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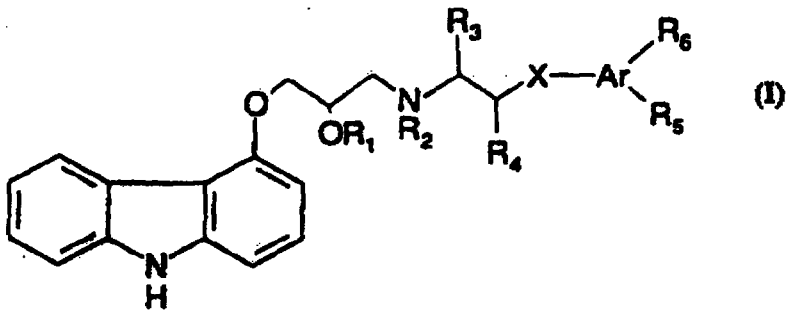
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(54) Title: USE OF CARBAZOLE COMPOUNDS FOR THE TREATMENT OF CONGESTIVE HEART FAILURE

(57) Abstract

A method of treatment using a compound of formula (I), wherein R_1 is hydrogen, lower alkanoyl of up to 6 carbon atoms or aroyl selected from benzoyl and naphthoyl; R_2 is hydrogen, lower alkyl of up to 6 carbon atoms or arylalkyl selected from benzyl, phenylethyl and phenylpropyl; R_3 is hydrogen or lower alkyl of up to 6 carbon atoms; R_4 is hydrogen or lower alkyl of up to 6 carbon atoms, or when X is oxygen, R_4 together with R_5 can represent $-CH_2-O-$; X is a valency bond, $-CH_2$, oxygen or sulfur; Ar is selected from phenyl, naphthyl, indanyl and tetrahydronaphthyl; R_5 and R_6



(I)

are individually selected from hydrogen, fluorine, chlorine, bromine, hydroxyl, lower alkyl of up to 6 carbon atoms, a $-CONH_2-$ group, lower alkoxy of up to 6 carbon atoms, benzyloxy, lower alkylthio of up to 6 carbon atoms, lower alkysulphonyl of up to 6 carbon atoms and lower alkylsulphonyl of up to 6 carbon atoms; or R_5 and R_6 together represent methylenedioxy; or a pharmaceutically acceptable salt thereof, preferably carvedilol, alone or in conjunction with one or more other therapeutic agents, said agents being selected from the group consisting of ACE inhibitors, diuretics, and cardiac glycosides for decreasing mortality resulting from congestive heart failure (CHF) in mammals, particularly humans.

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USE OF CARBAZOLE COMPOUNDS FOR THE TREATMENT OF CONGESTIVE HEART FAILURE

Field of the Invention

The present invention relates to a new method of treatment using compounds which are dual non-selective ß-adrenoceptor and α_1-adrenoceptor antagonists, in particular the carbazolyl-(4)-oxypropanolamine compounds of Formula I, preferably carvedilol, for decreasing the mortality of patients suffering from congestive heart failure (CHF). The invention also relates to a method of treatment using compounds which are dual non-selective ß-adrenoceptor and α_1-adrenoceptor antagonists, in particular the carbazolyl-(4)-oxypropanolamine compounds of Formula I, preferably carvedilol, in conjunction with one or more other therapeutic agents, said agents being selected from the group consisting of angiotensin converting enzyme (ACE) inhibitors, diuretics, and cardiac glycosides, for decreasing the mortality of patients suffering from CHF. The invention further relates to an incremental application scheme for administering compounds which are β-adrenoreceptor and α_1-adrenoreceptor antagonists.

Background of the Invention

Congestive heart failure occurs as a result of impaired pumping capability of the heart and is associated with abnormal retention of water and sodium. Traditionally, treatment of chronic mild failure has included limitation of physical activity, restriction of salt intake, and the use of a diuretic. If these measures are not suffcient, a cardiac glycoside, which is an agent that increases the force of mycardial contraction, is typically added to the treatment regimen.

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