AN INVESTIGATION OF CIGARETTE SMOKE AS AN AEROSOL WITH SPECIAL REFERENCE TO RETENTION IN LUNGS IN HUMAN SUBJECTS

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To illustrate some of the problems which are likely to be encountered in the investigation of the inhalation of aerosols, some experiments were performed using cigarette smoke (Baumberger, 1923; Greenberg, Lester and Haggard, 1952). Under suitable conditions the smoke can be generated so as to have reproducible characteristics. Since cigarette smoke contains a number of chemical constituents which can be measured in small amounts, some experiments were performed on human subjects to determine the retention in the lung of a few of these constituents of the smoke under certain types of breathing patterns.

METHODS

A burning cigarette was placed in a holder 6 cm. long and with a volume of about 5 cc. The cigarette and holder were then enclosed in a small container to which a tank supplied 0.4 liters of air per minute (Fig. 1). The system was so arranged that all of the air which left the chamber passed through the cigarette and holder. Smoke generated in this manner was quite concentrated so that particles increased in size due to coalescence. To prevent this type of change in particle size from continuing, the smoke upon leaving the holder was directed into a mixing tube where the particles were continuously diluted with air at the rate of 35 liters per minute or higher. The particle-size distribution of cigarette smoke generated in the above manner was found to be very reproducible.

The importance of rapid sampling in the case of fairly concentrated aerosols can be illustrated by the following example. If the air flow through the cigarette is increased to several liters per minute, the interval of time from the formation of the smoke to the moment of sampling can be varied from long to very short time intervals. The mass median diameters (M.M.D.'s) of the smoke particles corresponding to the following time intervals—0.05, 1, 11, 30 seconds—were, respectively, 0.3, 0.65, 1.4, and 1.6 microns in a typical trial.

One brand of cigarettes was used to obtain most of the results, but seven other brands were used for comparisons. The smoke was collected by impaction as described below, about two-thirds of each cigarette being used. The smoke particles, when examined microscopically, appeared to be clear droplets unless they remained airborne too long. A collected sample appeared as a

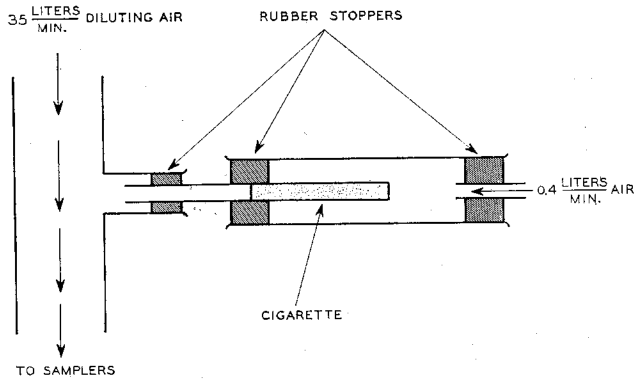

FIG. 1.—Apparatus used to produce constant characteristics in cigarette smoke.

brown viscous liquid. The following types of analyses were made on the samples.

Color.—To make a color analysis (First, Moschella, Silverman, and Berly, 1951) a sample of smoke was washed with absolute alcohol from the collecting device into a graduated test tube. The resulting mixture was then adjusted to a final volume of 10 cc. This final mixture, when stirred thoroughly, had a uniformly clear, yellow color which was read on a Klett colorimeter using a 420 mμ filter. Such color readings were found to be linear with concentration over a wide range of optical densities. The presence of small amounts of undissolved particles in the mixture did not appreciably alter the optical density.

Phenol.—If the alcohol is evaporated from a small aliquot of an alcoholic extract of smoke, the resulting material develops a blue color characteristic of the presence of phenol, using the Folin and Ciocalteau (1927) method of analysis for phenol. Since the Folin and Ciocalteau reagent is not specific for phenol we will simply call the combined substances detected by this reagent "Phenol". The mixtures were somewhat turbid. However, because of the wavelength used and because the turbidity was correlated with the blue color developed, the effect of the turbidity on the calculated percentages of retention was almost negligible as indicated by a comparison of values obtained on clear (centrifuged) and turbid samples. Hence, in most of the experiments the effect of turbidity was ignored.

259 mu.—The "259 mu" values were found by taking an aliquot of the sample in water, removing the alcohol, and acidifying with HCl to a pH of 1. The solution was then read at 259 millimicrons on a Beckman Model DU spectrophotometer. It was found that many other substances interfered with the nicotine values (Griffith and Jeffery, 1948) as obtained from readings at 236, 259, and 282 millimicrons; consequently, the values obtained at 259 were in reality rather independent of the amount of nicotine. The readings at the peak for nicotine, *i.e.*, at 259 millimicrons were not much different from the average of the other

TABLE 1.—Particle-size Distribution of Cigarette Smoke.

Cloud fraction (diameter)	Color (420 mμ)	Phenol	259 mμ	Nicotine
	Standard cloud			
3	1.1 ± 0.5	1.8 ± 0.7	2.0 ± 0.4	1.7 ± 0.7
4 (1.4 μ)	51.0 ± 2.0	55.0 ± 2.0	50.0 ± 1.0	53.0 ± 3.0
5_1 (0.76 μ)	26.0 ± 2.0	25.0 ± 3.0	27.0 ± 2.0	25.0 ± 4.0
5_{2s} (0.3 μ)	15.0 ± 1.0	12.0 ± 1.0	13.0 ± 1.0	15.0 ± 1.0
GW	6.4 ± 1.5	5.4 ± 0.5	8.0 ± 1.0	5.0 ± 1.0
M.M.D.	0.96	1.02	0.96	1.00

EXHALED SMOKE
(8-second cycle, 18 liters per minute)

	Color: No condensation	Color: With condensation	Phenol: No condensation	Phenol: With condensation	259 mμ: No condensation	259 mμ: With condensation	
3	2.0 ± 0.5	7.5	2.3 ± 0.2	9	4.0 ± 0.3	11	
4	39.0 ± 2.0	60.0	40.0 ± 2.0	54	40.0 ± 1.0	51	
5_1	28.0 ± 2.0	18.0	28.0 ± 3.0	21	25.0 ± 1.0	20	
5_{2S}	25.0 ± 2.0	12.0	24.0 ± 2.0	12	23.0 ± 3.0	14	
GW	6.0 ± 2.0	2.0	6.0 ± 2.0	3	8.0 ± 1.0	4	
M.M.D.	0.74	1.27	0.76	1.23	0.78	1.20	

two readings. Thus, although these values could not be considered as being due primarily to nicotine, they were useful to illustrate the fate of certain constituents when inhaled by human subjects.

Nicotine.—Since distillation resulted in so great a dilution, and since small amounts of materials were often involved, a colorimetric method sensitive to small amounts of nicotine (10-100 micrograms) was used (Landahl and Tracewell, unpubl.).

Particle-size distribution. — The relative amounts of a constituent in droplets of different sizes were obtained by means of glass impacting devices (May, 1945; Sonkin, 1946) through which the air passed in series. The first section used, section 3, collected the largest particles (fraction 3). Section 3 consisted of a right angle bend (over a distance of about 3 cm.) of a tube of inner diameter 4.0 mm. Fraction 4 was collected in section 4, in impinger with orifice 2.0 mm. jetting upon a surface 4 mm. away (Landahl and Black, 1947, Fig. 1). Fractions 5_1 and 5_{2s} were collected on similar impingers of orifice diameter 1.58 mm., the later having two 200-mesh, 0.002″-wire screens at the surface of impaction 4 mm. from the orifice. These impingers were from a laboratory model cascade impactor designed to be constructed easily from standard glass (or brass) tubing, the sections being joined, for example, by standard taper joints. Sections 1 and 2, which were not used in these experiments, were made respectively from 16 and 8 mm. inside diameter tubing, the right angle bends being fairly smooth, and without noticeable constrictions.

The sections of this impacting device were calibrated when possible by microscopic observations and by the instrument of May (1945). For very small values the sizes were estimated by producing larger particles containing a relatively volatile solvent which was then removed by evaporation. The mass median diameter of each section was found to depend somewhat on the amounts of materials in the sections preceding it. The following information enables one to take this into account. When the amount of material collected on sections 1, 2, 3, together with one half of that on 4 was 85% of the total, the M. M. D. for 4 was 2.0 microns. Similarly when 85% was on or above the midpoint of 2 or 3, respectively, the corresponding M. M. D.'s were about 13 and 5.8; the values corresponding to 5, 5_1, and 5_{2s} being 0.9, 0.9, and 0.25. Section 5 was an impinger of 1.40 mm. diameter orifice which could be used in place of 5_1 and 5_{2s} without changing the flow rate. When 50% of the mass of the particles was on or above the mid-point of section 1, its M.M.D. was estimated to be about 27 microns. Similarly for section 2, etc. the M.M.D.'s were, respectively 10, 4.5, 1.6, 0.6, 0.65, and 0.15 microns, the last value being an indirect estimate. When a criterion of 15% on or above the midpoint of a given section was used the M.M.D.'s were as follows: For 1, etc., the values were, respectively, 16, 7, 3.5, 1.3, 0.3, 0.4, and < 0.1 microns. By interpolating from these values, the M.M.D.'s of various cloud fractions can be estimated. If impingers are used instead of bent tubes for 1, 2, and 3, the orifice diameter should be about 15% larger than the tube diameters to obtain about the same results, the distance from orifice to plate being equal to the orifice diameter.

In series with the above devices and nearest to the pump (such capacity that pressure at pump was much less than one-half atmosphere), was an orifice about 2 mm. diameter which jetted onto 5 layers of glass wool cloth (fraction GW), about 4 mm. from the orifice. The fibers of the glass were 20 microns in diameter. The discs of glass wool cloth were held in a filter holder (Landahl and Black, 1947, Fig. 1, F) so that all the air passed through the glass wool filter at near the velocity of sound. Some experiments indicated that even particles much less than 0.1 microns are removed to a rather large extent by this glass wool impinger-filter, provided the pressure at the glass wool is sufficiently low. The flow rate, 18 liters per minute, was not appreciably changed by this last impinger.

Some observations indicated that several percent of the nicotine were lost by evaporation. However, the effects on the percentages retained are probably small since the exhaled and control samples were treated as much alike as possible.

Experimental Results

Particle-size distribution.—The results of experiments on particle size are given in Table 1. The results did not indicate any significant difference between any one brand and the average of all the brands of cigarettes, including one long cigarette and one with a built-in filter. The distribution using color as an index was the same as that for phenol, 259 mμ, and nicotine, except possibly the first and last fractions. These latter were unreliable, since they constituted such a small fraction of the total mass. As the material in the last fraction was spread over a relatively large surface, evaporation of nicotine could be responsible for its being somewhat less.

Smoke particles upon being inhaled and then exhaled into warmed collectors were found to have a slightly smaller average diameter than they had before being inhaled. Since the retention is about 50% under these conditions (see below) it is seen that the particles in cloud fraction 4 are retained more than those of 5_1 and 5_{2s}. On the other hand, the exhaled particles may have increased in size due to acquisition of moisture (cloud fraction 3). Under condensation (*e.g.*, collectors not warmed, about 25°C) one might expect to find considerable differences in the change in size for different sized particles if the particles were not fairly uniform in their composition. Since this does not occur, this again suggests similarity in composition of small and large particles for smoke produced under a given set of conditions.

A single impinger 5_{2s} collects all the material that falls above it as well as practically all that falls on it when in series with the others. Since this represents most of the material, the experiments to measure total retention in lungs were carried out using only such impingers with the orifice size being 1.40 mm. for 18 liters per minute and 2.54 mm. for 60 liters per minute.

TABLE 2.—Relative Concentration of Exhaled Smoke (per cent).[1]

Exhaled fraction	18 liters per minute		60 liters per minute			
	Color	Phenol	Color	Phenol	259 mu	Nicotine
	4-second cycle, 450 cc. tidal air		4-second cycle, 1500 cc. tidal air			
1	78	..	84	77	77	30
2	73	..	73	61	60	15
3	64	..	58	46	47	8
4	52	..	38	16	35	3
Totals	67	..	63	50	55	14
	8-second cycle, 900 cc. tidal air		8-second cycle, 3000 cc. tidal air			
1	80	72	79	..	..	18
2	51	34	54	..	..	4
3	38	28	36	..	..	0.6
4	27	18	22	..	..	0.5
Totals	49	38	48	39	34	6

[1] Relative concentration is defined as ratio of average concentration of substance in given portion of expired air to that of inspired air.

Brand variation.—One subject was used to measure the total per cent retention of smoke at the eight-second respiratory cycle, for various brands of cigarettes. The inspiratory and expiratory rates were both 18 liters per minute. All respiratory cycles used were divided into equal inhalation and exhalation periods of three-eighths of the cycle time, separated by pauses of one-eighth of the cycle time. From three to five trials were made with each brand with the following percentages retained: 49±2, 54±1, 49±1, 51±1, 53±2, 52±1, 52±3, 51±1. This gives an average value of 51.0±1.3%.

Of the 28 comparisons by pairs, only one pair showed a moderately significant difference. This is not unexpected in this many comparisons even if there were actually no differences. Furthermore, the correlation between the M. M. D.'s and the retentions of the materials from the various brands was not found to be significant.

Retention for various respiratory patterns.—Two subjects were used to measure the percentage retention for various patterns of respiration. From three to six trials were made on each subject for total retention on brand A. One subject was used in the experiments in which the expired air was fractionated into four equal serial fractions (exhaled fraction 1, 2, 3, 4 of Table 2, Landahl, Tracewell, and Lassen, 1951). Two to four trials were made in this situation. The results of these experiments are given in Table 2.

It may be seen from Table 2 that phenol, 259 mu, and especially nicotine are retained to a greater extent than color. This can be accounted for by the removal of these materials as vapor. Furthermore, the color is removed to a somewhat greater extent than triphenylphosphate particles (Landahl, Tracewell and Lassen, 1951, 1953) of corresponding size. Whether or not this can be accounted for by the absorption of moisture or by vaporization remains to be determined. We also note that the total retentions for color are less sensitive to changes in respiratory pattern than in the case of triphenylphosphate droplets. In the case of nicotine, the distillation from the particles to the walls of the respiratory passages appears to be as important as or more important than the removal of particles by settling, impaction, and diffusion (Landahl, 1950).

In addition to the experiments summarized in Table 2, one experiment was carried out at 18 liters per minute using a 12-second cycle and 1350 cc. tidal air. Only color was measured. The relative concentrations for the exhaled fractions 1 to 4 were, respectively, 73, 45, 33, and 22%. The total was 43%.

Summary

Experiments have been carried out to measure the particle-size distribution of cigarette smoke, generated in a fixed manner, as measured by various components. The results indicate that, for smoke generated under a given condition, the chemical composition of the droplets making up the smoke may be rather independent of the droplet size. Measurements carried out on exhaled smoke tended to confirm this latter generalization. Human subjects were used to measure retention under various respiratory patterns in which a few components were analyzed. The various components analyzed were found to be retained to different extents, demonstrating the importance of the volatility of the component. This may be illustrated by a comparison of the percentages retained for phenol and nicotine. A breathing pattern having a 4-second cycle and an inspiratory flow rate of 60 liters per minute gave, respectively, 50% and 86% retentions for phenol and for nicotine. Other conditions showed a similar result. Measurements were also made of the amounts of different components in various fractions of the expired smoke.

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