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Note

Magnesium salts of aldonic acids as analytical standards*†

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Metals and metal-containing compounds find use as standards for the determination of the relevant metal. In recent years, interest has developed in improved standards for the alkaline earth elements, particularly magnesium and calcium. Magnesium metal must be acid-washed to remove surface oxide, and then dried before weighing and dissolution in acid. Magnesium oxide is difficult to obtain and maintain in a high-assay form. Each of these standards has an unfavourable weighing factor. For clinical laboratories, water-soluble standards are preferable.

Alkaline earth salts of organic acids have received limited attention as standards. Magnesium acetate tetrahydrate has been mentioned as a standard for serum magnesium, but it is difficult to bring this salt to exact stoichiometry[1]. This salt, dried over calcium chloride, has been recommended as a chelometric standard[2]. Anhydrous magnesium acetate absorbs moisture less rapidly than high-assay magnesium oxide and is useful as a standard for serum magnesium[3]. Solutions in an organic solvent of alkaline earth salts of higher alkanoic acids have been utilized as standards for spectrochemical and atomic absorption spectrometric determinations of metals in petroleum products.

Aldonic acids (*e.g.*, xylonic[4], gluconic[5–7], and lactobionic acid[8]) form salts with various metals (*e.g.*, magnesium[4–6], calcium[6,8], and barium[7]) that have exact stoichiometry, and the alkaline earth salts show favourable water solubility. Some of the salts persist as stable, well-defined hydrates. The search for improved magnesium standards, especially for the clinical laboratory, prompted us to examine the alkaline earth salts of the aldonic acids.

Treatment of an aqueous solution of the aldonic acid with an insoluble alkaline earth carbonate, filtration of the resulting solution, and isolation of the metal aldonate remains a valid approach. Where the product is to serve as an analytical standard, the procedure must be so conducted that the isolated compound is both of high purity and high assay. For use as a reference standard for flame analytical techniques, the alkaline earth compound must be low in the content of the next higher alkaline

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earth. For example, for a magnesium standard, the calcium/magnesium weight ratio should be less than 1:2000.

Of the aldonic acids, D-gluconic acid is the most readily available; its magnesium salt has received attention in pharmaceutical and other applications. Our initial findings that magnesium D-gluconate dihydrate is an excellent standard for the determination of serum magnesium have been briefly reported[1].

We now report the preparation of high-assay, low-calcium magnesium D-gluconate dihydrate together with some relevant properties.

EXPERIMENTAL

Preparation of magnesium D-gluconate dihydrate (Ca <20 p.p.m.). — Technical grade 50% aqueous D-gluconic acid was diluted with an equal volume of deionized water, and the solution (1 litre) was passed slowly through a polyethylene column (75 × 2.5 cm) of Dowex 50W-X8 (H^+) resin (25 mesh).

Acid-washed, reagent-grade magnesium turnings (24 g) were treated at room temperature with M hydrochloric acid (2 litres) prepared by diluting high-purity hydrochloric acid (ULTREX® grade, J. T. Baker Chemical Co.) with high-purity water (resistance, 18 megohm/cm). The resulting solution was treated to pH 8 with 12% aqueous ammonium carbonate (reagent grade) previously filtered at 20 p.s.i. of nitrogen through a 0.2-μm cellulose acetate membrane filter. The precipitate was collected and washed exhaustively with *hot* high-purity water until the washings were chloride-free. The resulting low-calcium magnesium carbonate was dried at 150° in a polyfluorocarbon container.

To 800 ml of the purified solution of D-gluconic acid at room temperature, purified magnesium carbonate was added to pH 5.8. The mixture was filtered, active carbon was added to the hot filtrate, and the suspension was filtered hot. To the rapidly stirred, warm filtrate, 95% ethanol (350 ml, reagent grade) was added slowly. From the cooled mixture, magnesium D-gluconate dihydrate was collected and dried at 100–105°/0.1–0.5 mmHg (yellowing may be encountered at higher temperatures). The product (432 g, 80%) had a Ca/Mg ratio of 1:30,000.

Analytical data for first production batch: assay by chelometric weight titration against EDTA (photometric endpoint), 99.82% (average of 3 determinations); particulate matter (after dissolution in hot water), 0.0005%. Non-metallic impurities (p.p.m.): As <0.04, B 2, halide (as Cl) 2, N <20, PO_4 45, Si 0.7, SO_4 7. Metallic impurities (p.p.m.): Al 0.05, Ba <5, Bi <0.3, Cd <0.5, Ca 3, Cr <0.3, Co <0.3, Cu 0.5, Fe 1, Pb 0.5, Li <0.5, Mn 4, Hg 0.004, Mo <0.05, Ni 0.7, Nb <0.5. K 2, Ag 1, Na 90, Sr 2, Sn 0.3, Ti 0.05, V <0.05, Zn 3, Zr 0.3.

Warm, concentrated, aqueous solutions of magnesium D-gluconate deposit gelatinous precipitates on cooling to room temperature[9]. Isolation of magnesium D-gluconate dihydrate in 5–10 g amounts by addition of its aqueous solution to methanol has been reported[6], but gave gums on a larger scale. Addition of methanol or ethanol to an aqueous solution is a superior technique.

DISCUSSION

Criteria for a standard for the determination of magnesium include exact stoichiometry, a favorable weighing factor (*i.e.*, formula weight of the metal/formula weight of the standard), little change in weight on contact with moist air, and good storage stability. Additionally, water solubility is desirable and, for salts, the anion should not interfere.

Magnesium D-gluconate dihydrate meets all of these criteria. It has an extremely favourable weighing factor (0.05393), its solubility in water is ~16 g/dl at 25°, and the solubility is favourable in weakly acidic solution and in alkaline solution up to pH 11. The rate of moisture absorption[1] at 50% relative humidity is ~0.01%/min for the first 16 min and ~0.001%/min from 20–40 min. This rate is far less than that of high-assay magnesium oxide and anhydrous magnesium acetate. Consequently, magnesium D-gluconate dihydrate can be weighed without special precautions.

On storage of magnesium D-gluconate dihydrate over phosphorus pentoxide for 24 h, 0.30–0.35% of moisture is lost from 99.65% assay material; on more-prolonged storage, there was no further loss in weight, indicating that the dihydrate is not converted into the anhydrous salt under such conditions. Thus, high assay can be assured by desiccation of the standard over phosphorus pentoxide for a short time.

For use as a standard for the determination of magnesium by atomic absorption spectrometry, the magnesium D-gluconate dihydrate is used as a dilute solution in water, with nitric, perchloric, or hydrochloric acid added; the gluconate anion shows no effect on the flame characteristics or on the magnesium results[1].

Anhydrous calcium D-gluconate, of high assay (99.9% minimum), can also be prepared in high yield by a procedure which parallels that used for the magnesium analogue. The water solubility of this salt (3.5 g/dl at 25°) is adequate for use as a standard. The analytical use of this salt is being investigated.

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