maintenance (Flamm et al., Obstet. Gynecol., 70, 1987, 70 – 12), wound healing and infection, mastitis and placenta delivery, and osteoporosis. Additionally, oxytocin agonists may be useful for the diagnosis of both cancer and placental insufficiency.

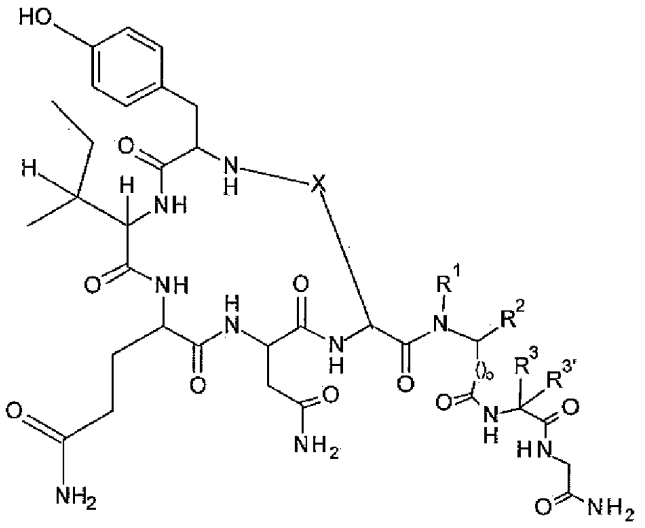
Furthermore, the Articles "Intranasal Oxytocin blocks alcohol withdrawal in human subjects" (Alcohol Clin Exp Res, Vol, No. 2012) and "Breaking the loop: Oxytocin as a potential treatment for drug addiction" (Hormones and Behavior, 61, 2012 , 331- 339) propose to treat alcohol withdrawal and drug addiction with a oxytocin agonist.

Oxytocin and its receptors exists in areas of the brain implicated in the symptoms of schizophrenia, such as the nucleus accumbens and the hippocampus. The oxytocin receptor agonists may be used for the treatment of autism, stress, including post traumatic stress disorder, anxiety, including anxiety disorders and depression, schizophrenia, Alzheimer's disease, psychiatric disorders, memory loss and metabolic diseases (WO2012/016229).

Objects of the embodiments disclosed herein are novel compounds of formula I and the use of compounds of formula I and their pharmaceutically acceptable salts for the treatment of CNS diseases related to the oxytocin receptor, which diseases are autism, stress, including post traumatic stress disorder, anxiety, including anxiety disorders and depression, schizophrenia, psychiatric disorders and memory loss, alcohol withdrawal,drug addiction and for the treatment of Prader-Willi Syndrom.

Further objects are the preparation of novel compounds of formula I and medicaments, containing them.

In one aspect, there is provided a compound of formula



I

wherein

R^1 is hydrogen, C_{1-7}-alkyl or C_{3-6}-cycloalkyl;

R^2 is hydrogen;

R^3 is hydrogen, C_{1-7}-alkyl, C_{1-7}-alkyl substituted by hydroxy, $-(CH_2)_2C(O)NH_2$, benzyl, phenyl, $-CH_2$-five membered aromatic heterocyclic group, CH_2-indolyl, $-CH_2-C_{3-6}$-cycloalkyl, C_{3-6}-cycloalkyl or $-(CH_2)_2-S-C_{1-7}$-alkyl;

$R^{3'}$ is hydrogen or C_{1-7}-alkyl; or

Xis $-C(O)-CHR^4-CHR^{4'}-C(O)-NH-CH_2-$

$R^4/R^{4'}$ are hydrogen or one of R^4 or $R^{4'}$ is amino:

o is 0 or 1;

or a pharmaceutically acceptable acid addition salt, a racemic mixture or its corresponding enantiomer and/or optical isomers thereof.

The present disclosure may provide selective, efficacious compounds, providing alternatives and/or improvements in the treatment of certain CNS diseases including autism, stress, including post traumatic stress disorder, anxiety, including anxiety disorders and depression, schizophrenia, psychiatric disorders and memory loss, alcohol withdrawal, drug addiction and for the treatment of Prader-Willi Syndrom.

In another aspect, there is provided a pharmaceutical composition comprising a compound as defined herein and a pharmaceutical acceptable carrier and/or adjuvant.

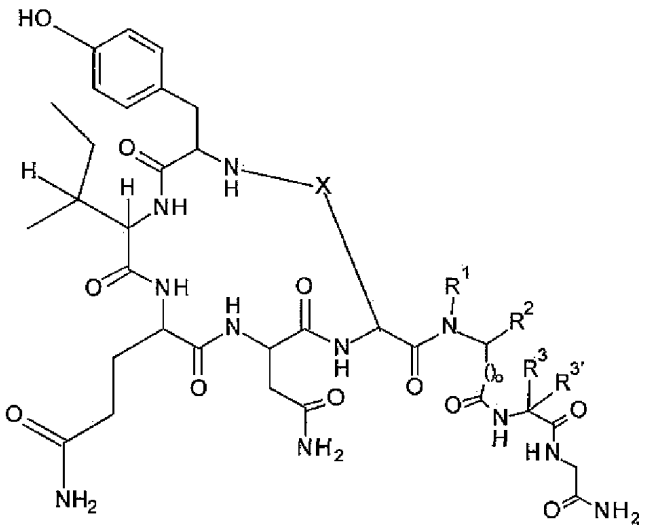
In another aspect, there is provided a pharmaceutical composition comprising a compound as defined herein and a pharmaceutical acceptable carrier and/or adjuvant for use in the treatment of autism, stress, including post traumatic stress disorder, anxiety, including anxiety disorders and depression, schizophrenia, psychiatric disorders and memory loss, alcohol withdrawal, drug addiction and for the treatment of Prader-Willi Syndrom.

In another aspect, there is provided a compound as defined herein for use as therapeutic active substances.

In another aspect, there is provided a compound as defined herein for use as therapeutic active substances in the treatment of autism, stress, including post traumatic stress disorder, anxiety, including anxiety disorders and depression, schizophrenia, psychiatric disorders and memory loss, alcohol withdrawal, drug addiction and for the treatment of Prader Willi Syndrom.

Claims

1. A compound of formula



I

wherein

R^1 is hydrogen, C_{1-7}-alkyl or C_{3-6}-cycloalkyl;

R^2 is hydrogen;

R^3 is hydrogen, C_{1-7}-alkyl, C_{1-7}-alkyl substituted by hydroxy, $-(CH_2)_2C(O)NH_2$, benzyl, phenyl, $-CH_2$-five membered aromatic heterocyclic group, CH_2-indolyl, $-CH_2-$ C_{3-6}-cycloalkyl, C_{3-6}-cycloalkyl or $-(CH_2)_2-S-$ C_{1-7}-alkyl;

$R^{3'}$ is hydrogen or C_{1-7}-alkyl; or

X is $-C(O)-CHR^4-CHR^{4'}-C(O)-NH-CH_2-$

$R^4/R^{4'}$ are hydrogen or one of R^4 or $R^{4'}$ is amino:

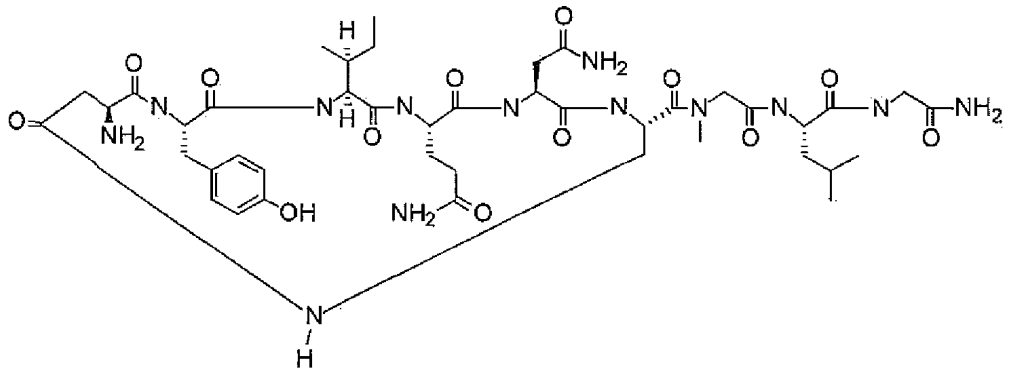
o is 0 or 1;

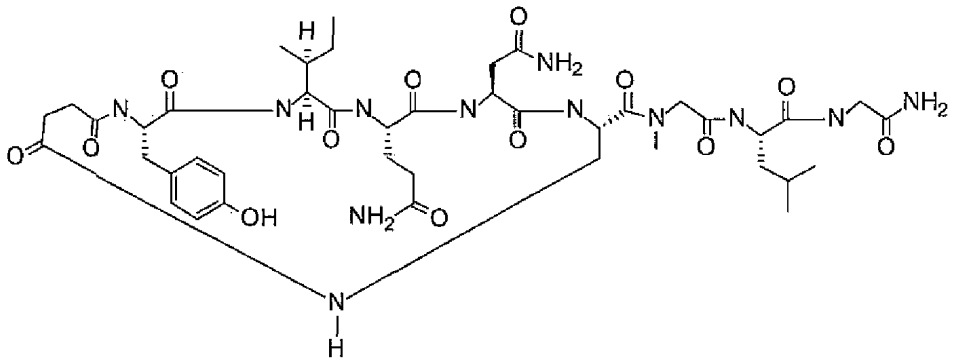
or a pharmaceutically acceptable acid addition salt, a racemic mixture or its corresponding enantiomer and/or optical isomers thereof.

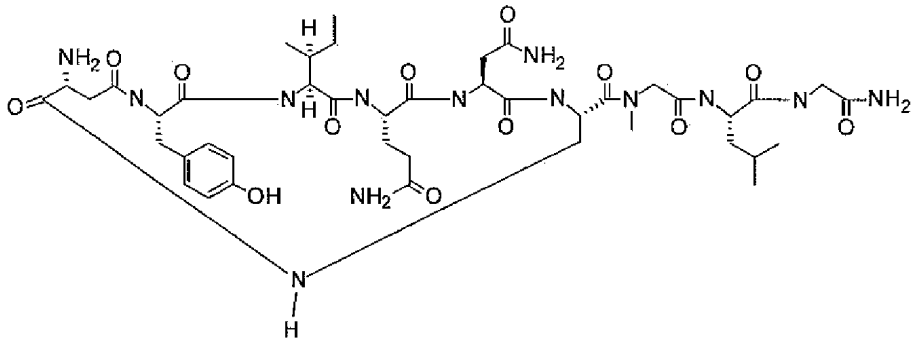
2. A compound of formula I according to claim 1, wherein R^1 is methyl or cyclopropyl.

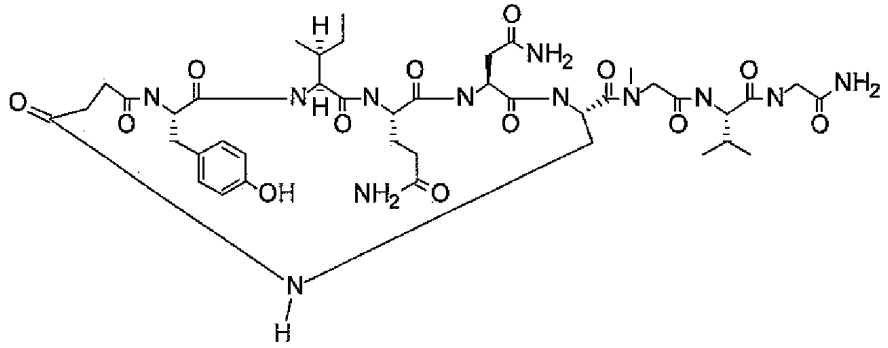
3. A compound of formula I according to claim 1, wherein o is 0.

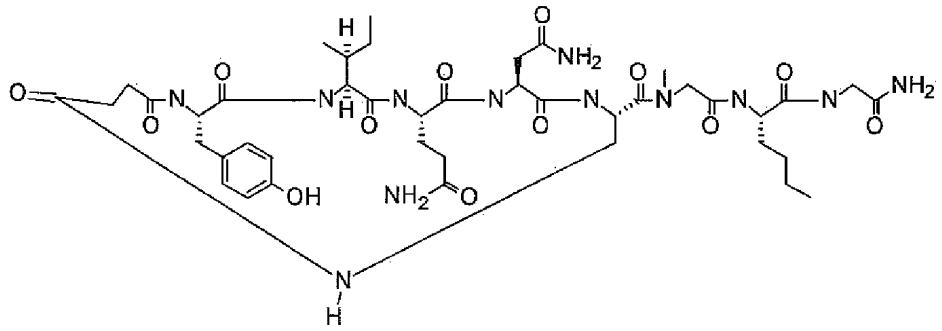
4. A compound of formula I accoccording to claim 1, wherein the compounds are

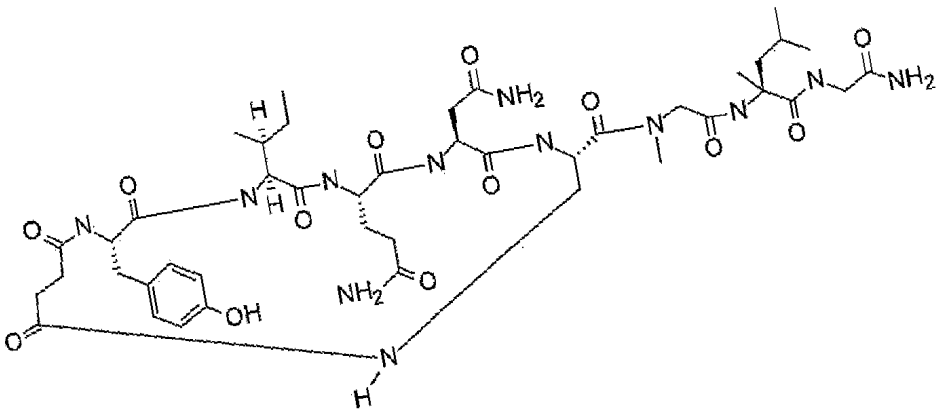


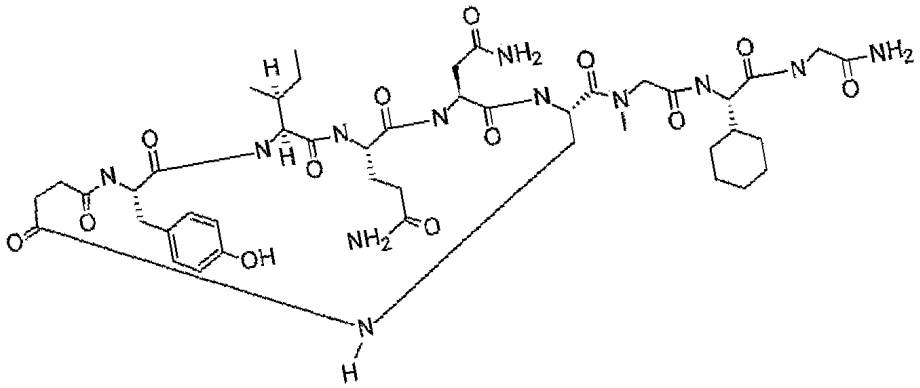


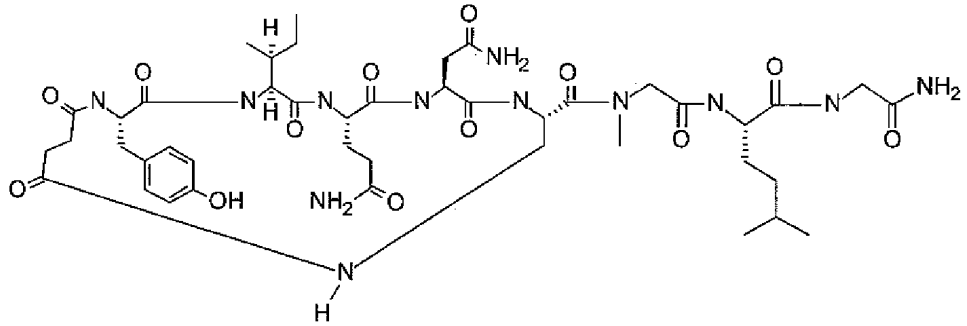


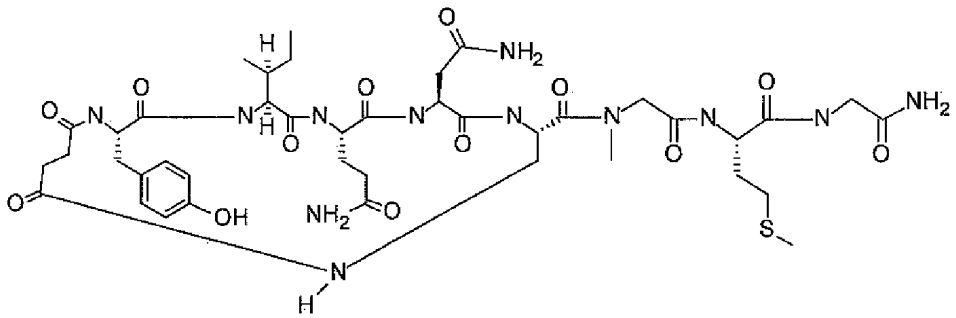


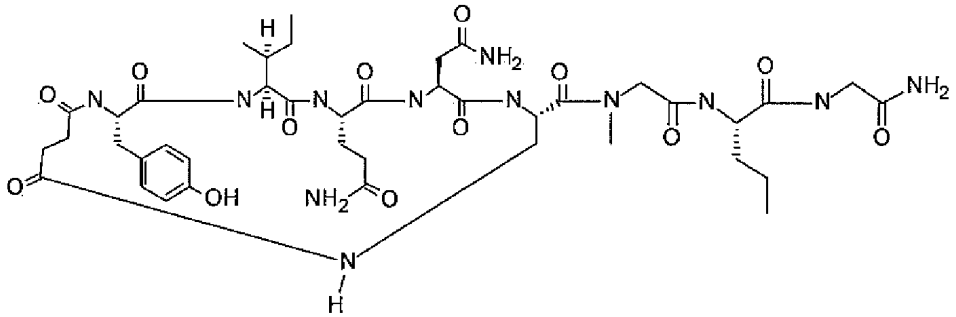


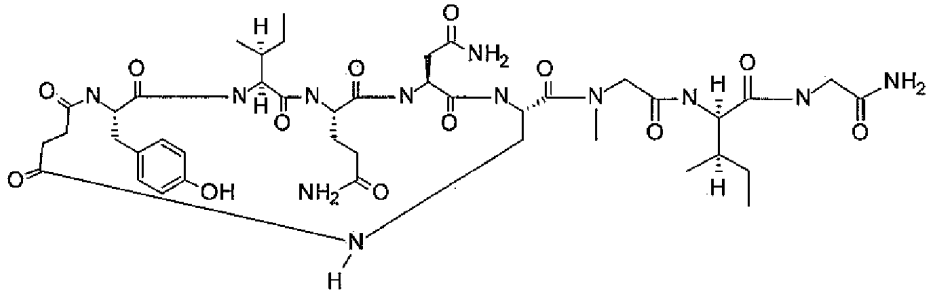


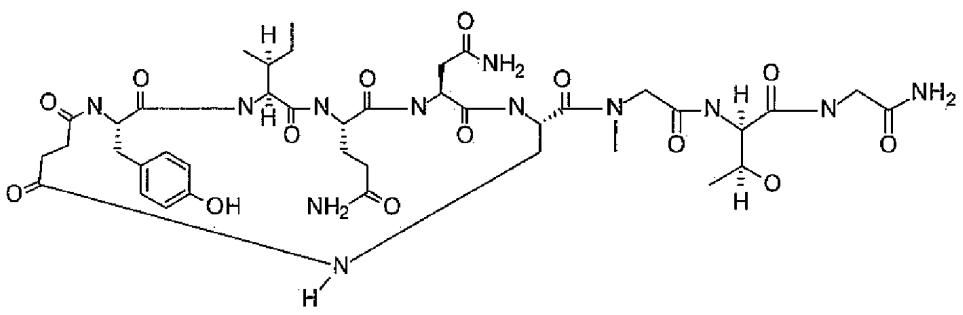


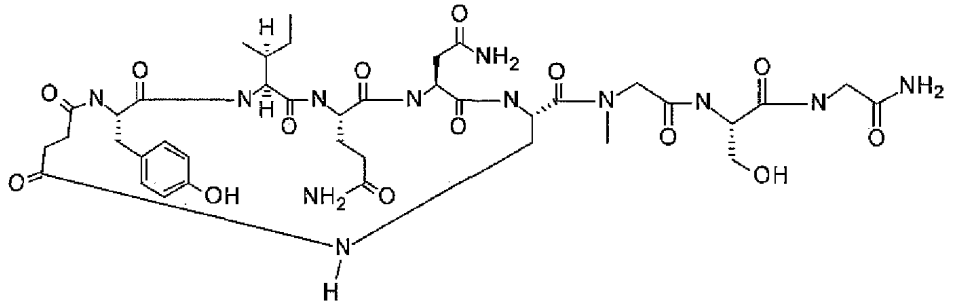


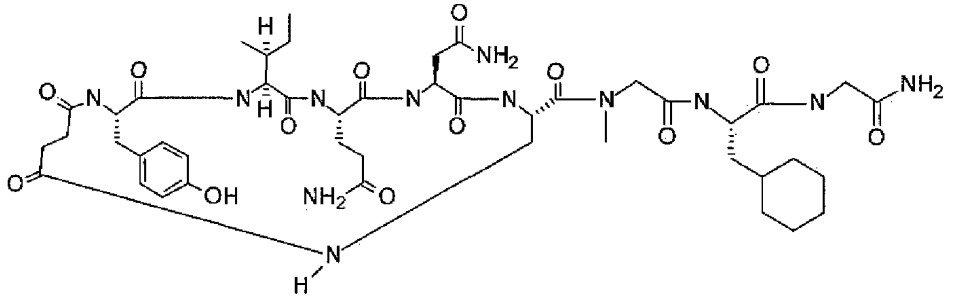


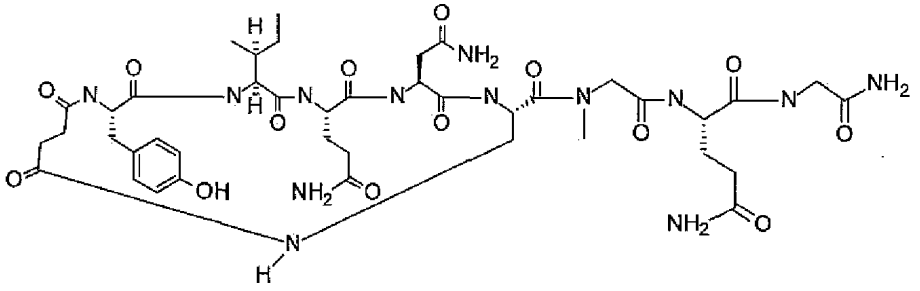


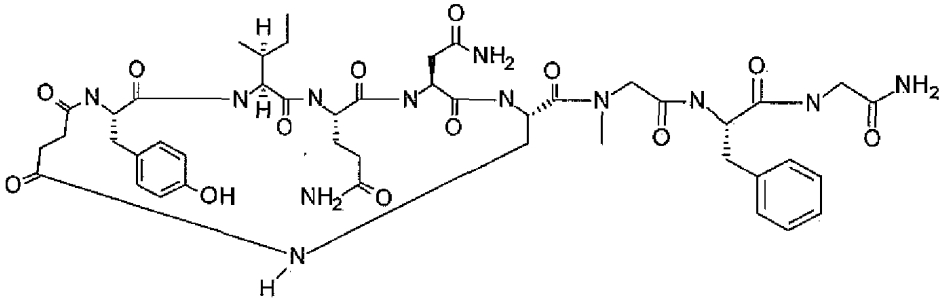


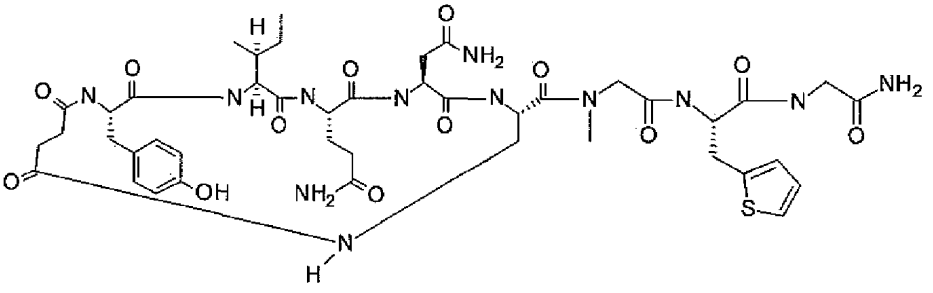


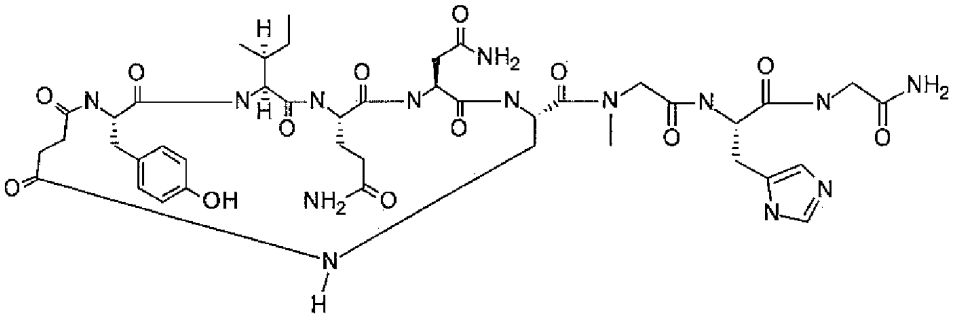


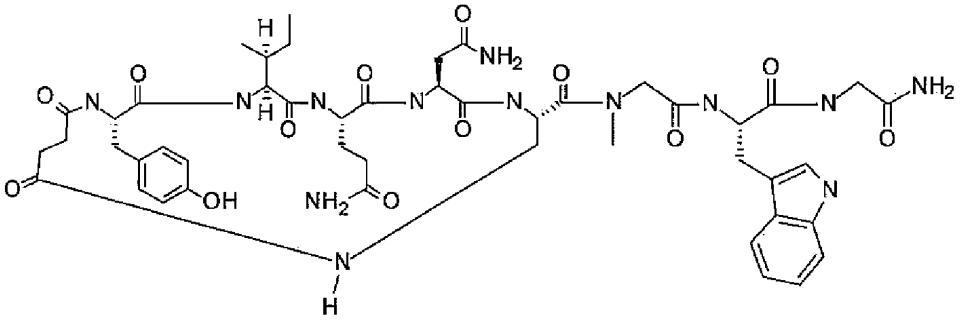


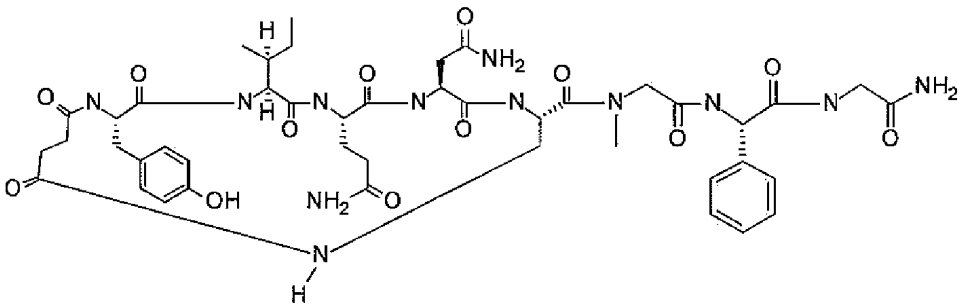


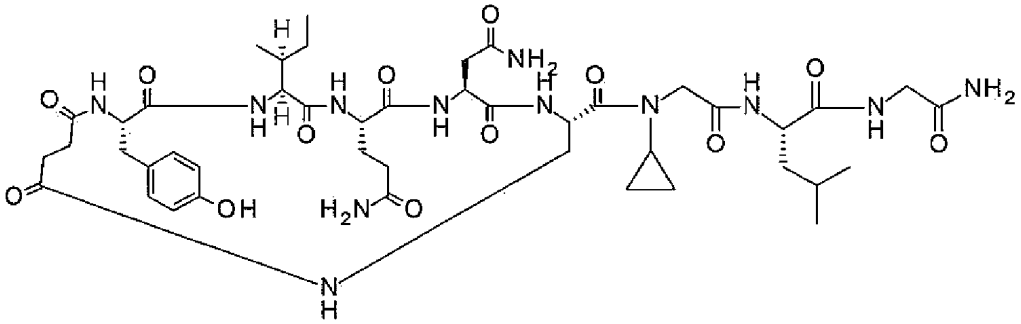


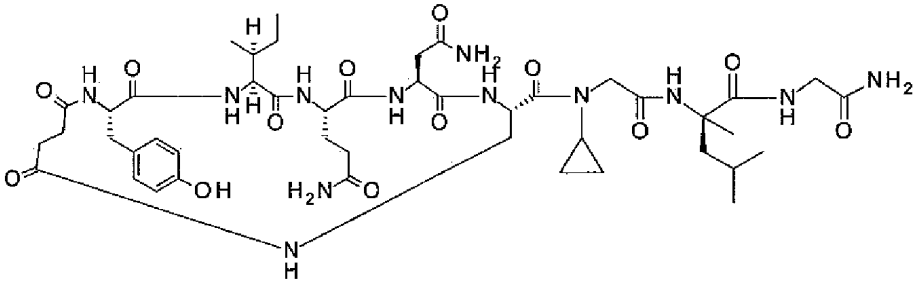


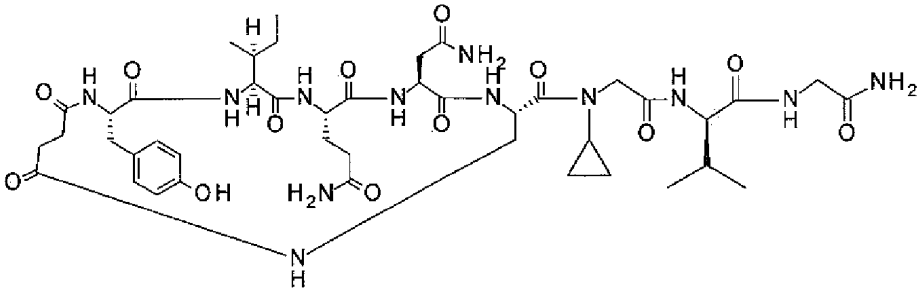


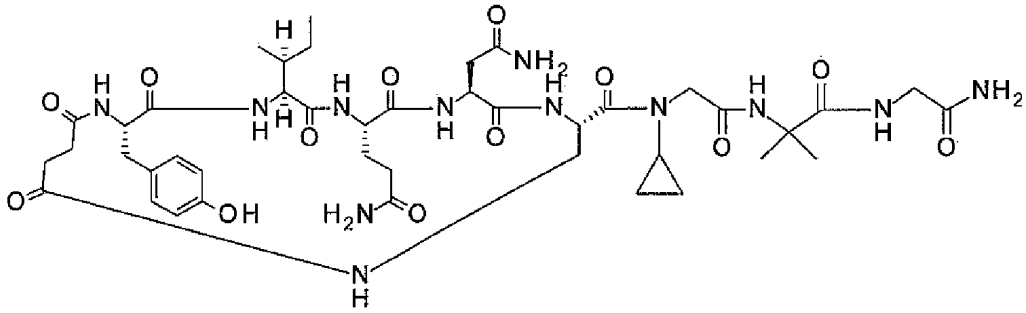


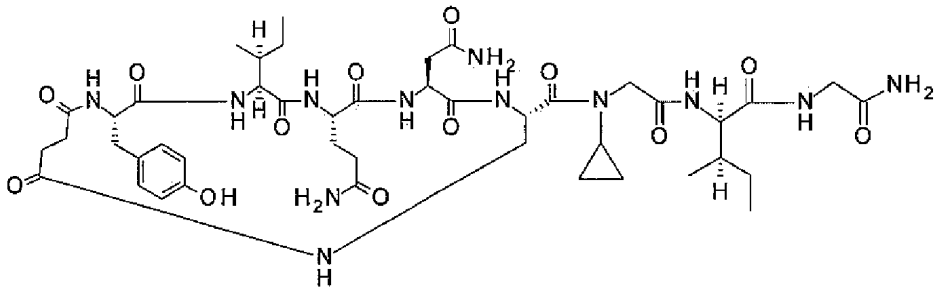


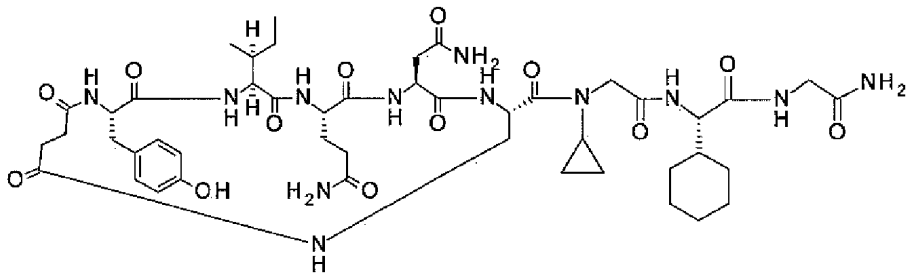


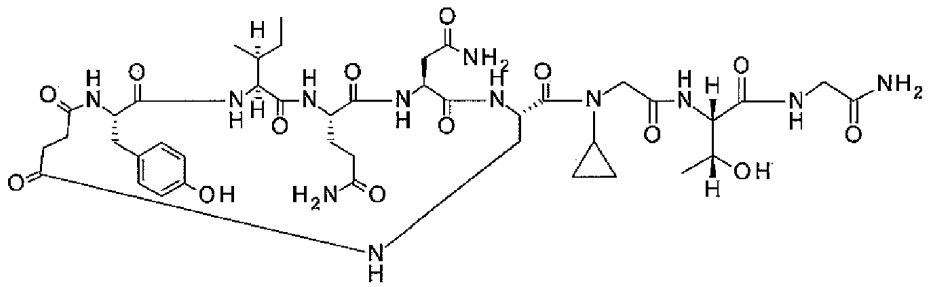


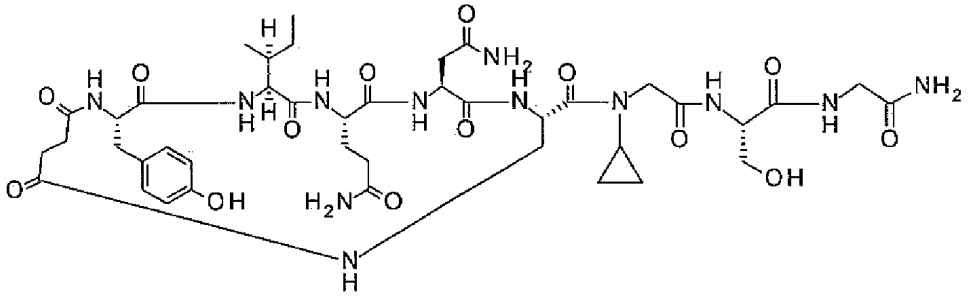












5. A pharmaceutical composition comprising a compound according to any one of claims 1 – 4 and a pharmaceutical acceptable carrier and/or adjuvant.

6. A pharmaceutical composition comprising a compound according to any one of claims 1–4 and a pharmaceutical acceptable carrier and/or adjuvant for use in the treatment of autism, stress, including post traumatic stress disorder, anxiety, including anxiety disorders and depression, schizophrenia, psychiatric disorders and memory loss, alcohol withdrawal, drug addiction and for the treatment of Prader-Willi Syndrom.

7. A compound according to any one of claims 1–4 for use as therapeutic active substances.

8. A compound according to any one of claims 1–4 for use as therapeutic active substances in the treatment of autism, stress, including post traumatic stress disorder, anxiety, including anxiety disorders and depression, schizophrenia, psychiatric disorders and memory loss, alcohol withdrawal, drug addiction and for the treatment of Prader Willi Syndrom.

9. The use of a compound according to any one of claims 1–4 for the preparation of medicaments for the therapeutic and/or prophylactic treatment of autism, stress, including post traumatic stress disorder, anxiety, including anxiety disorders and depression, schizophrenia, psychiatric disorders and memory loss, alcohol withdrawal, drug addiction and for the treatment of Prader-Willi Syndrom.