “energy drinks” but in too small amounts to exert effects beyond those of the caffeine and sugar ingredients (Smith and Atroch 2007.

B vitamins

51 Huang *et al* (2014) suggested that niacin (vitamin B3, nicotinamide) in an “energy drink” contributes to hepatic damage but it has been argued that this finding was confounded by subjects’ alcohol consumption, obesity (Robin *et al* (2018) and the presence of high levels of fructose (from the sucrose in the “energy drink”).

Reasons for, and patterns of, “energy drink” consumption

52 Several papers report results of surveys of 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, to enable direct comparison: 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.

53 Smit *et al* (2006) found that, although not of high caffeine content, “Lucozade Energy” brand drink (caffeine 121 mg/l, sugar 179 g/l) and a non-caffeine/non-glucose matched placebo 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 the drink due to its taste may have an influence on its perceived effects.

54 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, 6.2% of boys and 0.6% of girls of 11 years of age were in the highest “at least one “energy drink” a week” category. Weekly consumption of “energy drinks” increased with age, reaching 16.5% in 13-year-old boys and 8.6% in girls of this age. Consumption of “energy drinks” was also significantly associated with smoking ($p = 0.015$) and drinking alcohol ($p = 0.009$)

55 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 readily available, sometimes from parents, consumed for sport or to increase wakefulness. Taste was a positive factor, as were peer pressure and advertising. Adverse effects were also recognised and put some students off continued consumption.

56 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. However, overall, 69.5% of the “energy drink” consumers stated that they drank no more than 1 serving of drink per session and 24% stated that they drank no more than 2. Only 13 students out of 224 consumers stated that they drank more than this.

57 McCrory *et al* (2017) asked 41 young Canadian people aged 12 – 18 years about 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, in general “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.

58 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 in use, 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 influences on use, 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.

59 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 ($p = 0.007$).

60 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” included 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 were necessary. No

single dominant factor was identified as determining the consumption of “energy drinks” by young teenagers.

61 Reid *et al* (2017) polled young Canadians aged 12 – 17 years on their use of “energy drinks”. A total of 1103 adolescents took part in the study. Fifty seven per cent 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%) (contrast with para 60). Major reasons for consumption were curiosity/novelty (33 and 42%), taste (26 and 26%) and because friends drank them (23 and 28%). Three per cent and 16% respectively drank “energy drinks” in conjunction with alcohol.

62 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% were current users. Twenty-eight percent of users felt that the drinks posed a severe health threat, while 54% did not ($p < 0.05$). Thirty-six percent reported being exposed to “energy drink” advertising while 33% did not.

63 Kumar *et al* (2015) polled 779 adolescents in the US, 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. “Energy drink” consumption was positively correlated with these beliefs.

64 Aluqmany et al (2013) found that in a group of 600 female secondary school students in Saudi Arabia, 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 decide to stop drinking “energy drinks” only if they suffered side effects, while 8% declared they would stop if sales were restricted.

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)
EU countries	7		38	40		15	Zucconi *et al* (2013)
Bahrain	6.1	4.4	43.3	40	1.7	4.5	Nassaif *et al* 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	13	3	44	33	3	4	Faris (2013)
Pakistan (adults)	10	15	25	9	11	22	Usman *et al* (2015)

Effects on behaviour

65 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 ($p = 0.26$). This study, although reasonably large, was cross-sectional and self-reported.

66 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 normally. 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.

67 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.

68 A US Institute of Medicine and national Research Council joint workshop on adolescent risk-taking found that risk behaviour is a part of normal development and has a wide range of influences, including brain maturation, socioeconomic status and family situation. The report noted that the thought processes of adolescents and their evaluation of risk are different from those of adults.
https://www.ncbi.nlm.nih.gov/books/NBK53418/

69 Such findings add further complexity to the debate on how “energy drink” consumption may influence or be influenced by naturally occurring developmental processes.

Effects on sleep

70 Concerto *et al* (2017) polled a group of 70 Italian psychiatry residents (46 female, 24 male, aged 25 – 40 years) on their use of cigarettes, and caffeinated hot drinks, soft drinks 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. It was noted that the main source of caffeine consumption in this population was coffee. The authors recognised that the study was cross-sectional and the result might reflect the coffee-drinking culture of Southern Italy.

71 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 use of cigarettes and alcohol. The authors recognised that a longitudinal study would better allow the determination of any relationship between stimulant use and sleep quality.

72 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 years, 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.

73 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.

74 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

75 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 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.

76 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) students, $p<0.001$. 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, was self-reported and thus subject to personal bias, missed out the 8% of students in private or alternative schools and was without parental supervision, leading to possible non-

responders, and did not control for confounding factors such as abuse of other substances.

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

78 The current use of portable and other electronic devices (mobile phones, tablets, televisions and laptops) by children and adolescents may, to some extent be confounding attempts to ascribe poor school behaviour and daytime fatigue entirely to the consumption of "energy drinks". It is notable that there is an association between "energy drink" consumption and some of these activities. Lissak (2018) reviewed the reported adverse effects of "screen time" on young people. Sedentary behaviour, exposure to violent, fast-paced games and late-night exposure to the light from screens have all been reported to affect the health, psychological health and sleeping time of children and adolescents, even in the absence of "energy drink" consumption.

Adverse effects of "energy drinks".

79 A number of reviews were picked up in the PubMed search that covered the effects of "energy drinks" on the health of 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).

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

81 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.

82 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, of reports for "energy drinks" 15.2% were for moderate – major adverse effects (0.9% were major, n=7) compared with 39.3% of such reports 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 declined to 20 or fewer/month. Around half of the reported cases involved unintentional exposures by children < 6 years old.

83 In 2016/17, operatives at the services NHS111 (in England and Wales), NHS 24 (in Scotland) and NHS Direct (online) accessed the UK National Poisons Information Service (NPIS) TOXbase information page on caffeine 2116 times. Primary care centres accessed the same page 515 times.

84 A total of 855 exposures to “energy drinks” associated with adverse effects were reported to poison centres in Texas from 2010 – 2014, 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, the incidences of moderate and major adverse outcomes were 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 (Borron *et al,* 2018).

85 Kristjansson *et al* (2014) found a dose-response relationship between the prevalence of headaches, stomach aches, sleeping problems and low appetite and “energy drink” consumption in Icelandic children aged 10 – 12 years (none – <1 per day – 1+ per day). 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.

86 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 hyperactivity / inattention at school ($p< 0.006$). 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.

87 Park *et al* (2016) studied the effects of “energy drinks” on sleep, stress and suicidality in 68,043 Korean adolescents (aged 12 – 18 years). Sleep dissatisfaction, depressive mood, and with thinking of, planning and attempting suicide were significantly positively associated, in a dose related manner, with “energy drink”

consumption. Consumption of “junk food” (i.e. processed food high in sugar and/or fat) also correlated with “energy drink” consumption, which appeared to exacerbate the adverse effects arising from it. It was not possible to attribute causation to specific factors in this study.

88 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 were no longer apparent. 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.

89 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 determined, and the input relied on self-assessment.

90 Bashir *et al* (2016) reported on data in the US from 612 questionnaires completed by adolescents aged 12 to 18 years regarding consumption of “energy drinks” and subsequent subjective experiences. Frequent energy drink consumers were more likely to report experiencing 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.

91 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 in Canada. 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. The difference between the two groups was statistically significant (3.1% v 1.4%, OR 2.18 [95% CI 1.39–3.41]).

92 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.

Cardiovascular effects

93 A small number of recent case studies in adolescents have implied the involvement of "energy drink" consumption in their aetiology.

94 Cases have involved increased blood pressure (Usain and Jawaid, 2012) tachycardia (Di Rocco *et al*, 2013), dissection of the left descending coronary artery, cerebral vasoconstriction (Samanta 2015) and ECG ST segment elevation (Wilson *et al*, 2012). Following the appropriate symptomatic treatment, all of the subjects made a full recovery. All of these adverse events were reported subsequent to consumption of one or more "energy drinks" and, in the absence of medical history, the involvement of the drinks was inferred from the symptoms.

95 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.

96 The adults in these cases suffered myocardial infarction (Scott *et al,* 2011, Gharacholou *et al*, 2016, Solomin *et al,* 2015) ventricular tachycardia followed 3 days later by sudden cardiac arrest (Avci *et al,* 2013) and cerebral aneurysm with severe, catheter-induced vasospasm (Grant *et* al, 2016). In most cases there appeared to be no factors that confounded a diagnosis of the adverse events being attributable to acute or chronic excess consumption of "energy drinks", although it was not possible to establish causation unequivocally.

97 Studies have been conducted on healthy volunteers to observe the cardiovascular effects of "energy drink" consumption in the absence of disease states or excessive consumption: Hajsadeghi *et al* (2016), Steinke *et al* (2009), Kurtz *et al* (2013), Svatikova *et al* (2015), Grasser *et al* (2015), Sullivent *et al* (2012), Pommerening *et al* (2015), Nowak *et al* (2018), Molnar and Somberg (2014). Overall, the findings were mixed, with heart rate decreasing, increasing or unaffected, systolic blood pressure unaffected in some cases but mostly increasing, diastolic blood pressure likewise unaffected in some cases but mostly increasing. Effects on ECG parameters were observed in one study but not in another.

98 Detrimental effects of “energy drink” consumption on endothelial function were seen in one study (Worthley *et al* (2010), whereas Molnar and Somberg (2014) reported functional improvement.

99 The conclusions reached in these studies were largely that “energy drink” consumption should preferably be avoided by people with underlying cardiovascular problems.

Consumption of “energy drinks” relative to other substances

100 Several reports deal with co-consumption of “energy drinks” with other psychoactive substances, notably alcohol. A number of these reports consider the influence of this mixed consumption on “risky” behaviours such as drink driving and unsafe sex.

101 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.

102 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. The authors suggest that energy drink consumption is a risk marker for other substance consumption in this age group. Consumption of alcohol by the same age group did not appear to correlate with changes in later levels of alcohol consumption.

103 Kponee *et al* (2014) found in a survey of adolescents from Boston, Mass, USA that those who consumed “caffeinate alcoholic beverages”, 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 totalled 15.4%.

104 Scalese *et al* (2017) found that while mixing “energy drinks” with alcohol increased the probability of Italian adolescents in indulging in a wide range of risky behaviours such as binge drinking, cannabis and other drug use, unsafe sex, and fighting, the differences between the use of “energy drinks” alone and alcohol-plus-“energy drinks” 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.

105 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. Forty three percent 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.

106 ”Energy drink” 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.)

107 Williams *et aI* (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).

Reported beneficial effects of “energy drinks”

108 Consumption of “energy drinks” has been reported to maintain feelings of well-being, vitality and social extraversion for longer than seen with a placebo control (Seidl *et al*, 2000), increase significantly (p < 0.05) aerobic endurance and performance of subjects on cycle ergometers (Alford *et al*, 2001) and increase VO_2 (p<0.05) and time to exhaustion (p<0,05) relative to placebo, without significant differences in pre- and post-test heart rate or blood lactate, in treadmill tests (Rahnama *et al*, 2010).

109 Abian-Vicen *et al* (2014) found a small but significant (p < 0.05) increase in jump height but not in shooting precision in adolescent basketball players 60 minutes after ingestion of an” energy drink” and Prins *et al* (2014) found a small but significant (p = 0.016) improvement in running performance in a group of 18 late teens and early adults after consumption of an “energy drink”. Subjects’ rating of perceived exertion and mood were not altered by the “energy drink”. Smit *et al* (2004) found that “energy drinks” maintained arousal compared with a sensory-matched placebo and that caffeine “withdrawal reversal” was mainly responsible for this effect, with a very minor contribution from the carbohydrate content of the drink. The effect of carbonation on mood was variable but in some cases was consistent with reducing the uptake of caffeine and / or carbohydrates.

110 Souza *et al* (2017) reviewed the effects of a range of doses of caffeine (40 – 325 mg) and taurine (71 – 3105 mg) on jumping, muscle strength and endurance,

sport-specific actions and sprinting over 34 studies. Some studies showed no effect on the parameter measured, but across the meta-analysis there was a significant ($p<0.001$) improvement in all parameters except 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.

111 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 within sprints and at the end of the trial, with increased heart rate and blood lactate concentration. The athletes’ perception of their level of exertion was unaffected.

Expert opinions

EFSA Caffeine

112 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.*”

113 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 0.5 l 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.”*

114 EFSA (2011) collated the daily consumption data for 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. Forty-one per cent of adolescent “energy drink” consumers drank them in relation to sport.

115 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

116 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

117 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.”*

118 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.

119 EFSA (2015) stated that 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

120 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.

121 It was considered unlikely that D-glucurono-γ-lactone at the levels present in “energy drinks” would interact with caffeine, taurine, alcohol or physical exercise.

COT

122 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 substances 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

123 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, of those who were initially approached, had never consumed 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

124 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.

125 “Energy drinks” contain variable, but high, 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 or even lower than that in a serving of coffee from a high-street vendor, depending upon the make of each beverage.

126 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 and other diet-related diseases. New legislation may reduce the level of sugar in soft drinks and “energy drinks” alike.

127 The effects of caffeine consumption can be modified by dose, genetics, tolerance, withdrawal symptoms, expectations and social situations. The toxicological effects of caffeine include increased blood pressure, changes in heart rate, nervousness, irritability, anxiety, and insomnia and, at higher doses, tremor, tachycardia, palpitations and gastrointestinal upset.

128 Negative health-related effects are seen in both adolescents and adults and largely occur following ingestion of large quantities of “energy drinks”. They include poor sleep, reduced performance and acute physical effects, which are probably related to excess caffeine consumption.

129 It is not currently possible to determine whether adolescents are more susceptible than adults to the effects of excess caffeine consumption and hence an age before which to apply a restriction of sales of “energy drinks” on safety grounds is difficult to ascribe. However, even modest amounts of caffeine seem to exert measurable effects on heart rate and ECG parameters, although the changes that have been seen are not entirely consistent with each other. There may be a risk to health of people with underlying cardiovascular conditions

130 The constituents of “energy drinks” other than caffeine, including taurine have not been shown consistently to modify the effects of the caffeine or sugar in the drinks

131 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”.

132 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.

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

134 Use of “energy drinks” has been associated with a number of adverse effects in children and adolescents. However, modern social factors such as late-night use of electronic devices such as mobile phones and tablets also seem to bear some responsibility for adolescent “problematic” behaviour and sleep disruption.

135 “Energy drinks” are also consumed mixed with alcohol, which has been associated with the exacerbation of “risky” behaviours. However, most of the studies are cross-sectional or small-group longitudinal and any effects of “energy drinks” on adolescent behaviour overlie the already-documented behaviour patterns of this age group, arising from biological and social development. . Further studies would be necessary to determine how “energy drink” consumption affects or is affected by this background and hence the level of caffeine that would be of no concern in this age group.

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

137 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 constituents of “energy drinks”, caffeine and sugar, are well documented,

while those of other ingredients are either negligible or equivocal. 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. Other confounding factors may contribute to the behaviour that has been attributed to “energy drink” use.

COT Statement 2019/01

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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 “soft” 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

Baskin Robbins Cappachino Blast	234	710	330	7.55	4.11		
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		
Costa Flat white	277	450	616	8.94	4.86		
McDonalds	145	473	307	4.68	2.54		
Starbucks Caffe Latte Short	75	236	318	2.41	1.32		
Starbucks Caffe Latte Grande	150	472	317	4.84	2.68		
Caffe Nero Regular Americano	80	354	225	2.58	1.40		

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/