

Toxicological sciences in
‘Beitraege zur Tabakforschung International’
(BTFI)
during the last 55 years

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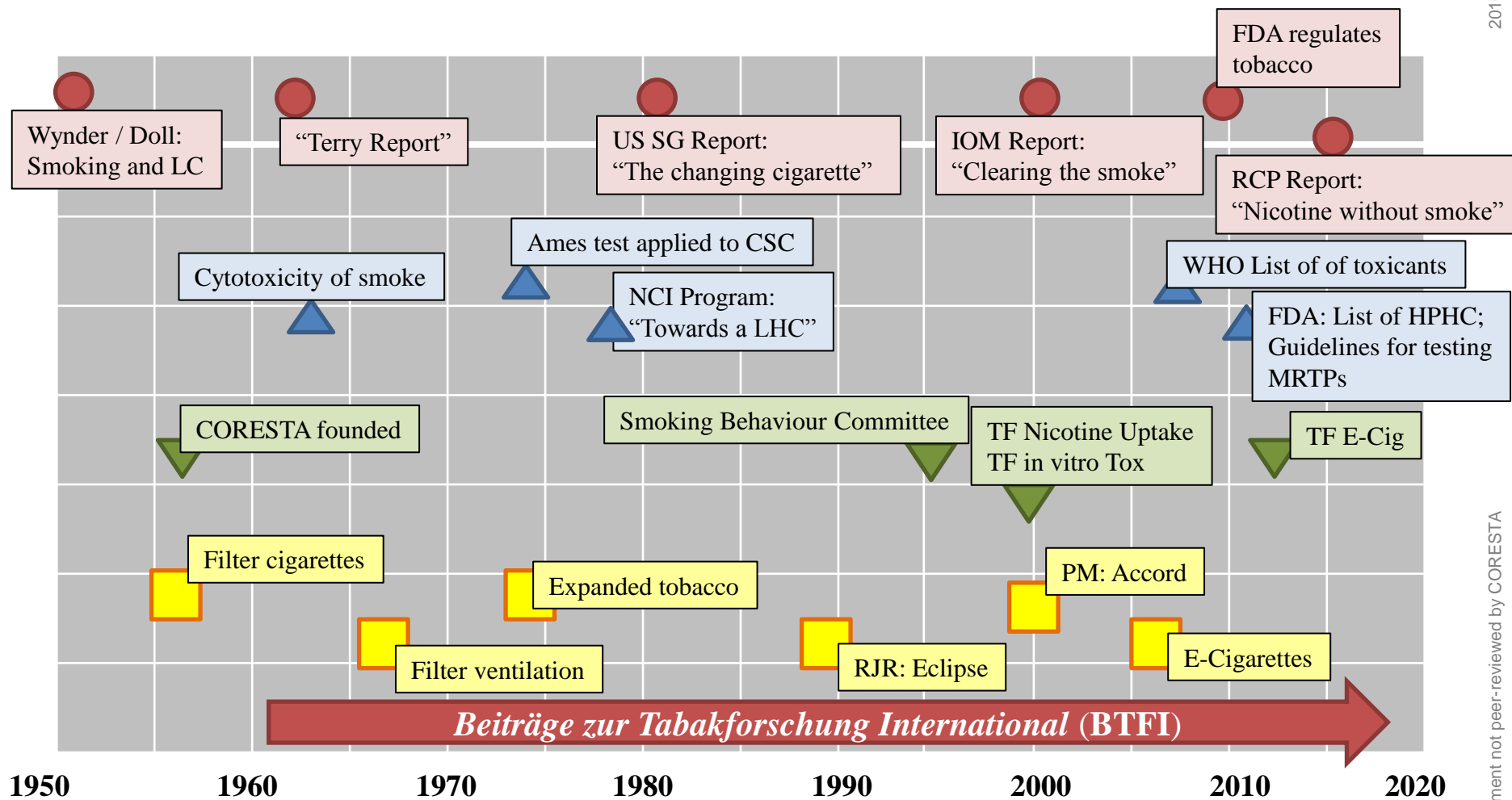
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Outline

- Events/milestones with impact on toxicology in tobacco research
- Toxicological aspects within the scope of BTFI
- Special toxicants in tobacco and tobacco smoke
- Human studies: Smoking behaviour / Nicotine effects
- Dosimetry: Mouth level exposure (MLE) / Respiratory retention / Biomarkers of exposure (BoE)
- *In vitro* toxicity studies
- Top 10 authors in BTFI
- Conclusions

Key events / milestones



Toxicological aspects within the scope of BTFI

1. *Fields covered by the Journal:* The Journal welcomes new, unpublished original contributions and review articles relating to the various aspects of tobacco science, including physical and chemical analysis of tobacco and tobacco smoke, pertinent matters to the manufacture of tobacco products, research into tobacco plants including biotechnology, plant treatment substances, protecting agents, leaf tobacco, statistical data processing, and human smoking behaviour including biomonitoring.

- Toxicants: **Nitrosamines / PAHs**
- Human studies: **Smoking behaviour / Nicotine dose/effects**
- Dose / Dosimetry: **MLE / Respiratory retention / BoEs**
- *In vitro* studies: **Cytotoxicity / Mutagenicity**

Toxicants in tobacco and smoke: PAHs

- PAHs are suggested to be carcinogenic for humans since the 18th century (“chimney sweepers’ carcinoma”), BaP was identified as a carcinogen in 1933 (Cook)
- In the mid of the 1950ies, the first publications on BaP in tobacco smoke appeared (Wynder)
- **BTFI**: 16 articles with the focus on PAHs were published.
- Already in the first volume of BTFI, two methods for BaP in CSC were published: Grimmer (1961), Barkemeyer (1962)

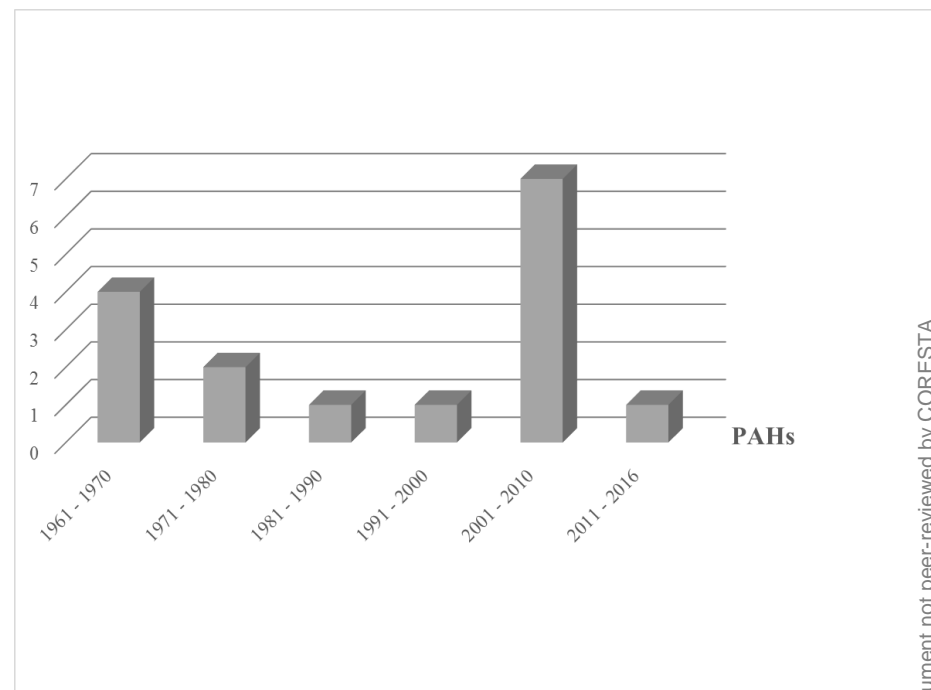
Beiträge zur Tabakforschung · Heft 3 · August 1961

DOI: 10.2478/cttr-2013-0017

Eine Methode zur Bestimmung von 3,4-Benzpyren in Tabakrauchkondensaten

von G. Grimmer

Biochemische Abteilung des Instituts für Organische Chemie der Universität Hamburg



Toxicants in tobacco and smoke: Nitrosamines

- In 1956, Barnes and McGee showed that N-nitrosamines are carcinogenic to rodents
- In 1962, Druckrey and Preussmann hypothesized that nitrosamines could be also present in tobacco smoke
- **BTFI**: 21 articles with the focus on nitrosamines
- Worth mentioning is a series of 3 papers of Neurath et al. between 1964 and 1966.

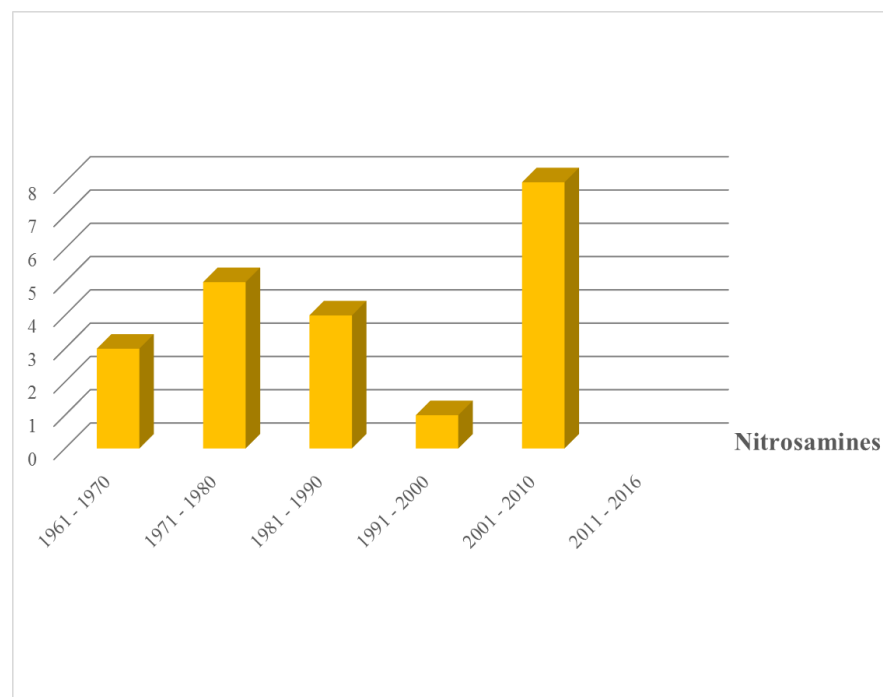
Beiträge zur Tabakforschung · Band 2 · Heft 7 · November 1964

DOI: 10.2478/cttr-2013-0084

Zur Frage der N-Nitrosoverbindungen im Tabakrauch

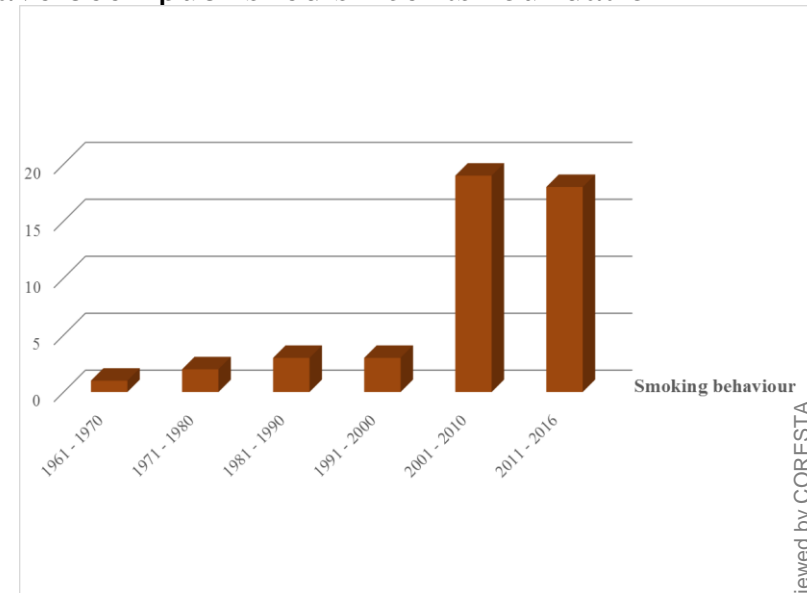
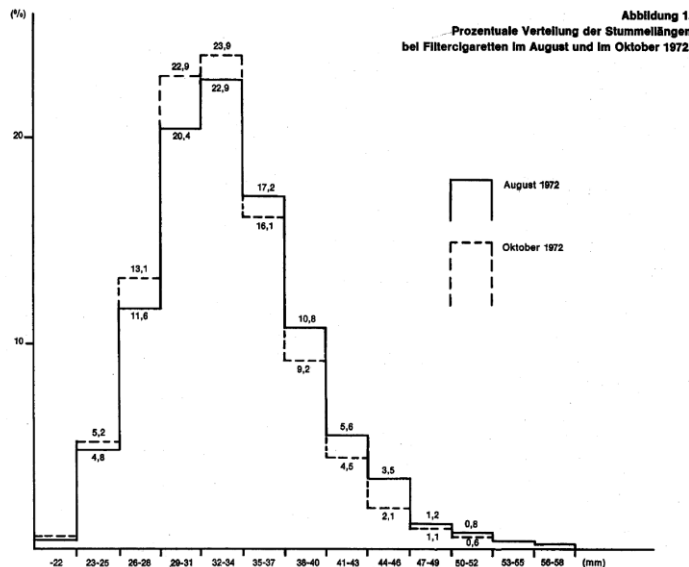
von G. Neurath, B. Pirmann und H. Wichern

Forschungslaboratorium H. F. & Ph. F. Reemtsma, Hamburg



Human studies: Smoking behaviour

- Smoking behaviour is an essential part of tobacco science with respect to both product design and health implication.
- **BTFI**: Smoking behaviour is an explicit part of the scope of the Journal. 46 articles dealing with various aspects of human smoking behaviour have been published since its foundation
- A rather exceptional aspect of smoking behaviour has been studied and published by W. Schulz between 1970 and 1986: The influence of tax increase or economic depression on cigarette butt length in the German population.



Human studies: Nicotine dose and effects

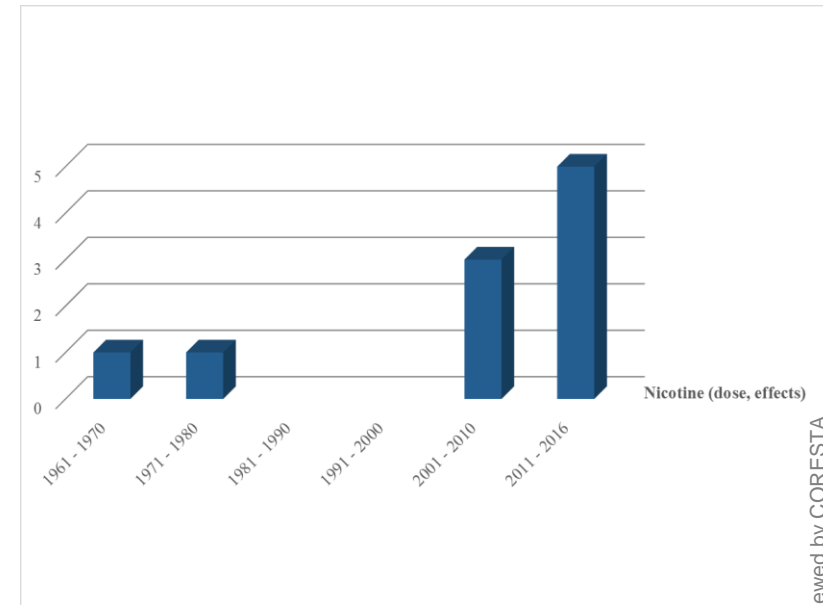
- By all accounts, nicotine is by far the most interesting and important compound in tobacco and tobacco smoke.
- **BTFI**: 10 articles with the focus on human nicotine dose and effects have been published in the Journal
- Two publications on the toxicology of nicotine are particularly noteworthy:
 - Schievelbein (1962): “Nicotine, smoking and organism”, 77 pages, 396 references (comprehensive review of the then scientific knowledge)
 - Nicotine workshop of 1974 in Stockholm, Sweden (published in 1976): with original contributions of well-known nicotine researchers (Schievelbein, Armitage, McKennis, Boyland, Gorrod, van Vunakis, Turner, Neelakantan, Feyerabend, Horning)

Beiträge zur Tabakforschung · Band 8 · Heft 5 · März 1976

Nicotine Workshop

arranged by

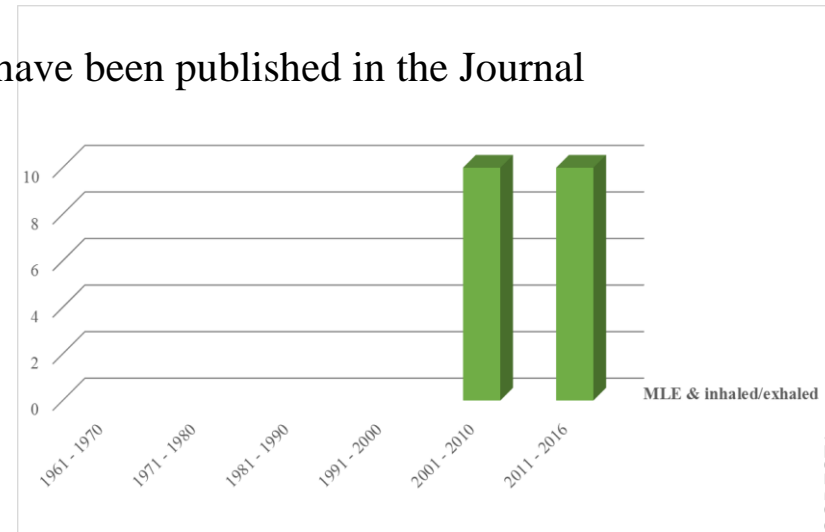
the Medical Advisory Board of the Swedish Tobacco Company, in Stockholm, in November 1974



DOI: 10.2478/cttr-2013-0391

Dose / Dosimetry: MLE and lung retention

- Dose and dosimetry are essential elements in toxicological studies. Determination of MLE measured by the part filter method and lung retention by measuring the difference of inhaled minus exhaled amounts are recent, non-invasive methodologies for assessing the human smoking dose.
- **BTFI**: 25 articles dealing with these technologies have been published in the Journal
- Two research teams are mainly associated with the development and application of these technologies:
 - St. Charles/Shepperd: MLE
 - Moldoveanu: Lung retention



Beiträge zur Tabakforschung International/Contributions to Tobacco Research

Volume 23 · No. 5 · September 2009

DOI: 10.2478/cttr-2013-0863

Beiträge zur Tabakforschung International/Contributions to Tobacco Research

Volume 23 · No. 3 · December 2008

DOI: 10.2478/cttr-2013-0857

A Robust Method for Estimating Human Smoked Cigarette Yields from Filter Analysis Data*

by

F.K. St.Charles¹, M. Ashley², C.J. Shepperd², P. Clayton², and G. Errington²

¹ Consultant, 2250 Hilltop Dr, Winston-Salem, NC 27106, USA

² British American Tobacco, Southampton SO15 8 TL, UK

A Pilot Study to Assess Solanesol Levels in Exhaled Cigarette Smoke*

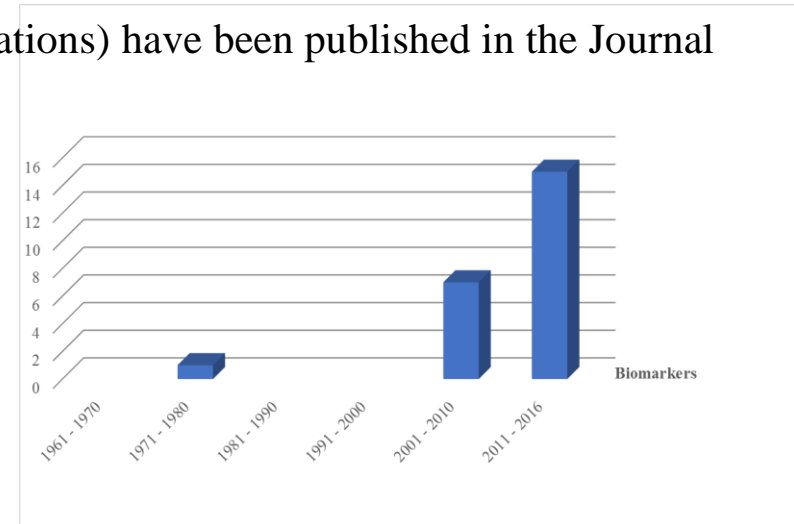
by

Serban C. Moldoveanu, William Coleman III

R.J. Reynolds Tobacco Co., 950 Reynolds Blvd, Winston-Salem, NC 27105, USA

Dose / Dosimetry: Biomarkers of exposure (BoEs)

- Depending on the body fluid used (blood, urine, saliva), application of BoEs can be either invasive or non-invasive. BoEs reflect the absorbed (internal) dose.
- **BTFI**: 23 articles dealing with BoEs (mostly applications) have been published in the Journal
- One of the first and a more recent publication of this category in BTFI were:
 - Grieder & Buser (1971): Method development for COHb and COex
 - Round et al. (2015): Changes in BoEs upon switching to new products.



Beiträge zur Tabakforschung · Band 6 · Heft 1 · Juli 1971

DOI: 10.2478/cttr-2013-0264

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Beiträge zur Tabakforschung International
Contributions to Tobacco Research
Volume 26 · No. 6 · June 2015
DOI: 10.1515/cttr-2015-0013

Gaschromatographische Bestimmung von Kohlenmonoxid in der Ausatemluft und im Blut*

von K. Grieder und H. Buser

Forschungslaboratorium Vereinigte Tabakfabriken AG, Neuchâtel, Schweiz

Changes in Biomarkers of Exposure and Subjective Effects When Smokers Switch to Dual Use of Cigarettes and Either Snus or a Dissolvable Tobacco Product: A Summary of Three Clinical Studies *

by

Elaine K. Round¹, Leanne R. Campbell¹, Mitchell F. Stiles¹, Michael Dixon², Michael F. Borgerding¹

¹ Research and Development Department, R.J. Reynolds Tobacco Company, Winston-Salem, N.C. 27102, USA

² Dixon Consultancy, Liphook Hampshire, UK

In vitro toxicity studies: Cytotoxicity

- Systematic *in vitro* cytotoxicity studies with tobacco smoke were reported since the 1960ies (W. Weiss).
- **BTFI**: 14 articles on smoke cytotoxicity have been published in the Journal
- A remarkably early study in this field was published by:
 - Brown & Fowler (1967): Toxicity of smoke solution to *Proteus Vulgaris* (effect of carbon filters, acrolein was identified as the strongest cytotoxic constituent in tobacco smoke)

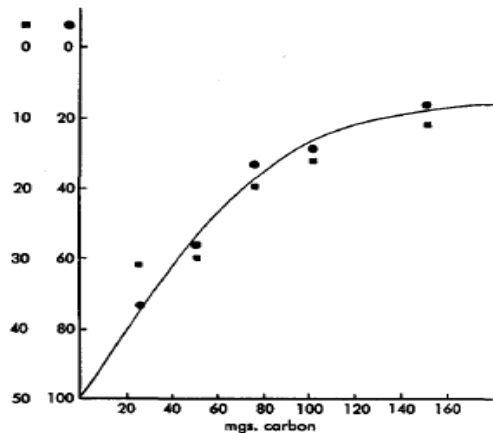
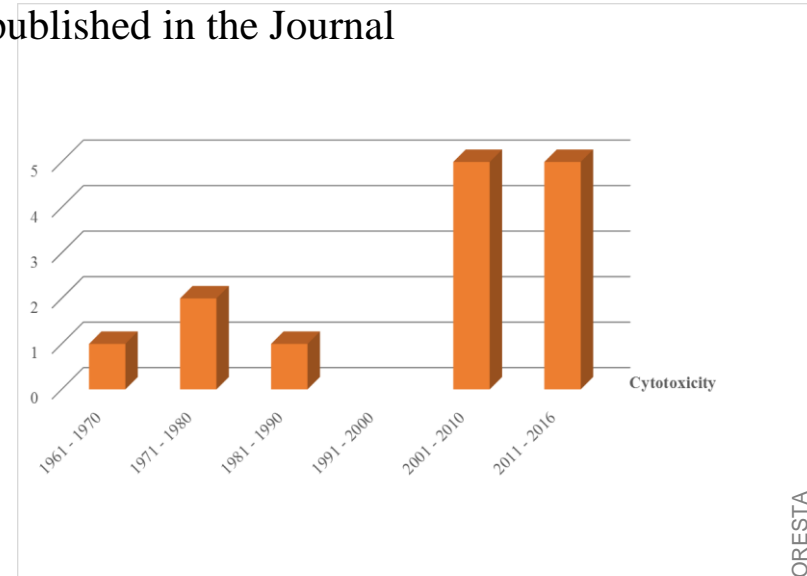


FIGURE 1

Reduction in toxicity and total aldehyde content of smoke solutions using various carbon loadings contained in recess filters

- Percentage reduction in growth as compared with control
- Percentage aldehyde content in smoke solution as compared with solution from "total vapour phase smoke solution"



Beiträge zur Tabakforschung · Band 4 · Heft 2 · Oktober 1967

DOI: 10.2478/cttr-2013-0172

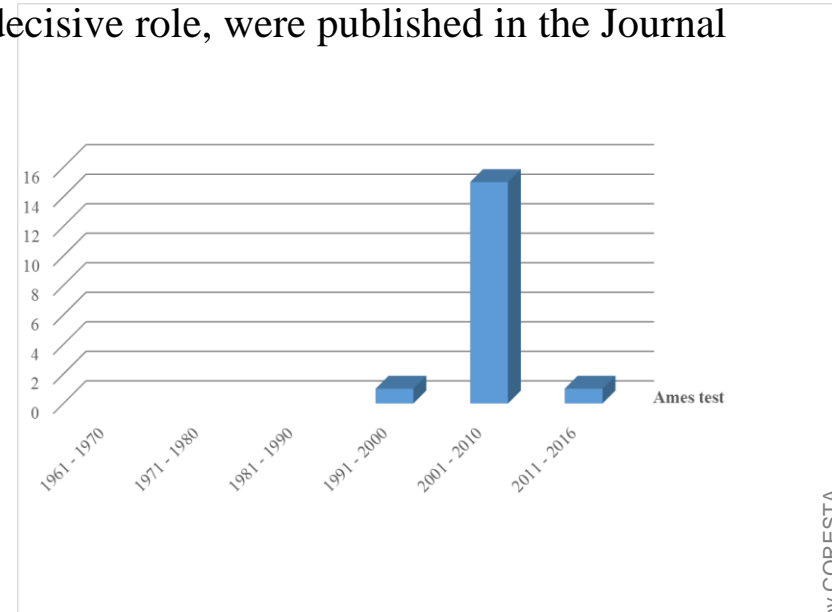
The Toxicity of Tobacco Smoke Solutions to *Proteus Vulgaris**

by P. W. Brown and C. A. Fowler

Carreras Limited, Research Division, Basildon, England

In vitro toxicity studies: **Mutagenicity (Ames test)**

- In 1974, the *S. typhimurium* assay (“Ames test”) was first applied to CSC (Kier, Yamasaki, Ames)
- **BTFI**: 21 articles, in which the Ames test plays a decisive role, were published in the Journal
- A remarkable paper on short-term tests for carcinogenic compounds has been published by Klein in the first volume of BTFI (1961, i.e. significantly earlier than the invention of the Ames test), briefly describing the following tests:
 - Mutagenicity tests with various cell systems, including bacteria
 - Cell transformations in various organ cell tissues
 - Inhibition of cell and tumor growth by carcinogens
 - Photodynamic (fluorescing) properties of carcinogens
 - Sebaceous gland test on mouse skin
 - Newt test (induction of hyperplasia with carcinogens)



Methoden zur Schnelltestung cancerogener Substanzen

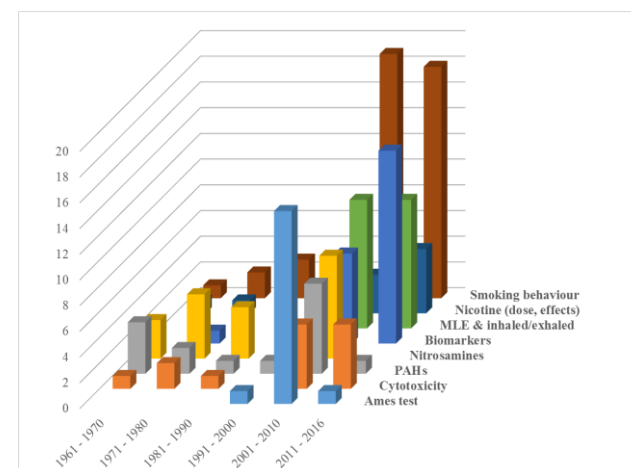
von U. E. Klein

Pathologisches Institut der Universität Hamburg

(Direktor: Prof. Dr. C. Krauspe)

Top 10 authors in BTFI (all topics)

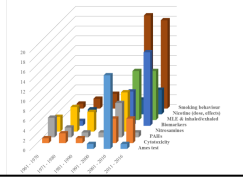
1.	F. Seehofer	48
2.	S. Moldoveanu*	26
3.	G. Neurath	25
4.	P. Coleman	21
5.	O. Chortyk*^o	20
6.	T. C. Tso^o / D. Hoffmann *^o	19
7.	A. Rodgman*	17
8.	S. Purkis	16
9.	T. Perfetti / H. Elmenhorst	15
10.	G. Lipp	14



* Mostly publishing in areas with relevance for toxicology

^o External (non-tobacco industry) scientist

Conclusions



- Despite the historical roots, toxicological aspects play a significant role in the published papers of BTFI, in fact from the start of the Journal
- In some toxicology-related areas of tobacco and tobacco smoke science, papers published in BTFI were actually “at the front”
- BTFI is also an attractive journal for non-industry scientists (this statement is also valid for toxicology-related research fields)
- As expected, published articles in BTFI dealing with toxicological aspects reflect political, scientific and industry-related developments in the area of smoking/tobacco and health
- Members of the “BTFI community” (authors, reviewers, advisory board, journal staff and editors) should support and strengthen the demonstrated developments so that the Journal can look ahead with confidence.