EQUILIBRIUM STUDY ON BINARY AND TERNARY COMPLEXES OF Pb (II) WITH COMMONLY USED DRUGS AND DIETARY LIGANDS UNDER PHYSIOLOGICAL CONDITIONS

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Introduction

Toxic metal ions can enter the human body through various means such as air, drinking water and food *etc.* Lead, cadmium, mercury, copper and arsenic are some of the common toxic metals. If the body's detoxification pathways of these toxic metal ions are not fast enough, they can accumulate in the body tissues and cause many health problems. They can be harmful even at low concentration levels. Urinary and fecal excretion by chelation therapy using synthetic or natural chelators is the only treatment to remove such heavy metals from the body (Laurie, 1975). Due to high usage of lead in industry, burning of coal and petroleum, and incineration of waste materials, lead is considered as the most widely distributed toxic metal. As a result of very high usage of motor vehicles, industrialisation, use of large amounts of pesticides on fruits and vegetables, and consumption of various types of canned foods and beverages Sri Lankans are also exposed to high levels of lead.

This study focused on the determination of formation constants of Pb(II)-binary and Pb(II)-mixed ligand (ternary) systems by mimicking *in vitro* conditions (physiological conditions). The objective of this research is to study the interaction between lead and some common drugs; ascorbic acid (AsC), salicylic acid (Sali) and Paracetamol (Para), dietary ligands; citric acid (Cit), caffeine (Caf) and nucleic acid uracil (Ura) using the Kelvin type pH titration method.

Materials and Methods

All reagents used were in analytical grade. Active ingredients of pharmaceuticals were obtained from State Pharmaceuticals Manufacturing Corporation. NaOH and HNO_3 solutions were standardised with primary standard pottasium hydrogen pthalate (KHP) and anhydrous sodium carbonate (Na_2CO_3) solutions respectively. Temperature and ionic strength of each reaction mixture were maintained at 37.0 +/- 0.2 ^{0}C and at 0.15 M $NaNO_3$, respectively. Further, nitrogen gas was purged to avoid interference from CO_2 in the atmosphere. The pH measurements were taken with a temperature controlled digital pH meter (MARTINI, MI151).

Formation constants of both systems were calculated using Irving –Rossotti equations. (Irving *et al.*,1954). Stability of ternary systems over binary systems was statistically calculated.

For any two ligands A, B forming complexes with a metal ion M^{n+}

statistical relationship can be given using following reactions.

$M + B \rightarrow MB$ (1)

K^{M}_{MB} = Stability constant for reaction 1

$MA + B \rightarrow MAB$ (2)

K^{MA}_{MAB} = Stability constant for reaction 2

$$\Delta \log K = \log K^{MA}_{MAB} - \log K^{M}_{MB}$$

If $\Delta \log K$ is positive, it means that the ternary system is more stable (Huber *et al.*, 1969).

Table 1. Different titration mixtures used

Titration mixture	0.03 M HNO_3/ ml	0.01 M A / ml	0.01M B / ml	0.01 M $Pb(NO_3)_2$/ml	Deionized water/ ml	Total / ml
(HNO_3+A)	10.00	00.00	00.00	00.00	30.00	40.00
	10.00	10.00	00.00	00.00	20.00	40.00
	10.00	10.00	00.00	10.00	10.00	40.00
(HNO_3+A+B)	10.00	10.00	10.00	00.00	10.00	40.00
	10.00	10.00	10.00	10.00	00.00	40.00

Results and Discussion

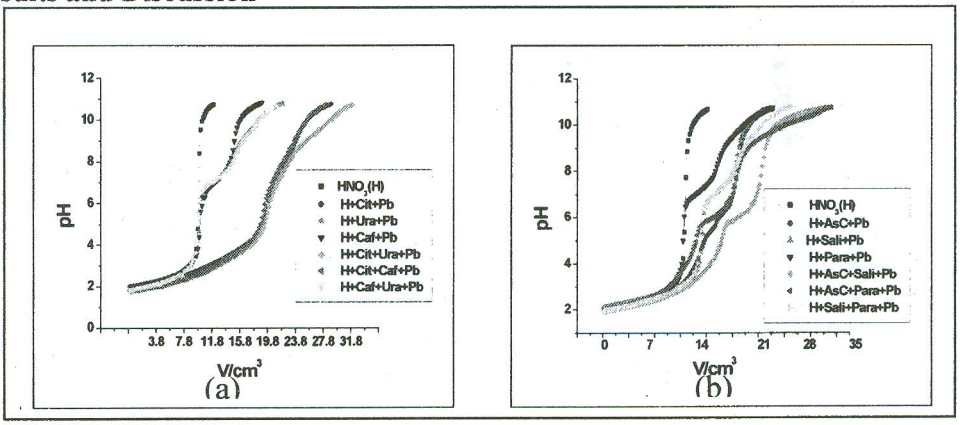

Figure 1. a) Titration curves for Cit, Ura, Caf Binary and ternary systems with Pb(II) b) Titration curves for AsC, Sali, Para Binary and ternary systems withPb(II)

The formation constants, K^{f}_{1} (first formation constant) and K^{f}_{2} (second formation constant) of both binary and ternary complex systems and $\Delta \log K$ values were obtained (Table 2) using the titration curves given in figure 1 (a) and (b).

Table 2. Formation constants and Δlog K values for different systems

System	Cit+Pb	Ura+Pb	Caf+Pb	Cit+Ura+Pb	Cit+Caf+Pb	Ura+Caf+Pb
Log K^{T}_{1}	10.29	13.55	2.43	17.89	9.22	8.11
Log K^{T}_{2}	3.05	4.88	-	4.82	4.14	2.96

System	AsC+Pb	Sali+Pb	Para+Pb	AsC+Sali+Pb	AsC+Para+Pb	Sali+Para+Pb
Log K^{T}_{1}	12.1	8.48	4.81	16.42	12.10	14.60
Log K^{T}_{2}	5.01	5.58	-	5.67	5.32	7.99

System	AsC+Sali+Pb	AsC+Para+Pb	Sali+Para+Pb	Cit+Ura+Pb	Cit+Caf+Pb	Ura+Caf+Pb
Δlog K	-2.81	0.51	3.18	-5.47	1.71	0.53

Complex formation was studied using UV absorption spectroscopy as well. Citric acid is contained in most beverages and some foods. Ascorbic acid, citric acid and caffeine can also be taken as dietary ligands. Therefore, these ligands can enter the stomach very often. Since stomach fluids are acidic in nature, for all the titrations, an acidic medium was maintained by the addition of a constant amount of 0.03 M nitric acid to each titration mixture to mimic physiological conditions.

Conclusion

Among the ligands considered, caffeine appears to interact weakly with Pb. This is evident even from the structure of caffeine which does not have functional groups suitable for binding to Pb. In many ternary systems, values obtained for Δlog K is positive showing that ternary systems are more stable. Hence ternary systems of metal complexes may play a much better role in chelation therapy.

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