DrugWatch Information Sheet
Caffeine & Energy Drinks

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Drug overview: Caffeine occurs naturally in plants such as tea, coffee and cocoa, and has been used for many years as a 'pep pill' and in exercise and diet supplements. It is also used as a bulking agent for both legal and illegal stimulant drugs, is an additive in make-up, soap, shampoo and shower gels, and there are even caffeinated tights. With the arrival of energy drinks however, increased caffeine consumption and associated risks and harms have been more prevalent, especially among adolescents.

Fig. 1 Coffee Arabica

Chemical name: Caffeine (1,3,7-trimethylxanthine).

Classification: Stimulant, methylxanthine, naturally occurring xanthine alkaloid.

Background: Caffeine was first isolated in 1820[1]; it is probably one of the most widely used drugs in the world and for many people is used safely. It is generally considered a functional drug because it can improve mood and alertness at low doses, and cups of tea or coffee help to focus attention and increase productivity[2]. However at high doses it can lead to withdrawal effects and even death (see Toxicity section below).

Fig. 3 One 160ml can of Monster contains 160mg of caffeine, more than 1½ times the recommended daily limit for adolescents.

Energy drinks: There is no widely agreed definition of energy drinks but they are generally recognised as higher-content caffeine drinks or supplements marketed as a mental and/or physical stimulator, containing legal stimulant drugs and other substances, sometimes herbal such as taurine, guarana, glucose and B vitamins[3-5]. Energy drinks first appeared in Europe in the 1960s but were not widely used until Red Bull appeared on the market in 1987[7]. By 2006 there were over 500 brands of energy drinks around the world[33] and their use has increased since then[8-11]. The British Soft Drinks Association reported that energy drink consumption in the UK has grown from 270 million litres in 2007 to 500 million litres in 2013[12].

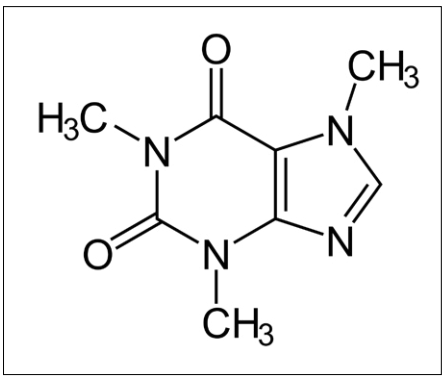

Fig.2 Caffeine's chemical structure

Cost:

Caffeine powder (prices quoted from online sources as of May 2015)			
100g	500g	1kg	20kg
£4	£15	£30	£340

Route of administration: Caffeine is usually consumed as a liquid. It can also be administered in pill or powder form but this can be more dangerous, as a greater amount can be taken at one time. There are user reports of nasal administration (sniffing) however this can be painful and is generally not recommended as an effective route of administration[13, 14]. IV use has been reported[15] however due to serious risks of harm this route of administration is not advised. Rectal administration (often in the form of enemas) has also been practiced.

Fig. 4 A shot of espresso can contain as much caffeine as an energy drink.

Dosage: NHS guidelines on caffeine dosages and intake are unclear. Health Canada find that for the general population of healthy adults caffeine does not have adverse effects if intake is limited to 400mg per day[16]. It has been recommended that children under 16 limit their daily consumption of caffeine to 2.5mg/kg body weight[17] and adolescents to limit consumption to 100mg per day[18].

Oral doses for adults[16, 17, 19, 20]					
Threshold/low dose[19]	Common dose	Strong dose	Very strong	Risk of toxicity[5, 21]	Risk of fatality[22]
10-20mg	50-150mg	150-400mg	400+mg	1000mg or more than 10mg/kg (4mg/kg in children)	More than 3000mg

Caffeine content estimations in popular foods and drinks[11, 23-25]

50g bar milk chocolate	50g bar of plain chocolate	Can of cola	Mug of tea	Mug of instant coffee	Shot of espresso	Energy drink	Energy shots
25mg	50mg	40mg	75mg	100-140mg	Can range from 50-320mg	Can range from 50 to 505mg	Can contain 200+ mg

Onset and duration: Caffeine is rapidly absorbed after ingestion, and provides an initial burst of energy which lasts approximately 30-40 minutes. The half life is up to 24 hours and active metabolites may also contribute to toxicity[2, 26]; in addition absorption and peak blood levels are delayed in overdosage. If stopping caffeine after continued use, symptoms of withdrawal may peak 1-2 days after cessation of intake and may persist for a week[27, 28].

Fig. 5 Caffeine powder

Coming up[14]	Duration	Coming down	Halflife
15-45 mins	1.5-5 hours	2-3 hours	Up to 24 hours

Brain chemistry: Caffeine inhibits the inhibitory effects of adenosine on dopamine, thereby increasing the psychoactivity of dopaminergenic systems and regulating the release of neurotransmitters such as glutamate and acetylcholine[29-31]. Unlike stronger dopaminergenic drugs such as amphetamine, caffeine does not produce reinforcing effects of "liking" and "wanting more", and so is generally not associated with strong cravings or urges to re-dose[32].

Effects: [2, 5, 6, 16, 33-41]

Desired effects	Negative/unwanted effects
Promote wakefulness and alertness	Tiredness
Improve focus	Headache
Increase energy	Agitation, insomnia, inability to focus
Increase confidence and mood	Tremor, palpitations
Quench thirst	Dehydration
Lose weight (stimulant/diuretic)	Reduced energy from diuretic effect
Increase athletic performance and endurance	Muscle stiffness and aches
Improve working memory	Increased heart rate and blood pressure
Increase reaction times	Chest pain, heartburn and dysrhythmias
Improve driving ability	Vomiting, nausea and abdominal pain
Enhance the experience of alcohol intoxication	Reduced reaction time
	Seizures, coma and death

Fig. 6 Caffeine 'pep' pills

Patterns of use: Since non-problematic caffeine use is so widespread, viewing it within the same framework as drugs such as alcohol or cocaine poses challenges, however the DSM-5 introduced new provisions for caffeine-related disorders[42]. Tolerance of its effects and withdrawal symptoms have also been described, with withdrawal effects including fatigue, insomnia, muscle aches, headaches, irritability and low mood[9, 26, 32].

Caffeine and young people: Children and adolescents have been reported as the fastest growing population of caffeine users with an increase in use of 70% in the past 30 years[43]. One study of 228 parents found that their 5-7 year old children drank approximately 52mg of caffeine daily and their 8-12 year old children drank 109mg daily[44], and others finding that an estimated 75-98% of children consume at least one caffeinated beverage daily[45, 46].

In 2012 an EU-wide survey on energy drinks was carried out involving more than 52,000 participants from 16 different EU Member States[7]. It found that the highest prevalence of consumption (68%) was for adolescents (aged 10-18) who also consumed more energy drinks mixed with alcohol, with prevalence of consumption around 53%.

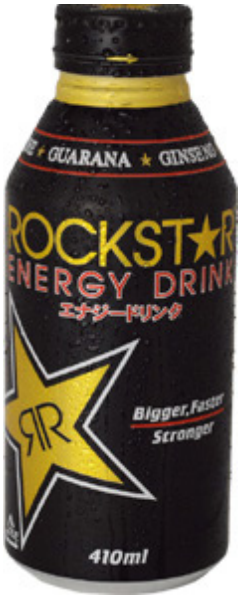

Fig. 7
Energy drinks are a global phenomenon

In October 2014 a report from the World Health Organisation highlighted concerns that energy drinks are aggressively marketed to young and inexperienced consumers[11] and surmised that "the risks of heavy consumption of energy drinks among young people have largely gone unaddressed and are poised to become a significant public health problem in the future"[47].

Mixing with alcohol: Many people assume that caffeine counteracts the sedative or depressant qualities of alcohol[48,49] and this is supported by some research[49-50]. Other studies challenge this and report no evidence of energy drinks countering alcohol's effects[51-53], however they find that as energy drinks might reduce some of the *sensations* of being drunk, this reduced sense of drunkenness can result in longer drinking sessions[11, 48, 54, 55]. One review of the evidence completed in 2012 suggests that while energy drinks may antagonise some aspects of alcohol-induced performance it is the alcohol, not the mixer that is leading to changes in behaviour[56].

Co-ingestion of caffeine and alcohol has been associated with increased risk-taking behaviours in teenagers and young people, such as increased number of sexual partners, binge drinking, unintentional injuries and riding with a driver who had been drinking alcohol[24, 57-59]. A contrasting view is that this is due to people with higher risk-taking personalities being attracted to drinks that mix alcohol with caffeine, although the authors of this study have received research funding from, among others, Red Bull GmbH[56].

Mixing with other drugs: Caffeine has been found as a bulking agent in street drugs such as amphetamine, cocaine and ecstasy[60, 112] and in a wide range of new psychoactive substances (NPS). One study tested seven branded NPS stimulants, none of which declared on the packet to contain caffeine. After testing all seven were found to containe amounts of caffeine ranging from approximately 20-96% (0.2-0.96g)[61] thereby placing individuals at risk of "significant caffeine toxicity". Caffeine can have a profound influence on psychostimulants such as cocaine and amphetamine[62], and these combinations have lead to death in rats when compared with administration of cocaine and amphetamine alone. In lower doses hyperthermia, increased seizures and serotonin loss have been observed[63]. Caffeine is also sold in tandem with stimulants such as ephedrine for weight loss, and some over the counter and prescription cough and asthma medications containing caffeine, ephedrine and theophylline have been used by bodybuilders as a performance aid[60, 65]. Toxicity and death are possible with these combinations[21, 66-69], and studies find that while some weight loss supplements may produce modest short-term results, they are most likely to produce adverse effects[68,69].

Toxicity: Caffeine toxicity is well recognised[2, 40, 71, 72] and although rare, if caffeine is consumed in large doses it can result in death[22, 73, 74]. One study reports the fatal overdose of a 39-year old man after ingesting approximately 12g of pure caffeine anhydrous[75]. Another identified five cases of fatal overdose from non-prescription drugs sold as appetite suppressants or stimulants; three of these cases had taken caffeine/ephedrine combinations and two had taken caffeine only[76]. Data collected over seven years from the Australian Poisons Information Centre found 21 subjects displaying signs of serious cardiac or neurological toxicity related to caffeine including hallucinations, seizures, arrhythmias or coronary heart disease[77].

Young people might be at more risk of harm from energy drinks mixed with alcohol. One article from 2010 discusses the case of a 17-year old boy who suffered acute kidney failure after consuming 3L of energy drink in combination with 1L of vodka[78]. Red Bull was implicated in the deaths of three young people in Sweden: two died after mixing it with vodka while out with friends and the third person died after drinking Red Bull after a strenuous gym workout[79]. The energy drink was not however found to be the cause of these deaths, and a spokesperson was reported to have said that the story was "not based on facts, and has been fuelled by speculation"[113].

Caffeine and mental health: In higher doses caffeine has been shown to exacerbate psychotic symptoms in some patients with schizophrenia, can complicate the management of depression[77] and can inhibit the metabolism of some psychotropic drugs[9, 80]. Caffeine has been reported to induce mania in bipolar patients[81, 82], manic symptoms in those without bipolar disorder[32, 83, 84], suicidiality in those with depression at doses of more that 300mg per day[85] and to induce or exacerbate anxiety at doses greater that 450 mg[32, 86]. Conversely, caffeine may be beneficial in treating OCD[87] and as some ADHD patients responded well to caffeine researchers concluded that despite the lack of clinical trials, caffeine is a candidate for treatment for ADHD[88,89].

Energy drink additives: Studies have been carried out to evaluate the effects of the additional ingredients in energy drinks. One study compared sugar-free Red Bull to a comparable amount of caffeine and concluded that the metabolic effects of sugar-free Red Bull are primarily due to caffeine alone[90]. Another study evaluated the effects of caffeine, taurine and glucose alone and in combination on cognitive performance and mood, and also concluded that despite the other ingredients having some effects that it is caffeine, not glucose or taurine that "is likely responsible for reported changes in cognitive performance"[35].

Guarana is a native South American plant (Paullinia spp.) which contains guaranine, a stimulant that is chemically similar to and contains mainly caffeine, along with other xanthine alkaloids, saponins, flavonoids and tannins[91]. In determining the overall caffeine content of a drink both the caffeine and guarana content must therefore be taken into account, with 1g of guarana equivalent to about 40mg caffeine[30, 92, 93]. Guarana has been suggested to improve cognitive performance, mental fatigue and mood[94, 95] and a number of articles have been published suggesting possible association between consumption of guarana and adverse effects, supported by four randomized clinical trials[92].

Fig. 8 Guarana

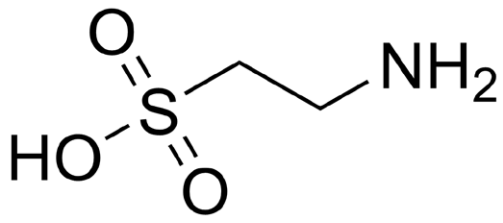

Fig. 9 Taurine molecule

Taurine is an amino acid found in large quantities in the human body that generally acts as an inhibitory neuromodulator[96]; it has been estimated that a 70kg human is likely to contain up to 70g taurine[97]. The average daily intake of taurine in humans has been estimated between 40 and 400mg; some energy drinks can contain up to 4000mg/L[98].

Research has shown that taurine can alleviate visual fatigue[99] while others have found that taurine alone can improve athletic performance[100]. Some studies find that its role on CNS effects is unclear and that it adds 'no significant benefit'[101], and concerns have been raised about the lack of research into the large quantities of taurine found in energy drinks[91].

Glucuronolactone is a naturally occurring metabolite formed from glucose in the liver and is found in a small number of foods. Those who drink two 250ml cans of energy drinks could exceed glucuronolactone intake from other food sources by up to 500%[102]. Some toxicity studies have been carried out on animals, however as the chemical is broken down very differently in humans the relevance of these studies is unknown[79].

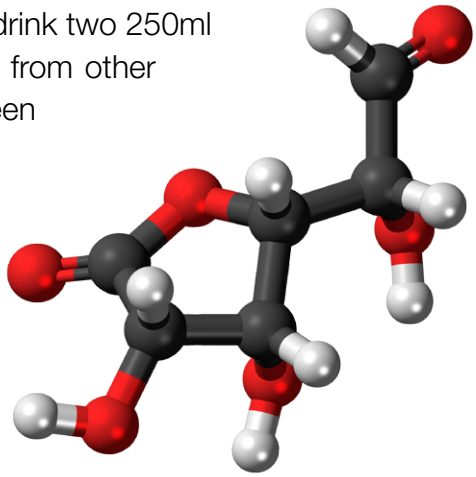

Fig. 10 Glucuronolactone molecule

Sugar (glucose, dextrose, sucrose) is present to various degrees in energy drinks and can have a short-acting alerting effect[103]. The typical sugar content in a large can of energy drink is 50-60g, which equates to 12.5-15 teaspoons of sugar[20]. The health risks of sugar are well documented and include obesity, an increased risk of heart disease and Type II diabetes[20, 104]. Sugar is known as a 'natural reward' that activates similar reward pathways as drugs such as cocaine, amphetamine and nicotine[105], and when paired with caffeine may increase the reinforcing properties of sweetened beverages[106, 107].

Legal status: Caffeine is not controlled in the UK. Caffeinated drinks belong to a class of food known as functional foods and at the date of this information sheet there is no legislation relating to the consumption of energy drinks in the UK or Ireland[79]. Other countries have certain restrictions on their sale and manufacture, for example Australia and New Zealand where the caffeine content of 'formulated caffeinated beverages' has been limited at 320 mg/L, and Lithuania which in 2014 became the first state in the world to explicitly ban selling energy drinks to under 18s[7].

Harm reduction advice:[26, 61]

- Early signs of caffeine toxicity can include tiredness and nausea. Please seek medical attention if you think you are experiencing these early signs.
- Signs of caffeine toxicity include anxiety/agitation, tremor, hallucinations, convulsions, vomiting, increased thirst or urination, rhabdomyolysis (breakdown of muscle tissue), abdominal pain, diarrhoea, seizure, breathing trouble, respiratory alkalosis (imbalance of carbon dioxide and oxygen in the blood, caused by hyperventilation), tachycardia (abnormal or faster than normal heart rhythm), high blood pressure and hypokalaemia (low potassium). If symptoms occur seek immediate medical attention.
- Caffeine is known to raise blood pressure[109]; people with hypertension have been advised to avoid use of caffeinated or energy drinks[108].
- When combined with psychostimulant drugs such as cocaine and amphetamine, caffeine can increase the risk of cardiovascular problems[62] and seizures[63], and when taken with MDMA can increase the risk of hyperthermia[110].
- Pregnancy has been shown to affect the rate that the body breaks down caffeine[79]. In 2008 the Food Standards Agency in the UK advised that a limit of 200mg of caffeine per day when pregnant will help to reduce risk[18, 25].
- It is recommended that you avoid ongoing use as a method of reducing sleep or to improve athletic performance.

Where to get help: We would advise anyone experiencing issues from caffeine or other substances to seek medical support via their GP or the NHS. There are a wide range of local drug services throughout the UK, to find out what is available in your area please use the links below:

England http://www.talktofrank.com/need-support

Scotland http://www.scottishdrugservices.com/sdd/homepage.htm

Wales http://dan247.org.uk

NI http://www.publichealth.hscni.net/publications/drug-and-alcohol-directories-services

ROI http://www.drugs.ie

This information sheet was written and designed by Mark Adley (www.thedrugswheel.com), in collaboration with UK DrugWatch and N2L. **UK DrugWatch** is currently an informal association of charities, organisations and individuals who share an interest in establishing a robust early warning system in the UK for all types of drugs. A list of current members, and a selection of information sheets can be found at: http://michaellinnell.org.uk/drugwatch.html. **N2L** (Never Too Late) is a confidential service for young people under 18 who live in North Tyneside and are experiencing difficulties in relation to the use of drugs and alcohol. Phone: (0191) 643 8802 or e-mail: n2l@northtyneside.gov.uk.

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Image references

Fig. 1 Coffee Arabica. Illustration of COFFEA arabica L. 106. from *Köhler's Medizinal-Pflanzen in naturgetreuen Abbildungen mit kurz erläuterndem*. Source text: Atlas zur Pharmacopoea germanica (1883-1914). Source: http://www.illustratedgarden.org/mobot/rarebooks/page.asp?relation=qk99a1k6318831914b2&identifier=0554. Author: Franz Eugen Köhler. Accessed online 16/05/2014: http://commons.wikimedia.org/wiki/File:Diagram_of_Coffea_arabica-cropped.jpg. *Licence: Public domain.*

Fig. 2 Structure of caffeine. Date: 20 February 2007. Source: Own work. Author: NEUROtiker http://commons.wikimedia.org/wiki/User:NEUROtiker. Accessed online 16/05/2014: http://commons.wikimedia.org/wiki/File:Koffein_-_Caffeine.svg. *Licence: Public domain.*

Fig. 3 Monster Energy can. Date: 5 July 2014. Source: Own work: Author: Juqao http://commons.wikimedia.org/w/index.php?title=User:Juqao&action=edit&redlink=1. Accessed online 16/05/2014: http://commons.wikimedia.org/wiki/File:Lata_de_Monster_Energy.jpg. *Licence: Public domain.*

Fig. 4 A photo of a cup of coffee. Date: 13 April 2005. Source: Own work. Author: Julius Schorzman http://assembleme.com/. Accessed online 16/05/2014: http://commons.wikimedia.org/wiki/File:A_small_cup_of_coffee.JPG. *Licence: Creative Commons Attribution ShareAlike 2.0* Note from author: I only require attribution if you publish this photo in print or if it is used in a for-profit project.

Fig. 5 Anhydrous USP grade Caffeine. Photographer: William Rafti of the William Rafti Institute. Date: 4 September 2005 (original upload date). Author: The original uploader was Rafti Institute at English Wikipedia. Accessed online 16/05/2014: http://commons.wikimedia.org/wiki/File:Caffeine_USP.jpg. *License: The copyright holder of this file allows anyone to use it for any purpose, provided that the copyright holder is properly attributed.*

Fig. 6 NoDoz caffeine tablets. NoDoz caffeine tablets containing 200 milligrams of caffeine each, distributed by Novartis Consumer Health, Inc. Date: 14 March 2008. Source: Own work. Author: Ragesoss: http://commons.wikimedia.org/wiki/User: Ragesoss. Accessed online 16/05/2014: http://commons.wikimedia.org/wiki/File:NoDoz_caffeine_tablets_on_black.jpg. *Licence: Permission is granted to copy, distribute and/or modify this document under the terms of the GNU Free Documentation License, Version 1.2.*

Fig. 7 Japanese Rockstar can. Description: ロックスター・エナジー・ドリンク. Source=OGB. Date: 20/08/2011. Author: OGB 市販清涼飲料水. Accessed online 16/05/2014: http://commons.wikimedia.org/wiki/File:200805can0.jpg. *Licence: This file is licensed under the Creative Commons Attribution-Share Alike 3.0 Unported license.*

Fig. 8 Sapindaceae: Paullinia cupana seen nr. Moyobamba, Peru. Date: 9 March 2012. Author: Geoff Gallice from Gainesville, FL, USA http://www.flickr.com/people/11014423@N07. Accessed online 16/05/2014: http://commons.wikimedia.org/wiki/File:Flickr_-_ggallice_-_Guarana.jpg. *Licence: This file is licensed under the Creative Commons Attribution 2.0 Generic license.*

Fig. 9 Taurine. Date: 6 May 2008. Source: Own work. Author: Yikrazuul http://commons.wikimedia.org/wiki/User:Yikrazuul. Accessed online 16/05/2014: http:// http://commons.wikimedia.org/wiki/File:Taurine.svg. *Licence: Public domain.*

Fig. 10 Glucuronolactone. Description: Ball-and-stick model of the glucuronolactone molecule showing the aldehyde form. Colour code: Carbon: black, Hydrogen: white, Oxygen: red. Date: 13 February 2011. Source: Own work. Author: Jynto http://commons.wikimedia.org/wiki/User:Jynto. Accessed online 16/05/2014: http://commons.wikimedia.org/wiki/File:Glucuronolactone-(aldehyde)-3D-balls.png. *Licence: This file is licensed under the Creative Commons CC0 1.0 Universal Public Domain Dedication.*