Bronchodilator Effects of Caffeine in Coffee*
A Dose-Response Study of Asthmatic Subjects

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Although caffeine is a universal drug and has multiple pharmacologic and physiologic actions in man, there are surprisingly few objective data about its effect on pulmonary function. We conducted a short-term, double-blind, randomized crossover study in nine asthmatic adults who ingested decaffeinated coffee containing varying amounts of added caffeine (mean of 0.2, 2.5, 5.6, and 7.2 mg/kg of body weight) on different days. The subjects also ingested decaffeinated coffee and aminophylline (200 mg) on a separate day of study. Baseline and post-drug determinations of serum levels of caffeine and theophylline, forced expired volume and flow, specific airway conductance (Gaw/Vl), vital signs, and reported symptoms were obtained. Peak increases in serum caffeine concentrations (mean, 12.4 μg/ml ± 1.5 μg/ml) occurred 45 minutes following the highest dose of caffeine (7.2 μg/kg), whereas the peak theophylline level (mean 3.8 μg/ml ± 0.4 μg/ml) occurred 90 minutes following oral administration of aminophylline (mean theophylline, 2.6 mg/kg). Comparable peak increases in the forced expiratory volume in one second (FEV1), the forced expiratory flow during the middle half of the forced vital capacity (FEF25-75%), and Gaw/Vl occurred at 120 minutes following aminophylline and the highest dose of caffeine, indicating that caffeine is an effective bronchodilator but is only 40 percent as active as an equivalent molar dose of theophylline. Regression analysis revealed statistically significant dose-response relationships between peak increases in serum caffeine concentrations and increases in FEV1, FEF25-75%, and Gaw/Vl from baseline values. These findings have diagnostic and therapeutic implications regarding the use of caffeine prior to tests of pulmonary function and as a dietary agent, alone or in combination with theophylline.

Caffeine (1,3,7-trimethylxanthine) is the most widely consumed drug in North America. The popularity of caffeine is related to its stimulant properties and its widespread availability in coffee, tea, soft drinks, and medications such as analgesics and cold preparations. Although the pharmacologic characteristics of caffeine are well known, there is surprisingly little published in vivo documentation and quantitation of the potential effect of caffeine on bronchomotor tone, particularly when compared to a related methylxanthine, theophylline. Some authorities have assumed (without supportive experimental data) that caffeine, like theophylline, relaxes bronchial smooth muscle in vivo, in part due to its similar chemical structure and its in vitro ability to inhibit phosphodiesterase enzyme activity, resulting in increased intracellular concentrations of 3':5'-cyclic adenosine monophosphate (cycle AMP). The notion of caffeine-induced bronchodilation is also evident in the common practice of advising patients to avoid caffeine-containing products prior to pulmonary function tests for clinical and research purposes. It is widely believed that caffeine might significantly alter bronchomotor tone and confound valid interpretation of results before and after the bronchodilator. The limited data on the effects of caffeine on airway function in man prompted us to investigate the hypothesis that caffeine exerts a short-term bronchodilator action which may be dose-related, similar to that of theophylline. We evaluated this possibility in nine adult asthmatic subjects who ingested realistic amounts of caffeine and compared these results to a single oral dose (200 mg) of aminophylline.

MATERIALS AND METHODS

We studied nine subjects (five women and four men; mean age, 35 years) with stable asthma, as defined by the American Thoracic Society, and no other clinically evident disorders, including hepatic disease or hypertension. Demographic characteristics, clinical history, including use of caffeine, and screening data on pulmonary function testing are presented in Table 1. For at least 12 years, the subjects had mild to moderately severe asthma which was allergic in nature in all but two subjects (subjects 3 and 8). The subjects used a wide range of medications to treat asthma: theophylline products (seven subjects); sympathomimetic agents (eight); inhaled (three) or...
Table 1—Demographic Data, Clinical History, and Screening Pulmonary Function Test Results of Subjects

<table>
<thead>
<tr>
<th>Subject, Sex, Age (yr)*</th>
<th>Height, cm</th>
<th>Weight, kg</th>
<th>Duration of Asthma, yr</th>
<th>Smoking History†</th>
<th>Routine Caffeine Use‡</th>
<th>FEV1/FVC, %</th>
<th>FEV1, L</th>
<th>FEF25-75%, L/sec</th>
<th>FEV1 after Bronchodilator, L</th>
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<tbody>
<tr>
<td>1, F, 23</td>
<td>155</td>
<td>55</td>
<td>23</td>
<td>ES + (t)</td>
<td>2.48 (76)</td>
<td>1.47 (49)</td>
<td>59 (22)</td>
<td>0.72 (32)</td>
<td>1.94 (32)</td>
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<tr>
<td>2, F, 32</td>
<td>162</td>
<td>59</td>
<td>12</td>
<td>ES –</td>
<td>3.54 (16)</td>
<td>2.19 (73)</td>
<td>60 (40)</td>
<td>1.38 (15)</td>
<td>2.52 (15)</td>
</tr>
<tr>
<td>3, M, 66</td>
<td>170</td>
<td>76</td>
<td>12</td>
<td>ES + (cof)</td>
<td>2.38 (61)</td>
<td>0.88 (31)</td>
<td>37 (10)</td>
<td>0.28 (20)</td>
<td>1.15 (20)</td>
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<tr>
<td>4, M, 60</td>
<td>178</td>
<td>77</td>
<td>39</td>
<td>Theophylline</td>
<td>– (cof)</td>
<td>3.29 (75)</td>
<td>1.39 (42)</td>
<td>42 (15)</td>
<td>0.50 (23)</td>
</tr>
<tr>
<td>5, F, 31</td>
<td>168</td>
<td>62</td>
<td>28</td>
<td>Pramidine mist</td>
<td>ES + (cof; M)</td>
<td>4.03 (110)</td>
<td>2.76 (86)</td>
<td>68 (48)</td>
<td>1.75 (11)</td>
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<td>59</td>
<td>15</td>
<td>Theophylline</td>
<td>S + (cof; t, col)</td>
<td>4.67 (100)</td>
<td>2.51 (61)</td>
<td>54 (29)</td>
<td>1.33 (37)</td>
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<tr>
<td>7, F, 31</td>
<td>163</td>
<td>66</td>
<td>16</td>
<td>Aminophylline;</td>
<td>ES + (cof; t)</td>
<td>2.92 (76)</td>
<td>1.60 (53)</td>
<td>55 (22)</td>
<td>0.78 (28)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pramidine mist</td>
<td>Marix –</td>
<td>2.86 (71)</td>
<td>1.75 (54)</td>
<td>61 (28)</td>
<td>1.08 (43)</td>
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<td>8, F, 19</td>
<td>162</td>
<td>55</td>
<td>14</td>
<td>Albuterol</td>
<td>S + (cof; col)</td>
<td>5.41 (101)</td>
<td>2.60 (62)</td>
<td>48 (23)</td>
<td>1.03 (19)</td>
</tr>
<tr>
<td>9, M, 30</td>
<td>178</td>
<td>70</td>
<td>27</td>
<td>Albuterol</td>
<td>–</td>
<td>3.51 (85)</td>
<td>1.91 (56)</td>
<td>54 (26)</td>
<td>0.98 (25)</td>
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<tr>
<td>Mean</td>
<td>167</td>
<td>64</td>
<td>21</td>
<td></td>
<td></td>
<td>1.02 (17)</td>
<td>0.64 (16)</td>
<td>10 (12)</td>
<td>0.46 (11)</td>
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<td>SD</td>
<td>8</td>
<td>8</td>
<td>9</td>
<td></td>
<td></td>
<td>1.20 (8)</td>
<td>0.64 (16)</td>
<td>10 (12)</td>
<td>0.46 (11)</td>
</tr>
</tbody>
</table>

*Mean age, 35 ± 17 years.
†ES, Ex-smoker; and S, current smoker.
‡cof, Coffee; t, tea; col, colas; and M, caffeine-containing medications.
§Numbers within parentheses are percent of predicted.
||Numbers within parentheses are percent change.
†This subject had positive methacholine bronchoprovocation prior to study.

oral (one) corticosteroids; and cromolyn sodium (one). No subject was receiving immunotherapy during the course of the study. Five subjects were ex-smokers, two were nonsmokers, and two smoked less than ten cigarettes per day. Six subjects routinely drank an average of two cups of brewed coffee each day (range, one to six cups per day), and two subjects (subjects 4 and 5) reported some associated improvement in breathing. The few daily drinkers of tea (one to three cups) and cola (16 oz) denied any noticeable effect of the beverage on their asthma. Three subjects (subjects 5, 6, and 8) consumed chocolate or cacao on a daily or frequent basis. The screening value for the forced expiratory volume in one second (FEV1) ranged from 31 to 86 percent of predicted, with a mean of 56 percent. The FEV1 improved 15 percent or more following two inhalations of aerosol isoproterenol from a metered-dose inhaler (75 µg per actuation) in eight subjects. The remaining subject (subject 5) improved her FEV1 by 11 percent following inhalation of isoproterenol but had clinically documented asthma and had demonstrated significant airway reversibility with inhalation of isoproterenol (FEV1 increased 18 percent) and a positive methacholine bronchoprovocation test several months prior to the present study. The mean improvement in FEV1, after the bronchodilator for the group was 25 ± 11 percent (± SD).

The protocol was approved by the UCLA School of Medicine Human Subject Protection Committee, and each subject signed an informed consent form. Each subject was instructed to withhold the following medications and products for the indicated duration (in parentheses) prior to each day of study: theophylline compounds (48 hours); adrenergic agents, oral (12 hours) and inhaled (eight hours); corticosteroids, oral (24 hours) and inhaled (12 hours); cromolyn sodium (24 hours); antihistamines (48 hours); caffeine-containing beverages and medications (12 hours); and theobromine products such as cocoa and chocolate (72 hours).

We used a double-blind, random-allocation, crossover experimental design, as indicated in Table 2. After fasting for at least four hours, subjects were studied at approximately the same time of day on each of five days of study separated by at least three days. On each day, subjects ingested a total of three 6-oz (180-ml) cups of a brewed decaffeinated coffee (Brim automatic-drip decaffeinated coffee) over a 15-minute period, without sugar or cream. Decaffeinated coffee was freshly prepared for each session in a standard fashion according to directions for the automatic-drip coffee maker (model HB5185; Norelco Dial-a-Brew II). Depending on the day of study, 150 mg of...
caffeine U.S.P. (Spectrum Pharmaceuticals) was dissolved in one, two, or three cups of the decaffeinated coffee vehicle. The amount of caffeine in a cup of brewed regular coffee is highly variable, with an average content of approximately 150 mg.14 To ensure uniformity, we therefore added 150 mg of caffeine to each cup of decaffeinated coffee to provide a standard amount of caffeine equivalent to that commonly consumed in a cup of brewed coffee. On two days, only decaffeinated coffee was used without any added caffeine. An aliquot of the resulting solutions was obtained each day, frozen, and subsequently analyzed for caffeine content, with appropriate dilutional corrections, by high-pressure liquid chromatography.15 The total amount of caffeine ingested was calculated on the basis of the measured caffeine concentration in the known volume of coffee solution ingested (Table 2). In addition, subjects on each day of study ingested an identical-appearing tablet containing either lactose (placebo) or 200 mg of aminophylline USP (active control drug) during the drinking of the last cup of coffee. For simplicity, the days using three cups of decaffeinated coffee alone with either a placebo or aminophylline tablet are designated as placebo and aminophylline days, respectively, whereas the other study conditions are designated as one, two, and three cups to indicate the number of cups of decaffeinated coffee to which the caffeine was added (Table 2).

Measurements during each day of study included serial sampling of venous blood from an indwelling heparinized catheter, whole-body plethysmography, spirometry, and recording of respiratory rate, heart rate, sitting blood pressure, and symptoms. Serum was frozen and subsequently analyzed in single-blind fashion for concentrations of caffeine, theophylline, and theobromine.16 Plethysmographic measurements, including airway resistance (Raw) and thoracic gas volume,17 with calculation of specific airway conductance (Gaw/Vl), were performed in a variable-pressure whole-body plethysmograph (Warren E. Collins). Spirometric measurements, including forced vital capacity (FVC), FEV, and forced expiratory flow rate between 25 and 75 percent of expired volume (FEF25-75%), were performed in triplicate at baseline and subsequently in duplicate using a computerized pneumotachograph spirometer (SC-20A, Cavitron Corp) which had been calibrated previously using a 3-L syringe and a Stead-Wells volumetric spirometer.18 The best FVC, FEV, and FEF25-75% were calculated from the best curve based on both the FVC and FEV,. Baseline (before coffee) measurements were performed following a 30-minute rest period. All measurements were repeated every 15 minutes after the end of the coffee-consuming period for the first hour, and then each 30 minutes thereafter for two hours.

The BMDP statistical software (University of California, Los Angeles) was used for statistical analyses. Data were primarily evaluated by two-way analysis of covariance (ANCOVA), grouped by subject and treatment; the baseline pulmonary function or serum drug concentration was used as the covariate. Two-way analysis of variance (ANOVA) was also used to evaluate baseline pulmonary function and serum drug concentrations and the area under the response-time curve (dependent variables), using subject and treatment as the two factors. A Friedman nonparametric two-way ANOVA was also used to analyze the area under the curve. When ANCOVA or ANOVA revealed significant differences across all treatment groups (p < 0.05), pairwise comparisons were performed using paired t-tests, with p values of less than 0.05 to less than 0.016 considered statistically significant, depending on the number of simultaneous tests performed (Bonferroni method). Linear regression analysis was used to determine dose-response relationships.

**RESULTS**

**Baseline Data**

Mean baseline (before drug) values for serum caffeine, theophylline, and theobromine concentrations and FEV, FEF25-75%, and Gaw/Vl (Table 3) were
not significantly different across all days of study according to two-way ANOVA. Forty-four of the 45 measurements of baseline serum caffeine level for the nine subjects showed either absent amounts of caffeine (34 measurements) or 1 μg/ml or less (ten measurements). Subject 2 had the highest baseline caffeine level (1.6 μg/ml) on her day of study with two cups of caffeinated coffee. Baseline serum theophylline level was zero in 11 instances, less than 1 μg/ml to 5 μg/ml in 24 instances, and 6 μg/ml to 12 μg/ml in nine measurements. Subject 3 had the highest baseline theophylline level (12 μg/ml on his day of study with two cups). In three subjects (subjects 3, 4, and 8), baseline theophylline values of 6 μg/ml or more were noted, possibly due to delayed theophylline metabolism or failure to completely abstain from their theophylline medications for the requested time prior to each day of study. Baseline serum theobromine concentrations were either zero to 1 μg/ml (40 measurements) or 1 μg/ml to 2 μg/ml (four measurements), except for subject 8 (2.2 μg/ml) on her day with three cups of caffeinated coffee.

**Serum Methylxanthine Changes**

The absolute mean changes from baseline in the serum caffeine level (excluding aminophylline day) and in the serum theophylline level (aminophylline day only) are depicted in Figure 1. Serum caffeine concentrations following ingestion of two and three cups of caffeinated coffee increased rapidly and peaked after 45 minutes at 9.9 μg/ml ± 1.8 μg/ml (± SE) and 12.4 μg/ml ± 1.5 μg/ml above baseline, respectively. On these same days the serum theophylline level increased maximally by 1.0 μg/ml ± 1.2 μg/ml and 1.9 μg/ml ± 1.2 μg/ml, respectively, after 180 minutes (data not shown). On the aminophylline day, the serum theophylline level increased maximally by 3.8 μg/ml ± 0.4 μg/ml at 90 minutes. Serial caffeine levels on the aminophylline and placebo days remained essentially unchanged (increments less than 0.3 μg/ml).

Changes in serum caffeine measurements were significantly different (by ANCOVA and paired t-tests, p < 0.01) between conditions except for three cups vs two cups (different only at 15 minutes), two cups vs one cup (different at 60, 120, and 150 minutes), and aminophylline vs placebo days (similar changes at all times). Serum theophylline levels were essentially similar at each measurement during the three days with caffeinated coffee, whereas theophylline concentrations on the aminophylline day were always higher than those on other studied days.

Serum theobromine concentrations increased modestly on every study day and reached mean peak changes of 0.64 μg/ml ± 0.31 μg/ml, 0.21 μg/ml ± 0.17 μg/ml, 0.10 μg/ml ± 0.12 μg/ml, 0.06 μg/ml ± 0.06 μg/ml, and −0.08 μg/ml ± 0.03 μg/ml during study days with three, two, and one cups, placebo, and aminophylline, respectively. The peak increases in serum theobromine level occurred more than 150

![Figure 1](image-url). Mean changes (± SE) in serum caffeine concentration (excluding aminophylline day) and serum theophylline concentration (aminophylline day only) from baseline over time.
minutes following ingestion of one, two, and three cups of caffeinated coffee. We chose to exclude further analysis of theobromine because of minimal increases in the concentration of this methylxanthine and its relatively weak physiologic potency, as suggested elsewhere.\textsuperscript{a,b}

**Physiologic Responses**

The bronchodilator effect of caffeine was investigated by comparing the changes in pulmonary function at each time during study days with three cups, aminophylline, and placebo. Changes in FEV\textsubscript{i}, FEF25-75\%, and Gaw/VL were analyzed with two-day ANCOVA, with baseline values as the covariate, and post hoc paired t-tests; a p value of <0.05/3 or <0.016 was considered significant, since three pairwise comparisons were performed at each time. The results are plotted as percent change from baseline in FEV\textsubscript{i} (Fig 2A), FEF25-75\% (Fig 2B), and Gaw/VL (Fig 2C) for ease of illustration.

Both FEV\textsubscript{i} and FEF25-75\% increased above baseline following three cups of caffeinated coffee and aminophylline and reached peak responses (more than 20 percent above baseline) by 120 minutes. These changes were significant compared to placebo. The area under the curve (AUC) for FEV\textsubscript{i} on the three-cup day was significantly different from that of placebo (p <0.011, two-way ANOVA; p<0.025, Friedman two-way ANOVA). The AUC for FEF25-75\% also showed significant differences from placebo (p = 0.004, ANOVA; p <0.025, Friedman two-way ANOVA). Aminophylline produced increments in FEV\textsubscript{i} and FEF 25-75\% which were not significantly different from those following three cups of caffeinated coffee.

Specific airway conductance similarly increased due to reductions in both Raw and thoracic gas volume and peaked (more than 50 percent above baseline) 120 minutes following ingestion of each active drug. Caffeine produced significantly greater increments in Gaw/VL than placebo at 60, 90, 120, and 180 minutes (ANOVA and paired t-test, p <0.04) (Fig 2C) and tended to be significant over the entire three-hour period after treatment by AUC (ANOVA and paired t-test, p = 0.06). Aminophylline produced significantly greater increments in Gaw/VL than placebo during 60 to 180 minutes by ANCOVA (p <0.005) and during the entire period after treatment (ANOVA for AUC, p = 0.009). Aminophylline-induced increments in Gaw/VL were not significantly different from those due to caffeine, although the former drug tended to produce greater increases during the last 1\% hours of the study.

Dose-response relationships were evaluated by linear regression analysis of the mean peak increases in FEV\textsubscript{i} (Fig 3A), FEF25-75\% (Fig 3B), and Gaw/VL (Fig 3C) vs the logarithmic peak increase in serum caffeine.

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**Figure 2.** Percent change (mean ± SE) from baseline in FEV\textsubscript{i} (A, top), FEF25-75\% (B, center) and Gaw/VL (C, bottom) over time. Three cups of caffeinated coffee and aminophylline alone are compared to placebo by two-way ANCOVA and post hoc paired t-tests. Asterisks indicate p<0.05; daggers indicate p<0.016.
Figure 3. Peak increases in FEV₁ (A, top), FEF25-75% (B, center), and Gw/Vt (C, bottom) vs peak increase in serum caffeine concentration plotted semilogarithmically following placebo and one, two, and three cups of caffeinated coffee. Equation of regression line by least-squares regression for FEV₁ is \( y = 0.134 + 0.346x \); for FEF25-75% is \( y = 0.183 + 0.396x \); and for Gw/Vt is \( y = 0.022 + 0.042 \log(\text{serum caffeine concentration}) \).
concentration on all study days except the aminophylline days and days with baseline theophylline levels more than 5 µg/ml (to avoid possible confounding interactions). Each point in the figures represents the peak response of each subject on a study day. The correlation coefficient was statistically significant for caffeine vs FEV₁ (p = 0.007), FEF25-75% (p = 0.005), and Gaw/Vl (p = 0.002).

Other cardiopulmonary responses were generally unchanged from baseline or showed minimal but statistically significant differences. Respiratory rate did not change from baseline on any study day. Heart rate decreased up to 9 percent from baseline at frequent times after the drug on each studied day using caffeinated coffee and on the aminophylline day. Blood pressure did not change except for small but statistically significant increases (12 percent) in diastolic pressure with two and three cups of caffeinated coffee.

Side effects were mild and were relatively more frequent with three cups of caffeinated coffee than with placebo or aminophylline. Three subjects reported increased nervousness and gastrointestinal upset with three cups, whereas only one individual reported these symptoms with aminophylline and placebo. Four subjects reported improved breathing with two and three cups, whereas only two subjects perceived similar improvement with aminophylline. The subjects could not consistently identify the caffeine content of beverages consumed.

**DISCUSSION**

As expected, orally administered caffeine was absorbed rapidly, and a peak serum concentration was reached within one hour after ingestion. Caffeine distributes into all tissues in proportion to their water content, and the rate of biotransformation is fairly uniform across individuals, the average half-life being at least 3.5 hours. Although coffee contains numerous chemicals which generate various metabolites, the exposure of most tissues to caffeine is greater than to any of its metabolites. Thus, the pharmacologic effects of coffee are primarily related to its content of caffeine.

The results of this study confirm and extend the findings of Becker and co-workers, who reported significant improvement in FVC, FEV₁, and FEF25-75% of asthmatic subjects one to six hours following ingestion of caffeine, with maximal bronchodilation at two hours. Unlike our study, their protocol used a parallel group design without placebo comparison and only a single, higher dose of caffeine (10 mg/kg) in younger asthmatic subjects (8 to 18 years).

We simulated the actual practice of coffee drinking by adults with a smaller dose of caffeine, similar to the amount ordinarily present in a brewed cup of regular coffee. Our results indicate that caffeine causes acute bronchodilation (Fig 2), with a significant dose-response relationship between serum caffeine concentration and pulmonary function (Fig 3). The significant increases in FEV₁, FEF25-75%, and Gaw/Vl following a 7-mg/kg dose of caffeine (three cups) were similar to those following 200 mg of aminophylline (theophylline, 170 mg or approximately 2.6 mg/kg). Therefore, caffeine is approximately 40 percent as potent as theophylline on a milligram-for-milligram basis in producing equivalent bronchodilation. This observation supports in vitro results which indicated that caffeine has a weaker relaxant effect than theophylline on bronchial smooth muscle. The short-term hemodynamic changes in heart rate and diastolic blood pressure in our subjects indicate other pharmacologic actions of caffeine and are similar to results reported by other investigators.

The mechanism of action of methylxanthines is controversial. The methylxanthines differ markedly in the intensity of their actions on various tissues, and it is postulated that these effects may be mediated by several basic cellular actions: (1) increasing amounts of the second messenger cyclic AMP (the traditional hypothesis); (2) translocations of intracellular calcium; and (3) blockade of receptors for adenosine. Caffeine may also relax bronchial smooth muscle by indirect mechanisms. Caffeine directly stimulates the adrenal medulla to release epinephrine and noradrenaline, which account for some short-term hemodynamic effects. Although we did not measure catecholamine levels, it is conceivable that endogenously released epinephrine could have contributed to the observed acute bronchodilation following caffeine ingestion. In addition, caffeine is partially metabolized to theophylline in adults. N-demethylation of caffeine constitutes a relatively minor metabolic pathway. Although the serum theophylline level was maximal at three hours following ingestion of three cups of caffeinated coffee, the maximal absolute increase in serum theophylline level after caffeine consumption was only 1.9 µg/ml and occurred one hour after the peak increases in pulmonary function. Although we might have observed higher theophylline levels at later times with a larger caffeine loading dose, the relatively small amount of theophylline generated from caffeine metabolism probably contributed minimally to the observed bronchodilation.

Our findings have diagnostic and therapeutic implications regarding the consumption of coffee and other methylxanthine-containing products by patients with bronchospastic disorders. Although the amount of caffeine in a cup of coffee varies considerably, even a single cup of strongly caffeinated coffee may quickly produce as much as a 15 percent increase in FEV₁. Therefore, consumption of coffee could produce falsely better "baseline" pulmonary function than anticipated.
in a “nonmedicated” patient with hyperreactive airways or could negate a significant bronchodilator response to an administered bronchodilator (or both). The potential confounding effect of prior caffeine ingestion must be avoided by having patients with caffeine habits use decaffeinated coffee or withhold all caffeine-containing products for at least 12 hours prior to pulmonary function testing with or without diagnostic bronchodilator administration. Prostration of theophylline agents and (probably) theobromine is also routinely indicated for similar reasons.

From a therapeutic standpoint, caffeine ingestion (eg, as coffee) has potentially both beneficial and adverse effects by virtue of its bronchodilator properties. Caffeine alone may be an effective bronchodilator when used on a short-term basis; however, a relatively large regular dosing of caffeine (eg, one to three cups of strong coffee every six hours or less) would be required for significant, sustained bronchodilatation, since caffeine is a relatively weak and short-acting bronchodilator. Toxic effects from caffeine and the possible development of tolerance may limit any therapeutic usefulness of long-term caffeine ingestion. Caffeine would also have minimal bronchodilator effects in patients with relatively fixed airway obstruction.

Caffeine may enhance the clinical effectiveness of concurrent bronchodilator therapy, due to its intrinsic effects on airway smooth muscle and to its partial metabolism to theophylline. Caffeine also competes with theophylline for common metabolic pathways and may suppress theophylline metabolism. Regular addition of caffeine to an existing theophylline pool (particularly if in the high therapeutic range) could increase the theophylline concentration and the possibility of methylxanthine-related toxic effects. The interactions and effects of concomitant use of caffeine and theophylline are unknown and require further investigation.

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Bronchodilator Effects of Caffeine in Coffee (Gong et al)