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(56) Documents Cited
US 4883182 A **US 4434893 A**
US 3702653 A

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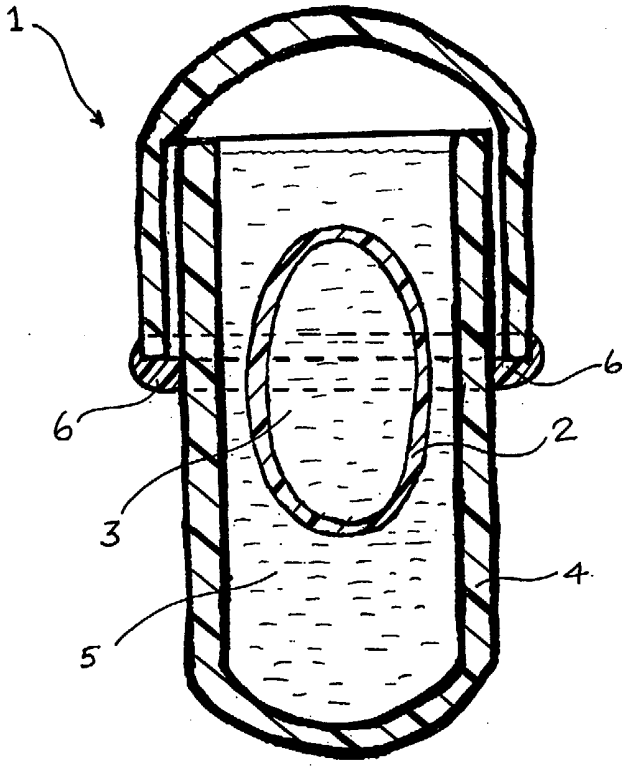
(54) Abstract Title
Tamper-proof capsules

(57) A tamper-evident capsule system (1) comprising an inner capsule (2) containing an active principle (3) and encapsulated within an outer capsule (4) at least partially filled with at least a tamper evident indicator (5).



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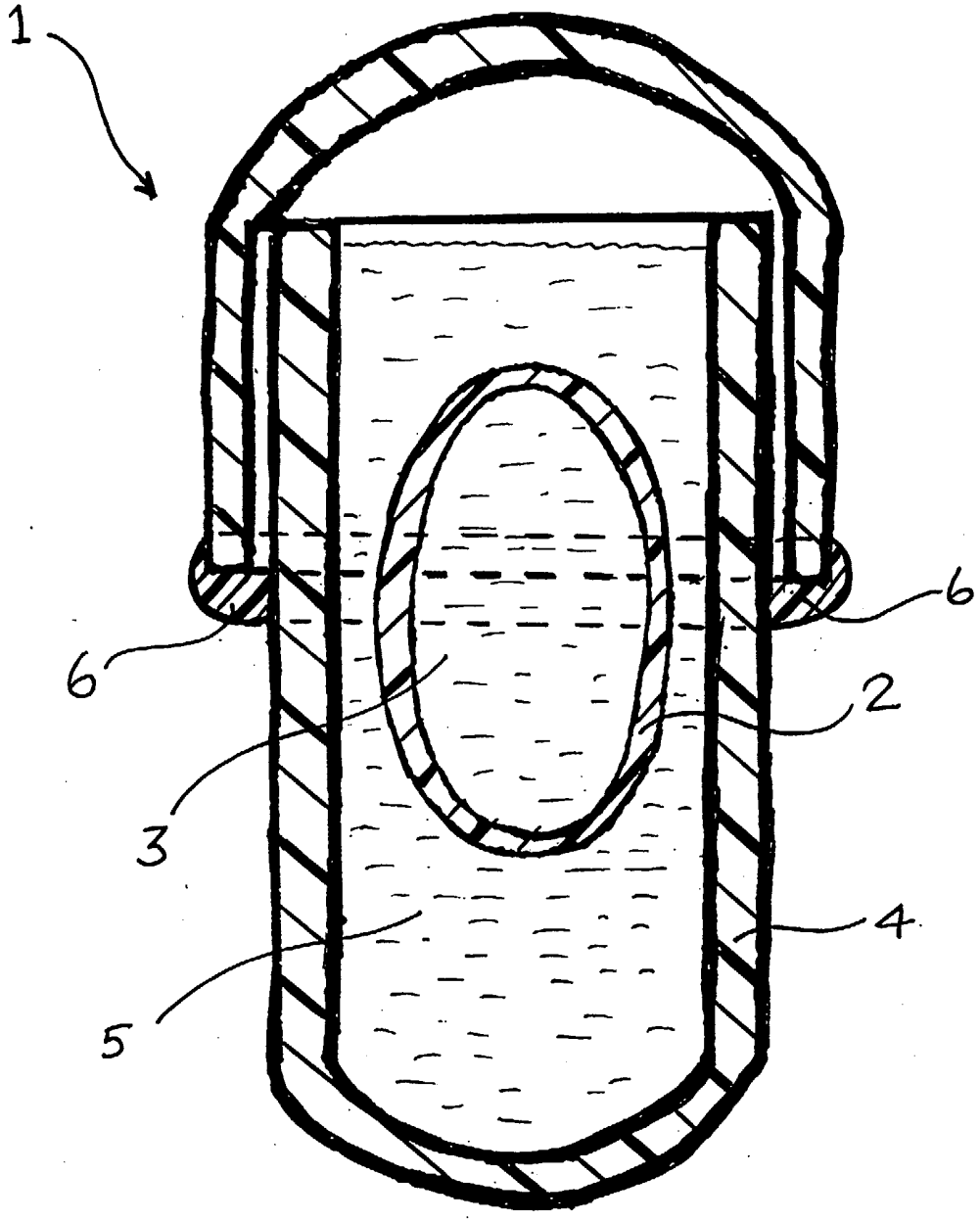
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TAMPER-EVIDENT CAPSULE SYSTEM

DESCRIPTION

This invention relates to a tamper-evident capsule system for the administration of at least one active principle in single or multiple therapy(ies).

Tampering with pharmaceutical products or other active principles encapsulated in two-piece capsules, has become of increasing concern.

Incidents, such as that in the United States of America where an individual adulterated capsules with cyanide resulting in the untimely death of several people, have resulted in agencies, such as the Federal Drug Administration, bringing out legislation requiring two-piece capsules to be banded as part of a tamper-evident system. As a consequence of this legislation, all prescription capsules in the United States of America are required to be tamper-evident and from the end of 1999, it has been a requirement for all US OTC two-piece capsules to be banded for tamper-evidence. Companies in Europe are now using similar means for the same purpose.

A major disadvantage associated with a banded two-piece capsule is that it will only show tamper-evidence if it has been split or separated. Small holes, such as those which can be caused by a hypodermic needle, leave little or no trace of the integrity of the capsule having been breached.

With hard capsules made of, say, hard gelatin, containing particulate material, a puncture hole formed in that material by, say, a hypodermic syringe, is usually sufficiently small for the particulate material to be retained in the capsule. As a consequence, tamper-evidence is not apparent.

Similarly, an associated blister pack could be punctured without evidence of tampering.

Thus, it is an object of the present invention to provide a tamper-evident capsule system which overcomes the disadvantages associated with known capsules and capsule systems discussed above, to provide evidence of tampering, particularly in relation to the contamination or other adulteration of the active principle contained therein.

Accordingly, a first aspect of the invention provides a tamper-evident capsule system comprising an inner capsule containing an active principle and encapsulated within an outer capsule at least partially filled with at least a tamper-evident indicator.

The inner capsule may be made of any suitable material, such as gelatin with or without a plasticiser, whilst the outer capsule is preferably made of hard gelatin or any other suitable material.

The indicator may be in any suitable form, as long as it is capable of being released from the outer capsule when the integrity thereof is breached.

A preferred indicator may be in the form of a liquid, more preferably of low viscosity, for example an oil, to provide tamper-evidence by visible means and/or smell.

However, any other suitable form of indicator may be employed, for example, a gas which, again, may provide tamper-evidence by visible means, such as colour, and/or smell.

Also, the indicator may be selected to provide a secondary indication of tamper-evidence, for example, by smell, colour change, phase change or

any combination thereof. Further, the indicator may be coloured or colourless, as long as detection of its leakage from the outer capsule when the integrity thereof is breached, is maximised.

Types of tamper-evident indicator other than those mentioned above may be used, for example, semi-solid, solid and/or gelatinous materials.

The outer capsule is preferably of two-part form and sealed by banding or any other suitable method, whilst the inner capsule containing the active principle may also be in two-piece form, again sealed by banding, with the active principle being particulate, liquid, semi-liquid, solid or semi-solid.

Further, the outer capsule may also contain, in addition to the tamper-evident indicator, an active principle or other material

The contents of the inner capsule may also include a colourant or other modifier, such as a pH indicator, capable of reacting with the indicator contained in the outer capsule when, say, the integrity of the inner capsule is breached.

The inner and outer capsules may be made from the same or different materials and one or both may be transparent. Where the outer capsule is transparent, changes to the indicator contained therein and/or the inner capsule would be more obvious than having the outer capsule opaque. Also, with a transparent outer capsule, the inner capsule could be readily identifiable by its colour markings and/or printing or any other identifying marks.

One or both of the inner and outer capsules may also be coated in known manner or uncoated, as required, and the system could comprise more than one inner capsule for, say, multi-therapy purposes.

Packaging, such as a blister pack could be used in addition to the innovative system discussed above as the integrity of such packaging could also be breached by, for example, a hypodermic syringe, with the outer capsule providing evidence of tampering.

A second aspect of the invention provides a method of rendering tamper-evident at least one capsule containing an active principle, which method comprises encapsulating the capsule(s) within an outer capsule containing a tamper-evident indicator.

The preferred characteristics of the outer capsule and/or tamper-evident indicator may be the same or similar to the preferences described above in relation to the first aspect of the invention.

In order that the various aspects of the invention may be more fully understood, a preferred embodiment in accordance therewith will now be described by way of example and with reference to the accompanying Figure which is a sectional view of a tamper-evident capsule system with an inner, soft gelatine capsule and an outer, hard gelatine capsule.

Referring now to the Figure, a tamper-evident capsule system, indicated generally at 1, comprises an inner one-piece, soft gelatine capsule 2 containing an active principle 3.

The inner capsule 2 and its contents of active principle 3 are encapsulated within an outer two-piece, hard gelatine capsule 4 at least partially filled with a tamper-evident indicator 5 which is of any suitable material capable of being released from the outer capsule 4 when the integrity

of the latter is breached, for instance, by being punctured by a hypodermic needle.

The outer capsule 4 is banded at 6 in a conventional manner.

The inner capsule 2 is made of any suitable material, in this particular case, plasticised gelatin, whilst the outer capsule 4 is made of a hard material, for example, non-plasticised gelatin, as is conventional in the art.

Thus, by encapsulating the inner capsule 2 and its contents 3 in the form of an active principle, within the outer capsule 4 filled, at least partially, with at least a tamper-evident indicator 5, there is provided a tamper-evident capsule system 1 which is capable of evidencing tampering, for example, by attempting to adulterate the contents thereof by injection of a hazardous material into the system 1 by, for example, use of a hypodermic syringe.

As discussed above, the indicator 5 is a coloured liquid, such as a low viscosity oil. However, it may take any other suitable form and may provide evidence of tampering by visual means, by smell or by a combination thereof.

Also, and in a modification of the capsule system 1 described above with reference to the drawing, a liquid active principle may be included with the indicator 5 in the outer capsule 4.

A further advantage of the present invention is that the outer capsule 4, and to a certain extent its contents 5, provides an additional layer of protection for the inner capsule 2 and its active principle contents 3.

CLAIMS

1. A tamper-evident capsule system comprising an inner capsule containing an active principle and encapsulated within an outer capsule at least partially filled with at least a tamper-evident indicator.

2. A system according to claim 1, wherein the inner capsule is made of gelatin with or without a plasticiser.

3. A system according to claim 1 or 2, wherein the outer capsule is made of hard gelatin.

4. A system according to claim 1, 2 or 3, wherein the indicator is in the form of a liquid, preferably of low viscosity.

5. A system according to claim 4, wherein the indicator is an oil.

6. A system according to claim 1, 2 or 3, wherein the indicator is a gas.

7. A system according to claim 1, 2 or 3, wherein the indicator is a semi-solid, solid and/or gelatinous material.

8. A system according to any preceding claim, wherein the indicator is arranged to provide tamper-evidence by visible means, such as colour, and/or smell.

9. A system according to any preceding claim, wherein the indicator is selected to provide a secondary indication of tamper-evidence, for example, by smell, colour change, phase change or any combination thereof.

10. A system according to any preceding claim, wherein the indicator is coloured or colourless.

11. A system according to any preceding claim, wherein the outer capsule is of two-part form, preferably sealed by banding.

12. A system according to any preceding claim, wherein the active principle is particulate, liquid, semi-liquid, solid or semi-solid.

13. A system according to any preceding claim, wherein the outer capsule also contains, in addition to the tamper-evident indicator, an active principle or other material.

14. A system according to any preceding claim, wherein the contents of the inner capsule include a colourant or other modifier, such as a pH indicator, capable of reacting with the indicator contained in the outer capsule.

15. A system according to any preceding claim, wherein the inner and outer capsules are made of the same material.

16. A system according to any of claims 1 to 14, wherein the inner and outer capsules are made of different materials.

17. A system according to any preceding claim, wherein one or both of the inner and outer capsules is or are transparent.

18. A system according to any preceding claim, wherein one or both of the inner and outer capsules is or are coated.

19. A system according to any preceding claim, comprising more than one inner capsule.

20. A system according to any preceding claim, including outer packaging, preferably in the form of a blister pack.

21. A tamper-evident capsule system substantially as hereinbefore described with reference to the accompanying drawing.

22. A method of rendering tamper-evident at least one capsule containing an active principle, which method comprises encapsulating the capsule(s) with an outer capsule containing a tamper-evident indicator.

23. A method according to claim 22, wherein the inner capsule is made of gelatin with or without a plasticiser.

24. A method according to claim 22 or 23, wherein the outer capsule is made of hard gelatin.

25. A method according to claim 22, 23 or 24, wherein the indicator is provided in the form of a liquid, preferably of low viscosity.

26. A method according to claim 25, wherein the indictor is provided as an oil.

27. A method according to claim 22, 23 or 24, wherein the indicator is provided as a gas.

28. A method according to claim 22, 23 or 24, wherein the indicator is provided as a semi-solid, solid and/or gelatinous material.

29. A method according to any of claims 22 to 28, wherein the indicator provides tamper-evidence means, such as colour, and/or smell.

30. A method according to any of claims 22 to 29, wherein the indicator provides a secondary indication of tamper-evidence, for example, by smell, colour change, phase change or any combination thereof.

31. A method according to any of claims 22 to 30, wherein the indicator is coloured or colourless.

32. A method according to any of claims 22 to 31, wherein the outer capsule is provided in two-part form, preferably sealed by banding.

33. A method according to any of claims 22 to 32, wherein the active principle is provided as a particulate, liquid, semi-liquid, solid or semi-solid.

34. A method according to any of claims 22 to 33, wherein the outer capsule also contains, in addition to the tamper-evident indicator, an active principle or other material.

35. A method according to any of claims 22 to 34, wherein the contents of the inner capsule are provided with a colourant or other modifier, such as a pH indicator, capable of reacting with the indicator contained in the outer capsule.

36. A method according to any of claims 22 to 35, wherein the inner and outer capsules are made of the same material.

37. A method according to any of claims 22 to 35, wherein the inner and outer capsules are made of different materials.

38. A method according to any of claims 22 to 37, wherein one or both of the inner and outer capsules is or are transparent.

39. A method according to any of claims 22 to 38, wherein one or both of the inner and outer capsules is or are coated.

40. A method according to any of claims 22 to 39, comprising more than one inner capsule.

41. A method according to any of claims 22 to 40, wherein tamper-evident rendered capsule is included in outer packaging, preferably in the form of a blister pack.

42. A method of rendering tamper-evident at least one capsule containing an active principle substantially as hereinbefore described with reference to the accompanying drawing.

Application No:	GB 0015523.4	**Examiner:**	Diane Davies
Claims searched:	1-42	**Date of search:**	16 November 2000

Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.R): A5B: BLJ, BLM

Int Cl (Ed.7): A61J 3/07; A61K 9/48

Other: Online databases: EPODOC, JAPIO, WPI

Documents considered to be relevant:

Category	Identity of document and relevant passage		Relevant to claims
X	US 4883182 A	(R.J. Hughes) Whole document: tamper-evident capsule with internal capsule.	At least claim 1
X	US 4434893 A	(Barlow Gordon Design) Whole document: tamper-proof package having capsules within two enclosures.	At least claim 1
X	US 3702653 A	(Parke Davis & Co.) Whole document: a conventional capsule is retained in a larger capsule with tamper-proof indicators.	At least claim 1

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.