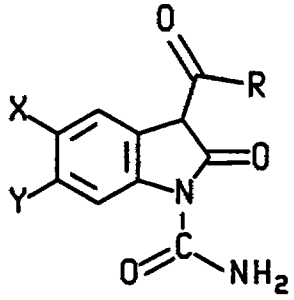
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INHIBITING PHOTODECOMPOSITION OF 3-SUBSTITUTED-2-OXINDOLES

Field of the Invention

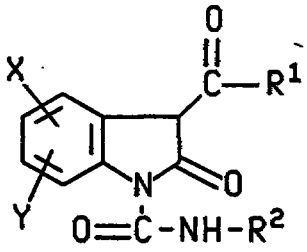
This invention relates to the inhibition of photodecomposition of certain 3-substituted-2-oxindole-1-carboxamides of the formula



and the pharmaceutically-acceptable base salts thereof wherein X is H, Cl or F; Y is H or Cl; and R is benzyl or thienyl, each optionally substituted with Cl or F.

Background of the Invention

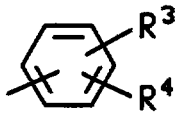
U.S. 4,569,942 discloses certain 2-oxindole-1-carboxamides of the formula



wherein X is H, fluoro, chloro, bromo, $(C_1\text{-}C_4)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_1\text{-}C_4)$alkoxy, $(C_1\text{-}C_4)$alkylthio, trifluoromethyl, $(C_1\text{-}C_4)$alkylsulfinyl, $(C_1\text{-}C_4)$alkylsulfonyl, nitro, phenyl, $(C_2\text{-}C_4)$alkanoyl, benzoyl, thenoyl, $(C_1\text{-}C_4)$alkanamido, benzamido or N,N-dialkylsulfamoyl having 1 to 3 carbons in each of said alkyls; Y is, H, fluoro, chloro, bromo, $(C_1\text{-}C_4)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_1\text{-}C_4)$alkoxy, $(C_1\text{-}C_4)$alkylthio and trifluoromethyl; R^1 is $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_4\text{-}C_7)$cycloalkenyl, phenyl, substituted phenyl, phenylalkyl having 1 to 3 carbons in said alkyl, (substituted phenyl)alkyl having 1 to 3 carbons in said alkyl, (substituted phenoxy)alkyl having 1 to 3 carbons in said alkyl, (thiophenoxy)alkyl having 1 to 3 carbons in said alkyl, naphthyl, bicyclo- [2.2.1]heptan-2-yl, bicyclo[2.2.1]hept-5-en-2-yl or $-(CH_2)_n\text{-}Q\text{-}R$; n is zero, 1 or 2; Q is a divalent radical derived from furan, thiophene, pyrrole, pyrazole, imidazole, thiazole, isothiazole, oxazole, isoxazole, 1,2,3-thiadiazole, 1,3,4-thiadiazole,

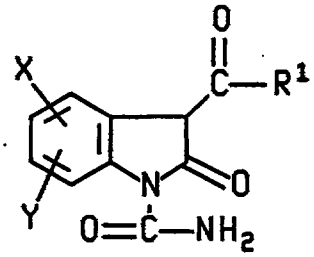
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1,2,5-thiadiazole, tetrahydrofuran, tetrahydrothiophene, tetrahydropyran, tetrahydrothiopyran, pyridine, pyrimidine, pyrazine, benzo[b]furan and benzo[b]-thiophene; and R^2 is $(C_1\text{-}C_6)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, benzyl, furyl, thienyl, pyridyl or



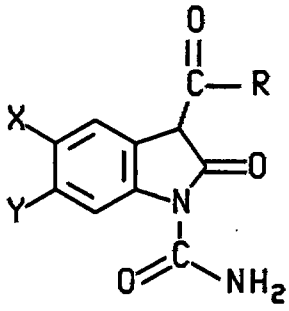
where R^3 and R^4 are each H, fluoro, chloro, $(C_1\text{-}C_4)$alkyl, $(C_1\text{-}C_4)$alkoxy or trifluoromethyl. That patent also discloses that said 2-oxindole-1-carboxamides are inhibitors of cyclooxygenase and lipoxygenase, possess analgesic activity in mammals and are useful in treatment of pain and alleviation of symptoms of chronic diseases such as inflammation and pain associated with rheumatoid arthritis and osteoarthritis.

U.S. Patent 4,556,672 discloses certain 3-acyl substituted- 2-oxindole-1-carboxamides of the formula



wherein X, Y and R^1 are as described above for the compounds of U.S. Patent No. 4,569,942.

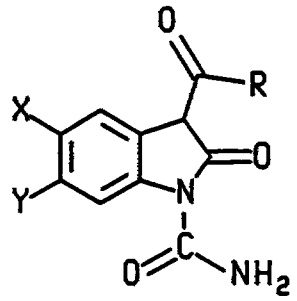
U.S. Patent No. 4,861,794 discloses the use of compounds of the formula



and the pharmaceutically-acceptable base salts thereof wherein X is H, Cl or F, Y is H or Cl and R is benzyl or thienyl to inhibit biosynthesis of interleukin-1 (IL-1) and to treat IL-1 mediated disorders and dysfunctions.

Summary of the Invention

This invention relates to a method of inhibiting photodecomposition of a compound of Formula I



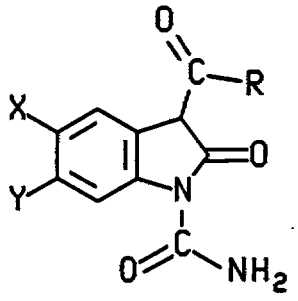
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and the enol form thereof or pharmaceutically acceptable salts thereof; wherein X is H, Cl or F; Y is H or Cl; and R is benzyl or thienyl, each optionally substituted with Cl or F; said photodecomposition resulting from light emanating from a light source which comprises introducing a light absorbing means between said compound and said light source.

In a preferred method of this invention said light absorbing means is a dye selected from the group consisting of yellow #6, red #40, red #3, yellow lake #6, red lake #40 and red lake #3.

In a further preferred method of this invention said light absorbing means is yellow #6.

In another aspect this invention relates to a tablet comprising a pharmaceutically active ingredient selected from a compound of the formula



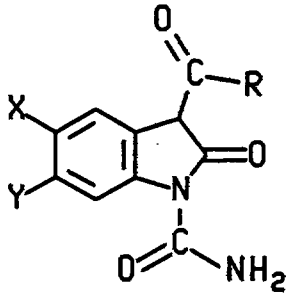
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or a pharmaceutically acceptable base salt thereof, wherein X is H, Cl or F; Y is H or Cl; and R is benzyl or thienyl, each optionally substituted with Cl or F; said tablet being coated with a coating containing a sufficient amount of yellow dye #6, red dye #40, red

dye #3, yellow lake #6, red lake #40 and red lake #3 to inhibit photodecomposition of said pharmaceutically active ingredient.

In a preferred aspect this invention comprises a coated tablet wherein said coating contains yellow dye #6 in sufficient amount to inhibit photodecomposition of said pharmaceutically active ingredient.

In another preferred aspect this invention comprises a capsule comprising a pharmaceutically active ingredient selected from a compound of the formula

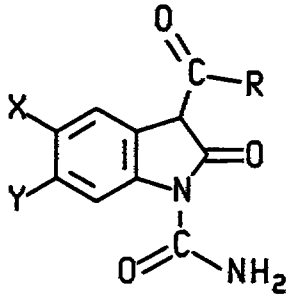


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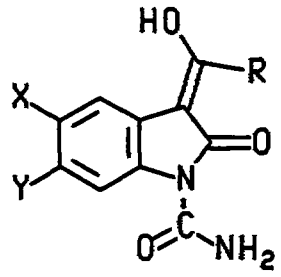
or a pharmaceutically acceptable base salt thereof, wherein X is H, Cl or F; Y is H or Cl; and R is benzyl or thienyl, each optionally substituted with Cl or F; said capsule shell containing a sufficient amount of yellow dye #6, red dye #40, red dye #3, yellow lake #6, red lake #40 and red lake #3 to inhibit photodecomposition of said pharmaceutically active ingredient.

Detailed Description of the Invention

Compounds of the formula



and the enol form:



and the pharmaceutically-acceptable base salts thereof wherein X is H, Cl or F; Y is H or Cl; and R is benzyl or thienyl optionally substituted with Cl or F and the preparation thereof are disclosed in U.S. Patent Nos. 4,556,672 and 5,290,802 the teachings of which are incorporated herein by reference. These compounds have been found to be photosensitive and are decomposed by light. This invention concerns methods for preventing photodecomposition of the compounds of Formula I and its enol form by inhibiting light from contacting said compounds.

As used within this document, "light source" means solar light or any artificial light source which produces light of wave lengths less than 600 nm. "Light absorbing means" means materials which block all or most wave lengths of light such as opaque glass or metals; or materials which absorb light with wave lengths of less than 600 nm such as ultra violet stabilizers or dyes.

The light absorbing means may be used in packaging materials such as blister packages, sachets or bottles. Chemical light absorbing means such as ultraviolet stabilizers may be incorporated in packaging material including blister packages, sachets or bottles or are preferably incorporated in capsule shells or tablet coatings. Chemical light absorbing means may also be mixed directly with the active ingredient prior to tableting or placing in a capsule shell.

"Inhibition of photodecomposition" means a statistically significant reduction in formation of light induced degradation products described herein below.

Of the methods of inhibiting photodecomposition described below, preferred therein are those where the compound employed is of the Formula I above wherein X is Cl, Y is H and R is thienyl; those wherein X is F, Y is Cl and R is thienyl or 4-chlorothien-2-yl; those wherein X is F, Y is Cl and R is 2-thienyl; and those wherein X is H, Y is Cl and R is benzyl. Particularly preferred are methods wherein X is Cl, Y is

H and R is 2-thienyl. The compounds of Formula I may exist in an enol form; all such enol forms and salts thereof are contemplated in this invention.

As disclosed in U.S. 4,556,672 and 5,290,802, the compounds protected by this invention are acidic and form base salts. All such base salts are within the scope of this invention and can be formed as taught by these patents. Such suitable salts, within the scope of this invention, include both the organic and inorganic types and include, but are not limited to, the salts formed with ammonia, organic amines, alkali metal hydroxides, alkali metal carbonates, alkali metal bicarbonates, alkali metal hydrides, alkali metal alkoxides, alkaline earth metal hydroxides, alkaline earth metal carbonates, alkaline earth metal hydrides and alkaline earth metal alkoxides. Representative examples of bases which form such base salts include ammonia, primary amines, such as n-propylamine, n-butylamine, aniline, cyclohexylamine, benzylamine, p-toluidine, ethanolamine and glucamine; secondary amines, such as diethylamine, diethanolamine, N-methylglucamine, N-methylaniline, morpholine, pyrrolidine and piperidine; tertiary amines, such as triethylamine, triethanolamine, N,N-dimethylaniline, N-ethylpiperidine and N-methylmorpholine; hydroxides, such as sodium hydroxide; alkoxides such as sodium ethoxide and potassium methoxide; hydrides such as calcium hydride and sodium hydride; and carbonates such as potassium carbonate and sodium carbonate. Preferred salts are those of sodium, potassium, ammonium, ethanolamine, diethanolamine and triethanolamine. Particularly preferred are the sodium salts. The compounds to which this invention is applicable include solvates such as the hemihydrates and monohydrates of the compounds hereinabove described.

Light-induced degradation of 3-substituted-oxindole-1-carboxamides occurs primarily at wave lengths of light less than 600 nm producing as decomposition products mainly benzoic or thenoic acid and oxindole-1-carboxamide. This degradation may be avoided by preventing light of wave lengths less than 600 nm from contacting the 3-substituted oxindole-1-carboxamide.

Red and yellow dyes have been found effective in preventing contact of light and the associated light-induced degradation of 3-substituted oxindole-1-carboxamides. Preferred dyes are FD&C red #40, FD&C red #3 and FD&C yellow #6. Yellow #6 is especially preferred. The dyes are effective in preventing light-induced degradation of 3-substituted-oxindole-1-carboxamides when mixed with the oxindole, applied to a

preformed tablet in a coating, or in a gelatin capsule containing the oxindole. The preferred method is the coating of tablets.

Film coating of pharmaceutical tablets is well known in the art and is described, for example, in United States Patents 4,828,841; 3,981,948; and 3,802,896 which are hereby incorporated by reference. Film coating materials such as white Opadry, Opadry II, Surelease, Aquacoat and Eudragit which are suitable for formulation with the selected dye are commercially available from Colorcon, West Point, PA; FMC Corp., Philadelphia, PA; Rohm Pharma, Weiterstadt, Germany respectively.

Dyes may also be formulated into gelatin capsules which are then filled with the oxindole. The technology for preparing capsules is well known to those of ordinary skill in this art. Capsules incorporating selected dyes are available commercially from Elanco Shinogi, Indianapolis, IN and Capsugel, Greenwood, SC. U.S. patent no. 3,784,684 describes the incorporation of opacifers and dyes in gelatine capsule shells.

The amount of dye in the coating or capsule shell is not critical except that sufficient dye must be incorporated to absorb any incident light. We have found that 1.2-2.8 mg/tablet of yellow #6 prevented decomposition while in capsule shells 0.28 to 0.5 mg/capsule afforded light stability.

A typical formulation of the coated tablets of this invention may be prepared as follows:

COMPONENT	mg/TABLET
Oxindole-1-carboxamide	21.74
Klucel EF	6.00
Lactose, Anhydrous	122.26
Ac-Di-Sol	6.00
Avicel PH102	40.00
Magnesium Stearate	3.60
Sodium Lauryl Sulfate	0.40
Total Weight (Core)	200.00
White Opadry (YS-5-7068)[a]	10.00
Distilled Water	
Yellow #6 Lake (39% Purity)[b]	1.15
Total Weight (Film coated tab)	211.15

[a] For the lots which will be film coated.

[b] For the lot which will contain dye.

The following Examples are presented to illustrate, but not to limit the invention which is defined by the claims.

EXAMPLE 1

Coated Tablets

Tablet cores of 5-chloro-2,3-dihydro-3-(hydroxy-2-thienylmethylene)-2-oxo-1H-indole-1-carboxamide (600 g) were prepared using the formulation described above.

Orange Opadry, containing yellow dye #6 obtained from Colorcon, West Point, PA (144 g) was suspended in 816 ml water. Tablet cores were changed to a Hi Coater HCT30 coating machine and held at 42°C while the orange Opadry suspension was applied.

Two coated and one uncoated lot of 5-chloro-2,3-dihydro-3-(hydroxy-2-thienylmethylene)-2-oxo-1H-indole-1-carboxamide (Formula I, X = Cl, Y = H) tablets were heated to 30°C and 50°C and held in a light cabinet for 6 weeks. Tablet cores were identical for all three lots. The coated tablets differ only in the amount of yellow #6 in the film coat. The intensity of the light cabinet was 400 foot candles (FC) in the center and 300 FC on the sides of the cabinet which was maintained at room temperature.

Appearances of the samples stored at 30°C and 50°C were not different from the appearance of the samples stored at 5°C. Flaking of the film coat was not observed for any tablets. The following visual observations were made on samples stored in the light cabinet for 6 weeks:

Lot 1 (core):	Slightly darkened, brown spots (compared to 5°C control)
Lot 2 (coated):	Slightly faded (compared to 5°C control)
Lot 3 (coated):	Slightly faded (compared to 5°C control)

The LC assay results for these lots are summarized in the table below. All samples were analyzed in triplicate. Assay values for the uncoated tablets were close to the intended 100 mg/g. Levels of thiophene-2-carboxylic acid, 6-chloro-1H-quinazoline-2,4-dione, thiophene-2-carboxylic acid 1-carbamoyl-5-chloro-2-oxo-2,3-dihydro 1H-indol-3-yl ester, 6-chloro-2-hydroxy-quinazoline-4-carboxylic acid and unknown #3 for the uncoated tablets increased significantly in the light cabinet (compared to 5°C control). No significant degradation was observed for the tablet cores stored at 5°C, 30°C or 50°C.

No significant degradation was observed for the coated tablets stored at 5°C, 30°C, 50°C or in the light cabinet. After 6 weeks, the levels of degradation in the light cabinet samples was approximately the same for both the coated tablet lots. Results of the above tests are shown in the table below.

40 mg 5-chloro-2,3-dihydro-3-(hydroxy-2-thienylmethylene)-2-oxo-1H-indole-1-carboxamide (Formula I, X = Cl, Y = H) Stability, 6 Weeks*				
LOT 1 (tablet core)				
6 weeks:	5°C	30°C	50°C	LC
5-chloro-2,3-dihydro-3-(hydroxy-2-thienylmethylene)-2-oxo-1H-indole-1-carboxamide (Formula I, X = Cl, Y = H) (mg/Tab)	39.4	39.7	39.8	38.7
5-chloro-2,3-dihydro-3-(hydroxy-2-thienylmethylene)-2-oxo-1H-indole-1-carboxamide (Formula I, X = Cl, Y = H) (mg/g)	99.0	99.8	100.8	97.8
% Thiophene-2-carboxylic acid	0.01	0.02	0.04	0.28
% 6-Chloro-1H-quinazoline-2,4-dione	ND	ND	<0.01	0.06
% Thiophene-2-carboxylic acid 1-carbamoyl-5-chloro-2-oxo-2,3-dihydro 1H-indol-3-yl ester	0.01	0.03	0.02	0.19
% 6-Chloro-2-hydroxy-quinazoline-4-carboxylic acid	0.01	0.03	0.04	0.29
% Unknown #3**	ND	ND	ND	0.03
LOT 2 (coated tablets, 1.35 mg yellow #6)				
6 weeks	5°C	30°C	LC	
5-chloro-2,3-dihydro-3-(hydroxy-2-thienylmethylene)-2-oxo-1H-indole-1-carboxamide (Formula I, X = Cl, Y = H) (mg/Tab)	39.5	39.4	38.7	
5-chloro-2,3-dihydro-3-(hydroxy-2-thienylmethylene)-2-oxo-1H-indole-1-carboxamide (Formula I, X = Cl, Y = H) (mg/g)	92.7	93.1	91.2	
% Thiophene-2-carboxylic acid	0.02	0.01	0.03	
% 6-Chloro-1H-quinazoline-2,4-dione	0.02	0.02	0.02	
% Thiophene-2-carboxylic acid 1-carbamoyl-5-chloro-2-oxo-2,3-dihydro-1H-indol-3-yl ester	0.01	0.01	0.01	
% 6-Chloro-2-hydroxy-quinazoline-4-carboxylic acid	0.03	0.02	0.04	

LOT 3 (coated tablets, 0.9 mg yellow #6)				
6 weeks	5°C	30°C	50°C	LC
5-chloro-2,3-dihydro-3-(hydroxy-2-thienylmethylene)-2-oxo-1H-indole-1-carboxamide (Formula I, X = Cl, Y = H) (mg/Tab)	39.5	39.6	39.0	39.0
5-chloro-2,3-dihydro-3-(hydroxy-2-thienylmethylene)-2-oxo-1H-indole-1-carboxamide (Formula I, X = Cl, Y = H) (mg/g)	94.9	94.8	94.3	93.3
% Thiophene-2-carboxylic acid	0.01	0.03	0.04	0.04
% 6-Chloro-1H-quinazoline-2,4-dione	0.01	0.01	0.01	0.01
% Thiophene-2-carboxylic acid 1-carbamoyl-5-chloro-2-oxo-2,3-dihydro 1H-indol-3-yl ester	0.01	0.02	0.02	0.02
% 6-Chloro-2-hydroxy-quinazoline-4-carboxylic acid	0.02	0.04	0.05	0.05
* Stability comparisons should be made against the 5°C control.				
** Area percent.				

EXAMPLE 2

Capsules

A formulation of a compound of Formula I where X is Cl, Y is H and R is thienyl was prepared from the following components:

	mg/unit
Compound of Formula I Sodium	128.205
Lactose, anhydrous	159.795
Pregelatinized Starch	112.500
Croscormellose Sodium	9.000
Magnesium Stearate	9.000

The above ingredients were mixed and a portion roller compacted, then milled and reblended with the remaining ingredients, lubricated and encapsulated in gelatin capsules obtained from Capsugel, a division of Warner-Lambert Company. A preferred

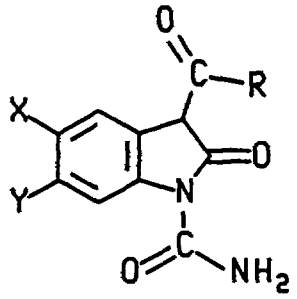
lubricant is sodium laurel sulfate. The capsules contained FD&C yellow dye 0.2651% of total dry weight in the capsule body and 0.1768% in the cap.

Capsules prepared in this manner were found to afford light stability to the compound of Formula I.

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CLAIMS

1. A method for inhibiting photodecomposition of a compound of the formula



and the enol form thereof or a pharmaceutically-acceptable base salt thereof, wherein X is H, Cl or F; Y is H or Cl; and R is benzyl or thienyl, each optionally substituted with Cl or F; said photodecomposition resulting from light emanating from a light source which comprises introducing a light absorbing means between said compound and said light source.

2. A method according to claim 1 wherein X is Cl; Y is H; and R is thienyl.

3. A method according to claim 2 wherein R is 2-thienyl.

4. The method according to claim 3 wherein the pharmaceutically-acceptable base salt is sodium.

5. A method according to claim 1 wherein X is F; Y is Cl; and R is thienyl or 4-chlorothien-2-yl.

6. The method according to claim 5 wherein R is 4-chlorothien-2-yl

7. The method according to claim 1 wherein X is H; Y is Cl; and R is benzyl.

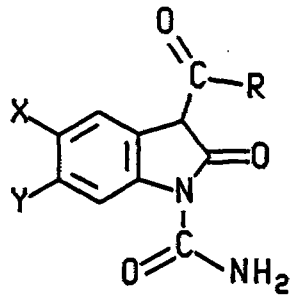
8. A method of claim 1 wherein said light absorbing means is a dye selected from the group consisting of yellow #6, red #40, red #3, yellow lake #6, red lake #40 and red lake #3.

9. A method of claim 8 wherein said light absorbing means is yellow #6.

10. A tablet comprising a pharmaceutically active ingredient selected from a compound of the formula

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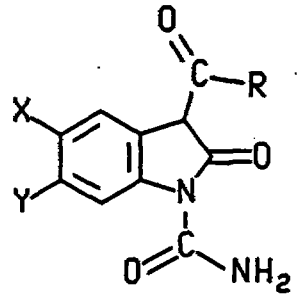


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or a pharmaceutically acceptable base salt thereof, wherein X is H, Cl or F; Y is H or Cl; and R is benzyl or thienyl, each optionally substituted with Cl or F; said tablet being coated with a coating containing a sufficient amount of yellow dye #6, red dye #40, red dye #3, yellow lake #6, red lake #40 and red lake #3 to inhibit photodecomposition of said pharmaceutically active ingredient.

11. A tablet of claim 10 wherein said coating contains yellow dye #6.

12. A capsule comprising a pharmaceutically active ingredient selected from a compound of the formula



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or a pharmaceutically acceptable base salt thereof, wherein X is H, Cl or F; Y is H or Cl; and R is benzyl or thienyl, each optionally substituted with Cl or F; said capsule shell containing a sufficient amount of yellow dye #6, red dye #40, red dye #3, yellow lake #6, red lake #40 and red lake #3 to inhibit photodecomposition of said pharmaceutically active ingredient.

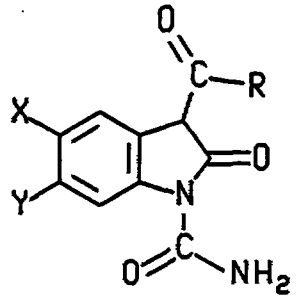
13. A capsule of claim 12 wherein said capsule shell contains yellow dye #6.

14. A method of claim 1 wherein said light absorbing means is packaging material which is effective in absorbing light.

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ABSTRACT

This invention relates to the protection of certain 3-substituted-2-oxindole-1-carboxamides of the formula



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and the pharmaceutically-acceptable base salts thereof wherein X is H, Cl or F; Y is H or Cl; and R is benzyl or thienyl, each optionally substituted with Cl or F from decomposition in the presence of light.

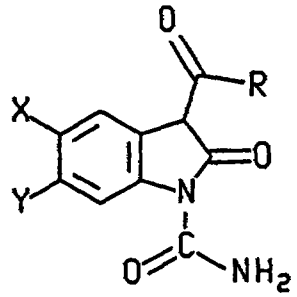
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INHIBITING PHOTODECOMPOSITION OF 3-SUBSTITUTED-2-OXINDOLES

Field of the Invention

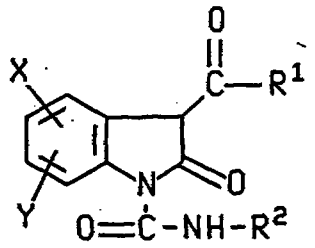
This invention relates to the inhibition of photodecomposition of certain 3-substituted-2-oxindole-1-carboxamides of the formula



and the pharmaceutically-acceptable base salts thereof wherein X is H, Cl or F; Y is H or Cl; and R is benzyl or thienyl, each optionally substituted with Cl or F.

Background of the Invention

U.S. 4,569,942 discloses certain 2-oxindole-1-carboxamides of the formula



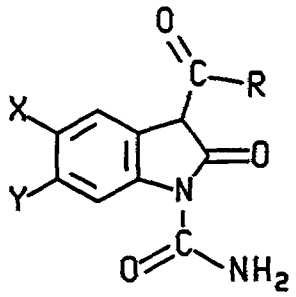
wherein X is H, fluoro, chloro, bromo, $(C_1\text{-}C_4)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_1\text{-}C_4)$alkoxy, $(C_1\text{-}C_4)$alkylthio, trifluoromethyl, $(C_1\text{-}C_4)$alkylsulfinyl, $(C_1\text{-}C_4)$alkylsulfonyl, nitro, phenyl, $(C_2\text{-}C_4)$alkanoyl, benzoyl, thenoyl, $(C_1\text{-}C_4)$alkanamido, benzamido or N,N-dialkylsulfamoyl having 1 to 3 carbons in each of said alkyls; Y is, H, fluoro, chloro, bromo, $(C_1\text{-}C_4)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_1\text{-}C_4)$alkoxy, $(C_1\text{-}C_4)$alkylthio and trifluoromethyl; R^1 is $(C_1\text{-}C_8)$alkyl, $(C_3\text{-}C_7)$cycloalkyl, $(C_4\text{-}C_7)$cycloalkenyl, phenyl, substituted phenyl, phenylalkyl having 1 to 3 carbons in said alkyl, (substituted phenyl)alkyl having 1 to 3 carbons in said alkyl, (substituted phenoxy)alkyl having 1 to 3 carbons in said alkyl, (thiophenoxy)alkyl having 1 to 3 carbons in said alkyl, naphthyl, bicyclo- [2.2.1]heptan-2-yl, bicyclo[2.2.1]hept-5-en-2-yl or $-(CH_2)_n\text{-}Q\text{-}R$; n is zero, 1 or 2; Q is a divalent radical derived from furan, thiophene, pyrrole, pyrazole, imidazole, thiazole, isothiazole, oxazole, isoxazole, 1,2,3-thiadiazole, 1,3,4-thiadiazole,

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CLAIMS

1. A method for inhibiting photodecomposition of a compound of the formula



and the enol form thereof or a pharmaceutically-acceptable base salt thereof, wherein X is H, Cl or F; Y is H or Cl; and R is benzyl or thienyl, each optionally substituted with Cl or F; said photodecomposition resulting from light emanating from a light source which comprises introducing a light absorbing means between said compound and said light source.

2. A method according to claim 1 wherein X is Cl; Y is H; and R is thienyl.

3. A method according to claim 2 wherein R is 2-thienyl.

4. The method according to claim 3 wherein the pharmaceutically-acceptable base salt is sodium.

5. A method according to claim 1 wherein X is F; Y is Cl; and R is thienyl or 4-chlorothien-2-yl.

6. The method according to claim 5 wherein R is 4-chlorothien-2-yl

7. The method according to claim 1 wherein X is H; Y is Cl; and R is benzyl.

8. A method of claim 1 wherein said light absorbing means is a dye selected from the group consisting of yellow #6, red #40, red #3, yellow lake #6, red lake #40 and red lake #3.

9. A method of claim 8 wherein said light absorbing means is yellow #6.

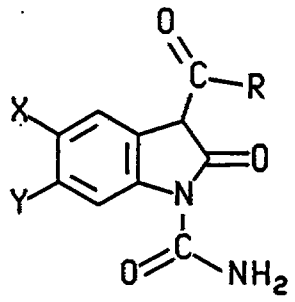
10. A tablet comprising a pharmaceutically active ingredient selected from a compound of the formula

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INHIBITING PHOTODECOMPOSITION OF 3-SUBSTITUTED-2-OXINDOLES

ABSTRACT

This invention relates to the protection of certain 3-substituted-2-oxindole-1-carboxamides of the formula



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and the pharmaceutically-acceptable base salts thereof wherein X is H, Cl or F; Y is H or Cl; and R is benzyl or thienyl, each optionally substituted with Cl or F from decomposition in the presence of light.