Opinion on Caffeine, Taurine and D-Glucurono - - Lactone as constituents of so-called "energy" drinks (expressed on 21 January 1999)

Terms of reference

To evaluate the safety of caffeine, taurine and D-glucurono- -lactone as constituents of so-called "energy" drinks.

Background

The Committee has been asked to evaluate the safety of caffeine, taurine and D-glucurono- -lactone (glucuronolactone) in the context of their inclusion as constituents of so-called "energy" drinks. The term "energy" drinks has been used in this opinion for convenience, to encompass a category of beverages that have appeared on the European market in recent years, which contain various combinations of substances, such as carbohydrates, vitamins and minerals, and many of which include one, or more of the three substances the Committee has been asked to evaluate. It should be noted however that the term "energy" drink is a commercial designation. It is neither an agreed legal term for a category of foods in the EU, nor does the Committee offer any view in this opinion as to whether claims that these drinks provide energy, in the conventional nutritional sense, are scientifically justified.

The Committee is aware that the term "energy drinks" is also used in a different way to mean beverages containing enhanced levels of carbohydrates which provide energy in the conventional nutritional sense, and which are often used by sportspersons and by people suffering from or recovering from illness. These types of beverages will not be further discussed.

Certain Member States have requested that the European Commission seek the opinion of the Scientific Committee on Food (SCF) about potential health effects from excessive consumption of "energy" drinks in certain sectors of the population. In these requests, neither the meaning of "excessive" nor the population groups of concern were defined. To the CommitteeÂ's knowledge, no surveillance information is available on the maximum intakes of "energy" drinks by individual consumers. It was agreed that initially the constituents caffeine, taurine and glucuronolactone should be evaluated for safety, taking into account the maximum concentrations currently known to be present in "energy" drinks available on the European market.

A collection of information on "energy" drinks and their constituents was submitted by Member States and by one company manufacturing "energy" drinks. The information comprised advertising material, lists of ingredients/constituents and their concentrations in various products, per capita estimates of intake in Austria, published opinions on "energy" drinks from independent scientists, and reviews of the safety of caffeine, taurine and glucuronolactone by scientists acting on behalf of one manufacturer. [1-3] The Committee itself therefore conducted an independent search of the published literature relating to taurine and glucuronolactone and updated its earlier opinion on caffeine [4] as a background to this opinion. This opinion covers only safety considerations of these three constituents.

Intake assumptions for "energy" drinks

Intake data for "energy" drinks are not available, with the exception of per capita estimates for Austria, [2] which has a well-established market for these types of drink. A per capita estimate of 1.85 litres/year which included non-consumers as well as consumers, was adjusted to take account of the fact that only 9% of the Austrian population are regular consumers of "energy" drinks. Assuming that 80% of "energy" drinks are consumed by regular consumers, it was estimated that the regular consumer drinks 16.4 litres/year or approximately 50ml/day averaged over one year.

However, the Committee considered that it was more appropriate for safety evaluation of "energy" drinks to consider likely consumption on any one day by regular consumers, rather than average consumption over one year. It would be reasonable to assume that a regular consumer of "energy" drinks might drink one to two 250 ml or 330 ml cans per day, and so in the estimates which follow in this opinion, a consumption figure of 0.5 litre of "energy" drink per day has been assumed as a reasonable estimate of possible intake on any one day by regular consumers. The Committee is of course aware that, on occasions, some individuals might drink amounts higher than this, for example, known high consumption of carbonated drinks in Europe is in excess of 1 litre/day and the intake of fluid that would be required to replace body fluids lost through sweating during, say, 2 hours of heavy exercise would be around 1 litre. The Committee considered that in the absence of comprehensive intake surveys, it was impossible to anticipate the maximum intakes of "energy" drinks which might be consumed in one day by extreme consumers, nor was it possible to anticipate the maximum that might consumed within a short period during the day by some consumers. The Committee has not therefore considered in detail the possible consequences of peak intakes in excess of 0.5 litre per day.

CAFFEINE

Previous SCF evaluation

The possible harm to health from the consumption of caffeine from food and beverages was considered by the SCF in 1983. [4] It concluded at that time that there was no apparent reason for concern about carcinogenic or mutagenic effects of caffeine in man at normal levels of intake. The data then reviewed did not reveal any teratogenic effects in humans, nor any adverse effects on human reproductive function, nor did they support any association between caffeine consumption and adverse pregnancy outcome. Neither did the animal studies point to clear permanent or adverse neurobehavioural effects in rodents even at severely toxic doses. There was little information on the effects of exposure to caffeine on the behaviour of children.

Levels in "energy" drinks and other foods and estimated intakes

A submission from the Austrian national food authority [1] included a list of the caffeine contents of 32 "energy" drinks, taken from a review of beverages on the Austrian market in March 1996. The stated caffeine content of most "energy" drinks ranged from 240-320 mg/l. Consumption of caffeine from "energy" drinks by regular consumers in Austria, which has a well-established market and where consumption is thought to be highest, has been estimated by one of the manufacturers of "energy" drinks to be about 14.4 mg/day on average, [3] equivalent to 0.24 mg/kg bw/day for a 60 kg person. However, using the CommitteeÂ's assumption for regular consumers of consumption of 0.5 l of "energy" drinks per day, containing the maximum level of 320 mg/l, caffeine intake would amount to 160 mg caffeine/day or 2.7 mg/kg bw/day for a 60 kg adult or 5.3 mg/kg bw/day for a 30 kg child.

A recent comprehensive survey in the UK of the caffeine content of "energy" drinks and other caffeine-containing products, such as cola drinks, tea, coffee and chocolate products, has revealed a wide range of caffeine concentrations in the respective product ranges. [6] Tea, coffee and chocolate drinks were made up using standardised procedures. The caffeine contents of 32 cola drinks ranged from 33-213 mg/l. Twenty-six "energy" drinks had a broad range of caffeine contents from 0.5-349 mg/l, but most contained over 110 mg/l, with a mean of 240 mg/l and a median of 293 mg/l. Tea infusions made from 14 samples of tea bags had caffeine contents ranging from 245-430 mg/l, while infusions made from 3 samples of loose leaf tea ranged from 95-105 mg/l. Caffeine levels in 16 standard instant coffees were 210-340 mg/l, while 8 filter and percolated coffees were 105-215 mg/l. Levels in 18 chocolate drinks ranged from 5.5-41 mg/l and levels in 6 chocolate bars ranged from 110-710 mg/kg. The UK survey did not offer any estimates of caffeine intakes but pointed out the need for data on the consumption of these products.

In its 1983 report on caffeine, [4] the Committee stated that for an average EEC consumer, the intake from cola-type beverages ranged from 0.013 mg/kg bw/day to 0.48 mg/kg bw/day, while caffeine exposure from all sources, including coffee, tea, chocolate, etc, ranged from 2.4 mg/kg bw/day to 4.5 mg/kg bw/day, averaging 3.5 mg/kg bw/day. Pregnant women were estimated to have lower average exposures of 2.0 mg/kg bw/day. More recent estimates of consumption of

caffeine by consumers are available for some European countries. In Germany, a median value of 7.8 mg/kg bw/day was estimated for adult coffee drinkers. [3] In Denmark the estimate for all consumers was a mean of 7mg/kg bw/day, and for heavy consumers (90 [th] percentile) 14.9mg/kg bw. [5] In the UK, the mean intake for all consumers was 4 mg/kg bw/day, and 7.5 mg/kg bw/day for heavy consumers (90 [th] percentile). [5] Estimates of mean intakes in pregnant women were slightly lower than for all consumers at 5.8 mg/kg bw/day and 3.4 mg/kg bw/day in Denmark and the UK respectively. [5]

Biological and toxicological information

The biological and toxicological behaviour of caffeine has been studied in numerous animal and human investigations. The evaluation which follows updates those aspects of the Committee's earlier opinion [4] which are considered to be most relevant to the consumption of caffeine in "energy" drinks, focusing on pregnant women and children.

Caffeine exposure during pregnancy in rodents is associated with intrauterine growth retardation, increases in resorptions and malformations, particularly facial clefts and ectrodactyly. [7] A recent 2-generation study in rats showed reduced pup weights. [8] Low dose exposure during pregnancy in rats caused only inconsistent post-weaning behavioural effects in the offspring. Higher doses were associated with lower birth weights and delayed physical development. [9-11] One study in primates has shown caffeine exposure to be associated with increased still births, miscarriages, reduced birth weight and impaired postnatal performance in a behavioural task. [12] Some studies suggest caffeine is a competitive inhibitor of benzodiazepine receptors at very high doses and at low doses to have a selective affinity for adenosine receptors, thus acting as an inhibitory neuro-modulator. [11] In general, the animal evidence indicates that doses around 10-20 mg/kg bw/day may be minimal effect levels for some effects such as behavioural changes and reduced birth weight, while higher bolus doses of 50-80 mg/kg bw/day or more are required to elicit teratogenic effects. [7]

Contradictory results have been noted in human studies on the effects of prenatal caffeine intake on birth weight. [13-19] Some reviews attribute apparent effects of caffeine on birth weight to the confounding effect of smoking. No clear association has been established between caffeine intake in early pregnancy and spontaneous abortion [14,19-23] or delayed conception. [14,24-29] Similarly there are no consistent associations between prenatal caffeine exposure and pre-term delivery [13,14,30,31] or congenital malformation. [13,14] A single, recent epidemiological study showed an association between heavy caffeine intake in pregnancy and sudden infant death syndrome. [32] In many of the human studies reviewed, caffeine consumers have been sub-divided into low, moderate and high consumers for analysis of data. In those studies indicating effects on pregnancy outcome, the association with caffeine was often confined to high consumers. In general, maternal caffeine consumption during pregnancy does not appear to have any measurable adverse consequences for the human foetus at intakes up to 300 mg/day.

Studies on prenatal caffeine exposure have shown no consistent behavioural or cognitive effects on children either at pre-school or school age. A long-term follow-up study in children whose mothers were exposed to 150-200 mg caffeine/day during pregnancy found no clear effects on mental development, psychomotor functions or behaviour up to 7 years of age. [33,34]

Caffeine appears in breast milk but has not been detected in the urine of breast-fed infants even when maternal caffeine consumption was high. [35] Studies on the effects of direct caffeine consumption by pre-school and school children have given variable results. In experimental studies in which single doses up to 10 mg/kg bw have been given to children, either no effect or small, inconsistent effects have been noted on mood, behavioural, cognitive and motor functions, some of which could be interpreted as beneficial. [35-42] Some of these studies indicated that a dose of 5 mg/kg bw increased arousal, irritability, nervousness or anxiety in some subjects, particularly if they were normally low consumers of caffeine.

In addition to reproductive and behavioural effects, the Committee has also considered whether there might be an

increased risk of cardiovascular effects from caffeine alone or caffeine in combination with other constituents, such as taurine, present in some types of "energy" drinks, particularly if consumed rapidly during or after intense exercise . The evidence from human studies, which have included normal individuals at rest, those undergoing intense exercise and those predisposed to cardiac arrythmias, have not indicated risks from normal intakes of caffeine alone. The possible effects from a combination of taurine and caffeine have not been studied.

Conclusions

A possible intake of 160 mg caffeine/day from 0.5l of "energy" drinks containing the maximum level of 320 mg caffeine/l could represent a significant contribution to total daily caffeine intake. However, this should be compared with possible intakes from other caffeine-containing beverages such as tea or coffee, many of which have caffeine contents in the range 100-400 mg/l. Such a comparison suggests that overall daily intake of caffeine is likely to be comparable, whether soft drinks including "energy" drinks, or tea and coffee, or a mixture of these, are selected, assuming that "energy" drinks replace other sources of caffeine. In the light of this, the contribution of "energy" drinks to overall caffeine intake does not appear to be a matter of concern for non-pregnant adults.

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. For example, consumption of 160 mg caffeine/day from 0.5l of "energy" drink would be equivalent to 5.3 mg/kg bw/day for a 10 year-old, 30 kg child. This could result in transient behavioural changes, such as increased arousal, irritability, nervousness or anxiety.

Risk assessment in relation to pregnancy is more difficult. Most of the available epidemiological data suggest there is no problem if total intake is below 300 mg caffeine/day. The question of possible effects on pregnancy and the offspring at regular intakes above this level remains open. This suggests that moderation of caffeine intake, from whatever source, is advisable during pregnancy.

TAURINE

Levels in "energy" drinks and other foods and estimated intakes

Taurine occurs naturally in food, especially in seafood and meat. The mean daily intake from omnivore diets was determined to be around 58 mg (range from 9 to 372 mg) and to be low or negligible from a strict vegan diet. [43] In another study taurine intake was estimated to be generally less than 200 mg/day, even in individuals eating a high meat diet. [44] According to another study, taurine consumption was estimated to vary between 40 to 400 mg/day. [45]

A submission from the Austrian National Food Authority [1] included a list of the contents of 32 "energy" drinks taken from a published review of drinks on the Austrian market in 1996. Some "energy" drinks did not contain any taurine. In those drinks in which taurine was present and its concentration declared, one contained 300 mg/l, one 2000 mg/l, and 11 contained 4000 mg/l. From the per capita intake of "energy" drinks averaged over a year for regular consumers in Austria (see earlier), [2] intakes of taurine can be estimated to average 200 mg/day from "energy" drinks containing 4000 mg/l. Using the CommitteeÂ's estimate of regular consumption of 0.5 l/day of "energy" drinks containing the highest level of taurine, daily intake of taurine would be 2000 mg/day. This is 5 times greater than the highest estimated intake of 400 mg/day from naturally occurring taurine in omnivore diets and at least an order of magnitude above average dietary intakes.

Biological and toxicological information

Taurine is present in the diet and is a normal metabolite in humans. It is a metabolic product of sulphur amino acids, mainly biosynthesised from cysteine in the liver. It participates in the formation of bile salts and the detoxification of certain xenobiotics. It is involved in a number of crucial physiological processes including modulation of calcium flux and neuronal excitability, osmoregulation, and membrane stabilisation. [46,47] However, the role of taurine in these

processes is not clearly understood and the influence of high taurine doses on these processes is uncertain.

Human clinical studies show that the oral intake of taurine can influence physiological functions. For example, taurine (3 or 6 g/day) decreased blood pressure in hypertension patients. [47,48] A similar effect was seen in animal models of hypertension but the mechanism of action is unknown. A substantial increase in the plasma concentration of growth hormone was reported in some epileptic patients during taurine tolerance testing (oral dose of 50 mg/kg bw/day), suggesting a potential to stimulate the hypothalamus and to modify neuroendocrine function, similar to that seen with certain other amino acids, such as arginine and histidine. [49] The effect on growth hormone is probably attributable to its known hypoglycaemic action. There is an indication that taurine (2 g/day) has some function in the maintenance and possibly in the induction of the psoriatic state. [50]

The effects of an "energy" drink on heart rate, plasma catecholamines, endurance time and other parameters were investigated in male, exercising endurance-athletes. [51] The subjects consumed an original "energy" drink containing taurine, glucuronolactone and caffeine and, at different times, control drinks, one without taurine and glucuronolactone and one without all three ingredients. The authors concluded that the study showed a positive effect of taurine-containing drinks on hormonal responses which led to a higher performance. However, the design of the study does not allow a distinction to be made between effects caused by taurine, or by glucuronolactone, or by both substances.

Toxicological studies did not reveal any indication for a genotoxic, carcinogenic or teratogenic potential of taurine. [52-64] However, there is no adequate study on chronic toxicity/carcinogenicity. Investigation of subacute/subchronic toxicity has also been fragmentary. [65-71] Overall, the available data are insufficient to establish an upper safe level for daily intake of taurine.

In a 6-week preliminary study in rats, a decrease in body weight was observed at 2000 ppm taurine in the diet. From this experiment, the dose causing a 10% reduction in body weight was estimated to be 1500 ppm, corresponding to 120 mg/kg bw/day. [54] The margin between this effect level and possible daily intakes in regular adult consumers of "energy" drinks (around 30 mg/kg b.w.) is small. Rats given taurine intravenously for 13 weeks showed an increase in water consumption at 1000 and 2000 mg/kg bw/day and haemosiderin deposition in the lungs at 2000 mg/kg bw/day. [69] The authors conclude, that the maximum no-effect dose was 500 mg/kg bw/day, while a group of reviewers has argued that 1000 mg/kg bw/day, is the more appropriate no-observed-adverse-effect level, because the minor nature of the effect and the likely relation to the osmotic activity of the test substance. [2] Administration of 0.4% taurine in drinking water to guinea pigs for 2 weeks, corresponding to 462 mg/kg bw/day, led to fatty infiltration of the liver. [64] In a 2-week study with rats receiving 1% taurine in drinking water (about 2.6 g/kg bw/day) changes in neutral lipids, phospholipids and enzyme activities related to lipid metabolism in liver microsomal membranes were observed. [66] In neither study was a no-effect level established. In other studies of longer duration, parameters corresponding to those described above were not examined.

Numerous publications describe special effects of taurine in different animal models, e.g. on behavior, blood pressure, serum glucose and serum cholesterol. Taurine was mostly applied in doses of 1000 mg/kg bw/day and above to induce these effects, using the oral route of administration. Intraperitoneal injection of taurine, however, seems to influence behavioral parameters at much lower doses. In one study, even a dose of 1.5 mg/kg bw was reported to decrease psychomotor activity. [72]

Animal experiments show that taurine protects against many adverse effects induced by xenobiotics. On the other hand, taurine also has the capacity to enhance chemically induced toxicity, e.g. taurine not only suppresses but also enhances lipid peroxide formation in the liver induced by carbon tetrachloride depending on the experimental conditions. [73,74] It should be noted that the combination of taurine with caffeine has not been studied with respect to any interactions.

Conclusions

The intake of taurine from regular consumption of some taurine-containing "energy" drinks is several times higher than

that from the rest of the diet. There is only limited information available either from human or conventional animal studies for risk assessment of taurine. There is a lack of scientific evidence to support the safety of taurine present in beverages at concentrations that may result in intakes several-fold higher than that usually obtained from the rest of the diet. Given the available information on involvement of taurine in a number of key physiological processes, together with the very limited data on possible adverse effects of taurine in humans and laboratory animals and the doses at which such effects were reported, the Committee considers it likely that the margin between normal daily intake of taurine from the diet (excluding consumption of "energy" drinks) and an adverse effect level in humans may be relatively small. At present, there is insufficient information on which to set an upper safe level for daily intake of taurine.

It may also be necessary to take into consideration, that absorption of taurine from beverages may be more rapid than from a food matrix. As, mentioned earlier, potential interactions between taurine and caffeine, both of which are present in several "energy" drinks, have not been sufficiently investigated.

Against this background, the Committee is unable to conclude that the safety-in-use of taurine in the concentration range reported for taurine in "energy" drinks has been adequately established. Further studies would be required to establish an upper safe level for daily intake of taurine.

D-GLUCURONO- -LACTONE

Levels in "energy" drinks and other foods and estimated intakes

A submission from the Austrian national food authority [1] included a list of the contents of 32 "energy drinks", taken from a published review of drinks on the Austrian market in March 1996. Not all "energy" drinks contain glucuronolactone. The stated concentrations in those drinks containing glucuronolactone ranged from 2000-2400 mg/l. From the per capita intake of "energy" drinks averaged over a year for regular consumers in Austria (see earlier), [2] intakes of glucuronolactone can be estimated to average 108 mg/day from "energy" drinks containing 2400 mg/l. This is equivalent to 1.8 and 3.6 mg/kg bw/day for mean and 90 [th] percentile intakes of 60 kg persons. [2] Using the CommitteeÂ's assumption of regular consumption of 0.5l/day, containing a maximum level of glucuronolactone of 2400 mg/l, would give an intake of 1200 mg/day, or 20 mg/kg bw/day for a 60 kg adult or 40 mg/kg bw/day for a 10 year-old, 30 kg child.

These estimates of intake from "energy" drinks can be compared with estimates of intake of glucuronolactone from other food sources. However, only a small number of foods have been identified as containing glucuronolactone and such comparisons should therefore be treated with caution. In the USA, mean and 90 [th] percentile intakes from other food sources have been estimated at 1.2 and 2.3 mg/day respectively among those consuming glucuronolactone containing foods, of which wine is the richest source (up to 20mg/l). [75] Based on this USA estimate, daily intake of glucuronolactone by regular consumers of two 250ml cans of energy drinks containing 2400 mg/l could exceed intake from other food sources by up to 500-fold.

Biological and toxicological information

D-Glucurono- -lactone is a normal human metabolite formed from glucose. At physiological pH, it is in equilibrium with glucuronic acid, its immediate precursor. Glucuronic acid occurs in plants, mainly in gums, but is in polymeric combination with other carbohydrates so is not readily bioavailable. Glucuronic acid is also an important constituent of fibrous and connective tissues in all animals. The available data [75] indicate that when glucuronolactone is administered orally to humans it is rapidly absorbed, metabolised and excreted as glucaric acid, xylitol and L-xylulose. Animals, such as rodents, which can synthesise vitamin C endogenously do so from glucuronic acid, either via its conversion to gulonic acid or to glucuronolactone, and hence to gulonolactone, then ascorbic acid. Such animals can also convert exogenously administered glucuronolactone into vitamin C. However, primates, including man, and guinea pigs do not possess this metabolic pathway. For this reason, the rodent may be an inappropriate model for man in the study of the effects of glucuronolactone.

The available toxicity studies are extremely limited. Acute toxicity studies have been carried out in rat, mouse, dog, rabbit and cat by oral, intravenous, intraperitoneal and subcutaneous routes. [76] It is of low acute toxicity, with the oral route being the least toxic; LD50 values ranged from 940 mg/kg bodyweight following intravenous administration in dog and rabbit, up to 10,700 mg/kg bodyweight and >20,000 mg/kg bodyweight following oral administration in rat and mouse respectively.

Glucuronolactone was administered to rats in a study designed to test the hypothesis that, as an inhibitor of -glucuronidase, it would increase longevity by increasing the rate of excretion of toxic substances as glucuronides. [77] The hypothesis was based on the assumption that intestinal -glucuronidase decreases the rate of excretion of toxic substances by allowing enterohepatic recirculation of aglycones split from glucuronides. Administration of glucuronolactone in the drinking water at 127 mg/day, equivalent to around 295-330 mg/kg bodyweight to rats from one year of age for the rest of their lifetime had no effect on fluid intake, bodyweight, time of death, or cause of death as determined by autopsy.

A study on glucuronolactone was carried out in dogs to follow up on observations that xylitol is a strong stimulator of insulin secretion in that species. [78] It was assumed that glucuronolactone would be converted to xylitol since, in the body, it is interconvertible with D-glucuronate which in turn is a precursor of xylitol in the glucuronate-xylulose cycle. A single intravenous injection of glucuronolactone at 400 mg/kg bodyweight caused only a slight increase in plasma insulin and glucose concentrations, which was small compared with the increase in plasma insulin elicited by xylitol or glucose itself. The authors concluded that glucuronolactone was either not converted to xylitol in dogs to any appreciable extent, or was metabolised in tissues other than the pancreatic islets, or was diverted to another metabolic pathway, such as formation of ascorbic acid. D-glucuronate is not a good stimulator of insulin release in rat pancreatic islets either. [79]

In a study of the antimutagenic activity of lactones in *Escherichia coli*, glucuronolactone was reported to be not mutagenic to *E.coli* strains WP2 and WP2s. Unlike some other lactones, it had no antimutagenic activity against two other established mutagens (4NQO and MNNG). [80]

A study on male endurance-athletes of the effects of an "energy" drink containing glucuronolactone, taurine and caffeine, which does not allow the effects of the three components to be evaluated separately, has already been mentioned earlier in the discussion on taurine. [51]

Glucuronolactone has also been used in long-term therapy of chronic carriers of the typhoid organism because of its ability to inhibit viral and bacterial -glucuronidase. It was stated that administration of between one and a few grams per day did not give rise to problems. [81]

Conclusions

Human metabolic considerations indicate the body is likely to handle small quantities of glucuronolactone without any problems. However, the intake of glucuronolactone from consumption of some "energy" drinks is possibly as much as two orders of magnitude greater than that from the rest of the diet. There is very little information available for risk assessment of glucuronolactone at such intakes. While there is no indication from the available data that there is any risk to health from consumption of high amounts of glucuronolactone, there is a lack of scientific evidence to support the safety of glucuronolactone present in beverages at concentrations that may result in intakes as much as two orders of magnitude greater than that obtained from the rest of the diet. As was the case with taurine, there is insufficient information on which to set an upper safe level for daily intake of glucuronolactone.

The Committee notes that the only study using chronic administration has been carried out in the rat and that rodents are known to metabolise glucuronolactone differently from man. Rodents may thus not be an appropriate model. There are no studies in mammalian species that include administration of high doses of glucuronolactone to growing animals. Knowledge of the influence, if any, of high doses of glucuronolactone on blood glucose homeostasis and metabolic pathways involving glucose would also be relevant for risk assessment in relation to children and diabetics.

Against this background, the Committee is unable to conclude that the safety-in-use of glucuronolactone in the concentration range reported for glucuronolactone in "energy" drinks has been adequately established. Further studies would be required to establish an upper safe level for daily intake of glucuronolactone.

Overall conclusions

"Energy" drinks are not traditional food products and contain some constituents, such as taurine and glucuronolactone, which, while not unique to these products, are present in much higher concentrations in "energy" drinks than are found in other food products and/or natural foods.

This opinion covers only the safety considerations for three constituents present in some "energy" drinks, caffeine, taurine and glucuronolactone. In the absence of comprehensive information about consumption patterns in Member States, and in particular a lack of information about maximum intakes among regular consumers, the Committee has based its considerations on an assumption that regular consumers of "energy" drinks might reasonably consume 0.5l/day and that some of these consumers may regularly select products containing the highest amounts of caffeine, taurine or glucuronolactone reported to be present in drinks on the market.

For caffeine, comparison of concentrations in "energy" drinks with concentrations present in other caffeine containing beverages such as tea and coffee suggest that overall daily intake of caffeine is likely to be comparable, whether soft drinks including "energy" drinks, or tea and coffee, or a mixture of these, are selected, based on the assumption that "energy" drinks replace other sources of caffeine. Under these circumstances, the Committee considers that the contribution of "energy" drinks to overall caffeine intake is not a matter of concern for non-pregnant adults.

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. The Committee considers that this could result in transient behavioural changes, such as increased arousal, irritability, nervousness or anxiety.

Risk assessment of caffeine in relation to pregnancy is more difficult. While intakes up to 300mg/day appear to be safe, the question of possible effects on pregnancy and the offspring at regular intakes above 300mg/day remains open. This suggests that moderation of caffeine intake, from whatever source, is advisable during pregnancy.

The Committee notes that the possible interactions of constituents of "energy" drinks have not been well studied and considers that the possible interactions between caffeine, taurine and alcohol may warrant investigation in humans, particularly under conditions of exercise and consequent dehydration through sweating .

For taurine and glucuronolactone, the Committee is unable to conclude that the safety-in-use of taurine and glucuronolactone in the concentration ranges reported for these constituents in "energy" drinks has been adequately established. Further studies would be required to establish upper safe levels for daily intake of taurine and glucuronolactone.

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