

Meadowlactone[®] An Effective Anti-Irritant

INTRODUCTION

The skin, which is the largest organ of the body, serves as a physical barrier to prevent both dehydration and infection. Irritation, as used in this report, refers to noticeable physical [pain](#) or discomfort. It may be accompanied by [inflammation](#) or painful reaction to [allergy](#) or cell-lining damage. Stimuli or agents that induce the state of irritation are typically chemical agents (for example strong bases and oxidizing agents) but mechanical, thermal (heat) and radioactive stimuli (for example [ultraviolet light](#)) can also cause irritation. The interaction between an irritant and the human skin depends on multiple factors: the intrinsic properties and the nature of the irritant itself, and specific individual- and environment-related variables. The main pathological mechanisms of irritancy include skin barrier disruption, induction of a cytokine cascade, and involvement of the oxidative stress network; all of them resulting in a visible or subclinical inflammatory reaction. In vivo, different non-invasive parameters for the evaluation of skin irritation and irritant potential of compounds and their specific formulations have been introduced, such as epidermal barrier function, skin hydration, surface pH, lipid composition, skin color and skin blood flow.¹

An anti-irritant may be defined as any ingredient that reduces certain signs of inflammation, such as swelling, tenderness, pain, itching, or redness. In the course of studying improved skin barrier function provided by a new naturally derived material called Meadowlactone, a very significant anti-irritancy property was noted.

Two separate investigations were initiated to confirm and quantify the anti-irritant properties of Meadowlactone. In addition, the testing and results of Meadowlactone as an agent in allergic contact sensitization is described.

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Meadowlactone:

Meadowlactone is a unique new functional ingredient derived from the natural vegetable oil of Meadowfoam (*Limnanthes alba*; see Figures 1 and 2). This lactone is a spatially oriented compound (see Figure 3) that can help re-establish a physiologically correct balance of oil and water in epidermal tissue and thereby restore skin to a healthy, youthful morphology. Meadowlactone is a delta-lactone whose chemical etiology is an anhydride formed by the removal of a water molecule from the hydroxyl and carboxyl radicals of hydroxy fatty acids. Meadowlactone is an amphoteric compound whose isomeric structures can shift between oil and water solubility as a function of pH. It has been observed that Meadowlactone, when applied to skin in reasonably low concentrations, produces marked sensory improvement in both feel and appearance. Even after a single application of as little as 1- 5%, panelists note a significant improvement in skin tone and texture.²

Figure 1. Meadowfoam flowers

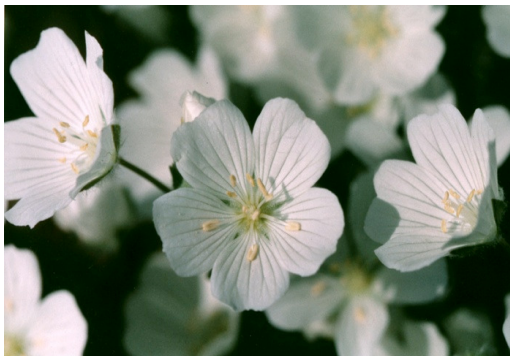
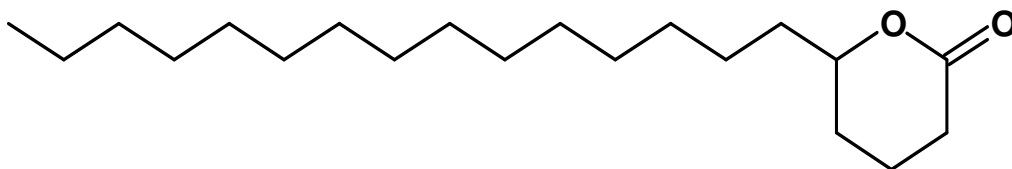


Figure 2. Meadowfoam in the field



Figure 3. Meadowlactone structure



Study No. 1: The Use of Meadowlactone in Hair Relaxers

Materials and Methods:

Hair relaxers are widely used to straighten curly hair. In most cases, the active ingredient is a strong base such as sodium hydroxide, which in a “regular strength” relaxer is present in approximately 2.2%. The process of relaxing (straightening) hair involves applying the cream relaxer formulation to the hair, working it into the virgin hair to break the emulsion and release the active agent (NaOH) onto the hair fibers and subsequent neutralization and conditioning. Some of the relaxer invariably gets to the client’s scalp and in a significant number of cases causes irritation ranging from very mild to extremely severe. Those individuals who experience irritation whenever they have their hair relaxed are referred to as “sensitive scalps”. For these studies, Meadowlactone was formulated directly into the relaxer at a level of 1%. The formulas used for these studies are shown in Figure 4.

Figure 4. Formulas for Control and Test Relaxers

INGREDIENT	INCI NAME	% CONTROL FORMULA	% TEST FORMULA
D.I. Water	Water	50.6	49.6
Propylene Glycol	Propylene Glycol	2.5	2.5
White Propet	Petrolatum	14.0	14.0
Mineral oil, 70 vis	Mineral oil	16.0	16.0
Fanwax SEW-P	Emulsifying wax, N.F.	11.0	11.0
Fancol LA-15	Laneth-15	1.0	1.0
Lan-Aqua-Sol 75:100	PEG-75 Lanolin	0.5	0.5
Meadowlactone	Meadowfoam delta-lactone	0.0	1.0
50% Sodium Hydroxide	Sodium Hydroxide	4.4	4.4

Appearance: white viscous cream

Viscosity (cps@25° C = 250,000 - 300,000)

The two products were coded with random numbers and submitted to the salon for use and evaluation. Salon evaluations were conducted using a “quarter-head” design such that the control and test formulas were applied alternately to four quadrants of the head thereby keeping the resident relaxer time equal for both products. Processing time on the hair was 15 to 18 minutes. Twenty female clients, ranging in age from 22 to 50 were included in the study.

Results:

In the case of the control relaxer (no Meadowlactone), 4 clients (20%) experienced significant irritation (severe) and 5 clients (25%) experienced definite but “milder” sensation. In the case of the test relaxer (1% Meadowlactone) there were no instances of irritation whatsoever, severe or mild (see Figure 5).

Figure 5: Results of Relaxer Studies in % Irritation

Relaxer	Severe Irritation %	Mild Irritation %	Total Irritation %
Control	20	25	45
Test (Meadowlactone)	0	0	0

Study No. 2: The Application of Meadowlactone after Skin Irritation Caused By Hair Dyes

Materials and Methods:

Permanent hair color is an oxidation dye system that utilizes ammonium hydroxide to provide a basic pH to swell the hair shaft and facilitate penetration of the dye into the hair fiber and hydrogen peroxide to “activate” and polymerize the color (dye intermediates). The addition of the combined alkali and oxidizing agent tends to be very irritating to skin. This system was used as a test to evaluate the anti-irritant benefits of Meadowlactone. The activator (see Figure 6) is added in equal quantity to the dye intermediates (see Figure 7) and mixed well immediately prior to application to the hair (see Figure 8).

Figure 6: Activator Formula

INGREDIENT INCI NAME	ACTIVATOR 1	ACTIVATOR 2
Acrylates/C10-30 alkyl acrylate crosspolymer	0.10	0.10
Cetyl alcohol, stearammonium chloride, ceteth-30, ethylhexyl palmitate, hydrogenated polyisobutene, glyceryl cocoate, paraffin	4.00	4.00
Butylene glycol	1.00	1.00
Etidronic acid	0.20	0.20
Disodium phosphate	0.38	0.38
Hydrogen peroxide (35% aq. Solution)	16.57	16.57
Behenyl alcohol	1.00	1.00
Tetrasodium EDTA	0.20	0.20
Meadowfoam delta lactone	0.20	5.00
Polyglutamic acid	1.00	1.00
Water	75.05	70.25
Phosphoric acid	0.30	0.30

Figure 7: Dye Intermediate Formula

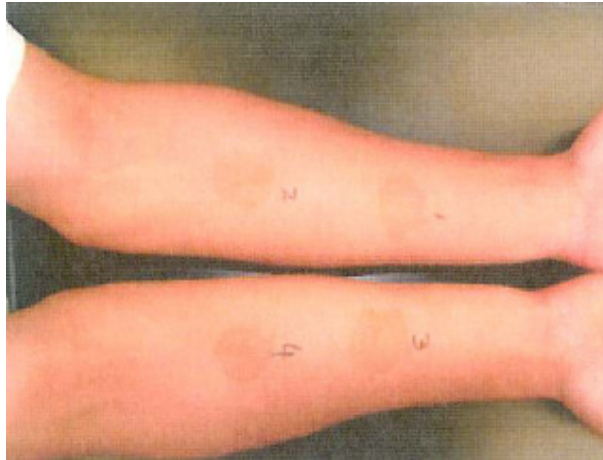
INGREDIENT	INCI NAME	DYE FORMULA 1	DYE FORMULA 2
	p-pheylenediamine	0.18	0.18
	Toluene-2,5-diamine	0.60	0.60
	<i>m</i> -aminophenol	0.07	0.07
	<i>o</i> -aminophenol	0.02	0.02
	Resorcinol	0.50	0.50
	Water	51.13	56.13
	Sodium sulfite	0.30	0.30
	Ascorbic acid	0.30	0.30
	Salicylic acid	0.10	0.10
	Pentetic acid	0.10	0.10
	Ethoxydiglycol	4.00	4.00
	Paraffin	10.00	10.00
	Hydrogenated lecithin	0.20	0.20
	Glyceryl stearate	1.20	1.20
	Oleth-3 phosphate	0.60	0.60
	Oleyl oleate	2.40	2.40
	Meadowfoam delta lactone	5.00	0.00
	Cetyl alcohol	5.00	5.00
	Ceteth-30	0.60	0.60
	Stearyl alcohol	4.00	4.00
	Aminomethyl propanol	3.50	3.50
	PEG-5 soy stearol	6.00	6.00
	Potassium carbonate	0.20	0.20
	Amonium hydroxide	4.00	4.00

Figure 8: Oxidized dye added to the hair and resulting Meadowlactone Content

PREPARATION NUMBER	DYE FORMULATION (50:50 MIXTURES)	RESULTING LEVEL OF MEADOWLACTONE
1	Activator 1 + Dye 2	0.1%
2	Activator 2 + Dye 2	2.5%
3	Activator 1 + Dye 1	2.6%
4	Activator 2 + Dye 1	5.0%

Immediately after mixing the hair dye (ammoniated) with the activator (oxidizer) at a ratio of 50:50, they were each applied to a 3cm area on the inside of both forearms. Therefore, each participant received a set of 4 preparations as noted in Figure 8 above.

Figure 9: Example of Application and Reaction on Forearms



Reaction to the application of the oxidative dye was monitored by noting the time when there was any sensation of irritation and/or the appearance of erythema or swelling in the area where the formula was placed.

Results:

As seen in Figure 10, Meadowlactone produced a marked reduction/elimination of irritation following the application of this tissue insult. Since formula Nos. 2 and 3 had approximately the same concentration of Meadowlactone, 2.5 and 2.6% respectively, the results for these participants were grouped together.

Figure 10: Results Following the Application of Oxidative Hair Dye with Meadowlactone

Formulation	1	2 and 3	4
Amount of Meadowlactone	0.1%	2.5%	5.0%
First Signs of Irritation	7.3min	22.0min	No irritation at any time
% of Participants with Irritation	100	50	0

The incorporation of Meadowlactone at a concentration of 2.5% increased the time before irritation by a factor of three-fold and decreased the incidence of irritation by 50%. At the higher level of 5%, Meadowlactone totally eliminated any signs of irritation.

Study No. 3: Repetitive Epidermal Contact with Meadowlactone to Determine Any Incidence of Primary or Cumulative Irritation and/or Allergic Contact Sensitization

This study is often referred to as an RIPT or Repeat Insult Patch Test. While it does not necessarily measure anti-irritancy with respect to reducing or eliminating irritation caused by an applied insult, it is indeed relevant since it demonstrates that the material itself, in “neat” form (i.e. 100% pure and undiluted) can be repeatedly applied directly to the skin without any indication of irritation or skin sensitization. In the event the material has the potential to be allergenic, skin sensitization is induced when a susceptible individual is exposed topically to the inducing chemical allergen. This chemical allergen provokes a cutaneous immune response which, if of the required magnitude and quality, will result in the development of contact sensitization³.

Materials and Methods:

One hundred and three (103) subjects, male and female, ranging in age from 18 to 79 years, completed this study. The upper back between the scapulae served as the area of application. Approximately 0.2 g of Meadowlactone was applied to the 1” x 1” absorbent pad portion of a clear adhesive dressing (TurMed Technologies, Inc. Burnsville, MN). This was applied to the treatment site to form a semi-occlusive patch.

Induction phase:

Patches were applied to the same sites 3 times/week (Monday, Wednesday and Friday) over a 3 week period for a total of nine applications. Each patch remained in place for 24 hrs. and was then removed and the area scored for any signs of irritation.

Challenge phase:

Two (2) weeks after the final induction patch application, a “challenge” patch was applied to a virgin test site adjacent to the original induction patch site. The patch was removed and the site scored twenty-four (24) and seventy-two (72) hours post-application.

Evaluation scoring and criteria:

SCORING	
0	No visible skin reaction
0.5	Barely perceptible
1	Mild
2	Moderate
3	Marked
4	Severe

Irritation and Sensitization Criteria
Edema
Dryness
Staining
Papules
Vesicles
Bullae
Ulceration
Spreading

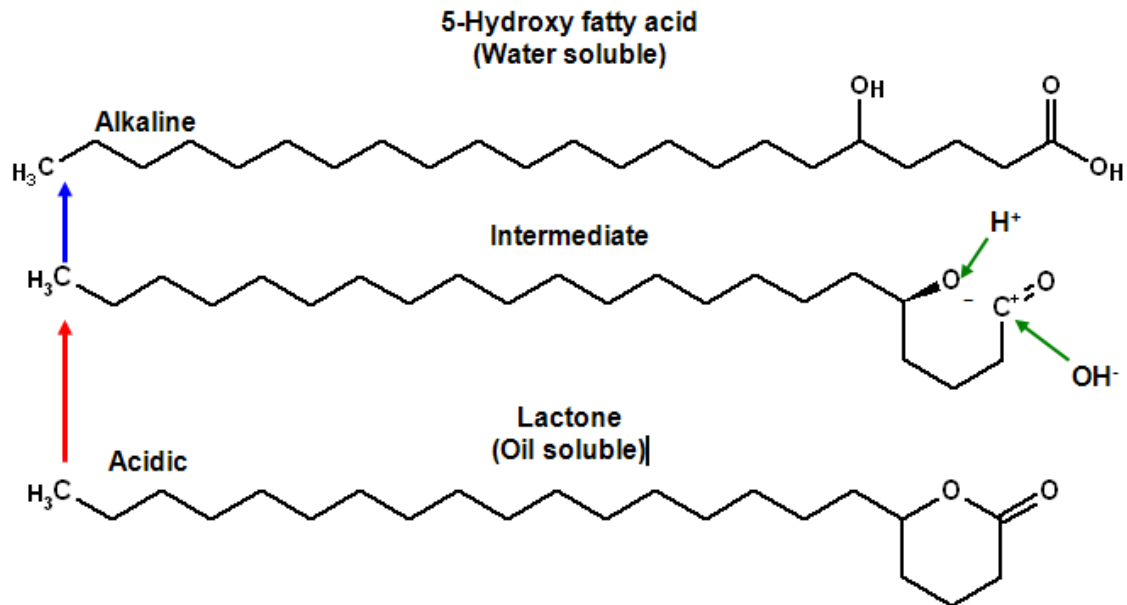
Results:

There was not a single incidence of irritation or sensitization among the entire 103 member panel at any time during the study. It was concluded that Meadowlactone, when repeatedly applied to the skin in a neat (undiluted) form, does not in any way cause irritation or elicit an allergic response.

DISCUSSION

The ability of Meadowlactone to serve as an anti-irritant is most likely derived from the molecules dynamic pH-dependent “isomerization”. In an attempt to better understand the biochemical mechanisms underlying the ability of this material to have such a pronounced effect on epidermal tissue, a series of physical chemistry studies were conducted to examine the structural configuration of the lactone under conditions simulating those likely to occur in tissue. The results of these studies are described in Figure 11.

Figure 11: Isomerization of Meadowlactone



Meadowlactone isomerizes, as a function of pH, between the more hydrophilic water soluble 5-hydroxy fatty acid and more lipophilic lactone. At the pH of skin, approximately 5.5, both forms are in equilibrium thereby providing the tissue with components that serve to complement both the water and oil phases within the epidermis. The process of isomerization *in vivo* translates to a pH buffering effect that modulates the insult caused by the application of an irritant. Irritation, with the accompany sensation of pain, is reduced or eliminated. In addition, there is a perceived softening of the skin with a long-lasting improvement in tone, feel and appearance. It is important to note that the RIPT (Repeat Insult Patch Test) showed that when Meadowlactone is applied as a pure material ("neat") it is non-irritating and is not allergenic. Therefore, it is reasonable to conclude that this material can be included in skin care formulations and used on a regular basis without concern for any adverse reactions caused by this ingredient.

References

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