ARTICLE IN PRESS
+ MODEL
Nutrition, Metabolism & Cardiovascular Diseases (2009) **xx**, 1—7

available at www.sciencedirect.com
ScienceDirect
journal homepage: www.elsevier.com/locate/nmcd

Nutrition, Metabolism & Cardiovascular Diseases

REVIEW

Carbonated beverages and gastrointestinal system: Between myth and reality

R. Cuomo [a,*], G. Sarnelli [a], M.F. Savarese [a], M. Buyckx [b]

[a] *Gastroenterology Unit, Department of Clinical and Experimental Medicine, University of Naples ''Federico II'', Via Sergio Pansini 5, 80131 Napoli, Italy*
[b] *The Beverage Institute for Health & Wellness, L.L.C., Coca Cola Company, Atlanta, USA*

Received 6 August 2008; received in revised form 13 March 2009; accepted 19 March 2009

KEYWORDS
Carbonated beverages;
Gastrointestinal system

Abstract A wealth of information has appeared on non-scientific publications, some suggesting a positive effect of carbonated beverages on gastrointestinal diseases or health, and others a negative one. The evaluation of the properties of carbonated beverages mainly involves the carbon dioxide with which they are charged. Scientific evidence suggests that the main interactions between carbon dioxide and the gastrointestinal system occur in the oral cavity, the esophagus and the stomach. The impact of carbonation determines modification in terms of the mouthfeel of beverages and has a minor role in tooth erosion. Some surveys showed a weak association between carbonated beverages and gastroesophageal reflux disease; however, the methodology employed was often inadequate and, on the overall, the evidence available on this topic is contradictory. Influence on stomach function appears related to both mechanical and chemical effects. Symptoms related to a gastric mechanical distress appear only when drinking more than 300 ml of a carbonated fluid. In conclusion there is now sufficient scientific evidence to understand the physiological impact of carbonated beverages on the gastrointestinal system, while providing a basis for further investigation on the related pathophysiological aspects. However, more studies are needed, particularly intervention trials, to support any claim on the possible beneficial effects of carbonated beverages on the gastrointestinal system, and clarify how they affect digestion. More epidemiological and mechanistic studies are also needed to evaluate the possible drawbacks of their consumption in terms of risk of tooth erosion and gastric distress.

The ''gossip'' about carbonated beverages

Natural bubbling or sparkling mineral waters have been popular for thousands of years. The ancient Greeks and Romans bathed in natural mineral springs and were familiar

* Corresponding author. Tel./fax: +39 081 7463892.
E-mail address: rcuomo@unina.it (R. Cuomo).

0939-4753/$ - see front matter © 2009 Elsevier B.V. All rights reserved.
doi:10.1016/j.numecd.2009.03.020

with the beneficial effects of bubbling waters from natural springs. A popular legend tells that, after crossing the Pyrenees, Hannibal, the famous general of the Carthaginian army, rested his troops and elephants at Les Bouillens in France, the location of the *Perrier* drinking water spring. Later, Europeans drank these naturally carbonated waters for their health. The story of carbonated beverages is a chapter of man's centuries-long attempts to imitate the products of nature, improve them, and adapt them as much as possible to his liking. Imitation of natural mineral waters and their mysterious effervescence was the objective [1].

Nowadays carbonated beverages are largely consumed all over the world. The global market in 2006 was close to 200 billion litres, the equivalent of 30.2 L per capita. This is 1.3 L more than in 2001, showing that the consumption in the last few years has markedly increased [2]. The consequence of this phenomenon is that people are increasingly interested in the effects of carbonated beverages on health, particularly on the gastrointestinal system. Different opinions are reported about the interaction of carbonated beverages and the gastrointestinal system, some suggesting a negative influence and other describing its benefits when consumed in a variety of conditions [3–12]. This trend appears to be paralleled by the increase in their commercial diffusion. The interest in carbonated beverages can be exemplified by two different articles attributing contrasting effect to their consumption. In one, the authors describe the cases of two children who experienced a pneumatic rupture of the esophagus – a condition occurring when gas under pressure is accidentally delivered into the oral cavity [13]. In the another, instead, the authors described the therapeutic property of carbonated drinks in the management of bolus obstruction in benign esophageal stricture [14]. These reports describe very borderline and unusual conditions, but there are studies that have verified the effect of their consumption on the gastrointestinal system and related diseases [7,15–18]. On the other hand, while the number of scientific reports on the effects of carbonated beverages is limited, a wealth of information has appeared on non-scientific publications, internet, popular articles, some suggesting a positive and others a negative effect on gastrointestinal diseases or health, often generating confusion in the public opinion on the true impact of carbonation on health. However there is now sufficient scientific evidence providing a basis for further investigation and answers as to what happens when a person drinks carbonated beverages and how they affect digestion. In examining the properties of carbonated beverages, it is necessary to consider three major points: a) the carbon dioxide with which these beverages are charged; b) the sugar or sweetener contained; c) the effect of other substances used by industries for their preparation. Of these, the most interesting and probably the most valuable one is carbon dioxide. The aim of this article is to explore the interaction of non-alcoholic carbonated beverages with the gastrointestinal system in humans.

This article reviews information available from articles retrieved using PubMed and other documents from other sources. The search on PubMed was performed utilizing as key word carbonated beverages, together with other terms describing the gastrointestinal system (i.e. esophagus, stomach etc).

Carbon dioxide and the gastrointestinal system

Carbon dioxide plays a key role in the body, almost like a hormone; it is produced by every tissue and probably acts on every organ.

Even if carbon dioxide is considered a waste product of cell respiration, it regulates body functions in at least 3 well defined ways: a) it is one of the prime factors in the blood's acid–base balance; b) it is the main factor controlling respiration; c) it exerts an essential tonic influence on the heart and the peripheral circulation. The level of carbon dioxide in the body is regulated by the release of excess molecules through the lungs [19].

At standard temperature and pressures, about 1 ml (2 mg) of carbon dioxide dissolves in 1 ml of neutral solution ($pH = 7$). In alkaline solutions, the gas is converted into carbonates and bicarbonates, and it is in this form that any ingested carbon dioxide is likely to be present in the intestinal tract. In general, one can assume that the daily average intake of carbon dioxide in food is equivalent to approximately 1 g daily of sodium bicarbonate or carbonate and therefore represents only a very small fraction of the amounts of these compounds in normal diets [20]

Most of the CO_2 in a carbonated beverage does not actually reach the stomach. Much is lost in the fizz when the can or bottle is opened, and some combines with swallowed air to cause belching. Therefore, most of the CO_2 present in a beverage does not reach the digestive tract and the small amount that does is readily and rapidly absorbed through the wall of the gastrointestinal system.

As the amount dissolved is a function of the pressure and temperature of the beverage, it is difficult to determine the amount ingested. With pressures used in commercial beverages, the volume of the gas will be 3–5 times the volume of the liquid (3–5 L of CO_2 in 1 L of liquid). Most of the gas escapes when the bottle is opened because of the sudden drop of pressure and it is estimated that ingestion ranges between 0.5 and 1.5 L of carbon dioxide at a time.

The gas ingested influences the alimentary tract through the nervous system and by direct mechanical and chemical means (see Fig. 1). Even the visual image of the bubbles in the beverage seemingly associated with pleasant reactions previously experienced with that same drink, can modify gastrointestinal perception [21,22].

Oral cavity and taste

In the oral cavity the ingested fluid is held for only a few seconds as swallowing moves the fluid into the esophagus and the stomach. If the beverage is ingested slowly, it induces a stimulating sensation and a slightly sour taste. These sensations can be modified by the different ingredients and physical properties of carbonated beverages [23]. The temperature of the beverage influences taste, with cooler drinks providing the most pleasant reaction – although this is susceptible to individual variations [24,25]. Mouthfeel differences between regular and diet cola beverages, rated by quantitative descriptive analysis, were indistinguishable because carbonation played such a large role in the sensory profiles of the two beverages [26]. When carbonation is too low or too high, the result is an overall

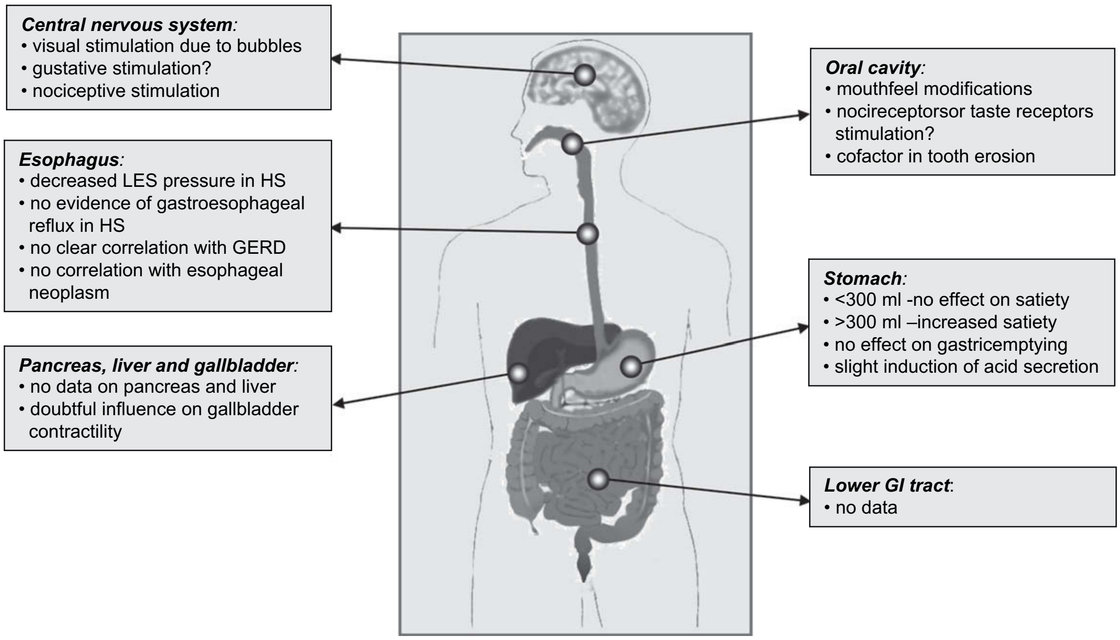

Figure 1 Effects of carbon dioxide in the beverages on gastrointestinal system. LES: lower esophageal sphincter; HS: healthy subjects; GERD: gastroesophageal reflux disease; GI: gastrointestinal.

unbalanced flavor [27]. The specific effects of carbonated beverages seem to be exerted only minimally in the oral cavity although nervous stimuli could influence the gastrointestinal tract [28,29]. The fizzy stimulation is caused by the diluted carbonic acid which induces a slight burning sensation by a mechanism defined as chemesthesis, rather than by the presence of bubbles [30,31]. Carbonated water excites lingual nociceptors via a carbonic anhydrase-dependent process, which in turn excites the neurons in the trigeminal subnucleus caudalis presumably involved in signaling oral irritant or chemesthetic sensations [31]. This perception is attributable to the conversion of CO_2 into carbonic acid, which is then capable of exciting lingual chemosensitive nociceptors [31]. However, a recent research has shown a specific taste modality for carbonated water in Drosophila [32], opening up the possibility that other organisms perceive the taste of oral carbonation. Against this background, an interesting field of research could be the exploration of the central nervous system and gastrointestinal system reactivity after carbon dioxide stimulation of the oral cavity.

The potential effect of carbonated beverages in determining dental caries in children has been hypothesized and evaluated in several studies, using different beverages [16,33—36]. In a study on eighty subjects conducted in Iceland, the authors found a significant relationship between carbonated cola and dental erosions independently of gastroesophageal reflux disease [16]. However in a research comparing patients affected by tooth erosion with healthy controls, the salivary pH in the patients with tooth erosions appeared lower in all of the following situations: basal, after drinking Coca-Cola, Sprite and carbonated water [36]. This means that saliva is basally altered in subjects with tooth erosion and carbonated beverages can only worsen the oral environment. Moreover both carbonated and non-carbonated beverages displayed a significant erosive effect on dental enamel showing that presence of carbonation in the beverages is not a major risk factor for tooth erosion [36].

In our opinion, the impact of carbonated beverages on the oral cavity has two important consequences. Firstly, the activation of the central nervous by carbon dioxide oral stimulation via a chemesthetic mechanism or by a putative gustative mechanism modifies the mouthfeel of beverages and could modulate the perception of digestive symptoms. Secondly, carbonation of beverages is one of the factors causing tooth erosion, although other synergic factors work to determine tooth damage such as the additional ingredients contained in the beverage and the basal alteration of saliva.

Esophagus

Most of the information on the relationship between the esophagus and carbonated beverages consumption is related to the problem of gastroesophageal reflux disease (GERD). The main symptom of this disease is heartburn, which frequently occurs when the esophagus is exposed to gastric acid. Recommendations generally made by physicians are to lose weight — if necessary, modify lifestyle behaviors, body posture and dietary habits, and often to limit the consumption of carbonated beverages. Very few studies have postulated that carbonated beverages cause GERD [37—39]. Fass and coworkers found that carbonated soft drink consumption was a predictor of GERD symptoms in a multivariate analysis [38]. Another small study on healthy individuals, performed by manometric evaluation, found decreased lower esophageal sphincter pressure immediately after, and also later on, following the ingestion of carbonated water compared to non-effervescent water [39]. The decrease in lower sphincter pressure after a carbonated beverage can be determined by increased fundus pressure due to carbon dioxide; on the other hand, the same authors failed to find

Please cite this article in press as: Cuomo R, et al., Carbonated beverages and gastrointestinal system: Between myth and reality, Nutr Metab Cardiovasc Dis (2009), doi:10.1016/j.numecd.2009.03.020

any increase in gastric reflux in the esophagus, confirming that gastroesophageal reflux is a multifactorial process. Moreover, a recent research performed on healthy subjects to verify the effect on the gastroesophageal reflux, of sweetened (sucrose 10%) water added with increasing concentrations of carbon dioxide showed no difference between carbonated and still water [40].

Other data derive from some surveys or epidemiologic studies. In a population-based telephone survey conducted in the USA, as part of the prevention strategies adopted to reduce heartburn, avoiding carbonated beverages appeared to decrease symptom; however in the same study, the authors failed to find any correlation between carbonated drink intake and heartburn [41]. In addition, epidemiologic studies exploring the consumption of carbonated drinks in patients with esophageal carcinoma ruled out a relationship between gastroesophageal reflux disease and carbonated beverages. In another population-based study no association was found between carbonated soft drinks and risk of esophageal adenocarcinoma [42]. A further epidemiologic study in the USA explored the relationship between amount of carbonated drinks consumed and the risk of four types of esophageal neoplasms (esophageal carcinoma, gastric cardia adenocarcinoma, esophageal squamous cell carcinoma and non-cardia gastric adenocarcinoma). Only esophageal carcinoma presented an inverse correlation with the drinks consumed, with greater consumption of drinks associated with lower risk of neoplasm. This data must be confirmed but suggests no role for carbonated beverage in determining esophageal neoplasm and, indirectly, gastroesophageal reflux [43].

The interaction between carbonated beverages and GERD is an important issue and needs a critical analysis of the quality of the studies reported. Overall, the experimental studies were performed with debatable methods and on small samples of mainly healthy subjects, whereas more regulated and objective research would be needed. Furthermore, telephone surveys and epidemiologic studies are useful to identify or rule out potential hazards but do not support any definitive conclusions.

Stomach

The hypothetical fate of carbon dioxide in a carbonated drink depends on the state of the gastric activity at the time of ingestion. When the stomach is empty, fluids pass rapidly into the duodenum where carbon dioxide is transformed into bicarbonate. The carbon dioxide dissolved is rapidly released in gaseous form as the fluid is warmed. The free carbon dioxide may be belched if the expanding gas increases the pressure and stimulates the gastric fundus, triggering the belching mechanism. Indeed, distension of the gastric fundus can increase transient lower esophageal sphincter relaxation [44]. If the carbonated fluid is taken while or after eating it tends to localize in the upper part of stomach and may produce a feeling of fullness. To this regard, there is need to underline some data in the literature. Very early observations showed that a rapid distension of the stomach induced by pumping air or carbon dioxide was able to inhibit any movement for 2–5 min after belching [45,46]. The same authors noted that ingestion of 150–200 cc of soda water inhibited all peristalsis for 2–3 min. These observations indicated that stomach stretching was related to motility.

Another study showed that, compared to still water, an alkaline solution with or without carbon dioxide was able to decrease gastric emptying, measured by fluoroscopy [47]. These observations suggest that alkali solutions decrease gastric emptying time and that carbon dioxide may not be the important link. Older studies mainly reported that carbonated water apparently decreased gastric emptying time, suggesting a possible effect on gastric motility [48,49]

A more recent article showed that adding carbonation to a drink does not significantly alter gastric function or the perception of gastrointestinal discomfort [50]. Pouderoux et al. also found no difference in gastric emptying or in feeling of fullness between 300 ml of carbonated and still water drunk with a meal of 700 calories, but showed an increased need to belch after carbonated water [51]. Similar results emerged from a study on healthy volunteers where 300 ml of sweetened beverages added or not with carbon dioxide did not influence the gastric emptying of a standard meal of 480 kcals [40].

Two studies performed during physical exercise showed that carbonated and non-carbonated beverages, administered alone, determined low gastrointestinal distress without clear evidence of influence on fluid intake [52,53]. In most of these studies the intake of beverages was ad libitum, with an average quantity of 1000 ml. Contrasting results come from two other studies. In the first one, performed with magnetic resonance imaging, the authors compared an intake of 800 ml of either water, a sweetened non-carbonated drink, a lightly carbonated drink, or regular cola, without a meal, and found an increased gastric distress and delayed gastric emptying only after drinking regular cola [54]. The second study aimed to verify the energy intake after a 590 ml preload beverage using regular cola and sparkling water; regular cola determined an initial increase in satiety without reduction of energy intake 175 min after drinking the beverage [55]. Both studies explored the effect of unusual volumes of beverages; moreover in the first study, the authors explored the effect of a large amount of beverage consumed without a meal.

The effects of carbonated water have also been assessed in patients affected by functional dyspepsia and constipation in a randomized double-blind study [7]. In these patients carbonated water decreased satiety and improved dyspeptic symptoms compared to still water, but did not influence gastric emptying. Also, in a recent study it was shown that drinking sweetened water with increasing concentrations of carbon dioxide does not affect gastric emptying in healthy volunteers [40].

In the past, several studies demonstrated that carbon dioxide plays a major role in the process of hydrochloric acid formation and secretion in the parietal cells of the gastric mucosa. Usually, carbon dioxide is supplied to the cells from the blood and interstitial fluids but, under some conditions, also from the lumen of the stomach. The diffusion of carbon dioxide into the cell is due to the weakness of carbonic acid and its liposolubility [56,60].

Using stomach pouches, some researchers found an inverse relationship between the amount of hydrochloric acid secreted by the stomach and the quantity of carbon

Please cite this article in press as: Cuomo R, et al., Carbonated beverages and gastrointestinal system: Between myth and reality, Nutr Metab Cardiovasc Dis (2009), doi:10.1016/j.numecd.2009.03.020

dioxide diffused in the lumen when secretion was stimulated by histamine [57]. In summary, after drinking carbonated beverages some of the carbon dioxide may be absorbed through the gastric wall, partly contributing, together with the carbon dioxide from the interstitial fluid and plasma, to the formation of hydrochloric acid.

Absorption of carbon dioxide is very high in the stomach. Equilibrium for carbon dioxide is reached within 80—90 min through the wall of the stomach while it takes longer for other gases, such as nitrogen, oxygen, or methane [58]. Water, alcohol, soluble gases and particularly carbon dioxide can be adsorbed efficiently from the stomach, contrarily to most foodstuffs are very little [59].

Compared to still water, an effervescent mixture also increased the absorption of acetylsalicylic acid. Sodium carbonate, sodium citrate and carbonated water also speeded up its absorption but to a lesser extent than the effervescent mixture [60].

Hence carbonated beverages seem to influence stomach function by both mechanical and chemical effects. Data from various studies underline that the mechanical effect depends on the pressure exerted by gas and fluid volume on the gastric wall. These studies showed that symptoms related to gastric distress appear only with intakes of carbonated fluid greater than 300 ml. On the other hand, a chemical effect related to carbon dioxide determines a slight increase in hydrochloric acid, which could influence positively the digestive process or worsen an acid related disease. Additional studies are needed to clarify these aspects.

Lower digestive tract

There is no clear evidence that the carbon dioxide ingested plays any pathophysiological role in the intestinal tract since it is almost totally absorbed before it reaches the lower digestive tract.

Accumulation of gas in the intestinal tract determines symptoms in many diseases, and intestinal flatus usually contains about 9.6% of carbon dioxide [61]. It needs to be further underlined that carbon dioxide diffuses rapidly across the gastrointestinal wall. If carbon dioxide is present in the intestine it will equilibrate with the amount already present in body fluids: therefore, if it is low it will diffuse from body fluids into the intestine and *vice versa*. In addition, it has been described that an intestinal trauma can decrease carbon dioxide absorption by 20% [62]. This is the only condition in which an increased carbon dioxide intake through a beverage might determine a greater presence of carbon dioxide in the intestinal lumen.

Pancreas, liver and gallbladder

There are scanty reports in the literature in this specific field. A rather dated article describes an increased activation of amylase in the saliva and pancreatic juice after contact with mineral spring water [63]. However, these authors did not consider that the effect did not depend on carbon dioxide but on the ionization of carbonic acid to hydrogen and bicarbonate ions. In a epidemiologic study on four hundred and ninety pancreas cancer patients, there was no link between pancreas cancer and past consumption of tea, carbonated beverages, beer, or spirits [17].

Some observations have been made on gallbladder activity. The first assessments of the effect of carbonated water on gallbladder contraction were performed by sonographic measurements in subject with dyspepsia and constipation [7]. One such study measured the contraction efficiency of the gallbladder before and after a treatment period of 15 days with 1.5 L of carbonated water compared to still water. At the end of treatment, gallbladder contraction improved only in patients treated with carbonated water. In a more recent experience, the acute administration of sweetened water with or without increasing concentrations of carbon dioxide in healthy subjects did not determine significant effects on gallbladder contraction compared to still water [40].

There are no references in the literature showing any relationship between carbonation of beverages and hepatic diseases.

Conclusions

The effects of beverages with carbon dioxide on the gastrointestinal system mainly involve the upper digestive tract, with a possible influence on taste, a causal role on tooth erosion, gastroesophageal reflux and on the modifications of gastric physiology. The data in the literature, while suggesting a minor role of carbonated beverages on tooth erosion, do not show a direct role of carbonated beverages as determining factor of gastroesophageal reflux; rather the epidemiological studies available do not sustain a causal relationship between regular drinking of carbonated beverages and gastroesophageal reflux disease. Further research in this field may elucidate the possible role of carbon dioxide.

The analysis of further observations, particularly on stomach physiology, shows that small volumes (300 ml) of carbonated beverages do not seem to influence the physiologic mechanisms, while greater volumes can modify the disposition of food in the stomach, producing satiety. Within this context, the ability of carbonated beverages to affect the feeling of satiation needs to be further explored; indeed, it could be a useful method to limit food intake; on the other hand, a chemical effect related to carbon dioxide determines a slight increase in hydrochloric acid, which could influence positively the digestive process or worsen an acid related disease.

Finally, an intriguing aspect is the role of carbon dioxide in sending gustatory signals to the central nervous system. The exploration of this matter could provide further insight into our understanding of the relationship between gustatory stimulation by carbon dioxide, modifications of stomach physiology, and gastrointestinal perception.

In conclusion there is now sufficient scientific evidence to understand the physiological impact of carbonated beverages on the gastrointestinal system, while providing a basis for further investigation on the related pathophysiological aspects. However, more studies are needed, particularly intervention trials, to support any claim on the possible beneficial effects of carbonated beverages on the gastrointestinal system, and clarify how they affect digestion. More

Please cite this article in press as: Cuomo R, et al., Carbonated beverages and gastrointestinal system: Between myth and reality, Nutr Metab Cardiovasc Dis (2009), doi:10.1016/j.numecd.2009.03.020

epidemiological and mechanistic studies are also needed to evaluate the possible drawbacks of their consumption in terms of risk of tooth erosion and gastric distress.

References

[1] Riley JJ. Scientific and medical origin of carbonated waters. Washington DC: American Bottlers of Carbonated Beverages; 1948.
[2] Reda A, Pattison J. The Global Carbonates report 2007. England: Canadean Ltd, www.candean.com.
[3] Malik VS, Schulze MB, Hu FB. Intake of sugar-sweetened beverages and weight gain: a systematic review. Am J Clin Nutr 2006 Aug;84(2):274—88.
[4] LaRowe TL, Moeller SM, Adams AK. Beverage patterns, diet quality, and body mass index of US preschool and school-aged children. J Am Diet Assoc 2007 Jul;107(7):1124—33.
[5] Tucker KL, Morita K, Qiao N, Hannan MT, Cupples LA, Kiel DP. Colas, but not other carbonated beverages, are associated with low bone mineral density in older women: the Framingham Osteoporosis Study. Am J Clin Nutr 2006 Oct;84(4):936—42.
[6] Mendel RW, Hofheins JE. Metabolic responses to the acute ingestion of two commercially available carbonated beverages: a pilot study. J Int Soc Sports Nutr 2007 Sep;14(4):7.
[7] Cuomo R, Grasso R, Sarnelli G, Capuano G, Nicolai E, Nardone G, et al. Effects of carbonated water on functional dyspepsia and constipation. Eur J Gastroenterol Hepatol 2002 Sep;14(9):991—9.
[8] Storey ML, Forshee RA, Anderson PA. Beverage consumption in the US population. J Am Diet Assoc 2006 Dec;106(12):1992—2000.
[9] Schulze MB, Manson JE, Ludwig DS, Colditz GA, Stampfer MJ, Willett WC, et al. Sugar-sweetened beverages, weight gain, and incidence of type 2 diabetes in young and middle-aged women. JAMA 2004 Aug 25;292(8):927—34.
[10] Cunningham MA, Marshall TA. Effectiveness of carbonated beverage education on dental students' knowledge and behavioral intent. J Dent Educ 2003 Sep;67(9):1011—5.
[11] Weizman Z. Cola drinks and rehydration in acute diarrhea. N Engl J Med 1986 Sep 18;315(12):768.
[12] Saldana TM, Basso O, Darden R, Sandler DP. Carbonated beverages and chronic kidney disease. Epidemiology 2007 Jul;18(4):501—6.
[13] Meyerovitch J, Ben Ami T, Rozenman J, Barzilay Z. Pneumatic rupture of the esophagus caused by carbonated drinks. Pediatr Radiol 1988;18(6):468—70.
[14] Karanjia ND, Rees M. The use of Coca-Cola in the management of bolus obstruction in benign oesophageal stricture. Ann R Coll Surg Engl 1993 Mar;75(2):94—5.
[15] Ibiebele TI, Hughes MC, O'Rourke P, Webb PM, Whiteman DC. Australian Cancer Study. Cancers of the esophagus and carbonated beverage consumption: a population-based case-control study. Cancer Causes Control 2008 Aug;19(6):577—84.
[16] Jensdottir T, Arnadottir IB, Thorsdottir I, Bardow A, Gudmundsson K, Theodors A, et al. Relationship between dental erosion, soft drink consumption, and gastroesophageal reflux among Icelanders. Clin Oral Investig 2004 Jun;8(2):91—6.
[17] Mack TM, Yu MC, Hanisch R, Henderson BE. Pancreas cancer and smoking, beverage consumption, and past medical history. J Natl Cancer Inst 1986 Jan;76(1):49—60.
[18] Feldman M, Barnett C. Relationships between the acidity and osmolality of popular beverages and reported postprandial heartburn. Gastroenterology 1995 Jan;108(1):125—31.
[19] Nelson LD, Cox MM, editors. Lehninger principles of biochemistry. Freman WH Publisher; 2008.
[20] Select committee on GRAS Substances. Evaluation of the health aspects of carbonates and bicarbonates as food ingredients (SCOGS-26). Bethesda: Life Sciences Research Office, Federation of America Societes for Experimental Biology; 1975.
[21] Verhagen JV, Engelen L. The neurocognitive bases of human multimodal food perception: sensory integration. Neurosci Biobehav Rev 2006;30(5):613—50.
[22] Sørensen LB, Møller P, Flint A, Martens M, Raben A. Effect of sensory perception of foods on appetite and food intake: a review of studies on humans. Int J Obes Relat Metab Disord 2003 Oct;27(10):1152—66.
[23] Kappes SM, Schmidt SJ, Lee SY. Relationship between physical properties and sensory attributes of carbonated beverages. J Food Sci 2007;72(1):S001—11.
[24] Meyer S, Riha WE. Optimizing sweetener blends for low-calorie beverages. Food Technol 2002;56:42—5.
[25] Ashurst PR. The chemistry and technology of soft drinks and fruit juices. Boca Raton, Fla: Sheffield Academic Press; 1998. p. 258.
[26] Shinozaki K, Shimizu Y, Shiina T, Morita H, Takewaki T. Relationship between taste-induced physiological reflexes and temperature of sweet taste. Physiol Behav 2008 Mar 18;93(4—5):1000—4.
[27] French SJ, Cecil JE. Oral, gastric and intestinal influences on human feeding. Physiol Behav 2001 Nov—Dec;74(4—5):729—34.
[28] Lavin JH, French SJ, Ruxton CH, Read NW. An investigation of the role of oro-sensory stimulation in sugar satiety? Int J Obes Relat Metab Disord 2002 Mar;26(3):384—8.
[29] Mattes RD. Physiologic responses to sensory stimulation by food: nutritional implications. J Am Diet Assoc 1997 Apr;97(4):406—13.
[30] Putnam RW, Filosa JA, Ritucci NA. Cellular mechanisms involved in CO(2) and acid signaling in chemosensitive neurons. Am J Physiol Cell Physiol 2004 Dec;287(6):C1493—526.
[31] Simons CT, Dessirier JM, Carstens MI, O'Mahony M, Carstens E. Neurobiological and psychophysical mechanisms underlying the oral sensation produced by carbonated water. J Neurosci 1999 Sep 15;19(18):8134—44.
[32] Fischler W, Kong P, Marella S, Scott K. The detection of carbonation by the Drosophila gustatory system. Nature 2007 Aug 30;448(7157):1054—7.
[33] Kitchens M, Owens BM. Effect of carbonated beverages, coffee, sports and high energy drinks, and bottled water on the in vitro erosion characteristics of dental enamel. J Clin Pediatr Dent 2007 Spring;31(3):153—9.
[34] Sohn W, Burt BA, Sowers MR. Carbonated soft drinks and dental caries in the primary dentition. J Dent Res 2006 Mar;85(3):262—6.
[35] Tahmassebi JF, Duggal MS, Malik-Kotru G, Curzon ME. Soft drinks and dental health: a review of the current literature. J Dent 2006 Jan;34(1):2—11.
[36] Sánchez GA, Fernandez De Preliasco MV. Salivary pH changes during soft drinks consumption in children. Int J Paediatr Dent 2003 Jul;13(4):251—7.
[37] Meining A, Classen M. The role of diet and lifestyle measures in the pathogenesis and treatment of gastroesophageal reflux disease. Am J Gastroenterol 2000;95:2692—7.
[38] Fass R, Quan SF, O'Connor GT, Ervin A, Iber C. Predictors of heartburn during sleep in a large prospective cohort study. Chest 2005;127:1658—66.
[39] Hamoui N, Lord RV, Hagen JA, Theisen J, Demeester TR, Crookes PF. Response of the lower esophageal sphincter to gastric distention by carbonated beverages. J Gastrointest Surg 2006 Jun;10(6):870—7.
[40] Cuomo R, Savarese MF, Sarnelli G, Vollono G, Rocco A, Coccoli P, et al. Sweetened carbonated drinks do not alter

upper digestive tract physiology in healthy subjects. Neurogastroenterol Motil 2008 Jul;20(7):780—9.
[41] Oliveria SA, Christos PJ, Talley NJ, Dannenberg AJ. Heartburn risk factors, knowledge, and prevention strategies: a population-based survey of individuals with heartburn. Arch Intern Med 1999 Jul 26;159(14):1592—8.
[42] Lagergren J, Viklund P, Jansson C. Carbonated soft drinks and risk of esophageal adenocarcinoma: a population-based case-control study. J Natl Cancer Inst 2006 Aug 16;98:1158—61.
[43] Mayne ST, Risch HA, Dubrow R, Chow WH, Gammon MD, Vaughan TL, et al. Carbonated soft drink consumption and risk of esophageal adenocarcinoma. J Natl Cancer Inst 2006 Jan 4; 98(1):72—5.
[44] Straathof JW, Ringers J, Lamers CB, Masclee AA. Provocation of transient lower esophageal sphincter relaxations by gastric distension with air. Am J Gastroenterol 2001;96(8):2317—23.
[45] Dickson WH, Wilson MJ. The control of motility of the human stomach by drugs and other means. J Pharmacol Exp Ther 1924;24:33.
[46] Dickson WH, Wilson MJ. Further observations on the motility of the human stomach. J Pharmacol Exp Ther 1928;34:65.
[47] Van Liere EJ, Sleeth CK. The emptying time of the normal human stomach as influenced by acid and alkali with a review of literature. Am J Dig Dis 1940;7:118.
[48] Carlson AJ. Contributions to the physiology of the stomach. Am J Physiol 1913;32:245.
[49] Hellebrandt FA, Houtz SJ. The influence on naturally carbonated mineral water on gastric motility and the secretion of hydrochloric acid. Arch Phys Med 1950;31:25.
[50] Zachwieja JJ, Costill DL, Beard GC, Robergs RA, Pascoe DD, Anderson DE. The effects of a carbonated carbohydrate drink on gastric emptying, gastrointestinal distress, and exercise performance. Int J Sport Nutr 1992;2:239—50.
[51] Pouderoux P, Friedman N, Shirazi P, Ringelstein JG, Keshavarzian A. Effect of carbonated water on gastric emptying and intragastric meal distribution. Dig Dis Sci 1997; 42:34—9.
[52] Hickey MS, Costill DL, Trappe SW. Drinking behavior and exercise-thermal stress: role of drink carbonation. Int J Sport Nutr 1994; 4(1):8—21.
[53] Lambert GP, Bleiler TL, Chang RT, Johnson AK, Gisolfi CV. Effects of carbonated and noncarbonated beverages at specific intervals during treadmill running in the heat. Int J Sport Nutr 1993;3(2): 177—93.
[54] Ploutz-Snyder Lori, Foley Jeanne, Ploutz-Snyder Robert, Kanaley Jill, Sagendorf Kenneth, Meyer Ronald. Gastric gas and fluid emptying assessed by magnetic resonance imaging. Eur J Appl Physiol 1999;79:212—20.
[55] Almiron-Roig E, Drewnowski A. Hunger, thirst, and energy intakes following consumption of caloric beverages. Physiol Behav 2003;79(4—5):767—73.
[56] Jacobs MN. The production of intracellular acidity by neutral and alkaline solutions containing carbon dioxide. Am J Physiol 1920;53:457.
[57] Kurtz LD, Clark BB. The inverse relationship of the secretion of hydrochloric acid to the tension of carbon dioxide in the stomach. Gastroenterology 1947;9:594.
[58] McIver MA, Redfield AC, Benedict EB. Gaseous exchange between the blood and the lumen of stomach and intestines. Am J Physiol 1926;76:92.
[59] Karel K. Gastric absorption. Physiol Rev 1948;28:433.
[60] Lolli G, Smith R. Effervescent mixture as adiuvants to rapid absorption of ingested drugs. N Engl J Med 1946;235:80.
[61] Tomlin J, Lowis C, Read NW. Investigation of normal flatus production in healthy volunteers. Gut 1991 Jun;32(6):665—9.
[62] Admiral J. Gas absorption in the intestine. Arch Neerland Physiol 1943;27:77.
[63] Loeper M, Mougeot A. Do spring waters containing carbon dioxide and hydrogen carbonates activate amylases? Compt Rend Soc Biol 1925;92:569.

Please cite this article in press as: Cuomo R, et al., Carbonated beverages and gastrointestinal system: Between myth and reality, Nutr Metab Cardiovasc Dis (2009), doi:10.1016/j.numecd.2009.03.020