Book Review

The Chemical Components of Tobacco and Tobacco Smoke

Alan Rodgman and Thomas A. Perfetti

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1836 pages

I highly recommend this book as an indispensable reference source for tobacco and smoke chemists as well as other scientists involved in the study of tobacco and its products. The compilation of proper chemical names, common names, Chemical Abstract Service numbers (CAS No.), and structures is alone worth the purchase price.

Collecting is a hobby enjoyed around the world. Collectable items include stamps, coins, antiques, butterflies, books, etc. The principal author of this book is a lifelong collector, but his collections are more information rather than items. For instance, he has a list of every book that he has ever read, and this list contains thousands of entries. I trust that many of us would like to have similar records, but few, if any, have had the foresight to maintain such an accounting. Furthermore, a list of books read during a lifetime, probably has little value to anyone other than the reader. However, ALAN RODGMAN's self-disciplined and enduring approach to meticulous recordkeeping is the foundation upon which this current book has been constructed. His collection of tobacco and tobacco smoke chemical component references began approximately in 1954 and is current in this book through 2007, a span of 53 years. It is fitting that this *magnum opus* is published a few months before the principal author's 85th birthday.

The authors of this book, ALAN RODGMAN and THOMAS A. PERFETTI, modestly state that their motivation for publishing *The Chemical Components of Tobacco and Tobacco Smoke (CCTTS)* is to update an earlier catalog of tobacco and smoke components published by R.L. STEDMAN in 1968 (1). STEDMAN voiced a similar purpose for his publication, i.e., a sequel to the catalog of JOHNSTONE and PLIMMER published in 1959 (2). Although it follows the general outline of STEDMAN's review, *CCTTS* is more than a simple and long overdue update; it is also a history book,

a textbook, and an autobiography of the authors' professional research into tobacco and smoke chemistry.

I can recall, as a newly employed tobacco and smoke chemist, that the publication of STEDMAN's catalog gave me great concern about my job security. Naively I thought, what is left to be done? However, the RODGMAN-PERFETTI publication is testimony to my lack of knowledge. Compare the following parameters between the STEDMAN and RODGMAN-PERFETTI catalogs:

Comparison of Stedman and Rodgman-Perfetti Catalogs of Tobacco and Smoke Components

Parameter	Stedman	Rodgman-Perfetti
Total pages	54	1836
References	666	6744
Tobacco constituents	Not available	4994
Smoke constituents	Not available	5315
Tobacco & Smoke constituents	~1200	8430

As may be seen from this comparison, there is approximately a tenfold difference in the number of references and a seven-fold difference in the total of tobacco and smoke constituents. These differences result principally from three factors: 1) Four decades of intense scrutiny of tobacco and smoke constituents; 2) Improvements in separation science and analytical chemistry methodologies; 3) Access to company documents under tobacco litigation.

The authors state (3), "Our goal was to present to the reader as many pertinent references as we could find for a particular component and permit the reader to decide which

references to study.” In terms of references, RODGMAN and PERFETTI have made ample use of information available on the Internet, e.g., www.rjrdocs.com 512875888 -5942. Some reviewers of early drafts of *CCTTS* questioned the use of electronic references because they can be unreliable. As the authors note at the beginning of the Bibliography (4), “NOTE: Every one of the following references that include an electronic reference was accessed and found to be functional during the period August 24–26, 2007.” Furthermore, between August 2007 and submission to the publisher of the Bibliography in November 2008, over two-thirds of the nearly 900 electronic references were used by the authors and all were found to be functional (5). However, websites are notoriously temporal and a valid web address in 2007–2008 may be gone today. The important service provided by this publication is to identify the reference and record it in a more permanent media. Furthermore, the authors have hard or electronic, i.e., PDF, copies of every reference listed in the book’s Bibliography (5). *CCTTS* is divided into twenty-eight chapters. Chapters 1–20, 22 and 27 deal with naturally occurring tobacco and smoke constituents; Chapter 21 discusses agronomic chemicals whose residues or pyrolytic products become constituents; and Chapter 24 reports on tobacco and tobacco smoke components used as tobacco product ingredients. Chapter 23 discusses the origins and significance of the “Hoffmann Analytes”; whose constituents are also found in other chapters, e.g., Chapter 15, *N*-Nitrosamines. Chapter 25 contains information on tobacco pyrolysis research and Chapter 26 covers carcinogens, tumorigens, mutagens, anticarcinogens, and antimutagens. These two chapters add few, if any, new constituents to the catalog. Chapter 28 summarizes the information in the preceding twenty-seven chapters and is similar to *CCTTS*’s Introduction.

A typical chemical class chapter contains the following:

- ▶ A historical perspective
- ▶ Analytical methodology used to characterize the presence of the component
- ▶ Quantification methodologies and results
- ▶ Smoke precursor studies
- ▶ Studies on the biological activity of a particular component
- ▶ Controversies related to the component(s)
- ▶ Tobacco modification, e.g., solvent extraction, flue-curing technology, and cigarette design technologies to reduce the levels of class constituents in tobacco products
- ▶ A table listing all reported class constituents found in tobacco, smoke and/or tobacco substitutes; multiple-function chemicals are listed in more than one chemical class

The discussion of some subjects is limited. There are quantitative data for fewer than 5% of the reported components principally because such data do not exist. In addition, the biological studies and controversies are almost entirely limited to carcinogenesis, tumorigenesis and mutagenesis. Several controversial subjects, e.g., smoke pH, human versus machine smoking, addiction, have either no or very limited discussion even though the authors have previously published papers on some of these subjects (6,7). In some regards, the included subjects reflect the autobiographical

nature of the book. Followers of tobacco and smoke literature will quickly realize that many of the discussions contained in *CCTTS* come almost directly from earlier publications by RODGMAN and/or PERFETTI. Although this in itself is not a deficiency, it does lead to redundancy, e.g., see discussions of the publication by VAN DUUREN *et al.* (8) in 1960 reporting the identification of dibenz[*a,h*]acridine, dibenz[*a,j*]acridine, and dibenzo[*c,g*]carbazole in tobacco smoke (9). However, many parts of *CCTTS* contain new, updated or previously unpublished discussions, e.g., Chapter 22 on Genes, Nucleotides, and Enzymes, Chapter 27 on Free Radicals.

The huge body of references that form the basis for *CCTTS* largely report on the pursuit of the two principal objectives of tobacco and smoke research. These objectives are to identify components of tobacco and its smoke that are important to the flavor, sensory experience, and consumer acceptance of tobacco products and to determine what components or class of tobacco components and its smoke may be responsible for the human health risks associated with tobacco use. Some progress has been made toward the first objective as discussed in Chapter 24 on Tobacco and/or Tobacco Smoke Components Used as Tobacco Ingredients. Another example is the identification of glucose and sucrose esters of 4-methylpentanoic acid and other “stench” acids in Oriental tobacco leaf whose pyrogenesis of the simple acids is so important to the smoke aroma and flavor of blended cigarettes. Progress on the second objective appears to be much more elusive. Although much has been alleged and many hypotheses have been generated, the status remains as stated by RODGMAN and PERFETTI (10), “Scores of citations over the past five decades have been issued by eminent scientists and health organizations in which it is stated that no single MSS component or class of components acting either individually or in concert can explain observations in human smokers or in laboratory animals treated with heroic doses of MSS.” This statement notwithstanding, studies discussed in Chapter 15 on *N*-Nitrosamines, e.g., reduction of tobacco specific nitrosamines during flue-curing of tobacco, may demonstrate beneficial progress. As RODGMAN and PERFETTI state in *CCTTS* (11), “Every practical effort should be made to reduce the amounts of alleged human carcinogens from tobacco products. However, whether the reduction or elimination of TSNAs from MSS will result in a “less hazardous” cigarette is unknown.”

The total of 8430 tobacco and smoke constituents listed in *CCTTS* will exacerbate the claims that tobacco and its products are very complicated chemical mixtures and thereby imply that this complexity in itself is unhealthy. The authors of *CCTTS* repeat the unreferenced claim that tobacco has been called a “chemical factory” (12). Furthermore, WAKEHAM’s (13) claim in 1971 that tobacco smoke itself may contain from ten to one hundred thousand smoke components yet to be identified, and they only account for the volatile compounds, as well as GROB’s statement in 1973 (14) that tobacco smoke is by far the most complex mixture available for analysis appear to be supported by *CCTTS*. Yet, these statements attest more to the long and intense scrutiny of tobacco and its smoke by skilled and diligent analytical chemists than anything else. As RODGMAN and PERFETTI state in *CCTTS* (11), “One thing has become apparent since

the mid-1950s: No other consumer product that involves a complex mixture has been defined in such detail as tobacco and/or its smoke, for example, the number of components identified to date in tobacco is almost twice that of the number identified in coffee." The question remains: Is tobacco chemically more complex than other crops and is its smoke more complex than other crops that have been heated or otherwise thermally treated?

In the preparation of *CCTTS*, the authors have been conservative in their listing of tobacco and smoke components. Basically, they have followed the practice of earlier catalogs (16), i.e., "The authors of some of the early reviews and catalogs on tobacco smoke composition listed the smoke components reported in the literature without regard to the analytical validity of their identification." Some exceptions to this policy do occur in *CCTTS*, e.g., the publication by VAN DUUREN *et al.* (8) in 1960 reporting the identification of dibenz[*a,h*]acridine, dibenz[*a,j*]acridine, and dibenzo[*c,g*]carbazole in tobacco smoke. RODGMAN and PERFETTI justified their approach by stating, "This problem has progressively decreased over the years as analytical technology has increased in sophistication." Although I agree about improvements in analytical technology, as a volunteer reviewer of tobacco and smoke publications, it is my experience that some investigators rely almost entirely on GC- or LC-mass spectrometry for identifications with commercially available, electronic mass spectral libraries. These identifications are not confirmed by any other evidence. Furthermore, the practice of including compounds not reported in the published literature might lead to a less rigorous threshold for identification.

One subject of great concern to analysts attempting to identify and quantify components of tobacco smoke is the formation of artifacts, i.e., the measured components should be representative of what the smoker is actually exposed to. This might be a significant, yet unproven problem considering the number of reactive chemical species found in smoke. How many of the 5315 smoke components reported in *CCTTS* are actually formed during the collection and subsequent aging of the concentrated tobacco smoke? This is a question that no one can answer with authority, but certainly artifacts do exist. DUBE and GREEN have previously discussed this potential problem (17). In *CCTTS*, RODGMAN and PERFETTI do not devote a chapter to artifact formation; however, the possibilities of artifacts are considered throughout and prominently discussed in Chapter 15 on *N*-Nitrosamines. Additionally, in Chapter 27 on Free Radicals there is an intriguing discussion on the most recent investigations of tobacco smoke free radicals (18) suggesting that simply separating smoke into its gaseous and particulate phases through the use of Cambridge filter pads may lead to artifact formation to the extent that:

... previously made biological assertions need to be reevaluated since the free radicals presumably present in MSS may not actually exist. The clear evidence of artifacts formed by the separation of whole smoke into particulate and vapor phases supports the total reexamination of the chemistry and biology of free radicals in tobacco smoke proposed by Bartalis *et al.* (27A05).

In conclusion, RODGMAN and PERFETTI have accomplished a remarkable task in updating and revising the catalog of tobacco and smoke components published by STEDMAN in

1968 (1). The publication of *CCTTS* ensures that a lifetime collection of references on tobacco and smoke components will not be lost. Any tobacco and smoke researcher as well as others interested in the subject will find the book to be a valuable desktop reference to learn whether a newly isolated tobacco or smoke component has been reported previously and, if so, what is already known about the component. This task will be greatly facilitated by the searchable CD-ROM included with the book.

The authors of *CCTTS* have written in its Summary the following (19):

If it were not for scientists' curiosity and the tremendous advances in analytical chemistry over the last fifty to sixty years, the need for this up-to-date catalog of compounds in tobacco and tobacco smoke would not be critical. As analytical technology advances, surely thousands of new chemical components in tobacco and tobacco smoke will be added to the listings found in this text.

And in the Introduction they state the following (20):

Years from now, just as we were surprised how paltry was the number of identified tobacco smoke components cataloged in 1954 by Kosak (2170), others will no doubt have similar remarks concerning this catalog. We hope the reader will be satisfied rather than frustrated with the progress that has been made by tobacco scientists over the last fifty plus years in furthering our knowledge base of components identified in tobacco and tobacco smoke. It should be noted the last published detailed catalog of tobacco and tobacco smoke components was that of Stedman (3797) in 1968.

The prophetic visions of RODGMAN and PERFETTI may be correct, but scientific curiosity and the challenge of understanding the complex chemistry and biological effects of tobacco products are insufficient in themselves to support research on the scale reported in *CCTTS*. Some "experts" claim that there is already sufficient knowledge while others argue the opposite as stated in *CCTTS* (19):

Hundreds of scientific articles (many of them referenced in this text) have stated that tobacco and tobacco smoke are complex mixtures. This is an accurate statement. But some have alluded to or emphasized that they are primarily complex, that is, these mixtures of chemicals are just too multifarious, too difficult to completely understand, or so complicated and/or convoluted that the normal individual could not possibly comprehend the totality of the concept or composition of the mixture. This was never the intent of the definition of a complex mixture, but nevertheless, some have implied that this multifaceted conglomeration of chemical components in tobacco and tobacco smoke is too difficult to explain and understand.

Whether or not an up-to-date catalog of tobacco and tobacco smoke constituents will be needed forty years hence is unknown. Regardless, RODGMAN and PERFETTI are commended for the foresight, hard work, and diligence required for publishing *CCTTS*.

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3. See *CCTTS*, Foreword, p. x.
4. See *CCTTS*, Bibliography, p. 1261.
5. Personal communication with A. Rodgman, December 2008.
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9. See *CCTTS*, pages 222, 488, 688, 707, 806, etc.
10. See *CCTTS*, Chapter 26, Carcinogens, Tumorigens, and Mutagens vs. Anticarcinogens, Inhibitors, and Antimutagens, p. 1180.
11. See *CCTTS*, Chapter 15, *N*-Nitrosamines, XV. H. Flue-curing and tobacco-specific *N*-nitrosamines, p. 712.
12. See *CCTTS*, Introduction, p. xxvii.
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16. See *CCTTS*, Chapter 1, The Hydrocarbons, p. 37.
17. Dube, M.F. and C.R. Green: Methods of collection of smoke for analytical purposes; Recent Adv. Tob. Sci. 8 (1982) 42–102 see pp. 74–77.
18. See *CCTTS*, Free Radicals, XXVII. E. Proposed mechanisms for the generation of free radicals in MSS, p. 1252.
19. See *CCTTS*, Summary, p. 1257.
20. See *CCTTS*, Introduction, Intent of the work, p. xxvii.