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Effects of Oral pH on Cigarette Smoking[1,2]

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KOZLOWSKI, L. T. AND R. M. KLEIMAN. *Effects of oral pH on cigarette smoking*. PHARMAC. BIOCHEM. BEHAV. 9(4) 477–480, 1978.—Permeability of nicotine across the oral mucosa had been shown to be a direct linear function of alkalinity in the oral cavity. Here, oral pH in cigarette smokers was manipulated from pH 5 to 8 by rinses with Sorenson's and McIlvaine's buffers. As alkalinity increased, cigarette taste was perceived as stronger, more bitter, and, in some cases, more unpleasant; and heart-rate accelerated slightly. Nicotine self-administration and blood pressure were not influenced. Differential absorption of nicotine and cross-adaptation of sour to bitter tastes are both discussed as explanations for the results.

Salivary pH   Cigarette smoking   Nicotine

URINARY pH affects the bioavailability of nicotine [4,20]: the formation of acid urine (pH≈5) causes roughly 35% of a dose of nicotine to be flushed out of the bloodstream unmetabolized, while the formation of alkaline urine (pH≈8) causes less than 1% of a dose to leave the circulatory system [4]. This effect is thought to be due to the relative impermeability of lipoidal barriers to ionized nicotine [3]. Recently the behavioral consequences of such dosage manipulations have been explored. Increases in urinary acidity lead to greater cigarette smoking [14]. Social activities [18] and stress [15]—both known to increase smoking—produce more acid urines than do control conditions. Psychological accounts of why smokers smoke more when stressed were pitted against a physiological account [16] which holds (a) that stress increases urinary acidity, which in turn increases nicotine excretion, and (b) that smokers smoke more cigarettes in order to maintain desired blood levels of nicotine. The biological explanation received compelling support.

Given the fruitfulness of these behavioral studies, other physiological systems with variations in pH were sought in hope of finding other influences on cigarette smoking. Nicotine absorption in the mouth (the oral mucosa provides a lipoidal barrier) is a linear function of pH [1, 2, 3, 17, 20]; at pH 5 about 3% of a nicotine dose is absorbed, this figure rising at pH 6 to about 10%, at pH 7 to about 15%, and at pH 8 to about 20% [3]. Similarly, oral irritation from nicotine is known to be a direct function of the amount of nicotine present in an un-ionized form [9]; in alkaline solution, more nicotine will be un-ionized. Nicotine has an acrid, burning taste that, given the common adjectives applied to taste, would be called bitter (alkaloids as a rule taste bitter [10]). No studies appear to have been conducted on the behavioral or psychological effects of oral pH on cigarette smoking. The first study was designed to see if physiologically normal variations (pH 5 to 8) of oral pH influence (a) cigarette taste—the more nicotine absorbed in the mouth, the greater the irritation or bitterness attributed to the cigarette, and (b) nicotine consumption—the more nicotine absorbed, the fewer cigarettes smoked (cf. [8]). Although in inhaling smokers, the relative dose manipulation caused by oral pH should be small (cf. [1]), perhaps the self-administration of nicotine is influenced by oral-hedonic factors (cf. [12]). Since nicotine is a cardiovascular stimulant, heart-rate and blood pressure were measured as indicators of the physiological effects of the oral pH manipulation of nicotine dose.

EXPERIMENT 1

METHOD

Subjects

Five males and 4 females were studied individually in five 1-hr sessions, after having been cigarette-deprived for 30 min. Each was paid $12.50. They smoked an average of 24 cigarettes per day (range: 10–35), and had been smoking regularly for 9 years (range: 1.5–16). These subjects were not college undergraduates and had an average age of 26 (range: 22–34).

Procedure

Sorenson's buffers (pH 5, 6, 7, 8) were used [19]. Order of presentation was balanced as much as possible. The first session always used spring water, and was discarded in analysis as a training trial.

Initial blood pressure readings were taken with a sphygmomanometer (Peerless Model No. 11i, Clayton Industries). Heart-rate was determined by 30 sec pulse count. Initial pH readings were taken from the dorsal surface of the tongue and the inside cheek with a Corning Model 5 pH meter fitted

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[2]Reprints are available from Lynn T. Kozlowski.

TABLE 1

MEAN EFFECTS OF ORAL pH ON TASTE, INTAKE, AND PHYSIOLOGICAL EFFECTS OF CIGARETTES

	pH of Buffer 5	6	7	8	Linear Trend F
Manipulation	6.03 (.27)*	6.27 (0.12)	6.96 (0.08)	7.41 (0.08)	107‡
Unpleasantness	0.02 (1.29)	0.24 (1.07)	0.27 (0.71)	0.08 (0.76)	0.06
Strength	0.64 (1.08)	0.81 (1.01)	1.42 (1.02)	1.34 (1.04)	10.35‡
Bitterness	0.57 (0.61)	0.79 (0.70)	1.21 (0.70)	1.36 (0.69)	15.11‡
Heart Rate (beats/min)	83.8 (8.57)	85.1 (12.53)	85.6 (10.09)	88.9 (9.75)	4.7†
Blood Pressure (Engel's Index)	120.15 (11.9)	118.0 (7.8)	116.2 (9.5)	119.0 (12.5)	0.65
Number of Puffs	16.44 (4.72)	15.67 (4.85)	15.67 (3.81)	16.56 (5.50)	0.12
Total Puff Time (sec)	25.94 (9.45)	24.49 (9.63)	24.14 (9.24)	27.00 (11.96)	0.27

*SD
†$p < 0.05$
‡$p < 0.01$

with a Markson No. 1207 flat glass electrode. Before each session each buffer was tasted and rated on nine 5-point unipolar scales (not-at-all to extremely) for Pleasant, Unpleasant, Bitter, Sweet, Salty, Sour, Acidic, Soapy, Flavorful. Acid buffers taste sour and some people confuse sour and bitter tastes [10]; basic buffers have a soapy taste to some people. Since we were interested in the effects of pH on cigarette taste, these buffer-taste ratings were included in order to evaluate their role as possible confounds to the results.

The pH manipulation and cigarette smoking. Subjects arranged 5 buffer-soaked dental cotton rolls in their mouths. Two rolls, 3.6 cm long, were placed upright along each side of the mouth as far back as possible between molars and cheek. One 1.7 cm roll was placed under the tongue (just behind the lower front teeth). In other words, the cotton was placed in close proximity to the parotid and submandibular salivary ducts. A plastic spray bottle was used to supplement the buffer manipulation. For a given spray command, the subject was to deliver 5 squirts to each of the upright cotton rolls, 5 to the roll under the tongue, and 5 to the tongue itself. Pilot studies had shown that the cotton roll and spraying procedure were able to minimize the effects of reactive salivation on oral pH. Manipulation checks consisted of pH readings from the tongue and cheek.

Smokers were then handed a lit cigarette and instructed to puff according to a series of taped commands (every 20 sec, a 2-sec puff). The cigarette was a Marlboro®; the pH of the smoke was about 5.5. After 3 puffs, a pH reading was taken and a cigarette rating sheet was given. This sheet consisted of six 9-point bipolar scales (Pleasant(+)/Unpleasant (–), Bad (–)/Good (+), Strong (+)/Weak (–), Harsh (–)/Mild (+), Soothing (+)/Irritating (–), and Tasteless (–)/Flavorful (+). This was followed by a set of the 9 solution taste ratings. The spraying regimen, the pH check, and the rating sheets were repeated 2 more times. The experimenter took the smoker's blood pressure and heart rate at the end of the Timed-Pull sequence.

Nicotine consumption. At this point, a Free-Smoke period began. The manipulation was repeated with fresh cotton rolls. The only restriction on the subject's smoking was that they would be told to spray every 75 sec, a time previously determined as necessary for the maintenance of the manipulation. Participants were told that blood pressure and heart-rate readings would follow the cigarette, but that it was necessary to wait at least 8 min from the first puff in order to get accurate results. This was done to reduce the possibility that the subject would extinguish the cigarette prematurely in order to hasten the progress of the session.

An observer was stationed behind a partially disguised one-way mirror directly opposite the subject and recorded the number of puffs taken by the subject, as well as the puff-times in sec with a Siliconix E110 electronic timer. Puff-time was measured as the time the cigarette was glowing while being puffed. After completing the first cigarette, the subject filled out another Cigarette Taste Rating Sheet. After the blood pressure and heart rate readings each smoker was instructed to repeat the Free-Smoke with a fresh cigarette and a new set of cotton rolls. The 8 min waiting time was used again. After the final cigarette taste rating, final blood pressure and heart-rate readings were taken. At the end of the final session, a general questionnaire concerning smoking and drinking habits was completed.

RESULTS AND DISCUSSION

Major results are given in Table 1. The oral pH manipulation was effective: pH measures in the table are the average of tongue and cheek readings for the last Timed-Puff and the last Free-Smoke scores. The cigarette-taste ratings are based on the average of the last Timed-Puff and the last Free-Smoke scores. (Separately, these ratings show the same pattern of results, at comparable levels of statistical significance.) An ANOVA test ($df=1,24$) for linear trends were computed; no higher-order trend components were significant.

Based on its use in pilot work, an Unpleasantness Index was calculated (Unpleasant + Bad + Harsh + Irritating, all scored as positive and divided by 4). As pH became more alkaline, subjects rated the cigarettes as Stronger, but not as more Unpleasant. The inconsistency of the Unpleasantness results with pilot work and with the results of Experiment 2 will be considered in the General Discussion. Two subjects felt that the acid (sour) buffers and the pH 5 cigarettes tasted very bitter. Perhaps they confused the bitter buffer taste with the cigarette taste. Bitterness means and their F-test in Table 1 do not include these subjects; if included, the effect is not significant statistically. See the General Discussion for more on the influence of buffer taste on the results.

As would be expected if alkaline pH causes more nicotine to be absorbed in the mouth, heart rate was somewhat higher as pH increased. Average blood pressure (using Engel's Index [6]) and number of puffs or puff-times were not affected by oral pH. Either our subjects were not regulators of their nicotine consumption [13], or the dose manipulation was not large enough to alter intake.

The evidence, though not without its flaws, indicates that oral pH does influence both cigarette taste ratings and heart-rate.

EXPERIMENT 2

Since the pH buffers have characteristic tastes of their own that might influence the cigarette taste ratings, we changed the buffer from Sorenson's to McIlvaine's citric-phosphate buffer [19]. This buffer has superior buffer capacity and tastes less sour at acid pH's than does Sorenson's[11]. In addition, we added a raspberry flavored syrup to half of the trials to try to mask the changes in buffer-taste as a function of pH, and to conceal the sour and bitter tastes of some of the solutions [11].

Our goal here was to reestablish the effects of oral pH on cigarette taste and on the cardiovascular system; no measures of nicotine consumption were included and the Free-Smoke period was omitted.

METHOD

Subjects

Four male and 7 female college students who had been cigarette-deprived for one-half hr were studied individually in two 2-hr sessions. They were paid $5.00. Subjects averaged 19 years of age (range: 18–21), smoking an average of 20 cigarettes per day (range: 2–40), and had been regular smokers for an average of 4.23 years (range: 2–7).

Procedure

Buffer manipulations were done as in Experiment 2, except that McIlvaine's citric-phosphate buffer was used. The 2 sessions per subject were identical except for the buffers being flavored in one session with from 10–30 ml of raspberry syrup to conceal some of the sourness and bitterness of the solutions. Flavoring had no effect on the solution's buffering capacity. Initial oral pH readings of the tongue and cheek, as well as initial heart-rate and blood pressure readings, were taken.

Participants were then presented with 4 solutions—spring water first and a random arrangement of the 3 buffered solutions. Tasting and rating procedures were as described in Experiment 1.

The major change in Experiment 2 is that the manipulation was collapsed into one session. The manipulation procedure remained the same as before. The Timed-Puff regimen was abbreviated to two cycles of three puffs, yielding a total of six timed-puffs of 2-sec duration.

No Free-Smoke followed, but instead, a 10-min pause, during which the Experimenter took blood pressure and heart rate readings, and prepared the apparatus for a new Timed-Puff cycle on the next buffer. This ten min period was necessary for the extinction of residual taste sensations, and avoided having the participant feel smoked out during the experiment. This procedure was repeated through the three sets of buffer-soaked cottons. The first set always contained spring water, flavored or unflavored depending on the session. The order of presentation of the buffers was randomized. A final questionnaire concerning smoking and drinking habits was completed at the end of the second session.

RESULTS AND DISCUSSION

There were no main effects or interactions involving the flavor manipulation that even approached statistical significance ($p>0.3$), so the mean score at each pH level was used for analysis. Table 2 shows the main results for the last Timed-Puff ratings. The pH manipulation was effective. As pH increases, Unpleasantness, Bitterness, and Heart rate increase. (Linear Trend F, $df=1/20$.) Consistent with this pattern, but only marginally significant statistically, Strength and Blood Pressure tend to increase.

TABLE 2

MEAN EFFECTS OF ORAL pH ON TASTE AND PHYSIOLOGICAL EFFECTS OF CIGARETTES

	pH of Buffer			
	5	6.6	8	Linear Trend F
Manipulation	5.4 (0.11)*	6.6 (0.09)	7.6 (0.11)	2,612§
Unpleasantness	0.52 (1.28)	0.96 (0.84)	1.69 (0.87)	12.69§
Strength	1.57 (1.13)	1.64 (0.91)	2.00 (1.01)	3.73†
Bitterness	0.77 (0.79)	0.77 (0.79)	(1.32) (1.15)	9.11§
Heart Rate	83.9 (6.93)	85.6 (7.43)	85.9 (5.42)	8.34‡
Blood Pressure	123.9 (6.9)	125.7 (7.12)	125.9 (6.64)	3.87†

*SD
†$p<0.10$
‡$p<0.05$
§$p<0.01$

GENERAL DISCUSSION

Buffer Taste as a Confound

Buffer tastes differed in Experiments 1 and 2; and in Experiment 2, there were major differences in buffer tastes—but not in cigarette taste—as a result of the raspberry flavoring. It is unlikely, then, that the unique tastes of the buffers caused the observed systematic effects on cigarette taste. The issue of cross-adaptation of sour to bitter substances should not be ignored [10]. Possibly the acid (sour) buffers caused our subjects to be adapted to the bitter taste of the cigarettes. This non-nicotine-absorption explanation requires that buffer bitterness increases directly with acidity. We do not feel confident in ruling out such an alternative account. Although there was no consistently significant association between buffer bitterness and pH (linear trends: Experiment 1, $p<0.01$; Experiment 2, unflavored, $p<0.10$, flavored, $p<0.25$), the pattern of means was consistent: acid buffers did tend to taste more bitter. Of course, it is possible that both cross-adaptation and pH-based nicotine absorption contribute to our results.

Cigarette Taste

Perceived Bitterness of the cigarette clearly increases as pH of the oral cavity increases. Perceived Strength of the cigarette appears to vary similarly as a function of oral pH: Experiment 1 supports this strongly, while Experiment 2 gives only modest support ($p<0.10$). Experiment 2 involved fewer puffs at each pH level than did Experiment 1; perhaps, more exposure is needed for a pronounced Strength effect to appear. The Unpleasantness effects are more complicated. In Experient 1, there is no hint of an effect, but in Experiment 2, there is impressive evidence that increased oral pH leads to increased cigarette Unpleasantness. This inconsistency is probably due to a complex relationship between Bitterness, Strength, and Unpleasantness. Perhaps the younger group (Experiment 2) is more unified in its dislike of bitter, strong cigarettes, while the older group (Experiment 1) is mixed in its reaction to them. (Subjects were older in Experiment 1, $t(18)-4.96$, $p<0.001$.) Also, the judgments of Bitterness and Strength are relatively objective, and the judgment of Unpleasantness is more a matter of preference.

Physiological Effects

The heart rate effects are quite small, but are statistically reliable. It is tempting to conclude that they constitute a bio-assay for nicotine, but it is possible that the effects of negative tastes were responsible for the heart rate changes. We have no direct evidence that plasma levels of nicotine varied as a function of oral pH. The failure of blood pressure effects to reach an acceptable level of statistical significance may be due to their greater sensitivity to extraneous, random factors.

Salivary pH is influenced by climate, diet, and psychological state [5,7]. Research is underway to evaluate whether some of the naturally occurring variations in oral pH influence cigarette taste or consumption.

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