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USE OF ANTIMONY (V) ARSENOSILICATE BEADS FOR ESTIMATION OF IRON CONTENT OF AYURVEDIC AND ALLOPATHIC PREPARATIONS

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Abstract: A method has been developed for the standardization of Indian ayurvedic drugs containing iron, using inorganic ion exchange material antimony (V) arsenosilicate cation exchanger. The iron present in the drug was absorbed quantitatively on the columns of the exchanger, eluted with a suitable solvent and then titrated against a standardized EDTA solution.

Key words: ayurvedic drugs iron content cation exchanger

INTRODUCTION

Inorganic ion exchangers have found application in the metal ion separation owing to their selective behaviour for certain metal ions (1). These materials have also demonstrated a potential use in the metal analysis of pharmaceuticals. Antimony (V) arsenosilicate (AAS), an ion exchanger synthesized in the investigation laboratory (2), has shown a high selectivity for Fe (III). It was considered worthwhile to explore the possibility of its use in estimating iron content of ayurvedic medicines used for the treatment of iron deficiency anaemias and for their standardization. Anaemia, especially caused by deficiency of iron, is in our population because malnutrition is very common. Parasite and helminth disease, infections and several other factors (3).

Several iron containing pharmaceutical preparations are available in the market manufactured by different pharmaceutical houses. Lohasava is one such preparation. Its method of preparation is described in standard ayurvedic texts, but in the absence of any available method for the estimation of its iron content, its therapeutic efficiency has always remained suspect as compared to iron preparations of modern system of medicine. The present attempt is in the direction of estimation of iron content of Lohasava manufactured by different pharmaceutical houses and in different batches of some established manufacturing houses. It is not only the low dose of iron which will leave the anaemia uncovered, an excessive dosage of iron may be harmful due to the deposition of unused Fe in various organs of the body (4). In view of this a judicious use of the drug is important for which its standardization is required. The following pages summarize the results of our attempt in this direction. Fesovit (Eskeyef), Fefol and Lohasavas of various companies have been quantitatively analysed for the presence of Fe, using antimony (V) arsenosilicate as the adsorbent.

EXPERIMENTAL

Reagents and chemicals: Potassium pyroantimonate [$KSb(OH)_6$] and sodium metasilicate [$Na_2SiO_3 . 5H_2O$] were obtained from Loba-Chemie

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(India) while sodium arsenate [$Na_2HAsO_4 . 7H_2O$] was a CDH product. Other reagents and chemicals were of Analar grade.

Preparation of the reagent solutions : Decimolar solutions of sodium metasilicate and sodium arsenate were prepared in demineralized water (DMW). Calculated amount of potassium pyroantimonate was dissolved in 5·8M HCl solution to obtain its 0·1M solution.

Synthesis of the ion-exchange material : Antimony (V) arsenosilicate was prepared by an earlier method (2), the main points of which are given below :

Decimolar aqueous solutions of sodium arsenate, potassium pyroantimonate and sodium metasilicate were mixed in the volume ratio 1:2:1, fixing the pH of the resulting gel in the range 0-1 by adding aqueous ammonia with constant stirring. The gel thus obtained was kept for 24 hrs at room temperature (~30°C) and filtered, removing the excess acid and washing with DMW, before drying the material in air oven at 45°C. The material was finally cracked into small granules of uniform size by putting in DMW. These granules were converted into the H^+ - form by treating with 1M HNO_3 for 24 hrs with occasional shaking, intermittently replacing the supernatant liquid with fresh acid. The material thus obtained was finally washed with DMW to remove the excess acid before drying at 45°C and obtaining particles of the size 50-70 mesh by sieving.

Distribution studies: Various 200 mg portions of the exchanger in H^+ - form were taken in 20 ml of the different metal solutions in the required medium and kept for 4 hours with intermittent shaking to attain equilibrium. The initial metal ion concentration was so adjusted that it may not exceed 3% of the total ion exchange capacity of the material. The metal ions in the solutions before and after equilibrium were determined by the EDTA titration (5). The alkali metal ions were determined by flame photometry. Distribution coefficient (Kd) were calculated by the formula

$$Kd = \frac{I - F}{F} \cdot \frac{V}{M} \text{ (ml/gm)}$$

where

I = Initial amount of the metal ion in the solution phase.

F = Final amount of the metal ion in the solution phase.

V = Volume of the solution (ml).

M = Amount of the exchanger (gm).

Treatment of the drug samples : To prepare the stock solution of the drug, one capsule of fefol or fesovit (allopathic drugs) was heated with a minimum amount (~ 10 ml) of the oxidizing mixture (Conc. HNO_3 + $HClO_4$, 1:2) to destory the organic matter completely till a clear solution is obtained. The volume of this solution was reduced to 1-2 ml to remove excess acid and was made 100 ml with DMW in a standard flask. "Lohasava" which is a liquid, was measured by volume, 5 ml of this drug was treated with the oxidizing mixture as above before following the rest of the procedure. This treatment transfers Fe (II) into Fe (III).

Adsorption of iron from drugs and its determination : 2 gm of the exchanger (50-70 mesh) in H^+ - form was taken in a glass tube with an internal diameter of ~ 0·6 cm and containing glass wool at its bottom. The column was washed thoroughly with DMW and 1 ml of the stock solution was loaded on it, maintaining a flow rate of 2-3 drops/min. The Fe(III) ions present in the solution are thus retained on the column due to the high selectivity of the material for these ions. They were then leached out with 1M NH_4NO_3 as eluant and the effluant was analyzed for the presence of Fe (III) - ions by EDTA titrations using Cu-PAN as indicator.

RESULTS

The Na^+ ion exchange capacity (*i.e.* c) of the material was obtained by the column process as usual (6) and was found to be 1·62 meq/dry gm.

The distribution coefficients (Kd) for some common metal ions on antimony (V) arsenosilicate in DMW and some other solvent systems are summarized in Table I. Tables II and III summarize the results of the determination of iron in the drugs.

TABLE I : Kd values of some metal ions on antimony (V) arsenosilicate cation exchanger.

Metal ions ↓	DMW	Solvents										
		0·01M HNO_3	0·1M HNO_3	1·0M HNO_3	0·01M $HClO_4$	0.1M $HClO_4$	1.0M $HClO_4$	CH_3OH	C_2H_5OH	C_3H_7OH	Citric acid 1.0%	Oxalic acid 1.0%
Na (I)	2400	150	38.8	5.26	233.3	78.57	51.50	2400	2400	2400	6140	2560
K (I)	1560	177.7	28.30	11.11	72.41	38.80	19.04	1566	1566	455	6950	203
Mg (II)	7100	620	80	44	620	140	44	7100	260	260	140	140
Ca (II)	7400	650	650	50	650	87.5	50	650	275	275	316	316
Sr (II)	2400	150	150	150	150	150	150	150	150	150	150	150
Ba (II)	5400	450	450	175	450	450	175	175	175	45	37.50	83.3
Mn (II)	7700	680	290	160	290	95	56	7700	7700	7700	316	316
Fe (III)	10400	10400	10400	10400	10400	10400	10400	10400	10400	10400	10400	10400
Co (II)	6400	6900	600	133	6900	600	600	6900	6900	600	600	6900
Ni (II)	7900	700	700	300	7900	7900	700	7900	7900	700	700	100
Cu (II)	6500	6500	560	230	6500	560	560	6500	6500	560	560	560
Zn (II)	8300	8300	8300	740	180	110	110	8300	740	320	110	320
Cd (II)	7100	7100	620	40	7100	620	620	7100	620	620	260	260
Hg (II)	6400	6400	6400	550	550	550	550	550	550	225	550	550
Pb (II)	7500	660	660	660	660	660	660	7500	660	660	26.6	280
Bi (III)	7500	7500	7500	7500	7500	7500	660	7500	7500	7500	660	660

TABLE II : Quantitative determination of iron from iron preparations using antimony (V) arsenosilicate columns.

Trade name of the drug	Labelled composition of the drug (each capsule)	Amount loaded (μg)	Amount found* (μg)	%Error	Standard deviation
Fesovit (Eskeyef)	Ferrous sulphate 150 mg, Ascorbic acid 50 mg, Riboflavin 2 mg, Thiamine mononitrate 2 mg, Nicotinamide 15 mg, Pyridoxine Hydrochloride 1 mg, Pantothenic acid 2·5 mg.	524·99	516·60	−1·6	2·5
Fefol (Eskeyef)	Ferrous sulphate 150 mg, Folic acid 0·5 mg.	544·50	536·20	−1·5	2·34

*Mean value of five replicates.

TABLE III : Quantitative determination of iron in various samples of Lohasava marketed in India using antimony (V) arsenosilicate columns.

Manufactured by	*Batch No.*	*Amount of iron loaded (mg/15 ml of drug)*	*Amount of rion found (mg/15 ml of drug)*	*% Error*
Dabur India Ltd.				
22 Site IV, Sahibabad - 201 010 (U.P.)	2016	18·431	18·009	-2·3
Regd. Office : 813 Asaf Ali Road, New Delhi	2031	16·755	16·335	-2·6
Shree Baidyanath				
Ayurved Bhawan Ltd.,	15	54·450	53·616	-1·6
Gwaliar Road, Jhansi	18	16·755	17·500	+4·3
Dhanvantari				
Karyalya Bijaigarh	22	41·88	42·700	+2·0
(Aligarh)	25	25·98	25·140	-3·3
Zandu				
70, Gokhale, South	5198	37·68	36·450	-3·4
Bombay- 400 025	5309	20·94	20·106	-4·2

DISCUSSION

The study was designed to employ an inorganic ion exchanger for the estimation of iron content of formulations used in modern and ayurvedic pharmaceutical products for their metal ion content. The results (Tables II and III) indicate that the method is quite precise for the quantitative adsorption of iron on the colum of Antimony (V) arsenosilicate which is highly selective for this metal ion. The method can, therefore, be utilized for the standardization of drugs containing iron.

The regulations for ayurvedic and other indigenous system of medicine are almost nonexistant. The formulations do vary in their constituents depending upon the source of ingradients. This is reflected in the observations of the present study. The products from modern medicines are required to be prepared under strict criteria, where "Good Manufacturing Practice" is adopted as a mandatory practice. In such products the chances of variation in the quantity of constituents are uncommon. The two products selected, Fesovit and Fefol, were found to possess the quantity of iron (II) as specified by the manufacturer.

Methods for the determination of active ingradients in ayurvedic preparations are few and often not too accurate to be used as standard techniques. The standards for ayurvedic medicines usually relate to their methods of preparation which should be in accordance with the formula described in the authoritative books of the system as indicated in the first schedule of drug control. The prerequisite for the preparation of ayurvedic drugs in the Act is the "raw materials" used in the preparation of the medicines.

The guidelines for the manufacture of ayurvedic medicines are vague as the raw materials obtained from different sources may vary in their active ingredients. The result in the lack of uniformity in the quantity of constitutents and consequently the benefit accrued to the patient may also vary.

Iron is absorbed more easily in ferrous form which passes directly into and through mucosal cells into the blood stream where it is immediately attached to transferrin. The absorption of the iron in ferric form is less and also erratic. Therefore the practice of use of oral iron in ferric form for therapeutic purpose in iron deficiency (7) 'anaemias' has been discarded. The iron contained in Lohasava is also in ferrous form. It appears

that the ferric form in which iron is added initially might have been converted into the ferrous form by the adjuvants of Lohasava.

Lohasava is administered orally in dose of 15 ml three times day. Different preparations of Lohasava contains elemental iron ranging from 16·775 to 41·88 mg in one dose whereas ferrous sulphate which is commonly used as 300 mg tablet and is also administered three times a day provides 60 mg of elemental iron per tablet.

Considering the low and variable iron content of different Lohasava preparations and also differences in the iron content of different batches from the same manufacturing house makes these preparations less reliable for therapeutic purposes in iron deficiency anaemias. However, these preparations do provide the estimated daily iron requirement of the body, which varies from 0·5-1·0 mg in adult male and from 1·0- 2·2 mg per day in adult female and hence may also be useful to treat mild anaemias when treated for a long duration.

This study was planned to determine the contents of iron in various preparations of Lohasava manufactured by ayurvedic pharmaceutical houses. The technique for determination of iron was selected after several trials and errors. The iron content of Lohasava was separated by an ion exchanger antimony (V) arsenosilicate, which is highly selective for Fe (III) ions, as is evident from the Kd values (Table I). The exchanger was syntesized in these loboratories for the purpose of extracting iron from Lohasava by the method already established earlier (2).

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