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Citation Classics

Spies, Joseph R & Chambers, Dorris C. Chemical determination of tryptophan in proteins. *Analytical Chemistry* **21**:1249-66, 1949.

Several variations of a method for colorimetric analysis of unhydrolyzed proteins are described. The basic method was based on fundamental studies of the behavior of free and peptide-linked tryptophan. These studies included a method of alkaline hydrolysis which protects tryptophan from external destruction at temperatures up to 185°C without addition of antioxidants to the solution. Dr. Spies, now retired, conducted his research in the Allergens Research Division of the U.S. Department of Agriculture. [The *SCI*® indicates that this paper was cited 739 times in the period 1961-1975.]

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January 24, 1977

"It is most gratifying that our paper is 'one of the most cited articles ever published.'

"Dissatisfaction, in the early 1940s, in the use of existing methods for the determination of tryptophan prompted our studies. The first of our several papers on the subject was published in 1948 and the last in 1967. Originally we never intended to get so involved. We started out by simply trying to substitute sulfuric acid for the concentrated hydrochloric acid used in some existing methods to avoid the corrosive fumes of the latter acid. But, one thing led to another, so that this small beginning led to over four years of full-time research with the excellent technical assistance of Dorris Chambers part of this time.

"The experimental research was just plain pleasure. But getting the results published was something else. Originally I attempted to publish the contents of this paper as four separate articles, little suspecting the grueling road that lay ahead. Three of these articles were submitted to the late Walter J. Murphy, Editor of *Analytical Chemistry*, on May 10, 1948, and the fourth on October 6, 1948. A total of 135 pages of manuscript was thus being considered at one time. The re-viewers were hard and in one case prejudiced to a point where I asked for and received his disqualification.

"During the ensuing months I answered the reviewers' many comments with a general statement and specific reply to each point raised. My responses totaled 62 pages over all with numerous revisions of the manuscripts. The final result was the combination of the four articles into one consisting of 71 pages of manuscript. Exactly one year to the day after the first submission, the revised manuscript was tentatively accepted for publication subject to more editorial revisions. The review process was onerous and a strong will was required to keep from giving it all up somewhere along the way. However, with one exception, I am deeply indebted to the anonymous reviewers who performed a difficult and seemingly thankless task. I am also indebted to Walter Murphy for his patience and fairness. Thanks are also due to Stella Anderson, Assistant Editor, and Miss Cordon for encouragement and editorial help in preparation of the manuscript. The resulting paper was much better than the original because of the cooperation of all of these persons. A final, as far as I am concerned, revision of the original method was published in 1967.[1] [Cited 76 times, 1967-1975.]

"Although many other papers on the determination of tryptophan have appeared, especially in the last decade, our method filled a considerable need by many researchers following its publication in 1949, and indeed the original method and its subsequent modification still enjoys considerable usage."

1. **Spies JR.** Determination of tryptophan in proteins. *Analytical Chemistry* **39**:1412-16, 1967.