(11) Application No. AU 2004264332 B2

(19) AUSTRALIAN PATENT OFFICE

(54) Title

Method and composition for treating burned skin

(51)[6] International Patent Classification(s)

A61K 31/405 8BMEP **A61P**
(2006.01) 17/02
A61P 17/02 (2006.01) 20060101ALI2006052
A61K 31/405 1BMWO
20060101AFI2005100 PCT/US2004/025260

(21) Application No: 2004264332 (22) Application Date: 2004.08.05

(87) WIPO No: WO05/016336

(30) Priority Data

(31) Number	(32) Date	(33) Country
10/636,404	2003.08.07	US

(43) Publication Date : 2005.02.24

(71) Applicant(s)

Lil Brat Pharmaceuticals

(72) Inventor(s)

Wayne, Dittrich D. O.

(74) Agent/Attorney

Watermark Patent and Trade Marks Attorneys, Level 2 302 Burwood Road, Hawthorn, VIC, 3122

(56) Related Art

US 5705196 A
US 4088754 A
JP 51765313 A,

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
24 February 2005 (24.02.2005)

PCT

(10) International Publication Number
WO 2005/016336 A1

(51) International Patent Classification[7]: A61K 31/405, A61P 17/02, A61K 9/10

(21) International Application Number: PCT/US2004/025260

(22) International Filing Date: 5 August 2004 (05.08.2004)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
10/636,404 7 August 2003 (07.08.2003) US

(71) Applicant *(for all designated States except US)*: **LIL BRAT PHARMACEUTICALS** [US/US]; 6772 Lorraine Street, Marlette, MI 48453 (US).

(72) Inventor: **WAYNE, Dittrich, D., O.**; 6723 Oakes Street, Marlette, MI 48453 (US).

(74) Agents: **MOORE, Todd, L.** et al.; Young & Basile, P.C., Suite 624, 3001 West Big Beaver Road, Troy, MI 48084-3107 (US).

(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 2005/016336 A1

(54) Title: METHOD AND COMPOSITION FOR TREATING BURNED SKIN

(57) Abstract: The present invention relates to a method and composition for treating sunburned skin. The present invention provides a method and composition for applying a mixture of indomethacin and moisturizing lotion topically to sunburned skin. The composition includes a mixture having substantially 100 milligrams of indomethacin per 30 cc of moisturizing lotion. The moisturizing lotion is marketed under the trade name Cetaphil® and includes the following ingredients: purified water, glycerin, hydrogenated polyisobutene, cetearyl alcohol (and) ceteareth-20, macadamia nut oil, dimethicone, tocopheryl acetate, stearoxytrimethylsilane (and) stearyl alcohol, panthenol, farnesol, benzyl alcohol, phenoxyethanol, acrylates/C10-30 alkyl acrylate crosspolymer, sodium hydroxide, and citric acid. It is theorized that the Cetaphil® provides certain pH and viscosity levels which allow for the stabilization and solubilation of the indomethacin within the Cetaphil®. The present invention may also be utilized for treating skin burns caused by radiation therapy and excessive heat.

METHOD AND COMPOSITION FOR TREATING BURNED SKIN

The subject application is a continuation-in-part of U.S. Patent Application Serial No. 10/636,404 filed on August 7, 2003.

Field of the Invention

The present invention relates to a method and composition for treating burned skin, and more particularly, a method and composition for a topical application of an indomethacin and moisturizing lotion formulation for the treatment of mild to moderate skin burns.

Background of the Invention

Although there has been substantial effort in recent years to reduce or eliminate the risk of sunburn (erythema) produced by certain wavelengths in the ultraviolet (UV) region of the spectrum, there are still circumstances wherein skin becomes exposed to UV radiation. Such exposure may, in some cases, cause sunburn. Such sunburn may cause irritation and pain to the skin thereby leading to the need for having the sunburn treated.

A number of prior art formulations have been developed for the treatment of sunburned skin. However, such treatments have certain disadvantages. For example, sunburn treatments that provide a spray mist or a petroleum-based composition to the sunburned area do not produce a sufficiently large heat transference effect to remove heat from the sunburned area. Furthermore, petroleum-based compositions tend to produce a residue that needs to be subsequently cleansed from the tender and sensitive area of the

sunburned skin. Such cleansing tends to cause further discomfort and irritation to the affected skin.

Preferably, a treatment for sunburn would satisfy several objectives simultaneously. The main objective for the treatment of sunburn would be to relieve pain, eliminate the source of heat, stop the burn progression, and, if necessary, help prevent infection. Thus, a useful treatment for sunburn preferably provides immediate relief from pain while also helping to promote healing. It would be desirable to have a formulation for treatment of sunburn to be combined in a reasonably convenient and cost-effective process wherein the prepared composition would remain stable during storage. Such a sunburn formulation should provide the relief and healing effects sought without producing an uncomfortable, sticky sensation and without soiling or sticking to one's clothing. In addition, the sunburn formulation should preferably not produce a residue that must be subsequently washed or removed from the sensitive sunburned area.

Since a sunburn is an inflammatory disorder, sunburn has been treated in the past with anti-inflammatory drugs. One of the most effective therapeutics is indomethacin [1-(p-chlorobenzoyl)-5-methoxy-2-methylindole-3-acetic acid], a non-steroid chemical compound that has been widely recognized for its outstanding anti-inflammatory, anti-pyretic, and analgesic properties. However, indomethacin can become unstable when mixed with certain carriers for topical applications, and therefore, oral administration is sometimes the preferred method of administration.

Oral administration of indomethacin has previously been reported as effective in relieving pain, reducing fever, and providing increased mobility in patients with inflammatory disorders, including those of a rheumatic nature. When orally administered, the

drug behaves as a systemic medicine that passes into the bloodstream for general distribution in the body. As in the case with numerous other drugs, not every one can satisfactorily accept this drug by the oral mode of administration, particularly over extending periods of therapy. In addition, oral administration does not provide for the direct and concentrated application of indomethacin on an affected area, such as an area of sunburned skin.

Similar deficiencies also exist in the treatment of skin burns as a result of radiation therapy. Past treatments have utilized moisturizing creams or ointments to soothe the skin burns, however, such creams and ointments do not contain active anti-inflammatory or anesthetic agents to reduce pain or itching. Topical hydrocortisone creams or ointments have been utilized to reduce inflammation and discomfort, but such treatments typically provide only temporary relief for up to 1-1 ½ hours. Topical anesthetic creams or ointments work to reduce pain, but similarly, only provide for the temporary relief of such pain. Other creams, such as silver sulfadiazine cream 1% (sold as Silvadene Cream®), are used to treat radiation burns having blistered areas and ulcerations in order to reduce the pain and incidence of secondary skin infection, however, such creams' effects are limited when applied to first degree burns.

It would be desirable to provide a non-oral method of administering indomethacin for the treatment of sunburned skin. In addition, it would be desirable to provide a carrier vehicle for the topical application of indomethacin whereby local treatment of inflammation is achieved to an area of sunburned skin. It would also be desirable to provide a carrier for indomethacin that provided a topical application which utilized a reasonably convenient and cost-effective process that remained stable during storage. It would be desirable to provide a

2004264332 23 Aug 2010

non-oral method of administering indomethacin for the treatment of mild to moderate skin burns caused by radiation therapy or excessive heat.

Summary Of The Invention

The present invention relates to a method and composition for treating mild to moderate skin burns. The method of the present invention comprises the steps of providing an indomethacin and a moisturizing lotion. The indomethacin and moisturizing lotion are combined to form a mixture for applying the mixture topically to burned skin to relieve the symptoms associated with burned skin. The mixture is applied one to two times daily to the burned skin.

According to a first aspect of the invention there is provided a method for treating burned skin, comprising the steps of:

a) providing a therapeutically effective amount of a composition comprising indomethacin and a moisturizing lotion, wherein the moisturizing lotion is an oil-and-water emulsion having a pH between about 6.3 and 6.5, and wherein indomethacin is maintained in stabilized and solubilized form in the moisturizing lotion wherein the moisturizing lotion comprises purified water, glycerin, hydrogenated polyisobutene, cetearyl alcohol (and) ceteareth-20, macadamia nut oil, dimethicone, tocopherylacetate, stearoxytrimethylsilane (and) stearyl alcohol, panthenol, farnesol, benzyl alcohol, phenoxyethanol, acrylates/C10-30 alkyl acrylate crosspolymer, sodium hydroxide, and citric acid; and

b) applying said composition topically to burned skin, and allowing the applied composition to remain in contact with the skin for an interval sufficient to deliver indomethacin transdermally to the burned skin.

In a second aspect of the invention there is provided a composition for treating sunburned skin, comprising a therapeutically effective amount of indomethacin and a moisturizing lotion, wherein the moisturizing lotion is an oil-and-water emulsion comprising purified water, glycerin, hydrogenated polisobutene, cetearyl alcohol (and) ceteareth-20, macadamia nut oil, dimethicone, tocopheryl acetate, stearoxytrimethylsilane (and) stearyl alcohol, panthenol, farnesol, benzyl alcohol, phenoxyethanol, acrylates/C10-30 alkyl acrylate crosspolymer, sodium hydroxide, and citric acid, and having a pH

COMS ID No: ARCS-289660 Received by IP Australia: Time (H:m) 16:56 Date (Y-M-d) 2010-08-23

2004264332 23 Aug 2010

between about 6.3 and 6.5, and wherein the indomethacin is present in a stabilized and solubilized form in the moisturizing lotion, and wherein said composition contains approximately 100 milligrams of indomethacin for every 30 cc's of moisturizing lotion.

The composition of the present invention provides a mixture of indomethacin and moisturizing lotion. The mixture provides substantially 100 milligrams of indomethacin per substantially 30 cc of moisturizing lotion. The moisturizing lotion may contain emollients and humectants. The moisturizing lotion may also contain purified water, glycerin, hydrogenated polyisobutene, cetearyl alcohol (and) ceteareth-20, macadamia nut oil, dimethicone, tocopheryl acetate, stearoxytrimethylsilane (and) stearyl alcohol, panthenol, farnesol, benzyl alcohol, phenoxyethanol, acrylates/C10-30 alkyl acrylate crosspolymer, sodium hydroxide, and citric acid. The moisturizing lotion may be marketed under the trade name Cetaphil®.

Description Of The Preferred Embodiment

The present invention will now be described in detail with reference to the disclosed embodiment.

COMS ID No: ARCS-289660 Received by IP Australia: Time (H:m) 16:56 Date (Y-M-d) 2010-08-23

The present invention provides a method and composition for treating sunburned skin of a human being. The composition includes a mixture of indomethacin and a moisturizing lotion. The composition is applied topically to the sunburned skin to provide highly effective relief of the symptoms associated with sunburned skin, including the local inflammation caused by the sunburn. It is believed that the skin, with the presence of the topical formulation, acts as a reservoir, absorbing large amounts of the indomethacin and slowly releasing the indomethacin into the skin and to other tissues. The skin may actually act as a depot or reservoir for the indomethacin. It is believed that the indomethacin is stabilized and solubilized by the moisturizing lotion wherein the moisturizing lotion enhances the absorption of the indomethacin through the skin and accordingly permits the drug to be employed topically for inflammation of the sunburned skin. Experimental results with the indomethacin have shown that far better results are achieved in relieving sunburned skin than other anti-inflammatory drugs, such as Motrin® and Tolectin®.

Experimental results have also shown that the use of the moisturizing lotion, marketed under the trademark Cetaphil® by Galderma Laboratories, Inc., Fort Worth, Texas 76133, performs well in stabilizing and solubilizing the indomethacin in creating the composition for treating sunburned skin. It is theorized that Cetaphil® provides the appropriate pH and viscosity levels to effectively stabilize and solubilize the indomethacin within the moisturizing lotion. The Cetaphil® provides emollients and humectants which are clinically proven to bind water to the skin and prevent moisture loss. The ingredients of Cetaphil® include purified water, glycerin, hydrogenated polyisobutene, cetearyl alcohol (and) ceteareth-20, macadamia nut oil, dimethicone, tocopheryl acetate, stearoxytrimethylsilane

(and) stearyl alcohol, panthenol, farnesol, benzyl alcohol, phenoxyethanol, acrylates/C10-30 alkyl acrylate crosspolymer, sodium hydroxide, and citric acid.

To provide an effective mixture of the indomethacin and the Cetaphil®, experimentation has found that a proper mixture having substantially 100 milligrams of indomethacin per 30 cc of Cetaphil® lotion will act as an effective treatment for sunburned skin. This mixture level allows the Cetaphil® to act as a proper stabilizer and solubilizer for the indomethacin. A stronger or weaker indomethacin mixture may be created depending on the treatment. However, experimentation has shown that the above-noted mixture remains an effective mixture for the treatment of sunburned skin.

In an alternative embodiment, the present invention may provide a method and composition for the treatment of mild to moderate skin burns sustained as a result of radiation therapy or excessive heat. The composition, as previously described, includes a mixture of indomethacin and a moisturizing lotion. The composition is applied topically to the burned skin to provide highly effective relief of the symptoms associated with burned skin, including pain, itching, irritation, and local inflammation. The same composition and method, as described in the previous embodiment, are used for the treatment of skin burned through radiation therapy or excessive heat.

It should be noted that the composition and method of the present invention are to be utilized on first degree burns wherein the skin is burned by excessive heat, radiation therapy, or the sun. Such first degree burns are best described as mild or moderate. The composition and method of the present invention should not be utilized on blistered, ulcerated or infected areas.

2004264332 23 Aug 2010

In use, the disclosed amounts of indomethacin and Cetaphil® are mixed to create the appropriate composition. The composition is applied to the sunburned areas thereby providing almost immediate relief of the pain and discomfort associated with sunburn. The moisturizing lotion provides moisture and a cooling sensation to the sunburned skin, and the indomethacin reduces the inflammation to the skin caused by the sunburn. The composition or mixture of indomethacin and Cetaphil®, should be applied to the sunburned areas one to two times daily. The same composition and method may be applied to skin that is burned by excessive heat or radiation therapy.

EXAMPLE

A comparison study of the effects of the invention, a combination of the non-steroidal anti-inflammatory drug (NSAID) indomethacin and a moisturizing lotion Cetaphil® (hereinafter the Treatment composition), and the composition of Iwaki et al; (JP 57165313A) on a sunburn model in human volunteers was conducted.

The particular formulation of the composition from Iwaki (hereinafter "the Iwaki composition"), determined from a translation thereof, was prepared according to the method outlined therein for the manufacture of a lotion (also translated as a "solution" in the document) is as follows:

Indomethacin	1 part/weight
Diisopropanolamine	1 part/weight
Ethyl alcohol	0-10 parts/weight
Glycerine	10-30 parts/weight
Carbopol®	0.1 part by weight

(Carbopol® is a commercially available (Lubrizol Advanced Materials, Inc.) acrylic acid polymer).

The aforementioned Iwaki composition at various composition amounts was prepared by the method outlined using the active ingredient indomethacin and admixed at 1 part by weight (pbw) purified water and 1 part by weight (pbw) indomethacin, added to the aqueous solution containing the water and 1 part by weight diisopropanolamine. Purified water was also added to a mixture

2004264332 23 Aug 2010

containing various amounts of ethyl alcohol (0 pbw and 10 pbw), Glycerine (10 pbw and 30 pbw), and carbopol 0.1 pbw. The indomethacin solution was added to the various glycerin materials. Sufficient water was added to constitute 100 parts.

The resulting compositions were runny watery solutions. The resulting materials were extremely runny and did not have the characteristics of an emulsion. It appeared that the indomethacin material was contained in aqueous media such as water. This observation is consistent with the data that indomethacin is considered to be sparingly soluble in alcohol and insoluble in water (see Physician's Desk Reference). The indomethacin appears to have dissolved in the diisopropanolamine and water solution. The fact that the indomethacin as apparently solubilized in the carrier indicates that it is present in a different chemical form from that contained in the oil and water emulsion.

The cream version of the Iwaki reference as outlined on pages 3 and 4 of Iwaki was prepared as follows:

One part diisopropanolamine was dissolved in 10 parts by weight purified water. One part indomethacin was added to this solution and dissolved. Glycerine compositions were prepared by admixing 0 and 10 parts by weight ethyl alcohol each with 10 and 30 parts glycerin, respectively. One part by weight carbopol was admixed with 30 parts by weight purified water in respective mixing containers. The respective glycerine-ethyl alcohol liquids were admixed with a Carbopol solution until evenly blended. The indomethacin solution was then added and admixed. Purified water was added to add up to 100 parts by weight.

The resulting materials were slightly opaque having a viscosity of slightly greater than 1 cps (centipoise) at room temperature indicating that the material was essentially water.

The resulting materials were thin materials that were somewhat runny and greasy. However, the materials were assessed as functional for further analysis, and the material containing 10 parts ethyl alcohol and 10 parts glycerin was selected for further examination. This material was evaluated against material compositions based on the claimed invention the "Treatment composition".

In evaluating the performance of the Iwaki and Treatment compositions, three volunteer subjects each exposed both of their forearms to direct sunlight for

COMS ID No: ARCS-289660 Received by IP Australia: Time (H:m) 16:56 Date (Y-M-d) 2010-08-23

1-1/2 hours, resulting in painful red skin. One hour following the exposure period, equal amounts of the Treatment and Iwaki compositions were applied to one or the other of each volunteer subject's forearms over a portion of the area of sunlight exposure. The remaining portion of the exposed area of each forearm was left untreated so as to serve as a control.

Each subject was evaluated for pain, erythema, and blistering at 1 hour following the exposure period and *before* application of the Treatment and Iwaki compositions, as well as at 1, 4, and 8 hours following application of the Treatment and Iwaki compositions. The results of these evaluations are set out in Table I, below.

In the following table, by way of explanation, a 1-4+ scale was employed to assess each subject's pain and erythema symptoms (blistering, or its absence, was assessed visually and its extent described). For purposes of assessing pain, a rating of 4+ corresponds to a subject's experiencing constant pain. The level of pain decreases from there to the point where the subject experiences no pain - a rating of 0. For purposes of assessing the level of erythema, the 0-4+ scale represents the degree of redness in each subject's skin following exposure as compared to the subject's normal skin color and their untreated "control area".

		Subject A			*Subject B*			*Subject C*		
		Control	Iwaki	Treatment	Control	Iwaki	Treatment	Control	Iwaki	Treatment
1 Hour after exposure/No treatment	Pain	4+	4+	4+	4+	4+	4+	4+	4+	4+
1 Hour after exposure/No treatment	Erythema	4+	4+	4+	4+	4+	4+	4+	4+	4+
1 Hour after exposure/No treatment	Blistering	None	None	None	None	None	None	None	None	None
1 Hour after treatment	Pain	4+	3+	1+	4+	4+/3+	1+	4+	3+	1+
1 Hour after	Erythema	4+	4+	2+/3+	4+	4+	3+	4+	4+	3+

		Subject A			Subject B			Subject C		
		Control	Iwaki	Treatment	Control	Iwaki	Treatment	Control	Iwaki	Treatment
Treatment										
1 Hour after treatment	Blistering	None	None	None	None	None	None	None	None	None
4 Hours after treatment	Pain	4+/3+	2+	0	4+	3+	0	4+/3+	3+/2+	0
4 Hours after treatmen	Erythema	4+	3+/2+	2+	4+	3+	3+/2+	4+	3+	3+
4 Hours after treatmen	Blistering	None	None	None	None	None	None	None	None	None
8 Hours after treatment	Pain	3+	2+	0	3+	2+	0	3+	2+	0
8 Hours after treatmen	Erythema	3+	2+	1+	3+	2+/1+	1+	3+	2+	0
8 Hours after treatmen	Blistering	Trace Amounts	Trace Amoun ts	None	Trace Amounts	None	None	Trace Amount s	Trace Amoun ts	None

As the results of Table 1 demonstrate, indomethacin, when combined with a moisturizing lotion, demonstrates superior treatment of the symptoms of sunburn than the application of indomethacin in the carrier of the Iwaki reference. For example, the Treatment composition demonstrated considerably more rapid reduction in the pain associated with sunburn than the Iwaki composition. The Treatment composition also eliminated the sunburn pain in the treatment subjects within 4 hours of treatment, whereas the pain experienced by volunteers subjected to treatment with the Iwaki composition was never eliminated. Furthermore, the Treatment composition prevented blister formulation in all of the treatment subjects; the Iwaki composition did not.

As observed and recorded in Table 1, one hour after exposure, subjects experience pain and erythema uniformly at 4+. One hour after treatment (2 hours after exposure), the pain and erythema noted for untreated areas was still reported at 4+. The Iwaki formulation had reduced reports for pain to 3+, but showed no effect for erythema. The Treatment composition elicited pain reports to 1+ and erythema to approximately 2+. This would support the conclusion that indomethacin was more effectively administered via an oil containing matrix.

The test was continued with observations at 4 hours post treatment. Slight pain reduction was reported in the control patches, but no appreciable change

2004264332 23 Aug 2010

was reported in erythema over the observations at 1 hour post treatment. The patches treated with the Iwaki composition evidenced some pain reduction to approximately 2+ to 3+. Erythema was reduced to approximately 3+. The Treatment composition material patches evidenced a reported pain reduction to zero (no pain), and a reduction in erythema to between 2+ and 3+.

The pain reduction achieved by the Treatment material was remarkable and is believed to be attributable to uptake of the topically applied indomethacin in the region proximate to application. Reduction in erythema was greater for the regions treated with the Treatment material over those treated with the Iwaki material in two of the three subjects.

At eight hours, the subjects were again evaluated. No subject reported pain in the regions treated by the Treatment material (in contrast, control regions evidenced pain at 3+ and regions treated by Iwaki evidenced pain at levels of 2+). Erythema was also evaluated at 1+ to 0 for the regions treated with the Treatment composition (in contrast erythema levels of 3+ were observed for untreated regions and approximately 2+ for the Iwaki material).

Blistering was also followed in the tests. The Treatment composition appears to have prevented blistering in all subjects. The Iwaki composition had no apparent effect on blistering.

To fully analyze the effect of indomethacin containing materials, Treatment compositions were prepared according to the present disclosure and were evaluated against composition without indomethacin (placebo material). Minor amounts of pain and erythema reduction were reported on regions treated with the placebo (attributable to the cooling effect of glycerine containing formulations). However, greater reductions in pain and erythema were reported with treatment by the indomethacin containing composition.

It is believed that the initial pain reduction can be attributable to the analgesic effect of the indomethacin delivered to the region to which the treatment composition is applied, while the prolonged reduction in pain and redness may be practically attributable to the anti-inflammatory action of the indomethacin delivered.

The various materials prepared according to the discussion in Iwaki, were further evaluated to ascertain their efficacy as moisturizing lotions. The Iwaki

COMS ID No: ARCS-289660 Received by IP Australia: Time (H:m) 16:56 Date (Y-M-d) 2010-08-23

materials were not desirable as moisturizing lotions. It is believed that this is due, at least in part, to the apparent lack of emollient materials present in the Iwaki composition.

Considering the results of the experiment as summarized in Table I, as well as earlier work in treating sunburn with various NSAIDs in other carriers (including indomethacin in the carrier of the Iwaki composition), (data not shown), it is concluded that the results obtained from the Treatment composition were highly unexpected.

The Cetaphil® preparation outlined and described in the specification contains the following ingredients: a combination of humectant(s), emollients, oils, waters, and emulsifiers, which are believed to be compounded for the following functions:

Water	aqueous carrier
glycerine	humectant
hydrogenated polyisobutylene	solvent
ceteryl alcohol	emulsifier
ceteareth 20	emulisifer
macadamia nut oil	oil
dimethicone	emollient
tocopheryl alcohol	humectant
phenoxyethanol	preservative
acrylates/C10-30	film forming agent
acylate crosspolymer	film forming agent
sodium hydroxide	pH adjustment
citric acid	Vitamin C

The composition outlined in the Iwaki reference lacks the emollient oil and emulsifier components outlined above. The materials of the Iwaki composition are believed to serve the following functions:

water	carrier
diisopronalolamine	solvent
ethyl alcohol	solvent
glycerin	humectant
carbopol	film forming agent

2004264332 23 Aug 2010

It is also noted that the Iwaki reference calls for the dissolution of indomethacin in diisopropanolamine-water solution, whereas the formulation as claimed is a mixture of indomethacin in a lotion composed of an oil-and-water emulsion containing emollients and humectants. It is not fully understood why, but it is believed that this difference may contribute to maintaining the indomethacin in a form that permits it to remain pharmacologically active in treating redness. This may contribute to the enhanced performance of the claimed invention.

In order to further understand the mechanism at work in the present invention, we evaluated compositions in which indomethacin was formulated with nonlipid containing aqueous carrier agents (i.e. calamine lotion results not shown) and found that the resulting material did not function to treat sunburn. It is believed that the absence of lipid components compromises uptake of indomethacin through the epidermal layer to inhibit inflammation.

Compositions containing indomethacin and pure lipid material appear to facilitate inclusion of indomethacin in the carrier but are equally problematic as the lipid material does not breach the lipid-water barrier present in the skin. Thus the indomethacin added to materials containing products on lipids such as petrolatum do not appear to function. It appears that an oil-and-water emulsion is preferred for effective uptake over either aqueous materials or pure lipid materials. It is further concluded that petrolatum is undesirable.

The Iwaki reference lacks the lipid material typically found in oils necessary to facilitate uptake of indomethacin through the epidermis. Without being bound to any theory, it is believed that any burn relief obtained by the Iwaki reference is attributable to the glycerine component as glycerine, particularly glycerine-in-water compositions, are known as a burn remedy.

The indomethacin component appears to be added to Iwaki for its UV absorbance (318) nm (see Iwaki, page 1). Thus, indomethacin is present for sunburn preventing characteristics, while the glycerine component is present for any sunburn treatment.

The indomethacin present in Iwaki is unavailable for uptake into the sunburn region. Hence, the lesser relief noted by the test subjects in the comparison studies.

2004264332 23 Aug 2010

These results are consonant with results reported by Kaidev et al. in J of Investigative Dermatology where it was posited that indomethacin carried in a base composed of propylene glycol-ethanol-dimethyl formamide 1:1:2 v/v applied topically failed to modify epidermal UV injury.

While the invention has been described in connection with what is presently considered to be the most practical and preferred embodiment, it is to be understood that the invention is not to be limited to the disclosed embodiments, but to the contrary, it is intended to cover various modifications and equivalent arrangements included within the spirit and scope of the appended claims. The scope is to be accorded the broadest interpretation so as to encompass all such modifications and equivalent structures as is performed under the law.

2004264332 23 Aug 2010

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A method for treating burned skin, comprising the steps of:

a) providing a therapeutically effective amount of a composition comprising indomethacin and a moisturizing lotion, wherein the moisturizing lotion is an oil-and-water emulsion having a pH between about 6.3 and 6.5, and wherein indomethacin is maintained in stabilized and solubilized form in the moisturizing lotion wherein the moisturizing lotion comprises purified water, glycerin, hydrogenated polyisobutene, cetearyl alcohol (and) ceteareth-20, macadamia nut oil, dimethicone, tocopherylacetate, stearoxytrimethylsilane (and) stearyl alcohol, panthenol, farnesol, benzyl alcohol, phenoxyethanol, acrylates/C10-30 alkyl acrylate crosspolymer, sodium hydroxide, and citric acid; and

b) applying said composition topically to burned skin, and allowing the applied composition to remain in contact with the skin for an interval sufficient to deliver indomethacin transdermally to the burned skin.

2. The method of claim 1, wherein the composition comprises approximately 100 milligrams of indomethacin for every 30 cc's of moisturizing lotion.

3. The method of claim 1 or 2, wherein the composition is applied from one to two times daily to burned skin.

4. The method of any one of claims 1 to 3, wherein the burned skin occurs by by any one of radiotherapy, radiation, or ultraviolet light.

5. The method of any one of claims 1 to 3, wherein the burned skin is a first degree burn and the burned skin has been burned by an agent selected from the group consisting of excessive heat, radiotherapy, radiation, or ultraviolet light.

6. A composition for treating burned skin, comprising a therapeutically effective amount of indomethacin and a moisturizing lotion, wherein the moisturizing lotion is an oil-and-water emulsion comprising purified water, glycerin, hydrogenated polisobutene, cetearyl alcohol (and) ceteareth-20, macadamia nut oil, dimethicone, tocopheryl acetate, stearoxytrimethylsilane (and)

COMS ID No: ARCS-289660 Received by IP Australia: Time (H:m) 16:56 Date (Y-M-d) 2010-08-23

2004264332 23 Aug 2010

stearyl alcohol, panthenol, farnesol, benzyl alcohol, phenoxyethanol, acrylates/C10-30 alkyl acrylate crosspolymer, sodium hydroxide, and citric acid, and having a pH between about 6.3 and 6.5, and wherein the indomethacin is present in a stabilized and solubilized form in the moisturizing lotion, and wherein said composition contains approximately 100 milligrams of indomethacin for every 30 cc's of moisturizing lotion.

LIL BRAT PHARMACEUTICALS

WATERMARK PATENT AND TRADE MARKS ATTORNEYS

P26743AU00

COMS ID No: ARCS-289660 Received by IP Australia: Time (H:m) 16:56 Date (Y-M-d) 2010-08-23