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FLUORESCENT SKIN-MARKING COMPOSITION

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ABSTRACT OF THE DISCLOSURE

A normally liquid, ultraviolet light-sensitive skin marking composition is disclosed as being useful for marking the skin of animals or humans, for instance to indicate areas on a patient's skin which are to be subjected to radiation therapy, for example for the treatment of cancer. The mark left by the composition is invisible in visible light but fluoresces under ultraviolet light. The composition consists essentially of polyvinyl acetate, a water-immiscible fluorescent brightening agent of the aminocoumarin type, organic solvent, and, optionally, water.

This invention is directed to marking compositions and an improved method of marking the skin of animals or humans, for instance to indicate target areas on the skin of patients to be subjected to radiation therapy. More particularly, it is directed to such a marking composition which, when applied to such skin, leaves a mark which is unnoticeable in ordinary, or visible, light but which fluoresces under ultraviolet light.

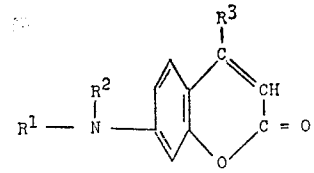
One field of use for the compositions of this invention is the treatment of cancer in humans by radiation therapy. It is the usual procedure to prepare the patient by visibly marking his skin to outline the diseased area to be irradiated. The marking material currently in use for this purpose is a bright purple dye which is visible in ordinary light. The mark left by the dye is resistant to removal by soap and water, this being a desired property since the treatment usually involves periodic irradiations over a period of about 6 to 8 weeks. While adequate for its intended purpose, the use of such a dye has a decided disadvantage—namely, the patient is adversely affected psychologically by the unsightly appearance of the mark and the fact that it must remain for such a long period of time. The problem is aggravated in cases where the mark is on a normally exposed area of the body such as the hands, face, neck, or throat.

A method of the present invention involves the application of the composition to the skin of the patient being prepared for radiation therapy to provide a normally invisible marking which, however, becomes quite visible under ultraviolet light, both long and short wave. The applied composition advantageously glows continuously under ultraviolet light without requiring visible light to activate the pigment. Thus, at the time for therapy the normally invisible marking can be illuminated with ultraviolet light to guide the radiation therapist in his treatment, but in the intervals between treatments the marking will remain virtually, if not in fact, invisible, being invisible under daylight, incandescent and fluorescent lighting.

The marking composition used in the method of the present invention has also been found to be effective without causing matting of the epidermal hair. It is essentially colorless and odorless. The composition is non-irritating, non-toxic and, when applied to the skin, leaves a tenacious film which conforms to surface irregularities. The mark left by the composition exhibits excellent resistance to scrubbing and repeated washings, such that one application will last at least several days, perhaps even weeks. If the mark becomes unsatisfactorily weak,

it can be traced over with a fresh application of the marking composition. Usually this will present no problem since radiation treatments are most often spaced about one week apart. Applying a fresh coating over the mark can be done, say, every other week. This tracing effort can be done by a nurse or technician and is far less time consuming than having to every so often relocate the area to be treated, a task which generally can be performed only by the physician.

The composition of the present invention consists essentially of a normally liquid solution of polyvinyl acetate, a water-immiscible fluorescent brightening agent of the aminocoumarin type, water-miscible organic solvent, and, optionally, water. The polyvinyl acetate component of the composition of the present invention has a molecular weight generally from about 30,000 to 60,000, preferably about 42,000 to 48,000. It is generally employed in amounts of about 4% to 12%, preferably about 7% to 9%, based on the weight of the total composition. The fluorescent brightening agent employed is a compound of the general formula:



wherein each of R^1, R^2 and R^3 is either hydrogen or alkyl of up to 3 carbon atoms. Preferably, each of R^1, R^2 and R^3 has up to 2 carbon atoms, for example being either methyl or ethyl. Most preferred of the compounds is 7-diethylamino-4-methylcoumarin, i.e. the compound represented by the above formula when R^1 and R^2 are both ethyl and R^3 is methyl. The amount of fluorescent brightening agent to be included in the composition is generally about 4% to 12%, preferably about 7% to 9%, based on the weight of the total composition. Mixtures of suitable brightening agents can be employed if desired. Also, the brightening agent can be in admixture with salts, such as sodium sulfate, which may be conventionally admixed therewith, for example to enhance certain solubility characteristics of the brightening agent. Thus, for instance, the preferred brightener for use in the composition of the present invention, 7-diethylamino-4-methylcoumarin, is supplied commercially both in pure form and diluted with a minor amount of sodium sulfate to enhance its solubility characteristics. Either form can be used in practicing the present invention.

The marking composition of the present invention advantageously includes an organic solvent in amounts sufficient to dissolve essentially all of the polyvinyl acetate and the brightening agent. These amounts will generally range from about 3 to 7 parts, preferably about 4 to 5 parts, per combined part by weight of the polyvinyl acetate and brightening agent. The solvent can comprise either just one or a mixture of two or more organic compounds. Often, for example, the polyvinyl acetate may be obtained from commercial sources in solution form in a suitable organic compound, e.g. in methanol, and the brightening agent obtained as a concentrated solution as well, but in a different, albeit suitable, medium. In such an instance these ingredients can be used in their predissolved forms in formulating the marking composition of the present invention. Any further solvent which may be desired—perhaps even a third compound—can be added separately. The totality of the solubilizing organic compounds present in the composition, whatever their source, is, then, what is referred to herein as the organic solvent.

Suitable organic solvents, then, are those which are miscible with water and are non-irritating to human skin of normal sensitivity. As examples of such may be mentioned, for instance, monohydric alkanols (both straight and branched-chain) of 1 to 4 carbon atoms, e.g., methanol, ethanol, isopropanol and n-butanol. Compounds such as ketone (e.g. acetone) and esters (e.g. ethylacetate) are generally irritating to human skin and, for this reason, should not be included in the organic solvent component. A preferred organic solvent is a mixture of about 50 to 70 weight percent of isopropanol and about 30 to 50 weight percent of methanol.

Water may be included in the composition of this invention, generally in amounts up to about 25 weight percent of the organic solvent. The water can serve as a cost-reducing extender for the composition, as well as a thinner. Thus, it is usually preferred that the marking composition have a viscosity at room temperature of about 15 to 18 seconds, optimally about 15 seconds, as measured with a Number 2 Zahn cup. Sufficient water to achieve a viscosity within this range is advantageously employed. Accordingly, the water will often be included in amounts of about 12 to 25, most preferably about 15 to 18, percent, based on the weight of the organic solvent.

The marking composition can be prepared by combining and mixing the several ingredients in any number which yields a normally liquid—i.e., liquid under ambient conditions—solution. Thus, for example, formulating can be carried out at room temperature by first dissolving the fluorescent brightening agent in a portion of the organic solvent, then adding the water, if employed, and finally adding the polyvinyl acetate as a solution in the remainder of the organic solvent.

The following examples will serve to illustrate, but not limit, the compositions and method of the present invention.

EXAMPLE I

Twenty-nine (29) pounds of "Calcofluor White RW" (a mixture of 90 weight percent 7-diethylamino-4-methylcoumarin and 10 weight percent sodium sulfate) was dissolved in 480 pounds of isopropanol at room temperature. To the resulting solution was added, with agitation, 108 pounds of water and 112 pounds of a 50 weight percent solution of polyvinyl acetate in methanol, the polyvinyl acetate having an average molecular weight of about 45,000. The resulting solution exhibited a room temperature viscosity in the range of about 15 to 18 seconds as measured with a number 2 Zahn cup. Samples of the solution were applied with cotton swabs to human arms. After evaporation of the volatiles, no visible residue was left. Illumination of the test area under ultraviolet light, however, rendered the residue visible as a fluorescent glow. The test subjects then washed their arms 20 times with soap and water, after which the coating appeared just as brilliant under ultraviolet light.

EXAMPLE II

A marking composition identical to that of Example I, except containing double the concentration of "Calcofluor White RW," was prepared and tested as in Example I. Equivalent results were obtained except that the marks applied with this composition were more durable than those applied with the composition of Example I. After two weeks of exposure to normal washing, abrasion, etc., the marks of this example still retained about 60% of their original visible strength under the ultraviolet light. After four weeks the marks were weak. When using the composition of this example, renewal of the mark need only be made about once every two weeks to assure excellent results.

The results obtained by using the compositions of the present invention were surprising, particularly since the following compositions, Compositions A, B, C and D, were found unsuitable.

Composition A had the following formulation. Instead of containing a brightening agent of the present invention, this composition was made with "Calcofluor ST," a brightener having a Colour Index number of 28. The composition was easily washed off the skin and, therefore, was unsuitable.

Ingredients:	Parts by weight
Isopropanol	66
"Calcofluor ST"	4
Water	15
Polyvinyl acetate	1.5
Methanol	7.5

The following Composition B likewise proved unsuccessful. The ingredients would not remain in suspension, the washability was poor, and the composition matted the epidermal hair and left a mark which was quite visible in daylight.

Ingredients:	Parts by weight
"Calcofluor ST"	4
Propylene glycol	3
Water	63
Poly (2-ethylhexyl methacrylate)	30

The following Composition C was tested and found to have the same deficiencies as that of Composition B.

Ingredients:	Parts by weight
"Calcofluor ST"	4
Propylene glycol	3
Water	63
Copolymer of vinyl acetate and 2-ethylhexyl methacrylate, 70:30 molar ratio, respectively	30

The following Composition D was also found to be unsuitable. It emitted a very strong and unpleasant odor and left a mark which was visible in daylight.

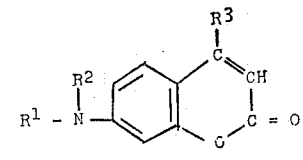
Ingredients:	Parts by weight
Methanol	16
Soya-alkyd resin	50
Calcium carbonate	40
Phosphorescent pigment having Colour Index number of 716 (Lawter Co.)	5
Aluminum stearate	0.3
Zinc oxide	1.5
Mineral spirits	15
24% solution of lead naphthenate	0.2
6% solution of cobalt naphthenate	0.2

It is claimed:

1. An ultraviolet light-sensitive skin marking composition consisting essentially of a normally-liquid solution of:

(a) about 4 to 12 percent (based on the weight of the total composition) of polyvinyl acetate having a molecular weight of about 30,000 to 60,000,

(b) about 4 to 12 percent (based on the weight of the total composition) of a water-immiscible fluorescent brightening agent of the formula:



wherein each of R^1, R^2 and R^3 is either hydrogen or alkyl of up to 3 carbon atoms,

(c) water-miscible organic solvent which is non-irritating to human skin of normal sensitivity, said solvent being present in an amount which is sufficient to dissolve essentially all of said components (a) and (b) and which is within the range of about 3 to 7 parts per combined part by weight of said components (a) and (b), and

(d) water in an amount up to about 25 weight percent of said organic solvent.

2. The composition of claim 1 wherein the organic solvent (component (c)) is selected from the group consisting of monohydric alkanols of 1 to 4 carbon atoms and mixtures thereof, and each of R^1, R^2 and R^3 is either methyl or ethyl.

3. The composition of claim 1 wherein the polyvinyl acetate (component (a)) has a molecular weight of about 42,000 to 48,000.

4. The composition of claim 1 wherein component (a) is present in amounts of about 7 to 9 percent; component (b) is present in amounts of about 7 to 9 percent; component (c) is present in amounts of about 4 to 5 parts per combined part by weight of said components (a) and (c); and component (d) is present in amounts of about 12 to 25 weight percent of said component (c).

5. The composition of claim 1 wherein the fluorescent brightening agent (component (b)) is 7-diethylamino-4-methylcoumarin.

6. The composition of claim 2 wherein the fluorescent brightening agent (component (b)) is 7-diethylamino-4-methylcoumarin.

7. The composition of claim 3 wherein the fluorescent brightening agent (component (b)) is 7-diethylamino-4-methylcoumarin.

8. The composition of claim 4 wherein the fluorescent brightening agent (component (b)) is 7-diethylamino-4-methylcoumarin.

9. An ultraviolet light-sensitive skin marking composition consisting essentially of a normally-liquid solution of:

(a) about 7 to 9 percent (based on the weight of the total composition) of polyvinyl acetate having a molecular weight of about 42,000 to 48,000,

(b) about 7 to 9 percent (based on the weight of the total composition) of 7 - diethylamino - 4-methylcoumarin,

(c) an amount within the range of about 4 to 5 parts per combined part by weight of said components (a) and (b), said amount being sufficient to dissolve essentially all of said components (a) and (b), of organic solvent selected from the group consisting of monohydric alkanols of 1 to 4 carbon atoms and mixtures thereof, and

(d) an amount within the range of about 12 to 25 percent, based on the weight of said component (c), said amount being sufficient to impart a room temperature viscosity to the composition of about 15 to 18 seconds, as measured with a Number 2 Zahn cup, of water.

10. The composition of claim 9 wherein the organic solvent (component (c)) consists essentially of about 50 to 70 weight percent of isopropanol and about 30 to 50 weight percent of methanol.

References Cited

UNITED STATES PATENTS

2,333,329	11/1943	Miglarese	117—1
2,347,644	5/1944	Sell	250—71
2,929,931	3/1960	Richter et al.	250—71
2,553,552	5/1951	Corper	424—9
3,309,274	3/1967	Brilliant	424—7

OTHER REFERENCES

Kirk-Othmer Encyclopedia of Chemical Technology, Interscience Encyclopedia, Inc., New York, N.Y., vol. 14 (1955), p. 692–3.

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