J Clin Gastroenterol 8(2): 150–153, 1986.

Effect of Regular and Decaffeinated Coffee on Serum Gastrin Levels

F. Acquaviva, A. DeFrancesco, A. Andriulli, P. Piantino, A. Arrigoni, P. Massarenti, and F. Balzola

We evaluated the hypothesis that the noncaffeine gastric acid stimulant effect of coffee might be by way of serum gastrin release. After 10 healthy volunteers drank 50 ml of coffee solution corresponding to one cup of home-made regular coffee containing 10 g of sugar and 240 mg/100 ml of caffeine, serum total gastrin levels peaked at 10 min and returned to basal values within 30 min; the response was of little significance (1.24 times the median basal value). Drinking 100 ml of sugared water (as control) resulted in occasional random elevations of serum gastrin which were not statistically significant. Drinking 100 ml of regular or decaffeinated coffee resulted in a prompt and lasting elevation of total gastrin; mean integrated outputs after regular or decaffeinated coffee were, respectively, 2.3 and 1.7 times the values in the control test. Regular and decaffeinated coffees share a strong gastrin-releasing property. Neither distension, osmolarity, calcium, nor amino acid content of the coffee solution can account for this property, which should be ascribed to some other unidentified ingredient. This property is at least partially lost during the process of caffeine removal.

Key Words: Coffee—Serum gastrin—Caffeine—Gastric acid secretion

From the Departments of Gastroenterology and Clinical Nutrition, Ospedale Maggiore, San Giovanni Battista, Torino, Italy.

Address correspondence and reprint requests to A. Andriulli, Department of Gastroenterology, Ospedale San Giovanni-Molinette, Corso Bramante 88, 10126 Torino, Italy.

Caffeine relaxes the lower esophageal sphincter (1–5) and stimulates gastric (2,6–12) and intestinal secretion (13,14) by inhibiting phosphodiesterase activity and increasing cyclic AMP concentrations (15,16).

At equal amounts of caffeine, both regular coffee and decaffeinated coffee are more potent stimulants of gastric acid output than caffeine alone (2). Presumably in coffee there is a noncaffeine acid stimulant that has not yet been isolated. That such a noncaffeine acid stimulant might act through gastrin release has not been thoroughly investigated. In one study ingestion of caffeine alone did not elevate plasma gastrin, but coffee and decaffeinated coffee produced instantaneous elevations (17). Later, when acid secretion and gastrin release in response to decaffeinated coffee proved greater than in response to a peptone meal, decaffeinated coffee appeared to be the most potent intragastric stimulant of acid secretion and gastrin release so far identified (18).

We have re-evaluated the effect of water and home-made regular or decaffeinated coffee on serum release of total gastrin and pepsinogen I.

MATERIALS AND METHODS

All studies were performed on fasting volunteers (ranging in age from 23 to 32 years) who had no history of gastrointestinal disease, were not currently taking any medications, and who gave informed consent.

Study 1 Design

Ten subjects (five men, five women) were given one cup of Italian home-made regular coffee at room temperature. The coffee solution was prepared from 17 g of coffee solids and 150 ml of water; of the final mixture, 50 ml corresponding to the total volume of one cup with 10 g of sugar was administered to each subject.

Chemical characteristics and amino acid content of the coffee mixture are shown in Table 1. Venous blood samples for gastrin determinations were drawn from an arm vein twice during the basal period and at +2, +5, +10, +15, and +30 min after coffee ingestion.

Study 2 Design

Ten healthy volunteers (five men, five women) were included; four were also evaluated in study 1. As control test, each subject received 100 ml of running water with 10 g of sugar. Blood was drawn twice before and at +2, +5, +10, +15, and +30 min after water ingestion. Following a 30-min interval, 100 ml of a sugared coffee solution was given, and blood was drawn at the same time intervals. A regular coffee solution was prepared as in study 1. On a separate day, the same subjects were given, after sugared water, equal amounts of a decaffeinated coffee mixture (100 ml), which was prepared from 17 g of decaffeinated coffee solids and 150 ml of running water. Chemical characteristics and amino acid content of the decaffeinated coffee are shown in Table 1. Blood specimens were drawn with the same schedule as for coffee.

Water, regular coffee, and decaffeinated coffee were given at their normal temperature (e.g., coffee at 60°C and water at 22°C).

Methods

Water, coffee, and decaffeinated coffee solutions were assayed for total nitrogen concentration by the Kjeldahl method (19), for total calcium content (20) and for caffeine concentration (21); moreover, concentrations of individual amino acids were analyzed in an amino acid analyzer, following acid hydrolysis (22). Gastrin values have been measured by a commercial kit following the manufacturer's directions. In the gastrin assay (Becton Dickinson, Orangeburg, New York) all molecular forms of gastrin are measured; this assay has been validated elsewhere (23).

TABLE 1. *Chemical characteristics and amino acid content of water and regular and decaffeinated coffee solutions*

	Water	Regular coffee	Decaffeinated coffee
Osmolarity (mOsm/kg H_2O)	315	451	451
Ca^{++} (mmol/liter)	1.42	1.38	1.26
Nitrogen (g/liter)	0.09	1.02	0.5
Caffeine (mg/100 ml)		240.8	5.9
Aspartic acid (mg/ml)		19.4	19.2
Threonine (mg/ml)		4.5	3.8
Serine (mg/ml)		4.3	3
Glutamic acid (mg/ml)		83.8	72.8
Glycine (mg/ml)		18.9	16.9
Alanine (mg/ml)		12.5	10.8
Isoleucine (mg/ml)		8.8	7.3
Leucine (mg/ml)		21.6	18.1
Tyrosine (mg/ml)		10.8	9.8
Phenylalanine (mg/ml)		12.7	12.2
Total amino acid content (mg/ml)		196.8	173.9

Data Analysis

The integrated gastrin output (IGO) after water and coffee in each subject was derived by computing the total area under the response curve. Experimental data are reported as mean values ± standard errors, and statistical differences in values have been checked by means of paired or unpaired Student's t test, as appropriate.

RESULTS

Study 1

After drinking one cup of regular coffee, gastrin response was characterized by a prompt increase in serum, which peaked at 10 min after the ingestion. The peak increase was of little significance (1.28 times the median basal level) with a p value approaching statistical significance when compared to basal value ($p = <0.06$); a positive response was appreciated in only 8 of the 10 subjects. At 30 min after the stimulus was given gastrin levels returned to basal value. The mean IGO value was 1.3 ± 0.5 pg/ml × min (Table 2).

Study 2

The administration of sugared water as a control test resulted in occasional random elevations of serum gastrin, which were not statistically significant. IGO values after administration of water did not vary between the two days of the study.

Coffee ingestion at a double dose of that given in study 1 was followed by a prompt increase in serum gastrin levels, which peaked at 15 min and remained elevated throughout the study. Mean IGO value was 2.3 times higher (Table 2) than the IGO after water ingestion, with a high statistical significance ($p < 0.001$). A response was evident in all subjects studied.

After administration of decaffeinated coffee, mean gastrin levels increased slightly and peaked at 15 min, thereafter remaining elevated throughout the study. Mean IGO response was 1.7 times higher (Table 2)

TABLE 2. *Integrated gastrin output* ($\bar{x} \pm SE$) *following ingestion of water, coffee, and decaffeinated coffee*

	Study 1		Study 2	
	Water	Coffee	Water	Decaffeinated
One cup	—	1.3 ± 0.15	—	—
Two cups	1.20 ± 0.05	2.71 ± 0.19	1.08 ± 0.06	1.8 ± 0.18

than those observed in the control study when water was administered; the difference was statistically significant ($p < 0.01$). A comparison between gastrin release after drinking regular coffee and that after drinking decaffeinated coffee reveals a statistically significant difference ($p < 0.005$).

DISCUSSION

We have confirmed that regular and decaffeinated coffees are potent stimulants of gastrin release. In the two previous studies on the gastrin-releasing effect of coffee, milk was added to the coffee in one (17) and only decaffeinated coffee was studied in the other (18).

The mechanism of gastrin release by coffee is unknown. Among the numerous agents which stimulate gastrin release are such luminal stimulants as peptides, amino acids or distension, neural vagal excitation, and blood-borne stimulants like calcium and hormones (24). Distension and osmolarity are unlikely to account for gastrin release by coffee since no gastrin response was observed in the control experiment when water was given. Intragastric or intravenous calcium increases serum gastrin levels and stimulates gastric acid secretion (25,26) but at concentrations several times higher than that present in the regular and decaffeinated coffees in our study. Therefore, the gastrin-releasing effect of coffee should be ascribed to some ingredients contained in coffee; caffeine is not the gastrin-releasing agent of coffee (17).

Only the aromatic amino acids, phenylalanine and tryptophan, have been shown to be potent stimulants of gastric secretion (27,28) and gastrin release (28) but at relatively larger concentrations than the amino acid content of an ordinary meal (28). Therefore, it seems extremely unlikely that the small amounts of amino acids in coffee hydrolysates are responsible for the stimulation of serum gastrin and gastric acid secretion in humans.

In search of an explanatory mechanism for the strong gastrin releasing property of coffee we can only speculate about some other unidentified ingredient(s). In this regard we have found that, following caffeine removal, decaffeinated coffee is still capable of releasing gastrin but at a lesser degree than regular coffee. This observation may suggest that in the process of caffeine removal some other constituent(s) with some gastrin releasing effect may be taken away. It would be of interest to compare the action of regular coffee with that of coffee that has undergone various chemical treatments.

REFERENCES

1. Dennish GW, Castell DO. Caffeine and the lower esophageal sphincter. *Am J Dig Dis* 1972;17:993–6.
2. Cohen D, Booth GH. Gastric acid secretion and lower esophageal sphincter pressure in response to coffee and caffeine. *N Engl J Med* 1975;293:897–9.
3. Cohen S. Pathogenesis of coffee-induced gastrointestinal symptoms. *N Engl J Med* 1980;303:122–4.
4. Thomas FB, Steinbaugh JT, Fromkes JJ, Caldwell JH. Inhibitory effect of coffee on lower esophageal sphincter pressure. *Gastroenterology* 1980; 79:1262–6.
5. Salmon PR, Fedail SS, Wurzner HP, et al. Effect of coffee on human lower esophageal function. *Digestion* 1981;21:69–73.
6. Roth JA, Ivy A. The effect of caffeine upon gastric secretion in the dog and man. *Am J Physiol* 1944;141:454–61.
7. Roth JA, Ivy AC. The synergistic effect of caffeine upon histamine in relation to gastric secretion. *Am J Physiol* 1944;142:107–13.
8. Littman A, Fox BW, Kammerling EM. A single aspiration caffeine gastric analysis in duodenal ulcer and control patients. *Gastroenterology* 1955;28:953–63.
9. Musick VH, Avey HT, Hopps HC. Gastric secretion in duodenal ulcer in remission: response to caffeine test meal. *Gastroenterology* 1946;7:332–9.
10. Debas HT, Cohen MM, Holubitsky IB. Caffeine-stimulated acid and pepsin secretion: dose-response studies. *Scand J Gastroenterol* 1971;6:453–7.
11. Cohen MM, Debas HT, Holubitsky IB, Harrison RC. Caffeine and pentagastrin stimulation of human gastric secretion. *Gastroenterology* 1971;61:440–4.
12. McArthur K, Hogan D, Isenberg JI. Relative stimulatory effects of commonly ingested beverages on gastric acid secretion in humans. *Gastroenterology* 1982;83:199–203.
13. Wald A, Back C, Bayless TM. Effect of caffeine on the human small intestine. *Gastroenterology* 1976;71:738–42.
14. Wagner SM, Mekhjian HS, Caldwell JH, Thomas FB. Effects of caffeine and coffee on fluid transport in the small intestine. *Gastroenterology* 1978;75:379–81.
15. Harris JB, Nigon K, Alonso D. Adenosine-3′5′-monophosphate: Intracellular mediator for methyl xanthine stimulation of gastric secretion. *Gastroenterology* 1969;57:377–84.
16. Harris JB, Alonso D. Stimulation of the gastric mucosa by adenosine-3′5′-monophosphate. *Fed Proc* 1965;24:1368–76.
17. Berkowitz JM, Shields JE, Andersen IH, Praissman M. Plasma gastrin response to coffee, Sanka, caffeine and water. *Gastroenterology* 1974;66:666.
18. Feldman EJ, Isenberg JI, Grossman MI. Gastric acid and gastrin response to decaffeinated coffee and a peptone meal. *JAMA* 1981;246:248–50.
19. Bradstreet RB. *The Kjeldahl method for organic nitrogen.* New York: Academic Press, 1965.
20. Bachra BM, Daner A, Sobel AE. The complexometric titration

of micro- and ultramicroquantities of calcium in blood, serum, urine and inorganic salt solutions. *Clin Chem* 1958;4:107.
21. Duplatre A, Tisse C, Estienne J. Contribution to determination of caffeine by liquid chromatography. *Analysis* 1981;9:404–5.
22. Mondino A. A new system of automatic amino acid analysis. *J Chromatography* 1967;30:100–4.
23. Gibson RG, Hirschowitz BI, Mihas AA. Evaluation of two commercial kits for serum gastrin assay, and comparison with a conventional radioimmunoassay procedure. *Clin Chem* 1977;23: 1046–51.
24. Walsh JH, Grossman MI. Gastrin. *N Engl J Med* 1975;292:1324–32.
25. Holtermuller KH, Goldsmith RS, Sizemore GW, Go VLW. Dissociation of gastric acid and serum gastrin responses to intraluminal calcium in man: Influence of calcitonin and parathyroid hormone. *Gastroenterology* 1974;67:1101–6.
26. Reeder DD, Becker HD, Thompson JC. Effect of intravenously administered calcium on serum gastrin and gastric acid secretion in man. *Surg Gynecol Obstet* 1974;138:847–51.
27. Taylor IL, Byrne WJ, Christie DL, et al. Effect of individual L-amino acids on gastric acid secretion and serum gastrin and pancreatic polypeptide release in humans. *Gastroenterology* 1982;83: 273–8.
28. McArthur KE, Isenberg JI, Hogan DL, Dreier SJ. Intravenous infusion of L-isomers of phenylalanine and tryptophan stimulate gastric acid secretion at physiologic plasma concentrations in normal subjects and after parietal cell vagotomy. *J Clin Invest* 1983;71:1254–62.