Use of Activation Analysis in Problems of Drug Control

By LEON M. REYNOLDS*, WAYNE V. KESSLER, JOHN E. CHRISTIAN, and PAUL L. ZIEMER

Two major problems in drug control are the manufacture of counterfeit drugs and the diversion of legitimate drugs into illegal underground channels of distribution. In this study the use of neutron activation analysis was investigated for identification of the source of a drug product by analysis of certain trace elements added to it during manufacture, or by analysis of natural trace elements or contaminants already present. The usefulness of added trace elements was found to depend on the levels of natural contaminants. A level too high of the latter would require the addition of larger amounts of additives than physiological considerations permit. Thus, each drug product should be considered individually, after first establishing its natural contaminant content. Samples of dextroamphetamine tablets and capsules from five manufacturers, along with common tablet and capsule ingredients, were analyzed for natural contaminants. In the group, 17 elements were detected in amounts of less than 1 part per billion to over 0.1 per cent. The contaminants present in the tablets and capsules from the five manufacturers indicated each product was readily distinguishable from the others.

THE INTRODUCTION of new classes of drugs, particularly barbiturates, tranquilizers, amphetamines, and more recently the hallucinogens, has created new and difficult problems of control for law enforcement agencies. The widespread abuse of these new products has been well documented in popular periodicals. The Food and Drug Administration (FDA) has estimated that half the barbiturates and amphetamines produced legally in the United States are diverted into illicit systems of distribution (1). This diversion is possible largely through pilferage and the smuggling of exported products back into the country (2). Legislation in the form of the Drug Abuse Control Amendments of 1965, enforced by the FDA, provides for safeguards in the distribution of depressant and stimulant drugs. A second aspect of the control problem is the small scale practice of drug counterfeiting, in which clandestinely manufactured imitations of brand name products are merchandised in normal channels (3).

Any aids in product source identification will obviously be of material assistance in the enforcement program. The present work explores various aspects of product source identification through the use of neutron activation analysis (NAA). One approach is to arbitrarily introduce minute quantities of trace elements, having no effect on drug quality, which will show up at any future time under NAA. Another approach is to investigate contaminants already present in the drugs in the hope of their proving distinctive with respect to origin.

According to Robinson (4), pharmaceutical manufacturers have long added small quantities of harmless substances to products for identification purposes. Such tracers, usually detected spectrographically, are considered by both manufacturer and the FDA to be trade secrets. The present study shows NAA to be a promising alternate tracer detection technique, with the additional prospect that natural contaminants of a product may also be used as a means of source identification. Others have reached similar conclusions. Pro (5) reports that he has suggested to the FDA a list of possible elements as markers.

NAA is a sensitive, powerful analytical tool, effective for about two-thirds of the elements. Activation is ordinarily carried out by placing the sample in a nuclear reactor, where the large quantities of thermal neutrons present create radioactive nuclides through an (n, γ) nuclear reaction. Analysis is achieved by measuring the radioactivity of the product nuclides after a radiochemical separation procedure, or by direct γ ray spectrometry, with a scintillation detector and multichannel analyzer. This work makes use of the latter. Basic principles and applications of NAA are amply described in the litera-

Received December 9, 1966, from the Bionucleonics Department, School of Pharmacy and Pharmacal Sciences, Purdue University, Lafayette, IN 47907
Accepted for publication January 11, 1967.
* Present address: Department of Physics, Ball State University, Muncie, IN 47306

ture. Four recent reference books (6–9) list hundreds of applications in a variety of disciplines, but surprisingly few in the pharmaceutical sciences.

Using direct γ ray spectrometry without radiochemical separation, several investigators have presented evidence indicating the possibility that sources of phenobarbital and pethidine hydrochloride (10), moonshine whiskey (11), meprobamate and heroin (12), and raw opium (13) are readily distinguishable on the basis of the presence and relative concentration of trace elements. Schlesinger *et al.* (12) also report a private communication from Dr. V. P. Guinn saying that his group had used these techniques successfully with amphetamine tablets.

With these same techniques, Tuckerman *et al.* (14) have identified 13 trace elements in samples of 40 drugs and drug ingredients, in concentrations of 0.01 mcg./Gm. to 5%.

The arbitrary addition of tracers is applicable to a variety of drug products. The studies reported here, however, are concerned entirely with dextroamphetamine sulfate tablets and capsules, and diluents commonly employed in tablet and capsule manufacture.

EXPERIMENTAL

Systems of Additives—Minute quantities of trace elements could be added to drugs during manufacture either as a single element or in groups. The number of elements having the desired properties is quite limited and, if used singly, the list would be quickly exhausted. Consequently, group or multicomponent systems would be required if a large number of separate distinguishable tags was desired. It is believed that, if differentiation is to be based on quantitative measurement of the amounts of the additives present, such measurements could only have validity if expressed in relation to some internal standard included as an additive. Thus, it was decided to investigate a four-component system in which one of the components serves merely as a standard, against which the other three are varied and measured.

The amounts of additives to be used will depend on the quantities needed to override the radioactivity produced by natural contaminants in the drug product. It was essential, therefore, to determine the levels of natural contaminants. The second phase of this study was devoted to that end.

Selection of Additives—The basic equation for neutron activation is (15)

$$A_m = \frac{m\sigma f\phi N_0}{A}(1 - e^{-\lambda t_r}) \qquad \text{(Eq. 1)}$$

where A_m is the activity of the sample of mass m, σ the thermal neutron activation cross-section, f the fractional isotopic abundance, ϕ the thermal neutron flux, N_0 Avogadro's number, A the atomic weight, λ the radioactive decay constant, and t_r the time of irradiation. Criteria for the selection of an additive which follow from Eq. 1 are high natural isotopic abundance, high neutron activation cross section, and short half-life (but not shorter than about 30 min. to allow reasonable time for counting). Additional criteria used were a high γ ray yield per disintegration, a reasonably simple γ ray spectrum, freedom from energy overlap with other radionuclides of other additives, freedom from interfering activities of other isotopes of the nuclide selected as an additive, availability in the form of a fine, nonhygroscopic powder, availability as a chemical compound in which the other constituents do not appreciably activate under neutron bombardment, absence as a natural contaminant at least in comparable quantities, nontoxicity, and reasonable availability and cost.

Results of the survey of elements are shown in Table I. The sensitivity values were calculated using Eq. 1 plus application of the γ ray yield factor. The asterisk in the last column indicates whether the spectrum is complex, due either to the presence of a large number of γ ray peaks or to multiple activities from the various isotopes present in the element.

TABLE I—POSSIBLE IDENTIFYING MARKERS

Nuclide	Abundance, %[a]	Activation Cross-Section, Barns[a]	Half-Life[a]	γ Ray Yield/ Dis.[b]	Peak Energy, Mev.[c]	Sensitivity, mcg.[d]	Complex Spectrum[a, c]
^{55}Mn	100	13.3	2.57 hr.	1	0.84	5	
^{63}Cu	69.1	4.3	12.8 hr.	1.2	0.51	20	
^{75}As	100	5.4	26.4 hr.	0.40	0.56	134	
^{121}Sb	57.2	6.8	2.8 day	0.7	0.56	430	
^{127}I	100	5.6	25 min.	0.17	0.44	9	
^{138}Ba	71.7	0.5	84 min.	0.26	0.16	330	
^{139}La	99.9	8.2	40.2 hr.	1	1.60	108	
^{151}Eu	47.8	1400	9.2 hr.	0.025	0.97	12	*
^{152}Sm	26.6	140	47.1 hr.	1	0.10	30	
^{164}Dy	28.2	2100	2.32 hr.	[e]	0.098		
^{174}Yb	31.8	60	4.1 day	0.07	0.40	1900	*
^{175}Lu	97.4	35	3.7 hr.	[e]	0.088		*
^{179}Hf	13.8	65	5.5 hr.	0.80	0.44	19	*
^{187}Re	62.9	66	16.7 hr.	0.09	0.16	120	*
^{197}Au	100	96	2.7 day	0.98	0.41	20	

[a] From Koch (6). [b] From Strominger *et al.* (16). [c] From Heath (18). [d] Amount of element required for a 10-min. irradiation at a 10^{10} neutron flux to produce immediately 100 counts/sec at 100% counting efficiency. [e] Not known.

In selecting nuclides from Table I for a four-component system, several opposing factors must be considered. Manganese and copper have the desired properties, but are already known to be present to some extent in drugs (14). Arsenic might be thought unsuitable, even at submicrogram levels, because of its toxicity. Iodine has an undesirably short half-life for many experimental arrangements, and a photopeak overlapping that of gold, preventing their simultaneous use. The samarium peak overlaps that of dysprosium. Based on these considerations, the major portion of this work was done with the seven additives listed in Table II.

Sample Preparation—Samples for irradiation were prepared in the form of fine, dry powders sealed in plastic containers. Since quantities of an additive required for irradiation and counting were much less than 1 mg., a dilution technique was required to provide samples of known weight. Lactose powder was found to be sufficiently inert under activation to serve as the basic diluent, although, as Table VI shows, mannitol would have been preferred, had the fact been known at the time. Stock mixes of the seven additives in lactose were prepared in concentrations ranging from 0.01% for Dy_2O_3 to 2% for La_2O_3. Geometric dilutions were carried out with a spatula on a pill tile, with a mixing period of 10 min. after each successive blending of equal portions. After blending on the pill tile was complete, the mixture was transferred to a 22-ml. glass vial, where it was further agitated for 30 min.

The first stock mixes prepared exhibited a variation in specific activity under neutron activation, as shown in Table III by Au stock mixes A and B, and by Cu stock mix A. Although first thought to be due to inadequate mixing, this variability turned out to be related to the fineness of the additive powders. In the case of Au, mixes A and B were prepared from purchased powder, passed through a 100-mesh screen, with mix B being more thoroughly mixed than A. Mix C was passed through a 100-mesh screen. The CuO powder was used as purchased in mix A, and further subdivided with a mortar and pestle before preparing mix B. The La_2O_3 powder as purchased was noticeably finer than the other oxides, as Table III indicates.

Both Lucite and polyethylene vials were used for the irradiations. Because both showed slight Mn and Na contamination, samples were transferred to other vials before counting. To facilitate transfer, the sample was usually encased in a plastic film.[1] This was done by centering the weighed powder on a 3-in. disk of the film, gathering up the edges and twisting, and then holding the twisted portion about 2 mm. from a heated soldering pencil until fused.

Activation and Analysis—For the investigation of the scheme of additives, the Purdue University reactor (with an available flux of about 2×10^{10} thermal neutrons/cm.^{2}/sec.) was used. Studies on the natural contaminants were carried out, using a flux of about 5×10^{12}, in the CP-5 reactor at Argonne National Laboratory. Neutron flux values were determined by use of gold foil or gold powder flux monitors, along with calibration of the counting assembly using a calibrated ^{137}Cs source. The duration of all irradiations except the last, which was 105.6 hr., was 10 or 30 min. Counting was begun as soon as possible after removal from the reactor (about 1 hr. for the Purdue reactor and 3 hr. for the CP-5). Counting was delayed 1 week after the long irradiation, to permit decay of the ^{24}Na.

The counting system consisted of a NaI(Tl) crystal mounted in a commercial steel shield[2] having 6-in. walls and inside dimensions of 20 × 20 × 36 in. The detector output was fed into a 400-channel analyzer.[3] Readout was by a high speed printer,[4] writing at 5 channels/sec. Two different detectors were used. All measurements on the additives were made with a 2-in. well crystal. All spectra of natural contaminants were collected with a 4 × 4-in. crystal.

Spectra of single photopeaks of the additives were analyzed by summing the counts in the seven central channels and dividing by the count accumulation time, the exponential decay factor, and the additive weight. The result was the specific activity at the end of irradiation. In a mixture of radionuclides, this calculation was carried out only on the outermost peak. The peak was then removed by instrumental stripping, with previously prepared standards (8, 14), before analysis of the next lower energy peak. Thus, for each component of the mixture, the specific activity, corrected for decay, was determined. Studies of 14 mixtures resulted in the data contained in Table II.

Gold was selected as the internal standard against which the other three components were varied and

TABLE II—EXPERIMENTAL DETERMINATION OF MARKER SENSITIVITIES[a]

Additive	Radionuclide Marker	Specific Activity, Relative to Au[b]
MnO_2	^{56}Mn	1.38
CuO	^{64}Cu	0.437
La_2O_3	^{140}La	0.14[c]
Eu_2O_3	^{152m}Eu	4.01
Sm_2O_3	^{153}Sm	1.22
Dy_2O_3	^{165}Dy	69
Au	^{198}Au	1

[a] A 2-in. diameter × 2-in. thick well detector was used. [b] The specific activity of Au was 4.12×10^5 counts/min./mg. of Au, for a 30-min. irradiation at a flux of approximately 2.1×10^{10} neutrons/cm.^{2}/sec. Counting rate was based on a seven-channel peak, corrected for decay, at 5 kev/channel. [c] A 15-channel peak was used.

TABLE III—UNIFORMITY OF STOCK MIXES

Stock Mix (in Lactose)		Replicates Analyzed, No.	Specific Activity— Coeff. of Variation, %	Activity— Range, % of Mean
0.25% Au	A	6	9.7	43
	B	6	9.3	28
	C	7	2.2	5.3
1.0% CuO	A	8	7.3	21
	B	8	1.7	6.1
2.0% La_2O_3		8	1.4	4.8

[1] Handi-Wrap, Dow Chemical Co., Midland, Mich.

[2] Packard Instrument Co., Downers Grove, Ill.
[3] Radiation Instrument Development Laboratory, Melrose Park, Ill.; model 34-12B.
[4] Hewlett-Packard Co., Palo Alto, Calif.; model 562 A digital recorder.

measured. Reasons for the choice were its high sensitivity, single sharp photopeak, intermediate photopeak energy value, and longer half-life. For ^{165}Dy the X-ray peak was used since it predominated, but because of its low energy an analyzer resolution of 5 kev/channel was required.

Mix Combinations—In order to prove the efficacy of a four-component system, mix combinations of additives were prepared and further diluted with lactose, to simulate a batch of drug product. Samples were then taken for irradiation and measurement. It was considered desirable to determine the amount of change in any amount or level necessary for it to be positively identifiable as "different." Or, stated in another way, it was desirable to determine the number of distinguishable tags possible through varying the amounts of additives over an order of magnitude relative to Au. Results of measurements on the first three mix combinations are shown in Fig. 1. The solid lines represent the expected activities relative to Au, based on data similar to those in Table II. The data points show results obtained from actual measurement. The levels shown in Fig. 1 were selected to approximate an interval of $\sqrt{2}$ between levels. Each dot corresponds to a sample of the mix combination.

Difficulty in maintaining the intended level was encountered only with ^{56}Mn. This was found to be the result of a particle size too large in the MnO_2 powder, which was composed of hard granules as purchased and had to be subdivided before dilution.

Determination of Natural Contaminants—Eight samples of dextroamphetamine sulfate tablets and capsules from five manufacturers, along with 10 ingredients commonly used in amphetamine and other drug products, were irradiated in the Argonne CP-5 reactor. Each material was analyzed following two 30-min. and one 105.6-hr. irradiations. Samples approximately 100 mg. in size were sealed by heat in $^2/_5$ dr. polyethylene vials for the short irradiations, and quartz ampuls for the long one. Samples were weighed after counting.

Identification of contaminants was based on determination of the peak energy and half-life, with both being required. γ Ray spectrum catalogs of Crouthamel (17), and particularly Heath (18), were helpful here. Data reduction was carried out as for the additives, though subtraction of the adjacent continuum was usually necessary to determine the seven-channel-peak counting rate.

Standards were prepared and irradiated along with the unknowns, when their need became apparent from the previous irradiation. Amounts of contaminants present were determined by the comparator method described by Lyon (8). The radionuclides ^{46}Sc, ^{51}Cr, ^{59}Fe, ^{60}Co, ^{65}Zn, ^{122}Sb, ^{124}Sb, and ^{233}Pa have longer half-lives and were detected only after the long irradiation. Amounts of these elements present were calculated by an absolute method using Eq. 1, and published data on cross sections (6) and decay schemes (16). To relate photopeak counting rates to sample disintegration rates, it was necessary to determine the counting efficiency of the detector system. This was done in the following manner.

A calibrated ^{137}Cs source with a γ ray emission of 4.95×10^5 γ rays/min. was prepared. A count of this source immediately gave the counting efficiency for the energy 0.66 Mev. The values for other energies were calculated from absolute detection efficiencies and peak-to-total ratios published by Heath (18). Values of counting efficiency as a function of energy for three different detectors are plotted in Fig. 2. Data points on the 2-in. well crystal were established by direct experimental comparison to the other two crystals. The validity of the absolute method is supported by the cross checks shown in the data in Table IV.

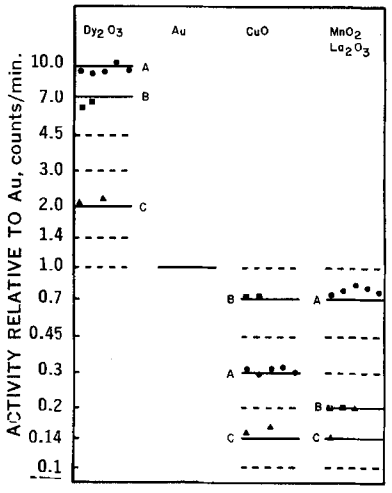

Fig. 1—Expected and measured levels of markers in three mix combinations, A, B, *and* C. *Key:* ●, A (*with* MnO_2); ■, B (*with* La_2O_3); ▲, C (*with* MnO_2).

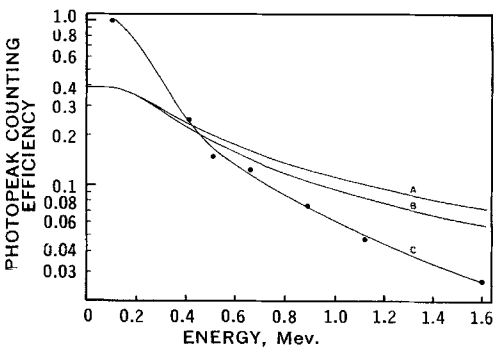

Fig. 2—Photopeak counting efficiencies for three different crystals. Source at minimum distance. Key: A, *4-in. crystal;* B, *3-in. crystal;* C, *2-in. well crystal.*

TABLE IV—MEASURED CONTAMINANT CONCENTRATIONS BY COMPARATOR AND ABSOLUTE METHODS

	Concn., mcg./Gm. of La in $CaSO_4 \cdot 2H_2O$	Au in Mannitol
Comparator method	0.17	
Comparator method involving two different irradiations	0.20	0.0014
Absolute method	0.16	0.0014

TABLE V—CONTAMINANTS IN COMMERCIAL DEXTROAMPHETAMINE TABLETS AND CAPSULES[a]

Element	Radionuclide Measured	Tablet Mfr. No. 1	Tablet Mfr. No. 2	Tablet Mfr. No. 3	Tablet Mfr. No. 4 Lot A[b]	Tablet Mfr. No. 4 Lot B	Tablet Mfr. No. 4 Lot C	Capsule Mfr. No. 4	Capsule Mfr. No. 5
Na	^{24}Na	400	200	300	200	200	200	60	60
Sc	^{46}Sc		0.008	0.02	0.02	0.02	0.01		
Ca	^{47}Ca		7%	4%	16%	16%	16%	13%	
Mn	^{56}Mn	0.9	10	0.7	2	1	1	0.06	0.1
Cu	^{64}Cu							1	2
Zn	^{65}Zn	30						2	2
Br	^{82}Br	2							0.5
Sr[c]	^{87m}Sr		600	300	800	800	800		
Sb[d]	^{122}Sb							0.03	0.07
La	^{140}La	0.01	0.02	0.02	0.04	0.05	0.03		
Au	^{198}Au							0.0005	

[a] Entries are in mcg./Gm. or per cent where designated. [b] Coded designation of lot numbers. Lot numbers were greatly different numerically, indicating lots manufactured at greatly differing times. [c] In every instance 64-day ^{85}Sr was also observed. [d] In every instance 60-day ^{124}Sb was also observed.

Application of Eq. 1 to contamination concentration determinations required measurement of the neutron flux for the long irradiation. This was done by six different determinations using La, Au, and Mn standards in two different irradiations, yielding as the result $(5.5 \pm 0.8) \times 10^{12}$ neutrons/cm.^{2}/sec.

Contaminants in Dextroamphetamine Tablets and Capsules—Contaminants observed in the dextroamphetamine sulfate tablets and capsules are shown in Table V. Polaroid photographs of samples of the spectra providing the data for Table V are shown in Fig. 3. Spectra of tablets from four different manufacturing sources, taken after a 30-min. irradiation and a 6-hr. waiting period, show the presence of only ^{24}Na, ^{56}Mn, and ^{87m}Sr, but in widely varying amounts. The longer lived nuclides are observable only with longer data collection times after the shorter ones have decayed. This effect is illustrated further with the capsules in Fig. 4, where *A* shows only the presence of ^{24}Na, ^{56}Mn, and ^{64}Cu. In *B*, the peak at 0.55 Mev. shows the presence of ^{82}Br in one manufacturer's product, but not in the other. In *C*, both sources show ^{65}Zn and ^{124}Sb, but ^{47}Ca is apparent in only the samples from manufacturer No. 4.

Contaminants in Drug Ingredients—Table VI shows contaminants present in a selection of nine commonly used tablet ingredients, and also in a commercial sample of pure dextroamphetamine sulfate crystals. Sodium was the one element found in all cases, but was present in a wide range of concentrations. Because the dextroamphetamine sulfate crystals were supplied by manufacturer No. 4, one might expect the same trace elements to appear in the tablets and capsules of manufacturer No. 4. That several do not is attributed to the fact that, because of sample sizes, the detection sensitivity for the pure dextroamphetamine sulfate sample is enhanced by a factor of about 50 over that of the tablets and capsules.

RESULTS AND CONCLUSIONS

Requirements for Additives—The experimental work has demonstrated that a four-component system of additives to provide product identification will work insofar as activation and counting techniques are concerned. In applying any such system to a particular drug product, the factor determining the amount of additives required will obviously be the principal activities produced by natural contaminants. For dextroamphetamine tablets, these activities would be due to Sr, Mn, and Na. Using a seven-channel-peak from a 4-in. detector at 10 kev/channel, the sensitivity ratios between ^{198}Au and ^{24}Na, ^{56}Mn, and ^{87m}Sr were 19, 0.16, and 29, respectively. If, in a four-component system, one assumes that Au used as an internal standard would need to produce a peak at least as large as that of any natural contaminants, when measured after a delay of the order of 3 hr., the Au concentrations required to match those of Na, Mn, and Sr for the tablets of Table V would be 13, 7, and 11 mcg./Gm., respectively. Such concentrations are unlikely to be granted official approval. A gain by a factor of 5–10 would be possible with an alternate approach using Sm_2O_3, Eu_2O_3, and CuO, together with Au, comprising the mixture, then waiting about 10 hr. until most of the ^{56}Mn and ^{87m}Sr had decayed, and removing the ^{24}Na by instrumental stripping. It is evident that

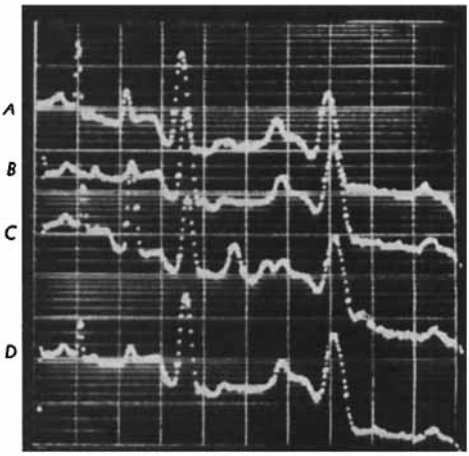

Fig. 3—Spectra of dextroamphetamine sulfate tablets from four manufacturers. Thirty-minute irradiation followed by 6-hr. decay; 0–4 Mev.; vertically displaced for clarity; scale of vertical axis is logarithmic. Key: A, manufacturer No. 4; B, manufacturer No. 1; C, manufacturer No. 2; D, manufacturer No. 3.

each drug product must be considered individually in designing a system of identifying additives, after first establishing the levels of natural contaminants.

Eu_2O_3 is suitable as an additive component, but only if irradiation time is in the range of 1 hr. or less, and assay made within about 10 hr. Though the spectrum is very complex, only the 9.3-hr. activity of ^{152m}Eu appears at first.

The number of separate identifiable tags possible under a four-component system also depends on how much the measurements are affected by natural contaminant activity. In a situation where one could use an arrangement such as shown in Fig. 1, 8^3 combinations are possible, if one includes the zero level. Not enough combinations were tried to be certain that all 512 combinations would be dis-

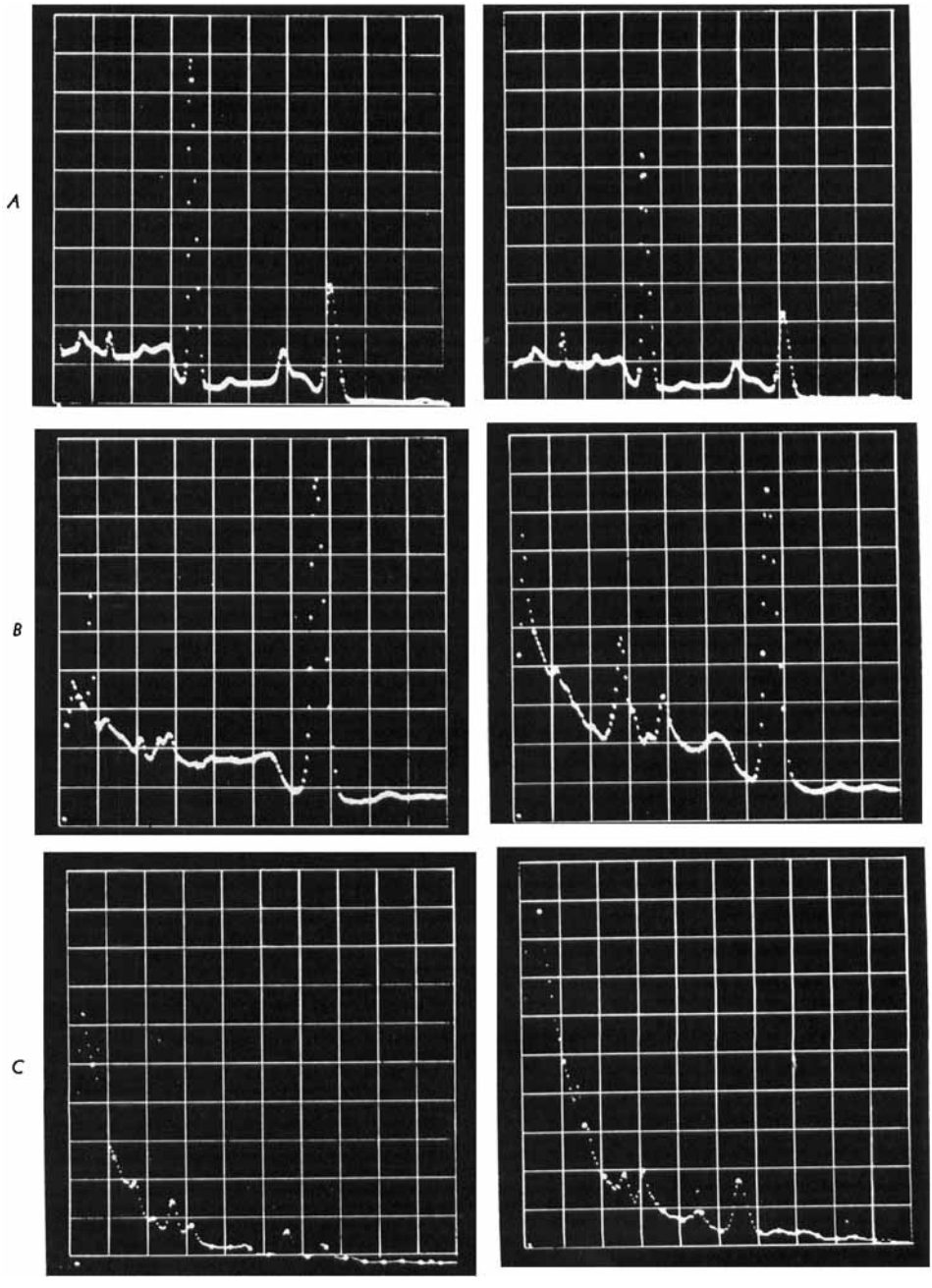

Fig. 4—Spectra of dextroamphetamine sulfate capsules from two manufacturers. Decay times: (manufacturer No. 4) A—7.3 hr., B—6.0 days, C—16 days; (manufacturer No. 5) A—7.7 hr., B—6.1 days, C—30 days. Scale of vertical axis is linear. Key: A, 0–4 Mev.; B, 0–2 Mev.; C, 0–2 Mev. Lefthand column, manufacturer No. 4; righthand column, manufacturer No. 5.

TABLE VI—CONTAMINANTS IN CERTAIN DRUG INGREDIENTS[a]

Element	Radionuclide Measured	Dextroamphetamine Sulfate	Mg Stearate	Wood Cellulose[b]	Microcrystalline Cellulose[c]	Mannitol	Calcium Sulfate Dihydrate	Dicalcium Phosphate Dihydrate	Lactose	Starch	Talc
Na	^{24}Na	10	700	600	6000	2	1	1000	40	200	400
Sc	^{46}Sc		0.07		0.001	0.001					0.7
Cr	^{51}Cr	0.2		2	0.07	0.4					
Mn	^{56}Mn	0.3		10		0.007	0.3	8		0.4	7
Fe	^{59}Fe	50	90	300		6					1000
Co	^{60}Co	0.1									
Cu	^{64}Cu	10		10							
Zn	^{65}Zn								0.6	20	
Br	^{82}Br									0.05	
Sr	^{87m}Sr						50				
Sb[d]	^{122}Sb	0.02	0.08	0.06	0.02	0.007			0.008		
La	^{140}La					0.006	0.2				0.4
Eu	^{152m}Eu						0.005				
Au	^{198}Au	0.0004			0.0004	0.001					
Hg	^{203}Hg		0.05							0.2	
Th	^{233}Pa										0.2

[a] Entries are in mcg./Gm. [b] Marketed as Solka-Floc by the Brown Co., Berlin, N. H. [c] Marketed as Avicel by the American Viscose Division, FMC Corp., Marcus Hook, Pa. [d] In every instance 60-day ^{124}Sb was also observed.

tinguishable; but it is evident that, with care, most could be used.

Single component additives have a distinct advantage. Quantitative differences would not be involved; only detection would be required for identification purposes, and far smaller amounts could be used. Table VI shows natural levels of Au of less than 1 part per billion were easily identified. Similar values would apply to other additives of comparable sensitivity.

Contaminants Detected—These results are generally consistent with those of Tuckerman *et al.* (14). In analyzing a somewhat different group of materials, the following additional trace elements were found: Cr, Fe, Zn, Sr, La, Eu, and Au. In the two compounds common to both studies, namely magnesium stearate and talc, these samples contained the same trace elements as those of Tuckerman, and in the same general levels; but other contaminants were also observed, as seen in Table VI.

Contaminants for Source Identification—Examination of Table V shows the six dextroamphetamine sulfate products from the five different manufacturers to be clearly and readily distinguishable from each other, on the basis of contaminants present and their relative concentrations. On the other hand, the three different lots of manufacturer No. 4, though apparently widely spaced in time, are so similar as to be indistinguishable. These results, then, provide further supporting evidence that natural contaminants may offer a means of determining the specific manufacturing source of amphetamine drug samples.

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