COMMONWEALTH of AUSTRALIA
PATENTS ACT 1952
APPLICATION FOR A STANDARD PATENT

CONCERN PHARMA of Route de Rehipont, 60-1328
OHAIN, Belgium
29896/84

We hereby apply for the grant of a Standard Patent for an invention entitled:

2-PENTANOYLAMINOACETIC ACID AND SALTS THEREOF

which is described in the accompanying specification.

Details of basic application:

Number: 84891
Convention Country: LUXEMBOURG
Date: June 30, 1983

The address for service is care of DAVIES & COLLISON, Patent Attorneys, of 1 Little Collins Street, Melbourne, in the State of Victoria, Commonwealth of Australia.

Dated this 26th day of June 1984.

[Signature]

For THE COMMISSIONER OF PATENTS

Davies & Collison, Melbourne and Canberra.
DECLARATION IN SUPPORT OF A CONVENTION OR NON-CONVENTION APPLICATION FOR A PATENT OR PATENT OF ADDITION

In support of the application made by ____________________________________________
for a patent for an invention entitled ____________________________________________

2-PENTANOYLAMINOACETIC ACID AND SALTS THEREOF

I/we, GEORGE KENNETH OBERHAUSEN of CONTINENTAL PHARMA of Route de Renipont, 50-1328 Ohain, Belgium.
do solemnly and sincerely declare as follows:

1. I am/we are the applicant(s) for the patent, or am / are authorised by the abovementioned applicant to make this declaration on its behalf.

2. The basic application(s) as defined by Section 141 of the Act was/were made in the following country or countries on the following date(s) by the following applicant(s) namely:

   Country, date and name of Applicant(s) for each basic application

   in Luxembourg on 30 June 1983
   by Continental Pharma

   in ____________________________________________ on ____________________________________________ 19
   by ____________________________________________

   ____________________________________________
   ____________________________________________
   ____________________________________________

3. The said basic application(s) was/were the first application(s) made in a Convention country in respect of the invention the subject of the application.

4. The actual inventor(s) of the said invention is/are Robert CAVALIER, Alexis COUDI, Claude GILLET, Philippe JANSSENS de VAREBEEKE, Paul NIEBES, Joseph ROBA, William VAN DORSSE, Georges LAMBERTIN, Michel FRANZ (see over for addresses)

5. The facts upon which the applicant(s) is/are entitled to make this application are as follows: The applicant would, if a patent were granted upon an application made by the said inventors, be entitled to have the patent assigned to it.

   DECLARED at Brussels this 29 day of May 1954

G.K. Oberhausen
Administrateur-déléguée
(Managing Director)

This form may be completed and filed after the filing of a patent application but the form must not be signed until after it has been completely filled in as indicated by the marginal notes. The place and date of signing must be filled in. Company stamps or seals should not be used.
4. Cont'd.

of rue de la Taillette, 2 a - 1330 Rixensart, Belgium
rue Inchebroux, 30 - 5890 Gistoux, Belgium
rue des Lovières, 14 - 5860 Blamont, Belgium
rue de la Bryle, 37 - 5989 Bossut-Gottechain, Belgium
rue du Lambais, 64 - 5980 Grez-Dolceau, Belgium
rue du Village, 1 - 1302 Dion-Valmont, Belgium
avenue de Wilsterzee, 62 - 1490 Court St-Etienne, Belgium
rue Cervantés, 31 -1190 Bruxelles, Belgium and
avenue du Haut-Champ, 52 - 1080 Bruxelles, Belgium,
respectively.
**Claim**

1. 2-pentanoylaminoacetic acid or a pharmaceutically acceptable salt thereof as a pharmaceuti- cal substance.
Complete specification for the invention entitled:

2-PENTANOYLAMINOACETIC ACID AND SALTS THEREOF

The following statement is a full description of this invention, including the best method of performing it known to us :-
This invention relates to 2-pentanoylaminocetic acid (I) and to pharmaceutical acceptable metal salts and addition salts with bases derived thereof, for use as pharmaceuticals.

\[
\text{CH}_3\text{(CH}_2)_3\text{-CO-NH-CH}_2\text{-COOH} \quad (I)
\]

The metal salts may be, for example, a sodium, a potassium, a lithium, a calcium, a magnesium, an aluminium or an iron salt. The addition salts may be formed by reaction with an inorganic base such as ammonia, or with an organic base which may be an aliphatic, a cycloaliphatic or an heterocyclic base, such as, for example, ethylamine, diethylamine, triethylamine, isopropylamine, ethanolamine, diethanolamine, triethanolamine. Said organic base may also be an amino-acid natural or not, such as, for example, lysine, ornithine or arginine.

A preferred salt of 2-pentanoylaminocetic acid is the sodium salt.

1. BACKGROUND OF THE INVENTION.

The compound of the present invention, 2-pentanoylaminocetic acid, is known for several years.

The publication of J. Katz et al., [C.A., 42].
describes the preparation of compound I.
In the form of its methyl ester, compound (I) has been isolated from cattle urine, and its structure has been confirmed by synthesis [S. Rikisaku et al., C.A. 81, 102,235v (1974); Agr. Biol. Chem., 38, 885-6 (1974)]. Other publications describe the synthesis of several acylglycines amongst which compound I, and the analysis of a mixture of these acylglycine derivatives by gaschromatography-mass spectrometry techniques, e.g. H.S. Ramsdell et al., J. Chromatogr., 181, 90-94 (1980); S.S. Tjoa et al., Clin. Chim. Acta, 95, 35-45 (1979).

However no biological activity of 2-pentanoylaminoacetic acid has been disclosed so far.

II. DESCRIPTION OF THE INVENTION.

It has surprisingly been found by the inventors that compound I and pharmaceutical acceptable salts thereof exhibit a potent anti-convulsant activity against convulsions induced by bicuculline in mice. This observation indicates that 2-pentanoylaminoacetic acid produces an effect on the central nervous system and in particular on the GABA-system, because as a matter of fact, bicuculline is known to be a specific antagonist of GABA (4-aminobutyric acid) [E. Roberts, Biochem. Pharmacol., 23, 2637-2649 (1974)].

It is clear that has also been found pharmaceutical compositions comprising compound I or a pharmaceutically acceptable salt thereof present great interest
for producing an effect on the central nervous
system, in particular in the treatment of various
forms of epilepsy, in the treatment of dyskinesiae
such as, for example, parkinsonism, in the treatment
of memory troubles, of psychic troubles such as, for
example, depression, and in the treatment of cerebral anoxia.

The activity of 2-pentanoylaminoacetic
acid and pharmaceutically acceptable salts thereof
has been evidenced by the pharmacological tests
described hereinafter.

II.1. Anti-convulsant activity.

The compounds tested, 2-pentanoylamino-
acetic acid (compound I), sodium 2-pentanoylamino-
acetate (compound II) or sodium valproate (a generally
accepted reference substance), have been administered
orally to 20 mice (CD1-Charles River) at a dose of
10 mg/kg as a suspension in a 1% tragacanth gum
mucilage. Administration has been done by means of
an intragastric tube.

Three hours later, bicuculline has been
administered at a dose of 0.7 mg/kg by intravenous
injection in the lateral vein of the tail.

The number of animals which exhibit tonic
extension has been noted and the results of the test
are represented in the form of "percentage of protec-
tion", i.e. the percentage of the animals which have
been protected against tonic extension.

The results obtained are given hereinafter and they clearly indicate that a potent anti-
convulsant activity is effected by the drugs
tested.
The anti-convulsant activity of the compounds has been further evaluated, using the technique described hereinabove, by examining the effect at different doses. From the experimental data, the ED₅₀ value has been calculated, i.e. the effective dose (mg/kg) providing protection against tonic extension of 50% of the animals. The results obtained are the following:

<table>
<thead>
<tr>
<th>Compound</th>
<th>% of protection</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-pentanoylaminooacetic acid</td>
<td>55</td>
</tr>
<tr>
<td>sodium 2-pentanoylaminooacetate</td>
<td>55</td>
</tr>
<tr>
<td>sodium valproate</td>
<td>40</td>
</tr>
</tbody>
</table>

These data indicate that 2-pentanoylaminooacetic acid and its sodium salt are more potent than sodium valproate in this test.

II. 2. Toxicity.

In further pharmacological tests the acute toxicity and the effect on behaviour have been examined. The effect on behaviour has been studied using a method derived from the one of S. Irvin (Gordon Res. Conf. on Medicinal Chemistry, p. 1933 (1959) as cited by R.A. Turner (Screening Methods in Pharmacology, Acad. Press, 1965, Chapter III, pages 22-34)).

The drug to be tested has been adminis-
tered orally as a 1% tragacanth gum mucilage, by means of an intragastric tube to groups of 3 or 5 mice, fasted for 18 hours. The compounds have been tested at a dose decreasing in a logarithmic way, starting from 3000 mg/kg, i.e. 3000, 1000, 300, 100, 30 and 10 mg/kg. No further testing has been made when a dose has been reached at which no abnormal behaviour or toxicity has been observed. Behaviour has been studied 2, 4, 6 and 24 hours after treatment and the observation has been extended if symptoms persisted at that moment. The deaths were registered for 14 days following the treatment. These observations allowed to determine the MTD value, i.e. the maximal tolerated dose, which is the maximal dose (mg/kg) which does not induce side effects or toxicity. The data so obtained are the following:

<table>
<thead>
<tr>
<th>Compound</th>
<th>MTD mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-pentanoylaminoacetic acid (I)</td>
<td>&gt;3000</td>
</tr>
<tr>
<td>sodium 2-pentanoylaminoacetate (II)</td>
<td>&gt;3000</td>
</tr>
<tr>
<td>sodium valproate</td>
<td>30</td>
</tr>
</tbody>
</table>

The LD_{50} value, i.e. the dose expressed in mg/kg which is lethal for 50% of the animals, has been calculated according to the Litchfield and Wilcoxon method [J. Pharmacol. Exp. Ther., 96, 99 (1949)].

The results obtained are shown hereinafter:

<table>
<thead>
<tr>
<th>Compound</th>
<th>LD_{50} mg/kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-pentanoylaminoacetic acid (I)</td>
<td>&gt;3000</td>
</tr>
<tr>
<td>sodium 2-pentanoylaminoacetate (II)</td>
<td>&gt;3000</td>
</tr>
<tr>
<td>sodium valproate</td>
<td>2250</td>
</tr>
</tbody>
</table>
It clearly results from these data that the toxicity and the effect on behaviour of 2-pentanoylaminoacetic acid and its sodium salt are very weak and it has to be noticed that at a dose of 3000 mg/kg per os no deaths have been observed for none of both compounds.

Hence 2-pentanoylaminoacetic acid and its sodium salt are better than sodium valproate; their superiority is evidenced quantitively by means of the therapeutical indexes TI-A and TI-B which corresponds, respectively, to the ratio of the LD_{50}/ED_{50} values and to the ratio of the MTD/ED_{50} values. The values of these therapeutical indexes are the following:

<table>
<thead>
<tr>
<th>Compound</th>
<th>TI-A (LD_{50}/ED_{50})</th>
<th>TI-B (MTD/ED_{50})</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-pentanoylaminoacetic acid (I)</td>
<td>&gt; 280</td>
<td>&gt; 280</td>
</tr>
<tr>
<td>Sodium 2-pentanoylaminoacetate (II)</td>
<td>&gt; 326</td>
<td>&gt; 326</td>
</tr>
<tr>
<td>Sodium valproate</td>
<td>78</td>
<td>1</td>
</tr>
</tbody>
</table>

The pharmacological data mentioned hereinbefore are evidencing the presence of potent anti-convulsant activity combined with weak toxicity and, hence, are emphasizing the pharmaceutical interest of 2-pentanoylaminoacetic acid and its suitable salts.

Compound I, 2-pentanoylaminoacetic acid, can be prepared by various art-known methods, one of which is indicated in scheme 1, hereinafter, given as a non limiting example.
Scheme 1.

\[ n.C_4H_9-\text{CO-A} + H_2N-Y \rightarrow n.C_4H_9-\text{CO-NH-Y} \rightarrow \]

III        IV                V

\[ n.C_4H_9-\text{CO-NH-CH}_2-\text{COOH} \]

In formula III, A is such that the radical \(-\text{CO-A}\) represents, for example, a carboxylic group, an alkoxy carbonyl group, an acide halide group, an anhydride group, a carbamoyl group or a \(N\)-carbonyl-imidazole group.

In formula IV and V, Y represents:

- either the \(\text{CH}_2-\text{COOH}\) group,
- either a precursor of said \(\text{CH}_2-\text{COOH}\) group, such as:
  - the \(-\text{CH}_2-Z\) group wherein Z represents, for example, an alkoxy carbonyl group or a formyl group optionally used in a protected form such as, e.g., a dithioacetal group, which may be cyclic or not.
  - the \(-\text{CH}_{B_1}B_2\) group wherein \(B_1\) and \(B_2\), which can be identical or not, represent, for example, an alkoxy carbonyl group on a carboxylic group.

According to the nature of the functional groups and to the reaction conditions, the acylation of amine IV by reagent III can directly yield compound I or a salt thereof, or yield intermediate V, which optionally can be isolated or not, before it is converted into compound I or a salt thereof.

According to the nature of the \(-\text{CO-A}\) group, the acylation is usually carried out by
reacting compound III with at least two equivalents of amine IV, or with one equivalent of amine IV and at least one equivalent of an organic or inorganic base, such as, for example, a tertiary amine, pyridine, an hydroxyde or a carbonate of an alkali or earthalkali metal. Usually, the reaction is carried out in an inert solvent or an excess of the organic base is used as solvent. If the -CO-A group, in reagent III, represents a carboxylic group, then the acylation of compound IV is classically made in the presence of a dehydrating agent such as, for example, phosphorus pentoxyde, or of a coupling agent such as, for example, dicyclohexylcarbodiimide or 1,1'-carbonyldiimidazole. If Y, in the intermediate V, represents a precursor of the -CH₂-COOH group, it is converted into said carboxymethyl group by well-known methods, chosen according to the nature of the group Y, such as, for example:

- by hydrolysis, carried out in an aqueous or alcoholic-aqueous medium in the presence of an acidic or basic catalyst,
- by oxydation, optionally combined with hydrolysis or proceeded by deprotection of the functional group,
- by decarboxylation in acidic medium at elevated temperature, optionally proceeded by hydrolysis.

It is clear that all reagents and reaction conditions used to achieve the acylation of compound IV and the conversion of compound V into compound I have to be chosen in such a way as to avoid undesired secondary reactions or degradation
of the molecule. In case 2-pentanoylaminoacetic acid is obtained as the free carboxylic acid it can easily be converted by art-known methods into its suitable metal salts, for example, by treatment in aqueous medium with the corresponding metal hydro-

xydes, carbonates or bicarbonates, or into its suitable addition salts by reaction in an inert solvent with the corresponding organic base. If, on the contrary, 2-pentanoylaminoacetic acid is obtained in the form of a metal or an addition salt, it can be transformed into the free carboxylic form by treatment with a suitable acid. Conversion of one salt into another salt can also be made by art-known methods. The preparation of 2-pentanoylaminoacetic acid and the sodium salt thereof is illustrated hereinafter by a non limiting example.

**Example 1: Synthesis of 2-pentanoylaminoacetic acid (compound I).**

\[
\begin{align*}
\text{CH}_3-(\text{CH}_2)_3-\text{CO-Cl} + \text{H}_2\text{N-CH}_2-\text{COOH} & \quad 1.\text{NaOH} \\
& \quad 2.\text{HCl} \\
\text{CH}_3-(\text{CH}_2)_3-\text{CO-NH-CH}_2-\text{COOH}
\end{align*}
\]

At \(0^\circ\text{C}\), \(10\) g \((0,133\) mole\) of glycine are dissolved in \(33,3\) ml \(4\text{N}\) \((0,133\) mole\) sodium hydroxyde. Then, with vigourous stirring, \(16\) g \((0,133\) mole\) pentanoylchloride and \(33,3\) ml \(4\text{N}\) sodium hydroxyde \((0,133\) mole\) are simultaneously added to the mixture. It is stirred until the characteristic smell of the acid chloride has disappeared, then acidified at \(0^\circ\text{C}\) with concentrated hydrochloric acid and extracted with ethyl acetate. The organic solution
is dried and the solvent is removed at diminished pressure. The residue is recrystallized from toluene, which yields 2-pentanylaminoacetic acid.

Melting point: 82°C

Elemental analysis:

<table>
<thead>
<tr>
<th></th>
<th>C</th>
<th>H</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>% calculated</td>
<td>52.82</td>
<td>8.23</td>
<td>8.50</td>
</tr>
<tr>
<td>% found</td>
<td>52.46</td>
<td>8.27</td>
<td>8.83</td>
</tr>
</tbody>
</table>

Example 2: Synthesis of sodium 2-pentanylaminoacetate (compound II).

\[
\text{CH}_3\text{(CH}_2\text{)}_3\text{CO-Cl + H}_2\text{N-CH}_2\text{-COO}Na \xrightarrow{\text{NaOH}} \text{CH}_3\text{(CH}_2\text{)}_3\text{CO-NH-CH}_2\text{-COO}Na
\]

At 0°C, 10 g (0.133 mole) of glycine are dissolved in 33.3 ml 4N (0.133 mole) sodium hydroxyde. Then, with vigourous stirring, 16 g (0.133 mole) pentanylyl chloride and 33.3 mole 4N (0.133 mole) sodium hydroxyde are simultaneously added. The mixture is stirred until the characteristic smell of the acid chloride has disappeared, then all water is distilled off and the residue is extracted by boiling isopropanol. The first crop of the crystallization yields sodium pentanoate. The next crops, obtained by cooling of the isopropanol solution, yield crude sodium 2-pentanylaminoacetate, which is purified by crystallization from ethanol.

Melting point: 190°C

Elemental analysis:

<table>
<thead>
<tr>
<th></th>
<th>C</th>
<th>H</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>% calculated</td>
<td>46.40</td>
<td>6.67</td>
<td>7.73</td>
</tr>
<tr>
<td>% found</td>
<td>46.00</td>
<td>6.66</td>
<td>7.69</td>
</tr>
</tbody>
</table>

In view of the pharmaceutical use of 2-pentanylamino-
acetic acid various pharmaceutical compositions may be formulated in order to be administered orally, rectally or parenterally, containing at least an effective amount of said compound or a salt thereof, usually in the presence of at least one pharmaceutical excipient. Thus, for example, the compositions to be administered orally can be liquids or solids and exist as tablets, sugar-coated pills, coated tablets, capsules, granules, powders, syrups or suspensions. The dry oral formulations comprise adjuvants and excipients commonly used in galenic pharmacy, inert diluents, disintegration agents, binders and lubricants, such as lactose, starch, talc, gelatin, stearic acid, cellulose and derivatives thereof, silicilic acid, magnesium stearate, polyvinylpyrrolidone, calcium phosphate, calcium carbonate and the like.

Such preparations can be made in order to prolong disintegration and consequently the active duration of the active element.

The aqueous suspensions, the emulsions and the oily solutions are prepared in the presence of sweetening agents, such as dextrose or glycerol, flavouring agents, such as vanillin for example, and can also contain thickening agents, wetting agents and preservation agents.

The oily emulsions and solutions are prepared in an oil of vegetal or animal origin and can contain emulsifiers, flavouring, dispersing, sweetening and antioxidant agents. For parenteral administration, sterile water, an aqueous polyvinylpyrrolidone...
The compositions to be administered rectally may be solids or liquids and may be presented in the form of suppositories, of gels, of solutions, of emulsions or of suspensions.

The suppositories may be prepared using fats such as cacao butter or semi-synthetic substances derived from triglycerides, or using hydrophilic products such as mixtures of polyethylene glycols.

The daily dose for administration of compound I or a salt thereof will be 100 mg to 5 g. In order to facilitate their use and their administration, the aforementioned pharmaceutical compositions are usually formulated in dosage unit form, the unit dose being 100 mg to 1 g. However, if necessary, the daily dose may be increased without danger, due to the low toxicity of compound I and its pharmaceutical suitable salts.

Hereinafter, a few galenic formulations in dosage unit form are given, suitable for systematic administration to human beings in accordance with the present invention. These examples are given as non limiting illustrations of the aforementioned pharmaceutical compositions. In these examples, the active product is designated by "compound A", which is either 2-pentanoylaminoacetic acid either sodium 2-pentanoylaminoacetate.
<table>
<thead>
<tr>
<th>Time (min)</th>
<th>Compound</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>30</td>
<td>Compound A</td>
<td>polyvinylpyrrolidone 10 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>corn starch 100 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>cutina HR R 10 mg</td>
</tr>
<tr>
<td>25</td>
<td>Compound A</td>
<td>gelatin 8 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>magnesium stearate 12 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>corn starch 20 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>lactose 110 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compound A 200 mg</td>
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<td>20</td>
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<td>magnesium stearate 2 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>talc 5 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>aerosil R 5 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>lactose 188 mg</td>
</tr>
<tr>
<td>15</td>
<td>Compound A</td>
<td>Compound A 100 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>magnesium stearate 15 mg</td>
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<td></td>
<td></td>
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</tr>
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<td></td>
<td></td>
<td>lactose 188 mg</td>
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<td>Compound A 500 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>corn starch 34 mg</td>
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<tr>
<td></td>
<td></td>
<td>Silartex R 25 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Aerosil 1 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Pharmacoat 606 R 15 mg</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compound A corn starch</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compound A starch Sta-RX</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compound A calcium phosphate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compound A magnesium stearate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compound A lactose</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compound A talc</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Compound A magnesium stearate</td>
</tr>
</tbody>
</table>

*Tables.*

<table>
<thead>
<tr>
<th>Tablets.</th>
<th>Compound A</th>
<th>500 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>corn starch</td>
<td>34 mg</td>
<td></td>
</tr>
<tr>
<td>Silartex R</td>
<td>25 mg</td>
<td></td>
</tr>
<tr>
<td>Aerosil R</td>
<td>1 mg</td>
<td></td>
</tr>
<tr>
<td>Pharmacoat 606 R</td>
<td>15 mg</td>
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</tr>
<tr>
<td></td>
<td>Tablets.</td>
<td>Compound A</td>
</tr>
<tr>
<td>starch Sta-RX 1500 R</td>
<td>180 mg</td>
<td></td>
</tr>
<tr>
<td>calcium phosphate</td>
<td>100 mg</td>
<td></td>
</tr>
<tr>
<td>aerosil R</td>
<td>5 mg</td>
<td></td>
</tr>
<tr>
<td>magnesium stearate</td>
<td>15 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tablets.</td>
<td>Compound A</td>
</tr>
<tr>
<td>corn starch</td>
<td>100 mg</td>
<td></td>
</tr>
<tr>
<td>lactose</td>
<td>188 mg</td>
<td></td>
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<tr>
<td>aerosil R</td>
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<td></td>
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<tr>
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<td></td>
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<tr>
<td>magnesium stearate</td>
<td>2 mg</td>
<td></td>
</tr>
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<td>Compound A</td>
</tr>
<tr>
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<td>corn starch</td>
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</tr>
<tr>
<td>magnesium stearate</td>
<td>12 mg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Capsules.</td>
<td>Compound A</td>
</tr>
<tr>
<td>polyvinylpyrrolidone</td>
<td>10 mg</td>
<td></td>
</tr>
<tr>
<td>corn starch</td>
<td>100 mg</td>
<td></td>
</tr>
<tr>
<td>cutina HR R</td>
<td>10 mg</td>
<td></td>
</tr>
</tbody>
</table>
I.M. or I.V. injectables.

- Compound A: 100 mg
- Sodium chloride: 20 mg
- Sodium acetate: 6 mg
- Distilled water for injectables: ad 5 ml

I.M. injectables.

- Compound A: 200 mg
- Benzylbenzoate: 1 mg
- Oil for injection: ad 5 ml

Syrup (containing a unit dose of 100 mg per 2 milliliters).

- Compound A: 5 g
- Citric acid: 0.5 g
- Nipasept®: 0.1 g
- Saccharose: 70 g
- Flavouring agent: 0.1 g
- Water: ad 100 ml

Solution (containing a unit dose of 100 mg per milliliters).

- Compound A: 2 g
- Sorbitol: 50 g
- Glycerin: 10 g
- Anise essence: 0.1 g
- Propylene glycol: 10 g
- Demineralized water: ad 100 ml

Suppositories.

- Compound A: 250 mg
- Butylhydroxyanisol: 10 mg
- Semi-synthetic glycerids: ad 3 g

R = registered trademark.
CLAIMS
THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. 2-pentanoylaminoacetic acid or a pharmaceutically acceptable salt thereof as a pharmaceutical substance.

2. Sodium 2-pentanoylaminoacetate as a pharmaceutical substance.

3. 2-pentanoylaminoacetic acid or a pharmaceutically acceptable salt thereof, according to claim 1, as an active therapeutic substance for producing an effect on the central nervous system, in particular in the treatment of various forms of epilepsy, of dyskinesias, of parkinsonism, of memory troubles, of psychic troubles, of depression and of cerebral anoxia.

4. Sodium 2-pentanoylaminoacetate according to claim 3, as an active therapeutic substance for producing an effect on the central nervous system, in particular in the treatment of various forms of epilepsy, of dyskinesias, of parkinsonism, of memory troubles, of psychic troubles, of depression and of cerebral anoxia.

5. 2-pentanoylaminoacetic acid or sodium 2-pentanoylaminoacetate as a pharmaceutical substance with anti-epileptic properties.

6. Pharmaceutical composition containing 2-pentanoylaminoacetic acid or a pharmaceutically acceptable salt thereof as active substance.

7. Pharmaceutical composition containing sodium 2-pentanoylaminoacetate as active substance.

8. Pharmaceutical composition containing 2-pentanoylaminoacetic acid, or sodium 2-pentanoyl-
aminoacetate or another pharmaceutically acceptable salt derived from 2-pentanoylaminooacid, and at least one suitable excipient, for producing an effect on the central nervous system, in particular in the treatment of various forms of epilepsy, of dyskinesiae, of parkinsonism, of memory troubles, of psychic troubles, of depression and of cerebral anoxia.

9. Method of use of 2-pentanoylaminoacetic acid, of sodium 2-pentanoylaminooacetate or of a pharmaceutically acceptable salt of 2-pentanoylaminooacid, which comprises administering an effective amount of one of said compounds to a person in need for such a treatment, to produce an effect on the central nervous system, in particular in the treatment of various forms of epilepsy, of dyskinesiae, of parkinsonism, of memory troubles, of depression and of cerebral anoxia.

10. Method of use of 2-pentanoylaminoacetic acid, of sodium 2-pentanoylaminooacetate or of a pharmaceutically acceptable salt of 2-pentanoylaminooacid, according to claim 9, which comprises administering this acid or salt orally, rectally or parenterally at a daily dose of 100 mg to 5 g.

11. The steps, features, compositions and compounds referred to or indicated in the specification and/or claims of this application, individually or collectively, and any and all combinations of any two or more of said steps or features.

DATED this 26th day of June 1984.

DAVIES COLLISON
Patent Attorneys for
CONTINENTAL PHARMA