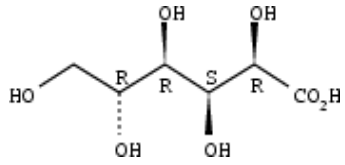
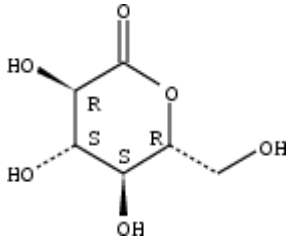
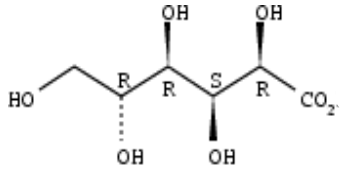
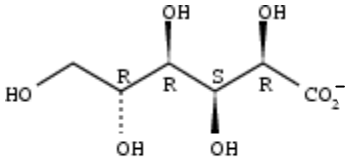
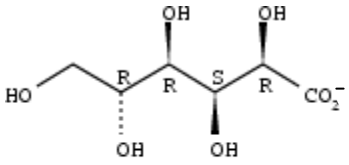
SIDS INITIAL ASSESSMENT PROFILE

CAS No.	Chemical	Structural formula
526-95-4	D-Gluconic acid	
90-80-2	Glucono-delta-lactone	
527-07-1	Sodium D-gluconate	 • 1Na
299-28-5 18016-24-5	Calcium D-gluconate	 • 1/2 Ca
299-27-4	Potassium D-gluconate	 • K

SUMMARY CONCLUSIONS OF THE SIAR

Category Rationale

Gluconate derivatives are presented as a category. Gluconic acid and its mineral salts freely dissociate to the gluconate anion and the respective cations. Glucono-delta-lactone (GDL), the 1,5-inner ester of gluconic acid, is formed from the free acid by the removal of water. On the basis of these spontaneous chemical rearrangements, glucono-delta-lactone, gluconic acid and its sodium, calcium and potassium salts can be considered as a category, with all members sharing the same representative moiety, the gluconate anion. Manufacturing and uses of the category members are also interlinked. The data summarized in this report are focused on the environmental and health effects from the gluconate anion and read-across to the lactone but do not deal with specific effects of the cations. Thus toxicological effects related to the cationic components are not part of the present report.

Human Health

Gluconic acid and its derivatives are naturally occurring substances. In mammalian organisms both D-gluconic acid and its 1,5-lactone are important intermediates in the carbohydrate metabolism. Gluconate is a metabolite of glucose oxidation. The daily production of gluconate from endogenous sources is about 450 mg/kg for a 60 kg person. A significant portion (60-85%) of parenterally administered gluconate is excreted unchanged in the urine.

The LD50 calculated after oral administration (gavage) of potassium gluconate on Wistar rats is 6060 mg/kg bw.

None of the repeated dose toxicity studies of any duration (4 weeks, 6 months, or 24 months) showed any significant toxicological effects of gluconates. Potential side effects were attributed to high doses of cation intake, evidenced by results from assays designed for the gluconate anion effect specifically. The NOAEL of sodium gluconate determined from the 28 days studies on rats was equal to 1000 mg/kg bw for males and 2000 mg/kg bw for females. These compounds are neither irritant to the eye or the skin nor show sensitizing properties.

The available in vitro and in vivo mutagenicity data with glucono-delta-lactone, sodium or calcium gluconate were negative. No carcinogenicity studies, and no inhalation toxicity data were available for any of the gluconates of the category.

SIDS testing requirements regarding reproductive toxicity were satisfied with histopathology of the reproductive organs in repeat dose studies on sodium gluconate and with developmental toxicity studies on glucono-delta-lactone. Indeed no changes were observed on the reproductive organs in 28 days oral studies with sodium gluconate (dosage up to 4400 mg/kg bw) and developmental toxicity studies on GDL on different species were all negative.

Environment

Gluconates are readily biodegradable both in aerobic and anaerobic conditions. As the sequestering tendency of gluconates decreases rapidly upon dilution or lowering pH, their chelated metal complexes are destroyed effectively and quickly by biological waste water treatment as well.

A closed bottle test for sodium D-gluconate showed that the Theoretical Oxygen Demand (ThOD) was 89% after 28 days which predicts 100% degradation; and an anaerobic study showed that 100% of sodium D-gluconate was degraded after 35 days.

Gluconic acid, its salts of sodium, potassium and calcium as well as glucono-delta-lactone are all characterised by a low vapour pressure (from 2.41e-009 hPa to 1.58e-022 hPa, estimated from the modified Grain Method), and a low octanol/water partition coefficient (estimated as -5.99 for the sodium salt, -7.51 for the calcium salt, - 5.99 for the potassium salt, -1.87 for the free acid and -1.98 for GDL). The dissociation constant of gluconic acid is in the range of 3.5 to 3.8. Because of their good water solubility (from 30 g/L for calcium gluconate to 590 g/L for sodium

gluconate) and low Log Ko/w, no bioaccumulation effects are to be expected, the substances were also shown to be readily metabolised.

Estimations from a level II/III fugacity model show that the main target compartments of gluconates are water (38.8 – 49.8 %) and soil (48.9-61.2%). The calculated Henry's law constants (1.38×10^{-4} $Pa.m^3$/mole for GDL, 4.74×10^{-8} $Pa.m^3$/mole for gluconic acid and 4.76×10^{-8} $Pa.m^3$/mole for sodium gluconate) indicate a low potential for volatilization and the estimated indirect photodegradation in the atmosphere with OH radicals (AOP (v1.91) program) gives a $t_{1/2}$ between 1.7 and 4.0 hours. The good water solubility and low vapour pressure designate water to be a major target compartment for these substances.

Acute toxicity to aquatic organisms (fish, daphnia, algae) was tested on sodium gluconate. In the range of concentrations tested, sodium gluconate did not show toxicity to any of the aquatic species: fish (LC0-96 hrs > 100 mg/l), daphnids (NOEC 24-48 hrs > 1000 mg/l), algae ($NOEC_r$ (24-72 h): 560 mg/l - E_rC_{50} (24-72 h): > 1000 mg/l)) The data from these studies were used for the other members of the category.

No terrestrial toxicity data for gluconates are available.

Exposure

Gluconic acid and its derivatives presented in this category are naturally occurring substances. In mammalian organisms both D-gluconic acid and its 1,5-lactone are important intermediates in the carbohydrate metabolism.

Most of these compounds are listed as permitted food additives, which may be added to all foodstuffs, following the "quantum satis" principle, as long as no special regulations restrict their use.

The manufacturing of gluconic acid is based on a fermentation process. Estimation of the worldwide industrial production per year for all the members of the gluconate category is around 65000 - 100000 tonnes. There is no production site in Belgium.

The typical industrial applications for the category are both dispersive and non-dispersive. The main non- dispersive applications are industrial cleaning, metal surface treatment, textile bleach stabiliser and aluminium processing.

When gluconates are used in wide dispersive applications such as chelating agents in cement set retarding, institutional and household cleaning, personal care products, pharmaceuticals and foodstuffs, their use might result in exposure to the environment. However, when used as sequestering agents in the building industry (concrete and mortar), the gluconate ions react with calcium ions present in the cement to form an insoluble and impermeable layer of calcium gluconate. Therefore, the gluconate is bound within the microcrystalline fibres of cement and is not free to migrate to cause any environmental pollution. Food applications could potentially contribute to spreading gluconates and glucono-delta-lactone in the environment, as these products are added in their crystalline or powder forms to food components such as meat, milk or soma at levels below 5 %w/w. However, since the final food is meant for human consumption and mostly gets ingested, there is no real potential for environmental distribution of gluconates from this application either.

Human exposure by all routes (including inhalation) is possible. Workers exposure will mainly be by inhalation and by skin contact. Consumers' exposure may be from the oral and dermal routes. Individual exposure of consumers to gluconates is expected to be limited because gluconates are mostly used as additives in the different consumer products typically in low dosages. Furthermore, Consumer exposure in personal care products, pharmaceuticals and foodstuffs applications are subject to specific regulatory provisions requiring an authorization procedure where the evaluation of the hazardous properties as well as the actual exposure is taken into account.

RECOMMENDATION

The chemicals in this category are currently of low priority for further work.

RATIONALE FOR THE RECOMMENDATION AND NATURE OF FURTHER WORK RECOMMENDED

The chemicals in this category are currently of low priority for further work because of their low hazard potential.