Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment

COT Statement on Adverse Reactions to Acid Sweets

Introduction

1. Since April 2003 the Food Standards Agency (FSA) has received a number of reports of adverse reactions in children eating sour acid sweets designed to be kept in prolonged contact with the tongue. Some reactions have been sufficiently severe for the children to attend hospital. At present there are no regulatory limits for acidity of confectionery products and no restriction on their sale in the UK. The COT was asked to consider the available data on acid sweets and whether it was the composition, pH or acidity, the method of use, or a combination of these factors, that was likely to be responsible for the adverse reactions.

Background

Acid Sweets

2. An increasing number of acid sweet products are available. These sweets are being manufactured by different countries, with some produced by UK manufacturers. Those reported to cause adverse reactions include both liquid and solid sweets. King Regal "Roll on King" (liquid sour candy), is part toy, part sweet and consists of syrup which is contained in a "roll on" bottle (50 ml) similar to deodorant container. These sweets are designed to be rolled on to the tongue, thus dispensing the sour candy directly onto the tongue. Public analyst reports have indicated that the pH of King Regal "Roll on King" was 2.14-2.26 and titratable acidity* expressed as citric acid was 6.3-6.7%. Brain Licker is a similar "roll on" product (60 ml). The pH of these products was reported to be 1.8-2.0 and titratable acidity as citric acid was 1.98-5%.

3. "Toxic Waste" is a solid sweet available in novelty drum containers. These sweets have an extremely sour soft centre with a hard outer coating. According to public analyst reports, some of the Toxic Waste sweets had a coating containing high levels of titratable acidity (39.8-64.2% as citric acid). When dissolved in water, the pH of the sweets was 2.2-2.7 and titratable acidity as citric acid 9.1-20.3%, calculated as a proportion of the whole sweet.

* Total dissociated plus undissociated acid measured by titration. When referring to a mixture of acids it is expressed as the acid assumed to be predominant.

There is a warning that Toxic Waste may cause temporary irritation to sensitive mouths, but consumers are encouraged to keep the sweets in their mouths for as long as possible to “show how tough they are.”

4. Complete compositional data are not available for acid sweets. According to the label, they contain sugars, acids, colours and preservatives. Of these the acids are most likely to be a contributing factor in the reported adverse effects. All of the products concerned contain citric, malic or lactic acid. Citric acid is the most commonly used acid.

Acids in foods

5. Acids are commonly used in the food industry to control pH, preserve food, chelate metal ions and enhance flavour. Organic acids are used in sugar confectionery to offset the general sweetness of sugar and to add flavour. There is a trend for use of a combination of two or more acids in formulated food products[1].

6. Citric acid occurs naturally in plants and animals as an intermediary substance in oxidative metabolism, being a component of the tricarboxylic acid cycle. Malic acid is also one of the steps in the tricarboxylic acid cycle and plays a role in cellular energy production. Lactic acid is a principal metabolic intermediate in glycogen breakdown and other metabolic processes in most living organisms and occurs naturally in small quantities in the body. Citric acid is found in the greatest amounts in citrus fruits. Malic acid is the principal acid contained in apples, apricots, peaches, plums and many other fruits and vegetables. Lactic acid is used in food and food applications as an acidifier, antimicrobial agent, curing agent, pH control agent and flavour enhancer and is present in many foods, both naturally or as product of microbial fermentation.

7. Citric acid anhydrous and monohydrate (E330), malic acid (E296) and lactic acid (E270) and their salts are permitted food additives in the European Union. Conditions of use are *“quantum satis”* which means that no maximum levels are set, but the additive must be used in the food concerned in accordance with good manufacturing practice and must not be used at a level higher than is necessary to achieve intended purpose. These acids are also listed as GRAS (Generally Recognised as Safe) in the USA, where maximum concentrations are specified for malic acid in foods as served: hard candy 6.9%; processed fruits and fruit juices 3.5%; non-alcoholic beverages 3.4%; soft candy 3.0%; jams and jellies 2.6%; 0.7% in all other foods when used in accordance with good manufacturing practice.

Toxicological considerations

Acidity

8. Organic acids are weak acids, in which the hydrogen ions are only partially dissociated from the base. In the mouth, the fully dissociated

hydrogen ions of a strong acid would be diluted by saliva, thereby raising the pH. In contrast, dilution of weak acids is likely to progressively release hydrogen ions, prolonging the low pH.

Irritation and sensitisation

9. Citric acid appears to be the most potent irritant of the three acids, although there are no direct comparative data. Eye irritation has been reported in the rat at 0.5% and 2% citric acid[2]. Neat malic acid caused severe ocular irritation in rabbits and was moderately irritating to rabbit skin[3]. Eye irritation has been reported in the rat at 10 - 20% lactic acid[2, 4]. Skin irritation has also been reported with application of neat lactic acid and slight skin irritation with occluded application of a 20% solution[4]

10. Skin irritation has been reported in humans at 3% citric acid[5]. Some studies have reported individual differences in the perception of a stinging sensation when 10% lactic acid solution was applied to the skin [6].

11. In a single report, citric and malic acid have been reported to cause skin sensitisation, as demonstrated by a reaction in 34 patients with atopic dermatitis who were patch tested with a 10% aqueous solution of the acids for 48 hours. Ten patients reacted to citric acid, six reacted to malic acid and 18 reacted to both. Rashes that were either generalised or on the extremities were observed 48 hours after challenge[7]. The test subjects appeared to be a highly selected group with respect to the severity and persistence of their symptoms. None of the controls, whether atopic or non-atopic reacted to citric or malic acid, suggesting that a sensitive subgroup exists.

Effects on dental enamel

12. Data from case studies suggest that ingestion of citric acid frequently or in large doses may cause erosion of teeth and local irritation, probably because of the low pH[8]. Tooth erosion is common in the UK: 50% of 5 year olds had evidence of tooth erosion in 1993[10]. However there are no data available on the extent to which citric acid may contribute to this prevalence.

13. Data from *in-vitro* studies indicate that the rate of enamel erosion associated with consumption of soft drinks, increases with decreasing pH for all acids[9]. Enamel erosion in the presence of citric, malic and lactic acids has been reported and factors such as exposure time, acid concentration, pH and presence of calcium have been shown to affect rate of dental erosion[11, 12,13].

Systemic effects

14. Toxicity of citric, malic and lactic acid has only been demonstrated at very high doses. Signs of acute toxicity in rats following ingestion of 11.7 g/kg body weight citric acid include motor ataxia, mydriasis (abnormal pupil dilation) and decreased rate of respiration and heart beat [14].

15. Mice and rats dosed with a single administration of a 25% malic acid solution showed signs of toxicity including ataxia, prostration and convulsions[15]. The World Health Organisation (WHO) stated that the oral lethal dose of L-malic acid for rabbits was 5 g/kg and for sodium malate in dogs was 1g/kg. The signs of acute poisoning in rats and mice were weakness, retraction of the abdomen, respiratory distress and cyanosis[16].

16. In rats given doses of lactic acid up to 1.3 g/kg body weight by gastric gavage, signs of toxicity included difficulty breathing, runny nose and abdominal inflation immediately after dosing[17].

17. The Joint FAO/WHO Expert Committee of Food Additives (JECFA) evaluated the safety of citric, malic and lactic acid and their calcium, potassium, sodium and ammonium salts[18]. Taking into account the well established metabolic pathways, JECFA concluded that there was no significant toxicological hazard posed by these compounds, hence no limits were set for their acceptable daily intake (ADI). However, a conditional ADI of 0-100 mg/kg body weight was recommended for D(-) and DL-malic acid and for D(-) and DL-lactic acid.

COT Evaluation

18. A number of factors may contribute to the reported acute effects of acid sweets on the oral mucosa. These include pH, total acid content, method of delivery direct onto the tongue and duration of contact. Conventional sweets such as acid drops are of low pH but stimulate salivary flow which reduces viscosity and raises the pH in the mouth. The liquid acid sweets are more viscous and are expected to inhibit salivary flow, which would reduce the buffering capacity of the saliva, thus further lowering the pH in the mouth.

19. It is possible that there is a subgroup with sensitivity to citric and malic acids. The available information indicates that allergic responses are rare and required challenge with very high concentrations of the acid. The reported allergic responses were systemic, producing reactions at sites distant from the site of patch-testing. In contrast, the reported adverse reactions to acid sweets were local effects, and are therefore more likely to have been irritant rather than allergic responses. However, the mode of application of the acid sweets and the irritancy of the acids could potentially act as an adjuvant, i.e. enhancing the sensitising effects of other ingredients in the sweets.

20. Damage to the oral mucosa was unpleasant but reversible, whereas damage to teeth would be permanent. As yet there was no evidence of a link between dental erosion and consumption of acid sweets. However there is evidence that high consumption of products such as cola beverages with a pH of 2.8 could be associated with dental erosion. Since the new acid sweets had a much lower pH it was likely that they could also lead to dental erosion. Concern was also expressed about possible long term health implications of repeated exposure.

21. Based on the case reports, a pH of 2.5 might be considered as a level below which acute effects would be expected. However, the variability of the product in terms of manufacturing was unknown, the reported pH of 2.5 could not be taken as representative. There could be difficulties in measuring low pH accurately, which could result in significant inter-laboratory variability making interpretation of results difficult and inconsistent. Therefore the reliability of this value was uncertain.

22. Because the effects were related to a combination of factors it would be difficult to set a level at which an individual might adversely react based on pH alone. It might be possible to investigate key characteristics in determining a response in a human volunteer study, which would need to be conducted in adults for ethical reasons. The mode of application would be difficult to replicate in animals. Some *in-vitro* tests for skin corrosion, such as those used for industrial chemicals, might provide a benchmark against materials already classified as corrosive. However, the issue was complex, with several variables being involved, i.e. acidity, pH and buffering capacity; even exposure to pH 4 could be a problem if individuals were exposed to it for a prolonged period.

23. Safe product design is the responsibility of the manufacturer. If products are shown to be harmful, the relevant regulatory authorities could take action under the appropriate legislation.

Conclusions

24. We *conclude* that the acute effects of acid sweets in the mouth appear to be attributable to a combination of the acid content, the method of application and duration of contact.

25. We *consider* that whilst the acute effects are reversible, acid sweets may also have the potential to contribute to long term irreversible damage to dental enamel. There is also uncertainty with respect to the long term implications of repeated exposure on the oral mucosa.

26. We *recommend* that the manufacturers and distributors should be required to provide evidence of the safety of acid sweets to the relevant regulatory authorities.

COT statement 2004/05
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