On 10th December 2013, the European Food Safety Authority (EFSA) published a scientific opinion on the safety assessment of the low calorie sweetener aspartame, alongside responses it received during the consultation process, which reconfirmed its safety at the current Acceptable Daily Intake (ADI). The ADI is an estimate of the amount of a food additive that can be consumed daily over a lifetime without appreciable risk to health. The safety assessment was conducted following a request in 2011 from the European (EU) Commission to re-evaluate the safety of aspartame after concerns were raised by Members of the EU parliament.

To conduct this full risk assessment, EFSA carried out an in-depth re-evaluation of peer-reviewed scientific and other literature on aspartame and its breakdown products, including human studies. This thorough review was made possible by the large body of scientific evidence made available from two public calls for data (both published and unpublished). It included the 112 documents that were used in the safety assessment of aspartame in the early 1980s. EFSA has published a full list of the scientific studies supporting the review on its website.

**Background to the new safety assessment**

EFSA was due to re-evaluate all food additives authorised in the EU prior to 2009, including aspartame, by 2020, however any food additive can be re-prioritised at any time. Since EFSA’s establishment in 2002, the Authority has kept the safety of aspartame under regular review and has issued advice via its scientific panels on new studies in 2006, 2009 and 2011. In all of these instances, the Authority concluded that new data did not give reason to re-evaluate the safety of aspartame or to revise the ADI of 40 mg/kg of bodyweight. The safety of aspartame has continually raised interest and at times controversy, mainly due to concerns relating to some of the early experimental animal studies utilised to evaluate its safety. However, extensive reviews on aspartame have been carried out by many national and international regulatory and advisory bodies, which have all concluded that the scientific evidence supports the safety of human consumption of aspartame at intakes below the ADI.

In 2010, two studies were published that prompted the timing of the re-evaluation of aspartame. The studies investigated possible health risks relating to the consumption of low calorie sweeteners including aspartame and included an epidemiological study on the association between intakes of low calorie sweetened soft drinks and increased incidence of preterm delivery (Halldorsson et al. 2010) and a carcinogenicity study in mice exposed to aspartame through feed (Soffritti et al. 2010). EFSA’s assessment of the Halldorsson et al. (2010) publication concluded that the findings of this study did not demonstrate any causal relationship between the consumption of low calorie sweetened soft drinks and premature birth and that additional studies are needed to either confirm or refute an association. EFSA recommended that future studies should also explore other important confounding factors, such as exposure to other dietary components that might affect delivery outcomes.

The Soffritti et al. (2010) study evaluated the potential of aspartame to induce carcinogenic effects in male and female Swiss mice treated with differing doses of aspartame (5 different dose levels from 0 parts per million (ppm) to 32,000ppm) from prenatal life (12 days of gestation) until death. The study found that aspartame induced cancers of the liver and lung in male mice but no carcinogenic effects were observed in female mice. The authors suggest that this is due to both spontaneously occurring and treatment-induced tumours being more common in males than females. Interestingly, the authors concluded that because aspartame is completely
metabolised to phenylalanine, aspartic acid and methanol in the gastrointestinal tract, the observed carcinogenic effects were not caused by aspartame itself but rather by its metabolites, namely methanol. However, methanol is naturally present in the diet and necessary for a range of body functions at the molecular level. Toxicity of methanol only becomes a safety concern when consumption and exposure is high, such as from intake of certain alcoholic spirits, particularly home-distilled varieties. EFSA’s review of the study concluded that there are flaws in its validity and statistical approach, and therefore the results cannot be interpreted fully. This was the case for similar previous studies conducted by the same team who have been criticised for failing to follow internationally accepted guidelines for toxicology testing (Soffritti et al. 2005 was the topic of a Facts Behind the Headlines article in Nutrition Bulletin (Stanner 2005)). In addition, EFSA added that Swiss mice (as used in this study) are known to have a high incidence of spontaneous tumours and the incidence of tumours reported in the study for all dose groups falls within the control range recorded for these tumours in mice. Importantly, hepatic tumours in mice are not regarded by toxicologists as being relevant for human risk when they are caused by non-genotoxic substances (i.e. substances which do not damage the DNA) such as aspartame.

After the end of the public consultation on the draft opinion on the re-evaluation of aspartame in February 2013, two additional papers were brought to the attention of EFSA as relevant for the evaluation of aspartame. One was the evaluation by Gift et al. (2013) of several studies carried out by the European Ramazzini Foundation (ERF) and the second was a toxicological review of methanol (non-cancer) by the United States Environmental Protection Agency (US-EPA). The Panel provided a separate statement on these papers which can be found here.

The panel noted that the Gift et al. (2013) review of the ERF studies is consistent with EFSA’s conclusions on the lack of carcinogenic activity of aspartame. The Panel also analysed US-EPA’s Toxicological Review of Methanol (Non-cancer) in the context of the safety assessment of aspartame. The Panel noted that the combination of the endpoint used, a benchmark dose response (BMR) of 5% and the uncertainty factors applied, resulted in a Reference Dose (RfD) for exogenous methanol of 2 mg/kg bw/day that was overly conservative. This RfD was by definition in addition to dietary intakes of methanol which were included in the background exposure estimates used by the US EPA. Taking all these factors into consideration, the Panel concluded that the toxicological review of methanol by US-EPA and the review by Gift et al. (2013) do not alter the conclusions on the risk assessment of aspartame performed by EFSA. EFSA confirmed the Acceptable Daily Intake (ADI) for aspartame of 40 mg/kg bw/day.

Findings of the latest review

In EFSA’s 2013 scientific opinion of the safety of aspartame, the Authority concluded that aspartame and its breakdown products pose no toxicity concern for consumers at current levels of exposure. The current ADI for aspartame is deemed to be safe for the general population. Although current intakes were not measured in the re-evaluation, an adult would have to consume 14 cans of a sugar-free drink containing maximum permitted levels of aspartame every day before reaching the ADI. In reality as most drinks use aspartame in combination with other sweeteners and the aspartame level actually used is considerably lower than the maximum permitted levels.

Following the extensive review of evidence in animal and human studies, the opinion of EFSA experts is that there is no risk of aspartame causing damage to genes and inducing cancer.
EFSA’s experts also concluded that aspartame does not harm the brain, the nervous system or affect behaviour or cognitive function in children or adults. The opinion makes clear that the breakdown products of aspartame (phenylalanine, methanol and aspartic acid) are also naturally present in other foods (for instance, methanol is found in fruit and vegetables) and that the contribution of aspartame to total dietary exposure of these substances is low.

Phenylalanine, one of aspartame’s breakdown products, is an amino acid found in many protein-containing foods, which can be toxic at high intakes, in particular to the developing foetus in women with the medical condition phenylketonuria (PKU). The Authority confirmed the ADI, which has been set for the general population, is not applicable to people who suffer from PKU as they must adhere strictly to a low phenylalanine diet. Furthermore, if aspartame is stored under certain conditions, then it can break down into an impurity product named 5-benzyl-3,6-dioxo-2-piperazine acetic acid (also known as ‘Di-ketopiperazine’ or DKP). EFSA’s review found that, based on exposure levels of aspartame, exposure to DKP from all foods and drinks containing aspartame would be below the ADI for DKP and therefore consumer safety is not at risk from exposure to DKP from aspartame.

For pregnant women, the Panel noted that there was no risk to the foetus from phenylalanine derived from aspartame at the current ADI (40 mg/kg bw/day) excluding women with PKU.

Key References


