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A REVIEW OF TOBACCO ADDITIVES

Additives have been in common use in the tobacco industry for many years not only as casings and flavourings but also for such specific functions as controlling burn rate, ash formation and smoke amelioration. Dyes have also been used. This review, however, is specifically concerned with the use of additives to alter smoke composition and, in particular, to reduce the biological activity of cigarette smoke.

At present, the main criterion for determining the biological activity of smoke condensate is the mouse skin painting test. Each test takes up to two years to complete. In consequence, since interest in this field of work is quite recent, only a limited number of mouse skin painting experiments have been undertaken to determine the effect of additives on the biological activity of cigarette smoke condensate. Other, more rapid methods of bio-assay have been examined and results indicate that the hyperplasia (skin thickening) test may be correlated to the mouse skin painting test (1) and this will enable a rapid screening of additives to be undertaken.

In addition to the above, such tests as the Paramecium, Tetrahymena, rabbit trachea and clam gill may be used to evaluate the effect of additives on the cytotoxicity of tobacco smoke.

Work, which will be detailed later, indicates that the biological activity of smoke condensate, as determined by mouse skin painting, may be related to the concentration of benzo(a)pyrene (BaP). Thus additives which reduce BaP, aromatic polycyclic hydrocarbons (APHs) and other undesirable smoke constituents may also achieve the objective of reducing the biological activity of smoke.

Wynder and Hoffmann(2) smoked treated cigarettes and determined BaP content of the cigarette smoke condensate and also evaluated the biological activity of the smoke by mouse skin painting.

Table 1

Effect of additives on BaP content and biological activity of cigarette smoke condensate

Additive (4-5%)	BaP	Papillomas %-15 months	Carcinomas % - 15 months
Control	1.15	44	14
Aluminium oxide tri-hydrate	1.8	58	?
Cobalt (III) oxide	1.1	44	?
Calcium carbonate	1.0	18	2
Copper (II) nitrate	0.8	6	2

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Further work by the same authors (3) confirmed the above results for copper nitrate and also showed that nickel acetate reduced the biological activity of smoke condensate.

Table 2

Effect of additives on BaP and Phenol content and biological activity of cigarette smoke condensate

Additive	BaP ppm	Phenol mg/g	Papillomas %-18 months
Control	1.4	3.4	29
Control	1.4	3.2	28
Nickel Acetate	0.8	2.8	13
Copper Nitrate	0.75	2.5	8
Copper Nitrate	0.6	2.3	3

Treatment of tobacco with 8.3% sodium nitrate, according to Hoffman and Wynder (4) reduced BaP from 1.05 to 0.60 ppm and phenol from 3.46 to 3.18 mg/g; at the same time the tumor rate falling from 25 to 4% (18 months). Other work, including investigations carried out in R. & D.E., has confirmed these changes in smoke composition but shows increases in the deliveries of aldehydes, oxides of nitrogen and HCN (5, 6, 7, 8, 9).

In a number of mouse skin painting experiments carried out by Harrogate the tumorigenicity of smoke condensate from treated cigarettes has been evaluated. For some condensates, APHI and hyperplasia Area Activity Ratings (AAR) have also been determined. The results are detailed in Table 3.

Table 3

Summary of Harrogate experiments on treated cigarettes

Cigarette	Additive	Tumorigenicity Dose mg./week	CDE Final Index	Hyperplasia(4) A.A.R. micron days	APHI(5) %
T12	Copper nitrate(5%)	300 S.W.S.(2)	109	75	55
T11	Cu K malate(1)	do.	306		100
T 7	Malic acid	do.	233		122
T10	Potassium nitrate	do.	133		61
T 8	" malate	do.	386	99	105
T 9	KH malate	do.	298		106
T 6	Control	75/150/300 F.A.S.(2)	50/188/122	100	
T13	Potassium carbonate	ditto	152/261/319	109	
T22	Sodium nitrate	108/180/300	45/100/127(3)	45	
T21	Potassium nitrite		94/164/271		
T23	Ammonium sulphamate		171/235/342		
T24	Control		139/177/286	97	
-	Folie B (Gerlach)	225	51	68	
-	Blend B		204	95	
T25	F.c. control	108/180/300	41/220/305(3)		
T26	Schweitzer		64/196/168		
T27	Lamina		158/181/326		
T28	Stem		56/98/184		

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(1) Additive levels T11 :- Cu as in T12
T10 :- nitrate as in T12
T 9 :- K as in T11
T 8 :- K as in T10
T 7 :- Acid as in T11

(2) S.W.S. ≡ Month old condensate; F.A.S. ≡ freshly assayed smoke.
(3) Predicted values. These may be revised.
(4) Cigarette B.O. = 100. Differences less than 10 not significan
Determined by Batelle.
(5) Determined by R. & D.E., Southampton.

In the first series of experiments, for which there is no proper control, copper nitrate and potassium nitrate would appear to be the most effective. From the other results sodium nitrate and possibly potassium nitrite appear to reduce tumorigenicity but potassium carbonate and ammonium sulphamate have had an adverse effect. For comparison, results obtained from reconstituted tobaccos - Folie B and Schweitzer -, and from stem and lamina are included.

Projects CONQUEROR and LOCHINVAR examined the activity of smoke from a number of treated cigarettes by the Clam Gill and Rabbit Trachea tests (10). Results are summarized in Table 4. The lower the result the more toxic the smoke; differences less than ±1 are not considered significant.

Table 4

Toxicity of smoke to Clam Gill and Rabbit Trachea

Cigarette	Additive	Activity Rating		Mean BZ
		Clam Gill	Rabbit Trachea	
238R	Control	5.6	6.2	5.9
239R	Ammonia	5.6	7.1	6.4
291R	Potassium Carbonate	9.5	5.6	7.6
294R	Lamina	6.3	8.1	7.2
287R	50/50 Lamina/CRS	8.0	6.2	7.1
288R	C.R.S.	4.2	5.5	4.9
520A	Control	7.1	5.5	6.3
520B	Glycerol	5.7	5.1	5.4
520C	Propylene glycol	8.3	5.7	7.0
520D	Diethylene glycol	6.9	7.3	7.1

For comparison, results on lamina and C.R.S. cigarettes have been included. Only potassium carbonate would appear to be effective in reducing the cilia-toxicity of cigarette smoke while C.R.S. would appear to be more toxic than lamina. Of the humectants examined the results indicate that glycerol has a more toxic effect than propylene glycol and diethylene glycol.

Hyperplasia tests (1) on tobacco smoke from cigarettes treated with potassium carbonate (291R) and ammonia 239R gave A.A.R.s of 131 and 150 micron days compared with 148 for the CN.102 Control (276 R).

St. Pauli treated cigarettes (11) and Folie B and Folie E (Gerlach reconstituted tobacco) (12) were also subjected to the hyperplasia test. Results are detailed in Table 5.

Table 5

Hyperplasia Tests

Cigarette	Treatment	A.A.R. (Micron days).
Blend B	Normal blend	95
Folie B	Reconstituted Tobacco (Gerlach)	68
Blend E	Normal blend	83
Folie E1	Reconstituted tobacco 30 g./m^2	62
Folie E2	70 g./m^2	44
Folie E3	70 g./m^2 + 8% Sodium Nitrate	40
VK51	4.5% K carbonate on stem. Steam treated.	87
VK52	Normal blend.	100
VK 54	4.5% K carbonate on total blend. Steam treated.	109

These results indicate that tobacco reconstitution is a major factor in reducing the toxicity of smoke as determined by the hyperplasia test. It should be noted that the results obtained on the St. Pauli treated cigarettes do not correlate with the Kracht "Tumorigenic Index" (13) which gave values of 137, 182 and 318 respectively.

Wynder and Hoffmann (2) also determined the effect of smoke from treated cigarettes on the number of papillomas in mice after 15 months application of smoke condensate. Their results are summarized in Table 6. No BaP or phenol deliveries were quoted.

Table 6

Effect of additives on biological activity of cigarette smoke condensate

Additives	% Papillomas
Control	44
Aluminium oxide (aerated)	48
Boric acid	43
Aluminium oxide (activated)	41
Aluminium oxide	36
Magnesium oxide	29
Aluminium silicate (1%)	27
Aluminium silicate (4%)	23

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Aluminium silicate and magnesium oxide would appear effective in reducing the biological activity of the cigarette smoke.

Many workers have studied the effect of additive on smoke deliveries. Table 7 summarizes results obtained within the B-A.T. Group.

Since 1955 various workers have been interested in the reduction of "tar" delivery by the addition of inorganic oxides or salts. Their results are summarized in table 8.

Table 8

Reduction in "Tar" delivery

Additive	Level %	"Tar" Reduction %	Reference
Cuprene	4	59	14
Attapulgite	10	25	15
Activated Alumina	9	35	16
Activated Kaolin + Lime	5 + 5	30	17
Attapulgite	10	42	18
"Micra Al"	-	36	19
Alumina	10	17	20
Alumina	9	21	21

Most of these results are based on analytical techniques of unknown validity and require confirmation. It would appear, however, that various types of activated clays and alumina may be effective in reducing T.P.M. delivery.

Wynder and Hoffmam determined the BaP content of smoke condensate from cigarettes treated with aluminium oxide trihydrate, ammonium nitrate, cholic acid, nickel nitrate, cobalt oxide, calcium carbonate/iron oxide, calcium carbonate and copper nitrate[2]. Only copper nitrate gave a significant reduction in BaP concentration.

Bently and Burgan[22] found potassium nitrate, copper nitrate, sodium nitrite, ammonium sulphanate, glycerol and ethylene glycol effective in reducing BaP deliveries.

Lowering combustion temperature has been suggested as a means of reducing BaP delivery. Aluminium and nickel foils (29-32), alumina-ferrous materials (33), potassium chloride and nitrate (34), silicone (35), alkali metal bicarbonates and ruthenates (36), sodium dihydrogen phosphate (37), aluminium trihydrate (38) and metallic salts of silicates, phosphates, borates and boric oxide (39), have been claimed in this conte--

P.J. Nicholl.

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