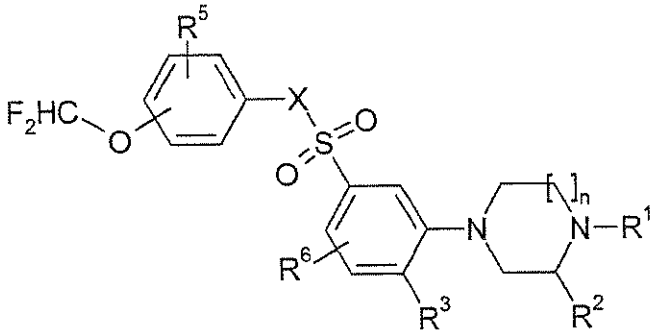
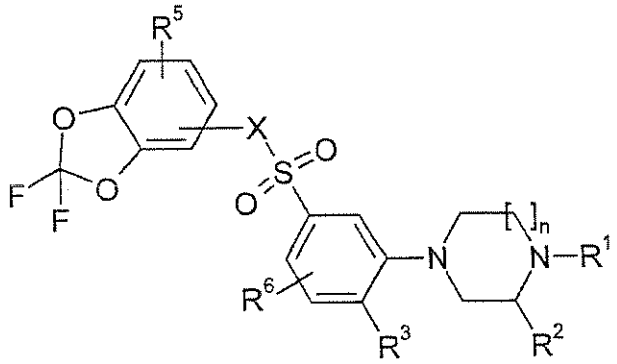
The compounds should also have good pharmacological profile, e.g. a good bioavailability and/or a good metabolic stability.

SUMMARY ~~OF THE INVENTION~~

In a first aspect, t~~T~~he present disclosure~~invention~~ relates to N-phenyl-(piperazinyl or homopiperazinyl)-benzenesulfonamides or benzenesulfonyl-phenyl-(piperazines or homopiperazines) of formula (I) or (I')



(I)



(I')

wherein

X is a bond or a group N-R^4;

R^1 is hydrogen or methyl;

R^2 is hydrogen or methyl;

R^3 is hydrogen, C_1-C_3 alkyl (e.g. methyl), fluorine, C_1-C_2 alkoxy (e.g. methoxy) or fluorinated C_1-C_2 alkoxy;

R^4 is hydrogen C_1-C_4 alkyl (e.g. methyl, ethyl, n-propyl, isopropyl), C_3-C_4 cycloalkyl, or -CH_2-C_3-C_4 cycloalkyl (e.g. cyclopropylmethyl);

R^5 is hydrogen, fluorine, chlorine, C_1-C_2 alkyl (e.g. methyl), fluorinated C_1-C_2 alkyl, C_1-C_2 alkoxy (e.g. methoxy) or fluorinated C_1-C_2 alkoxy;

R^6 is hydrogen, fluorine or chlorine; and

n is 1 or 2,

and physiologically tolerated acid addition salts and the N-oxides thereof.

In a second aspect, the present disclosure also relates to a pharmaceutical composition comprising at least one compound as defined above, optionally together with at least one physiologically acceptable carrier or auxiliary substance.

Said compounds, i.e., the N-phenyl-(piperazinyl or homopiperazinyl)-benzenesulfonamides or benzenesulfonyl-phenyl-piperazines or -homopiperazines and

their physiologically tolerated acid addition salts and the N-oxides thereof, exhibit to a surprising and unexpected degree, a high binding affinity to the 5-HT_6 receptor and are thus useful as pharmaceuticals.

The present ~~invention~~disclosure thus further relates to the compounds of formula (I) or (I') for use in therapy.

The present ~~invention~~disclosure also relates to pharmaceutical compositions which comprise a compound of formula (I) or (I') and, optionally, a physiologically acceptable carrier and/or an auxiliary substance.

In particular, said compounds, i.e., the N-phenyl-(piperazinyl or homopiperazinyl)-benzenesulfonamides or benzenesulfonyl-phenyl-(piperazines or homopiperazines) and their physiologically tolerated acid addition salts and the N-oxides thereof, are modulators of the 5-HT_6 receptor.

The present ~~invention~~disclosure thus further relates to the compounds of formula (I) or (I') for use in modulating the 5-HT_6 receptor.

The present ~~invention~~disclosure also relates to the use of the compounds of formula (I) or (I') in the manufacture of a medicament for modulating the 5-HT_6 receptor and corresponding methods of modulating the 5-HT_6 receptor.

Modulators of the 5-HT_6 receptor and in particular antagonists of the 5-HT_6 receptor are known to be useful in treating a variety of disorders.

The present ~~invention~~disclosure thus further relates to the compounds of formula (I) or (I') for use in treating said disorders.

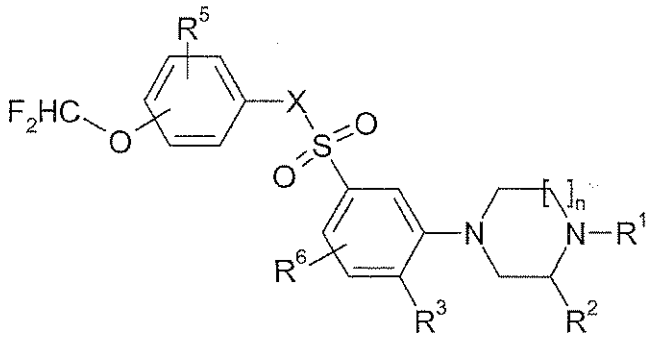
The present ~~invention~~disclosure also relates to the use of the compounds of formula (I) or (I') in the manufacture of a medicament for treating said disorders and corresponding methods of treating said disorders.

DETAILED DESCRIPTION OF THE INVENTION

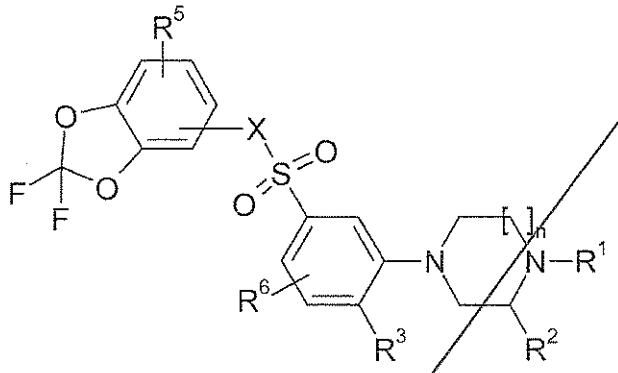
The disorders diseases which are susceptible to treatment with a compound of the formula (I) or (I') include, e.g., disorders and diseases of the central nervous system, in particular cognitive dysfunctions, such as a deficit in memory, cognition and learning, in particular associated with Alzheimer's disease, age-related cognitive decline and mild cognitive impairment, attention deficit disorder/hyperactivity syndrome (ADHD), personality disorders, such as schizophrenia, in particular cognitive deficits related with schizophrenia, affective disorders such as depression, anxiety and obsessive

We claim:

1. N-Phenyl-(piperazinyl or homopiperazinyl)-benzenesulfonamide or benzenesulfonyl-phenyl-(piperazine or homopiperazine) of formula (I) or (I')



(I)



(I')

wherein

X is a bond or a group N-R^4;

R^1 is hydrogen or methyl;

R^2 is hydrogen or methyl;

R^3 is hydrogen, C_1-C_3 alkyl, fluorine, C_1-C_2 alkoxy or fluorinated C_1-C_2 alkoxy;

R^4 is hydrogen, C_1-C_4 alkyl, C_3-C_4 cycloalkyl, or C_3-C_4 cycloalkyl-CH_2-;

R^5 is hydrogen, fluorine, chlorine, C_1-C_2 alkyl, fluorinated C_1-C_2 alkyl, C_1-C_2 alkoxy or fluorinated C_1-C_2 alkoxy;

R^6 is hydrogen, fluorine or chlorine; and

n is 1 or 2,

or a physiologically tolerated acid addition salt or an N-oxide thereof.

2. The compound as claimed in claim 1, wherein R^5 is hydrogen, fluorine, C_1-C_2 alkyl, fluorinated C_1-C_2 alkyl, C_1-C_2 alkoxy or fluorinated C_1-C_2 alkoxy

3. The compound as claimed in claim 1 or 2, where R^1 is hydrogen.

4. The compound as claimed in any one of claims 1 to 3, wherein R^2 is hydrogen.

5. The compound as claimed in any one of claims 1 to 32, wherein R^2 is methyl.

6. The compound as claimed in any one of claims 1 to 5, wherein X is a group N-R^4.

7. The compound as claimed in any one of claims 1 to 6, wherein n is 1.

8. The compound as claimed in any one of claims 1 to 7, wherein R^3 is methyl or methoxy.

9. The compound as claimed in any of claims 1 to 7, wherein R^3 is hydrogen or fluorine.

10. The compound as claimed in any one of claims 1 to 9, wherein R^4 is hydrogen, C_1-C_4 alkyl or cyclopropylmethyl.

11. The compound as claimed in claim 10, wherein R^4 is hydrogen.

12. The compound as claimed in any one of claims 1 to 11, wherein R^5 is hydrogen.

13. The compound as claimed in any one of claims 1 to 11, wherein R^5 is methyl, methoxy or difluoromethoxy.

14. The compound as claimed in any one of claims 1 to 11, wherein R^5 is chlorine or fluorine.

15. The compound as claimed in any one of claims 1 to 14, wherein R^6 is hydrogen.

16. The compound as claimed in any of claims 1 to 7, wherein R^5 and R^6 are hydrogen, R^3 is selected from the group consisting of C_1-C_2 alkyl and C_1-C_2 alkoxy, and R^4 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, or cyclopropylmethyl.

17. The compound as claimed in claim 1, wherein
X is a bond or a group N-R^4;
R^1 is hydrogen or methyl;
R^2 is hydrogen;
R^3 is hydrogen, C_1-C_2 alkyl, C_1-C_2 alkoxy ;
R^4 is hydrogen, methyl, ethyl, n-propyl, isopropyl or cyclopropylmethyl;
R^5 is hydrogen, methyl or methoxy;
R^6 is hydrogen; and
n is 1 or 2.

18. The compound as claimed in claim 17, wherein R^3 is methyl.

19. The compound as claimed in claim 17 or 18, wherein R^5 is hydrogen

20. The compound as claimed in claim 17, 18 or 19, wherein R^4 is hydrogen.

21. The compound as claimed in claim 17, 18, 19 or 20, wherein R^1 is hydrogen.

22. The compound as claimed in claim 17, 18, 19, 20 or 21, wherein X is a group N-R^4.

23. The compound as claimed in claim 17, 18, 19, 20, 21 or 22, wherein n is 1.

24. The compound as claimed in any one of claims 1 to 23, wherein the $OCHF_2$-radical in formula I is located on the benzene ring in the ortho-position with respect to X.

25. The compound as claimed in any of claims 1 to 23, wherein the $OCHF_2$-radical in formula I is located on the benzene ring in the meta-position with respect to X.

26. The compound as claimed in any of claims 1 to 23, wherein the $OCHF_2$-radical in formula I is located on the benzene ring in the para-position with respect to X.

27. The compound as claimed in any one of claims 1 to 26 for use in therapy.

28. A pharmaceutical composition comprising at least one compound as claimed in any one of claims 1 to 26, optionally together with at least one physiologically acceptable carrier or auxiliary substance.

29. The compound as claimed in any one of claims 1 to 26 for use in treating a disorder selected from diseases of the central nervous system, addiction diseases or obesity.

30. A method for treating a disorder selected from diseases of the central nervous system, addiction diseases or obesity, said method comprising administering an effective amount of at least one compound as claimed in any one of claims 1 to 26 to a subject in need thereof.

31. The method as claimed in claim 30, wherein the disorder is a disease of the central nervous system.

32. The method as claimed in claim 31, wherein the disease of the central nervous system is a cognitive dysfunction.

33. The method as claimed in claim 32, wherein the cognitive dysfunctions is associated with Alzheimer's disease.

34. The method as claimed in claim 32, wherein the cognitive dysfunctions is associated with schizophrenia.

35. The method as claimed in claim 30, wherein the disorder is an addiction disease.

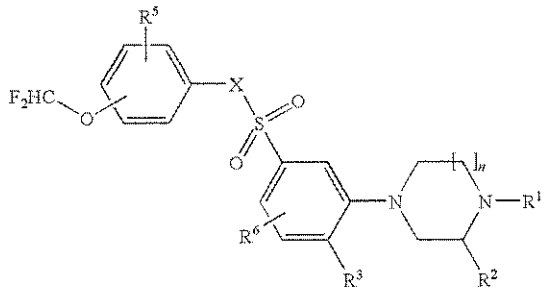
36. The method as claimed in claim 30, wherein the disorder is obesity.

37. The use of a compound as claimed in any of claims 1 to 26 in the manufacture of a medicament for the treatment of a disorder wherein the disorder is defined as in any one of claims 30 to 36.

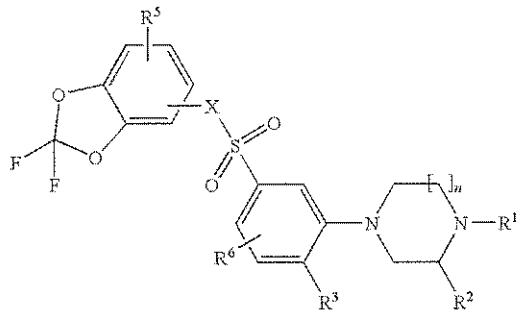
CLAIMS:

1. N-Phenyl-(piperazinyl or homopiperazinyl)-benzenesulfonamide or benzenesulfonyl-phenyl-(piperazine or homopiperazine) of formula (I) or (I')

(I)



(I')



wherein

X is a bond or a group N-R^4;

R^1 is hydrogen or methyl;

R^2 is hydrogen or methyl;

R^3 is hydrogen, C_1-C_3 alkyl, fluorine, C_1-C_2 alkoxy or fluorinated C_1-C_2 alkoxy;

R^4 is hydrogen, C_1-C_4 alkyl, C_3-C_4 cycloalkyl, or C_3-C_4 cycloalkyl-CH_2-;

R^5 is hydrogen, fluorine, chlorine, C_1-C_2 alkyl, fluorinated C_1-C_2 alkyl, C_1-C_2 alkoxy or fluorinated C_1-C_2 alkoxy;

R^6 is hydrogen, fluorine or chlorine; and

n is 1 or 2,

or a physiologically tolerated acid addition salt or an N-oxide thereof.

2. The compound as claimed in claim 1, wherein R^5 is hydrogen, fluorine, C_1-C_2 alkyl, fluorinated C_1-C_2 alkyl, C_1-C_2 alkoxy or fluorinated C_1-C_2 alkoxy.

3. The compound of claim 1, where R^1 is hydrogen.

4. The compound of claim 1, wherein R^2 is hydrogen.

5. The compound of claim 1, wherein R^2 is methyl.

6. The compound of claim 1, wherein X is a group N—R^4.

7. The compound of claim 1, wherein n is 1.

8. The compound of claim 1, wherein R^3 is methyl or methoxy.

9. The compound of claim 1, wherein R^3 is hydrogen or fluorine.

10. The compound of claim 1, wherein R^4 is hydrogen, C_1-C_4 alkyl or cyclopropylmethyl.

11. The compound of claim 1, wherein R^4 is hydrogen.

12. The compound of claim 1, wherein R^5 is hydrogen.

13. The compound of claim 1, wherein R^5 is methyl, methoxy or difluoromethoxy.

14. The compound of claim 1, wherein R^5 is chlorine or fluorine.

15. The compound of claim 1, wherein R^6 is hydrogen.

16. The compound of claim 1, wherein R^5 and R^6 are hydrogen, R^3 is selected from the group consisting of C_1-C_2 alkyl and C_1-C_2 alkoxy, and R^4 is selected from the group consisting of hydrogen, C_1-C_4 alkyl, or cyclopropylmethyl.

17. The compound of claim 1, wherein

X is a bond or a group N—R^4;

R^1 is hydrogen or methyl;

R^2 is hydrogen;

R^3 is hydrogen, C_1-C_2 alkyl, C_1-C_2 alkoxy ;

R^4 is hydrogen, methyl, ethyl, n-propyl, isopropyl or cyclopropylmethyl;

R^5 is hydrogen, methyl or methoxy;

R^6 is hydrogen; and

n is 1 or 2.

18. The compound of claim 17, wherein R^3 is methyl.

19. The compound of claim 18, wherein R^5 is hydrogen.

20. The compound of claim 19, wherein R^4 is hydrogen.

21. The compound of claim 20, wherein R^1 is hydrogen.

22. The compound of claim 21, wherein X is a group N—R^4.

23. The compound of claim 22, wherein n is 1.

24. The compound of claim 23, wherein the $OCHF_2$-radical in formula I is located on the benzene ring in the ortho-position with respect to X.

25. The compound of claim 23, wherein the $OCHF_2$-radical in formula I is located on the benzene ring in the meta-position with respect to X.

26. The compound of claim 23, wherein the $OCHF_2$-radical in formula I is located on the benzene ring in the para-position with respect to X.

27. A pharmaceutical composition comprising at least one compound of claim 1, optionally together with at least one physiologically acceptable carrier or auxiliary substance.