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PREPARATION AND CHARACTERIZATION OF COMPLEXES OF ALUMINIUM-SORBITOL; SORBITOL-CITRIC ACID-SORBITOL-DEXTRIN AND CITRIC ACID-SUCROSE-GLUCOSE AND DEXTRIN

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Preparation and characterization of the complexes of aluminium with sorbitol; sorbitol-citric acid; sorbitol-dextrin and citric-acid; surcose; glucose and dextrin have been studied. With the exception of Al-sorbitol complex which is unstable below pH 8.0 showing precipitation with acid, the complexes are stable between pH 4.5 and above.

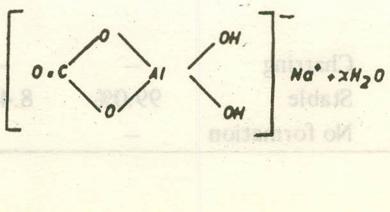
INTRODUCTION

Aluminium is distributed in varied amounts in about 48 body tissues and fluids. Lungs [1] and trachea contain 2.5-4.5 mg/g and 0.2 mg/g ash respectively. It is present in the heart in concentrations of 0.327-4.16 mg/kg/wet wt. Liver contains 3-23 mg/kg dry wt., kidney 1.5-27 mg/kg dry wt. blood 0.10-0.72 mg/l, and urine 100-1000 mcg/24 hr.

Some aluminium compounds have been studied as food additives in animals. In small amounts (1-2%) it stimulates the growth [2], but in higher amounts it gives rise to the retardation of growth accompanied by gross disturbances of phosphate and calcium metabolism. In human beings excessive occupational exposure leads to increased aluminium uptake with recorded changes in some serum enzymes.

Aluminium hydroxide gel, gelat in aluminium hydroxide; and colloidal aluminium hydroxide are used as antacid. It is used to provide symptomatic relief in gastric and duodenal ulcer and in reflux oesophagatis. It is also used in the treatment of hyperchlorhydria Diluted with 2-3 parts of water the aluminium hydroxide gel is used as intragastric drip. It is also used as an adjuvant in adsorbed vaccines to increase their potency and to reduce the incidence of undesirable reaction either by delaying the release of antigen or by altering tissue reactivity. Aluminium hydroxide in allergen injections acts by modifying tissue reactivity rather than by delaying the release of antigen from the tissue.

Complexes of aluminium have also been used as antacid. These are sodium polyhydro mono-carbonate-hexitol [3] and dihydroxy aluminium carbonate [4]. The latter has the following structure.



The aluminium complexes studied in the present paper are non-ionic, colloidal, hexitol and carbohydrate chelates. Preparation and characterization of aluminium-sorbitol, -sorbitol, citric acid, -sorbitol, dextrin and citric acid have been studied. The complexes with sucrose, glucose and dextrin reported [5] in the literature have also been incorporated for comparison. Studies on their efficiency as antacid are being undertaken and will be reported in another paper.

Methods and characterization of the complex: Aluminium chloride, $AlCl_3$ $6H_2O$ (8.9 g), equivalent to elemental aluminium (1 g) was dissolved in water (10 ml) and 15% sodium-hydroxide (30 ml) was added to it dropwise with vigorous stirring to obtain a precipitate of aluminium hydroxide. It was washed first with tap water and then with distilled water to get rid of electrolytes.

The wet aluminium hydroxide was taken in a dish, and the required quantities of carbohydrate, sorbitol, sodium hydroxide and citric acid was admixed thoroughly and heated at different temperatures for the periods indicated in the Tables. A dark brown cake which gave clear solution when dissolved in water was obtained. The solution was centrifuged and analysed. Different ratios were tried to get the ideal complex, but only successful results have been recorded. At low temperature or when the time of beating is shorter, the solution of the final product looks turbid against reflected light. On boiling the solution of such a complex gel formation took place.

Estimation: Aluminium complex (1 ml) was digested with 2 ml concentrated nitric acid and sulphuric acid (1:1) in a Kjeldhel flask adding nitric acid in a small portion (0.5-1 ml) until on evaporation it gave off white fumes of sulphuric acid and colourless solution was obtained. After cooling, water (2-3 ml) was added and the solution evaporated to white fumes. The same process was repeated twice to destroy nitrosyl sulphuric acid. Finally the solution was boiled with a little water and after cooling was made up to a definite volume (200 ml) with acetate buffer (pH 5.4) in a volumetric flask. Aluminium was estimated colorimetrically using 8-hydroxy quinoline, 1% in chloroform at 410 nm.

Stability of the complex on boiling: The complex containing 1% aluminium was ampouled and boiled at 100° for 1 hr. or at 115° for 30 min. in an autoclave. The stable complex remained clear and transparent while the unstable complex became turbid or formed micelles or gel.

Reaction on admixture with egg albumin: Fresh egg albumin was prepared by mixing with water in the ratio of 1:6 according to the method of Hawk. To this solution were added 5 ml. of aluminium chloride (0.1%) and admixed thoroughly. The precipitation of albumin started on the addition of 0.2 mg of elemental aluminium while complete precipitation was observed on the addition of 0.25 mg.

The aluminium complexes (pH 7.1-7.0) were also added in the same manner but no preciptation was observed on the addition of 2.5 mg elemental aluminium which is 10 times that of ionic aluminium.

Stability on admixture with saline: The solution of 0.9% sodium chloride (100 ml) was added to 1% aluminium complex (10 ml) and mixed thoroughly. The solution on keeping for 24 hr. at room temperature did not show any visual sedimentation, coagulation or gel formation.

Stability on admixture with other metal complex: Aluminium complexes containing 1% elemental aluminium were admixed thorughly with 1% iron, cobalt and zinc complexes in a ratio of 1:1 and kept for 24 hr. at room temperature. The solution remained clear, showing no sedimentation, coagulation or gel formation. This solution was then ampouled and autoclaved at 115° for 30 min. It remained clear and transparent against reflected light showing no adverse deterioration in its stability.

Stability at different pH: The pH of the preparation in auqeous solution was regulated within the range of 1-8 with 0.1-1.0 N hydrochloric acid in accordance with the method of Nissim [6] and Robson. The Al concentration in all the solutions was 1 mg/ml. After the solution had been kept standing for 24 hr. at room temperature, the precipitate was removed by centrifugation and the aluminium contents and pH in the supernatent determined. The results from these studies showed that the complexed precipitated within the pH range of 4.3-3.2. There was no precipitation between pH 4.5–8.

Density and viscosity: The density and viscosity of the aqueous solution containing 1% aluminium of the best samples [No. 2 (Table 1), No. 2 (Table 2), No. 3 (Table 3)] were 1.228, 0.00536 poise; 1.0580, 0.00155 poise and 1.0533, 0.0014 poise respectively.

DISCUSSION

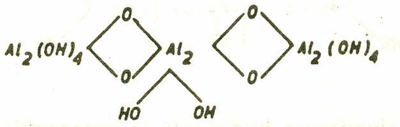
Aluminium chloride was dissolved in boiled water and a calculated amount of sodium hydroxide was added for the preparation of aluminium hydroxide. In excess alkali

Table 1. Al-Sorbitol complexes

Expt. No.	Ratio of Al:sorbitol in g.	Ratio of Al:NaOH in g.	Temperature (°C)	Time in hours	pH of the complex	Stability on long boiling	Metal in complex	Isoelectric point
				Sorbitol variable				
1.	1 : 25	1 : 3.0	170°	3.00	12.1	Stable	98.0%	8.2-8.0
2.	1 : 20	1 : 3.0	170	3.00	12.0	Stable	97.0%	8.4-8.0
3.	1 : 10	1 : 3.0	170	3.00	11.6	Unstable	–	–
				Alkali variable				
4.	1 : 20	1 : 3.0	170	3.5	12.0	Stable	97.0%	8.4-8.0
5.	1 : 20	1 : 2.5	170	3.5	11.8	Stable	96.2%	8.5-8.0
6.	1 : 20	1 : 1.0	170	3.5	11.0	Unstable	–	–
				Temperature variable				
7.	1 : 20	1 : 3.0	200	2.5	–	Charring	–	–
8.	1 : 20	1 : 3.0	170	3.00	12.00	Stable	99.0%	8.4-8.0
9.	1 : 20	1 : 3.0	150	3.50	–	No formation	–	

aluminate is formed. The metal hydroxide was washed with distilled water quickly to free it from electrolytes. Complex formation does not take place if freshly prepared aluminnium hydroxide is not used. D. Tommasi [7] found that $Al(OH)_3$ formed with ammonia on keeping turned into a difficulty soluble product. Its solubility in hydrochloric, nitric, or acetic acid or in alkali lye is said to be as difficult as that of the calcined oxide. Tommasi suggested that the hydroxide perhaps became a crystalline hydrate. R. Phillip [8] also noted that aluminium hydrogel, freshly precipitated and washed in the cold, is readily soluble in acids, but if kept under water for some days, becomes sparingly soluble. This phenomenon has been observed by many workers. By means of X-radiogram J. Bohm [9] noted the passage from the amorphous to the crystalline state during the ageing of the gel and behaving like aluminium oxide. When the last washing of aluminium hydroxide was tested for chlorides, the test with silver nitrate was very negligible. This freshly prepared aluminium hydroxide suspension gives no indication of the presence of chloride. This, however, is more apparent than real. From the literature was found that metal hydroxides retained traces of chlorides [10]. Later on, when an aluminium complex is formed from such hydroxide, the soluble finished product does show the presence of chloride. The presence of such traces of chloride apparently has no effect on the formation of the ultimate complex. When the washing is insufficient larger quantities of chlorides are left adsorbed on the aluminium hydroxide. The carbohydrate complex formed from such chlorides containing hydroxides may give a clear solution but on long boiling produce sediments or gel.

The composition of the precipitated aluminium hydroxide according to E. Schlumberger [11] is not very definite and he claimed to have made $Al_{10}O_{22}H_{11}$, i.e. 10 $Al(OH)_3$ less $8H_2O$ or 5 $Al_2O_3 . 5H_2O$. The latter hydrate is represented by the formula:



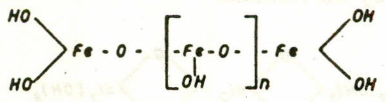
In another way 6 $Al(OH)_3$ less $4H_2O$ i.e. $3Al_2O_3$ $5H_2O$ may also be represented by two molecules of $3Al(OH)_3$ less $2H_2O$ or $Al_3O_7H_5$. This is isomorphic with ferrichydroxide ($Fe_3O_7H_5$) or $3Fe(OH)_3$ less $2H_2O$. This phenomenon has been observed with precipitated ferric and several other oxides as well. J.M. Bemmelen [12] called them absorption compounds and considered that the moist preparation contains either (i) water mechanically mixed with a precipitate or (ii) absorbed water. The amount of water is dependent on (i) the method of formation, (ii) the time, (iii) the temperature, and (iv) the presence of foreign

Table 2. Al-Sorbitol citric acid complexes

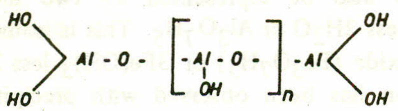
Expt. No.	Ratio of Al:S.C.A. in g.	Ratio of Al:NaOH in g.	Temperature (°C)	Time in hours	pH of the complex	Stability on long boiling	Metal in complex	Isoelectric point
Sorbitol variable								
1.	1:25:2	1:1.5	170	3.00	10.5	Stable	95.0%	3.6-3.3
2.	1:20:2	1:1.5	170	3.00	10.0	Stable	95.3%	3.05-3.0
3.	1:15:2	1:1.5	170	3.00	9.8	Stable	81.4%	3.8-3.5
Alkali variable								
4.	1:20:2	1:3.0	170	3.00	12.0	Stable	79.0%	3.4-3.2
5.	1:20:2	1:2.5	170	3.00	10.3	Stable	82.0%	3.4-3.2
6.	1:20:2	1:1.5	170	3.00	10.0	Stable	95.3%	3.5
7.	1:20:2	1:0.75	170	3.00	8.1	Unstable	–	
Temperature variable								
8.	1:20:2	1:1.5	200	2.50	–	Charring	–	
9.	1:20:2	1:1.5	180	2.00	10.0	Stable	81.0%	3.5-3.2
10.	1:20:2	1:1.5	170	3.00	10.0	Stable	95.4%	3.4-3.2

substances. H.W. Foote [13] found this to be the case with ferric, aluminium and zirconium hydroxides. In other words aluminium hydroxide $6Al(OH)_3$ less $4H_2O$ i.e. $3Al_2O_3$. $5H_2O$ is isomorphic with ferric hydroxide $6Fe(OH)_3$ less $4H_2O$ or Fe_2O_3 $5H_2O$ or $Fe_3O_7H_5$.

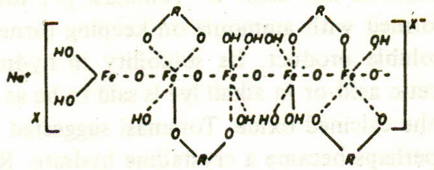
Schwietzer [14] has proposed the following structure for the colloidal oxide of iron.



and since aluminium hydroxide is isomorphic with ferric hydroxide it may be represented as follows:



For saccharated oxide of iron having an excess of alkali be proposed the structure (R = sucrose).



The structure of colloidal aluminium hydroxide chelate would likewise be as follows: (R = hexitol or carbohydrate).

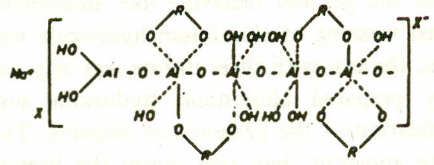


Table 3. Al-Sorbitol-dextrin-citric acid complexes

Expt. No.	Ratio of Al:S:D:C.A. in g.	Ratio of Al:NaOH in g.	Temperature (^oC)	Time of heating in hours	pH of the complex	Stability on long boiling	Metal in complex	Isoelectric point
				Sorbitol variable				
1.	1:15:4:2	1:1.5	170	3.00	8.0	Stable	94.0%	2.5-2.0
2.	1:10:4:2	1:1.5	170	3.00	8.5	Stable	96.2%	2.4-2.1
3.	1:5:4:2	1:1.5	170	3.00	9.00	Stable	93.9%	3.1-3.0
				Dextrin variable				
4.	1:5:4:2	1:1.5	170	3.00	9.7	Stable	93.8%	3.00
5.	1:5:3:2	1:1.5	170	3.00	9.45	Stable	96.0%	3.1-3.0
6.	1:5:1.5:2	1:1.5	170	3.00	9.1	Stable	94.4%	3.2-3.0
				Alkali variable				
7.	1:5:4:2	1:2.25	170	3.00	9.7	Stable	95.0%	2.3-2.1
8.	1:5:4:2	1:1.50	170	3.00	9.0	Stable	94.3%	3.1-3.0
9.	1:5:4:2	1:1.25	170	3.00	–	No formation	–	
				Temperature variable				
10.	1:5:4:2	1:1.5	180	2.00	9.6	Stable	88.0%	4.5-4.2
11.	1:5:4:2	1:1.5	170	3.00	9.45	Stable	88.2%	3.3-3.1
12.	1:5:4:2	1:1.5	150	3.00	–	No formation	–	

Table 4. Al-sucrose complexes

Expt. No.	Ratio of Al:sucrose in g.	Ratio of Al:NaOH in g.	Tempera-ture (°C)	Time of heating in hours	pH of the complex	Stability on long boiling	Metal in complex	Isoelectric point
Sorbitol variable								
1.	1:20.0	1:3.0	170	3.00	8.9	Stable	91.2%	4.1-3.9
2.	1:10.0	1:3.0	170	3.00	8.6	Stable	88.0%	4.0-3.8
3.	1:5.0	1:3.0	170	3.00	8.6	Unstable	–	–
Alkali variable								
4.	1:1.0	1:3.0	170	2.75	8.9	Stable	90.0%	3.8-3.6
5.	1:10.0	1:2.0	170	2.75	8.6	Stable	88.0%	3.4-3
6.	1:10.0	1:1.0	170	2.75	7.5	Unstable	–	–
Temperature variable								
7.	1:10.0	1:2.0	180	2.75	8.6	Stable	91.0%	4.0-3.8
8.	1:10.0	1:2.0	170	2.75	8.4	Stable	91.2%	3.5-3.0
9.	1:10.0	1:2.0	150	2.75	8.4	No formation		

Table 5. Al-glucose complexes

Expt. No.	Ratio of Al:glucose in g.	Ratio of Al:NaOH in g.	Tempera-ture (°C)	Time of heating in hours	pH of the complex	Stability on long boiling	Metal in complex	Isoelectric point
Glucose variable								
1.	1:20.0	1:3.0	170	3.00	7.65	Stable	91.3%	4.4-4.1
2.	1:10.0	1:3.0	170	3.00	7.50	Stable	90.0%	4.4-4.2
3.	1:5.0	1:3.0	170	3.00	7.5	Unstable	–	–
Alkali variable								
4.	1:10.0	1:3.0	170	3.0	7.8	Stable	84.0%	4.0-3.8
5.	1:10.0	1:2.0	170	3.00	7.6	Stable	83.0%	3.9-3.6
6.	1:10.0	1:1.0	170	3.00	7.5	Unstable	–	–
Time variable								
7.	1:10.0	1:3.0	170	3.00	7.8	Stable	91.0%	4.4-4.1
8.	1:10.0	1:3.0	170	2.50	7.6	Stable	90.0%	4.3-4.1
9.	1:10.0	1:3.0	170	2.00	7.6	Unstable	–	–

Table 6. Al-dextrin complexes

Expt. No.	Ratio of Al:Dextrin in g.	Ratio of Al:NaOH in g.	Tempera-ture (°C)	Time of heating in hours	pH of the complex	Stability on long boiling	Metal in complex	Isoelectric point
Dextrin variable								
1.	1:15.0	1:2.24	170	3.00	8.00	Stable	88.88%	3.9-3.7
2.	1:10.0	1:2.24	170	3.00	9.0	Stable	80.0%	3.9-3.6
3.	1: 5.0	1:2.24	170	3.00	9.6	Unstable	–	–
Alkali variable								
4.	1:15	1:3.00	170	3.00	10.0	Stable	87.03%	3.5-3.2
5.	1:15	1:2.24	170	3.00	9.6	Stable	88.80%	3.4-3.2
6.	1:15	1:1.50	170	3.00	8.2	Stable	80.00%	3.4-3.0
Temperature variable								
7.	1:15.0	1:2.24	200	2.30	– Charring –			
8.	1:15.0	1:2.24	180	2.50	9.6	Stable	88.0%	3.4-3.2
9.	1:15.0	1:2.24	170	3.00	9.8	Stable	85.0%	3.9-3.7

Aluminium forms a complex with sorbitol alone in ratio of Al 1g. Sorbitol (20 g) and NaOH (3 g) Table 1). We found in the case of iron [15] that its complexes with sorbitol are not stable on storage. After 2-3 months sedimentation took place and the concentration of the metal dropped. Its isoelectric point ranged between pH 7.5-6.5. The isoelectric point of aluminium-sorbitol complex ranged between pH 8.4-8.2. Although on storage sedimentation did not take place. It is unsuitable for oral or parentral use.

It formed a stable complex with sorbitol and citric acid in a ratio of Al (1 g), sorbitol (20 g), citric acid (2 g), (Table 2) and sorbitol, dextrin and citric acid in a ratio of Al(1 g), sorbitol (5 g), dextrin (4 g) and citric acid (2 g) (Table 3).

The isoelectric point or the pH at which precipitation take place with acid is a valuable means for determining the stability of the complexes. This is due to the fact that these complexes are alkaline and the binding of Al with hexitol and carbohydrates is more firm if the pH of the precipitation is lower towards the acidic side. The isoelectric point of aluminium complexes ranged between pH 4.3-3.2, with the exception of Al-sorbitol.

The tests with egg albumin substantiate the finding that metal ions interact with protein while non-ionic complexes do not. Aluminium chloride in concentration of 0.2-2.5 mg precipitated the egg albumin while aluminium complexes upto 2.5 mg did not have any effect.

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