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Intestinal Gas Capsules: A Proof-of-Concept Demonstration

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Production of certain gases and their relative concentrations affect gut function, may have pathogenic roles in several gastrointestinal (GI) disorders, and can, therefore, be useful as biomarkers for specific diseases.[1] Under normal gut conditions, the most prevalent gases include CH_4, CO_2, H_2, H_2S, and NO.[1,2] One of the major difficulties in understanding their physiology and functional capacity is the lack of direct access, because sampling through insertion of tubes into mouth or anus is inconvenient and invasive.[2] We have previously introduced the concept of swallowable gas capsules,[2] which can be readily made with standards acceptable for evaluation in animal and human subjects, in a similar fashion to camera and pH capsule counterparts.[3,4] The first stages for deploying of such capsules include the demonstration of their safe performance and benchmarking. Herein, we report an indigestible, noninvasive, swallowable gas capsule to perform in vivo gas measurements along the GI tract of a pig model system on low-fiber and high-fiber diets. Ethics approval was received from the Faculty of Veterinary Science at the Melbourne University (ID 1312821).

Description of Technology

The capsules were designed and fabricated at RMIT University. They are made of an indigestible cladding, gas-permeable membrane, $H_2/CH_4/CO_2$ gas sensor, microcontroller, wireless transmitter (433 MHz) and silver oxide battery (Figure 1*A*–*C*). A custom-made receiver decodes, stores, and displays the gas profiles in time. Data are transmitted every 5 minutes. The capsules were tested on pigs under high-fiber (2 pigs) and low-fiber diets (2 pigs).

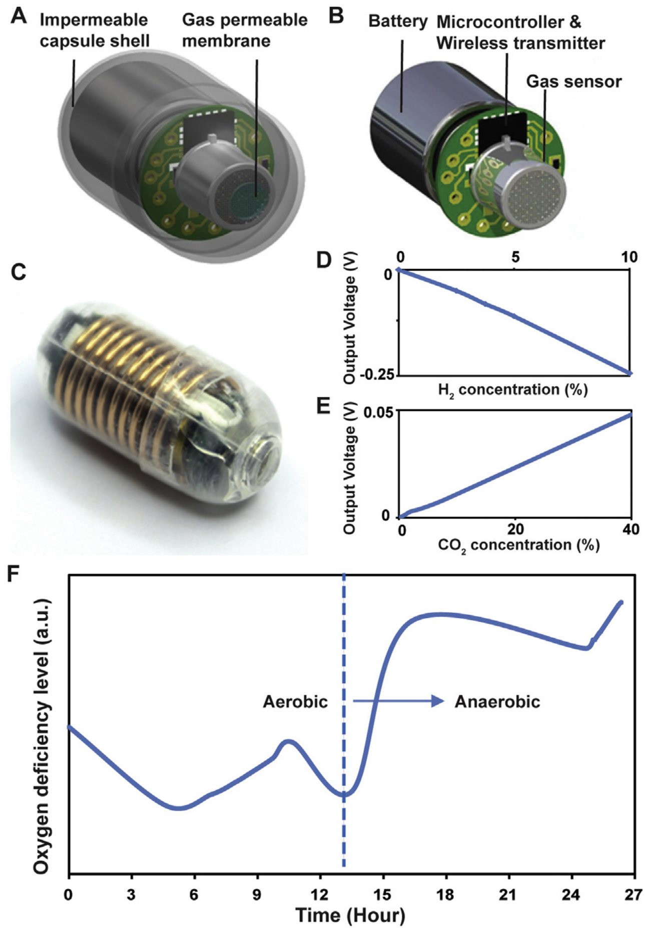

Figure 1. (*A*, *B*) Schematic of capsules with and without cladding. (*C*) Capsule photo. (*D*, *E*) Gas sensor characteristics. (*F*) Output of an oxygen sensitive test capsule.

Abbreviations used in this paper: **GI, gastrointestinal.**

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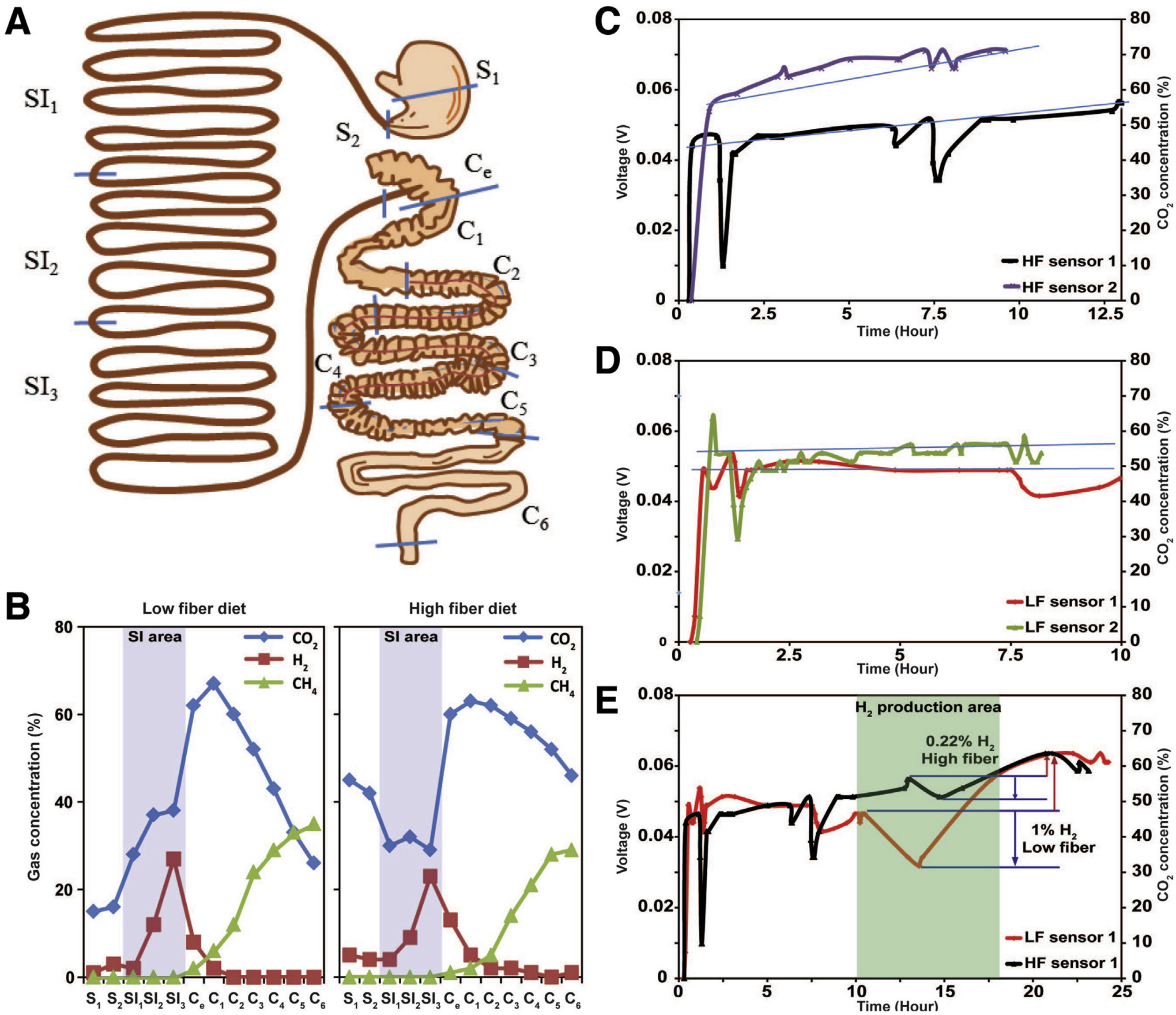

Figure 2. (*A*) Sampling sites. C, colon; Ce, cecum; S, stomach; SI, small intestine. (*B*) Concentration of gases from various regions of the gastrointestinal (GI) tract of pigs on low-fiber (LF) and high-fiber (HF) diets. Adopted from ref 5 with permission. (*C*, *D*) CO_2 concentration and their trend lines for pigs on HF and LF diets. (*E*) Response of 2 capsules on HF and LF diets.

Video Description

Benchmarking

The gas capsules' operation was benchmarked against classical measurements in pigs fed with high- and low-fiber diets, by Jensen and Jørgensen in 1994.[5] They described a virtual absence of CH_4 in the stomach and small intestine (Figure 2*A*, *B*). The highest concentration for H_2 was found in the ileum. From respiration chamber measurements, CO_2 production per day for the pigs on the high-fiber diet was significantly higher than those on the low-fiber diet (212 and 46 L/d for each pig, respectively).

Our Measurements

Initial tests with an oxygen-sensitive sensor illustrated that the transition of the capsule from aerobic to anaerobic environment occurred at 10-14 hours (Figure 1*F*). In the benchmarking experiments, this represented the ileum in the pig. Four capsules with sensors of characteristics shown in Figure 1 subsequently were gavaged in pigs (2 high-fiber, 2 low-fiber): 2 stopped transmitting information after nearly 10 hours and 2 after 25 hours. Four observations were made (Figure 2*C*–*E*). (1) After each feeding, large declines in responses were observed. Such declines probably reflected excess air entering the GI tract in response to feeding. This phenomenon disappeared in <2 hours. Water consumption did not affect the measurements. (2) As expected, pigs on high-fiber diet showed CO_2 increasing in concentration (Figure 2*C*), whereas those on a low-fiber diet did not show any discernible change from the baseline (Figure 2*D*), as described in the benchmarking experiments.[5] (3) Troughs at 13 hours (low fiber) and 14.5

hours (high fiber) were seen in the 2 measurements that exceeded 20 hours (Figure 2*E*). If the transition characteristics of these capsules were similar to the initial test (Figure 1*F*), it was most likely that they reached the anaerobic regions of the GI tract where active fermentation of the added fiber was occurring. In the benchmarking data, increased relative amounts of H_2 were documented, particularly in association with the low-fiber diet where it was 4-fold greater.[5] This would reduce the measured % CO_2. Although the H_2 concentrations were much lower in the current study (1% for low fiber and 0.22% for high fiber) compared with those reported by Jensen and Jørgensen in post mortem pigs,[5] the ratio (9/2) was almost identical to their in vitro measurements. (4) Reaching the 18-hour mark, all capsules entered an area where the percentages of CO_2 from the 2 pigs were again similar, likely to represent exhaustion of fermentation of the added dietary fiber.[6]

Take Home Message

We demonstrated successful operation of gas capsules using a pig model on low- and high-fiber diets with similar CO_2 and H_2 profiles to those from the classical work of Jensen and Jørgensen.[5] These novel capsules potentially provide a noninvasive and economical assessment method for a range of putative gas biomarkers important for the future of GI research, and for point-of-care and clinical assessments. Issues yet to be addressed include (1) enhancing capsule durability and reliability, (2) preventing capsule retention by high-quality manufacturing, reducing size, and improving hydrodynamics, (3) inclusion of >1 gas and vapor sensor for multigas measurements, (4) better defining the anatomic position of the capsules (eg, by incorporating pH or oxygen sensors), (5) exploring relationships between intestinal gas constituents, gut microorganisms, and health, and (6) establishment of libraries based on health status and gas constituents.

Supplementary Material

Note: To access the supplementary material accompanying this article, visit the online version of *Gastroenterology* at www.gastrojournal.org, and at http://dx.doi.org/10.1053/j.gastro.2015.07.072.

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Conflicts of interest
The authors disclose no conflicts.

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