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**Smith E L & Page J E.** The acid-binding properties of long-chain aliphatic amines.
*J. Soc. Chem. Ind.* 67:48-51, 1948.
[Research Division, Glaxo Laboratories Ltd., Greenford, Middlesex, England]

Long-chain tertiary aliphatic amines, such as methyldioctylamine, are more efficient as acid-binders than are primary or secondary amines and can extract strong acids from mixtures with weak acids. Analytical and industrial applications of the technique are suggested. [The *SCI*® indicates that this paper has been cited in over 170 publications.]

## Long-Chain Amines as Anion Exchangers

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In 1943, as part of a wartime Therapeutic Research Corporation programme, my colleagues in the Chemical Research Department of Glaxo Laboratories at Greenford prepared and tested for activity against the tubercle bacillus and other microorganisms a number of primary, secondary, and tertiary long-chain aliphatic amines.[1] Unfortunately, although secondary and tertiary amines with 17 to 20 carbon atoms inhibited, *in vitro*, the growth of *Mycobacterium tuberculosis* and were highly active against other organisms, they proved to be inactive *in vivo*. Nevertheless, a colleague, J. Ungar, started a study of the metabolism of methyldioctylamine and I, while developing a colorimetric method for its determination in urine and tissue extracts, observed that salts of long-chain amines with mineral acids are almost insoluble in water but are readily soluble in organic solvents, such as chloroform.[2] This property is illustrated by the almost complete extraction of hydrochloric acid from strong aqueous solution.

The availability of the range of amines encouraged E. Lester Smith and me to investigate their acid-binding properties and to look for industrial applications. Our first experiments were concerned with wartime projects, such as the purification of penicillin and the removal of mineral acids from acid-hydrolysates of protein. At that time, towards the end of World War II, protein hydrolysates were being considered (they were later found to be of no value) for use by medical teams treating malnutrition in liberated Europe. Experiments on the extraction of organic acids from biological material and fermentation liquors and on the recovery of metals, such as chromium and vanadium, gave promising results and indicated the wide utility of the technique.

After the work had been written up for publication, our interest in long-chain amines flagged. Smith undertook exciting work on the antipernicious anaemia factor (vitamin $B_{12}$) and I became involved with spectrophotometry.

It therefore came as a surprise when, in 1952, papers started to appear from the Oak Ridge National Laboratory and other laboratories describing the value of the technique for, *inter alia*, separating niobium and tantalum[3] and extracting uranium, applications in fields remote from those for which we had prepared the amines.

Looking back over 40 years, it is pleasing to see that the anion-exchange properties of long-chain amines continue to find use in industrial and analytical laboratories. They are featured in biochemical, geological, and metallurgical analyses and are the subject of basic physical studies. Thus, cadmium, copper, and lead in urine are determined by atomic absorption spectrometry after extraction of iodide complexes as ion pairs with tri-*n*-octylamine,[4] and work goes on at Oak Ridge on problems of aggregation and of liquid third-phase formation.[5]

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1. **Borrows E T, Hargreaves B M C, Page J E, Resuggan J C L & Robinson F A.** Preparation and properties of some long-chain aliphatic amines. *J. Chem. Soc.* 1947:197-202. (Cited 15 times.)
2. **Hopewell B M C & Page J E.** *Colorimetric estimation of long-chain aliphatic amines. Analyst* 70:17, 1945.
3. **Leddicotte G W & Moore F L.** A new solvent extraction method for the separation of niobium and tantalum. *J. Amer. Chem. Soc.* 74:1618, 1952. (Cited 55 times.)
4. **Flanjak J & Hodda A.** Determination of cadmium, copper and lead in urine. *Anal. Chim. Acta* 172:313-6, 1985.
5. **Moyer B A.** Alkane-insoluble trialkylammonium double salts involving the dodecamolybdophosphate anion. *Solvent Extr.* 5:195-203, 1987.

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