and cellulose hydroxyl groups has been proposed (4).

A comparison of the adsorption by the three varieties of cornstarch indicates that Amioca adsorbed all dyes to the greatest extent, U.S.P. cornstarch next, and then Amylon. This trend is related to the amylopectin content. Recent studies concerned with anionic dye binding of soluble starches have shown the opposite results (5): the less interaction occurring, the higher the proportion of amylopectin. This is attributed to the greater rigidity of the branched portions of starch in solution compared to the more flexible linear amylose chains. One would not necessarily expect interactions involving the intact starch grain to be the same as that in solution. The results presented here confirm this.

The lack of anionic dye adsorption on potato starch is apparently because of the presence of phosphate esters (6) which impart a negative charge to the potato starch grain, but which are absent in the other starches. Schoch and Maywald (7) have shown that potato starch and carboxylated starches adsorb cationic dyes strongly but do not adsorb anionic dyes. Adsorption of anionic dyes on potato starch has been observed when neutral electrolytes are added (8). These would be expected to reduce the repulsive forces between the dye and starch by breaking down the electric double layer.

In view of the observed affinity of anionic certified dyes for starch it would appear that the addition of starch to a tablet granulation before the addition of the dye solution should aid in preventing color migration. A recent communication (9) has indicated that starch does enhance color distribution and prevent migration when added to tablet granulations.

In general, it is proposed that adsorption isotherm data can be used to study color migration problems. These isotherms indicate the amount of dye adsorbed as a function of that amount remaining in solution. Since it is the dye in solution which migrates upon drying, the objective should be to minimize this concentration while increasing the amount adsorbed. For systems described by the Langmuir equation the constants, k_1 and k_2 can be considered as a measure of the extent of adsorption for a given dye concentration and the maximum amount of adsorption, respectively. Therefore, by measuring adsorption as a function of such factors as temperature, solvent, electrolyte concentration, and the presence of tablet components, it should be possible to pick systems giving maximum dye adsorption with a minimum of dissolved dye, resulting in maximum color distribution.

Further studies are being conducted and will be reported in a future communication.

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Reduction of 1,2,3-Trimercaptopropane Content of Dimercaprol

By EDWARD G. RIPPIE† and ALBERT A. KONDRITZER

A multiple batch extraction procedure is described which can serve to reduce the trithiol content of dimercaprol to levels conforming to the U.S.P. XVI monograph.

Previous reports (1, 2) indicate the presence of the trithiol, 1,2,3-trimercaptopropane, in many laboratory, pilot plant, and commercial lots of dimercaprol (BAL). The toxicity of BAL is substantially increased by this impurity and the revised monograph on dimercaprol appearing in the first U.S.P. XVI supplement contains limits on the concentration in which it may be present. Many lots of BAL, presently available for drug use, contain far more than the established 1.5% limit of the trithiol. Since BAL is not currently manufactured in this country, a purification process is needed.

This report presents the results of a study of the removal of 1,2,3-trimercaptopropane from BAL by a liquid-liquid extraction procedure, using petroleum ether as the extracting solvent. This method may be used with a variety of solvents under various experimental conditions, *e.g.*, BAL saturated with water to increase the partitioning of the trithiol into the organic solvent phase to obtain basic information of value for the development of a commercial process for the purification of BAL containing excessive quantities of the trithiol impurity.

EXPERIMENTAL

Materials.—BAL purified by passage through a partition chromatographic column, followed by distillation at low pressure; 1,2,3-trimercaptopropane, hereinafter designated as TSH; petroleum ether, shaken with concentrated sulfuric acid over a period of several days and distilled between 35–50° were employed.

Procedure.—Known concentrations of TSH in BAL were equilibrated with petroleum ether. The volume of the BAL was chosen sufficiently large so that it was not significantly changed by the extraction. The petroleum ether phase was analyzed for sulfhydryl content, and the resultant data utilized in calculations of extraction efficiency.

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TABLE I.—RESULTS OF EXTRACTION OF TSH FROM BAL WITH PETROLEUM ETHER

1	2	3	4	5	6	7	8
	Before Extn.		Iodine Titer per ml. Petroleum Ether		TSH mg./ml. Petroleum		
Ampul No.	BAL mg.	TSH mg.	BAL + TSH	TSH	Ether Phase	BAL Phase	K
1	2431.6	21.1	0.988	0.127	0.592	10.1	.0586
2	2487.0	64.1	1.223	0.377	1.758	29.6	.0594
3	2443.9	122.9	1.529	0.703	3.277	56.5	.0580
4	2545.2	236.8	1.945	1.151	5.366	101.3	.0529
5	2535.4	329.5	2.217	1.449	6.755	137.7	.0489
6	Pure BAL	.....	0.868	0.000	...	...	Av. (1–4)
7	.....	Pure TSH	10.119	10.119	47.175	...	.0572

Approximately 2-ml. volumes of BAL were weighed into glass ampuls. The TSH, in varying amounts, was then weighed into the ampuls to give the desired concentrations. Exactly 2 ml. of petroleum ether was pipetted into each ampul and the ampuls quickly sealed with an oxygen-gas flame and shaken for 3 hours in a thermostated water bath at 24.5°. After removing each ampul from the bath, a 1-ml. sample of the petroleum ether phase was withdrawn as quickly as possible and pipetted into an excess of 0.1 *N* iodine; back titration was carried out with 0.1 *N* thiosulfate solution.

RESULTS

The data are presented in Table I. Columns *2* and *3* represent the quantities of BAL and TSH weighed into each ampul. The iodine titer of the petroleum ether phase, representing the sum of BAL and TSH, is given in column *4*. The iodine titer due to the TSH content of each ampul was calculated as follows. The iodine titer of the petroleum ether extract of the pure BAL (ampul 6) was multiplied by the mole fraction of BAL in the BAL phase of each ampul; the resultant corrected iodine titer due to the BAL in the petroleum ether extract of each ampul was subtracted from the corresponding titer of column *4* to give column *5*. The TSH content of the petroleum ether phase in mg./ml. is given in column *6*. The amounts of BAL and TSH in the BAL phase were then recalculated for the amount removed by extraction, and the concentration of TSH in the BAL phase is given in column *7*. The partition coefficient in column *8* is the mg. TSH per ml. petroleum phase divided by mg. TSH per ml. BAL phase. The average partition coefficient obtained, $K = 0.0572$, may be used in calculations applicable to the purification of BAL contaminated with trithiol.

The feasibility of the extraction method was verified by the multiple extraction of a typical BAL sample. A volume of petroleum ether equal to that of the BAL was used for each successive extraction step. The fraction of trithiol originally present which remains in the BAL after n extractions under these conditions is $(1 + K)^{-n}$. Therefore, 41 extractions would be expected to result in a 10-fold reduction in trithiol concentration. This was found to be the case experimentally. The percentage loss of BAL into the petroleum ether equals 0.435 × (number of volumes of petroleum ether used in the extraction). Except for convenience, little is gained in the way of efficiency by use of continuous extraction against a multiple extraction performed in this way.

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Identification of Some Barbiturates in Blood by Use of Thin-Layer Chromatography

By JOHN A. PETZOLD, WALTER J. R. CAMP, and ERNST R. KIRCH

A simple, rapid method for the identification of mixtures of barbiturates when present in blood is described. This procedure is especially useful in differentiating between amobarbital and pentobarbital.

THE PROCEDURES involving the identification of certain barbiturates leave much to be desired. This is particularly true when it is necessary to establish the presence of barbiturates in the blood and urine as the agents causing comas in hospital patients or deaths in medical-legal cases.

Two popular approaches of identification using paper seem to be those similar to Algeri, *et al.* (1), and Stevens (2), involving either the treatment of the paper chromatogram after elution of the barbiturate or treatment of the barbiturate before spotting in order to differentiate between saturated and unsaturated groupings attached to the pyrimidine ring. Among the many investigators using thin-layer chromatography, Frahm, *et al.* (3), using piperidine: petroleum ether as the mobile phase, and Eberhardt, *et al.* (4), using isopropanol: ammonia: chloroform as the mobile phase, have reported success in the separation of several barbiturates.

We would like to report a simple, rapid method of

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