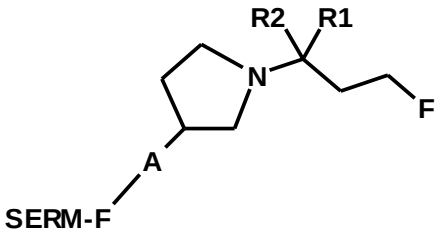
CLAIMS

1. Compounds of the formula (I-A):

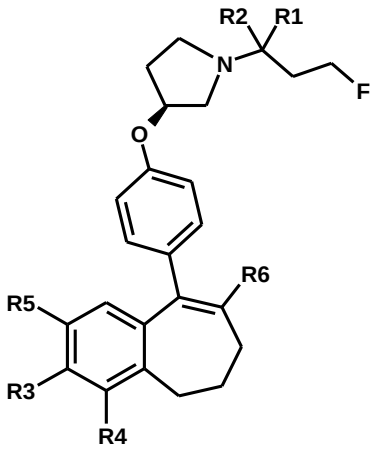


(I-A)

wherein:

- R1 and R2 represent independently a hydrogen atom or a deuterium atom;
- A represents an oxygen or nitrogen atom; and
- SERM-F represents a selective estrogen receptor modulator fragment comprising an aryl or heteroaryl group linked to the adjacent “A” group;

with the proviso that the compounds of formula (I-B) below are excluded:



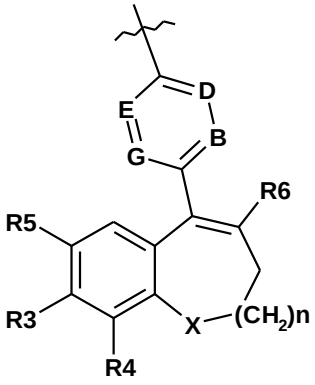
(I-B)

wherein, in formula (I-B):

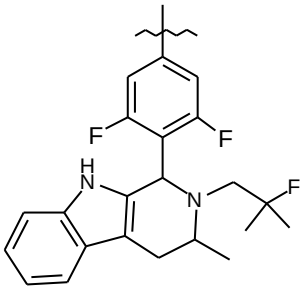
- R1 and R2 represent independently a hydrogen atom or a deuterium atom;
- R3 represents a hydrogen atom, a -COOH group, a -OH group or a $-OPO(OH)_2$ group;
- R4 represents a hydrogen atom or a fluorine atom;
- R5 represents a hydrogen atom or a -OH group;
- wherein:
  - at least one of R3 or R5 is different from a hydrogen atom;
  - when R3 represents a -COOH group, a -OH group or a $-OPO(OH)_2$ group, then R5 represents a hydrogen atom;
  - when R5 represents a -OH group, then R3 and R4 represent hydrogen atoms;

- R6 is selected from:
  - a phenyl group or a heteroaryl group comprising 3 to 9 carbon atoms and comprising from 1 to 3 heteroatoms independently selected from oxygen, nitrogen and sulphur, said phenyl and heteroaryl groups being unsubstituted or substituted with 1 to 3 substituents independently selected from:
    a (C_1-C_6)-alkyl group unsubstituted or substituted with one or more (such as 1, 2 or 3) fluorine atoms; a halogen atom; a -OH group; a (C_1-C_6)-alkoxy group unsubstituted or substituted with one or more (such as 1, 2 or 3) fluorine atoms; a cyano group; a sulphur group substituted with 5 fluorine atoms or (C_1-C_6)-alkyl groups substituted with two or more (such as 2 or 3) fluorine atoms; a sulfonyl-(C_1-C_6)-alkyl group wherein said (C_1-C_6)-alkyl group are unsubstitued or substituted with two or more (such as 2 or 3) fluorine atoms; a silane group substituted with 3 (C_1-C_6)-alkyl groups; an amine group unsubstituted or substituted with one or more (such as 1 or 2) (C_1-C_6)-alkyl groups; an amide group unsubstituted or substituted with one or more (such as 1 or 2) (C_1-C_6)-alkyl groups; a heterocycloalkyl group saturated or partially saturated, comprising 3 to 5 carbon atoms and comprising 1 or 2 heteroatoms independently selected from oxygen, nitrogen or sulphur; or a heteroaryl group comprising 2 to 4 carbon atoms and comprising 1 to 3 heteroatoms selected from oxygen, nitrogen or sulphur and being unsubstituted or substituted with an oxo group; and
  - a cycloalkyl group or a heterocycloalkyl group comprising 4 to 9 carbon atoms and comprising 1 or 2 heteroatoms independently selected from oxygen, nitrogen or sulphur, said cycloalkyl or heterocycloalkyl groups being saturated or partially saturated and being unsubstituted or substituted with 1 to 4 substituents independently selected from:
    a fluorine atom; a -OH group; a (C_1-C_6)-alkyl group; a -COOR7 group wherein R7 is a (C_1-C_6)-alkyl group; or an oxo group;
    or a pharmaceutically acceptable salt thereof.

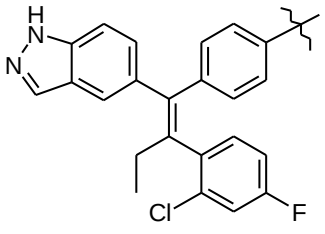
2. The compounds of formula (I-A) according to claim 1, characterized in that SERM-F is selected from the following structures (aI), (bII), (cIII) and (dIV), provided that when A represents a nitrogen atom then SERM-F represents the structure (aI):



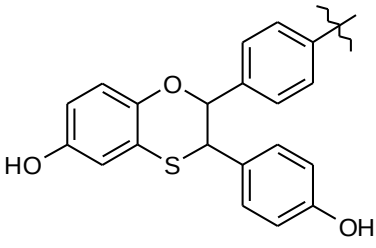
(aI)



(bII)



(cIII)



(dIV)

wherein:

- B, D, E and G represent independently =CH- or nitrogen atoms;
- n is an integer selected from 0 and 1;
- X represents -CH_2-, -O-, -S-, -SO- or -SO_2-;
- when n = 1 and X = CH_2, then at least one of A, B, D, E or G is a nitrogen atom;
- R3 represents a hydrogen atom or an -OH, -COOH or -$OPO(OH)_2$ group;
- R4 represents a hydrogen, fluorine or chlorine atom or a methyl group;
- R5 represents a hydrogen, fluorine or chlorine atom, or a methyl or -OH group;
- wherein R3 and R5 do not simultaneously represent -OH groups or hydrogen atoms;
- R6 is selected from:
  - a phenyl group, which is unsubstituted or substituted with 1 to 3 substituents independently selected from:

a (C_1-C_6)-alkyl group unsubstituted or substituted with one or more fluorine atoms or -OH groups; a halogen atom; an -OH group; a (C_1-C_6)-alkoxy group unsubstituted or substituted with one or more fluorine atoms, (C_1-C_6)-alkoxy or heterocycloalkyl groups; a cyano group; a sulphur group substituted with 5 fluorine atoms or with a (C_1-C_6)-alkyl group substituted with two or more fluorine atoms; a sulfonyl-(C_1-C_6)-alkyl group wherein said (C_1-C_6)-alkyl group is unsubstituted or substituted with two or more fluorine atoms; a silane group substituted with three (C_1-C_6)-alkyl groups; an amine group unsubstituted or substituted with one or more (C_1-C_6)-alkyl groups; an amide group unsubstituted or

substituted with one or more (C_1-C_6)-alkyl or (C_1-C_6)-alkoxy groups; a heterocycloalkyl group saturated or partially saturated, comprising 3 to 5 carbon atoms and comprising 1 or 2 heteroatoms independently selected from oxygen, nitrogen and sulphur; a heteroaryl group comprising 2 to 4 carbon atoms and comprising 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur and being unsubstituted or substituted with an oxo group; a -SO_2NH_2 group; a -COOH group; a -O-cycloalkyl group; a -O-heterocycloalkyl group; and a –OCD_3 group;

- a heteroaryl group comprising 3 to 9 carbon atoms and comprising between 1 to 3 heteroatoms independently selected from oxygen, nitrogen and sulphur, said heteroaryl group being unsubstituted or substituted with 1 to 3 substituents independently selected from:

a (C_1-C_6)-alkyl group unsubstituted or substituted with one or more fluorine atoms; a halogen atom; an -OH group; a (C_1-C_6)-alkoxy group unsubstituted or substituted with one or more fluorine atoms; a cyano group; a sulphur group substituted with 5 fluorine atoms or with a (C_1-C_6)-alkyl group substituted with two or more fluorine atoms; a sulfonyl-(C_1-C_6)-alkyl group wherein said (C_1-C_6)-alkyl group is unsubstituted or substituted with two or more fluorine atoms; a silane group substituted with three (C_1-C_6)-alkyl groups; an amine group unsubstituted or substituted with one or more (C_1-C_6)-alkyl groups; an amide group unsubstituted or substituted with one or more (C_1-C_6)-alkyl or (C_1-C_6)-alkoxy groups; a heterocycloalkyl group saturated or partially saturated, comprising 3 to 5 carbon atoms and comprising 1 or 2 heteroatoms independently selected from oxygen, nitrogen and sulphur; a heteroaryl group comprising 2 to 4 carbon atoms and comprising 1 to 3 heteroatoms selected from oxygen, nitrogen and sulphur and being unsubstituted or substituted with an oxo group; a -COO-(C_1-C_6)-alkyl group; and an oxo group;

- a cycloalkyl group comprising 4 to 9 carbon atoms, which is saturated or partially saturated, and which is unsubstituted or substituted with 1 to 4 substituents independently selected from:

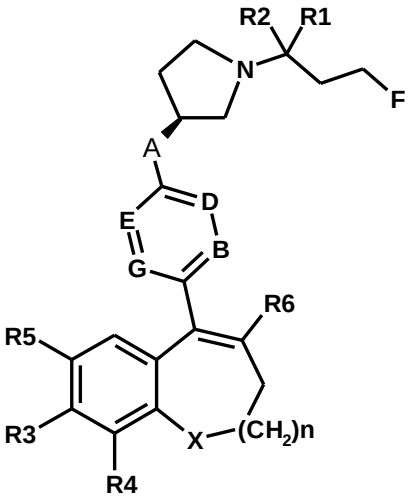
a fluorine atom; an -OH group; a (C_1-C_6)-alkyl group; a -COOR7 group wherein R7 is a (C_1-C_6)-alkyl group; and an oxo group; and

- a heterocycloalkyl group comprising 4 to 9 carbon atoms and comprising 1 or 2 heteroatoms independently selected from oxygen, nitrogen and sulphur, said heterocycloalkyl group being saturated or partially saturated and being unsubstituted or substituted with 1 to 4 substituents independently selected from:

a fluorine atom; an -OH group; a (C_1-C_6)-alkyl group; a -COOR7 group wherein R7 is a (C_1-C_6)-alkyl group; and an oxo group;

or a pharmaceutically acceptable salt thereof.

3. The compounds according to claim 1 or 2, characterized in that they respond to formula (I), wherein R1, R2, R3, R4, R5, R6, A, B, D, E, G, X and n are as defined in claim 1 or 2:



(I)

or a pharmaceutically acceptable salt thereof.

4. The compounds according to any of claims 1 to 3, characterized in that R6 is selected from:

- a phenyl group, which is unsubstituted or substituted with 1, 2 or 3 substituents independently selected from:

a (C_1-C_6)-alkyl group unsubstituted or substituted with one or more fluorine atoms or -OH groups; a halogen atom; an -OH group; a (C_1-C_6)-alkoxy group unsubstituted or substituted with one or more fluorine atoms, (C_1-C_6)-alkoxy or heterocycloalkyl groups; a sulphur group substituted with a (C_1-C_6)-alkyl group substituted with two or more fluorine atoms; a sulfonyl-(C_1-C_6)-alkyl group; an amine group unsubstituted or substituted with one or more (C_1-C_6)-alkyl groups; an amide group substituted with an (C_1-C_6)-alkoxy groups; a -SO_2NH_2 group; a -COOH group; a -O-cycloalkyl group; a -O-heterocycloalkyl group; and a -OCD_3 group;

- a heteroaryl group selected from an indole, pyridinyl, benzofuran, isoxazole, quinolyl and thiazolyl group, said heteroaryl group being unsubstituted or substituted with 1 to 3 substituents independently selected from:

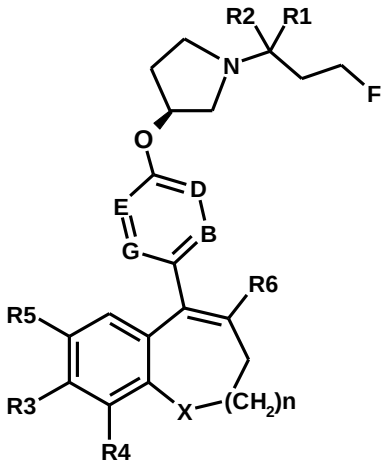
a (C_1-C_6)-alkyl group; a halogen atom; an -OH group; a (C_1-C_6)-alkoxy group; an amine group; an amide group substituted with a (C_1-C_6)-alkoxy group; and

- a heterocycloalkyl group selected from an indolinyl, dihydroazaindolinyl, dihydrobenzodioxinyl, benzodioxolyl, 2,3-dihydrobenzofuranyl, dihydrobenzoxazinyl and 5,6-dihydro-2H-pyranyl group, said heterocycloalkyl group being being unsubstituted or substituted with 1 to 4 substituents independently selected from:

a fluorine atom; a (C_1-C_6)-alkyl group; a -COOR7 group wherein R7 is a (C_1-C_6)-alkyl group; and an oxo group;

or a pharmaceutically acceptable salt thereof.

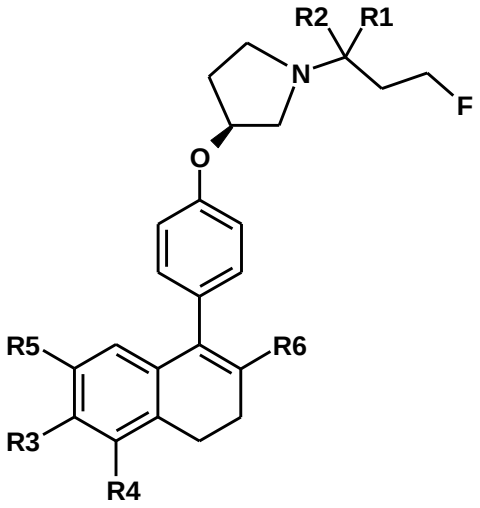
5. The compounds according to any of claims 1 to 4, characterized in that they respond to formula (I-2), wherein X, n, R1, R2, R3, R4, R5, R6, B, D, E and G are as defined in claim 2 or 3:



(I-2)

or a pharmaceutically acceptable salt thereof.

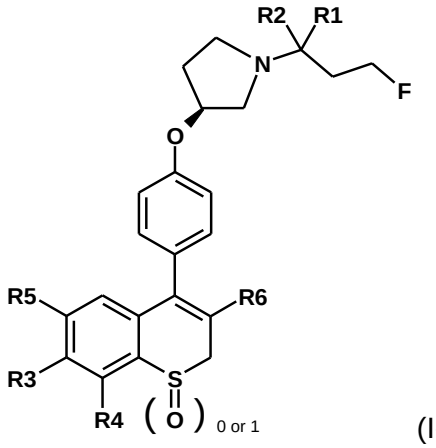
6. The compounds according to any of claims 1 to 4, characterized in that they respond to formula (I-3), wherein R1, R2, R3, R4, R5 and R6 are as defined in claim 2 or 3:



(I-3)

or a pharmaceutically acceptable salt thereof.

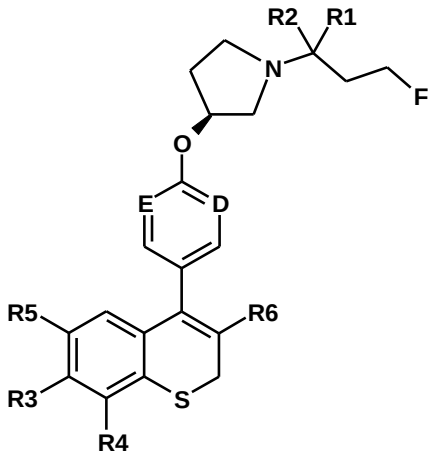
7. The compounds according to any of claims 1 to 4, characterized in that they respond to formula (I-4), wherein R1, R2, R3, R4, R5 and R6 are as defined in claim 2 or 3:



(I-4)

or a pharmaceutically acceptable salt thereof.

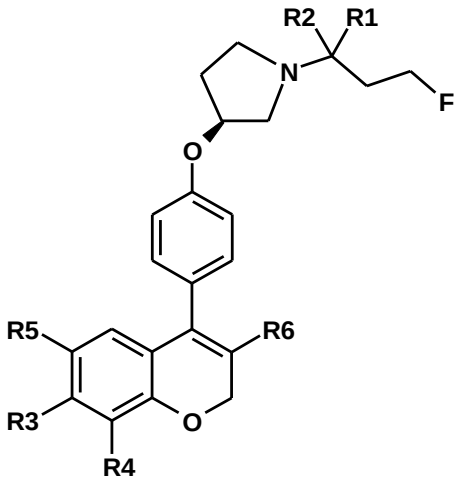
8. The compounds according to any of claims 1 to 4, characterized in that they respond to formula (I-5), wherein E, D, R1, R2, R3, R4, R5 and R6 are as defined in claim 2 or 3 and wherein one or two of E and D represent nitrogen atoms:



(I-5)

or a pharmaceutically acceptable salt thereof.

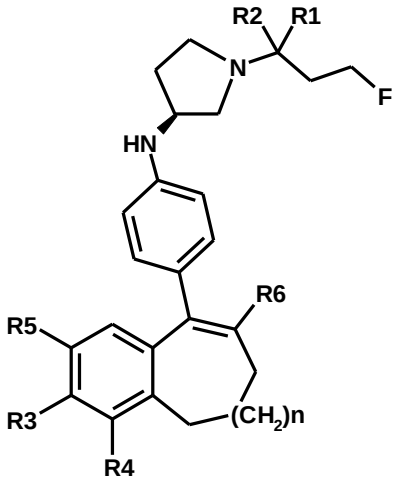
9. The compounds according to any of claims 1 to 4, characterized in that they respond to formula (I-6), wherein R1, R2, R3, R4, R5 and R6 are as defined in claim 2 or 3:



(I-6)

or a pharmaceutically acceptable salt thereof.

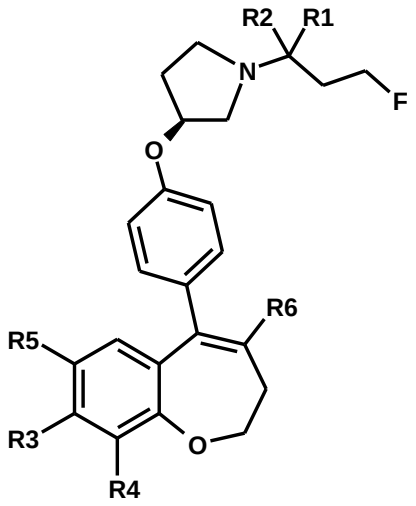
10. The compounds according to any of claims 1 to 4, characterized in that they respond to formula (I-7), wherein n, R1, R2, R3, R4, R5 and R6 are as defined in claim 2 or 3:



(I-7)

or a pharmaceutically acceptable salt thereof.

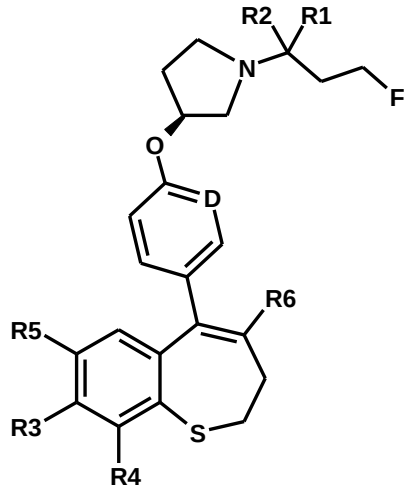
11. The compounds according to any of claims 1 to 4, characterized in that they respond to formula (I-8), wherein R1, R2, R3, R4, R5 and R6 are as defined in claim 2 or 3:



(I-8)

or a pharmaceutically acceptable salt thereof.

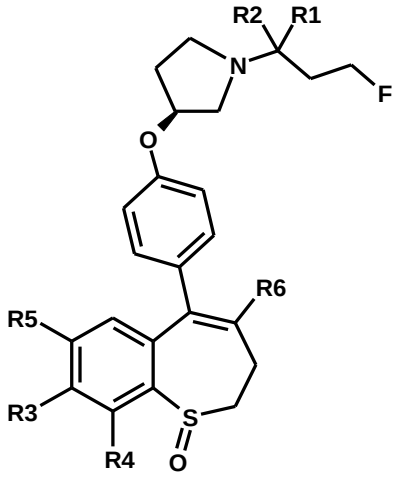
12. The compounds according to any of claims 1 to 4, characterized in that they respond to formula (I-9), wherein D, R1, R2, R3, R4, R5 and R6 are as defined in claim 2 or 3:



(I-9)

or a pharmaceutically acceptable salt thereof.

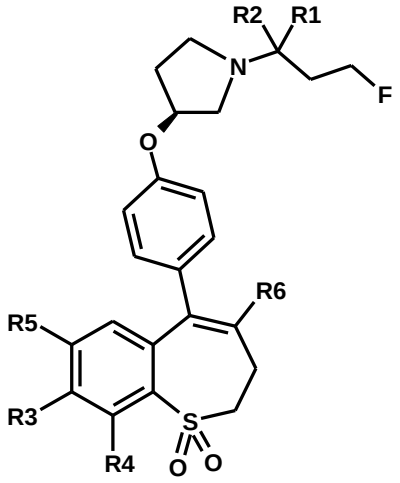
13. The compounds according to any of claims 1 to 4, characterized in that they respond to formula (I-10), wherein R1, R2, R3, R4, R5 and R6 are as defined in claim 2 or 3:



(I-10)

or a pharmaceutically acceptable salt thereof.

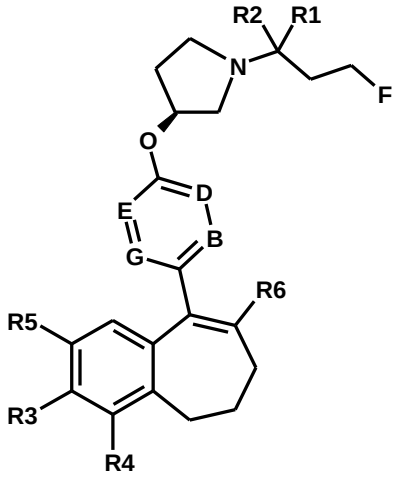
14. The compounds according to any of claims 1 to 4, characterized in that they respond to formula (I-11), wherein R1, R2, R3, R4, R5 and R6 are as defined in claim 2 or 3:



(I-11)

or a pharmaceutically acceptable salt thereof.

15. The compounds according to any of claims 1 to 4, characterized in that they respond to formula (I-12), wherein B, D, E, G, R1, R2, R3, R4, R5 and R6 are as defined in claim 2 or 3:



(I-12)

or a pharmaceutically acceptable salt thereof.

16. A medicament, characterized in that it comprises a compound according to any of claims 1 to 15, or a pharmaceutically acceptable salt thereof.

17. A pharmaceutical composition, characterized in that it comprises a compound according to any of claims 1 to 15, or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

18. A compound according to any of claims 1 to 15 for use as an inhibitor and degrader of estrogen receptors.

19. A compound according to any of claims 1 to 15 for use in the treatment of ovulatory dysfunction, cancer, endometriosis, osteoporosis, benign prostatic hypertrophy or inflammation.

20. A compound according to claim 19 for use in the treatment of an estrogen receptor dependent cancer.

21. A compound according to claim 19 or 20, for use in the treatment of breast, ovarian, endometrial, prostate, uterine, cervical or lung cancer, or a metastasis thereof.

22. A compound according to any of claims 19 to 21, for use in the treatment of a cancer which is resistant to anti-hormonal treatment.