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Determination of zinc in pharmaceutical preparations by atomic absorption spectrophotometry

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The analysis for Zn content of a variety of pharmaceutical preparations by atomic absorption spectrophotometry is recorded. The method for creams, ointments and pastes involves extraction with ether, dissolving the residue in HCl, followed by suitable dilution of the extract to bring the Zn content within the limits of the calibration graph, and measurement of the Zn content using the 213·9 nm resonance line. For lotions and dusting powders the initial ether extraction is neglected; for liquid preparations a simple dilution is required. The method showed a good degree of accuracy and precision and was specific for Zn no interference being encountered from a variety of metals and other common excipient materials that are used in pharmaceutical preparations.

Pharmaceutical preparations containing zinc are usually analysed by (a) direct ignition e.g. zinc ointment B.P.; (b) chelometric titration with the disodium salt of ethylenediaminetetraacetic acid (EDTA) e.g. zinc undecenoate ointment B.P.; or (c) titration with hydrochloric or sulphuric acid e.g. dusting powder of zinc and salicylic acid B.P.C. All these methods have their limitations due to matrix interferences (Garratt, 1964).

Atomic absorption spectrophotometry has been used to determine zinc in zinc insulin preparations (Spielholtz & Toralballa, 1969) and for the determination of a variety of other metals in pharmaceuticals (Dalrymple & Kenner, 1969; Leaton, 1970). Flame radiation interferences in such methods are relatively few and fairly readily surmounted. They are caused by elements or other components that chemically bind the atoms of the element of interest to form undissociated compounds, which prevents those atoms from participating in the absorption process. Such interferences, particularly marked with anions, can be overcome by the introduction of an additive substance, such as hydrochloric acid (HCl), to the blank, test and standard solutions, thus converting the metal ion to a single chemical form whose concentration is anion independent. We report an atomic absorption spectrophotometric method for the analysis of zinc in pharmaceutical preparations.

METHODS

Apparatus

Atomic absorption spectrophotometer: Perkin-Elmer model 290B equipped with a multi-element (Ca-Mg-Zn) hollow cathode lamp. The standard single slot burner head was used at a wavelength of 213·9 nm (instrument setting 084) and a slit width of 7 Å. An air-acetylene flame was used, the flow rates of each being adjusted to give a

lean, blue flame as recommended in the manufacturer's handbook. Atomizer flow rate was 3·8 cm^3 min^{-1}. A servoscribe recorder was used at a setting of 10 mV.*

Reagents

Blank solution. A 1 % v/v HCl solution is used as blank. It is used for making all dilutions of test and of standard zinc solutions.

Standard solution of zinc. Weigh accurately about 2·5 g of analytical grade zinc metal (BDH); dissolve it in a minimum amount of dilute HCl and transfer the solution to a 1000 cm^3 graduated flask, dilute to the mark with water and mix thoroughly (solution A).

Preparation of standard zinc solutions for atomic absorption. Dilute solution A 1 in 100; take 20 cm^3 of the resulting solution and dilute to 250 cm^3. The zinc content of this solution is about 2·0 μg cm^{-3}. From this diluted solution prepare a series of standards in the range 0·2 to 1·0 ppm. These standards and the 2·0 μg cm^{-3} solution were prepared every two days.

Procedures

1. *Preparation of zinc test solutions:* (specific dilutions are not given below for samples because of the variety of concentrations of zinc in the discussed preparations. As a general guide, prepare dilutions of samples that will give a theoretical concentration of zinc corresponding to the mid-point of the concentration range of the standards).

(*a*) *Creams, ointments and pastes:* thoroughly mix the preparation. Weigh out accurately about 0·1 g of the preparation into a 10 cm^3 centrifuge tube. Extract twice with solvent ether (approximately 5 cm^3) each time centrifuging, the ether layer being discarded. Add 1 cm^3 of concentrated HCl and warm to dissolve the residue. If necessary filter through Whatman No. 4 filter paper to remove any undissolved solids that are present. Dilute the extract or filtrate to exactly 50 cm^3 with deionized water (solution B). Make an appropriate dilution from this solution to give a final concentration of zinc in about the middle of the calibration graph, e.g. for zinc ointment B.P. containing 15·0 % Zn oxide, a 1 in 400 dilution is necessary.

In all cases two equivalent dilutions of solution B are prepared and the mean response obtained taken as the best estimate of the concentration of zinc present.

(b) *Calamine powder, calamine lotion, dusting powders:* the same method as described above is used with the exception that the preliminary extraction with ether is not required.

(c) *Liquid preparations:* dilute the liquid with blank solution to give a final concentration of zinc in about the middle of the calibration graph.

2. *Instrumental procedure:* let the instrument and lamp equilibrate for about 30 min before use. Set the wavelength dial to 084 and set the zero by aspirating the blank solution. Optimize the flame setting by raising or lowering the burner head when aspirating a standard solution. Aspirate standards, starting from the lowest to the highest, then aspirate blank. Analyse tests, followed by the standards again. Plot the percentage absorption against the concentration of zinc and determine the μg cm^{-3} of tests.

* The use of a titanium coated atomizer and burner head (available from Perkin-Elmer) is recommended, as prolonged use of HCl will lead to corrosion of the atomizer components, and pitting of the burner head if stainless steel is used; such corrosion will, in time, adversely affect precision.

RESULTS AND DISCUSSION

A comparison was made between the official assay methods and the atomic absorption method for the analysis of zinc content of a variety of official creams, ointments and pastes (see Table 1). Comparison of the means obtained shows that there is good agreement between the two methods in all cases. It can be concluded that the atomic absorption method in general has the same degree of accuracy as the official method for determining the content of zinc of these preparations.

Use was made of the F-test (Downie & Heath, 1970) to compare the precision of the two methods. F has a critical value of 3·18 (at the 5% level) for nine degrees of freedom. Comparison of the variances showed that except for two instances there was no significant difference in precision between the two methods. The precision for the zinc and salicylic acid paste was much better using the B.P. method and for zinc undecenoate ointment much better using the atomic absorption method.

Tables 2 and 3 record the results for the determination of zinc content in official dusting powders and liquids. These preparations were made up according to the B.P.C. specifications and a direct comparison made between the estimated content of zinc and the known content. The accuracy and precision of the atomic absorption method is good, particularly with the liquid preparations. The higher standard deviations recorded for the dusting powders are similar to those for the ointments, creams and pastes. This would suggest that the method is testing the uniformity of mixing.

The results of the determination of zinc content of a variety of calamine preparations are shown in Table 4. Again the precision and accuracy of the atomic absorption method compares favourably with the official assay method. As no official assay method is specified for calamine B.P. or calamine lotion B.P., this method may prove useful.

Table 1. *Results of the analysis for zinc in zinc creams, ointments and pastes by atomic absorption and by the official assay procedure.*

Preparation	Declared amount of zinc oxide (%)	Amount found by Atomic absorption [1] Mean and s.d. (%)	Relative s.d. (%)	Official assay [1] Mean and s.d. (%)	Relative s.d. (%)	F value
Zinc ointment B.P.	15·0	15·0 ± 0·40	2·7	15·2 ± 0·27	1·8	2·20
Compound zinc paste B.P.	25·0	25·1 ± 0·49	2·0	24·6 ± 0·37	1·5	1·80
Cream of zinc B.P.	32·0	32·0 ± 0·70	2·2	31·9 ± 0·44	1·4	2·53
Coal tar paste B.P.C.	24·2	24·4 ± 0·53	2·2	24·6 ± 0·38	1·6	1·95
Cream of zinc and ichthammol B.P.C.	26·3	26·6 ± 0·51	1·9	26·3 ± 0·41	1·6	1·68
Zinc and salicylic acid paste B.P.	24·0	23·7 ± 1·01	4·3	24·3 ± 0·13	0·5	60·37
Zinc and castor oil ointment B.P.	7·5	7·2 ± 0·27	3·8	7·4 ± 0·16	2·2	2·85
Compound ointment of resorcinol B.P.C.	4·0	4·1 ± 0·08	2·0	4·0 ± 0·08	2·0	1·00
Zinc undecenoate ointment B.P.	20·0*	19·4 ± 0·04	0·2	19·2 ± 0·25	1·3	39·05

* Results calculated as % Zinc undecenoate; [1] Mean and standard deviation (s.d.) of 10 determinations.

Table 2. *Results of the analysis for zinc in dusting powders by atomic absorption.*

Preparation[2]	Declared amount of zinc oxide (%)	Amount found by atomic absorption [1] Mean and s.d. (%)	Relative s.d. (%)
Dusting powder of alum and zinc B.P.C.	42·3	42·1 ± 0·57	1·4
Dusting powder of zinc and salicylic acid B.P.C.	20·1	20·3 ± 0·39	1·9
Dusting powder of zinc, compound B.P.C.	25·2	25·6 ± 0·50	2·0

[1] Mean and standard deviation (s.d.) of 10 determinations.
[2] These preparations were made up according to the B.P.C. specifications, the declared amount of zinc oxide being the amount present.

Table 3. *Results of the analysis for zinc in liquid preparations.*

Preparation	Declared amount of zinc sulphate (%)	Amount found by Atomic absorption [1] Mean and s.d. (%)	Relative s.d. (%)
Eye drops of zinc sulphate B.P.C.	0·25	0·25 ± 0·004	1·6
Compound eye lotion of zinc B.P.C.	0·35	0·35 ± 0·004	1·1
Lotion of copper and zinc sulphate B.P.C.	1·37	1·37 ± 0·010	0·7
Mouth-wash of zinc sulphate and zinc chloride B.P.C.	1·00*	1·098 ± 0·017	0·7
Lotion of zinc sulphate B.P.C.	1·00	1·02 ± 0·008	0·8

* Calculated as zinc content; [1] Mean and standard deviation of 10 determinations.

Table 4. *Results of the analysis for zinc in calamine preparations by atomic absorption and by the official assay method where appropriate.*

Preparation	Declared amount of zinc (%)	Amount found by Atomic absorption [1] Mean and s.d. (%)	Relative s.d. (%)	Official assay [1] Mean and s.d. (%)	Relative s.d. (%)	F value
Calamine powder B.P.	No official limit	57·8 ± 0·40	0·7	—	—	—
Cream of calamine B.P.C.	4·8	4·8 ± 0·11	2·3	4·7 ± 0·07	1·5	2·47
Calamine lotion B.P.	No official limit	11·0 ± 0·20	1·8	—	—	—
Oily lotion of calamine B.P.C.	2·9	2·8 ± 0·10	3·6	2·9 ± 0·08	2·8	1·56
Compound ointment of calamine B.P.C.	17·0	16·8 ± 0·38	1·8	16·9 ± 0·28	1·7	1·84

[1] Mean and standard deviation of 10 determinations.

Table 5. *Results of the analysis for zinc in some proprietary preparations by atomic absorption.*

Preparation	Declared amount of zinc or zinc compound	Amount found by atomic absorption [1] Mean and s.d. (%)	Relative s.d. (%)	Percentage of stated amount (%)
Vasogen Silicone A.A.[2] (Pharmax)	7·5% Zinc oxide; Calamine 1·5%	8·3* ± 0·09	1·1	96·5
Tinnefax (Burrough's Wellcome)	10% Zinc	10·5 ± 0·17	1·6	105·0
Thovaline (Ilon)	21·8% Zinc oxide	21·5 ± 0·48	2·2	98·6
Cream of calamine (Boots)	5·0% Zinc oxide; Calamine 15·0%	15·5* ± 0·20	1·3	100·0
Vasozinc (Smith, Miller and Patch)	0·25% Zinc sulphate	0·25 ± 0·003	1·2	100·0

* Calculated as % zinc oxide; [1] mean and standard deviation (n = 10); [2] acetone used as solvent instead of ether.

Table 5 shows the applicability of the given method to the determination of zinc content of a few proprietary preparations. The results obtained agree favourably with the stated amounts.

Atomic absorption has an advantage over other methods of analysis of zinc in that it has general applicability to a variety of preparations entailing the use of one general method of preparation of the sample for analysis. It is also rapid, sensitive and specific for zinc. The preparations chosen contained a variety of other metals such as iron, aluminium, copper and other common materials used in pharmaceutical formulations such as talc, starch, ointment bases. These had no significant effect on the results except for the one instance of zinc and salicylic acid paste B.P.

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