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Acute Oral Toxicity of Hydrofluoric Acid Controlled with Gq-300® Additive Fixed Dose Procedure-Acute Oral Toxicity -Ocde420

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Abstract

This paper demonstrates the tolerable acute oral toxicity of a solution composed of Hydrofluoric acid (HF) at 24% concentration and GQ-300® as a controlling additive. The literature describes pure HF as a liquid, corrosive, colorless, fuming, (identifying CAS number 7664-39-3). GQ-300®, additive consisting of a strongly acidic chemical composition and safe for human use, obtained by the mixing of strong acids with the aim of achieving a balanced mixture of acids which allows, by means of additivation, the control and safe handling of other strong and corrosive acids commonly used in water treatment, cleaning of scale of silicates, in sites with contents of silicates to enhance recovery of metal, non-metal mining and hydrocarbon such as oil and gas. Since there is no precise information about the toxicity of this mixture, or it is expected that the test material is toxic, the study of oral toxicity uses varying volumes of fixed oral doses of three solutions of different concentrations of HF Controlled with the GQ - 300® additive Administered in rats in order to know the tolerable acute toxicity of the mixture. Obtaining as a result that the HF mixture controlled with GQ-300®, administered to rats wistar by mouth in a volume of 20 µl with a range of 275 to 289 mg/kg, have a tolerable dose of acute toxicity greater than the pure HF to 48% , which means that this GQ controller minimizes the toxic action of the HF.

Keywords: Acute; Additivation; Controller; Hidrofluoric Acid; GQ-300; Toxicity

Introduction

Hydrofluoric acid (HF) is a weak inorganic acid with a dissociation constant (KA) of 3.45 highly dangerous, corrosive, of acute and penetrating odour, is produced from the chemical reaction between calcium fluoride and sulfuric acid to produce HF gas that When cooled, it is stored as a colorless liquid, with a density similar to that of water [1, 2]. The most widely known property of the HF is to attack glass, enamels, cement, rubber, leather, metals (especially iron), and organic compounds [3]. In oil Refineries It is used to obtain high octane gasoline through the process of renting the HF [4]. Your identification Card CAS number 7664-39-3 [5]. It is one of

the most dangerous acids, so it should be handled with great caution. With serious health effects according to their route of administration: Inhalation causes respiratory Irritations, can cause bronchitis bronchopneumonia pulmonary edema. Dermal wounds of difficult healing, ocular: Burns blindness (irreversible optic nerve injury), orally burns in esophagus and stomach, severe pain, with risk of perforation, vomiting spasms [3]. The absorption by mouth is associated with a high mortality rate, due to the severe hypokalemia that occurs, demonstrated by the electrocardiographic changes with prolongation of the QT wave, in addition to this, other alterations have been found in the Electrocardiogram as ventricular fibrillation and polymorphic ventricular tachycardia [6]. Additionally, fluorine is direct-toxic, activating adenylate cyclase resulting in an increase in the formation of cyclic adenosine monofosfato that produces cardiac irritability [7].

The Product GQ-300 is an intellectual property of Globalquimica A.L.C.A. 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 [8]. 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.

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 [9]. It Must be kept in mind that strong and corrosive acids such as Sulfuric Acid, Hydrochloric, Hydrofluoric etc, are low PH; that is to say. their negative logarithms of the concentration of hydrogen ions is extremely low which gives them a higher concentration of Hydrogens and exposure to agents with extreme acidity PH < 2 is associated with severe tissue damage.

In order to mitigate the impact of risks by using large volumes of strong and corrosive acids throughout the industrial area where they are used, and especially in the metal, Non-metallic and energetic mining operations, the Product GQ-300, It has a wide range of applications allowing to maintain its low pH, its concentration of hydrogen but minimizing the risks to the extreme exposure of the acidity and preventing the tissue damage.

According to the foregoing, evaluate the acute oral toxicity of the hydrofluoric acid mixture with the GQ-300® controller. Since there is no precise information about the toxicity of this mixture, or it is expected that the test material is toxic, the study of oral toxicity uses varying volumes of fixed oral doses of three solutions of different concentrations of HF Controlled with the GQ - 300® additive administered in rats with the aim of discovering the tolerable acute exposure of the solution of hydrofluoric acid with GQ - 300® controller and its action in the mix.

Materials and Methods

The Initial observation test was carried out with the half of the maximum volume of liquid that can be administered in a single dose to rats of 500 microliters (µl), increasing or decreasing the volume according to the toxic effects that the experimental animals demonstrated, dying animals, or animals obviously sore, showing signs of severe and long-lasting anguish, will be killed humanely, and considered equally as those who died immediately in the study, Likewise there will not be administration of pure, highly toxic corrosive substances as hydrofluoric acid to 24% of concentration that is known to be orally lethal according to their Technical Data Sheets for the protection of the animals, therefore the references made in notes ½ of the CAS Number will be used as reference control. The HF solutions controlled with GQ - 300® additive were labeled according to their individual concentrations of HF: HF with GQ - 300® additive (02) 73.4%, HF with GQ - 300® additive (03) 67%, and HF with GQ - 300® additive 56.7% (04).

The animals used for testing were female Wistar rats at 6 weeks of age, kept in sterile conditions, used three animals per experimental group HF (02), HF (03), HF (04), using 05 dose levels for a total of 45 Wistar rats and 05 experimental control rats that will be administered the volume of GQ – 300 solution equal to the other experimental rats, the other component of the mixture (hydrofluoric acid) is not used as control because it is highly toxic, its CAS card is to be used as reference, this is

acceptable according to the Protocol OCDE 420, 425 [10, 11], and the globally harmonized system of classification and labelling of products chemical (SGA) in its fourth edition United Nations New York and Geneva 2011 [14]. All the procedures used in this study were approved by the committee of ethics in animal research (CEBIOULA117/18) of the Council of Scientific, Humanistic, Technologic and Artistic Development of the University of Los Andes, Merida, Venezuela, which were in compliant with international standards of animal care and veterinary medical practice.

The study begins with two fixed volumes of different solutions, the high volume 500 µl and the low volume 200 µl. After observing the lethal effects in these groups with these administered volumes according to protocol OCDE 420, another group will be utilized decreasing the administered volumes due to effects caused at 100µl and 50µl if the toxic effects continue the volumen for administration to other animal groups Will decrease with 20µl obtaining survivability of 50% of the animals. As such the study was conducted in decreasing form from the fixed volumen of the test article. The animals were maintained in the care unit #2 of the ULA University Vivarium at a temperature of 22ºC (+ 3ºC) and a relative humidity of 30% - 70%, Illumination: cycle of 12 hours of light and 12 hours of darkness. Feeding and hydration ad Libitum, feeding was suspended 12 hours prior to administration of the test substances, they were organized in cages by experimental Group with n=03.

Study Conditions

The administration of fixed volumes was realized in a unique dose for the experimental groups by quantitiy of administered volumen, in a decreasing manner with HF (02), HF(03), HF(04), these were colorless, fuming, transparent liquids, for each experimental Group the volumes of oral administration were 500 µl, 200 µl,100 µl, 50 µl y 20 µl, the administered is directly, via plastic canulas inserted in insulin syringes. It is important to note that the administration protocol for fixed volumes in a unique dose of 500µL and 200µL, were utilized in parallel as volumes for initial observation where two wide ranges of volumes were it was expected to find the initial toxic findings of the substances, notwithstanding these volumes caused death in 100% of the administered population. The difference was the time of death even when survivability was very short in these two groups, the results of these two experimental groups are shown on Tables 1-3. The study continues with administration of a lower fixed volume than the initial Group, taking as a fixed dose and single dose of 100µl, where immediate toxic effects were immediate and death occured at 2 hours of having administered the test articles to three groups. With these results the administration volume was lowered further for the HF(02), HF(03), HF(04) solutions to half of the previous administered volume given that death was not instantaneous, but even with this dose of 50µl symptoms of acute toxicity were markedly present and similar to those observed with previous volumes administered, the animals of the 3 groups were observed for 4 hours and then sacrificed due to high levels of suffering and toxicity of the animals, and finally a fixed and single dose of 20µl was administered where signs of slightly tolerable toxicity were demonstrated with half of the animals succumbing to death and the surviving animals sacrificed at the 7 day point after administration, results shown on Tables 4-6, It is important to note that a control Group was maintained that was only receiving the same volumes as the others but only of the GQ-300® product [10].

Animal	Severity				Type of Damage	Tox Start	Tox Stop	Death
	Mild	Moderate	Severe	Death				
01 HF(02) 148 grams V=500 µl				X	After 5 minutes caused instant death with a volume of oral administration 0.5 cc = 500µl	5-min	Death	5 -min
02 HF(02) 147grams V=500 µl				X	After 5 minutes caused instant death with a volume of oral administration 0.5 cc = 500µl	5-min	Death	5-min
03 HF(02) 127grams V=500 µl				X	After 5 minutes caused instant death with a volume of oral administration 0.5 cc = 500µl	5-min	Death	5 -min
01 HF(02) 150grams V=200 µl			X		Difficulty breathing, drooling, body weakness, possibly by trachea wheezing, convulsions within half an	5-min	Death	30-min

					hour of the dosing, dies			
02 HF(02) 167grams V=200 µl			X		It presents the same clinical manifestations but takes more time to die, at one hour after administering the dose.	5-min	Death	1 hour
03 HF(02) 133grams V=200 µl			X		Difficulty breathing, drooling, body weakness, possibly by trachea wheezing, convulsions within half an hour of the dosing, dies	5-min	Death	30-min
01 HF(03) 153grams V=500 µl				X	After 5 minutes caused instant death	5-min	Death	5 - min
02 HF(03) 184grams V=500 µl				X	After 5 minutes caused instant death	5-min	Death	5-min
03 HF(03) 138grams V=500 µl				X	After 5 minutes caused instant death	5-min	Death	5-min

Table 1: Effects of Hydrofluoric Acid "Controlled with GQ-300®" HF (02) HF (03) HF (04) Solutions with fixed volumes of 500 y 200µl.

Animal	Severity				Type of Damage	Tox Start	Tox Stop	Death
	Mild	Moderate	Severe	Death				
01 HF(03) 154 grams V=200 µl			X		Manifestation of pain, body weakness, tachycardia, these animals increased weakness of the animal over time	5 minutes	Death	2 hours
02 HF(03) 118grams V=200 µl			X		Equal to the previous manifestations	5 minutes	Death	2 hours
03 HF(03) 152grams V=200 µl			X		Equal to the previous manifestations	5 minutes	Death	2 hours
01 HF(04) 161grams V=500 µl				X	After 5 minutes caused instant death	Immediate	Death	5 min
02 HF(04) 168grams V=500 µl				X	After 5 minutes caused instant death	Immediate	Death	5 min
03 HF(04) 132grams V=500 µl				X	After 5 minutes caused instant death	Immediate	Death	5 min
01 HF(04) 106grams V=200 µl			X		They presented serious clinical manifestations, bodily weakness, retching, wheezing	Immediate	Death	20min
02 HF(04) 142grams V=200 µl				X	They presented serious clinical manifestations, bodily weakness, retching, wheezing	Immediate	Death	20 min
03 HF(04) 157grams V=200				X	They presented serious clinical manifestations, bodily	Immediate	Death	At 1 hour

µl					weakness, retching, wheezing			and 30 min
Control GQ (01) 154grams V=500 µl	X				A bit of body weakness, tachycardia, still remained alive	10 minutes	Euthan asia	14 days
Control GQ (02) 158grams V=200 µl	X				A bit of body weakness, tachycardia, still remained alive	10 minutes	Euthan asia	14 days

Table 1: Effects of Hydrofluoric Acid "Controlled with GQ-300®" HF (02) HF (03) HF (04) Solutions with fixed Volumes of 500 y 200µl (Continued) Source Morales, et al. 2019.

Animals	Behavior	SCV	S.Respiratorio	S. Locomotor	Irritación	Mucous Membranes
General	Motor weakness	Decrease in blood supply	Difficulty	Slow	Ocular, gastric, regurgitations	Reddish Mouths

Table 2: Clinical Signs of Toxicity Hydrofluoric Acid "Controlled With GQ-300®" HF (02) HF (03) HF (04) Volume OF 500 Y 200µl. Source Morales, et al. 2019.

Animals	Necropsy Findings	Pathological findings
Animals with administration of 500 and 200 µl volumes. In general the two groups	They presented features of burns in the stomach wall, filled with air, irritated gastric mucosa, perforation of the stomach with emptying intestines of the liquid	ϖ Damage at the stomach level, intestine, trachea
		ϖ Low blood supply at the abdominal level
		ϖ Signs of Burns at the abdominal level

Table 3: Postmortem Signs of Toxicity, Hydrofluoric Acid "Controlled With GQ-300®" HF (02) HF (03) HF (04) volume of 500 y 200µl Source Morales, et al. 2019.

Animals	Behavior	SCV	S. Respiratory	S. Locomotor	Irritación	Mucous Membranes
The Three Groups	Majority of time spent in resting state, lethargy.	Decrease in blood supply	Slow Breathing	Few and Slow Movement	Ocular, gastric regurgitations	Low salivation, decreased intake of food and water

Table 4: CLINICAL Signs of Toxicity Hydrofluoric Acid "Controlled With GQ-300®" HF (02) HF (03) HF (04) Volume of 20µl Source Morales, et al. 2019.

Animal	Severity				Type of Damage	Tox Start	Tox Stop	Duration.
	Mild	Moderate	Severe	Death				
HF(02) 01=84 grams 02=79 grams 03=76 grams V=20µl		X		One (01) animal (Nª02)	They expressed unrest upon administering the subsequent dose lethargy, body weakness, tachycardia, piloerection, found lethargic after two hours continue the same for 7 days but with considerable weight loss.	Immediately	Euthanasia	7 days
HF(03) 01=79 grams		X		Two (02) Animales	They showed signs of suffocation at the beginning, a little shortness of breath, they were slower than	Immediately	Euthanasia	7 days

02=80 grams 03=75 grams V=20µl				(01,03)	the HF Group (02), piloerection remained equally for 7 days also with weight loss			
03 HF(04) 01=76 grams 02=81 grams 03=73 grams V=20µl		X		One (01) animal (Nª03)	They showed signs of suffocation at the start, regurgitation, piloerection remained equally for 7 days also with weight loss	Immediately	Euthanasia	7 days
Control with GQ (02) 76grams V=20µl	X				A bit of body weakness, tachycardia, still remained alive for 7 days	10 minutes		14 days

Table 5: Effects of Hydrofluoric Acid "Controlled With GQ-300® HF (02) HF (03) HF (04) Volume of 20µl Source Morales, et al. 2019.

Animals	Necropsy Findings	Pathological findings
In General All Groups	Presented burn scars on stomach wall, empty stomach, intestines with signs of burns, grayish color, and gastric mucousa irritated brownish yellow color.	ϖ Presented damage at the level of the stomach, intestines, trachea
		ϖ Scars of Burns at the abdominal level

Table 6: Postmortem Signs Of Toxicity Hydrofluoric Acid "Controlled With GQ-300®" HF (02) HF (03) HF (04) volume of 20µl Source Morales, et al. 2019.

Discussion of the Results

The present study was realized with the objective of discovering the tolerable acute toxicity of an HF – Hydrofluoric Acid solution with the controlling agent GQ-300®, that has as a function of use, the ability to control or diminish the toxic effects of pure HF – Hydrofluoric Acid, for which it is necessary to evaluate the estimated acute toxicity (EAT) with lethal dose 50 (LD_{50}) of this solution. The pure HF at 48% concentration, has a Safety Data Sheet, of which we have included as control for this study, the reference for pure HF at 48% concentration, reported by Carl Roth, purveyor of the Safety Data Sheet with Registry Nº 2015/830/UE, Of HF of 48% concentration and with comercial name (Rotipuran**®),** whose concentration and commercial name refer to having an estimated acute oral toxcitiy of 5mg/kg of body weight as demonstrated on Table 7**.**

Substance	CAS No.	Exposure Route	EAT
Hydrogen Fluoride	7664-39-3	Oral	5 mg/Kg
Hydrogen Fluoride	7664-39-3	Skin	5 mg/Kg
Hydrogen Fluoride	7664-39-3	Inhalation: Gas	100 ppmV/4h

Table 7: Estimated Acute Toxicity (EAT) of HF – Hydrofluoric Acid at 48% concentration.
Taken from HF 48% Rotipuran® (REACH) Safety Data Sheet modified by 2015/830/UE

Then, according to the observation of the experimental results obtained from the development of the OCDE420 protocols, we can infer that three (3) solutions with HF, are substances which presented evidence of acute toxicity in an active toxic level with a dose of 22 mg/kg of body

weight in a fixed volume of 20 µl for oral administration as described in Table 8.

Study Group	HF Concentration in mg	GQ-300 Concentration in mg	Estimated Acute Toxicity (Eat)	Average Body Weight (RATS)	ETA
HF02	16.15 mg	5.85 mg	22mg/kg body weight	80 g	275mg/kg
HF03	14.74 mg	7.26 mg	22mg/kg body weight	78 g	282mg/kg
HF04	12.47 mg	9.53 mg	22mg/kg body weight	76 g	289mg/kg

Table 8: Acute ORAL Toxicity-Maximum Tolerable dose of Controlled HF with GQ-300® Source Yasmin Morales 2019

The Solution of HYDROFLUORIC ACID "CONTROLLED WITH GQ-300®" administered orally to Wistar rats of six weeks of age at a rango of 275 to 289 mg/kg of concentration, did not cause immediate death, they survived. Nonetheless, they presented some signs of toxicity during the 4 days following administration, but maintaining survivability for 7 days, at which time they were euthanized following ethics protocols [10,11]. In agreement with what was established in the standard OCDE420 [12] with a fixed volume, single dose solution of hydrofluoric acid - HF controlled with GQ - 300® and an LD50 of 22 mg/kg of body weight, this solution is classified as a toxic substance type B.

These experimental results also permit Classification under Global Harmonized System (SGA) Edition IV of United Nations, New York and Geneva 2011 [14,15], to classify the Hydrofluoric Acid solution controlled with GQ-300® in a single dose range of 22mg/kg to a volume less than or equal to 20µl with an acute oral toxicity in categories (03), and acute organ toxicity category (03), Category (3) danger to health, toxic in case of ingestión.

By comparing these classifications of acute oral toxicity of hydrofluoric acid - HF solutions (02) 73.4%, HF (03) 67%, HF (04) 56.7 concentration and controlled with GQ - 300®, with those of the hydrofluoric acid - pure HF to 48% of concentration and not controlled, We conclude that the GQ-controlled HF - 300®, has a more tolerable acute toxicity per single dose, which means that this GQ - 300® controlling agent minimizes the toxic effect of hydrofluoric acid - HF.

With these results, the study meets the objective of the present study, that was to show that the controlled hydrofluoric acid with the GQ - 300®, additive can provide the most safe handling of the acid hydrofluoric-HF that today is in the market, as well as allowing a reversible effect, in case of accident, which hydrofluoric acid - HF does not offer when not controlled.

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