(12) UK Patent (19) GB (11) 2554444 (13) B

(45) Date of B Publication 13.10.2021

(54) Title of the Invention: A device for sampling gastro-intestinal material

(51) INT CL: ***A61B 10/00*** (2006.01)

(21) Application No: **1616464.2**

(22) Date of Filing: **28.09.2016**

(43) Date of A Publication **04.04.2018**

(56) Documents Cited:
WO 2014/140334 A1
WO 2002/102243 A1
US 20030017195 A1
WO 2006/026504 A2
US 4481952 A

(58) Field of Search:
As for published application 2554444 A viz:
INT CL **A61B**
Other: **EPODOC, WPI and TXTA**
updated as appropriate

Additional Fields
Other: **None**

(72) Inventor(s):
Samuel Rees
Luke Ashton
Chris Iveson
Agnieszka Chomka
Soren Thomsen
Natasha Hui Jin NG
Patrick Albers
Matthias Thurner
Rasmus Aarup Poulsen

(73) Proprietor(s):
BioMe Oxford Limited
4 Hadow Road, Marston, Oxford, Oxfordshire, OX3 0JW, United Kingdom

(74) Agent and/or Address for Service:
J A Kemp LLP
Gray's Inn, 14 South Square, Holborn, LONDON, WC1R 5JJ, United Kingdom

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Fig. 1

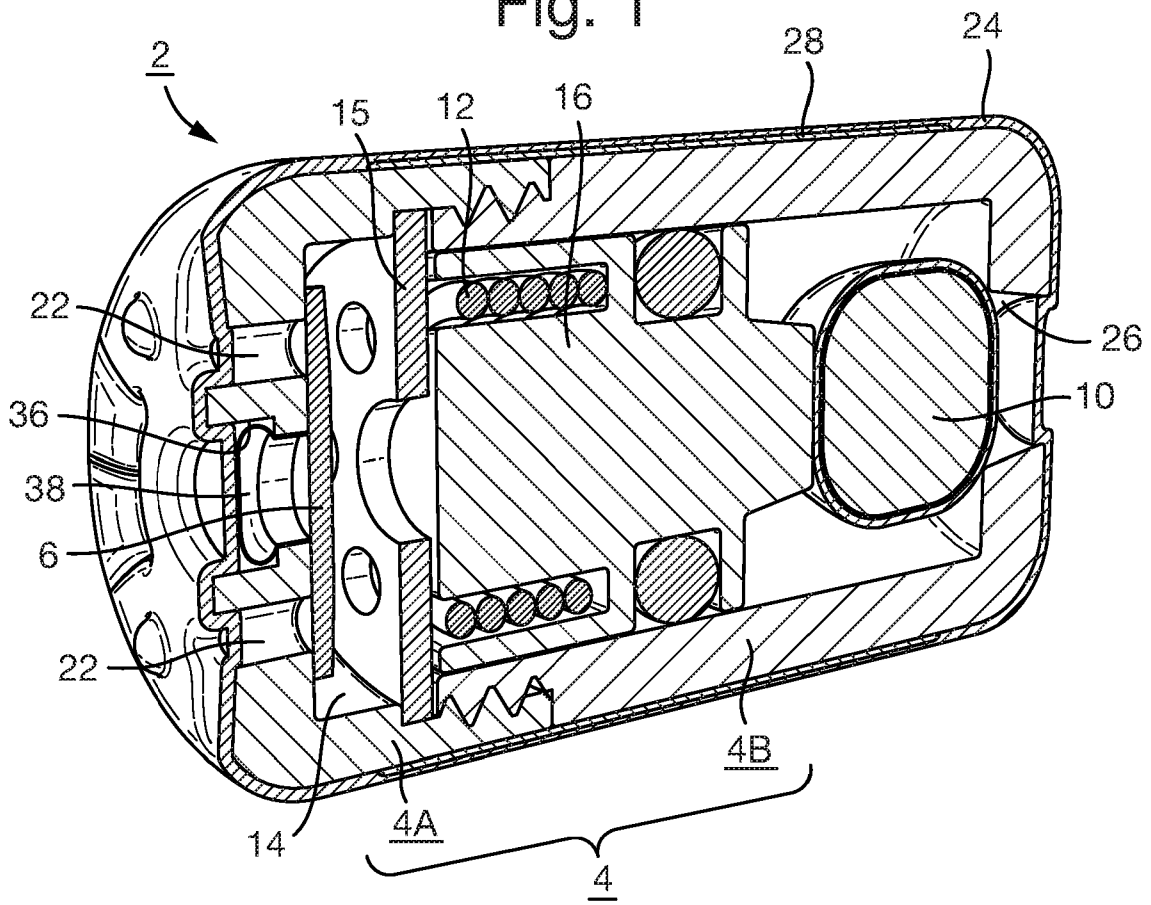
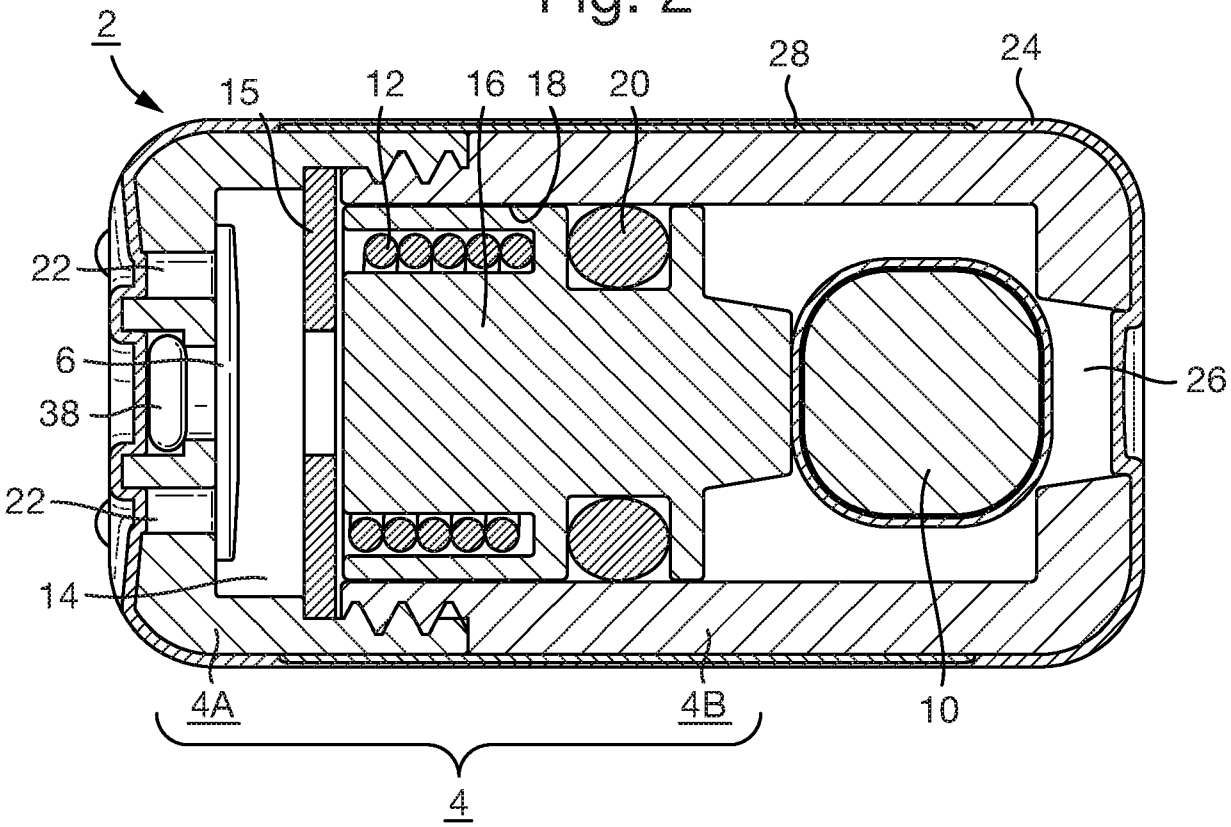


Fig. 2



12 12 17

Fig. 3

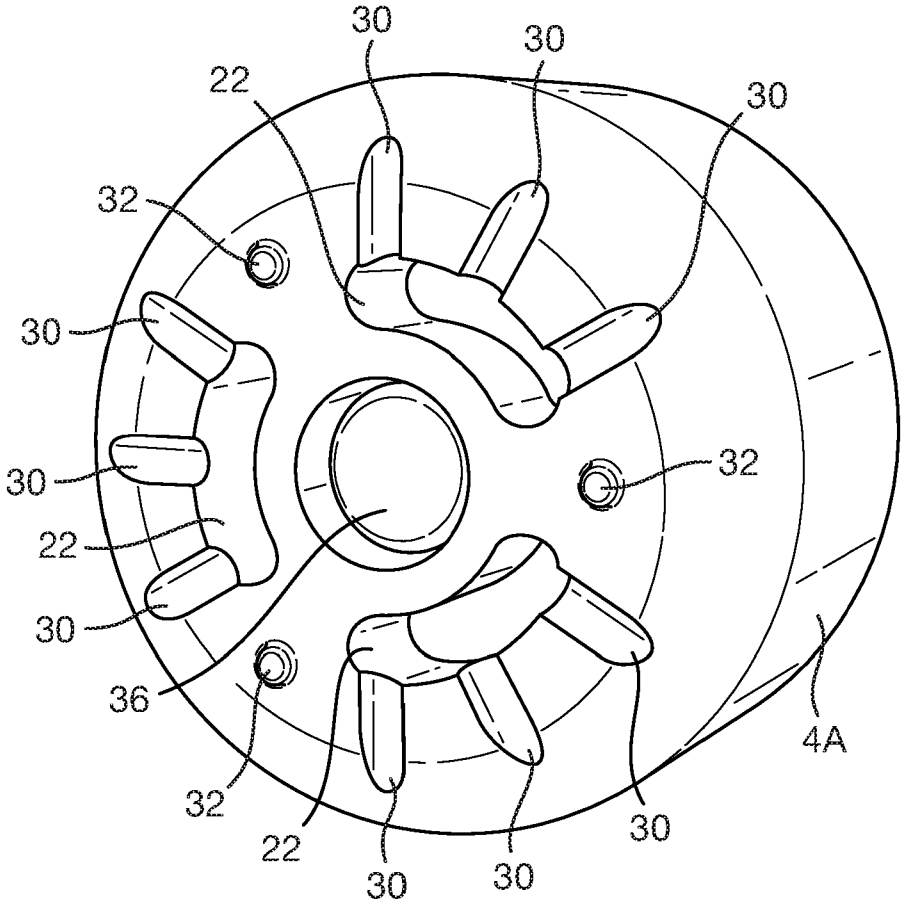


Fig. 4

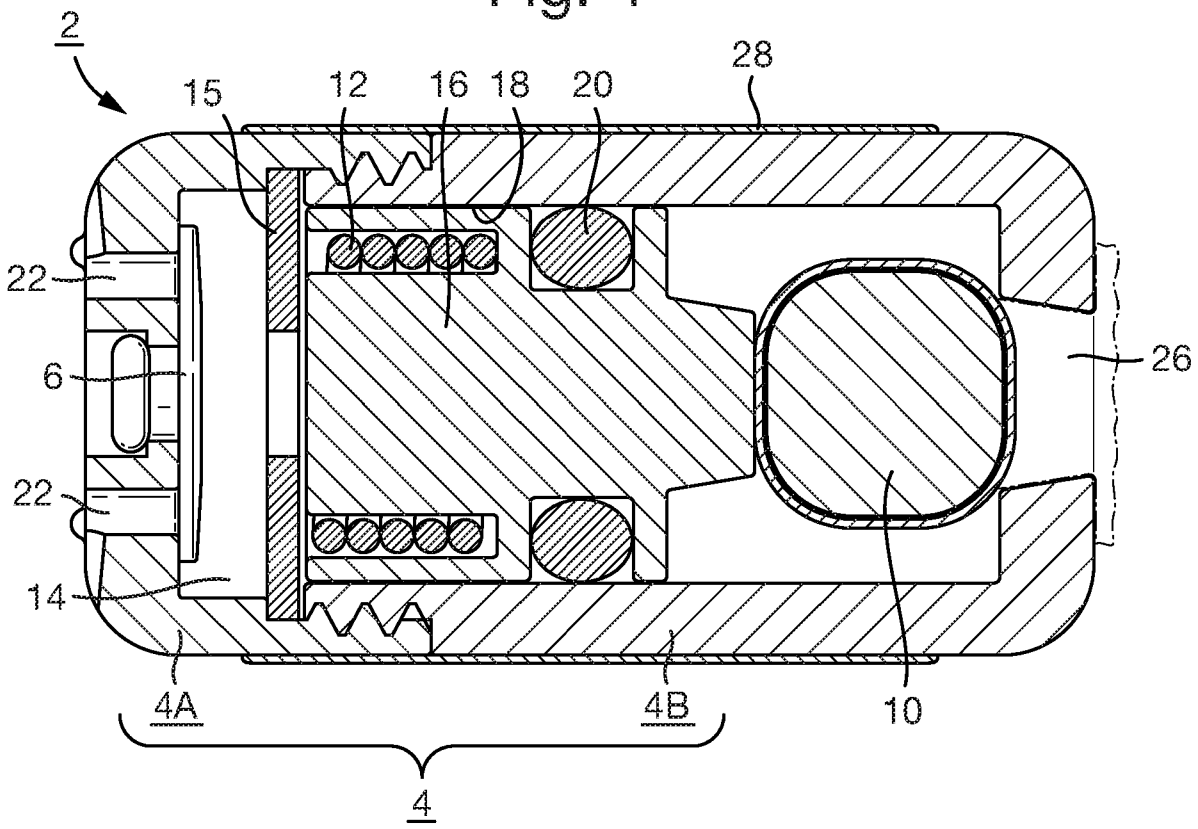
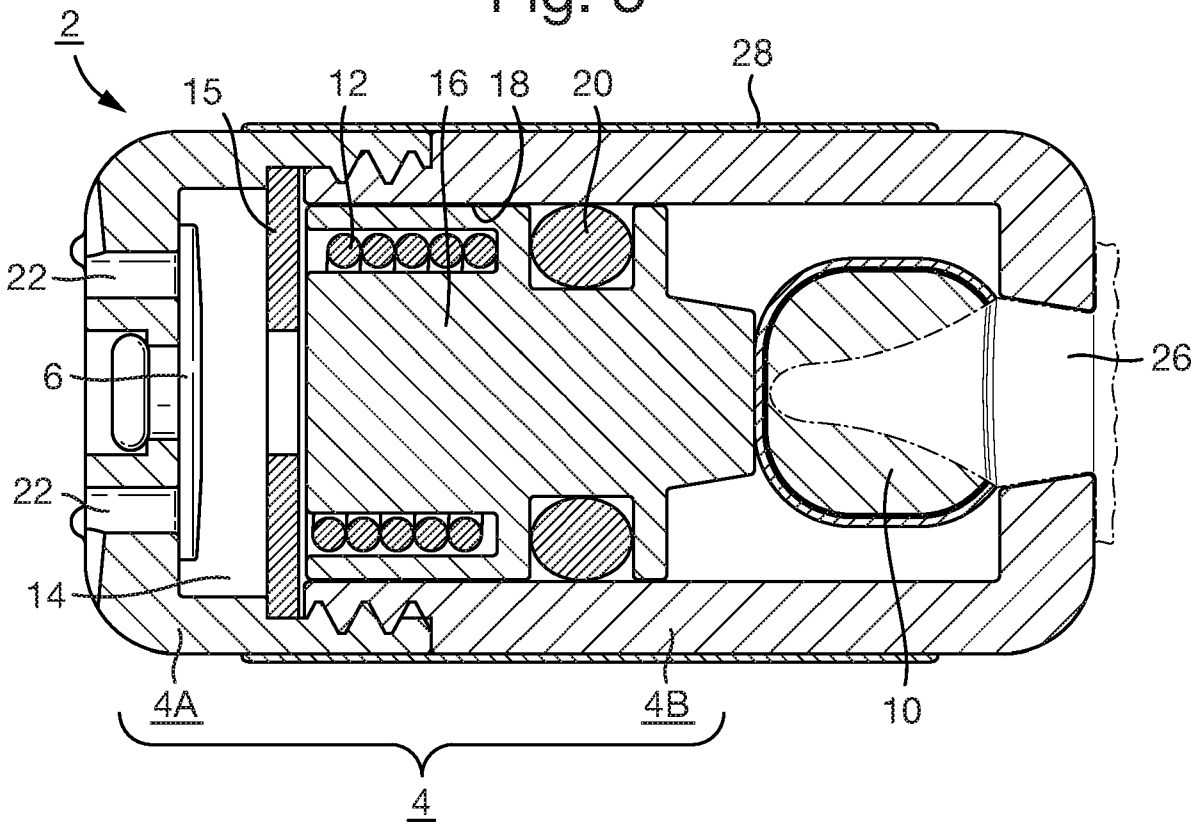


Fig. 5



12 12 17

Fig. 6

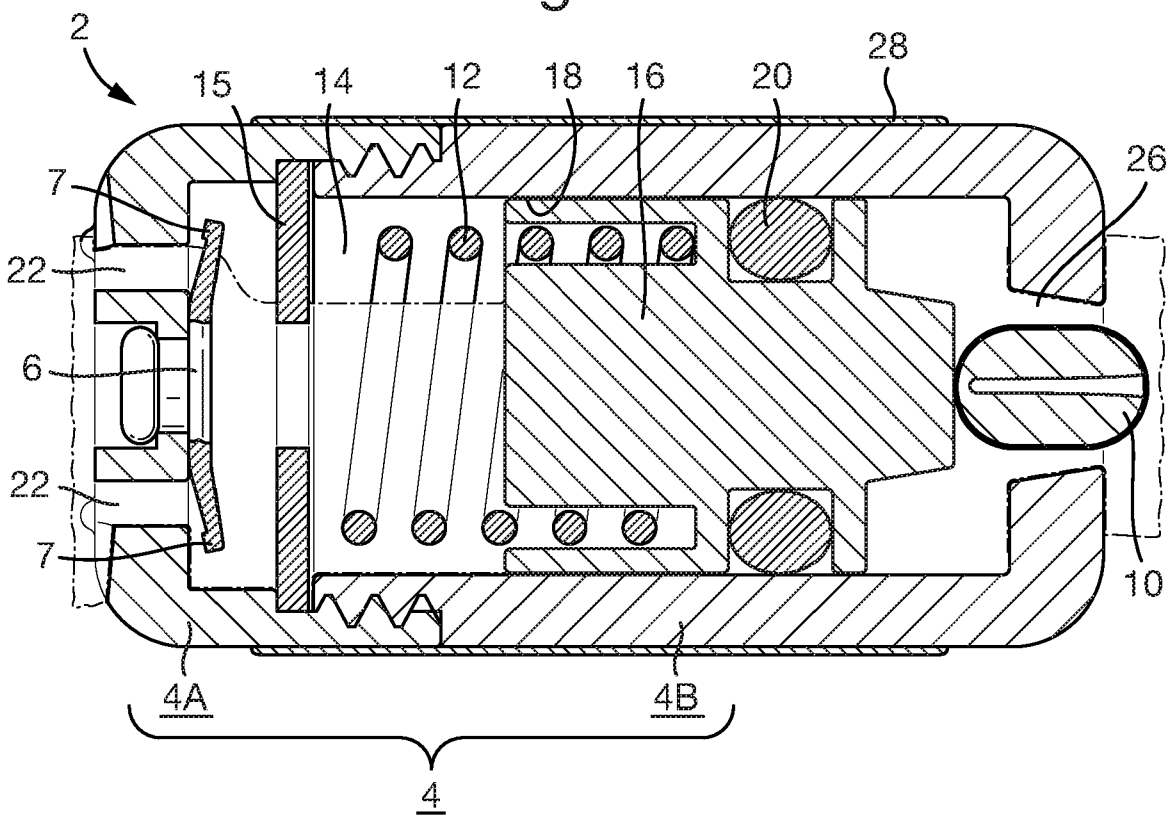
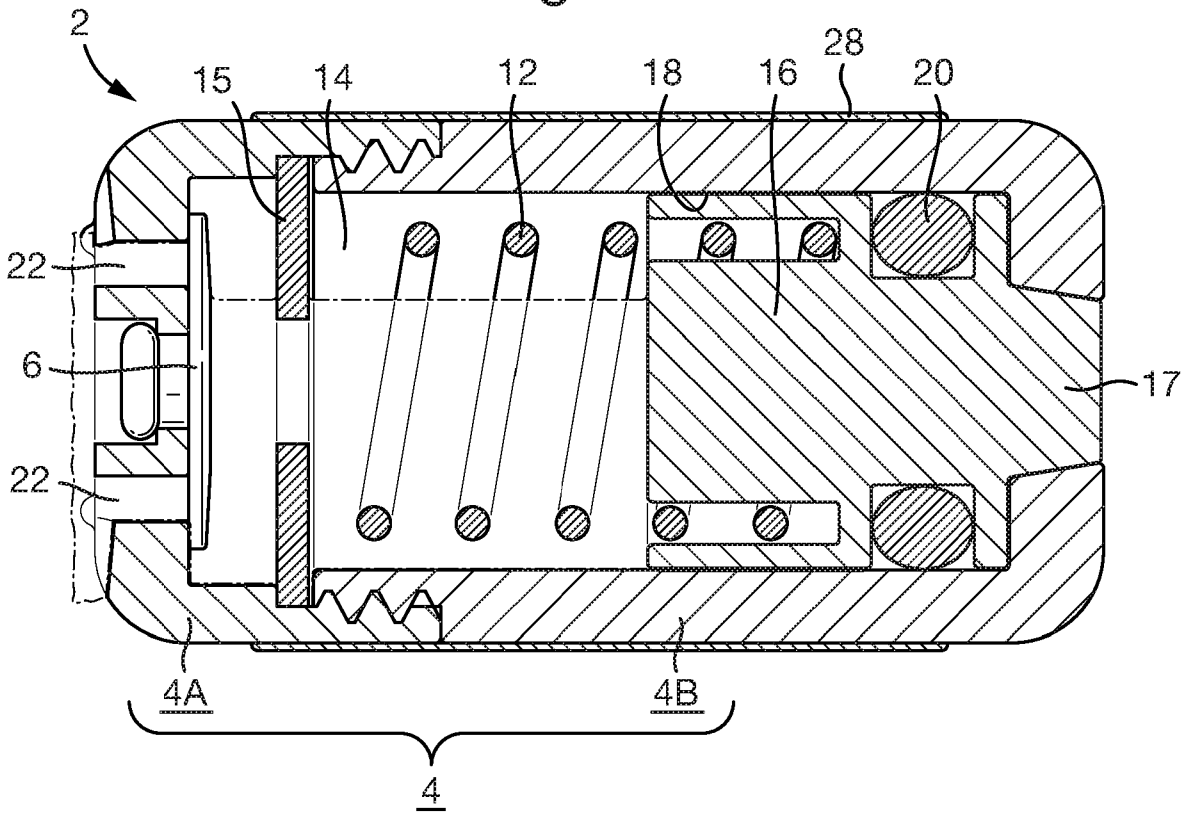


Fig. 7



12 12 17

A DEVICE FOR SAMPLING GASTRO-INTESTINAL MATERIAL

The invention relates to a device for sampling gastro-intestinal material.

Valuable information about the health of a subject can be obtained by analysing gastro-intestinal material. It is proven challenging however to extract gastro-intestinal material in a reliable and cost-effective manner, and without contaminating or otherwise disrupting the extracted material relative to its native state within the gastro-intestinal tract.

A promising approach has been to provide an ingestible device which can be opened to extract material at an appropriate position within the gastro-intestinal tract. An example of such a device is disclosed in US 2015/0011874 A1. The device uses a motor coupled to a rotatable element to open and close an access port to a chamber within the ingestible device which can store a sample of the material to be extracted. Electrical sensors are provided for sensing properties of the environment around the device. Opening of the access port by the motor can be triggered in response to an output from the electrical sensors. Ingestible devices of this type are relatively costly and complex.

It is an object of the invention to provide a device for sampling of gastro-intestinal material which has high reliability and low cost.

According to an aspect, there is provided a device for sampling gastro-intestinal material, comprising: a capsule body having a sample input valve; a suction mechanism configured to generate a partial vacuum within the capsule body and thereby draw gastro-intestinal material into the capsule body through the sample input valve; and an actuator configured to actuate the suction mechanism, wherein: the actuator comprises a dissolvable element and is configured so that the dissolvable element dissolves in a predetermined region of the gastro-intestinal tract and the dissolving of the dissolvable element causes actuation of the suction mechanism.

Thus, a device is provided which can actuate using purely mechanical means and with no need for mechanical or other links to the environment outside of body. The actuation mechanism is mechanically simple due to the reliance on dissolution of a dissolvable element, facilitating high reliability and low cost. No electrical input or machinery is required, either for actuation or for sensing properties of the environment. This also facilitates low cost and high reliability, as well as reducing the risk of injury or discomfort which may be caused by electrical elements and/or heat generated thereby.

In an embodiment, the suction mechanism comprises a biasing member restrained by the dissolvable element prior to actuation of the suction mechanism; and the dissolving of the dissolvable element releases the biasing member.

This approach can be implemented particularly efficiently and reliably. The biasing member may be implemented using a spring for example. Springs are cheap and readily available in biocompatible materials.

In an embodiment, the sample input valve is configured to allow a pressure gradient driven passage

of material from the outside of the capsule body to the inside of the capsule body through one or more sample collection openings, and to seal the one or more sample collection openings in the absence of a pressure gradient; and an exterior surface of the capsule body is provided with one or more indented channels leading to one or more of the sample collection openings to reduce blocking of the one or more sample collection openings by tissue or material within the gastro-intestinal tract. The indented channels thereby improve reliability.

In an embodiment, one or more of the sample collection openings is non-circular. This reduces or prevents blocking of sample collection openings by tissue or material (e.g. food particles) with the gastro-intestinal tract, thereby improving reliability.

In an embodiment, the device further comprises one or more protruding members protruding outwards relative to an average level of an outer surface of the capsule body adjacent to the sample input valve, for reducing suction-based adhesion of the device to tissue or material within the gastro-intestinal tract. This reduces or prevents blocking of sample collection openings, thereby improving reliability.

In an embodiment, the device is coated with a muco-adhesive material configured to promote adhesion between the device and a lining of the intestinal wall when the muco-adhesive material contacts the lining of the intestinal wall. The adherence provided by the muco-adhesive material improves the stability of the device during the extraction of material into the device. In an embodiment, the muco-adhesive material is arranged on a portion of the outer surface of the device that is selected such that adhesion of the device to the lining of the intestinal wall is promoted in an orientation of the device which allows gastro-intestinal material to be drawn into the capsule body through the sample input valve. The orientation may be such that collection openings and actuator openings are not covered by any part of the lining of the intestinal wall when the device is adhered to the lining of the intestinal wall. Extraction of material by the device 2 can therefore be carried out with high reliability.

Embodiments of the invention will now be described, by way of example only, with reference to the accompanying drawings in which corresponding reference symbols represent corresponding parts, and in which:

Figure 1 is a perspective sectional view of a device for sampling gastro-intestinal material;

Figure 2 is a side sectional view of the device of Figure 1;

Figure 3 is a perspective view of a front sub-unit of the capsule body of the device of Figures 1 and 2, showing example indented channels and protruding members; and

Figures 4-7 are side sectional views of the device of Figures 1 and 2 at different stages of actuation.

In an embodiment, an example of which is depicted in Figures 1-7, there is provided a device 2 for sampling gastro-intestinal material. Gastro-intestinal material encompasses any material found naturally within the gastro-intestinal tract.

The device 2 comprises a capsule body 4 having a sample input valve 6. In an embodiment the

sample input valve 6 comprises a one-way valve. In an embodiment the sample input value 6 comprises an umbrella valve, but other valve types could be used instead (e.g. duckbill valve). In the embodiment shown, the capsule body 4 comprises a front sub-unit 4A and a rear sub-unit 4B that can be screwed together for ease of assembly. Other arrangements for connecting together front and rear sub-units are possible, including for example a snap fastening mechanism, a pressure fitting, a ratchet mechanism or adhesive. The overall shape and size of the capsule body 4 is designed to be suitable for a human patient to swallow safely, and preferably without significant discomfort. Edges can be smoothed (rounded) to improve comfort and reduce risk of injury. In the embodiment shown the capsule body 4 has a substantially cylindrical form to allow space for a bore 18 within which a movable element 16 can move longitudinally (see below) without the overall dimensions of the device 2 becoming too large. In an embodiment the device 2 has an overall length of between 10mm and 30mm, optionally between 10mm and 20mm, optionally between 14mm and 18mm, optionally about 16mm. In an embodiment the device 2 has a maximal diameter (perpendicular to the length direction) of between 6mm and 12mm, optionally between 6mm and 10mm, optionally between 7mm and 9mm, optionally about 8mm.

The sample input valve 6 is secured within the front sub-unit 4A by means of a bung 38 of the sample input valve 6 engaging within an opening 36 in the front sub-unit 4A.

The device 2 further comprises a suction mechanism capable of generating a partial vacuum within the capsule body 4 and thereby drawing gastro-intestinal material into the capsule body 4 through the sample input valve 6. An actuator is provided for actuating the suction mechanism. The actuator comprises a dissolvable element 10. The actuator is configured so that the dissolvable element 10 dissolves in a predetermined region of the gastro-intestinal tract and the dissolving of the dissolvable element 10 causes actuation of the suction mechanism.

In the embodiment shown, the suction mechanism comprises a biasing member 12 restrained by the dissolvable element 10 prior to actuation of the suction mechanism. In the embodiment shown the biasing member 12 comprises a spring, but other mechanisms are possible. In the case where a spring is used the inventors have found that a compression spring arrangement is more practical than a tension spring arrangement, as it makes better use of the small amount of space available. Springs are relatively cheap and readily available in biocompatible materials. Springs can also be provided in a suitably small size to fit within the device 2 while still providing the necessary forces to achieve actuation. The biasing member 12 presses against a support member 15 (having holes to allow material to flow through the support member 15) that is fixedly attached to the capsule body 4. The provision of the support member 15 prevents the biasing member 12 from pressing against, or otherwise interfering with, the sample input valve 6. The dissolving of the dissolvable element 10 releases the biasing member 12. The biasing member 12 expands a sample chamber 14 within the capsule body 4 on release of the biasing member 12 and thereby generates the partial vacuum within the capsule body 4. In the embodiment shown, the suction mechanism comprises a movable

element 16 engaged within a bore 18 via a sliding seal 20. The biasing member 12 expands the sample chamber 14 by driving movement of the movable element 16 within the bore 18.

In the embodiment shown the sliding seal 20 is implemented by means of an o-ring engaging outwardly against the bore 18. Various materials can be used for the o-ring, including for example nitrile (NBR), silicone, fluorocarbon (FKM), ethylene propylene (EPDM), isoprene rubber (IR), and thermoplastic (TP). It is desirable to provide a relatively small sliding seal force (i.e. force resisting movement in the sliding direction). Providing a relatively small sliding seal force means that the biasing member 12 can be configured to provide a smaller force. The risk of injury in the event of failure of the device is thereby reduced.

The sample input valve 6 is configured to allow a pressure gradient driven passage of material from the outside of the capsule body 4 to the inside of the capsule body 4 through sample collection openings 22, and to seal the sample collection openings 22 in the absence of a pressure gradient. Thus, when the partial vacuum is generated by the biasing member 12, the pressure gradient thereby generated opens the sample input valve 6 (see Figure 6) and allows material to be driven by the pressure gradient into the sample chamber 14 until the pressure gradient falls to a level which is no longer high enough to hold the sample input valve 6 open (see Figure 7). At this point the sample input valve 6 closes and the extracted material is sealed within the sample chamber 14 ready for removal and analysis at a later time.

In the embodiment shown, the capsule body 4 comprises an actuator opening 26 (more than one actuator opening may be provided in other embodiments) via which the gastro-intestinal material can contact the dissolvable element 10 and dissolve the dissolvable element 10 when the actuator opening 26 is unsealed. The actuator opening 26 is separated from the sample collection openings 22, thereby reducing or avoiding contamination of the material extracted into the sample chamber 14 by material originating from the dissolvable element 10. In the embodiment shown the risk of contamination is further reduced or avoided by providing the actuator opening 26 on an opposite side of the capsule body 4 to the sample collection openings.

In an embodiment the device 2 is configured to be taken orally. For example, the actuator is configured so that the dissolvable element 10 remains intact during transit from the mouth to the predetermined region at which it is desired to extract material, and dissolves in the predetermined region. This may be achieved by coating the device 2 and/or dissolvable element 10 in such a way that the device and/or dissolvable element 10 only become uncovered when the device 2 is in the predetermined region. Alternatively or additionally, the dissolvable element 10 may be configured such that it is resistant to material in the gastro-intestinal tract in all regions prior to the predetermined region at which it is desired to extract material but dissolves in material present in the predetermined region.

The device 2 is thus actuated based on selectively dissolving the dissolvable member 10 in the predetermined region (and not before). Various differences in the composition of material found in different

regions of the gastro-intestinal tract may be used as the basis for achieving the selective dissolving. For example, there is a large pH gradient between the stomach and the small intestine, which can be used to ensure actuation of the device 2 in the small intestine (or even in a specific region of the small intestine). Various different coatings are available commercially that dissolve at different pH levels and which would allow such targeting. The pH gradient is much smaller between the small intestine and the large intestine, which may favour use of non-pH based methods of achieving the selective dissolving. In one embodiment, a coating is used which is broken down by one or more enzymes which are found in the predetermined region of interest (e.g. the large intestine) and not in any earlier portion of the gastro-intestinal tract (e.g. section of the small intestine or stomach).

In the embodiment shown, the device 2 is entirely encapsulated by a sealing material 24 that is configured such that when the device is taken orally, the sealing material 24 will dissolve only when the device 2 reaches the predetermined region of the gastro-intestinal tract. It is not essential for the sealing material 24 to entirely encapsulate the device 2. In other embodiments the sealing material 24 may only partially encapsulate the device 2. For example, the sealing material 24 may cover (and thereby seal until it dissolves) the actuator opening 26 and not cover selected other regions of the outer surface of the device 2. Alternatively or additionally, the sealing material 24 may cover (and thereby seal until it dissolves) the sample collection openings 22. In an embodiment the sealing material 24 comprises an enteric coating. The sealing material 24 may be applied by spray coating, for example.

The dissolvable element 10 is formed from a material that is safe for consumption and does not significantly modify the gut microbiome (i.e. materials containing sugar or other materials which may be consumed by bacteria should be avoided). The dissolvable element 10 also needs to be dissolvable, at least in the material found in the predetermined region (optionally in other liquids where the dissolvable element 10 is coated). Various materials are suitable, including one or more of the following in any combination: hypromellose, polyvinylpyrrolidone, sodium carboxymethyl cellulose, and sodium starch glycolate. The dissolvable element 10 may be solid or hollow.

In an embodiment, the dissolvable element 10 comprises a first material coated with a second material. The first material may be fully encapsulated by the second material. The second material may be configured such that when the device 2 is taken orally, the second material will dissolve only when the device 2 reaches the predetermined region of the gastro-intestinal tract. The second material may comprise an enteric coating for example. The first material provides the necessary bulk for the dissolvable element 10 to mechanically restrain the biasing member 12, while the second material provides the selective dissolving functionality necessary to ensure that the device 2 actuates in the desired predetermined region of the gastro-intestinal tract.

Other coatings may be provided to the device 2 to improve functionality. For example, in an embodiment the device is coated with a muco-adhesive material 28 configured to promote adhesion between

the device 2 and a lining of the intestinal wall when the muco-adhesive material 28 contacts the lining of the intestinal wall. In the example shown in Figures 1 and 2 the muco-adhesive material 28 is covered initially by the sealing material 24 so that the muco-adhesive material 28 only becomes exposed (and thereby prone to adhering to the lining of the intestinal wall) in the predetermined region of the gastro-intestinal tract. The adherence provided by the muco-adhesive material 28 improves the stability of the device 2 during the extraction of material into the sample chamber 14. The adhesion is not strong enough to prevent the device 2 from being passed through the gastro-intestinal tract nor to risk any damage to the gastro-intestinal tract. Various materials, including for example polymers, lectins, and liposome-based formulations are known which provide the required functionality. Non-limiting examples developed for oral delivery include: chitosan, poly(acrylic acid), alginate, poly(methacrylic acid) and sodium carboxymethyl cellulose.

In the embodiment shown the muco-adhesive material is arranged on a portion of the outer surface of the device 2 that is selected such that adhesion of the device 2 to the lining of the intestinal wall is promoted in an orientation of the device 2 which allows gastro-intestinal material to be drawn into the capsule body through the sample input valve 6. The orientation may be such that both collection openings 22 and actuator openings 26 are not covered by any part of the lining of the intestinal wall when the device 2 is adhered to the lining of the intestinal wall. In the embodiment shown this is achieved by providing the muco-adhesive material on an outer lateral surface that is substantially perpendicular to the surface in which the sample collection openings 22 are provided and substantially perpendicular to the surface in which the actuator opening 26 is provided, but it will be appreciated that other arrangements are possible, depending on the particular geometry of the device 2 and the positioning of the collection openings 22 and actuator openings 26.

Various features may be provided to promote efficient extraction of material through the collection openings 22. An example configuration for a front sub-unit 4A of the capsule body 4, comprising examples of such features, is shown in Figure 3.

In an embodiment, as depicted in Figure 3, an exterior surface of the front sub-unit 4A is provided with indented channels 30. Each of the indented channels 30 leads to one of three sample collection openings 22 in this particular example. Other arrangements are possible (e.g. different numbers of sample collection openings and/or indented channels 30). The indented channels 30 are configured to reduce or prevent blocking of the sample collection openings 22 by tissue or material (e.g. food particles) within the gastro-intestinal tract.

In order to further reduce or prevent blocking of the sample collection openings 22, one or more of the sample collection openings 22 may be non-circular, for example elongate. In the embodiment shown, three such non-circular (and elongate) collection openings 22 are provided.

In an embodiment, as depicted in Figure 3, one or more protruding members 32 are provided. The protruding members 32 protrude outwards relative to an average level of an outer surface of the capsule body

4 adjacent to the sample input valve 6 (and collection openings 22). The protruding members 32 are configured to reducing suction-based adhesion of the device 2 to tissue or material within the gastro-intestinal tract. The protruding members 32 prevent any large substantially planar surface being available that could otherwise become attached via suction-based adhesion to tissue or material within the gastro-intestinal tract, thereby potentially blocking (partially or completely) one or more of the collection openings 22. The protruding members 32 effectively allow the device 2 to stand away from the intestinal wall and allow fluid to flow in between (preventing the build up of any vacuum).

Figures 4-7 illustrate operation of the embodiment described above with reference to Figures 1-3.

Figure 4 depicts the device 2 after it has reached the predetermined region in the gastro-intestinal tract and the sealing material 24 (shown in Figures 1 and 2) has dissolved away. For example, the sealing material 24 may comprise an enteric coating that protects the device 2 from the acidic environment in the stomach until it passes through into the small intestine. Once in the small intestine the pH levels rise due to the introduction of bile and sodium carbonate. This causes the sealing material 24 to dissolve. The dissolving of the sealing material 24 exposes the collection openings 22, the muco-adhesive material 28 and the dissolvable element 10 to material at the predetermined region in the gastro-intestinal tract.

Figure 5 depicts the device 2 at a subsequent time when the dissolvable element 10 has started to dissolve. The dissolvable element 10 is shaped so that the dissolution occurs at the desired rate and achieves the desired aim of actuating the device 2.

Figure 6 depicts the device 2 at a subsequent time when the shape of the dissolvable element 10 has changed due to the dissolution (e.g. partially collapsed) in such a way that the biasing member 12 is released. The released biasing member 12 pushes the movable element 16 to the right in the orientation of the figure. The sample chamber 14 is expanded. The expansion generates a partial vacuum in the sample chamber 14. The partial vacuum provides a pressure gradient between the outside of the device 2 and the sample chamber 14. The pressure gradient forces open the sample input valve 6 (depicted in Figure 6 by the pulling back of the peripheral edges 7 of the sample input valve 6). Opening of the sample input valve 6 allows material to be driven by the pressure gradient into the sample chamber 14.

Figure 7 depicts the device 2 after the actuation process is complete. The movable element 16 has been pushed all the way to the extreme end of its travel, sealing the actuator opening 26 via a portion 17 having a form complementary to the form of the actuator opening 26. The pressure difference between the sample chamber 14 and the outside of the device 2 is now low enough that the sample input valve 6 is closed. The sample chamber 14 is filled with material extracted from the predetermined region of the gastro-intestinal tract, as desired, and sealed, ready for removal and analysis at a later time.

In an embodiment the sample chamber 14 may be pre-filled (optionally partially) with a substance (e.g. a preservative), which acts in a desirable way on material that has been extracted into the sample chamber 14 during the time between extraction from the gastro-intestinal tract and removal for analysis at a

later time (e.g. preventing or reducing degradation of the extracted material).

CLAIMS

1. A device for sampling gastro-intestinal material, comprising:

a capsule body having a sample input valve;

a suction mechanism configured to generate a partial vacuum within the capsule body and thereby draw gastro-intestinal material into the capsule body through the sample input valve; and

an actuator configured to actuate the suction mechanism, wherein:

the actuator comprises a dissolvable element and is configured so that the dissolvable element dissolves in a predetermined region of the gastro-intestinal tract and the dissolving of the dissolvable element causes actuation of the suction mechanism;

the suction mechanism comprises a biasing member restrained by the dissolvable element prior to actuation of the suction mechanism;

the dissolving of the dissolvable element releases the biasing member; and

the biasing member is configured to expand a sample chamber within the capsule body, without any change to the outer shape and size of the capsule body, on release of the biasing member and thereby generate the partial vacuum within the capsule body.

2. The device of claim 1, wherein the device is configured to be taken orally.

3. The device of claim 2, wherein the actuator is configured so that the dissolvable element remains intact during transit from the mouth to the predetermined region and dissolves in the predetermined region.

4. The device of any preceding claim, wherein the suction mechanism comprises a movable element engaged within a bore via a sliding seal, and the biasing member is configured to expand the sample chamber by driving movement of the movable element within the bore.

5. The device of any preceding claim, wherein the biasing member comprises a spring.

6. The device of any preceding claim, wherein the device is coated with a muco-adhesive material configured to promote adhesion between the device and a lining of the intestinal wall when the muco-adhesive material contacts the lining of the intestinal wall.

7. The device of claim 6, wherein the muco-adhesive material is coated so as only to become exposed when the device reaches the predetermined region of the gastro-intestinal tract.

8. The device of any preceding claim, wherein the sample input valve is configured to allow a pressure gradient driven passage of material from the outside of the capsule body to the inside of the capsule body through one or more sample collection openings, and to seal the one or more sample collection openings in the absence of a pressure gradient.

9. The device of claim 8, wherein the capsule body comprises one or more actuator openings via which the gastro-intestinal material can contact the dissolvable element and dissolve the dissolvable element when the one or more actuator openings are unsealed, wherein the one or more actuator openings are separated from the one or more sample collection openings.

10. The device of claim 9, wherein the one or more actuator openings are on an opposite side of the capsule body to the one or more sample collection openings.

11. The device of claim 9 or 10, wherein the one or more actuator openings are sealed by a sealing material, the sealing material being configured such that when the device is taken orally, the sealing material will dissolve only when the device reaches the predetermined region of the gastro-intestinal tract.

12. The device of claim 11, wherein the device is coated with a muco-adhesive material configured to promote adhesion between the device and a lining of the intestinal wall when the muco-adhesive material contacts the lining of the intestinal wall.

13. The device of claim 12, wherein the sealing material is provided over the muco-adhesive material, such that the muco-adhesive material is exposed only when the device reaches the predetermined region of the gastro-intestinal tract.

14. The device of any of claims 11-13, wherein the sealing material comprises an enteric coating.

15. The device of any of claims 6, 7 and 12-14, wherein the muco-adhesive material is arranged on a portion of the outer surface of the device that is selected such that adhesion of the device to the lining of the intestinal wall is promoted in an orientation of the device which allows gastro-intestinal material to be drawn into the capsule body through the sample input valve.

16. The device of any preceding claim, wherein:

the sample input valve is configured to allow a pressure gradient driven passage of material from the outside of the capsule body to the inside of the capsule body through one or more sample collection

openings, and to seal the one or more sample collection openings in the absence of a pressure gradient; and

an exterior surface of the capsule body is provided with one or more indented channels leading to one or more of the sample collection openings to reduce blocking of the one or more sample collection openings by tissue or material within the gastro-intestinal tract.

17. The device of any preceding claim, wherein:

the sample input valve is configured to allow a pressure gradient driven passage of material from the outside of the capsule body to the inside of the capsule body through one or more sample collection openings, and to seal the one or more sample collection openings in the absence of a pressure gradient; and

one or more of the sample collection openings is non-circular.

18. The device of any preceding claim, further comprising one or more protruding members protruding outwards relative to an average level of an outer surface of the capsule body adjacent to the sample input valve, for reducing suction-based adhesion of the device to tissue or material within the gastro-intestinal tract.

19. The device of any preceding claim, wherein the dissolvable element comprises one or more of the following: hypromellose, polyvinylpyrrolidone, sodium carboxymethyl cellulose, and sodium starch glycolate.

20. The device of any preceding claim, wherein the dissolvable element comprises a first material coated with a second material.

21. The device of claim 20, wherein the first material is fully encapsulated by the second material.

22. The device of claim 20 or 21, wherein the second material is configured such that when the device is taken orally, the second material will dissolve only when the device reaches the predetermined region of the gastro-intestinal tract.

23. The device of any of claims 20-22, wherein the second material comprises an enteric coating.