Study of Aluminum Gallic Acid and Aluminum Gallic Acid Methyl Ester Potentiometrically using Computer Program BEST

SHABANA AMIN, ZAHIDA T. MAQSOOD AND S. ARIF KAZMI*
Department of Chemistry, University of Karachi, Karachi- 75270, Pakistan

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Summary: Potentiometric studies on complexation reaction between Al^{3+} (which has recently been implicated in neurological dysfunctions including Alzheimer's disease) and 3,4,5-Trihydroxybenzoic acid (gallic acid) and its methyl ester has been investigated. A computer program BEST was use to analyse the data. It is found that gallic acid forms 1:1 complex up to pH 8.5 and a 1:2 complex between pH 8.5 and 11.0. Log β_1 and log β_2 values are 18.76 and 29.52, which are higher than those of Fe^{3+} complex of the same ligand. The methyl ester of gallic acid forms 1:1, 1:2 as well as 1:3 complexes with log β_1 log β_2 and log β_3 values of 23.8, 33.83 and 39.63 respectively. Implications of these formation constants for polyphenol complexes of Al^{3+} upon Al absorption and resulting toxicity are discussed.

Introduction

Aluminum is the most abundant element in the lithosphere, after oxygen and silicon. In nature it is not implicated in any known biological, biochemical or metabolic function and it is normally excreted by kidneys without any damage to the organism. If excess aluminum is absorbed or its excretion is disturbed, it accumulates in the tissues impairing their functions [1]. Aluminum has been implicated in the pathogenesis of Alzheimer's disease which is also called senile dementia [2,3].

In order to understand the relationship of aluminum and its pathogenic characteristics in Alzheimer's diseases [4], the following information would be desirable.

1) How and in what chemical form aluminum is absorbed ?
2) How aluminum is transferred through the GIT ?
3) What is the nature of the toxic species ?
4) Does it interfere with an essential biological element ?

To attempt to answer some of these questions, we have undertaken a study of complexation of Al by potential ligands found in nutritional matrix, such as 3,4,5-trihydroxy benzoic acid (Gallic acid) and its methyl ester. These compounds are ultimate hydrolysis products of condensed polyphenols found in foods like tannins of tea [5,6]. Some characteristics of Al^{3+} complexation by biological ligands have been reported [7,8,9]. Complexation of Aluminum by these molecules may have an effect on its absorption.

The present work describes a Potentiometric study of interaction of Al^{3+} with Gallic acid and Gallic acid methyl ester.

Results and Discussion

The potentiometric titration curves (pH vs volume of base added) for 3,4,5-trihydroxybenzoic acid and its Al^{3+} complex are shown in Figure 1 and for the methyl ester and its Al^{3+} complex are shown

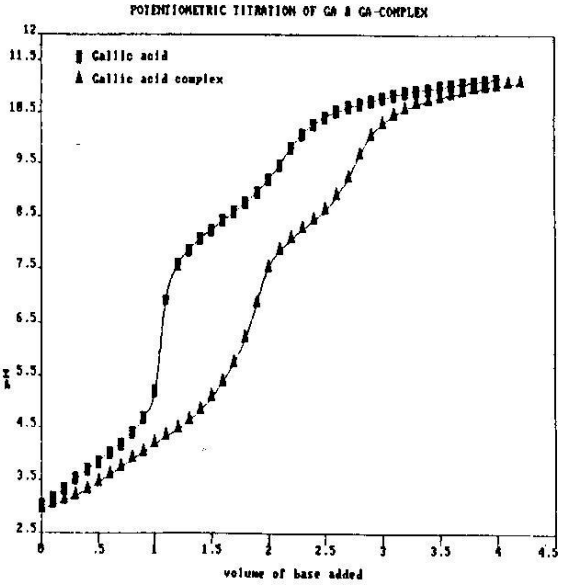

Fig. 1: pH-titration of 100.0 ml ($5x10^{-3}$M) Gallic acid (GA) and 100.0 ml of Al^{3+}-Gallic acid mixture mixed in (1:5) ratio with $[Al^{3+}]=1x10^{-3}$M with 1.20 M NaOH.

*To whom all correspondance should be addressed.

in Figure 2. The data was analyzed by the computer program BEST [11]. The steps in treatment of potentiometric data by BEST has been described earlier [10]. Tables 1 and 2 list the species and their respective log β values obtained as the best fits of the data for the gallic acid - aluminum system (sigma fit = 0.041) and the gallic acid methyl ester-aluminum system (sigmafit = 0.021). Figures 3 and 4 are the species distribution curves (percent species *vs* pH) for the aluminum complexes of gallic acid and its methyl ester.

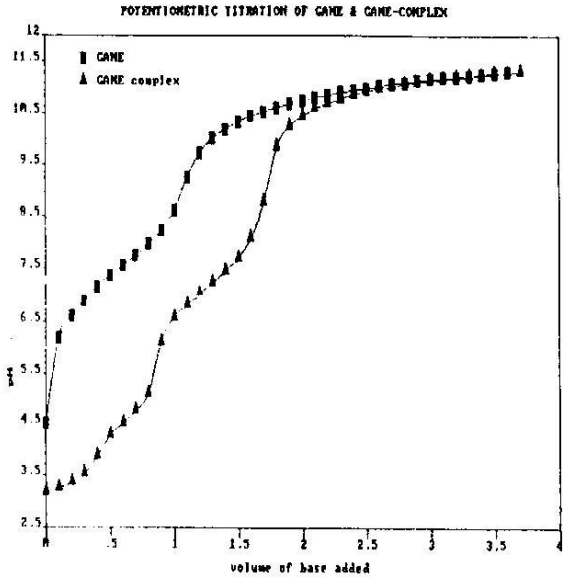

Fig. 2: pH-titration of 100.0ml ($5x10^{-3}$M) Gallic acid methyl ester (GAME) and 100.0 ml of Al^{3+} -Gallic acid methyl ester mixture mixed in (1:5) ratio with $[Al^{3+}]=1x10^{-3}$M with 1.10 M NaOH.

Table 1: Best sigfit (0.041) was obtained when the following species were considered

Species	pH range	log β
1A1:1GA:1H	3.0-4.0	23.76
1A1:1GA	4.0-8.5	18.76
1A1:2GA	8.5-11.0	29.52

Table 2: Best sigfit (0.021) was obtained when the following species were considered.

Species	pH range	logβ
1A1.1GAME	4.0-7.0	23.80
1A1.1GAME:10H		11.82
1A1:2GAME	7.0-10.5	33.83
1A1:2GAME:20H		10.16
1A1:3GAME	10.5-12.0	39.63

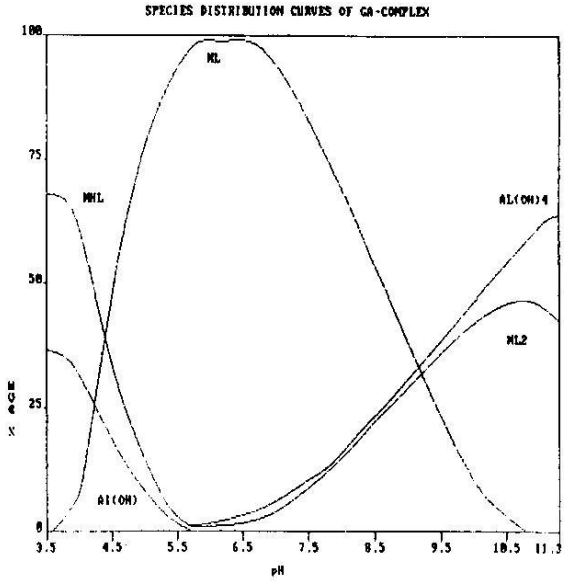

Fig. 3: Distribution of various species of Al^{3+} complex with Gallic acid as a function of pH.

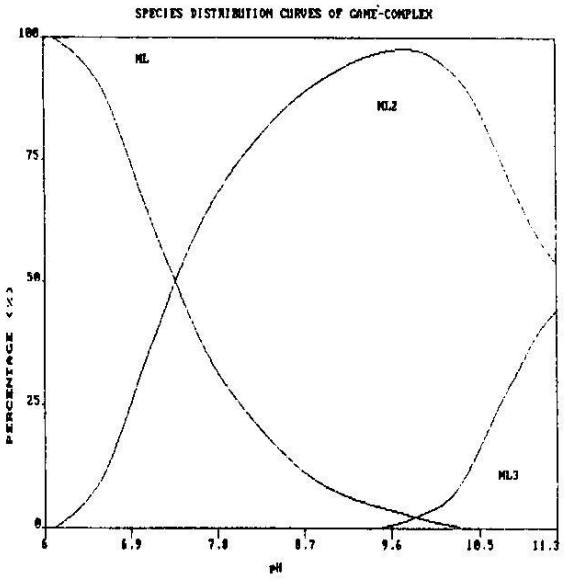

Fig. 4: Distribution of various species of Al^{3+} complex with methyl ester of gallic acid at different pH.

Other species which were also considered inclu -ded 1A1:1GA:10H; 1A1:2GA:1H; 1A1:2GA:2H; 1A1:2GA:10H and 1A1:2GA:20H and the corresponding species for gallic acid methyl ester. Inclusion of these species gave sigmafits of the order of 0.45-0.50 whereas their exclusion species by specie or by groups of species failed to improve the sigmafit sig-

nificantly till the species as postulated in Table 1 and 2 alone were considered. The noteworthy observation here is that for the methyl ester we see a higher stoichiometry (1A1:3MEGA) compared to the gallic acid complex. A1 (III) has a very small ionic radius and radius ratio rules would predict a low co-ordination number. At high pH, gallic acid would have extra negative charge (COO^- and OH^-) and these -ve charges would repel each other causing instability of such species. In the methyl ester case on the other hand, since there is no negatively charged carboxylate group we see a 1:3 complex.

It is seen that up to pH 8.5 only one molecule of gallic acid co-ordinates with each Al^{3+} ion. Above this pH and up to a pH of 11.00 two molecules of gallic acid co-ordinate with each Al^{3+}. The β values for complexation of Al^{3+} by gallic acid are higher than the corresponding values for complexation of Fe^{3+} by this ligand. On the other hand methyl ester of gallic acid forms complexes of three different stoichiometries, i.e. 1:1, 1:2, and 1:3. Like the Al^{3+} complexes of gallic acid, those of its methyl ester analog are more stable than their corresponding Fe^{3+} complexes, i.e., the β values (formation constants) of Al^{3+} complexes are higher. Polyphenols and their hydrolysis products are implicated in reduced absorption of iron [12]. The higher stability constant values for these aluminum complexes may mean even less A1 absorption unless stronger A1 receptors are available or if these complexes have somehow increased penetration of blood-brain barrier to deposit in brain.

Experimental

All reagents used were of AR or reagent grade. Solutions were made in deionized distilled water (Deionizer CSW-300) freed from CO_2 by boiling for 10 minutes. This water was cooled in an air tight flask. For all pH measurement Orion pH-meter, model SA 720, was used. A 0.05 M solution of potassium hydrogen pthalate, which has pH value 4.010 at room temperature (25°C) was used to calibrate the pH meter along with a standard buffer solutions made from BDH standard chemicals.

Procedure

For potentiometric titrations a double walled glass cell was used which was designed in our laboratory. The temperature was controlled by circulating thermostated water through the jacket. The solution was protected from the atmosphere.

Potentiometric Titrations

These experiments were done as described earlier for Fe^{3+} complexes [10] 100 cm^3 of deionized and CO_2 free water was taken in the above mentioned cell. 5 m moles of gallic acid or its methyl ester and 1mmole of aluminum sulphate were dissolved in this water. The solutions were purged with purified nitrogen gas for half an hour. The temperature was controlled at 30°C by means of circulating water from a thermostated water bath.

Gallic acid-Al^{3+} system was titrated against 1.2 M sodium hydroxide solution. Small increments (0.1 cm^3) were added till equilibrium conditions as determined by a constant meter reading ±0.002 pH unit was maintained for 2 minutes. Similarly titration for Gallic acid and its methyl ester (metal-free) were performed to confirm their respective PKa values.

The methyl ester analog was similarly titrated against 1.1 M NaOH.

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