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Alcloxa

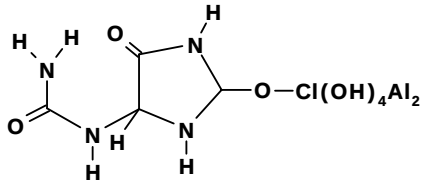
1. Overview

Alcloxa is an optimal active ingredient for safe and effective antiperspirant, anti-acne and grease skin formulations.
It is an aluminum salt of Allantoin that possess the skin protectant keratolytic, soothing and healing properties of Allantoin together with the astringent, mild antimicrobial properties of the aluminum compounds. The aluminum component reduces sweat by reducing the sweat gland ducts to swell, the allantoin component minimize the irritation caused by the aluminum component.
This compound shows a moderate acidity without the skin irritant characteristic of the aluminum salts or the damage of such salts on cloths.

2. Chemical structure

Empirical formula: $C_4 H_9 O_7 Al_2 Cl N_4$

Structural formula:



Molecular weight: 314.56
Hydratation water: 3,4 mol
Molar ratio Al/Cl/Allantoin: 2/1/1

3. Codex and names

CTFA name:	Alcloxa
JSCI name:	Aluminum Chlorhydroxy Allantoinate
EINECS name:	Aluminum, Chloro [(2,5-Dioxo-4-Imidazolidinyl) Ureato] Tetrahydroxydi-
CAS number:	[1317-25-5]
EINECS number:	215-262-3
JSCI number:	S0017

4. Specification data

Appearance:	fine powder
Colour:	white
Odour:	odourless
Identification:	corresponds to C.T.F.A. IR spectrum
Assay (Al_2O_3):	26.0% - 30.0%
Allantoin (as nitrogen):	38.0% – 42.0%
Nitrogen:	14.0% min
pH (1% water solution):	4.0 – 5.0
Chloride:	8.5% - 10.5%
Sulphate:	0.05% max
Heavy metals (Pb):	less than 20 ppm
Shelf life:	5 years in original packing

5. General description

Alcloxa is a aluminum allantoinate compound obtained from the reaction of allantoin with aluminum chlorohydrate in the molar ratio 1:1.

Allantoin has a long history of use in skin treatment for its mild keratolytic, skin moisturizing, anti-irritant and healing properties.
The *keratolytic action* of allantoin (due both to the dissolution of intercellular matrix and to disruption of keratin structure) helps the natural desquamation of the superficial corneocytes. These desquamation stimulates the proliferation of the basal cells, expose the underneath more hydrated-soften skin layers and favourite the penetration in the stratum corneum of other active compounds of the formulation.
The skin *moisturizing effect* results from the ability of Allantoin to increase the water binding to the intercellular matrix and to keratin of the stratum corneum.
The *anti-irritant* and *soothing effect* arise from its ability to form complexes and neutralize many irritants and sensitizing agents, reducing the irritation effects caused by several raw materials such as preservatives and surfactants. For this reason Allantoin may be considered a *skin protectant*, as can reduce the irritation potential of some formulations.
Allantoin stimulates cell-proliferation and speed up *wound healing:* it assists the regeneration of cells of damaged epithelium, stimulate the granulation tissue, the fibrinolysis of damaged tissue and the removal of the necrotic area.

Aluminum chlorohydrate is a coordination complex of basic aluminum chloride and water. This complex represent an improvement of previous used aluminium chloride salts that were more acidic. Aluminum chlorohydrate has a pH of 4-5, is considerably less irritating to the skin and showed reduced clothing damage.
In spite of the very large reduction in irritancy and clothing damage offered by aluminium chlorohydrate over the more acidic aluminum chloride salts, even this compound is not completely free of problems, in fact a significant number of users (upto 10%) experienced stinging, redness and itching.
The *mechanism of antiperspirant activity* of this aluminum compound is due to the reduction of the sweat diffusion to the skin surface. According to the so-called "Plug theory" the hydrolysis of the compound and the diffusion in the acidic media of sweat duct form an amorphous aluminum hydroxide agglomerate that physically plugs the sweat duct.

Alcloxa is a compound that combine the properties of aluminum salts with the properties of allantoin. It is more effective than the single components, as it acts as a chemical entity.
The *allantoin component* enhances the action of the aluminum salts and serves to overcome irritations experienced by many individuals who may be sensitive to the use of aluminum salts.
The *aluminum component* reduces sweat by causing the sweat gland ducts to swell.
Alcloxa also add to the antiperspirant properties the deodorant effect because of its *bacteriostatic action*. It showed bacteriostatic properties at concentrations of 0.2% particularly against Gram + bacteria (*B. subtilis, S. aureus, P. vulgaris, Pityrosporum ovale*). The agar diffusion test revealed inhibition zones of 6 mm for *Staphylococcus aureus* and of 20 mm for *Pityrosporum ovale*.
This is ascribable to two different mechanisms: first bacterial growth is retarded due to a decrease in the amount of water present, second aluminum salt have itself an antimicrobial action.
Alcloxa for the moderate acidity and for the anti-irritant action of allantoin represents within the group of aluminum antiperspirants the compound with the best tolerability.

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6. Deodorant efficacy studies

The deodorant action of Alcloxa was tested on eight female and one male subjects. An *ointment* containing 0.2% Alcloxa was rubbed into the axillae once daily and the effects on the axillary odour were noted. In all nine subjects there was a complete inhibition of odour formation already after one application. The inhibition lasted for about 24 hours. There was no sign of irritation or sensitization in any of the subjects tested.

A *lotion* containing 0.65% Alcloxa was tested for its antiperspirant and deodorant action in the axillae of 5 healthy male and 12 female subjects who applied it daily for periods of 6-16 weeks. All subjects gave most favourable reports. None developed any primary irritation or sensitization , even after prolonged use of these products. Three female subjects who did not tolerate commercial preparations could use the lotion and cream containing Alcloxa without any ill effect. The majority of subjects volunteered he information that the new preparations had a deodorant effect of considerably longer duration than any of the other antiperspirants previously used by them. This prolonged action was especially pronounced in case in which synthetic fabrics were worn. These fabrics are unable to absorb moisture and therefore they further the bacterial decomposition of sweat resulting odour. The Alcloxa preparations prevented perspiration for at least 24-48 hours after a single application. Therefore Alcloxa in a 0.2% solution or ointment is an effective deodorant agent.

In vitro Alcloxa inhibited odour formation and bacterial decomposition of pulverized human epidermal scales. The scales were obtained from a patient with exfoliative dermatitis, characterized by a great deal of exudation. The scales were pulverized in a Wiley mill, defatted with ether and suspended in a 0.2% Alcloxa solution. Control scales from the same patient were suspended in water. After 24 hours the scales suspended in water developed a foul odour and a green colour appeared in the solution. There was no change in colour or odour in the scales treated with Alcloxa.

7. Characteristics

Alcloxa is ***soluble*** in water at 1%, very slightly soluble in alcohols and not soluble in propylene glycol and mineral oil.

SOLVENTS	***Temperature***	***SOLUBILITY % w/w$_{solvent}$***
Water	25°C	1
	40°C	2
	70°C	4
Propylene glycol	70°C	<0.01
Ethanol	25°C	0.01
Methanol	25°C	0.05
Mineral oil	25°C	<0.01

The pH of 1% aqueous solution is between 4.0-5.0.

8. Applications

Alcloxa is a soluble salt retaining the skin softening, healing, keratolytic and anti-irritant action of allantoin together with a mild astringency exerted by aluminum compounds.
Alcloxa is an active ingredient for antiperspirant, anti-acne and grease skin products, it can be used in form of acqueous, hydro-alcoholic solutions and emulsions.

In ***antiperspirants*** and ***deodorants*** the addition of Alcloxa alleviates the slight irritation deriving from the use of these products. It may be used in hydro-alcoholic solutions and emulsions in aerosols, pump sprays, rolls on, sticks, gels, creams at levels of 0.25-0.5%.

Alcloxa may be used for its astringent antibacterial properties in ***oral care products***. It is very indicated in formulations for sensitive teeth, periodontal and gum diseases (like gingivitis, irritable and bleeding gums).
Dentifrice compositions containing Alcloxa are valuable in the treatment of *hypersensitive dentin*. Hypersensitive dentin is a dental problem in which the tooth surfaces are depleted for erosion of the enamel, and dentin and cementum are exposed for the recession of the gingival. This condition exhibit itself as a painful sensation in response to ordinary stimuli at the surface of the teeth (temperature, acidity, mechanical forces and food). The addition of Alcloxa to a dentifrice composition provides soothing and pain relieving properties.(ref. 1).
The use of Alcloxa in dentifrice combat sensitive periodontal tissue and promotes the healing of *inflamed and bleeding gums* (ref. 2).
Alcloxa gives to oral formulations a slightly astringent and reinforces the bacteriostatic properties. It is compatible with other normal components of these products and does not alter the taste and tones.
The recommended levels of use for *toothpastes* are between 0.1-1% and in *mouthwashes* between 0.15%-0.2%.

In ***antiacne*** products the slightly astringent effect favours healing of pustules and oozing lesions. It reduces the extension of infected skin eruptions, healing them and developing a soothing action. Alcloxa may be equally combined with anti microbial agents in order to fight acne more effectively.
Levels of 0.5%-2% are recommended.

In ***shave products*** helps to regenerate the surface lesions and sooths the irritations produced by shaving.
For these products, a dose of 0.2% to 0.25% of Alcloxa is recommended.

In ***foot products*** (powder and creams) for its mild astringency, protective and antiseptic properties it is useful for daily hygiene to control perspiration and odour. It may be also indicated for a variety of clinical foot problems such as athlete's foot, onychomycosis, hyperhydrosis, dermatophytosis, epidermal macerations, inflamed and areas of oseus prominence.

In ***baby products*** is indicated, for its healing reparative action, in the treatment of diaper rash.

Alcloxa is also approved in ***haemorrhoidal products*** for its soothing and keratolytic action. The rationale for its use is that the lysis of the outer layer of the skin allows medications that are applied to the anus and perianal area to penetrate into the deeper tissue. The use levels are 0.2-2.0%.

Alcloxa for its effectiveness, toxicological profile, absence of toxic impurities and environmental implications, represents a suitable alternative to the use of Triclosan in many applications.
The use of ***Triclosan*** in cosmetic products is very questioned today, on the basis of many toxicological and environmental considerations.

The multiple cosmetic applications and use levels of Alcloxa are summarized in the following table.

Application	***Form***	***Use level***
Antiperspirants, deodorants	Creams, spray, lotions	0.25-0.5%
Oral products	Toothpastes, mouthwashing	0.15-1%
Anti-acne products	Lotions, creams	0.5-2%
After-shave products	Lotions	0.2-0.25%
Shaving products	Soaps, creams	
Hair products	Lotions	0.25%
Foot care products	Lotions, creams, powders, spray	0.2-0.3%
Baby products	Creams, powders	0.2-0.5%
Hemorrhoidal products	Gels, Creams	0.2-2%

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9. Toxicological data

In toxicological tests conducted on animals (ref. 3), Alcloxa and aluminum allantoinates were found ***non-sensitizing*** and ***non-irritating.***
Preliminary usage tests on human subjects also indicate that these salts have no harmful effect on human skin.
There is no evidence that Aluminum is adsorbed through the skin. FDA judge aluminum antiperspirant safe and effective, as the level of exposure to aluminum from antiperspirants (dermal, inhalation, olfactory) is negligible. The level of exposure is small in comparison to levels from all other sources. For these reasons the association of Alzeheimer's and neurodegenerative diseases with the use of antiperspirant products containing aluminium was judged unsubstantiated by FDA and CTFA.(ref. 4)

Acute oral toxicity (rat, mouse)
The oral LD50 was > 8000 mg/Kg.

Acute dermal toxicity (rabbit)
The dermal LD50 on normal and abraded skin was > 8000 mg/Kg.

Eye irritation (rabbit)
A 24% water solution of the test material applied to the eyes of rabbits (Draize method) causes a mild irritation.
Alcloxa in powder is eyes irritant.

Sensitization (guinea pig)
The average response to a challenge injection of 25% test suspension was not greater than the average response for each animal. The test material is not sensitizing to guinea pigs.

Primary skin irritation (guinea pig)
The test material was applied to the normal skin of healthy guinea pigs. There was no irritation at test concentration, so Alcloxa is not considered a primary skin irritant.
The purpose of these experiments was to test whether or not Alcloxa had primary irritating and sensitizing properties when applied to the skin. The following preparations were used:
1. Alcloxa suspension (25%) in 5% Sodium Lauryl Sulfate (SLS) water solution.
2. An "antiperspirant cream" containing 0.25% Alcloxa.

Each of these test substances was applied to the skin of three adult male guinea pigs, a total of 12 animals. A 4 inch sq. area on the backs of the animals was shaved and the test substances were rubbed for one minute on alternating days over 8 days, a total of 4 applications.
In preliminary studies, 5% SLS was applied in the same way, to rule out the possible irritating effect of the suspending medium. During the experimental period the appearance of the skin, the weight and general health of the animals were under

constant observation. After the 4th application a week was allowed to elapse, before the fifth, sensitizing dose was applied.
The treated skin areas remained perfectly normal throughout the entire course of the experiment. There was no immediate or delayed skin reaction after the first 4 th application, indicating any primary irritating effect of the preparation used.
The fifth, sensitizing application, had equally no visible effect whatsoever on the appearance of the skin. There was not the slightest evidence of erythema or oozing ; there was no edema or loss of hair. The skin retained its normal aspect even though some of the ointments remained on the skin surface from one application to the next.
The experimental conditions of testing with 25% suspensions of Alcloxa in SLS solution were much more severe than one would expect to encounter in everyday usage. The concentrations of the test substances were 30 to 100 times higher than in the commercial preparations. Moreover SLS has been shown to potentiate the sensitizing powers of metallic salts both in guinea pigs (Nilzen and Wilkstroem : Acta Derm. Ven. : 35, 292, 1955) and in man. In spite of these additional factors Alcloxa proved to be completely non-irritating and non-sensitizing under the conditions of testing.
Alcloxa proved to be without any primary irritating and sensitizing properties, when tested on the skin of guinea pigs. The absence of any harmful effect on the skin was the more noteworthy, as half of the tests were performed under severe conditions of testing.

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Alcohol Soluble Alcloxa Modified

10. Overview

Alcohol Soluble Alcloxa Modified is the alcohol soluble form of Alcloxa, obtained by the complexation with propylene glycol. This complex is in form of white micropowder, possess all the antiperspirant, deodorant and anti irritant properties of Alcloxa and is designed for formulations with high alcohol content and aerosols.

11. Codex and names

Chemical name:	Aluminum Chlorhydroxy Allantoinate alcohol soluble modified

12. Specification data

Appearance:	fine powder
Colour:	white
Odour:	odourless or slight characteristic
Assay (Al_2O_3):	35.3% min.
Allantoin (as nitrogen):	1.6 ± 0.5%
Propylene glycol:	21.5% min.
Chloride:	12.2% min.
Sulphate:	0.05% max.
Heavy metals (Pb):	less than 20 ppm
Shelf life:	5 years in original packing

13. Solubility

A. S. Alcloxa Modified is soluble in water, propylene glycol, glycerin, ethanol and methanol and practically insoluble in mineral oil, benzyl alcohol, acetone and isopropanol.

14. Applications

A. S. Alcloxa Modified may be used at concentrations of 6-20% in preparations with high content of alcohol, such as aftershave lotions, deodorants and antiperspirants (aerosol, rolls-on, deodorant sticks, solutions).

15. Toxicological data

The toxicity tests conducted has shown that A.S. Alcloxa Modified is non-sensitizing and non-irritating for skin and eyes.

Acute oral toxicity (rat):
thirty healthy rats, equally divided as to sex were used in this study. The test material was administered orally by a rigid stomach tube. The method of Litchfield and Wilcoxon was used in calculating LD50 oral. The oral LD50 was ≥ 2000 mg/Kg.

Acute dermal toxicity (rabbit):
ten normal healthy rabbits of both sexes were used in this study. The test material was applied to the normal and abraded skin of animals. The dermal (normal and abraded) LD50 was ≥ 2000 mg/Kg.

Eye irritation (rabbit):
Powder is eyes irritant. At 10% aqueous solution of the test material was applied to the eyes of rabbits without washout. According to the Draize method there was no eye irritation. The test material is not an eye irritant at 10% concentration.

Primary skin irritation (human):
A series of 100 white females were subjected to prophetic patch tests with the following products for the purpose of determining whether the ingredients contained therein were capable of producing primary irritation or sensitization of the skin.
1)Antiperspirant spray, 10% Modified A.S. Alcloxa.
2)Modified A.S. Alcloxa 10% aqueous.
The patch were performed in the following manner: the entire upper back was thoroughly cleansed with alcohol (isopropyl 70%). The material to be tested was then impregnated into a one-half inch square of clean white blotting paper. This was then applied to the previously cleansed skin site and covered with an “Elasto-Patch” plaster and allowed to remain in contact with the skin for 48 hours. Upon removal of the patches, the test areas were observed at once for *immediate reaction.* A final examination for delayed reactions was made 72 hours after application of the patch test. Retests were performed 14 days later employing the same technique as described above. There was no evidence of primary irritation on the initial 48 hour patch test, and no indication of any sensitization of the skin on the retest performed 14 days later. It is the opinion of the dermatologist that the above mentioned products are not primary irritants, and the sensitizing potential, if existent at all, is exceedingly low.

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