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Acute Dermic Toxicity Study of Controlled Hydrofluoric Acid with Gq-300® Additive

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Research Article

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Abstract

Acute dermal toxicity is the adverse effect that occurs within a short period of 24 hours after exposure. The test provides basic information to classify and label the products, being an initial step for other more lasting exposure studies. The Test Substance is a solution composed of 24% Hydrofluoric Acid (HF), controlled with the additive GQ-300®, which is a strongly acidic chemical composition and safe for human use, obtained by mixing strong acids with the purpose of achieving a balanced mixture of acids which allows, through additivation, the control and safe handling of other strong and corrosive acids. The objective of this study is to know the effect and absorption by the cutaneous route that this mixture has, for which it is used with a fixed volume of three labeled solutions and of different concentrations of HF, administered in Female Rats BIUO: Wistar in young age, adult rats and female mice BIOU: NMRI in young adult age. In conclusion the solutions of HF Controlled with Gq-300® Additive. They cause skin irritation and the degree of irritation will depend on the type of skin, being in the most sensitive and young skin, where the irritation damage and the necrosis caused by regeneration of it will be more pronounced in a short period of time. The Controlled Fluorhydric Acid with the additive GQ-300, could provide the safest handling that the 48% pure Hydrofluoric Acid (HF), which today does not have, besides allowing a reversible effect, in case of an accident, which does not offer the pure HF of 48%.

Keywords: Dermic Toxicity; Hydrofluoric Acid; Additives; Azeotropic Mixture

Introduction

The skin is the most extensive organ of expression of the body that surrounds and insulates other organs of the environment [1]. Not only is it an external protection cover, but it also performs multiple functions, some more complex than others, such as protection, thermoregulation, immune response capacity,

biochemical synthesis and excretion of water and fat, among others. It is also the sensory organ that receives tactile, thermal and painful stimuli [2]. The dermal layer can be considered as a border in two media, the internal and external that may reflect some damage of the individual. The thickness of the skin varies considerably according to the regions of the body. The proportions between the epidermis and the dermis are also variable. However, permeability almost always keeps an inverse proportion to the thickness of the stratum corneum. In some areas, differences in lipid concentration affect absorption by the skin depending on the lipophilic or hydrophobic properties of an individual drug or substance. Thus, penetration is greater in the face, in intertriginous areas and especially in the perineum. Consequently, the application of any xenobiotics in these areas is more likely to cause sensitization, irritation and drug atrophy problems [3].

On the other hand, when we talk about acute dermal toxicity, it is the adverse effect that occurs within a short period of time after application to the skin of one or multiple doses for a period of 24 hours. The test provides basic information to classify and label the products, being an initial step for other studies of more lasting exposure, as well as to know the absorption by this route [3]. The OECD standards establish that the relationship between the exposure of animals to the substance, the incidence and severity of all observed anomalies, both behavioral and clinical anomalies and their reversibility must be included in dermal toxicity studies. Macroscopic lesions, changes in body weight, the effect on mortality, or any other type of toxic effect [4].

Hydrofluoric Acid (HF) is a liquid, corrosive, transparent, colorless smoking and corrosive (identification sheet, CAS number 7664-39-3) [5]. It is a compound often used in industry, because of its extensive use; many countries have reported burns from this substance usually. The most common accidents occur due to skin exposure and ingestion. In contact with the skin it can cause serious burns that can even endanger the life of the victim as they can produce metabolic acidosis, fluoride poisoning and ventricular arrhythmias.

However, the test substance that was used in this study is a solution of Hydrofluoric Acid (HF), with a concentration of 24% and controlled with the GQ-300®. The GQ-300® additive consists of a Strong and Corrosive Acid Controller Additive. It Is characterized as a balanced azeotropic mixture of acids, which once in equilibrium, facilitates its use as an additive to modify properties of other strong acids, as it induces equilibrium in acid strength in dissolution, KA or acid ionization constant of Every strong acid you want to control. Among the changes of properties, which induces in other acids that it controls, are the reduction of vapors, change of the freezing point by variation of its azeotropic activity and the reduction of hydroniums ions. All this balance facilitates the safe use of highly dangerous acids with these new properties, in industries: food, drugs, mining operations, metallurgy, naval operations, agriculture, extraction and treatment of Hydrocarbons, Arms and water treatment industry, among others [6].

Extreme pH acids are capable of producing severe injuries in live tissues similar to those produced by heat and are called chemical burns by caustics. The chemical characteristics inherent in the substance determine the type and extent of tissue damage that they can produce [6]. Due to there not being precise information regarding absorption through skin and the effect thereof of this mixture, this dermal toxicity study is performed with a fixed volume of 3 named solutions and of different concentrations of HF: HF(02) 73.4%, HF(03) 67% and HF(04) 56.7% Controlled with the GQ-300® additive administered in two rodent species Female Rats BIUO: Wistar Young with 2 months of age and adult rats with 6 months of age, Female Rats BIOU: NMRI Young adult age**.** An initial observation study is conducted where dying animals, or animals obviously injured or in pain, that could demonstrate signs of severe or lasting pain, are humanely sacrificed, for this study said application was not necessary.

Materials and Methods

We utilized one N=01 of animal per experimental solution and specie applied by age for which then the study counted with 03 Wistar rats of Young age, 03 Wistar rats of adult age, and 03 NMRI rats of young adult age. The administered doses of the experimental solutions HF(02), HF(03) y HF(04) was of a single volume of 20µl for the BIOU Wistar rats (young and adult) and 10 µl in BIOU NMRI rats. The experimental animals had an acclimation period of 03 days where they were shaven a day before applying the dermal dose. The animals were maintained in care unit 03 of the Universidad de Los Andes vivarium at a temperature of: 22ºC (+ 3ºC), with adequate relative humidity, Lighting: 12 Light / 12 Dark Cycle. Feeding and Hydration was ad libitum, they were classified in a cage by specie and age, the animals were labeled as follows (02) with two black hoops on the tail, HF(03), three black hoops on the tail and HF(04) four black hoops on the tail. The solution was applied on the dorsal side of each animal

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with a volumetric micro pipette described for each animal.

Study Conditions

The administered substances of HF(02), HF(03), HF(04), were transparent, colorless, fuming liquids, the observations and notes in accordance with the established for Draize grading: the modified Draize method, developed by Murphy and colleagues, consists in applying the substance topically on the dorsal of the rat shaved 24 hours prior at 3 different concentrations, the site of dermal dose of each animal shall be evaluated previously and in use after 6 hours of the products for 14 days. Following is described the Draize scoring which includes Erythema, Edema [7] (Tables 1 & 2).

Erythema Formation	Value	EDEMA Formation
Very Slight Erythema (Barely Perceptible)	1	Very Slight edema (Barely Perceptible)
Well defined Erythema	2	Slight edema (edges of area well defined)
Moderate to Severe Erythema	3	Moderate edema (raised approximately 1mm)
Severe Erythema (beet red) to slight Eschar formation	4	Severe edema (raised more than 1mm & extending beyond the area of exposure)
Total		

Table 1: Evaluating reactions in skin [8].

Skin Pigmentation	Pointscale
Pigmentation not perceptible	0
Defined Pigmentation (Light coffee) with defined borders	1
Moderate Pigmentation (coffee)	2
Strong Pigmentation, (Dark Coffee)	3
Intense Pigmentation (Intensely Pigmented or Black)	4

Table 2: Photo Pigmentation [9].

During the study the administration of analgesics or the sacrificing of animals was not necessary due to intense manifestation of pain. The dorsal observations of each animal after single dose administration are reported in Tables 3-5.

HF Solution (02)	Edema	T.A	Erythema	T.A	P.P	T.A	Necrosis
Young Wistar Rat	1	-	1		1	5	NO
Adult Wistar Rat	2	5 min	2	5 min	2	5	NO
Young Adult Rat	2	2 min	3	2 min	3	5	YES

Table 3: Dermal observation of HF (02).
T.A = Time of Appearance / P.P = Photo Pigmentation.

HF Solution (03)	Edema	T.A	Erythema	T.A	P.P	T.A	Necrosis
Young Wistar Rat	1	-	1		1	5	NO
Adult Wistar Rat	2	5 mint	2	5 mint	2	5	NO
Young Adult Rat	2	5 mint	3	2 mint	3	5	YES

Table 4: Dermal observation of HF (03).
T.A = Time of Appearance / P.P = Photo Pigmentation.

HF Solution (04)	Edema	T.A	Erythema	T.A	P.P	T.A	Necrosis
Young Wistar Rat	1	-	1		1	5	NO
Adult Wistar Rat	1	-	2	-	1	5	NO
Young Adult Rat	1	-	3	2 mint	3	5	YES

Table 5: Dermal observation of HF (04).
T.A = Time of Appearance / P.P = Photo Pigmentation

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Results and Discussion

In the present experimental work it could be observed that the skin of the BIOU-NMRI mice was more sensitive than the skin of the BIO-Wistar rats to these solutions of hydrofluoric acid (HF(02), HF(03) and HF(04)) controlled with additive GQ-300®. NMRI mice showed more pronounced erythema, which inferred irritation of the substance in sensitive skins. The skin of the Young BIOU Wistar rats was less sensitive to the three solutions of which the hydrofluoric acid solution (HF04) controlled with additive GQ-300 ®, was even less sensitive because it did not present erythema or edema only a little reddish photopigmentation Pronounced with respect to the other solutions [7]. The skin of the adult rats was more sensitive than the young rats; the erythema was marked in the three solutions with a higher degree than in the young. The mice showed more pronounced erythema and necrosis, however, at 14 days the healing process was created forming a dry crust without humidity in the area during the observations for 14 days. After 14 days, the animals were euthanized without apparent pathological findings [7].

The rat rodent species has been the most common species used for in vivo dermal penetration testing, and remains a requirement as part of the pesticide Safety Assessment in North America [9]. However, the in vivo rat test method is considered to have some value due to the "generation of systemic kinetic and metabolic information" that may be related to man [10].

It is important to note that the pure hydrofluoric acid-HF without control at 48% of concentration is not applied as a control group solution because its safety data sheet declares it to be a corrosive and irritating substance with irreversible lesions to the skin, the same safety data sheet is used as reference. For the present study, the safety data sheet of pure hydrofluoric acid-HF at 48% of concentration, as reported by Carl Roth, supplier of the safety data sheet with Registry Nº2015/830/UE with commercial name (Rotipuran® [11], therefore the animals are not subjected to suffering that this solution of pure and uncontrolled hydrofluoric acid HF at 48% concentration can cause. As such we refer:" if it is clear that if a substance is very toxic by skin, the study of skin irritation/corrosion may not be practicable, since the amount of substance to be applied exceeds the toxic dose and therefore would entail the death of Animals tested"[12]. Annual Globally Harmonized System (SGA) IV United Nations edition New York and Geneva 2011. The SGA hazard classification report for pure and uncontrolled HF at 48% of concentration is in Table 6.

Section	Hazard Class	Hazard class and category	Hazard statement
3.1O	Acute toxicity (oral)	(Acute Tox.2)	H300
3.1 D	Acute toxicity (dermal)	(Acute Tox.1)	H310
3.1 I	Acute toxicity (inhal.)	(Acute Tox.2)	H330
3.2	Skin corrosión/irritation	(Skin Corr.1A)	H314
3.3	Serious eye damage/eye irritation	(Eye Dam.1)	H318

Table 6: SGA Classification of pure hydrofluoric acid at 48% concentration.
Taken from the safety data sheet HF 48% Rotipuran® (REACH) amended by 2015/830/UE.

This safety data sheet classifies according to the GHS system pure hydrofluoric acid (HF) of 48% of concentration at cutaneous level as corrosive/irritant 1a, by the degree of cutaneous irritation as acute toxicity in the category of danger as 1 irreversible damage.

- According to the results obtained in this research work, hydrofluoric acid-HF at 24% concentration and controlled with additive GQ-300®, and classifying, according to the Globally Harmonized System (GHS).
- The animals showed reversible dermal irritation, so the skin toxicity would be in the classification (1b): The substance produces dermal irritation.
- The degree of skin irritation would be in grade (03) because it is reversible and does not generate secondary damage such as alopecia, hyperkeratosis, hyperplasia and scaling.
- Due to the PH, irritation potential of the solution is in category (1) for its acidic pH.

In conclusion, the solutions of hydrofluoric acid-HF at 24% concentration and controlled with GQ-300 ® additive, cause skin irritation. The degree of irritation will depend on the type of skin, being in the most sensitive skins where the irritation damage and the necrosis caused will be more pronounced, but with regeneration of the same in a short period of time.

When comparing these results of hydrofluoric acid-HF at 24% concentration and controlled with additive GQ-

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300 ® with pure uncontrolled hydrofluoric acid (HF) at 48% concentration, the objective of the test is fulfilled: to demonstrate that hydrofluoric acid-HF At 24% concentration controlled with the additive GQ-300 ®, is safer to handle and manage than the pure hydrofluoric acid (HF) at 48% concentration, which does not exist today, in addition to allowing a reversible effect, in case of accident, which hydrofluoric acid -Pure HF at 48% concentration does not offer.

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