

## Citation Classics

**Schneider W C.** Phosphorus compounds in animal tissues. I. Extraction and estimation of desoxypentose nucleic acid and of pentose nucleic acid. *J. Biol. Chem.* 161: 293-303, 1945.

**This new extraction method consists in heating the tissue in 5 ml. of 5 percent trichloroacetic acid for 15 minutes at 90° after removal of phospholipids and acid-soluble phosphorus compounds. The tissue is then cooled and centrifuged. The residue is resuspended in 2.5 ml. of 5 percent trichloroacetic acid and centrifuged. The trichloroacetic acid extracts are combined to form the nucleic acid extract. [The SC<sup>®</sup> indicates that this paper was cited 1,518 times in the period 1961-1975.]**

Walter C. Schneider, Ph.D.  
National Institutes of Health  
Bethesda, Maryland 20014

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"It is indeed most gratifying to learn 31 years after publishing my paper that it is one of the most cited scientific papers. It is not entirely surprising to me that this should be the case since methods are the backbone of all scientific research. Consequently, my method for the extraction of nucleic acids from tissues and for their analysis might be expected to be referred to more frequently than average...

"To my mind there were two reasons for the popularity of the method. In the first place it was simple-both nucleic acids could be extracted from tissues with a single hot trichloroacetic acid treatment and then measured colorimetrically. More important, however, was the fact that the method dealt with nucleic acids, molecules that have engrossed the scientific community for more than 30 years and will continue to do so for many more...

"The fact that the paper should be cited so frequently is also a source of great satisfaction to me for another reason. This paper was based upon my doctoral dissertation and was thus my first as a sole author. I was fortunate to have Van R. Potter of the University of Wisconsin guide me into doing this work, which was designed to provide methods for measuring DNA and RNA in fractionations of tissue homogenates by

differential centrifugation so that the recovery of subcellular organelles could be measured biochemically. The methods served admirably for this purpose and were instrumental in developing new methods for isolating nuclei, mitochondria, and microsomes, and in studying the subcellular localisation of biochemical functions.

"A few sidelights should also be noted. As I have confessed to friends and colleagues from time to time, the discovery that both nucleic acids could be extracted from tissues with hot trichloroacetic acid was not due to some great inspiration on my part but rather to my misreading one of Zacharias Dische's papers in the *Biochemisches Zeitschrift*. I have noticed a number of times during the intervening years that other scientific breakthroughs could be traced to similar fortunate mistakes-such is the progress of science. Also, imagine my surprise and chagrin upon opening the journal in which my paper appeared to find a paper on the same subject by Gerhard Schmidt and S.J. Thannhauser.<sup>1</sup> Their paper permitted the separation of DNA from RNA, which mine did not, but not the separation of DNA from protein, which mine did. It was immediately obvious to me that the ideal method for measuring nucleic acids would combine the best features of the two methods. I hurried to the laboratory to work out the details and the results were published the following year in the same journal....

"It may be of interest that I continue to use the method essentially unchanged. Although I have followed the literature diligently seeking for improvements that I could adopt, only a few have proved useful. One of these was the neutralisation of the tissue suspension after the initial extractions with cold trichloroacetic acid to avoid loss of protein during the extractions with alcohol. Another was the use of lower concentrations of alkali and shorter extraction times suggested by Fleck and Munro to solubilize RNA. Finally, the more sensitive diphenylamine reaction of Burton and the fluorimetric procedure of Kissane and Robins have proved most useful in more recent years for measuring the small amounts of DNA present in cytoplasmic organelles."

1. **Schmidt G & Thannhauser S J.** A method for the determination of desoxyribonucleic acid, ribonucleic acid, and phosphoproteins in animal tissues. *J. Biol. Chem.* 161:83-89, 1945.