

Summary

[0004] According to a first aspect, there is provided an intravesical drug delivery device including a housing defining a reservoir, a first unit in the form of a solid tablet contained within the reservoir in a first position, the first unit including a drug; and a second unit in the form of a solid tablet contained within the reservoir in a second position distinct from the first position, the first and second positions being in fluid communication with one another, wherein the second unit contains an osmotic agent which facilitates in vivo release of the drug from the housing, wherein the device is elastically deformable from a relatively straightened shape suited for insertion through the urethra of a patient and into the patient's bladder and a retention shape suited to retain the device within the bladder.

[0004a] According to a second aspect, there is provided an intravesical drug delivery device including: a housing which comprises a water permeable elastomeric tube, which comprises (i) a lumen defining a reservoir, and (ii) a drug release orifice in communication with the reservoir; a plurality of first tablets which comprise a drug, the first tablets being contained within the reservoir at one or more first positions; and a plurality of second tablets which comprise an osmotic agent, the second tablets being contained within the reservoir at one or more second positions which are different from and in fluid communication with the one or more first positions, wherein the device is elastically deformable between a relatively straightened shape suited for insertion through the urethra of a patient and into the patient's bladder and a retention shape suited to retain the device within the bladder, and wherein the device is configured, following intravesical insertion, to permit the first and second tablets to be solubilized by urine diffusing into the reservoir and to release solubilized drug through the drug release orifice by osmotic pressure generated in the reservoir.

[0004b] According to a third aspect, there is provided an intravesical drug delivery device including: a housing which comprises a water permeable silicone tube, which comprises (i) a lumen defining a cylindrical reservoir, and (ii) a drug release orifice in a sidewall of the silicone tube, the drug release orifice being in communication with the cylindrical reservoir; a plurality of drug tablets which comprise at least 75 wt% gemcitabine; and a plurality of osmotic agent tablets which comprise at least 85 wt% urea, wherein the osmotic agent tablets are positioned within opposed end regions of the cylindrical reservoir and the drug tablets are positioned within a middle region in the cylindrical reservoir between osmotic agent tablets.

[0005] Disclosed herein is an intravesical drug delivery device, including a first housing portion loaded with a drug formulation which includes a drug, and a second housing portion loaded with an excipient. The device is configured to release the drug according to a first release profile and is configured to release the excipient according to a second release profile which differs from the first release profile.

[0006] Disclosed herein is a method of administering a drug to a patient, including inserting an intravesical drug delivery device as disclosed herein into a patient, and releasing the drug from the inserted device.

Brief Description of the Drawings

[0007] **FIG. 1** is a cross-sectional view of an embodiment of a prior art drug delivery device.

[0008] **FIG. 2** is a cross-sectional view of one embodiment of a multi-unit drug delivery device.

[0009] **FIG. 3** is a cross-sectional view of another embodiment of a multi-unit drug delivery device.

[00010] **FIG. 4** is a cross-sectional view of another embodiment of a multi-unit drug delivery device.

[00011] **FIG. 5** is a cross-sectional view of one embodiment of a multi-unit drug delivery device.

[00012] **FIG. 6** is a perspective view of a portion of the multi-unit drug delivery device of **FIG. 5**.

[00013] **FIG. 7** illustrates example configurations for drug delivery devices having more than one drug housing portion.

[00014] **FIG. 8** is a plan view of an embodiment of a drug delivery device having more than one drug housing portion.

[00015] **FIG. 9** is a graph showing the percent drug release over time of a single tablet drug delivery device and a two tablet drug delivery device.

CLAIMS

1. An intravesical drug delivery device comprising:
 - a housing defining a reservoir;
 - a first unit in the form of a solid tablet contained within the reservoir in a first position, the first unit comprising a drug; and
 - a second unit in the form of a solid tablet contained within the reservoir in a second position distinct from the first position, the first and second positions being in fluid communication with one another,
 - wherein the second unit comprises an osmotic agent that facilitates in vivo release of the drug from the housing,
 - wherein the device is elastically deformable from a relatively straightened shape suited for insertion through the urethra of a patient and into the patient's bladder and a retention shape suited to retain the device within the bladder.
2. The device of claim 1, wherein the housing comprises a water permeable wall portion defining at least part of the reservoir.
3. The device of claim 2, wherein the water permeable wall portion is substantially impermeable to the drug in aqueous solution.
4. The device of claim 2, wherein the water permeable wall portion is permeable to the drug in aqueous solution.
5. The device of claim 1, wherein the housing comprises at least one aperture configured to permit a fluid to enter the reservoir in vivo.
6. The device of claim 1, wherein the housing comprises at least one drug release orifice, which is in fluid communication with the reservoir.
7. The device of claim 1, wherein the housing comprises an elongated, annular tube and the reservoir comprises the annulus of the annular tube.

8. The device of claim 7, wherein a drug release orifice is provided in an end plug located at an end of the tube.
9. The device of claim 7, wherein a drug release orifice is provided in a sidewall of the tube.
10. The device of claim 8, wherein the first unit is located closer than the second unit to the drug release orifice.
11. The device of claim 7, wherein the housing has no release orifice and is configured to release the drug through a drug permeable wall bounding the reservoir.
12. The device of claim 11, wherein the drug permeable wall comprises a disk stabilized in the annulus of the tube at, or near, an end of the tube.
13. The device of claim 12, wherein the disk is sandwiched between an inner washer and an outer washer.
14. The device of claim 11, wherein the drug permeable wall is part of a sidewall of the tube.
15. The device of claim 11, wherein the drug permeable wall is part of an end plug located at an end of the tube.
16. The device of any one of claims 1 to 15, wherein the drug is a low solubility drug.
17. The device of claim 1, wherein the device is configured to release a therapeutically effective amount of the drug over a period from 2 days to 30 days.
18. The device of claim 1, wherein the housing comprises an elongated annular tube, the annular tube comprising a water permeable wall portion and a water impermeable wall portion.

19. The device of claim 18, wherein the water impermeable wall portion comprises a water impermeable coating.
20. The device of claim 11, wherein the first unit is located closer than the second unit to the drug permeable wall.
21. The device of claim 1 or claim 18, wherein the housing comprises an elongated, annular tube having a wall thickness from 0.1 to 0.4 mm.
22. The device of claim 1 or claim 18, wherein the housing has a durometer from 25A to 80A.
23. The device of claim 1 or claim 18, wherein the housing comprises silicone, a thermoplastic polyurethane, ethylene-co-vinyl acetate (EVA), or a combination thereof.
24. The device of any one of claims 1 to 23, wherein the drug comprises lidocaine, gemcitabine, docetaxel, carboplatin, cisplatin, oxaliplatin, trospium, tolterodine, or mitomycin C.
25. The device of claim 1, wherein the drug comprises gemcitabine and the osmotic agent comprises urea.
26. The device of claim 25, wherein the first unit comprises at least 75 percent by weight gemcitabine HCl and the second unit comprises at least 85 percent by weight urea.
27. The device of any one of claims 1 to 26, comprising a plurality of the first units and a plurality of the second units.
28. The device of claim 1, wherein:
 - the housing comprises a water permeable, elongated, annular tube having an inner diameter from about 2 to about 5 mm,

the solid tablet of the first unit has a diameter substantially the same as the inner diameter of the elongated annular tube, the one or more solid tablets of the first unit filling a length from about 1 cm to about 3 cm of the annulus of the annular tube, and

the solid tablet of the second unit has a diameter substantially the same as the inner diameter of the elongated annular tube, the one or more solid tablets of the second unit filling a length from about 10 cm to about 15 cm of the annulus of the annular tube.

29. The device of claim 1 or claim 28, wherein a ratio of volume of the first unit to volume of the second unit is from about 0.05 to about 0.5.
30. The device of claim 1, wherein the device is configured to spontaneously assume a shape in the absence of a compressive load, which shape comprises an interconnected and overlapping pair of coils.
31. The device of claim 1 or claim 30, wherein the housing further comprises a retention frame lumen and a retention frame positioned in the retention frame lumen.
32. The device of claim 31, wherein the retention frame comprises a superelastic alloy or other elastic wire.
33. The device of claim 1, wherein the reservoir comprises a flow modulator channel between the first and second units.
34. The device of claim 1, wherein:
 - the housing is water permeable,
 - the first unit comprises a first tablet that comprises a low solubility drug, and
 - the second unit comprises a second tablet that comprises the osmotic agent that facilitates release of the drug from the housing by osmotic pressure.

35. The device of claim 34, wherein the drug comprises gemcitabine and the osmotic agent comprises urea.
36. The device of claim 1, wherein the device is configured, following deployment of the device into a patient, to permit water or urine to enter the reservoir and solubilize the first and second units.
37. The device of claim 1, wherein the osmotic agent is configured to expedite solubilization of the drug.
38. The device of claim 1, wherein the device is configured to release the drug and the osmotic agent from the housing.
39. An intravesical drug delivery device comprising:
a housing which comprises a water permeable elastomeric tube, which comprises (i) a lumen defining a reservoir, and (ii) a drug release orifice in communication with the reservoir;
a plurality of first tablets which comprise a drug, the first tablets being contained within the reservoir at one or more first positions; and
a plurality of second tablets which comprise an osmotic agent, the second tablets being contained within the reservoir at one or more second positions which are different from and in fluid communication with the one or more first positions,
wherein the device is elastically deformable between a relatively straightened shape suited for insertion through the urethra of a patient and into the patient's bladder and a retention shape suited to retain the device within the bladder, and
wherein the device is configured, following intravesical insertion, to permit the first and second tablets to be solubilized by urine diffusing into the reservoir and to release solubilized drug through the drug release orifice by osmotic pressure generated in the reservoir.
40. The device of claim 39, wherein the drug comprises gemcitabine and the osmotic agent comprises urea.

41. The device of claim 39 or 40, wherein:
the second tablets are positioned within opposed end regions of the reservoir,
the first tablets are positioned within a middle region in the reservoir between the second tablets, and
the drug release orifice is located in a sidewall of the elastomeric tube adjacent to the first tablets.
42. An intravesical drug delivery device comprising:
a housing which comprises a water permeable silicone tube, which comprises (i) a lumen defining a cylindrical reservoir, and (ii) a drug release orifice in a sidewall of the silicone tube, the drug release orifice being in communication with the cylindrical reservoir;
a plurality of drug tablets which comprise at least 75 wt% gemcitabine; and
a plurality of osmotic agent tablets which comprise at least 85 wt% urea,
wherein the osmotic agent tablets are positioned within opposed end regions of the cylindrical reservoir and the drug tablets are positioned within a middle region in the cylindrical reservoir between osmotic agent tablets.
43. The intravesical drug delivery device of claim 42, wherein the drug tablets are centered about the drug release orifice.
44. The intravesical drug delivery device of claim 42 or 43, wherein the device is configured, following intravesical insertion, to permit the first and second tablets to be solubilized by urine diffusing into the reservoir and to release gemcitabine through the drug release orifice by osmotic pressure generated in the reservoir.