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2,807,566

METHOD OF POTENTIATING DRUGS AFFECTING THE CENTRAL NERVOUS SYSTEM AND COMPOSITIONS THEREFOR

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This invention relates to a new composition affecting the central nervous system and method of potentiating drugs affecting the central nervous system.

The composition in accordance with this invention has been found to be of great efficacy in treating, for example, conditions requiring sedative, hypnosis and/or anti-convulsant action and which have heretofore been treated with barbiturates which are sedative-hypnotics and/or anti-convulsants, paraldehyde, chloral hydrate, 2-monobromisovalerylurea, allylisopropylacetyl-carbamide and bromdiethylacetylurea.

The composition according to this invention comprises the combination of a centrally acting drug, that is, a drug having an affect on the central nervous system, and a compound which potentiates said drug.

More specifically, the drug used in the composition of this invention and which affects the central nervous system is a sedative-hypnotic and/or anti-convulsant barbiturate, paraldehyde, chloral hydrate, 2-monobromisovalerylurea, allylisopropylacetylcarbamide or bromdiethylacetylurea.

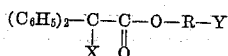
The following are exemplary of the barbiturates:

- 5-phenyl-5-ethylbarbituric acid (Phenobarbital)
- 5-isoamyl-5-ethylbarbituric acid (Amobarbital)
- 5-ethyl-5-(1-methylbutyl)-barbituric acid (Pentobarbital)
- N-methyl-5-cyclohexenyl-5-methyl barbituric acid ("Evipal")
- 5-allyl-5-(1-methylbutyl) barbituric acid ("Seconal")
- N-methyl-5-ethyl-5-phenylbarbituric acid ("Mebaral")
- 5-N-butyl-5-ethyl barbituric acid ("Butethal")

and alkali metal salts of these compounds. Where a salt is used the sodium salt is preferred.

Although the above barbiturates are preferred and are particularly advantageous with this invention, it will be appreciated that other barbiturates can be used equivalently.

The potentiating compound which is utilized in the composition in accordance with this invention is an amino-alkyl ester of a diphenyl acetic acid derivative or an acid addition salt thereof, the ester having the following structural formula:



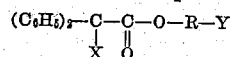
where X=alkyl having not in excess of 8 carbon atoms or alkenyl having not in excess of 8 carbon atoms; R=alkylene having from 2 to 8 carbon atoms; Y=a nitrogen-linked radical selected from the group consisting of piperidino, NH₂, NHR₁, NR₁R₂, where R₁ and R₂ are selected from the group consisting of alkyl not in excess of 8 carbon atoms, cycloalkyl radicals not in excess of 8 carbon atoms, phenyl radicals and phenylalkyl radicals, the alkyl portion of the phenylalkyl not exceeding 8 carbon atoms.

The ester potentiates the central nervous effect of these drugs as evidenced, for example, by increasing the duration of their effect.

Due to the markedly superior potentiation which re-

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sults through its use, a potentiating compound within the scope of the following formula is preferred:



where X=alkyl having 1 to 4 carbon atoms or alkenyl having 3 to 4 carbon atoms; R=alkylene having from 2 to 4 carbon atoms; Y=a nitrogen-linked radical selected from the group consisting of piperidino, NH₂, NHR₁, NR₁R₂, where R₁ and R₂ are selected from the group consisting of alkyl not in excess of 4 carbon atoms, cycloalkyl having from 5 to 6 carbon atoms, benzyl and phenethyl.

The following are illustrative of potentiating compounds which may be used in forming the composition in accordance with this invention:

- 1-diethylamino-2-ethyl-3-propyl 2,2-diphenyl-4-pentenoate
- 1-diethylamino-2-ethyl-3-propyl 2,2-diphenyl-4-pentenoate hydrochloride
- 1-diethylamino-6-hexyl 2,2-diphenyl-4-pentenoate
- 1-diethylamino-6-hexyl 2,2-diphenyl-4-pentenoate hydrochloride
- 1-diethylamino-5-pentyl 2,2-diphenyl-4-pentenoate hydrochloride
- 1-diethylamino-4-butyl 2,2-diphenyl-4-pentenoate hydrobromide
- 1-diethylamino-5-pentyl 2,2-diphenyl-4-pentenoate sulfate
- 1-diethylamino-6-hexyl 2,2-diphenyl-4-pentenoate tartrate
- β-Diethylaminoethyl 2,2-diphenyl pentanoate
- β-Diethylaminoethyl 2,2-diphenyl-4-pentenoate
- β-Diethylaminoethyl 2,2-diphenyl-4-pentenoate hydrochloride
- β-Diethylaminoethyl 2,2-diphenyl-4-pentenoate hydrobromide
- β-Diethylaminoethyl 2,2-diphenyl-4-pentenoate sulfate
- β-Dimethylaminoethyl 2,2-diphenyl-4-pentenoate
- β-Dimethylaminoethyl 2,2-diphenyl-4-pentenoate tartrate
- β-Dimethylaminoethyl 2,2-diphenyl-4-pentenoate hydrobromide
- β-Dimethylaminoethyl 2,2-diphenyl-4-pentenoate benzoate
- β-Dimethylaminoethyl 2,2-diphenyl-4-methyl-4-pentenoate
- β-Dimethylaminoethyl 2,2-diphenyl-4-methyl-4-pentenoate hydrochloride
- β-Dimethylaminoethyl 2,2-diphenyl-4-methyl-4-pentenoate hydrobromide
- β-Dimethylaminoethyl 2,2-diphenyl-4-methyl-4-pentenoate citrate
- β-Piperidinoethyl 2,2-diphenyl-4-pentenoate
- β-Piperidinoethyl 2,2-diphenyl-4-pentenoate hydrochloride
- β-Piperidinoethyl 2,2-diphenyl-4-pentenoate hydrobromide
- β-Piperidinoethyl 2,2-diphenyl-4-pentenoate sulfate
- β-Piperidinoethyl 2,2-diphenylpentanoate
- β-Piperidinoethyl 2,2-diphenylpentanoate hydrochloride
- β-Piperidinoethyl 2,2-diphenylpentanoate acetate
- β-Piperidinoethyl 2,2-diphenylpentanoate sulfate
- β-Diethylaminoethyl 2,2-diphenyl-4-methylpentanoate
- β-Diethylaminoethyl 2,2-diphenyl-4-methylpentanoate hydrochloride
- β-Diethylaminoethyl 2,2-diphenyl-4-methylpentanoate hydrobromide
- β-Diethylaminoethyl 2,2-diphenyl-4-methylpentanoate phosphate
- β-Dimethylaminoethyl 2,2-diphenylpentanoate
- β-Dimethylaminoethyl 2,2-diphenylpentanoate hydrochloride
- β-Dimethylaminoethyl 2,2-diphenylpentanoate hydrobromide
- β-Dimethylaminoethyl 2,2-diphenylpentanoate acetate
- β-Diethylaminoethyl 2,2-diphenylpentanoate
- β-Diethylaminoethyl 2,2-diphenylpentanoate hydrochloride

β -Diethylaminoethyl 2,2-diphenylpentanoate hydrobromide
 β -Diethylaminoethyl 2,2-diphenylpentanoate sulfate
 β - (Phenylethylamino) - propyl 2,2 - diphenyl - 3 - methyl-4-pentenoate
 β -Diethylaminoethyl 2,2-diphenylpentanoate citrate
 β -Diethylaminoethyl 2,2-diphenylpentanoate benzoate
 β - (Phenylethylamino) - propyl 2,2 - diphenyl - 3 - methyl-4-pentenoate hydrochloride
 β - (Phenylethylamino) - propyl 2,2 - diphenyl - 3 - methyl-4-pentenoate tartrate
 β - (Phenylethylamino) - propyl 2,2 - diphenyl - 3 - methyl-4-pentenoate benzoate
 γ -Dibenzylaminopropyl 2,2-diphenyl-4-hexenoate
 γ -Dibenzylaminopropyl 2,2-diphenyl-4-hexenoate hydrochloride
 γ -Dibenzylaminopropyl 2,2-diphenyl-4-hexenoate acetate
 γ -Dibenzylaminopropyl 2,2-diphenyl-4-hexenoate sulfate
 β -Aminoethyl 2,2-diphenylhexanoate
 β -Aminoethyl 2,2-diphenylhexanoate hydrochloride
 β -Aminoethyl 2,2-diphenylhexanoate hydrobromide
 β -Aminoethyl 2,2-diphenylhexanoate sulfate
 β -Benzylmethylaminoethyl 2,2-diphenylpentanoate
 β -Benzylmethylaminoethyl 2,2-diphenylpentanoate hydrochloride
 β -Benzylmethylaminoethyl 2,2-diphenylpentanoate hydrobromide
 β -Benzylmethylaminoethyl 2,2-diphenylpentanoate benzoate
 β -Methylaminoethyl 2,2-diphenylpentanoate
 β -Methylaminoethyl 2,2-diphenylpentanoate hydrochloride
 β -Methylaminoethyl 2,2-diphenylpentanoate hydrobromide
 β -Methylaminoethyl 2,2-diphenylpentanoate sulfate
 β -Diethylaminoethyl 2,2-diphenyl-4-methyl-4-pentenoate
 β -Diethylaminoethyl 2,2-diphenyl-4-methyl-4-pentenoate hydrochloride
 β -Diethylaminoethyl 2,2-diphenyl-4-methyl-4-pentenoate tartrate
 β -Diethylaminoethyl 2,2-diphenyl-4-methyl-4-pentenoate sulfate
 β -(Cyclopentylethylamino)-ethyl 2,2-diphenylpentanoate
 β -(Cyclopentylethylamino) - ethyl 2,2 - diphenylpentanoate hydrochloride
 β -(Cyclopentylethylamino)-ethyl 2,2-diphenylpentanoate hydrobromide
 β -(Cyclopentylethylamino)-ethyl 2,2-diphenylpentanoate citrate
 β -(Cyclohexylethylamino)-ethyl 2,2-diphenylpentanoate
 β -(Cyclohexylethylamino)-ethyl 2,2-diphenylpentanoate hydrochloride
 β -(Cyclohexylethylamino)-ethyl 2,2-diphenylpentanoate hydrobromide
 β -(Cyclohexylethylamino)-ethyl 2,2-diphenylpentanoate sulfate
 β -Dibenzylaminoethyl 2,2-diphenylhexanoate
 β -Dibenzylaminoethyl 2,2-diphenylhexanoate hydrochloride
 β -Dibenzylaminoethyl 2,2 - diphenylhexanoate hydrobromide
 β -Dibenzylaminoethyl 2,2-diphenylhexanoate sulfate

Aminoalkyl esters of diphenyl acetic acid having the above structural formula and the acid addition salts thereof are well known to the art and several methods suitable for their preparation are known. Thus, for example, reference may be had to the following:

1. Craig, Witt, Ulliot, "Abstracts of the 116th Meeting of the American Chemical Society," September 18-23 (1949), page 4L. Smith, Kline & French Laboratories.
2. Craig, Witt, Macko, Dacanay, Fellows and Ulliot, J. A. C. S. 73, 1939 (1951), March—Smith, Kline & French Laboratories.
3. Larsen, Ruddy, Elpern, McMullin, J. A. C. S. 71, 532 (1949), February—Sterling Winthrop Research Institute.

The essential ingredients of the composition according to this invention will preferably be intimately admixed and

may be included in widely varying proportions. It has been found that maximum potentiation occurs when the potentiating compound acts first. Thus, the composition of this invention is used to excellent advantage in multiple doses and in timed delay tablets, and the like.

Generally speaking, the selected potentiating ester will be used in an amount of from about 7 mgm./kgm. of body weight to about 20 mgm./kgm. of body weight. It is, however, preferred to use the selected potentiating ester in an amount of from about 3 mgm./kgm. of body weight to about 10 mgm./kgm. of body weight. The amount of potentiating ester will, of course, vary widely depending upon the centrally acting drug selected and the amount of potentiation desired.

Expressed in absolute amounts a satisfactory range of the potentiating ester is from 60 mg. to 1200 mg. and a preferred range is from 180 mg. to 600 mg.

The amount of the selected centrally acting drug to be potentiated will vary widely depending on the physiological effect to be achieved. Generally speaking, it is desirable to have from about the standard effective therapeutic dose (U. S. P.) of the selected drug to about one-fourth of the standard dose. It is preferred to use an amount in the range of from the standard effective therapeutic dose to one-half of the standard dose. The standard effective therapeutic doses for the centrally acting drugs used in the composition of this invention are well known in the art.

The method in accordance with this invention comprises the administration internally of the essential ingredients of the above composition for concurrent physiological action. It is preferred to administer the potentiating ester first for maximum potentiation. The administration may be, for example, oral or by intravenous injection; and, if desired, the essential ingredients may be administered in a different manner, i. e., one orally and one intravenously. The ranges given above for the essential ingredients are applicable to the method whether these ingredients are administered together or separately.

For administration the composition may be made up in various forms, as, for example, in a tablet, in a capsule, a powder, or a liquid, such as water, for oral administration. The essential ingredients may be extended with any desired excipient as, for example, sugar of milk or starch. When prepared for injection, the essential ingredients may be mixed with any suitable vehicle, such as, for example, water, a polyhydric alcohol or a mixture thereof.

A highly efficient preparation for oral use in accordance with this invention and based on an average body weight of about 150 lbs. may be made up on any of the following formulae, it being appreciated that numerous other combinations and varying amounts of the individual ingredients can be utilized.

Example 1

	Grams
55 Chloral hydrate -----	0.6
β -Diethylaminoethyl 2,2-diphenylpentanoate -----	0.5

Example 2

Paraldehyde -----	3.0
60 β -Diethylaminoethyl 2,2-diphenylpentanoate -----	0.5

Example 3

5-phenyl-5-ethylbarbituric acid -----	0.15
β -Diethylaminoethyl 2,2-diphenylpentanoate -----	0.5

Example 4

5-isoamyl-5-ethylbarbituric acid -----	0.2
β -Diethylaminoethyl 2,2-diphenylpentanoate -----	0.5

Example 5

70 Sodium 5-ethyl-5-(1-methylbutyl)-barbiturate -----	0.1
β -Diethylaminoethyl 2,2-diphenylpentanoate -----	0.5

Example 6

N-methyl-5-cyclohexenyl-5-methylbarbituric acid -----	0.25
75 β -Diethylaminoethyl 2,2-diphenylpentanoate -----	0.5

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Example 7

Sodium 5-allyl-5-(1-methylbutyl)-barbiturate	0.1
β -Diethylaminoethyl 2,2-diphenylpentanoate	0.5

Example 8

N-methyl-5-ethyl-5-phenylbarbituric acid	0.1
β -Diethylaminoethyl 2,2-diphenylpentanoate	0.5

Example 9

2-monobromisovalerylurea	0.75
β -Diethylaminoethyl 2,2-diphenylpentanoate	0.5

Example 10

Bromdiethylacetylurea	0.9
β -Diethylaminoethyl 2,2-diphenylpentanoate	0.5

Example 11

Allylisopropylacetylcarbamide	0.375
β -Diethylaminoethyl 2,2-diphenylpentanoate	0.5

Example 12

N-methyl-5-cyclohexenyl-5-methylbarbituric acid	0.25
β -Dimethylaminoethyl 2,2-diphenyl-4-pentenoate	0.5

Example 13

5-phenyl-5-ethylbarbituric acid	0.15
β -Dimethylaminoethyl 2,2-diphenyl-4-pentenoate	0.5

Example 14

Chloral hydrate	0.6
β -Diethylaminoethyl 2,2-diphenyl-4-pentenoate	0.5

Example 15

Paraldehyde	3.0
β -Diethylaminoethyl 2,2-diphenyl-4-pentenoate	0.5

Example 16

5-phenyl-5-ethylbarbituric acid	0.15
β -Dimethylaminoethyl 2,2-diphenyl-4-methyl-4-pentenoate	0.5

Example 17

5-isoamyl-5-ethylbarbituric acid	0.2
β -Piperidinoethyl 2,2-diphenyl-4-pentenoate	0.5

Example 18

Sodium 5-ethyl-5-(1-methylbutyl)-barbiturate	0.1
β -Piperidinoethyl 2,2-diphenylpentanoate	0.5

Example 19

N-methyl-5-cyclohexenyl-5-methylbarbituric acid	0.25
β -Diethylaminoethyl 2,2-diphenyl-4-methylpentanoate	0.5

Example 20

Sodium 5-allyl-5-(1-methylbutyl)-barbiturate	0.1
β -Dimethylaminoethyl 2,2-diphenylpentanoate	0.5

Example 21

N-methyl-5-ethyl-5-phenylbarbituric acid	0.1
β -(Phenylethylamino)-propyl 2,2-diphenyl-3-methyl-4-pentenoate	0.5

Example 22

2-monobromisovalerylurea	0.75
γ -Dibenzylaminopropyl 2,2-diphenyl-4-hexenoate	0.6

Example 23

Bromdiethylacetylurea	0.9
β -Aminoethyl 2,2-diphenylhexanoate	0.4

Example 24

Allylisopropylacetylcarbamide	0.375
β -Benzylmethylaminoethyl 2,2-diphenylpentanoate	0.5

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Example 25

N-methyl-5-cyclohexenyl-5-methylbarbituric acid	0.25
β -Diethylaminoethyl 2,2-diphenyl-4-methyl-4-pentenoate	0.5

Example 26

5-phenyl-5-ethylbarbituric acid	0.15
β -(Cyclopentylethylamino)-ethyl 2,2-diphenylpentanoate	0.6

Example 27

Chloral hydrate	0.6
β -(Cyclohexylethylamino)-ethyl 2,2-diphenylpentanoate	0.6

Example 28

Paraldehyde	3.0
β -(Cyclohexylethylamino)-ethyl 2,2-diphenylpentanoate	0.6

Example 29

5-phenyl-5-ethylbarbituric acid	0.15
β -Dibenzylaminoethyl 2,2-diphenylhexanoate	0.6

Example 30

5-isoamyl-5-ethylbarbituric acid	0.2
β -Dimethylaminoethyl 2,2-diphenyl-4-pentenoate	0.5

Example 31

N-methyl-5-ethyl-5-phenylbarbituric acid	0.1
β -Dimethylaminoethyl 2,2-diphenyl-4-pentenoate	0.5

Example 32

N-methyl-5-cyclohexenyl-5-methylbarbituric acid	0.25
β -Dimethylaminoethyl 2,2-diphenyl-4-pentenoate	0.5

Example 33

N-methyl-5-cyclohexenyl-5-methylbarbituric acid	0.25
β -Piperidinoethyl 2,2-diphenyl-4-pentenoate	0.5

Example 34

N-methyl-5-cyclohexenyl-5-methylbarbituric acid	0.25
β -Methylaminoethyl 2,2-diphenylpentanoate	0.4

Example 35

Sodium allyl-5-(1-methylbutyl)-barbiturate	0.1
β -Dimethylaminoethyl 2,2-diphenyl-4-pentenoate	0.5

Example 36

Sodium 5-allyl-5-(1-methylbutyl)-barbiturate	0.1
β -Piperidinoethyl 2,2-diphenyl-4-pentenoate	0.5

Example 37

Sodium 5-allyl-5-(1-methylbutyl)-barbiturate	0.1
β -Diethylaminoethyl 2,2-diphenyl-4-methylpentanoate	0.5

Example 38

Sodium 5-allyl-5-(1-methylbutyl)-barbiturate	0.1
β -Methylaminoethyl 2,2-diphenylpentanoate	0.4

Example 39

N-methyl-5-ethyl-5-phenylbarbituric acid	0.1
β -Dimethylaminoethyl 2,2-diphenyl-4-pentenoate	0.5

Example 40

N-methyl-5-ethyl-5-phenylbarbituric acid	0.1
β -Piperidinoethyl 2,2-diphenyl-4-pentenoate	0.5

Example 41

N-methyl-5-ethyl-5-phenylbarbituric acid	0.1
β -Diethylaminoethyl 2,2-diphenyl-4-methylpentanoate	0.5

Example 42

N-methyl-5-ethyl-5-phenylbarbituric acid	0.1
β -Methylaminoethyl 2,2-diphenylpentanoate	0.5

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Example 43

Chloral hydrate	0.6
β -Diethylaminoethyl 2,2-diphenylpentanoate hydrochloride	0.5

Example 44

Paraldehyde	3.0
β -Diethylaminoethyl 2,2-diphenylpentanoate hydrochloride	0.5

Example 45

5-phenyl-5-ethylbarbituric acid	0.15
β -Diethylaminoethyl 2,2-diphenylpentanoate	0.5

Example 46

5-isoamyl-5-ethylbarbituric acid	0.2
β -Diethylaminoethyl 2,2-diphenylpentanoate hydrobromide	0.5

Example 47

Sodium 5-ethyl-5-(1-methylbutyl)-barbiturate	0.1
β -Diethylaminoethyl 2,2-diphenylpentanoate citrate	0.5

Example 48

N-methyl-5-cyclohexenyl-5-methylbarbituric acid	0.25
β -Diethylaminoethyl 2,2-diphenylpentanoate citrate	0.5

Example 49

Sodium 5-allyl-5-(1-methylbutyl)-barbiturate	0.1
β -Diethylaminoethyl 2,2-diphenylpentanoate acetate	0.5

Example 50

N-methyl-5-ethyl-5-phenylbarbituric acid	0.1
β -Diethylaminoethyl 2,2-diphenylpentanoate succinate	0.5

Example 51

2-monobromisovalerylurea	0.75
β -Diethylaminoethyl 2,2-diphenylpentanoate hydrochloride	0.5

Example 52

Bromdiethylacetylurea	0.9
β -Diethylaminoethyl 2,2-diphenylpentanoate tartrate	0.5

Example 53

Allylisopropylacetylcarbamide	0.375
β -Diethylaminoethyl 2,2-diphenylpentanoate benzoate	0.5

Example 54

N-methyl-5-cyclohexenyl-5-methylbarbituric acid	0.5
β -Dimethylaminoethyl 2,2-diphenyl-4-pentenoate sulfate	0

Example 55

5-phenyl-5-ethylbarbituric acid	0.15
β -Dimethylaminoethyl 2,2-diphenyl-4-pentenoate phosphate	0

Example 56

Chloral hydrate	0.6
β -Diethylaminoethyl 2,2-diphenyl-4-pentenoate hydrochloride	0.5

Example 57

Paraldehyde	3.0
β -Diethylaminoethyl 2,2-diphenyl-4-pentenoate hydrochloride	0.5

Example 58

5-phenyl-5-ethylbarbituric acid	0.15
β -Dimethylaminoethyl 2,2-diphenyl-4-methyl-4-pentenoate tartrate	0.5

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Example 59

5-isoamyl-5-ethylbarbituric acid	0.2
β -Piperidinoethyl 2,2-diphenyl-4-pentenoate hydrobromide	0.5

Example 60

Sodium 5-ethyl-5-(1-methylbutyl)-barbiturate	0.1
β -Piperidinoethyl 2,2-diphenylpentanoate citrate	0.5

Example 61

N-methyl-5-cyclohexenyl-5-methylbarbituric acid	0.25
β -Diethylaminoethyl 2,2-diphenyl-4-methyl-pentanoate citrate	0.5

Example 62

Sodium 5-allyl-5-(1-methylbutyl)-barbiturate	0.1
β -Dimethylaminoethyl 2,2-diphenylpentanoate acetate	0.5

Example 63

N-methyl-5-ethyl-5-phenylbarbituric acid	0.1
β -(Phenylethylamino)-propyl 2,2-diphenyl-3-methyl-4-pentenoate succinate	0.6

Example 64

2-monobromisovalerylurea	0.75
γ -Dibenzylaminopropyl 2,2-diphenyl-4-hexenoate hydrochloride	0.6

Example 65

Bromdiethylacetylurea	0.9
β -Aminoethyl 2,2-diphenylhexanoate tartrate	0.4

Example 66

Allylisopropylacetylcarbamide	0.375
β -Benzylmethylaminoethyl 2,2-diphenylpentanoate benzoate	0.5

Example 67

Sodium 5-phenyl-5-ethylbarbiturate	0.15
β -Diethylaminoethyl 2,2-diphenylpentanoate hydrochloride	0.5

Example 68

Sodium 5-isoamyl-5-ethylbarbiturate	0.2
β -Diethylaminoethyl 2,2-diphenylpentanoate hydrochloride	0.5

Example 69

5-ethyl-5-(1-methylbutyl)-barbituric acid	0.1
β -Diethylaminoethyl 2,2-diphenylpentanoate hydrochloride	0.5

Example 70

Sodium N-methyl-5-cyclohexenyl-5-methylbarbiturate	0.25
β -Diethylaminoethyl 2,2-diphenylpentanoate hydrochloride	0.5

Example 71

5-allyl-5-(1-methylbutyl)-barbituric acid	0.1
β -Diethylaminoethyl 2,2-diphenylpentanoate hydrochloride	0.5

Example 72

Sodium N-methyl-5-ethyl-5-phenylbarbiturate	0.1
β -Diethylaminoethyl 2,2-diphenylpentanoate hydrochloride	0.5

Example 73

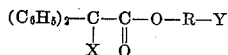
5-N-butyl-5-ethylbarbituric acid	0.1
β -Diethylaminoethyl 2,2-diphenylpentanoate hydrochloride	0.5

It is not desired to be limited except as set forth in the following claims, it being understood that the above examples are merely illustrative.

This application is a continuation-in-part of application Serial No. 310,141, filed September 17, 1952, now abandoned.

What is claimed is:

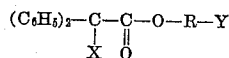
1. A medicinal preparation comprising a centrally acting drug selected from the group consisting of barbiturates, 2-monobromisovalerylurea, allylisopropylacetylcarbamide and bromdiethylacetylurea and a component to substantially increase the effectiveness of the centrally acting drug, said component being selected from the group consisting of an ester of a diphenylacetic acid derivative and organic and inorganic acid addition salts of said ester, the ester having the following structural formula:



wherein X is selected from a group consisting of alkyl having not in excess of 4 carbon atoms and alkenyl having from 3 to 4 carbon atoms, R is alkylene having from 2 to 4 carbon atoms and Y is a nitrogen-linked radical selected from the group consisting of piperidino, primary amino, secondary alkyl amino having not in excess of 4 carbon atoms, di-alkyl amino with each alkyl group having not in excess of 4 carbon atoms, secondary cycloalkyl amino having from 5 to 6 carbon atoms, di-cycloalkyl amino having from 5 to 6 carbon atoms in each cycloalkyl group, secondary benzylamino, dibenzylamino, secondary phenethylamino and diphenethylamino.

2. The method of potentiating the sedative-hypnotic effect of a centrally acting drug selected from the group consisting of a barbiturate, 2-monobromisovalerylurea, allylisopropylacetylcarbamide and bromdiethylacetylurea,

which comprises administering internally for concurrent physiological action with said drug a member selected from the group consisting of an ester of a diphenylacetic acid derivative and organic and inorganic acid addition salts of said ester, the ester having the following structural formula:



10 wherein X is selected from the group consisting of alkyl having not in excess of 4 carbon atoms and alkenyl having from 3 to 4 carbon atoms, R is alkylene having from 2 to 4 carbon atoms and Y is a nitrogen-linked radical selected from the group consisting of piperidino, primary
15 amino, secondary alkyl amino having not in excess of 4 carbon atoms, di-alkyl amino with each alkyl group having not in excess of 4 carbon atoms, secondary cycloalkyl amino having from 5 to 6 carbon atoms, di-cycloalkyl amino having from 5 to 6 carbon atoms in each
20 cycloalkyl group, secondary benzylamino, dibenzylamino, secondary phenethylamino and diphenethylamino.

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