Calcium Gluconate versus Hexafluorine in the Treatment of Hydrofluoric Acid Exposure

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Abstract

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Hydrofluoric acid (HF) is the inorganic acid of elemental fluorine and causes tissue damage in humans by two mechanisms; free hydrogen ions cause a caustic burn and fluoride ions penetrate tissues resulting in chemical burns. The mode of action this acid assumes is to bind to calcium and magnesium when it comes into contact with skin and tissues. Once HF is absorbed through the skin or eyes, it dissociates and can cause extensive damage to tissues by the formation of insoluble fluoride salts. If enough Ca and Mg are absorbed, there may be an inadequate supply available for vital body functions. Exposures to hydrofluoric acid must be treated immediately, as sudden death has been reported from acid burns to as little as 2.5% of body surface area. Two treatments available today include calcium gluconate and Hexafluorine. Calcium gluconate works by combining with free fluoride ions to form insoluble calcium fluoride,

thus preventing the burns that result from the extraction of calcium from tissue and bones. Depending on the surrounding circumstances, calcium gluconate can also be administered by injection or intra-arterial infusion.

Hexafluorine has both absorption and chelating capacities enabling it to trap H+ and F+ ions immediately as it contacts HF. This ability prevents the superficial layers of skin from being destroyed and also halts the fluoride ion advancement.

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I would like to thank my family for their support during my pursuit of this degree and through the process of this research. I would also like to thank the risk control staff and my advisor John Olson for their guidance and for giving me the opportunity to further my education. Finally, I want to thank my friends for the endless amount of help they have given me. I hope that our relationships will carry on during our professional careers in the field of Risk Control.

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Chapter I
Statement of the Problem

Introduction

Since its birth in the 1950's, the semiconductor industry has been continuously growing. Today it is approaching sales of $200 billion dollars per year worldwide. This industry is growing faster than all other "mature" industries indicating that microchips have yet a lot of growth potential (Van Zant, P., 2000).

The semiconductor industry supplies us with many luxuries that we have come to take for granted including computers, televisions, telecommunications equipment, industrial machinery, aircraft, and military equipment (Moris, F., 1996). In order to provide these amenities and stay competitive in the industry, semiconductor companies need to use the best available technology. Many times, this technology requires the use of a variety of chemicals. In fact, microchip fabrication is primarily a series of chemical processes. Up to 20% of all process steps are wafer surface preparation or cleaning, requiring semiconductor companies to consume large quantities of chemicals. If all the costs of production are summed, chemicals can be up to 40% of manufacturing costs (Van Zant, P., 2000).

Semiconductor companies must implement stringent engineering and administrative controls to help prevent exposure and reduce the risks associated with chemicals. Risks are managed by developing employee knowledge, skill, and awareness through training programs and inspections, however employee exposure to hazardous chemicals continues to be a problem (Van Zant, P., 2000). Many of these chemicals have the potential to seriously harm human beings causing burns, systemic poisoning, and in some cases leading to death. Hydrofluoric acid (HF) is a chemical with unique characteristics that make it extremely toxic to humans, and immediate treatment following exposure is imperative. This study will analyze the effectiveness, availability, and cost of treatment methodologies used for HF exposures.

Purpose

The purpose of this study is to compare and contrast calcium gluconate and Hexafluorine as treatments for hydrofluoric exposure.

Objectives

1.0 Examine processes in the semiconductor industry that utilize hydrofluoric acid.
    1.1 Analyze the properties and toxicity of hydrofluoric acid.
2.0 Analyze and evaluate calcium gluconate and Hexafluorine to establish which is the preeminent treatment methodology.

Background and Significance

Hydrofluoric acid has been used in the industrial setting since the late seventeenth century when it was discovered that the acid had the ability to dissolve silica (Dowback, Rose, and Rohrich, 1994). The semiconductor industry has implemented HF into various processes including silicon dioxide wet etching, reaction chamber cleaning, and oxide etching. Hydrofluoric acid has become the most common burn-producing chemical in the semiconductor industry and its use in operational processes presents the industry with a unique chemical hazard (Edelman, 1986). The distinctive characteristics of HF make it highly toxic to humans. Exposures to the skin and eyes have been associated with severe symptoms such as eschar formation, liquefaction necrosis, and sloughing, which develop as a result of the hydrogen ion, and systemic fluoride poisoning or death due to the fluoride ion. (Upfal and Doyle, 1990).

A variety of treatment options have been utilized however the majority of them have proven to be ineffective (Mistry and Wainwright, 1992). Two treatment methodologies available today include calcium gluconate and a product called Hexafluorine. Calcium gluconate can be administered to an exposed employee in the form of a topical gel, injection, infusion, or eye drop solution and manages hydrofluoric acid burns by precipitating the fluoride ion in the form of an insoluble salt (Mistry and Wainwright, 1992). Hexafluorine is a first aid treatment that is used in aqueous form as a rinse or wash. This product has the ability to absorb the corrosive hydrogen ions and bind to the fluoride ion, which may eliminate the need for further medical treatment (Hall, Blomet, Gross, and Nehles, 1999).

When deciding which of these products to use, a semiconductor company must carefully consider their needs and look at the advantages and disadvantages of each. All aspects of each treatment methodology should be weighed however ultimately; the most efficacious treatment should be used. This paper focuses on the effectiveness and cost of each option in order to establish which is the preeminent treatment.

Limitations of the Study

This study was highly directed toward the semiconductor industry. Although hydrofluoric acid is utilized by other industries that may have benefited from the information contained in this paper, those industries were not researched in this study.

Definition of Terms

Cardiac Arrhythmia	Irregularity of the heartbeat.
Chemosis	Eye disorder marked by swelling of the conjunctiva around the cornea.
Conjuctival Inflammation	Inflammation of the thin transparent mucus that lines the inside of the eyelid and the exposed surface of the anterior sclera up to the border of the cornea.
Eschar	Scab or slough.
Erythema	Redness of the skin.
Hypocalcemia	Marked reduction of calcium in the blood.
Induration	The hardening of tissue.
Liquefaction Necrosis	Complete and rapid dissolution of cells by enzymes, forming circumscribed areas of softened tissue with semi-fluid exudates.
Sloughing	A mass of dead tissue separating from or being only partially attached to a living structure.
Subungual	Beneath the nail of a toe or finger.

**Terms taken from <u>Melloni's Illustrated Medical Dictionary</u>

Chapter II
Review of Literature

Introduction

The purpose of this study is to compare and contrast the effectiveness of calcium gluconate and Hexafluorine as treatments for hydrofluoric exposure. The literature review will explain the semiconductor processes that utilize hydrofluoric acid, HF toxicity, effectiveness of each treatment methodology, and provide comparisons and contrasts in order to establish a basis for the goals and objectives of this study.

Use of Hydrofluoric Acid in the Semiconductor Industry

The semiconductor industry has a variety of chemical processes that involve the use of hydrofluoric acid (HF). These processes include the silicon dioxide wet etching process, the removal of oxides from the silicon surface, and reaction chamber cleaning. In the silicon dioxide wet etching process, the silicon dioxide is thermally grown and then etched with HF. The hydrofluoric acid dissolves the silicon dioxide but does not attack the silicon. The etch rate of the acid is so fast however, that it needs to be mixed with water and ammonium fluoride in order to slow the process. The resulting compound, NH_4 – HF, is referred to as buffered oxide etch (BOE). The concentration of the BOE is adjusted as needed (VanZant, 1993).

Hydrofluoric acid is also utilized in the removal of oxides from the wafer. Oxide layers are grown in heated chemical baths after first being cleaned in 49% HF. The layers are thin but have proven to be sufficient in preventing the silicon surface from reacting during other processes. When it comes time for the oxide removal process, HF has been the chemical of choice. It is used in conjunction with water to form a solution of varying concentrations. The ratio of water to HF ranges from 100:1 to 10:7 depending on the thickness of the oxide layer (VanZant, 1993).

The reaction chamber is a component of the tube furnace system in which wafers are oxidized. It protects the wafers from being contaminated and functions to even out the temperature in the tubes of the system. The reaction chamber is commonly composed of high-purity quartz. Quartz is used because of its ability to withstand high temperatures and also because it is, for the most part, a clean substance. However, quartz tubes do require periodic cleaning. One method is to use hydrofluoric acid or a solution of water and HF. The acid cleans the tubes by removing a thin layer of the quartz and therefore, over time, the tubes are weakened by the HF cleaning process (VanZant, 1993).

Hydrofluoric acid is the most common burn-producing chemical in the semiconductor industry, and its use in operational processes presents the industry with a unique chemical hazard. The acid's distinctive characteristics are what make it so highly toxic to humans (Edelman, 1986). Maintenance employees and "chemical handlers" refilling reservoirs are most often at risk of being exposed to the higher concentrations of HF. However, all employees must be aware of the risks involved regardless of whether the acid is being used a 3% solution at an etch station or as a 50% solution in a quartz cleaning operation (Edelman, 1986).

Properties and Toxicity of Hydrofluoric Acid

Hydrofluoric acid, sometimes referred to as hydrogen fluoride, hydrofluoride, or monohydride, is the inorganic acid of elemental fluorine (Dowback, Rose, & Rohrich, 1994). The properties of HF can be found in Table I.

Table I

Properties of HF

Appearance	Indistinguishable from water at low concentrations; Fuming liquid at high concentrations
Odor	Pungent Odor at concentrations less than 1 ppm
Molecular Weight	20.01 daltons
Boiling Point	20 degrees Celsius
Vapor Pressure	400 mmHg
Vapor Density	0.7
Flammability	Nonflammable
Corrosiveness	Highly Corrosive

Hydrofluoric acid is commonly thought of as a strong acid however it is actually a very weak acid. It has a low dissociation constant (3.5×10^{-4}) resulting from the strong electronegativity of the fluoride ion. The fluoride ion, thus, does not readily dissociate from the hydrogen ion. This low ionicity makes HF lipophilic and highly permeable across membranes (Beiran, Miller, & Bentur, 1997). In this way, HF acts more like a base than an acid. This characteristic is why hydrofluoric acid causes significantly less surface damage following exposure than do hydrochloric and sulfuric acids (Mistry & Wainwright, 1992). However, even minor topical injury caused by the hydrogen ion alters the protective barrier enough to assist in the penetration of the fluoride ions into body tissues (Vance et. al., 1986). Once the fluoride ion is free, it seeks out calcium and magnesium and forms insoluble fluoride salts. This action lowers the calcium and magnesium content of cell membranes thus increasing permeability to potassium (Beiran et. al., 1997). The ionic shift due to potassium is responsible for the extreme pain associated with HF exposure (Mistry & Wainwright, 1992). As calcium is immobilized, the result is the formation of tissue abnormalities, cellular metabolism impairment, cell injury, and cell death with subsequent tissue necrosis (Vance et. al., 1986). If the fluoride ion is not fully bound in the superficial tissues it will progress and decalcify bone causing hypocalcemia, cardiac arrhythmia, and potentially death (Mistry & Wainwright, 1992).

Symptoms

Exposure to hydrofluoric acid can occur via inhalation, ingestion, or dermal contact. Most poisonings occur after HF comes into contact with the skin or eyes and is absorbed into the body (www.mednets.com). The extent of injury is dependent upon variables such as the concentration of the acid, the amount of HF involved, the condition of the skin or eyes, and the surface area involved (Upfal & Doyle, 1990). Hydrofluoric acid assumes the same mode of action for the eyes and skin however the resulting damage is unique to each organ and warrants discussion.

Cutaneous Exposure

Hydrofluoric acid burns to the skin usually exhibit a consistent pattern although brief contact with a high concentration of HF or exposure to low concentrations of the acid can cause the onset of symptoms to be delayed (Vance et. al., 1986). Exposure to HF solutions below 20% can be considerably painful however long-term morbidity is usually not a result (Upfal & Doyle, 1990). A delay of up to 24 hours before the onset of pain is not uncommon with solutions under 50 percent (Edelman, 1986). The associated pain has been described as “deep”, “throbbing”, “burning”, and “excruciating” (Vance et. al., 1986). Physical signs of swelling and erythema might be faint at this point. If erythema is present, it can be well demarcated and localized or diffuse. An area of induration has been observed in some cases and the skin may appear brown or black in color (Edelman, 1986). Blistering is uncommon, especially if the exposure is to the fingertips. Subungual exposure typically produces a gray, black, or bluish discoloration of the nail bed, which is a very important sign of a serious injury (Edelman, 1986). Concentrations of hydrofluoric acid above 50% are frequently associated with immediate pain. Exposed skin may take on a blanched appearance and feel leathery. It is common to see skin lines obliterated by edema fluid causing the area to be raised (Edelman, 1986). Eschar formation and lequefaction necrosis may also be seen along with tissue sloughing (Upfal and Doyle, 1990).

Ocular Exposure

The lipophilic characteristic of hydrofluoric acid allows it to deeply penetrate the cornea of the eye (Beiran et. al., 1997). The effects of the exposure are usually noted within one day although one case of corneal damage was reported to have been delayed until the fourth day after exposure (Upfal and Doyle, 1990). The symptoms of ocular exposure include conjunctival inflammation, corneal epithelial coagulation and sloughing, and chemosis. Later effects include the development of chronic conjunctival and corneal inflammation and scarring (Upfal and Doyle, 1990).

Treatment

Exposures to hydrofluoric acid need to be treated promptly in order to prevent systemic fluoride poisoning (Vance et. al., 1986). If left untreated, 7 milliliters of 99% HF could theoretically bind to all of the calcium in a 154-pound person (Mistry & Wainwright, 1992). In the case of 100% hydrofluoric acid, death has been a result of a burn to only 2.5% of the body surface area (Edelman, 1986). Historically, hydrofluoric acid burns have been treated using tannic acid, zinc oxide, silver nitrate, and steroids, however none of these methods are accepted today (Mistry & Wainwright, 1992). More recent methods have included benzalkonium chloride or benzithonium chloride, magnesium oxide, and sulfate ointments. These methods have also been unable to prove themselves effective in the binding of free fluoride ions (Mistry & Wainwright, 1992). Today, the preferred method of treatment in the United States for both cutaneous and ocular exposures is immediate irrigation with water for 15 to 20 minutes to wash away excess acid and to dilute the remaining HF. Calcium gluconate is used following this process to treat the exposed area. (Mistry & Wainwright, 1992). In Europe, particulary in France and Germany, a product called Hexafluorine is gaining popularity.

Treatment of Cutaneous Exposures With Calcium Gluconate

Calcium gluconate manages hydrofluoric acid burns by precipitating the fluoride in the form of an insoluble salt (Upfal & Doyle, 1990). Calcium gluconate is often administered to an exposed individual in one of, or a combination of, three ways: as a topical gel, as an injection, or intra-arterially (Mistry & Wainwright, 1992). Following a 15 to 20 minute water lavage, topical therapy should be initiated. Calcium gluconate gel consists of 2.5% calcium gluconate and a lubricant such as KY-jelly. The gel is easily applied to the affected area and is painless. The disadvantage to this gel is that it may have limited effectiveness in treating burns with delayed onset of symptoms, as its penetration might not be adequate to bind to fluoride ions deep in the tissues. Subcutaneous injections are often the next mode of action if pain persists for more than 45 minutes following exposure (Mistry & Wainwright, 1992).

Injections are typically 5% to 10% calcium gluconate and are administered with a small-gauge needle directly into and approximately 0.5 cm peripheral to the burn (Upfal & Doyle,1990). Anesthesia is commonly avoided; as pain is an indicator that more aggressive therapy is required (Mistry & Wainwright, 1992). The volume of calcium gluconate injections should be no more than 0.5 mL per square centimeter of tissue and for fingers, no more than 0.5 mL per digit. Injecting a larger volume could potentially cause local compartment syndrome (Upfal & Doyle, 1990). This could present difficulties as there may not be enough calcium to bind to all of the fluoride ions. For example, 0.5 mL of 10% calcium gluconate contains only 4.2 mg of elemental calcium. This amount has been calculated to neutralize only 0.025 mL of 20% hydrofluoric acid. Injections can also be painful, particularly in subungual exposures, as injections may have to be made directly into the nail bed. This is accomplished by either creating burr holes in the fingernails or by completely removing them. Injections can be repeated as needed to bind fluoride ions, treat pain, and limit tissue damage (Upfal & Doyle, 1990).

An alternative to subcutaneous calcium gluconate injections, especially useful in treating digital burns, are 4-hour, intra-arterial infusions through the radial or brachial artery. This method provides the best calcium delivery and eliminates the need for fingernail removal. It also reduces the probability of subsequent skin grafting. Risks involved with intra-arterial infusion of calcium gluconate include arterial spasm and local bleeding. Therefore, this treatment method is reserved for severe digital burns (Upfal & Doyle, 1990).

Case Studies - Calcium Gluconate

Various case histories and studies have indicated that calcium gluconate is an effective treatment for dermal hydrofluoric acid burns. In July of 1980, a man entered the Royal Brisbane Hospital complaining of pain in his right hand. It was learned that he had been working with 50% hydrofluoric acid for approximately 12 hours prior to his presentation at the hospital. Two hours after his arrival, rinsing with copious amounts of water and application of topical treatments were not successful in alleviating his pain. At this time he was complaining of pain in the palm of his hand and under his nailbeds. He was in distress and suffering erythema and oedema of his hand. He was treated by inta-arterial infusion of 30 mL of 10% calcium gluconate, which resulted in immediate relief of pain. After complaining of residual pain in his fingertips, he was injected with 10% calcium gluconate subcutaneously and his nails were removed to allow infiltration of the nail bed. Twenty-four hours later, he again complained of pain in his fingertips and was given two additional injections of calcium gluconate. He received one more injection on the following day. An X-ray examination of his hand showed no atopic calcification and normal bone consistency. He was discharged from the hospital 4 days later and gained full recovery of his hand (Pegg, Siu, & Gillett, 1985).

Between January 1997 and December 1999, 10 patients were admitted to Kaohsiung Medical University Hospital in Taiwan with hydrofluoric acid dermal burns. The burns were to the digits and were caused by variable concentrations of the acid. They were treated using intra-arterial infusions of 10% calcium gluconate with the infusion rate set at 10 mL per 12-hour periods. This was adjusted based on subjective reports of pain. The patients' heart rate, blood pressure, and electrocardiograph were monitored. Pain relief was almost immediate after infusion and none of the patients received pain medications. The average delay between HF dermal burns and treatment was13.5 hours, the average infusion time was 39 hours and the total infusion dose 18.3 mL. The average healing time of the digits was 5.8 days. No major complications were noted and all of the exposed digits were completely functional and had good cosmetic appearance following treatment (Lin, Tsai, Lin & Lai, 2000).

In another study, 48 of 53 patients with hydrofluoric acid burns were successfully treated with calcium gluconate gel alone while the remaining 5 patients responded to gel followed by calcium gluconate injections. There were no complications noted (Mistry & Wainwright, 1992).

Mistry and Wainwright also describe a case of a laboratory technician who handled hydrofluoric acid of an unknown concentration at work and developed intense pain at the tip of her finger. She sought medical attention and was prescribed topical calcium gluconate. Her pain was still severe after 12 hours and she again sought attention at an emergency department. A gray area of skin, 1 cm in diameter, was noted at the tip of her right index finger. There was evidence of extension under the fingernail. The distal half of the nail was removed and the nail bed was irrigated with water. The patient spent one night in the hospital so that 2.5% calcium gluconate gel could be applied every four hours until the pain ceased. The burn to the finger healed and there were no deformities upon re-growth of the fingernail (1992).

In 1987, a 26-year-old male enter a hospital suffering from an exposure to 25% hydrofluoric acid. He was treated with ice-water packs to his fingers and hands. They were also soaked in a saline/calcium gluconate solution. This treatment was not successful in relieving his pain, and visible blistering and discoloration became apparent. He was transferred to the intensive care unit where he received 10% calcium gluconate through the brachial artery. This relieved his pain temporarily however; residual pain began to occur about 2 hours after the infusion. At that time, another infusion was administered and pain did not recur during the remainder of his hospital stay. On the fourth day following exposure and subsequent treatment, there was a large blister containing a thick, yellow exudate, which was surrounded by an area of erythema. There was also a small black area in the nail bed surrounded by an area of coagulation. By day 7, there was noticeable improvement, and by day 10, there was complete healing of the burned areas including the nail bed. At this time, the patient was discharged from the hospital and suffered no further adverse effects (Edinburg, M. and Swift, R., 1988).

Treatment of Ocular Exposures With Calcium Gluconate

Upon ocular exposure to hydrofluoric acid, water should be used to irrigate the eyes for a minimum of 15 minutes. The exposed individual should then be brought to medical attention for further treatment, including additional water irrigation and the administering of 1% calcium gluconate solution (Upfal & Doyle, 1990).

Case Studies - Calcium Gluconate

Beiran, Miller, and Bentur carried out a study on rabbit eyes to determine the efficacy of calcium gluconate in ocular hydrofluoric acid burns. One eye of each rabbit was exposed to 0.05 mL of 2% hydrofluoric after they had been anaesthetized. One minute after the introduction of the HF, they underwent treatment with 500 mL normal saline, 1% calcium gluconate eyedrops, and additional or substitute methods in some cases. The study indicated that 1% calcium gluconate, administered as drops, might be advantageous over alternative therapies but that subconjunctival injections have a possible adverse effect (1997).

A clinical report explained by Beiran, Miller, and Bentur documented 1% calcium gluconate drops as a treatment for ocular HF burns in humans. A patient was treated with the drops for 5 days and in a follow-up two months later was still suffering from visual impairment (1997).

Treatment of Cutaneous Exposures With Hexafluorine

While rinsing with water only washes away hydrofluoric acid on the surface of skin, the product called Hexafluorine, manufactured by Laboratoire PREVOR in France, rinses and absorbs HF simultaneously. Hexafluorine is able absorb the corrosive hydrogen ions and bind to fluoride ions using its hypertonicity and chelating properties. It has greater chemical bond energy for HF than do skin tissue receptors therefore rinsing with the product immediately following exposure may eliminate the need for further treatment. The amount of Hexafluorine used depends on the duration of contact and the extent of surface area involved. Hexafluorine showers in 5-liter volumes can be used to decontaminate skin within 2 minutes following exposure (Hall, Blomet, Gross & Nehles, 1999).

Case Studies - Hexafluorine

Case histories and studies in Europe have indicated that Hexafluorine is effective in hydrofluoric acid burn treatment. During the 4-year period between 1994 and 1998, 11 workers sustained splashes from hydrofluoric acid. Six of these burns involved 6% HF/15% HNO_3 and 5 involved 40% HF. Exposed areas included the face, eyes, upper and lower extremities, hands and thorax. All patients were decontaminated with Hexafluorine and no chemical burns or adverse effects were noted in any of the workers. None of them had any lost work time (Hall et. al., 1999)

Three cases of workers who were treated with Hexafluorine following hydrofluoric acid exposure have been reported to Labortoire PREVOR. All of the exposures involved 20% HF splashes to the skin. The surface area involved was less than 5% of total body surface area in all instances. The workers were decontaminated with Hexafluorine and no burns developed (Josset, Blomet, Lym, Jahan & Meyer, 1992).

Hall et. al. discuss another case report in which a worker fell into a bath containing 1,505 liters of water, 30 liters of hydrochloric acid and 233 liters of 59% HF. His entire body and head were immersed in the solution. He was decontaminated with Hexafluorine and also used water to rinse his eyes. He developed minor burns on his back and stomach. Although there was a corneal burn to the left eye, the right eye sustained no damage (1999).

Between 1998-1999, there were 16 ocular and cutaneous incidents involving HF. Two of the splashes involved 70% HF and the others a mixture of hydrofluoric acid and nitric acid at a pH of 1. The splashes were all rinsed with Hexafluorine and rinsing began within 1 minute of exposure for 75% of the cases. Three splashes were rinsed after an hour of contact. All of the exposed individuals had immediate pain relief during or following the rinsing. 60% of the workers were sent to the hospital for follow-up medical examinations but none suffered any damage. One of the ocular splashes suffered residual pain and one had some blisters on the outside of the eyelid the day after treatment. There were no sequelae in the majority of the cases and no secondary care was needed for any of the individuals. The average number of days away from work was 0.9 days (Barbe, J., Blomet, J. and Mathieu, L., 2000).

Treatment of Ocular Exposures With Hexafluorine

As demonstrated in the previous case studies, Hexaflourine can be used for the eyes in the same manner it is used for dermal exposures. For ocular exposures, applying 500 mL of the product within 2 minutes following exposure has proven to be effective (Hall et. al., 1999).

Case Studies - Hexafluorine

Various case studies have supported the efficacy of Hexafluorine in ocular hydrofluoric acid burn treatment. In July of 1995, a worker sustained a splash of 38% HF to the eye from a defective pipe. He rinsed his eye with Hexafluorine, sustained no injury, and returned to work the following day (Siewe, Nehles, Blomet & Gross, 1998).

A worker in 1995 sustained an ocular and dermal exposure involving 40% hydrofluoric acid. His clothes were saturated with HF. The clothes were torn from his body and coworkers rinsed him with Hexafluorine. His eyes were rinsed one more time with the product and he was taken to the hospital where he was examined. No damage was found and he returned to work the following day (Siewe et. al., 1998).

Comparison of Calcium Gluconate and Hexafluorine

An in vitro study was carried out to simulate decontamination effects without flushing. Ten milliliters of 0.1 Normal hydrofluoric acid (0.2%) was placed into a beaker, and water along with either 10% calcium gluconate or Hexafluorine were added. The pH and pF were subsequently measured. It was concluded that water had very little effect on either variable. It was also discovered that Hexafluorine bound the hydrogen ion 100 times greater than calcium gluconate. The final pH value with Hexafluorine was 6.5 while it was 4.5 with calcium gluconate. The causticity limit of the hydrogen ion is a pH value of 5.5 indicating that despite the use of calcium gluconate, a caustic injury still may occur. The final pF value with calcium gluconate was 3.0 versus 6.0 for Hexafluorine. The toxicity limit is a pF value less than 5.0. The results then indicate that although fluoride tissue toxicity should not occur following the use of Hexafluorine, it may occur despite the use of calcium gluconate (Hall et. al. 1999).

In a recent animal study, 120 New Zealand albino rabbits were separated into 6 groups and exposed to 70% hydrofluoric acid. The exposure was carried out by applying a piece of filter paper, saturated in HF, to a surface area of less than 1% of the body. After the exposure, the areas were flushed with water for 5 minutes followed by an application of 2.5% calcium gluconate gel, or decontamination with Hexafluorine for 3 minutes at a rate of 0.2 liters per minute. Observations were made at 10 minutes, 1 hour, 2 hours, and every 24 hours for 6 days. At 10 minutes, 1 hour, and 2 hours, no burns were visible on the rabbits treated with calcium gluconate. However, burns were visible on the first and second days and were severe on the third through sixth days. The rabbits irrigated with Hexafluorine showed no burns at any time during the study (Hall et. al. 1999).

Another animal study was conducted using 62 adult male Charles River Wistar rats. They were divided into groups of 20 animals and the remaining 2 were used as unexposed controls. All of the rats and burns induced by application of a 1 centimeter square piece of filter paper saturated with 70% hydrofluoric acid to the skin. The three groups were then treated using 3 different methods: water irrigation alone, water irrigation plus calcium gluconate inunction, and rinsing with Hexafluorine. Serum calcium levels were measured to determine if hypocalcemia occurred and if there were differences in patterns over time in the animals undergoing the different methods of treatment. With the water irrigation alone and water irrigation plus calcium gluconate inunction, hypocalcemia was present from 10 minutes to 4 hours following exposure. Over a five-day period, the serum calcium levels returned to normal. With Hexafluorine irrigation, the pronounced calcium deficiency was not seen at the four-hour mark as it was in the first two animal groups. At the five-day mark, levels were similar to control values (Blomet, J., Gross, M., Hall, A., Nehles, J., 1999).

Summary

This literature review presented information regarding the hazards associated with hydrofluoric acid use and described the effectiveness of the treatment methodologies in question. Comparisons were made between calcium gluconate and Hexafluorine with respect to application, mode of action, and effectiveness. This data is essential in providing a basis for even further comparison of these two products in Chapter 4.

Chapter III
Methodology

This chapter will outline the methods used for research in this study. Information was gained through a review of professional literature and was also obtained via vendors and manufacturers. The process that follows was used in gathering data relevant to the purpose and objectives of this study:

1.0 A literature search and review of hydrofluoric acid use in the semiconductor industry and the hazards associated with its use.

2.0 Research of professional literature to determine:

- Use and effectiveness of calcium gluconate as treatment following HF exposure through analysis of case studies
- Benefits and/or adverse effects of calcium gluconate

3.0 Research of professional literature to determine:

- Use and effectiveness of Hexafluorine as treatment following HF exposure through analysis of case studies
- Benefits and/or adverse effects of Hexafluorine

4.0 Obtain information from vendors and manufacturers via phone, company literature, and case studies to assist in establishing which is the preeminent treatment.

5.0 Use information gained from literature review to compare and contrast the above treatments in the areas of effectiveness, benefits and/or adverse effects, and cost.

Chapter IV
The Study

The purpose of this study is to compare and contrast calcium gluconate and Hexafluorine as treatments for hydrofluoric acid exposure. Information on the characteristics, effectiveness, availability, and cost of each option is formatted to provide a clear understanding of the differences between the treatment methodologies.

Efficacy of Calcium Gluconate

Data has shown that calcium gluconate is an effective treatment for hydrofluoric acid exposure. In most cases, individuals who sustain an exposure to HF have full recovery of the affected areas following treatment. However, calcium gluconate has a limited ability to neutralize hydrogen ions and thus allows for initial and secondary caustic burns of the exposed area. Calcium gluconate gel is very easy to use, but has limited efficacy, as it cannot bind to fluoride ions that have penetrated deep into the body tissues. It is also common for the gel to have to be repeatedly applied for a period of days or sometimes weeks, and it is often necessary to follow its application with injections or intra-arterial infusions. Injections of calcium gluconate are effective but can be painful considering fingernails may need to be removed, and the calcium gluconate itself can burn upon entering the body. Intra-arterial infusions of calcium gluconate have proven to be effective as well, however the treatment is invasive and sometimes results in adverse effects such as arterial spasm and local bleeding. In addition, calcium gluconate has limited effectiveness as a treatment for ocular exposure and can actually produce a toxic effect if injected into the eye.

Availability of Calcium Gluconate

Since its approval by the Food and Drug Administration, calcium gluconate has become the standard treatment for hydrofluoric acid burns in the United States. Calcium gluconate can be purchased through a variety of vendors however; Pharmascience Inc. in Quebec, Canada is the main supplier (Segal, E., 2000). A semiconductor company also has the option of mixing their own solutions. Topical gel (2.5% calcium gluconate) can be produced by mixing one 10-mL ampule (10%) per 1 ounce of K-Y Lubricating Jelly, and eye wash solutions can be made by mixing one 10-mL ampule (10%) per 90 mL of saline to get a 1% calcium gluconate solution. The shelf life for these mixtures has not been determined and it is recommended that they be replaced after a 6-month period.

Cost of Calcium Gluconate

Semiconductor companies can save on cost if they choose to mix their own calcium gluconate solutions, however many companies opt to buy from a vendor. Calcium gluconate gel is available through Pharmascience Inc. at a cost of $264.60 for 12, 25-g tubes plus an additional charge of 5% for shipping and handling. Quantities of 6 are available for $165.30. The 10% calcium gluconate solution used for injections and intra-arterial infusions can be found at some hospital pharmacies for a cost of $5.89 per 10-mL. The cost of calcium gluconate appears to be low however in the unlikely event that an exposure to hydrofluoric acid should occur, this cost could become much higher. In some cases, calcium gluconate gel has proven to be sufficient to stop damages from HF, however in many cases, additional treatment at a medical facility is necessary. As noted in Chapter II case studies, hospital visits can last anywhere from hours to days. An overnight stay in one hospital was reported to be $868 per night not including anything additional, such as cost of medications and treatment. In addition to this cost is the employee's paid time away from work. According to Francisco Moris (2000), the average wage for a semiconductor production worker in 1995 was $14.59 per hour. It should be mentioned that as an employer, you are expected to pay 100% medical and disability benefits which vary in accordance with the injury. When a semiconductor company adds up the costs, they may find that treatment of a severe HF exposure with calcium gluconate could end up costing upwards of $1,000 per day for the duration of the treatment.

Efficacy of Hexafluorine

The information collected through various studies indicates that Hexafluorine is also an effective treatment for hydrofluoric acid exposures. Hexafluorine is used as an aqueous wash and is equally effective for both the skin and eyes. This product has the ability to bind both the hydrogen and fluoride ions preventing both caustic burns and systemic fluoride poisoning. The manufacturer recommends that Hexafluorine be utilized immediately, within 2 minutes, after exposure. Hexafluorine replaces the need for initial rinsing with water, which is why this window of time is so small. If used within this time frame, this product has shown that it has the ability to prevent all adverse effects. If Hexafluorine were to be utilized, say after 1 hour, it would be effective in treating any further damage but would not correct the damages that have already occurred. There has not been an observed secondary burn as of today following decontamination with this product and additional treatment is rarely necessary.

Availability of Hexafluorine

Hexafluorine is available in all of Europe and is being extensively used in France and Germany. It is also available in Taiwan and China, however it is not yet available in Japan due to customs issues. Hexafluorine is available in the United States as a 5L volume portable shower, which is to be used as a decontaminant for skin exposures but not as an eyewash solution. The FDA has not yet approved the use of Hexafluorine as first aid for the eyes, as this type of use would be considered medical rather than cosmetic in nature. Laboratoire PREVOR, the manufacturer of Hexafluorine, has a vendor in the United States called Safe Stride, which is located in Washington State. It should also be noted that Hexafluorine has a shelf life of 2 years.

Cost of Hexafluorine

There are very few semiconductor companies utilizing Hexafluorine in the United States, although there are several semiconductor equipment manufacturers that do use the product. This could be in part due to lack of knowledge or possibly because it is only available in the 5L volume shower. Most semiconductor companies deal with hydrofluoric acid exposures small enough that this large quantity would not be required. The cost of Hexafluorine is $1,620 per 5 liters, which initially is much higher than the cost of calcium gluconate solutions. However, decontamination of a hydrofluoric acid exposure with Hexafluorine can eliminate the need for additional medical treatment keeping additional costs at a minimum. Although exposed individuals are often sent for a medical evaluation following a rinsing with Hexafluorine, they often sustain no damages and do not require a hospital stay or an extended period of time away from work.

Therefore, the cost of Hexafluorine should be viewed as the cost of conformance versus that of non-conformance, as the cost of non-conformance is a sunk cost; there is no return on your investment.

Table II
Comparison of Calcium Gluconate and Hexafluorine

	Calcium Gluconate	**Hexafluorine**
Application	Gel, Injection, Intra-arterial Infusion following water lavage.	Used in aqueous form as a rinsing solution.
Mode of Action	Binds to fluoride ion forming insoluble fluoride salt.	Binds to both the hydrogen and fluoride ions.
Efficacy	Limited ability to bind to hydrogen ion. Usually results in full recovery following cutaneous exposure. Limited efficacy when used to treat ocular exposures.	Equally effective for cutaneous and ocular exposures. No secondary burns have been reported following its use.
Availability	Widely available in the United States.	Available in the United States through a vendor in the state of Washington.
	Main supplier located in Quebec Canada.	
Cost	Varies; Company can manufacture their own to reduce initial cost. Costs associated with secondary medical treatment can be substantial.	5-Liter shower- $1,620. Costs associated with secondary medical treatment commonly eliminated.
FDA Approval	Yes	Approved as a decontaminant for the skin Not approved as an eyewash solution.
Shelf-Life	6 months	1.5 Years

Summary

Chapter IV supplied information as to the effectiveness, availability, and cost of both calcium gluconate and Hexafluorine. The comparisons drawn in this chapter are the basis from which conclusions can be made regarding both treatment methodologies.

Chapter V
Conclusions and Recommendations

Introduction

The purpose of this study was to compare and contrast calcium gluconate and Hexafluorine as treatments for hydrofluoric acid exposure. Chapters two and four examined the efficacy, availability, and cost of each treatment methodology. To fulfill the purpose of the study, objectives were set and achieved.

Specific objectives of the study were:

3.0 Examine processes in the semiconductor industry that utilize hydrofluoric acid.
    3.1 Analyze the properties and toxicity of hydrofluoric acid.
4.0 Analyze and evaluate calcium gluconate and Hexafluorine to establish which is the preeminent treatment methodology.

Conclusion

The conclusions of this study are based on information gathered from vendors, manufacturers, and the literature review. They are drawn from comparisons made in Chapter IV and are organized according to the corresponding goals. The first objective of the study was to examine processes in the semiconductor industry that utilize hydrofluoric acid. This included doing an analysis of the properties and toxicity of HF. Semiconductor companies utilize hydrofluoric acid in several processes including silicon dioxide wet etching, reaction chamber cleaning, and the removal of oxides from silicon surfaces. This wide use of HF has facilitated it becoming the most common burn-producing chemical in the industry. Hydrofluoric acid possesses unique properties that make it very toxic to humans. HF has a low dissociation constant thus making it highly lipophilic. Once absorbed into the body, the hydrogen and fluoride ions separate. The hydrogen ion is then free to cause a secondary burn, which includes symptoms such as eschar formation, liquefaction necrosis and sloughing. The fluoride ion seeks out calcium in the body, which can lead to hypocalcemia and death. The severity of the symptoms associated with hydrofluoric acid exposure indicate that immediate treatment is imperative.

The second objective was to analyze and evaluate calcium gluconate and Hexafluorine to establish which is the preeminent treatment. Both treatment methodologies researched have proven to be effective treatments following exposure to this chemical. Calcium gluconate has the ability to bind to the fluoride ion thus preventing systemic poisoning however; it has limited efficacy in binding the hydrogen ion and therefore allows for secondary caustic burns. In addition, there is debate as to whether it is effective as a treatment for ocular exposures. It has become the standard treatment for hydrofluoric acid burns in the United States since its approval by the Food and Drug Administration. Semiconductor companies have the option of producing their own calcium gluconate gel and solutions, or purchasing it from a vendor. The initial cost of calcium gluconate is low however; case studies show that hydrofluoric acid exposures treated with this product commonly require secondary treatment at a medical facility increasing cost tremendously.

Hexafluorine has the ability to bind both the hydrogen and fluoride ions preventing both caustic burns and systemic fluoride poisoning. There has not been an observed secondary burn as of today following decontamination with this product and secondary treatments are rarely necessary. The FDA has approved Hexafluorine in the United States as a skin decontaminant but it has not been approved as an eyewash solution. Therefore, semiconductor companies in the U.S. can purchase Hexafluorine in the 5-Liter volume but not in the smaller volume that would be used for rinsing the eyes. Although the initial cost of Hexafluorine is much higher than calcium gluconate, the costs associated with secondary treatment, which can be substantial, are commonly eliminated following treatment with this product.

Although availability and cost of each product are aspects that semiconductor companies may consider; when dealing with an exposure of such severity it is important that the most efficacious treatment be used. The information gathered in this study shows that Hexafluorine is the most efficacious treatment for hydrofluoric acid exposures.

Recommendations

When dealing with a chemical as hazardous as hydrofluoric acid, it is important that semiconductor companies have stringent engineering and administrative controls in place to control the associated risks. Although prevention is the best treatment, in the event of an exposure to HF immediate treatment with the most efficacious treatment available is imperative.

Hexafluorine has proven to be the preeminent HF treatment methodology available at the present time. Although it has been approved in the U.S. as a decontaminant for the skin, it is recommended that the Food and Drug Administration further examine all information available on this product and consider approving Hexafluorine as a decontaminant for the eyes as well.

It is also recommended that all semiconductor companies that utilize hydrofluoric acid have Hexafluorine available for immediate decontamination of cutaneous exposures at their facilities. Calcium gluconate solution (1%) should be available for exposures sustained to the eyes, as Hexafluorine has not yet been approved as a treatment for ocular exposures. Cutaneous exposures associated with small volumes and low concentrations of hydrofluoric acid may also be successfully treated using calcium gluconate. Calcium gluconate gel might also be applied following decontamination with Hexafluorine to ensure optimal results.

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