AMENDED SPECIFICATION

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PATENT SPECIFICATION

1,069,341



1,069,341

NO DRAWINGS

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COMPLETE SPECIFICATION

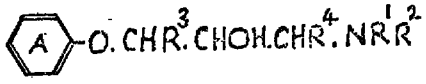
Pharmaceutical Compositions containing Alkanolamine Derivatives

We, IMPERIAL CHEMICAL INDUSTRIES LIMITED of Imperial Chemical House, Millbank, London, S.W.1, a British Company, do hereby declare the invention, for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to new pharmaceutical compositions containing alkanolamine derivatives which possess β-adrenergic blocking activity and which are therefore useful in the treatment or prophylaxis of coronary artery disease.

Certain 1 - amino - 3 - phenoxy - 2 - propanol derivatives are known, but it was not known heretofore that compounds of this type possess β-adrenergic blocking activity.

According to the invention we provide pharmaceutical compositions comprising as active ingredient at least on racemic alkanolamine derivative of the formula:—



wherein R^1 stands for hydrogen; wherein R^2 stands for an alkyl radical of not more than 10 carbon atoms which is branched at the α-carbon atoms, or for a cycloalkyl radical of not more than 5 carbon atoms, or for the 2 - hydroxy - 1,1 - dimethylethyl or 1-methyl - 3 - phenylpropyl radical; wherein R^3 and R^4, which may be the same or different, stand for hydrogen or for alkyl radicals of not more than 5 carbon atoms; and wherein the benzene ring (A) bears at least one additional substituent selected from halogen atoms, alkyl radicals containing not more than 4 carbon atoms, alkoxy, alkylthio, alkanoyl, aralkanoyl, aroyl, aryl, aryloxy, alkylaryloxy, arylthio, arylsulphonyl, arylamino, aralkyl, aralkoxy and alkenyl radicals each containing not more than 10 carbon atoms, halogenoalkyl radicals containing not more than 5 carbon atoms and hydroxy and nitro radicals, provided that the 2- and 6-positions of the benzene ring (A) are not both substituted; or a carboxylic ester thereof; or a salt thereof; together with a pharmaceutically-acceptable diluent or carrier, but excluding simple non-sterile solutions of the active ingredients in common organic solvents or in water, and excluding simple aqueous suspensions of the active ingredients in the absence of a suspending agent.

It is to be understood that the above definition of alkanolamine derivatives encompasses all possible stereoisomeric racemates thereof, and mixtures thereof.

As a suitable value for R^2 when it stands for an alkyl radical of not more than 10

carbon atoms there may be mentioned, for example, the isopropyl, s-butyl or t-butyl radical. As a suitable value for R^2 when it stands for a cycloalkyl radical of not more than 5 carbon atoms there may be mentioned, for example, the cyclopentyl radical.

As a suitable value for R^3 or R^4 when it stands for an alkyl radical of not more than 5 carbon atoms there may be mentioned, for example, the methyl radical.

As suitable additional substituents on the benzene ring (A) there may be mentioned, for example, one or more substituents selected from fluorine, chlorine, bromine and iodine atoms, and methyl, ethyl, isopropyl, t-butyl, methoxy, ethoxy, n-butoxy, methylthio, acetyl, benzoyl, hydroxy, trifluoromethyl, phenyl, phenoxy, 4-tolyloxy, phenylthio, phenylsulphonyl, anilino, benzyl, α,α-dimethylbenzyl, benzyloxy and nitro radicals.

Racemic alkanolamine derivatives which may be used as active ingredients in the pharmaceutical compositions of the invention include, for example, the known racemic compound 1 - (2 - chlorophenoxy) - 3 - isopropylamino - 2 - propanol, and the new racemic alkanolamine derivatives described in United Kingdom Patent Specification No. 1,069,345. As particularly valuable compounds there may be mentioned, for example, the known racemic compounds 1 - (2 - chlorophenoxy) - 3 - isopropylamino - 2 - propanol and the new racemic compounds 1 - (3 - tolyloxy)-, 1 - (4-tolyloxy)-, 1 - (2,3 - dimethylphenoxy)-, 1 - (2,4 - dimethylphenoxy)-, 1 - (3,4 - dimethylphenoxy)-, 1 - (3,5 - dimethylphenoxy)-, 1 - (3 - ethyl - 5 - methylphenoxy)-, 1 - (3-chlorophenoxy)-, 1 - (2,3 - dichlorophenoxy)-, 1 - (3,5 - dichlorophenoxy)-, 1 - (2,4,5-trichlorophenoxy)-, 1 - (3 - fluorophenoxy)-, 1 - (4 - chloro - 3 - methylphenoxy)-, 1-(3 - methoxyphenoxy)-, 1 - (2 - hydroxyphenoxy)-, 1 - (3 - nitrophenoxy)-, 1 - (3-trifluoromethylphenoxy)-, 1 - (2 - phenylphenoxy)-, 1 - (2 - phenoxyphenoxy)-, 1 - (3-phenoxyphenoxy)-, 1 - (2 - benzoyl - 5-methoxyphenoxy)-, 1 - (4 - anilinophenoxy)-, and 1 - [2 - (4 - tolyloxy)phenoxy] - 3-isopropylamino - 2 - propanol, and 1 - (3,5-dimethylphenoxy) - 3 - (1 - methyl - 3-phenylpropylamino) - 2 - propanol, 1 - (2,3-dichlorophenoxy) - 3 - s - butylamino - 2-propanol, 1 - (2 - hydroxy - 1,1 - dimethylethylamino) - 3 - (3 - tolyloxy) - 2 - propanol and 1 - t - butylamino - 3 - (3 - tolyloxy) - 2 - propanol, and the salts thereof; and the preferred compounds of these are 1 - (3 - tolyloxy)-, 1 - (3,5 - dimethylphenoxy)-, 1 - (3 - chlorophenoxy)-, 1 - (2,3-dichlorophenoxy)-, 1 - (3,5 - dichlorophenoxy)-, 1 - (2 - phenoxyphenoxy)- and 1-[2 - (4 - tolyloxy)phenoxy] - 3 - isopropylamino - 2 - propanol, and 1 - (3,5 - dimethylphenoxy) - 3 - (1 - methyl - 3 - phenylpropylamino) - 2 - propanol and 1 - t - butylamino - 3 - (3 - tolyloxy) - 2 - propanol, and the salts thereof.

As suitable alkanolamine carboxylic esters there may be mentioned, for example, *O*-esters derived from a saturated or unsaturated aliphatic carboxylic acid of not more than 20 carbon atoms, for example acetic, palmitic, stearic or oleic acid, or *O*-esters derived from an aromatic carboxylic acid of not more than 15 carbon atoms, for example benzoic acid.

As suitable salts of the alkanolamines and alkanolamine carboxylic esters which may be used as active ingredients in the pharmaceutical compositions of the invention there may be mentioned acid-addition salts derived from inorganic acids, for example hydrochlorides, hydrobromides, phosphates or sulphates, or derived from organic acids, for example oxalates, lactates, tartarates, acetates, salicylates, citrates, benzoates, β-naphthoates, adipates or 1,1′ - methylene - bis - (2 - hydroxy - 3-naphthoates), or derived from acidic synthetic resins, for example sulphonated polystyrene resins, for example "Zeo-Karb" 225 ("Zeo-Karb" is a Trade Mark). Relatively insoluble salts, for example the 1,1′ - methylene bis-(2 - hydroxy - 3 - naphthoates), have the advantage that they afford prolonged blood levels of the medicament.

The pharmaceutical compositions of the invention may be in the form of tablets, capsules, aqueous or oily solutions, aqueous or oily suspensions, emulsions, sterile injectable aqueous or oily solutions or suspensions, or dispersible powders.

Suitable tablets may be formulated by admixture of the active ingredient(s) with known pharmaceutical excipients, for example inert diluents, for example calcium carbonate, calcium phosphate or lactose, disintegrating agents, for example maize starch or alginic acid, binding agents, for example starch, gelatin or acacia mucilage, and lubricating agents, for example magnesium stearate, stearic acid or talc. Such tablets may optionally be coated by known techniques in order to delay disintegration in the stomach and thus to provide a sustained action over an extended period.

The aqueous suspensions, emulsions, oily solutions and suspensions of the invention generally contain a sweetening agent, for example glycerol, dextrose or sucrose, and a flavouring agent, for example vanillin or orange extract, in order to provide a palatable product. The aqueous suspensions of the invention may also contain suspending or thickening agents, for example sodium carboxymethylcellulose, and wetting agents, for example condensation products of fatty alcohols with ethylene oxide.

The emulsions of the invention may contain the active ingredient(s) dissolved in an oil of vegetable or animal origin, for example

arachis oil or cod liver oil, and may also contain sweetening agents and flavouring agents which may with advantage be essential oils. The said emulsions may also contain emulsifying agents and dispersing agents, for example soya bean lecithin, polyoxyethylene sorbitan mono-oleate, gum acacia, gum tragacanth or casein, and anti-oxidants, for example propyl gallate.

The oily solutions of the invention likewise contain the active ingredient(s) in solution in an oil of vegetable or animal origin and may optionally contain flavouring agents to mask the taste and improve oral acceptability. Such oily solutions may advantageously be filled into soft gelatin capsules. The oily solutions may also contain sweetening agents, for example icing sugar, in which case, the oil phase may in addition contain a suspending agent, for example beeswax, to maintain the redispersion properties of the suspension.

Oral compositions in the form of gelatin capsules may consist of capsules containing active ingredient(s) only or the capsules may contain the active ingredient(s) in admixture with inert diluents, for example lactose or sorbitol.

The sterile injectable aqueous suspensions of the invention may contain a suspending or thickening agent, for example sodium carboxymethylcellulose, and a wetting or dispersing agent, for example a phenol-polyethylene oxide condensate, for example the condensation product of octylcresol with about 8—10 molecular proportions of ethylene oxide. The sterile injectable oily solutions of the invention may be prepared from a non-toxic injectable oil, for example arachis oil or ethyl oleate, and they may additionally contain gelling agents, for example aluminium stearate, to delay absorption within the body. These oily injectable preparations may contain one or more preservatives, for example methyl or n-propyl *p*-hydroxybenzoate, or chlorobutanol.

The invention is illustrated but not limited by the following Examples in which the parts are by weight:—

EXAMPLE 1

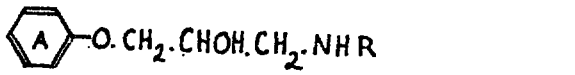
A mixture of 50 parts of 1 - (2 - chlorophenoxy) - 3 - isopropylamino - 2 - propanol, 125 parts of maize starch, 270 parts of calcium phosphate and 1 part of magnesium stearate is compressed, and the compressed material is then broken down into granules by passage through a 16-mesh screen. The resultant granules are compressed into tablets according to the known art. There are thus obtained tablets which are suitable for oral use for therapeutic purposes.

The 1 - (2 - chlorophenoxy) - 3 - isopropylamino - 2 - propanol is replaced by any one of the 1 - amino - 3 - phenoxy - 2 - propanol derivatives described in United Kingdom Patent Specification No. 1,069,345 and in a similar manner there are obtained tablets which are suitable for oral use for therapeutic purposes.

EXAMPLE 2

89 Parts of spray-dried lactose are passed through a 60-mesh sieve, and then mixed with 5 parts of maize starch and 1 part of magnesium stearate. The mixture is passed through a 60-mesh sieve, and then thoroughly mixed with 5 parts of 1 - isopropylamino-3 - (3 - tolyloxy) - 2 - propanol hydrochloride. The mixture is passed through a 60-mesh sieve, and then compressed into tablets according to the known art. There are thus obtained tablets which are suitable for oral use for therapeutic purposes.

The 1 - isopropylamino - 3 -(3 - tolyloxy)-2 - propanol hydrochloride is replaced by the hydrochloride of any of the compounds listed in the following table, and in a similar manner there are obtained tablets which are suitable for oral use for therapeutic purposes:—



	R
2-chlorophenyl	isopropyl
3-tolyl	isopropyl
4-tolyl	isopropyl
2,3-dimethylphenyl	isopropyl
2,4-dimethylphenyl	isopropyl
3,4-dimethylphenyl	isopropyl
3,5-dimethylphenyl	isopropyl
3-ethyl-5-methylphenyl	isopropyl
3-chlorophenyl	isopropyl
2,3-dichlorophenyl	isopropyl
3,5-dichlorophenyl	isopropyl
2,4,5-trichlorophenyl	isopropyl
3-fluorophenyl	isopropyl
4-chloro-3-methylphenyl	isopropyl
3-methoxyphenyl	isopropyl
2-hydroxyphenyl	isopropyl
3-nitrophenyl	isopropyl
3-trifluoromethylphenyl	isopropyl
2-diphenylyl	isopropyl
3,5-dimethylphenyl	1-methyl-3-phenylpropyl
2,3-diflourophenyl	s-butyl
3-tolyl	2-hydroxy-1,1-dimethylethyl
3-tolyl	t-butyl
2-phenoxyphenyl	isopropyl

	R
3-phenoxyphenyl	isopropyl
2-benzoyl-5-methoxyphenyl	isopropyl
4-anilinophenyl	isopropyl
2-(4-tolyloxy)phenyl	isopropyl

EXAMPLE 3

A mixture of 50 parts of 1 - (4 - chlorophenoxy) - 3 - isopropylamino - 2 - propanol and 150 parts of maize starch is filled into hard gelatine capsules. The composition so obtained is suitable for oral use for therapeutic purposes.

EXAMPLE 4

200 Parts of coconut oil, 780 parts of arachis oil and 20 parts of beeswax are melted together at a temperature not exceeding 100° C., and 0.75 part of propyl gallate is then added and dissolved by stirring. The oily solution is stirred and allowed to cool to ambient temperature. 0.4 Part of 1 - isopropylamino - 3 - (3 - tolyloxy) - 2 - propanol hydrochloride, 40 parts of icing sugar and 0.6 part of saccharin sodium are mixed together for 10 minutes, and 58.6 parts of the abovementioned oily solution are added slowly with continual stirring. A suitable flavouring agent is added, and mixing is continued for 30 minutes. There is thus obtained an oily suspension suitable for oral administration for therapeutic purposes.

EXAMPLE 5

A solution of 1 part of 1 - isopropylamino-3 - (3 - tolyloxy) - 2 - propanol hydrochloride in 100 parts of distilled water is filled into ampoules. The ampoules are sealed and then heated at 115° C. for 30 minutes. There are thus obtained ampoules containing a sterile aqueous solution suitable for parenteral administration for therapeutic purposes.

The above process is repeated except that a solution of 0.1 part of sodium metabisulphite and 1 part of 1 - isopropylamino-3 - (3- tolyloxy) - 2 - propanol hydrochloride in 100 parts of distilled water is filled into ampoules and then treated as described above. There are thus obtained ampoules containing a sterile aqueous solution suitable for parenteral administration for therapeutic purposes.

EXAMPLE 6

A solution of 1 part of 1 - isopropylamino-3 - (3 - tolyloxy) - 2 - propanol hydrochloride in 100 parts of distilled water is passed through a sterilising filter. The sterile filtrate is filled into sterile ampoules under aseptic conditions. There are thus obtained ampoules containing a sterile aqueous solution suitable for parenteral administration for therapeutic purposes.

EXAMPLE 7

A mixture of 1 part of di - [1 - isopropylamino - 3 - (3 - tolyloxy) - 2 - propanol]-1,1' - methylene - bis - (2 - hydroxy - 3-naphthoate, 40 parts of sucrose, 0.5 part of a cetyl alcohol-polyethylene oxide-condensate, 1 part of polyvinylpyrrolidone, 0.25 part of methyl *p*-hydroxybenzoate and 100 parts of water is ball-milled for several hours. After the incorporation of suitable colouring and flavouring agents there is obtained a suspension suitable for oral administration for therapeutic purposes.

EXAMPLE 8

200 Parts of di - [1 - isopropylamino-3 - (3 - tolyloxy) - 2 - propanol] 1,1'-methylene - bis - (2 - hydroxy - 3 - naphthoate) are milled to a fine powder, sterilised by heating at 120° C. for 3 hours, and then mixed with 20 parts of sterile, finely-powdered sodium carboxymethylcellulose. The resulting powder is thoroughly mixed together with 100 parts of a sterile 2% solution of polyoxyethylenesorbitan mono-oleate in water, and the resulting mixture is dried. The dry, sterile product is introduced into vials which are then sealed. Addition of sterile water to the powder, followed by shaking, produces a suspension suitable for intramuscular injection for therapeutic purposes.

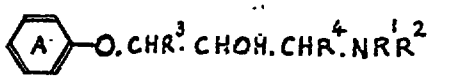
EXAMPLE 9

A mixture of 2 parts of aluminium stearate and 98 parts of arachis oil is gelled and sterilised by stirring and heating at 150° C.

The mixture is then cooled, 1 part of sterile 1 - isopropylamino -3 - (3 - tolyloxy) - 2-propanol hydrochloride is added, and the mixture is ball-milled under sterile conditions to reduce the particle size of the active ingredient to below 50 microns. There is thus obtained a sterile oily suspension suitable for intramuscular injection for therapeutic purposes.

WHAT WE CLAIM IS:—

1. Pharmaceutical compositions comprising as active ingredient at least one racemic alkanolamine derivative of the formula:—



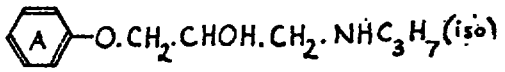
wherein R^1 stands for hydrogen; wherein R^2 stands for an alkyl radical of not more than 10 carbon atoms which is branched at the α-carbon atom, or for a cycloalkyl radical of not more than 5 carbon atoms, or for the 2 - hydroxy - 1,1 - dimethylethyl or 1-methyl - 3 - phenylpropyl radical; wherein R^3 and R^4, which may be the same or different, stand for hydrogen or for alkyl radicals of not more than 5 carbon atoms; and wherein the benzene ring (A) bears at least one additional substituent selected from halogen atoms, alkyl radicals containing not more than 4 carbon atoms, alkoxy, alkylthio, alkanoyl, aralkanoyl, aroyl, aryl, aryloxy, alkylaryloxy, arylthio, arylsulphonyl, arylamino, aralkyl, aralkoxy and alkenyl radicals each containing not more than 10 carbon atoms, halogenoalkyl radicals containing not more than 5 carbon atoms, and hydroxy and nitro radicals, provided that the 2- and 6-positions of the benzene ring (A) are not both substituted; or a carboxylic ester thereof, or a salt thereof, together with a pharmaceutically-acceptable diluent or carrier, but excluding simple non-sterile solutions of the active ingredients in common organic solvents or in water, and excluding simple aqueous suspensions of the active ingredients in the absence of a suspending agent.

2. Pharmaceutical compositions comprising as active ingredient at least one racemic alkanolamine derivative of the formula:—



wherein R^1 stands for hydrogen; wherein R^2 stands for an alkyl radical of not more than 10 carbon atoms which is branched at the α-carbon atom, or for a cycloalkyl radical of not more than 5 carbon atoms, or for the 2-hydroxyl - 1,1 - dimethylethyl or 1 - methyl-3 - phenylpropyl radical; wherein R^3 and R^4, which may be the same or different, stand for hydrogen or for alkyl radicals of not more than 5 carbon atoms; and wherein the benzene ring (A) bears at least one additional substituent selected from halogen atoms, alkyl radicals containing not more than 4 carbon atoms, alkoxy, alkanoyl, aralkanoyl, aroyl, aryl, aryloxy, arylthio, arylsulphonyl, aralkyl and alkenyl radicals each containing not more than 10 carbon atoms, halogenoalkyl radicals of not more than 5 carbon atoms, and hydroxy and nitro radicals, provided that the 2- and 6-positions of the benzene ring (A) are not both substituted; or a salt thereof, together with a pharmaceutically-acceptable diluent or carrier, but excluding simple non-sterile solutions of the active ingredients in common organic solvents or in water, and excluding simple aqueous suspensions of the active ingredient in the absence of a suspending agent.

3. Pharmaceutical compositions comprising as active ingredient at least one racemic alkanolamine derivative of the formula:



wherein the benzene ring (A) is further substituted as stated in claim 2, or a salt thereof, together with a pharmaceutically-acceptable diluent or carrier, but excluding simple non-sterile solutions of the active ingredients in common organic solvents or in water, and excluding simple aqueous suspensions of the active ingredient in the absence of a suspending agent.

4. Compositions as claimed in claim 1 or 2 wherein R^2 stands for the isopropyl, s-butyl or t-butyl radical.

5. Compositions as claimed in claim 1 or 2 wherein R^2 stands for the cyclopentyl radical.

6. Compositions as claimed in any one of claims 1, 2, 4 and 5 wherein R^3 or R^4 stands for the methyl radical.

7. Compositions as claimed in any one of claims 1 and 4—6 wherein the benzene ring (A) bears one or more substituents selected from fluorine, chlorine, bromine and iodine atoms and methyl, ethyl, isopropyl, t-butyl, methoxy, ethoxy, n-butoxy, methylthio, acetyl, benzoyl, hydroxy, trifluoromethyl, phenyl, phenoxy, 4-tolyloxy, phenylthio, phenylsulphonyl, anilino, benzyl, α,α-dimethylbenzyl, benzyloxy and nitro radicals.

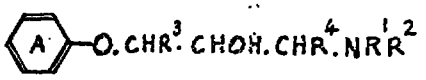
8. Compositions as claimed in any of claims 2—6 wherein the benzene ring (A) bears one or more additional substituents selected from fluorine, chlorine and bromine atoms and methyl, ethyl, isopropyl, t-butyl, methoxy, ethoxy, n-butoxy, acetyl, benzoyl, hydroxy, trifluoromethyl, phenyl, phenoxy, phenylthio, phenylsulphonyl, benzyl and nitro radicals.

9. Pharmaceutical compositions comprising as active ingredient racemic 1 - (3 - tolyloxy)-

The mixture is then cooled, 1 part of sterile 1 - isopropylamino -3 - (3 - tolyloxy) - 2-propanol hydrochloride is added, and the mixture is ball-milled under sterile conditions to reduce the particle size of the active ingredient to below 50 microns. There is thus obtained a sterile oily suspension suitable for intramuscular injection for therapeutic purposes.

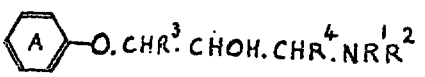
WHAT WE CLAIM IS:—

1. Pharmaceutical compositions comprising as active ingredient at least one racemic alkanolamine derivative of the formula:—



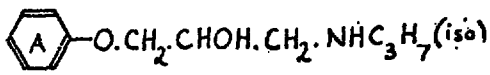
wherein R^1 stands for hydrogen; wherein R^2 stands for an alkyl radical of not more than 10 carbon atoms which is branched at the α-carbon atom, or for a cycloalkyl radical of not more than 5 carbon atoms, or for the 2 - hydroxy - 1,1 - dimethylethyl or 1-methyl - 3 - phenylpropyl radical; wherein R^3 and R^4, which may be the same or different, stand for hydrogen or for alkyl radicals of not more than 5 carbon atoms; and wherein the benzene ring (A) bears at least one additional substituent selected from halogen atoms, alkyl radicals containing not more than 4 carbon atoms, alkoxy, alkylthio, alkanoyl, aralkanoyl, aroyl, aryl, aryloxy, alkylaryloxy, arylthio, arylsulphonyl, arylamino, aralkyl, aralkoxy and alkenyl radicals each containing not more than 10 carbon atoms, halogenoalkyl radicals containing not more than 5 carbon atoms, and hydroxy and nitro radicals, provided that the 2- and 6-positions of the benzene ring (A) are not both substituted; or a carboxylic ester thereof, or a salt thereof, together with a pharmaceutically-acceptable diluent or carrier, but excluding simple non-sterile solutions of the active ingredients in common organic solvents or in water, and excluding simple aqueous suspensions of the active ingredients in the absence of a suspending agent.

2. Pharmaceutical compositions comprising as active ingredient at least one racemic alkanolamine derivative of the formula:—



wherein R^1 stands for hydrogen; wherein R^2 stands for an alkyl radical of not more than 10 carbon atoms which is branched at the α-carbon atom, or for a cycloalkyl radical of not more than 5 carbon atoms, or for the 2-hydroxyl - 1,1 - dimethylethyl or 1 - methyl-3 - phenylpropyl radical; wherein R^3 and R^4, which may be the same or different, stand for hydrogen or for alkyl radicals of not more than 5 carbon atoms; and wherein the benzene ring (A) bears at least one additional substituent selected from halogen atoms, alkyl radicals containing not more than 4 carbon atoms, alkoxy, alkanoyl, aralkanoyl, aroyl, aryl, aryloxy, arylthio, arylsulphonyl, aralkyl and alkenyl radicals each containing not more than 10 carbon atoms, halogenoalkyl radicals of not more than 5 carbon atoms, and hydroxy and nitro radicals, provided that the 2- and 6-positions of the benzene ring (A) are not both substituted; or a salt thereof, together with a pharmaceutically-acceptable diluent or carrier, but excluding simple non-sterile solutions of the active ingredients in common organic solvents or in water, and excluding simple aqueous suspensions of the active ingredient in the absence of a suspending agent.

3. Pharmaceutical compositions comprising as active ingredient at least one racemic alkanolamine derivative of the formula:



wherein the benzene ring (A) is further substituted as stated in claim 2, or a salt thereof, together with a pharmaceutically-acceptable diluent or carrier, but excluding simple non-sterile solutions of the active ingredients in common organic solvents or in water, and excluding simple aqueous suspensions of the active ingredient in the absence of a suspending agent.

4. Compositions as claimed in claim 1 or 2 wherein R^2 stands for the isopropyl, s-butyl or t-butyl radical.

5. Compositions as claimed in claim 1 or 2 wherein R^2 stands for the cyclopentyl radical.

6. Compositions as claimed in any one of claims 1, 2, 4 and 5 wherein R^3 or R^4 stands for the methyl radical.

7. Compositions as claimed in any one of claims 1 and 4—6 wherein the benzene ring (A) bears one or more substituents selected from fluorine, chlorine, bromine and iodine atoms and methyl, ethyl, isopropyl, t-butyl, methoxy, ethoxy, n-butoxy, methylthio, acetyl, benzoyl, hydroxy, trifluoromethyl, phenyl, phenoxy, 4-tolyloxy, phenylthio, phenylsulphonyl, anilino, benzyl, α,α-dimethylbenzyl, benzyloxy and nitro radicals.

8. Compositions as claimed in any of claims 2—6 wherein the benzene ring (A) bears one or more additional substituents selected from fluorine, chlorine and bromine atoms and methyl, ethyl, isopropyl, t-butyl, methoxy, ethoxy, n-butoxy, acetyl, benzoyl, hydroxy, trifluoromethyl, phenyl, phenoxy, phenylthio, phenylsulphonyl, benzyl and nitro radicals.

9. Pharmaceutical compositions comprising as active ingredient racemic 1 - (3 - tolyloxy)-

3 - isopropylamino - 2 - propanol or a salt thereof together with a pharmaceutically-acceptable diluent or carrier.

10. Pharmaceutical compositions comprising as active ingredient racemic 1 - (4 - tolyloxy)- or 1 - (2,3 - dimethylphenoxy) - 3-isopropylamino - 2 - propanol, or a salt thereof, together with a pharmaceutically-acceptable diluent or carrier.

11. Pharmaceutical compositions comprising as active ingredient racemic 1 - (2,4 - dimethylphenoxy)-, 1 - (3,4 - dimethylphenoxy)-,1 - (3,5 - dimethylphenoxy)-, 1 - (3-ethyl - 5 - methylphenoxy)-, 1 - (3 - chlorophenoxy)-, 1 - (2,3 - dichlorophenoxy)-, 1-(3,5 - dichlorophenoxy)-, 1 - (3 - fluorophenoxy)-, 1 - (4 - chloro - 3 - methylphenoxy)-, 1 - (3 - methoxyphenoxy)-, 1 - (2-hydroxyphenoxy)-, 1 - (3 - nitrophenoxy)-, 1 - (3 - trifluoromethylphenoxy)-, 1 - (2-phenylphenoxy)-, 1 - (2 - phenoxyphenoxy)- or 1 - (2 - benzoyl - 5 - methoxyphenoxy)-3 - isopropylamino - 2 - propanol, or 1-(2,3 - dichlorophenoxy) - 3 - s - butylamino-2 - propanol, 1 - (2 - hydroxy - 1,1 - dimethylethylamino) - 3 - (3 - tolyloxy) - 2-propanol or 1 - t - butylamino - 3 - (3 - tolyloxy) - 2 - propanol, or a salt thereof, together with a pharmaceutically-acceptable diluent or carrier.

12. Pharmaceutical compositions comprising as active ingredient racemic 1 - (2,4,5 - trichlorophenoxy)-, 1 - (3 - phenoxyphenoxy)-, 1 - (4 - anilinophenoxy)- or 1 - [2 - (4-tolyloxy)phenoxy] - 3 - isopropylamino - 2-propanol, or 1 - (3,5 - dimethylphenoxy) - 3-(1 - methyl - 3 - phenylpropylamino) - 2-propanol, or a salt thereof, together with a pharmaceutically-acceptable diluent or carrier.

13. Pharmaceutical compositions comprising as active ingredient racemic 1 - (2-chlorophenoxy) - 3 - isopropylamino - 2-propanol or a salt thereof together with a pharmaceutically-acceptable diluent or carrier, but excluding simple solutions of the active ingredient in common organic solvents or in water, and excluding simple aqueous suspensions of the active ingredient in the absence of a suspending agent.

14. Compositions as claimed in any one of claims 1—8 wherein the carboxylic ester is an *O*-ester derived from a saturated or unsaturated aliphatic carboxylic acid of not more than 20 carbon atoms, for example acetic, palmitic, stearic or oleic acid, or an *O*-ester derived from an aromatic carboxylic acid of not more than 15 carbon atoms, for example benzoic acid.

15. Compositions as claimed in any one of claims 1—14 wherein the salt of the alkanolamine or alkanolamine ester is an acid-addition salt derived from an inorganic acid, for example a hydrochloride, hydrobromide, phosphate or sulphate, or derived from an organic acid, for example an oxalate, lactate, tartrate, acetate, salicylate, citrate, benzoate, β-naphthoate, adipate or 1,1′ - methylene - bis - (2-hydroxy - 3 - naphthoate), or derived from an acidic synthetic resin, for example a sulphonated polystyrene resin.

16. Compositions as claimed in any one of claims 1—15 which are in the form of tablets, capsules, aqueous or oily solutions, aqueous or oily suspensions, emulsions, sterile injectable aqueous or oily solutions or suspensions, or dispersible powders.

17. Tablets as claimed in claim 16 which are formulated by admixture of the active ingredient(s) with known pharmaceutical excipients, for example inert diluents, for example calcium carbonate, calcium phosphate or lactose, disintegrating agents, for example maize starch or alkinic acid, binding agents, for example starch, gelatin or acacia mucilage, and lubricating agents, for example magnesium stearate, stearic acid or talc.

18. Tablets as claimed in claim 17 which are coated by known techniques in order to delay disintegration in the stomach.

19. Aqueous suspensions, emulsions, oily solutions and suspensions as claimed in claim 16 which contain a sweetening agent, for example glycerol, dextrose or sucrose, and a flavouring agent, for example vanillin or orange extract.

20. Aqueous suspensions as claimed in claim 16 or 19 which contain a suspending or thickening agent, for example sodium carboxymethylcellulose and a wetting agent, for example a condensation product of a fatty alcohol with ethylene oxide.

21. Emulsions as claimed in claim 16 or 19 which contain the active ingredient(s) dissolved in an oil of vegetable or animal origin, for example arachis oil or cod liver oil.

22. Emulsions as claimed in claim 21 which contain emulsifying agents and dispersing agents, for example soya bean lecithin, polyoxyethylene sorbitan monooleate, gum acacia, gum tragacanth or casein, and anti-oxidants, for example propyl gallate.

23. Oily solutions as claimed in claim 16 or 19 which contain the active ingredient(s) in solution in an oil of vegetable or animal origin.

24. Soft gelatin capsules containing an oily solution as claimed in claim 23.

25. Oily solutions as claimed in claim 19 which contain a sweetening agent, for example icing sugar, and a suspending agent, for example beeswax.

26. Capsules as claimed in claim 16 which contain the active ingredient(s) only or which contain the active ingredient(s) in admixture with inert diluents, for example lactose or sorbitol.

27. Sterile injectable aqueous suspensions as claimed in claim 16 which contain a suspending or thickening agent, for example sodium

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carboxymethylcellulose, and a wetting or dispersing agent, for example a phenol-polyethylene oxide condensate, for example the condensation product of octylcresol with about 8—10 molecular proportions of ethylene oxide.

28. Sterile injectable oily solutions as claimed in claim 16 which contain a non-toxic injectable oil, for example arachis oil or ethyl oleate.

29. Sterile injectable oily solutions as claimed in claim 28 which contain a gelling agent, for example aluminium stearate.

30. Sterile injectable oily preparations as claimed in claim 28 or 29 which contain one or more preservatives, for example methyl or n-propyl *p*-hydroxybenzoate or chlorobutanol.

31. Pharmaceutical compositions, claimed in any one of claims 1—30, substantially as described in the foregoing Examples 1—9.

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