

lungszeiten und damit gleichzeitig drei unterschiedliche Gesamtdosen angewendet, um die Abtötung, wenn *auch nur mit wenigen Punkten*, für jede Intensität kurvenmässig zu ermitteln. Es wurde dabei so verfahren, dass jeweils bei den verschiedenen Intensitäten durch entsprechende Verlängerung der Bestrahlungszeit gleiche Gesamtdosen resultierten (Intensität · Zeit = konstant). Die diesbezüglichen Verhältnisse sind in dem beigefügten Bestrahlungsschema wiedergegeben.

Bestrahlungsschema

Intensität	Erg cm ⁻² sec ⁻¹	Bestrahlungszeiten		
1	4 · 10 ⁴	30''	1'	2'
1/10	4 · 10 ³	5'	10'	20'
1/50	0,8 · 10 ³	25'	50'	100'

In der beigefügten Abbildung sind die Ergebnisse dieser Versuche kurvenmässig dargestellt, wobei jeder Punkt der Kurve den Mittelwert aus durchschnittlich 15 Einzelbestimmungen darstellt. Man ersieht, dass der photodynamische Wirkungsgrad, gemessen an der Abtötung der Hefezellen, bei konstanter Benzpyren-Konzentration und einer Strahlendosis von $48 \cdot 10^4$ Erg bei der Intensität 1 ungefähr 6–8mal so gross ist wie bei der Intensität 1/10 und 1/50. In dem von uns untersuchten Intensitätsbereich ist also eine deutliche Abhängigkeit der photodynamischen Wirkung des Benzpyrens von der Intensität des UV.-Lichtes vorhanden, indem mit abnehmender Intensität die Wirkung konstanter Strahlendosen ziemlich steil abfällt.

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Summary

(1) The relation between photodynamic effect and intensity of ultra-violet radiation was investigated by means of the lethal-curve of yeast cells treated with benzpyrene as photosensibilizer.

(2) If the dosis of radiation ist kept constant, the resulting photodynamic effect decreases rapidly with diminishing intensity.

¹ Teilergebnisse der Dissertation.

The Composition of Tobacco Smoke¹

The report by GRAHAM, WYNDER, and CRONINGER² that tobacco smoke condensate has produced tumors in a large percentage of the mice on whom it was painted, ESSENBERG's work on the effects of tobacco smoke inhalation³, and the recent statistical studies on the relationship between smoking and the incidence of lung

¹ This work was supported by a grant from the Damon Runyon Memorial Fund for Cancer Research.

² E. A. GRAHAM, E. L. WYNDER, and A. B. CRONINGER, *Science* 116, 521 (1952). – E. L. WYNDER, private communication.

³ J. M. ESSENBERG, *Science* 116, 561 (1952).

cancer in humans¹ have rearoused interest in the chemical nature of tobacco smoke.

Communications in the literature note the occurrence in this smoke of a large number of chemical individuals and groups; these reports have been reviewed and are briefly summarized here. The diversity of methods and interests of the various investigators limits their data as a reliable source of information on the chemical components of tobacco smoke. Thus, there has been no uniformity in the type of smoking machine used by workers in this field, nor in the values chosen for such parameters as the frequency of puffing, the duration of the puff, the volume of the puff, and the moisture content of the tobacco; we deem it probable, however, that the variation in the composition of the smoke resulting from this lack of standardization has been quantitative in nature rather than qualitative.

Of more importance is the fact that collection of the smoke, in virtually all published work, seems to have been incomplete; the collection trains have been designed to retain vapors rather than aerosols. A second major point of uncertainty is that the several investigators have employed different varieties and blends of tobacco, cured in divers ways, and smoked in the form of cigarets, cigars, and pipe tobacco. This variation in the nature of the material smoked may have resulted in the presence or absence of a particular component in a "tar" (as reported by WENUSCH³ to be true of certain of the alkaloids), but here, too, the apparently minor qualitative differences between various tobaccos would indicate that almost all of the compounds demonstrated to be present in the smoke from any one source exist in most tobacco smokes.

The smoke from tobaccos which have been impregnated with considerable quantities of additives will, of course, contain these foreign materials or their decomposition products.

In the accompanying table we have summarized the qualitative data of previous investigators. For the reasons cited above, as well as the frequent absence of such data, we have not included quantitative information here. A single question mark following the name of a compound indicates that we do not consider the evidence cited in the literature to be definitive proof of the identity of the compound. The superscript "a" identifies those materials which have been tested for carcinogenic activity³; unless otherwise indicated these compounds are reported to be non-carcinogenic.

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Zusammenfassung

Die Literatur über die verschiedenen Bestandteile des Tabakrauchs ist kritisch gesichtet worden, und die kanzerogene Eigenschaft einzelner Verbindungen wurde angeführt.

¹ E.g. E. L. WYNDER, *Arch. Ind. Hyg. Occupational Med.* 3, 218 (1952).

² A. WENUSCH, *Der Tabakrauch* (Geist, Bremen, 1939), pp. 75–79.

³ J. L. HARTWELL, *Survey of Compounds Which Have Been Tested for Carcinogenic Activity*, Federal Security Agency, Public Health Service, Bethesda, Md., 2nd edition (1951).

Class	Compound	Reference ^f
aldehydes	formaldehyde ^a	7, 8, 9
	acetaldehyde ^a	8, 10
	butyraldehyde	8
	acrolein ^a ?	9
	benzaldehyde ^a	8
ketones	furfural ^a	11, 12
	diethyl ketone	8
	dipropyl ketone	8
	dipalmityl ketone?	13
	biacetyl	14, 15
acids	"higher" ketones?	8
	formic acid	8, 16
	acetic acid ^a	8, 12, 16
	butyric acid ^a	8, 17, 18
	valeric acid	8
alcohols	caproic acid	8
	seven and eight carbon aliphatic acids?	8
	succinic acid?	12, 19
	fumaric acid ^a	12
	citric acid?	12
alkaloids	benzoic acid ^a	8, 11
	phenolic acids?	12
	methanol ^a	7, 9, 11, 12, 20, 21
	glycerol ^{a, b}	22
	diethylene glycol ^{a, b}	22
	ethylene glycol ^{a, b}	23
	phenol?	11, 24
	"phenols"?	9, 18
	pyrocatechol	11, 25
	nicotine ^{a, c}	8
	pyridyl ethyl ketone	5, 11
	myosmine	5, 11, 26, 27
	nicotyrine	5, 11
	α -socratine	5, 26, 27, 28
	β -socratine	5, 27
	γ -socratine	5, 27
	obelin	5, 27
	lohitam	5, 27
	anodmin	5, 27
	lathraein	5, 27
	poikiline	55
	gudham	60

Class	Compound	Reference ^f
other nitrogen compounds	pyrrole ^a	12, 18, 24, 29, 30
	"pyrroles"?	11, 31
	"N-methyl-pyrrolidines"?	11, 12
	pyridine ^a	9, 12, 24, 25, 29, 32, 33
	"picoline"?	9, 11
	"lutidine"?	9, 11
	"collidine"?	9, 11
	"pyridine bases"?	9, 18, 30, 34, 35
	methylamine?	18, 30
	"chlorophyll degradation products"?	12, 36
hydrocarbons	"uric acids"?	36
	hentriacontane?	12, 13, 17, 25, 36, 37
	acetylene	38
	"unsaturated hydrocarbons"	38
	azulene	24
	phenanthrene ^{a, d}	12
	anthracene ^{a, d}	12
	benzopyrene ^{a, d}	39
	"condensed aromatics"?	12
miscellaneous	levoglucosan (1,6-anhydro- β -D-glucopyranose)	11, 40
	"phytosterol"?	13, 53
	C ₁₀ H ₁₄ O (a furan?)	13
	"resins"?	11, 41
	"resin acids"?	11, 36
inorganic compounds	ammonia	8
	carbon dioxide	12, 17, 18, 38, 42
	carbon monoxide	12, 17, 18, 21, 25, 38, 43, 44, 45
	hydrogen sulfide ^a	9, 11, 18, 21, 25, 38, 46, 47
	hydrogen cyanide ^a	11, 18, 25, 30, 46, 48
	thiocyanic acid?	11
	oxygen	42
	arsenic ^{a, e}	9, 49, 57, 58, 59
	"cyanides"?	9
	"nitrates"?	9, 12
	"acetates"?	12
	"chlorides"?	12

^a Tested for carcinogenic activity; see text.
^b These alcohols are not derived from the tobacco itself but are compounds added as humectants.
^c It has been reported that at least part of the nicotine is present in the smoke in the form of salts of organic acids¹.
^d These polynuclear hydrocarbons were identified (only some incomplete spectral data were cited) in a material obtained by the destructive distillation, rather than the smoking, of tobacco. The work is open to question inasmuch as other investigators who have specifically sought for evidence of the polynuclear aromatics in tobacco smoke² have been unable to find any. Benzopyrene is, of course, carcinogenic³.
^e The arsenic is probably present as As₂O₃⁴. Arsenic is a carcinogen⁵.
^f Relatively few references to papers published before 1918 have been included since the early work in this field has been well summarized by KISSLING⁶.
^g The references to these compounds are too numerous to cite.

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The Vasoconstrictor Factor of Platelets

RAND and REID¹, studying the source of RAPPORT's serotonin², obtained active preparations only in cases in which the serum was made from whole blood or platelet rich plasma. On the basis of these results they conclude that "the appearance of RAPPORT's serotonin in serum depends on the presence of the lighter elements of the blood (probably platelets) at the time of clotting". The possible identification of the platelet vasoconstrictor

factor with serotonin is questioned also by QUICK¹ and STEFANINI². With the intention of solving the problem, we prepared platelets, free of plasma and other blood elements, by means of fractional centrifugations in a refrigerated centrifuge. From ethanol extracts of platelets, obtained from rabbit and sheep blood, it has been possible to separate by chromatographic procedure a fraction, which with EHRLICH's reagent gives the same color as serotonin, and which with diazotized sulphanilic acid develops a pink color not changing to orange following exposure to hydrochloric acid vapors. We used WHATMAN paper n° 1, employing as a solvent a mixture of ethanol, water and chloroform, in the ratio 80:20:50.

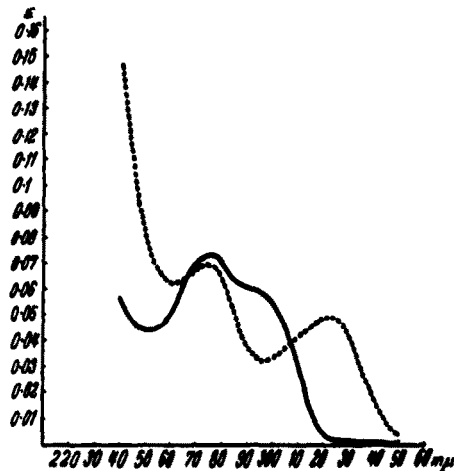


Fig. 1.—Extract of 0.02 cm³ of fresh platelets of rabbit. Eluate of the paper section giving violet color with EHRLICH's reagent: ultraviolet absorption spectrum in water at pH 7.8 (solid line) and pH 12 (dotted line).

The eluate of this section of the chromatographic strip gives in neutral water an ultraviolet absorption spectrum identical with that of RAPPORT's serotonin. Following alkalization, the spectrum undergoes the same changes

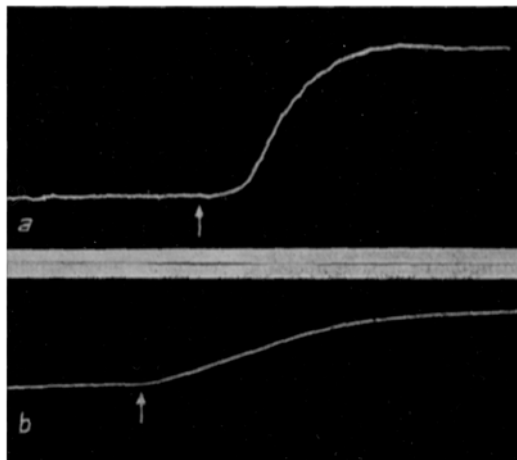


Fig. 2.—Extract of 0.005 cm³ of fresh platelets of rabbit. Eluate of the paper section giving violet colour with EHRLICH's reagent: (a) activity on isolated guinea pig gut suspended in 10 cm³ of TYRODE's solution; (b) activity on isolated rat uterus suspended in 10 cm³ of TYRODE's solution.

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