Convenient Method of Simultaneously Analyzing Aluminum and Magnesium in Pharmaceutical Dosage Forms Using Californium-252 Thermal Neutron Activation

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Abstract □ A commercial antacid suspension containing aluminum hydroxide and magnesium hydroxide products was used as a model sample to study the use of a californium-252 thermal neutron activation as a method for quantifying aluminum content as well as for the simultaneous assay of aluminum and magnesium. A 3.5-μg californium-252 source was used for the activation, and the induced aluminum-28 and magnesium-27 activity was simultaneously measured by sodium iodide crystal gamma-ray spectrometry using dual single-channel analyzers and scalers. The antacid suspension was contained in a chamber designed with the unique capability of serving as the container for counting the induced radioactivity in addition to being the irradiation chamber itself. Ten replicate irradiations were performed, and the precision was compared with 10 replicate analyses of the antacid suspension using the official ethylenediaminetetraacetic acid titration method. For aluminum the precision was 1.4 *versus* 0.62% for the titration method. For the magnesium the precision was 5.3 *versus* 0.79% for the titration method. This pilot study demonstrated that use of more intense californium-252 sources, which are commonly available, would provide a method that is competitive with the ethylenediaminetetraacetic acid titration method in precision and in other aspects as well.

Keyphrases □ Californium-252—thermal neutron activation, method of simultaneously analyzing aluminum and magnesium in pharmaceutical dosage forms □ Dosage forms—method of simultaneously analyzing aluminum and magnesium using californium-252 thermal neutron activation □ Aluminum—method of anlaysis in pharmaceutical dosage forms using californium-252 thermal neutron activation □ Magnesium—method of analysis in pharmaceutical dosage forms using californium-252 thermal neutron activation

Analysis of aluminum in pharmaceutical formulations by thermal neutron activation in a reactor has been proposed (1) as an alternative to the official but somewhat cumbersome ethylenediaminetetraacetic acid titration method (2). However, limited access to reactors often makes neutron activation an uneconomical and inconvenient analysis technique. The recent availability of high intensity, relatively inexpensive, californium-252 neutron sources provides another means of analyzing pharmaceuticals for certain activable constituents. This report is a study of the feasibility of using californium-252 neutron activation analysis for aluminum quantification as well as for the simultaneous assay of aluminum and magnesium. A commercial antacid suspension containing aluminum hydroxide and magnesium hydroxide products was chosen as a typical sample for this study. However, the technique should apply to other products containing one or both of these minerals such as aluminum hydroxychloride or sterile penicillin G procaine suspension, which often is formulated with aluminum stearate.

EXPERIMENTAL

The californium-252 neutron source was in the form of a needle 5-cm long and 0.5-cm in diameter. The californium-252 content at the time of irradiation was 3.5 μg, which gave an emission rate of 8.1×10^6 neutrons/sec.

The chamber (Fig. 1) in which the suspension was contained during irradiation also had the unique capability of serving as the chamber for counting the induced radioactivity following irradiation. During irradiation the chamber was placed upright in a tank of water moderator, such that the level of the water was the same height as the level of solution in the chamber. After irradiation the californium-252 source and its surrounding plexiglass moderator sleeve were removed from the chamber. The chamber was then simply inverted and placed over a sodium iodide crystal for counting, thereby resembling a Marinelli-type counting chamber. All irradiations were for exactly 36 min, followed by a 90-sec delay, and then a 36-min count. The predominant activation reactions of aluminum and magnesium (Table I) are caused by neutrons thermalized by the water moderator and by water present in the antacid suspension.

The instrumentation required for analysis of the gamma rays emitted from the magnesium-27 and aluminum-28 can be economically assembled by using dual single-channel analyzers and scalers. One analyzer–scaler was used to count the 0.83-MeV full-energy peak of magnesium-27 and the other analyzer–scaler simultaneously counted the 1.78-MeV peak of aluminum-28. The magnesium-27 analyzer was calibrated with a manganese-54 (0.835 MeV) standard source, and the aluminum-28 analyzer was calibrated with an aluminum-26 (1.81 MeV) standard. Figure 2 is a gamma-ray spectrum obtained using a multichannel analyzer to count the antacid sample showing the two full energy peak bands used to measure the magnesium-27 and aluminum-28 with the dual single-channel analyzers.

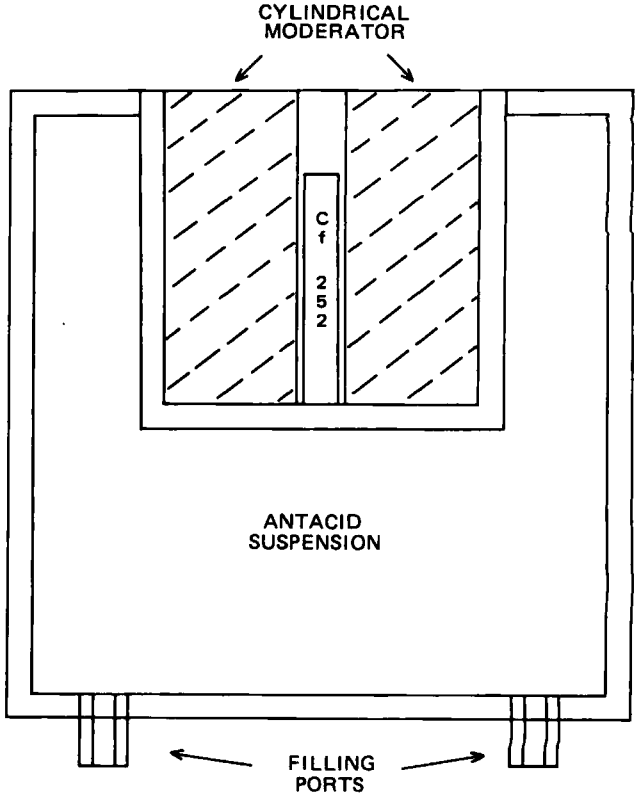

Figure 1—*Cross-section of cylindrical irradiation–counting chamber showing the californium-252 (Cf 252) source position. Diameter = 14.5 cm; height = 14.5 cm; volume = 2.1 liters.*

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Table I—Magnesium and Aluminum Reaction Parameters (3)

Parameter	Magnesium	Aluminum
Reaction	$^{26}Mg(n,\gamma)^{27}Mg$	$^{27}Al(n,\gamma)^{28}Al$
Isotope abundance	11.2%	100%
Cross section (thermal)	27 mb[a]	210 mb
Half-life	9.5 min	2.3 min
Gamma-ray energy	0.83, 0.01 MeV	1.78 MeV
Interferences	None	$^{27}Al(n,p)^{27}Mg$
Cross section	—	3 mb

[a] Millibarns.

Table II—Aluminum and Magnesium Analysis of Commercial Antacid Suspension by Californium-252 Neutron Activation Analysis and by the Official Ethylenediaminetetraacetic Acid Titration Method

Neutron Activation, net counts[a]		USP Method, %	
Aluminum 28	Magnesium 27	Equivalent Aluminum Oxide	Magnesium Hydroxide
5218	1221	2.20	4.04
5384	1147	2.21	4.00
5333	1102	2.19	3.98
5243	1244	2.18	3.96
5333	1180	2.20	3.97
5165	1127	2.17	3.99
5347	1080	2.20	4.03
5285	1121	2.20	3.97
5224	1187	2.18	4.05
5154	1146	2.21	4.01
Mean 5229	1166	2.19	4.00
SD 75.6	61.2	0.0135	0.0316
(1.4%)	(5.3%)	(0.62%)	(0.79%)

[a] Aluminum-28 background = 252 counts; magnesium-27 background = 1282 counts.

Ten replicate irradiations of the commercial antacid suspension were performed over a 16-day period. The counts of all replicates were normalized to the time of the first irradiation in order to correct for the decay of the californium-252 during the course of the experiment. A separate irradiation of only aluminum, in the form of a commercial aluminum hydroxide gel containing 9% equivalent aluminum oxide, was used to determine the Compton contribution of the aluminum-28 activity to the 0.830-MeV peak of magnesium-27. This constant ratio of the aluminum-28 peak counts to the counts in the magnesium-27 peak from aluminum-28 was used to remove the aluminum-28 contribution to the total magnesium-27 counts for each of the 10 irradiations.

Because of its low cross-section, the $^{27}Al(n,p)^{27}Mg$-interference reaction should not contribute significantly to the magnesium-27 peak. However, any contribution from that reaction would be eliminated when the Compton contribution to the magnesium-27 peak from aluminum-28 was subtracted.

To compare the precision of the californium-252 neutron activation analysis method with that of the official method, replicate analyses of the commercial antacid suspension were performed on 10 different days over a 2-week period by the official ethylenediaminetetraacetic acid titration method (2).

RESULTS AND DISCUSSION

The gross counting rates for the magnesium-27 and aluminum-28 peak channels were corrected for background, and in the case of the magnesium-27, for the aluminum-28 contribution to the 0.83-MeV magnesium-27 peak. The results are given in Table II along with the results of the ethylenediaminetetraacetic acid titration analysis.

It can be seen from Table II that the californium-252 method provides a precision for aluminum-28 that is considerably better than for magnesium-27. This is expected because of the higher thermal neutron activation cross section (Table I) for the $^{27}Al(n,\gamma)^{28}Al$-reaction. The precision for both aluminum and magnesium can be improved considerably by using a more intense californium-252 source than the relatively weak one which was used for this pilot study. Because of the large volumes used and the minimum amount of sample manipulation required, it can be assumed that the overall error in this technique is due entirely to the counting error. In this case the precision, expressed as the counting error, decreases inversely as the ratio of the square root of the total counts. Consequently, for example, if a californium-252 source 30 times the strength of the source utilized in this experiment were used, the magnesium-27 precision would be improved to $(\sqrt{1166}/\sqrt{1166 \times 30})$ (5.3%) = 0.97%, and the aluminum-28 precision would be improved by the same factor to a value of 0.26%.

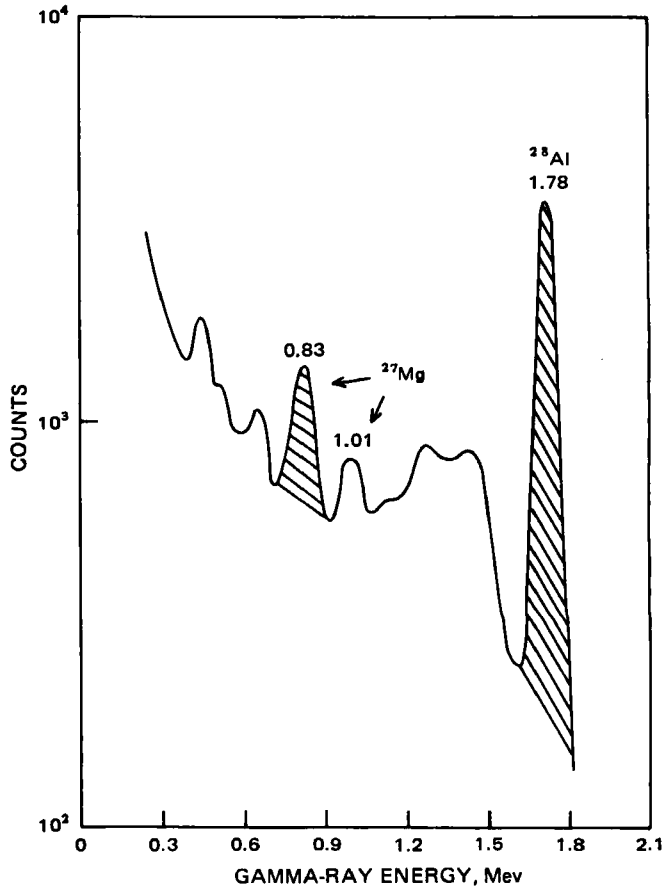

Figure 2—*Gamma-ray spectrum of neutron irradiated antacid suspension containing magnesium and aluminum showing the magnesium-27 and aluminum-28 peaks.*

This improved magnesium-27 value is competitive with the precision for the USP magnesium hydroxide method shown in Table II, and the aluminum-28 determination is more precise than the USP method for aluminum. Sources of californium-252 of this intensity, ~100 μg, are commonly available, relatively inexpensive, and the amount of shielding required is not restrictive. This technique, when used with an appropriate companion standard, should have potential application as an accurate, in-house quality control technique for products containing aluminum and magnesium.

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