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Detection of Drugs Using XAD-2 Resin. I: Choice of Resin, Chromatographic Conditions, and Recovery Studies

In 1969 Fujimoto and Wang [*1*] introduced a new drug extraction technique when they applied Amberlite®XAD-2, a nonionic polystyrene divinylbenzene resin, to the analysis of narcotic analgesics in urine. The resin was prepared by washing it with water and methanol, and after the urine sample was poured through a column containing the resin the adsorbed drugs were eluted with methanol and subsequently analyzed by thin-layer chromatography (TLC). Morphine, meperidine, codeine, methadone, levorphanol, pentazocine, and dihydromorphinone were detected in therapeutic concentrations. Many modifications of the original procedure successfully applied XAD-2 and other similar resins to the extraction of drugs from urine and, more recently, other biological fluids and tissues.

Research into optimal chromatographic conditions for the system was concerned with different types of resin columns [*2–4*] as well as pH conditions and eluting solvents. Bastos et al [*5*], Kullberg et al [*6*], and Miller et al [*7*] found a pH of 8.5 ± 1.0 to be optimum for the single simultaneous extraction of morphine, amphetamines, and phenobarbital. Kullberg and Gorodetzky [*8*] used pH 8.5 for the extraction of acidic, basic, and neutral drugs, and overall recoveries ranged from 63 to 78%. Sawada et al [*9*] demonstrated that the adsorption of benzodiazepines was not affected by urinary pH. Since the pH range of 8 to 8.5 appears to be optimal for morphine without significantly affecting recoveries of other basic drugs while still producing acceptable recovery for barbiturates, it has generally been accepted as the optimum pH for XAD-2 resin extractions. A variety of eluting solvents has been studied for the desorption of drugs from the resin. Methanol was very effective but the resulting extracts were impure [*1,10,11,12*]. Mulé et al [*2*] selected a chloroform/isopropanol (3:1) mixture as the most efficient. The other solvents tested included ethyl acetate, 1,2-dichloroethane, 1,2-dichloroethane/isopropanol (9:1), 1,2-dichloroethane/isopropanol (3:1), 1,2-dichloroethane/ethyl acetate (2:3), and chloroform/methanol (9:1). Bastos et al [*13*] proposed a sequential elution of the resin using first isopropyl ether, followed by two elutions with chloroform/isopropanol (3:1). Kullberg et al [*6*] observed that amphetamine required a higher polarity solvent, such as isopropanol/ethyl acetate/dichloroethane (25:45:30), and later modified

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the procedure to use acetone followed by chloroform/methanol (3:1) [*8*]. Ethyl acetate followed by an equal amount of methanol has been used by Pranitis et al [*3*]. Consistent results have been obtained with chloroform/isopropanol (3:1) [*2,5,13*]. Ethyl acetate/dichloroethane (1:2) has been recommended for the elution of commercial columns and for the elution of phenobarbital [*6*] and morphine [*7*]. Machata and Vycudilik [*14*] found this mixture superior to chloroform/isopropanol or to methanol because of the impure extracts that resulted from the use of the latter two solvents.

Application of XAD-2 resin techniques to biological tissues and fluids other than urine has been limited. Missen and Lewin [*15*] studied the recovery of amobarbital, methaqualone, and amitriptyline from whole blood. Results obtained by the XAD-2 procedure when compared to those of solvent extraction and protein precipitation showed that the resin produced the cleanest extracts and was the least complicated. Recoveries for amobarbital, methaqualone, and amitriptyline were 81, 74, and 61%, respectively, while solvent extraction techniques yielded 76, 73, and 17%, respectively. The protein precipitation method showed 72% amobarbital and 36% methaqualone recovered. Vycudilik [*16*] used XAD-4 resin for the isolation of phentermine from blood with recoveries ranging from 92 to 95%. Pranitis et al [*3*] extended the XAD-2 resin extraction technique to blood, serum, bile, gastric contents, and tissues. Urine and serum were extracted without special preparation, while blood and gastric content were diluted with water and bile was autoclaved in the presence of hydrochloric acid. Tissue was homogenized with 2% hydrochloric acid and, after a mild steam bath hydrolysis, the homogenate was centrifuged and the supernatant analyzed. The hydrolysis improved drug recovery 30 to 206%. Thin-layer chromatographic and sequential chromogenic spraying were used for drug detection and identification with recoveries ranging from 76 to 98.7% for blood and 56.8 to 96% for brain, liver, and kidney. Techniques using direct chloroform/isopropanol extraction were shown to be less efficient than the XAD-2 resin. Ibrahim et al [*17*] reported a classical Stas-Otto procedure to prepare a tissue extract for subsequent extraction by XAD-2 resin. Blood was extracted directly and gastric contents were extracted either directly or following dialysis. Recoveries ranged from 60% for secobarbital to 76% for propoxyphene. Pranitis and Stolman [*4*] reported the differential separation of drugs from blood using sequential elution in four steps. After adsorption and elution of acidic and neutral drugs with chloroform, the pH of the XAD-2 resin column was changed from 4.5 to 11.6 and basic drugs were eluted with a mixture of chloroform and isopropanol. Recovery of a number of drugs ranged from 56 to 95%. The differential elution technique simplified TLC identification since each class of drugs appeared in a separate solvent fraction.

The increasing use of drugs in today's society has placed an increased demand on the toxicologist for a practical, rapid procedure applicable to simultaneous toxicologic screening of many tissue samples. This and subsequent papers will discuss the application of XAD-2 resin to the analysis of drugs in biological specimens in the effort to develop suitable, comprehensive, analytical methods for the detection of acidic, basic, and neutral drugs.

Materials and Methods

Columns

Glass chromatography columns (Chromaflex, 13 by 250 mm) with a 200-ml upper reservoir were used throughout the study. The only exception was the recovery study of drugs at pH 8.5 and 9.5; adsorbent cartridges prepacked with XAD-2 resin (Brinkmann Instruments, Inc., Westbury, N.Y.) were used.

Preparation of Resins

Amberlite XAD-2, XAD-4, and XAD-7 resins were obtained from Rohm and Haas Co., Philadelphia, Pa. The resins were washed by mechanically stirring with three times their volume of methanol for 1 h. The methanol was decanted and washing repeated twice with additional quantities of methanol. The methanol washes were followed by three washes with three similar volumes of water. After preparation, the resin was stored under water in a refrigerator. A cotton plug was placed in the bottom of the chromatography columns to retain the resin. The prepared resin was added as a slurry to the columns and allowed to settle by gravity to a height of 10 cm. This volume was equivalent to 5 or 6 g of resin. Flow rate was regulated by a stopcock at the bottom of the column.

Choice of Resins

Aqueous drug standard solutions (1 mg/100 ml) of codeine, morphine, meperidine, and pentobarbital (200 ml) were passed through the columns packed with XAD-2, XAD-4, or XAD-7 resin. A mixture of ethyl acetate/1,2-dichloroethane (3:2) (100 ml) was used to elute the drugs. The total amount of each of the drugs was determined by using ultraviolet (UV) and gas chromatographic (GC) techniques before and after passage through the resin column. Direct extraction of the eluting solvent with 0.1*N* sulfuric acid was used to determine the concentrations of morphine, codeine, and meperidine in the eluate. In the case of pentobarbital, the solvent was first evaporated and the residue subsequently dissolved in 0.45*N* sodium hydroxide. (When ethyl acetate/1,2-dichloroethane is extracted directly with sodium hydroxide, ethyl acetate is hydrolyzed and the acetic acid formed changes the pH of the aqueous basic solution and causes interference with the UV determination of barbiturates.)

Quantity of Resin, Flow Rate, and Eluting Solvent

A pentobarbital solution (1 mg/100 ml, 200 ml, pH 8) was passed through various quantities (5 to 20 g) of XAD-2 resin to determine the relative efficiency of recovery.

Morphine, meperidine, and pentobarbital solutions (1 mg/100 ml, 200 ml, pH 8) were passed through columns at flow rates varying between 1.5 and 15 ml/min to determine the effect of flow on the efficiency of recovery of the drugs.

The same group of drugs was eluted from the XAD-2 resin with a variety of organic solvents or solvent mixtures to evaluate the ability of each to remove adsorbed drugs from the resin. The solvents included chloroform/methanol (3:1); isopropanol/chloroform (1:3); ethyl acetate/methanol (1:1); 1,2-dichloroethane, *n*-butyl chloride, 20% isopropanol in chloroform, and ethyl acetate/1,2-dichloroethane (3:2).

Drug Efficiency Studies

Aqueous drug standards (amobarbital, pentobarbital, phenobarbital, secobarbital, morphine, codeine, meperidine, and methadone) were added to distilled water (200 ml) to prepare 1 mg/100 ml solutions. Solid sodium bicarbonate (2 to 3 g) was added until the solution reached pH 8. The basic solution was passed through an XAD-2 resin column at a flow rate of 10 to 15 ml/min. The drugs were eluted with a mixture of ethyl acetate and 1,2-dichloroethane (3:2) (100 ml) and the eluate was evaporated to dryness after the addition of 1% hydrochloric acid in methanol (one or two drops). The residue was analyzed with TLC. In addition, samples were removed at various stages of the procedure and assayed. Radioimmunoassay kits (Roche Diagnostics, Division of Hoffmann-La Roche, Inc., Nutley, N.J.) and an Abbott Laboratories Logic Series gamma

scintillation well counter, Model 111-B, were used for morphine and barbiturates. Codeine, methadone, and meperidine were determined by UV and GC procedures.

Thin-Layer Chromatography

The eluates from the XAD-2 resin chromatography were acidified and evaporated to dryness. The residue was redissolved in a mixture of chloroform and methanol (1:1) and applied to a silica gel TLC plate (0.25 mm, 20 by 20 cm, Analtech). The plate was developed in the Davidow et al system [*18*] (ethyl acetate/methanol/ammonium hydroxide [75:10:5]) after the system had been equilibrated for 1 h. Following developing and air drying, the plate was lightly sprayed with diphenylcarbazone solution (0.1%), then with mercurous nitrate solution (0.3% in 0.04*N* nitric acid) to detect the barbiturates, and, after drying, with iodoplatinate solution (0.5% in 2% potassium iodide) to detect the basic drugs.

Losses occurring during the extraction of TLC spots (TLC losses) were determined by applying 10 μl of ethanol drug standard (codeine, morphine, methadone, meperidine, phenobarbital, pentobarbital, amobarbital, and secobarbital; 1 mg/ml), spraying the plates with the appropriate solutions, and quantitating the drugs by using UV or GC techniques after they were extracted from the silica gel with organic solvents.

Ultraviolet Spectrophotometry

Barbiturates were analyzed with the Broughton modification of the procedure of Goldbaum [*19*] after separation by removing the spot from the TLC plate, suspending the silica gel in 0.1*N* sulfuric acid (2 to 3 ml), extracting the suspension with chloroform (60 ml), and back-extracting the chloroform into 0.45*N* sodium hydroxide (5 ml). A UV spectrum of the sample was recorded with a Beckman DK2A ratio recording spectrophotometer.

Basic drugs were analyzed after TLC separation by removing the spot and suspending the silica gel in 0.1*N* sulfuric acid (2 or 3 ml). The acid was adjusted to pH 8 to 8.5 with sodium bicarbonate and the aqueous basic solution extracted twice with chloroform (30 ml). The chloroform was back-extracted into 0.1*N* sulfuric acid (3 ml), and a UV spectrum of the sample was produced as before.

Gas Chromatography

Drugs were analyzed after TLC separation by removing the spot from the plate and suspending the silica gel in 0.1*N* sulfuric acid. The pH was adjusted to 8.5 to 9. The basic aqueous solution was extracted with three times its volume of *n*-butyl chloride for 15 min on a modified Burrell® shaker [*20*] and then centrifuged for 5 min at 2000 rpm. The *n*-butyl chloride fraction was separated and extracted with 1*N* sulfuric acid (3 ml). The organic layer was removed by aspiration. The acid solution (2 ml) was made basic with sodium hydroxide (0.5 ml) (this step converts norpropoxyphene to norpropoxyphene amide) and then neutralized with 1*N* sulfuric acid, and the pH was adjusted to 9 with pH 9 carbonate-bicarbonate buffer. This solution was extracted with a mixture of *n*-docosane (10 μg/ml) in chloroform (0.1 ml), and a 1-μl aliquot was injected into a F & M Biomedical gas chromatograph (Model 400) equipped with a 1.2-m (4-ft) by 2-mm U-shaped glass column packed with 3% OV-17 on Gas Chrom Q, 100-120 mesh (oven temperature, 210°C and flow rate of nitrogen, 25 to 30 ml/min).

Results and Discussion

Choice of Resin

Table 1 shows the percentage of recovery of codeine, morphine, meperidine, and pentobarbital when a solution of each was passed through each of XAD-2, XAD-4, and XAD-7 resins. XAD-2 resin gave somewhat better recoveries for codeine, XAD-4 for meperidine and morphine, and XAD-7 for pentobarbital. The recovery for each drug from each of the three resins was generally similar and no statistically significant difference was noted. The average recovery for the four drugs was 80% (estimated standard deviation $s = 11.5$) with XAD-2, 83% ($s = 9.4$) with XAD-4, and 75% ($s = 11.2$) with XAD-7.

TABLE 1—*Percent recovery of drugs from XAD resins.* [a]

	Resin					
	XAD-2		XAD-4		XAD-7	
Drug	Mean	*s*	Mean	*s*	Mean	*s*
Codeine	94	1.2	92	4.9	88	9.4
Morphine	78	2.6	82	3.2	62	7.3
Meperidine	81	4.6	87	12.3	80	5.1
Pentobarbital	66	7.7	70	6.2	71	5.8

[a] Aqueous drug solutions (1 mg/100 ml, 200 ml, pH 8) were passed through the resin column and subsequently eluted with ethyl acetate/1,2-dichloroethane (3:2) (100 ml). Results are of a minimum of five analyses in each case.

XAD-4 and XAD-7 resins did not seem to offer any significant advantage when compared to XAD-2 resin. Since XAD-4 and XAD-7 had been recently developed, only one report [*16*] on using XAD-4 for the analysis of phentermine in blood has appeared in the literature. On the other hand, XAD-2 is available commercially from Brinkmann Instruments, Inc. (Westbury, N.Y.), Bio-Rad Laboratories (Richmond, Calif.), and Eastman Kodak Co. (Rochester, N.Y.), and numerous applications to drug analysis, particularly in urine, have been reported [*1-14*]. Therefore, there appears to be no advantage to XAD-4 or XAD-7 resins for general drug analysis.

Quantity of Resin, Flow Rate, and Eluting Solvent

Table 2 shows the effect of varying quantities of XAD-2 resin on the recovery of pentobarbital from 200 ml of an aqueous 1 mg/100 ml solution. No difference in percentage of recovery was observed as the amount of resin was varied between 5 and 20 g. Ibrahim et al [*17*] passed an extract obtained from 500 g of tissue through 1 to 2 g of XAD-2 resin and found that the resin was neither overloaded nor the extraction process hindered by components present in the extract.

Table 3 shows the effect of changing column flow rate during adsorption on the recovery of morphine, meperidine, and pentobarbital from XAD-2 resin. The flow rate of eluting solvent was not controlled. The fastest possible flow rate obtainable with the columns used was approximately 15 ml/min (by gravitational flow). However, decreasing the flow rate as much as tenfold did not result in improved recoveries. With a flow rate of 1 to 2 ml/min, it would take several hours for a 200-ml extract to pass through the column. Since the flow rate did not affect drug adsorption, a 10-to 15-ml/min flow rate was used to shorten the time of analysis.

TABLE 2—*Percent recovery of pentobarbital from various amounts of XAD-2 resin.* [a]

Amount of Resin, g	Recovery, [b] %
5	75
10	73
20	73
...	mean, 74[c]

[a] Pentobarbital solution (1 mg/100 ml, 200 ml, pH 8) was passed through the resin column and subsequently eluted with ethyl acetate/1,2-dichloroethane (3:2) (100 ml).

[b] Results are of a minimum of three analyses.

[c] $s = 1.1$.

TABLE 3—*The effect of flow rate on percent recovery of drugs from aqueous solution using XAD-2 resin.* [a]

	Flow Rate, ml/min			
Drug	1.5	5.0	10	15
Morphine	95	93	100	97
Meperidine	100	109	108	103
Pentobarbital	104	104	108	112

[a] Recoveries corrected for determined XAD-2 and TLC losses. Results are of a minimum of three analyses.

Solvents or solvent mixtures of various polarities (ranging from methanol to *n*-butyl chloride) were evaluated for their efficiency in the elution of drugs from XAD-2 resin. The more polar solvents such as methanol and isopropanol, alone or in combination with chloroform or ethyl acetate, produced highly impure extracts. The high polarity of these solvents caused significant amounts of organic material to be stripped from the resin and eluted along with the drugs, thus making the subsequent TLC analysis difficult. On the other hand, solvents of low polarity such as 1,2-dichloroethane and *n*-butyl chloride yielded the least amount of interfering substances, but recovery of drugs was below 40% with 1,2-dichloroethane and below 17% with *n*-butyl chloride. A mixture of ethyl acetate and 1,2-dichloroethane (3:2) was found to give the best overall recovery (66 to 94%). The resulting extract was free of interfering substances, thereby requiring no additional clean-up procedure.

pH of Extraction

Recovery studies for morphine, codeine, methadone, amobarbital, and phenobarbital were performed with XAD-2 resin at pH 8.5 and 9.5. The effects of varying the pH are shown in Table 4. The best recoveries for the drugs studied were achieved at pH 8.5. Therefore, pH 8.5 is recommended as an optimum pH for comprehensive analysis and has also been recommended by Kullberg and Gorodetzky [*8*], Bastos et al [*5*], and Miller et al [*7*].

Drug Extraction Efficiency Studies

Recovery studies were conducted on spiked aqueous samples. Known amounts of acidic (amobarbital, secobarbital, pentobarbital, phenobarbital) and basic (codeine, morphine,

TABLE 4—*Percent recovery from aqueous solution using XAD-2 resin.*[a]

Drug	pH 9.5	pH 8.5
Morphine	68	93
Codeine	100	100
Methadone	93	93
Amobarbital	56	69
Phenobarbital	31	73

[a] 100 μg of drug in 25 ml water was passed through a commercially prepacked Brinkmann column. Results of a minimum of three analyses.

meperidine, methadone) drugs were added to the aqueous test solutions. The solutions were analyzed with XAD-2 resin and drug losses occurring during the various stages of the XAD-2 extraction procedure determined. The recovery of four basic and four acidic drugs during the extraction of aqueous solutions with XAD-2 resin is shown in Table 5. Drugs were adsorbed onto the resin from the aqueous solution. Only a relatively small amount (0 to 5%) of the drugs was not adsorbed by the resin, that is, was detected in the aqueous effluent. This amount is referred to as "adsorption loss." Drugs were further eluted from the resin with ethyl acetate/1,2-dichloroethane (3:2). Amounts of drugs varying from 6 to 40% remained on the resin. This amount, not desorbed from the resin, is referred to as "desorption loss." Finally, during the analysis of TLC spots additional losses occur that are referred to as "TLC loss." These losses for codeine, morphine, methadone, meperidine, phenobarbital, pentobarbital, amobarbital, and secobarbital ranged from 0% (methadone) to 25% (phenobarbital), with an average of 12% ($s = 8.3$). Phenobarbital showed the greatest loss among the four barbiturates tested. This was expected since phenobarbital is the least stable compound in the group. The relatively high losses of morphine and meperidine can be attributed to the inability of organic solvents to extract these compounds efficiently from the aqueous acid suspension of silica gel.

Radioimmunoassay, because of its high sensitivity, small sample size (100 μl) requirement, and good precision in quantitatively measuring dilute solutions, was used to determine and differentiate adsorption and desorption losses occurring during the XAD-2 resin extraction procedure for those drugs applicable. A combined adsorption and desorption loss (extraction loss) was determined for codeine, methadone, and meperidine by measuring the amount of drug before the solution was poured onto the resin and the amount recovered in the eluting solvent. Since the adsorption losses for morphine and the four barbiturates as determined by radioimmunoassay ranged from 0 to 5%, while desorption losses for the same drugs ranged from 14 to 40%, it is reasonable to assume that the combined extraction loss for codeine, methadone, and meperidine is due mainly to the desorption loss as well.

The recovery of drugs from aqueous solutions analyzed with the XAD-2 resin and corrected for adsorption and desorption losses are listed in Table 6 along with recoveries reported in the literature with other XAD-2 resin methods for the extraction of drugs from urine. Urine was chosen for comparison because it is essentially aqueous in nature and responds to the resin in a manner similar to water. Recoveries resulting from the present study were essentially the same as the average values reported in the literature. For phenobarbital, morphine, and codeine, the results of this study (85, 82, and 94%, respectively) showed an improvement of 4 to 23% when compared to the literature data for the same drugs (81.5, 71, and 72%). On the other hand, amobarbital, pentobarbital, secobarbital, methadone, and meperidine were recovered less efficiently in this study (67, 60, 60, 81, and 57%, respectively) to the extent of 4 to 28% when compared to the literature data (71, 68, 76.5, 83.5, and 66.5%). Kullberg and Gorodetzky [8] reported

TABLE 5—*Losses of drugs at different stages of XAD-2 resin extraction from aqueous solutions.*

	Amobarbital[a]		Pentobarbital[a]		Phenobarbital[a]		Secobarbital[a]		Morphine[a]		Codeine		Meperidine		Methadone	
	Mean	*s*	Mean	*s*	Mean	*s*	Mean	*s*	Mean	*s*	Mean	*s*	Mean	*s*	Mean	*s*
Amount added, μg	100	...	100	...	100	...	100	...	100	...	100	...	100	...	100	...
Adsorption loss, μg	5	1.5	0	0	0	0	0	0	4	4.5	6[b]	1.2	19[b]	4.7	43[b]	9.2
Desorption loss, μg	28	10.6	40	7.7	15	4.1	40	4.0	14	2.8						
TLC loss, μg	7	1.7	7	3.0	25	2.5	12	3.4	19	4.2	8	3.4	20	2.1	0	6.5
Total loss, μg	40	...	47	...	40	...	52	...	37	...	14	...	39	...	43	...
Amount recovered,[c] %	...	...	65	10.1	47	4.1	...	...	56	7.8	71	7.8	61	6.7	24	3.3
Corrected recovery, %	...	...	112	...	83	...	...	...	93	...	85	...	100	...	67	...

[a] Adsorption and desorption losses determined by radioimmunoassay.
[b] Combined adsorption and desorption loss.
[c] Average of a minimum of 20 analyses.

TABLE 6—*Recovery of drugs using the XAD-2 resin extraction method compared with literature data.*

Drug	Recovery, %		
	This Study[a]	Literature[b]	Reference
Amobarbital	67	71	*8*
Secobarbital	60	68	*8*
Pentobarbital	60	76.5 (88, 65)	*2, 8*
Phenobarbital	85	81.5 (80, 83)	*6, 2*
Codeine	94	72	*8*
Morphine	82	71 (85, 64, 65)	*7, 2, 8*
Meperidine	81	83.5 (89, 78)	*2, 8*
Methadone	57	66.5 (55, 78)	*2, 8*

[a] Recoveries corrected for adsorption and desorption losses.
[b] Average of literature data with individual values in parentheses.

that up to 25% of drugs can be lost in seemingly unimportant steps of their procedure (adsorption of drugs to the sides of glassware, transfer of residue from the concentration tubes to TLC plates, and so forth). These losses, which can explain the low recoveries for some drugs, were considered as operational losses that could be minimized with careful laboratory technique.

Summary

Amberlite XAD-2, a nonionic polystyrene divinylbenzene resin, was first used for the analysis of drugs in urine and a number of reports have described the development at optimal conditions for extraction, including type of resin columns, pH conditions, and eluting solvents. XAD-4 and XAD-7 resins were compared to the similarly structured XAD-2 resin and no significant advantage over the XAD-2 resin for drug screening was observed. A quantity of 5 to 6 g of resin was found to have sufficient capacity for the extraction of 200 ml of pentobarbital solution (1 mg/100 ml). A column flow rate of approximately 15 ml/min (gravitational flow) was sufficient for analysis and slower rates were not more efficient. A mixture of ethyl acetate and 1,2-dichloroethane (3:2) was found to give best overall recovery (66 to 94%) of drugs, the resulting extracts being reasonably free of interfering substances. A pH value of 8.5 is recommended as optimum for comprehensive analysis of acidic and basic drugs. Recovery studies were conducted on spiked samples to determine drug losses occurring during various steps in the XAD-2 extraction procedure for four acidic (amobarbital, secobarbital, pentobarbital, and phenobarbital) and four basic (morphine, codeine, meperidine, and methadone) drugs. A relatively small amount (0 to 5%) of the drugs was not adsorbed by the resin and amounts varying from 6 to 40% failed to be desorbed by the eluting solvent. Additional losses occurred during the removal and analysis of TLC spots. Recovery of drugs from aqueous solutions analyzed with the XAD-2 resin were compared to recoveries reported in the literature with other XAD-2 resin methods for the extraction of drugs from urine. Recovery of phenobarbital, morphine, and codeine improved by 4 to 23% while recoveries of amobarbital, pentobarbital, secobarbital, methadone, and meperidine were 4 to 28% less efficient when compared to literature data.

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