Experimental evaluation of chemical burns and their decontamination:

the case of sulphuric acid

- Laurence Mathieu[1], Céline Fosse[1], Hervé Coudouel[1], Alan Hall[2,3], Joël Blomet[1]

1 Prevor Laboratory, Valmondois, France,

2 Dept. of Preventive and Biometric Medicine, Univ. of Colorado Health Sciences Center, Denver, CO, USA, 3Service of Medical Translation and Toxicological Consulting Inc., Laramie, WY, USA

- Elian Lati, Laurent Peno Mazzarino, M. P. Gasser, D. Bouzoud

BIO-EC Laboratory, Longjumeau, France

Mechanism of the chemical burn

- Chemical burns are the result of the action of corrosive and irritant products on the components on the skin and the eye.

- The severity of the chemical burn is due to:
  - The nature and the concentration of the chemical agent,
  - The energy of the reaction,
  - The time of contact.

- And also depends on:
  - Physical parameters such as temperature and pressure,
  - Surface of the affected area,
  - Quality of the tissues, damaged or not.

What is the chemical risk in the world and in Europe?

- **49.375.672** organic and inorganic substances[i].
  - Registered in the Chemical Abstract Service (data 08/13/09)
- About **600,000** are commonly used by industries.
- Several thousand new molecules are created each year by research.
- More than **25,000** irritant and corrosive chemicals have been identified as having the potential to cause burns[ii].
- In Europe[iii], **104.031** commercial chemical substances have been recognized and numbered
  - 100.204 under EINECS (European INventory of Existing Commercial chemical Substances)
  - 4.381 under ELINCS Information System (European LIst of Notified Chemical Substances)
  - **1.261** chemical substances can be identified as irritant or corrosive with Xi et C risk sentences.

[ii] www.cas.org

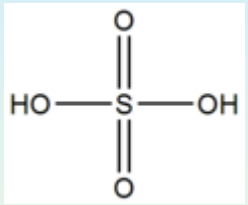
[ii] *Liao C-C, Rossignol AM. (2000). 'Landmarks in burn prevention'. Burns, Vol.26, pp.422-434.*

[iii] *http://ecb.jrc.ec.europa.eu/esis/index.php?PGM=cla*

Sulphuric acid H_2SO_4

- can induce severe burns for a concentration ≤ 15% [i] because
  - Strong corrosive and diacid
    - When used concentrated (about 95%), concentration is 18 M = 36 N
  - Can induce associated thermal burn due to heat release
- **It is widely used in industry**
  - approximately 150, 000, 000 tonnes a year worldwide
- It is also often used as a weapon[ii] in violence to women.
- Even it is widely used, few experimental studies and reviews have been performed to understand its mechanism.

CAS n°7664-93-9



Sulphuric acid can release 2 H^+ ions successively in an aqueous solution:

$$H_2SO_4 + H_2O \longrightarrow H_3O^+ + HSO_4^- \qquad pK_1 = -2$$

$$HSO_4^- + H_2O \rightleftharpoons H_3O^+ + SO_4^{2-} \qquad pK_1 = 2$$

In contact with water, sulphur trioxide produces sulphuric acid with heat release:

$$SO_3 + H_2O \xrightleftharpoons{88\ kJ} H_2SO_4$$

[i] *Flamminger A, Maibach H. (2006) 'Sulfuric Acid Burns (corrosion and acute irritation): evidence-based overview to management', Cutaneous and Ocular Toxicology, Vol. 25, pp.55-61*

[ii] *www.acidsurvivors.org/*

Burns induced by sulfuric acid

- When concentrated, the pain is immediate.
  - On the skin, necrosis is rapid with an appearance of dark brown color. There is a risk of side effects such as retractile fibrosis and /or keloid scarring.
  - In the eyes, the cornea becomes opaque. There is a risk of ocular perforation and loss of visual acuity.
  - In the event of inhalation, there is a risk of acute, more or less delayed lung edema.

Flamminger A, Maibach HI 2006, 'Cut and Ocul Tox, vol. 25, pp.55-61

Milton R, Mathieu L, Hall AH, Maibach HI, Accepted in Burns

Human skin explant model

Objectives of the model :

- to highlight the extent of epidermal and dermal lesions following contact with a strong corrosive on living explants of human skin,

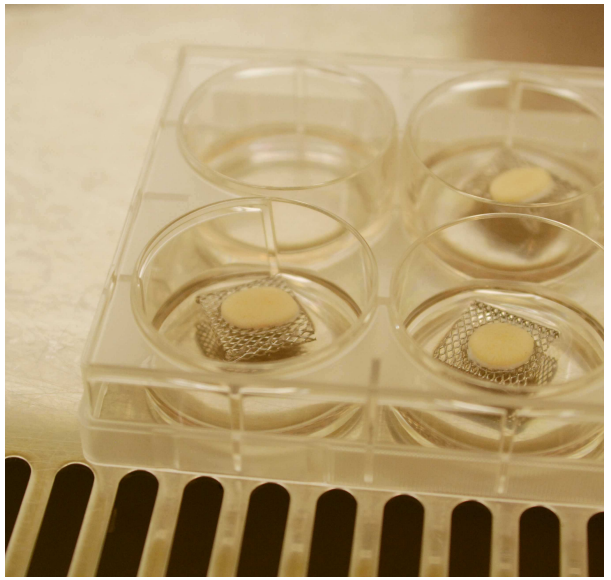
- to compare the efficacy of different decontamination solutions.

Advantages of the model:

- **no need of pre treatment of the skin (shaving,etc)**
- **a lot of spots of burns with a small skin surface**
  - **obtained from abdominoplasty**
- **a medium culture that can keep explants alive for 11 days**

Mathieu L, Burgher F, Hall AH, Maibach HI, to be published

Diffusion of sulphuric acid through the skin: Material and method



- **Tested substance**
- 95% sulphuric acid (RECTAPUR Ref. 20692).

- **Application of sulphuric acid**
- By deposit of 30 µl soaked on a disk of filter paper of 1 cm in diameter.

- **Preparation of the explants**
- 39 explants, with a diameter of 1 cm, have been prepared from an abdominoplasty of a woman (57 years old) (reference P673).
- Explants were put in survival in a BEM medium of BIO-EC at 37℃ in a wet atmosphere, enriched by 5 % of CO_2.

- **These explants were distributed in 3 groups of 2 explants in duplicate and another non treated explant at T0:**
  - **Blank group (unexposed to H_2SO_4) at T0, 24h, 48h, 6 and 11 days.**
  - **Explants + H_2SO_4 exposed and observed after during 25s, 40 s, 1 min, 2 min, 3 min, 4 h, 5 h, 6 h, 7 h, 8 h, 9 h, 10 h, 24 h, 48 h.**
  - **Explants + H_2SO_4 applied during only 25 s, then in survival during 48 h, 6 and 11 days.**

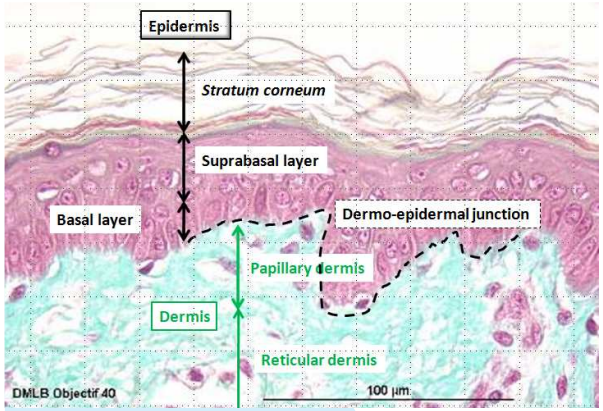
- **Sampling for histology**
- At each time of survival, the 2 explants of each group are sampled and fixed in an ordinary Bouin solution.

Results

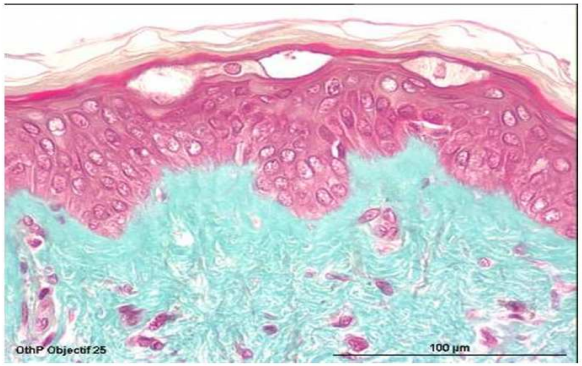
In these experimental conditions,

- There are **no change in the controlled group**.
- there are **marked lesions in the epidermis with marked alterations of cellular structures at 25 seconds**.
- **At 3 minutes, marked alterations of cellular structures** in the **papillary dermis**.
- **After 4 hours of contact until 48h**, H_2SO_4 induces **marked alterations in the papillary and superior reticular dermis**.
- The application of **95% H2SO4 during 25 seconds** on explants maintained alive during 11 days shows **marked alterations in the epidermis without signs of epidermal reconstruction**.

Results of histology



Normal (unexposed) skin



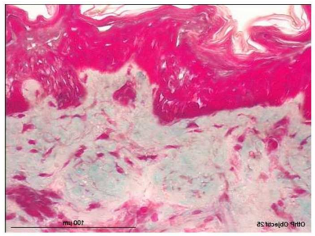
Sulphuric acid after 3 min

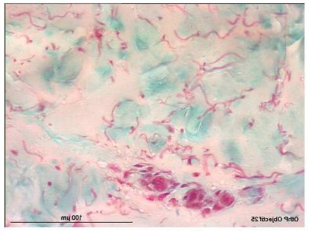
- **In the epidermis, strong alterations.**
- **In the papillary dermis, beginning of hyalinisation** near the dermo-epidermic junction. The cellular structures present a morphology sharply altered with sharply acidophilic cytoplasm and piknotic nuclei.

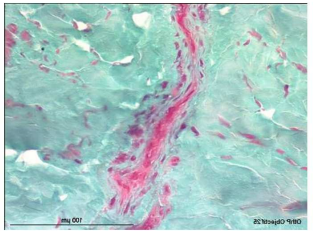
AIOH Canberra December 2009

Sulphuric acid after 25s

- **In the epidermis, strong alterations**, acantolysis with bubles, nuclear and cytoplasmic lysis of the keratinocytes with acidophilic cytoplasm.
- **In the papillary dermis, weak alteration** with a lightly acidophilic cytoplasm.







Sulphuric acid after 4h

- **In the epidermis, strong alterations.**
- **In the papillary dermis, clear hyalinisation** with very marked alteration of cell structures.
- **In the superior reticular dermis, clear hyalinisation** with very acidophilic cells.
- In the inferior reticular dermis, cell structures are moderately acidophilic.

		Epidermis	Papillary dermis		Superior reticular dermis		Inferior reticular dermis	
Group	Time of observation	Cellular structures	Hyalinized collagen	Cellular structures	Hyalinized collagen	Cellular structures	Hyalinized collagen	Cellular structures
Control	0 sec	-	-	-	-	-	-	-
Burn	25 sec	++	-	+	-	-	-	-
Burn	40 sec	+++	-	++	-	-	-	-
Burn	1 min	+++	-	++	-	-	-	-
Burn	2 min	+++	-	++	-	-	-	-
Burn	3 min	+++	+	+++	-	-	-	-
Burn	4 h	++++	+++	+++	+++	+++	-	++
Burn	5 h	++++	+++	+++	+++	+++	-	++
Burn	6 h	++++	+++	+++	+++	+++	-	++
Burn	7h	++++	+++	+++	+	++	-	+
Burn	8 h	++++	+++	+++	++	++	-	+
Burn	9 h	++++	+++	+++	++	+++	+	++
Burn	10 h	++++	+++	+++	+	+++	-	++
Control	24 h	-	-	-	-	-	-	-
Burn	24 h	++++	+++	+++	+++	+++	-	+
Control	48 h	-	-	-	-	-	-	-
Burn	48 h	++++	+++	+++	++	+	+	+
Healing	48 h	+++	-	++	-	-	-	-
Control	6 J	-	-	-	-	-	-	-
Healing	6 J	+++	-	++	-	-	-	-
Control	11J	-	-	-	-	-	-	-
Healing	11J	+++	-	+	-	-	-	-

Conclusion H_2SO_4

- The model of human skin explant is reproducible.
- After 25 seconds, the burn has already appeared.
  - The washing must be performed within the first minute.
- The burn affects the upper dermis within 3 minutes.
- There is a delay of some hours before burn appearance in the deep dermis.
- There is no spontaneous healing with only a 25 s contact.
  - This can explain the bad scarring process due to H_2SO_4
- We need to decrease time of contact with sulphuric acid, about 20 s, in order to evaluate decontamination solutions.

What do we know about decontamination?

- Need for external decontamination and dilution
  - Can be obtained with water washing
- Need to avoid or decrease penetration of eyes/skin
  - Can be obtained with hyperosmolar solution
- Need for « soft neutralization » of the acid
  - Can be obtained with amphoteric agents

Hall AH, Maibach HI 2006, Cut and Ocul Toxicol, vol. 25 no.2, pp.67-83.

What do we know about Diphotérine®?

- **Effective decontamination within the first minute**
- **Advantages to be used even as a secondary decontamination**

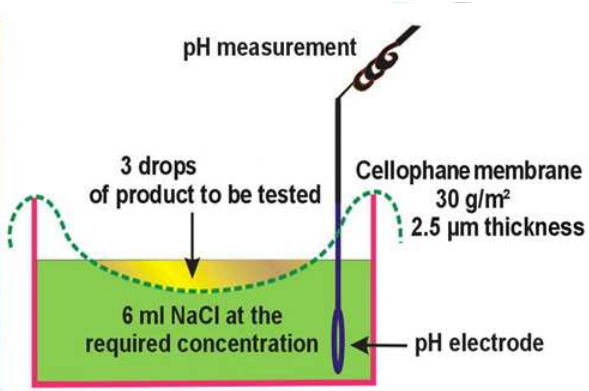
- **How long will the decontamination be effective?**

Hall AH, Blomet J, Mathieu L 2002 Vet Human Toxicol 44(4) 228-231

Nehles J, Hall AH, Blomet J, Mathieu L, 2006 Cut and Ocul Toxicol, 25, 249-258

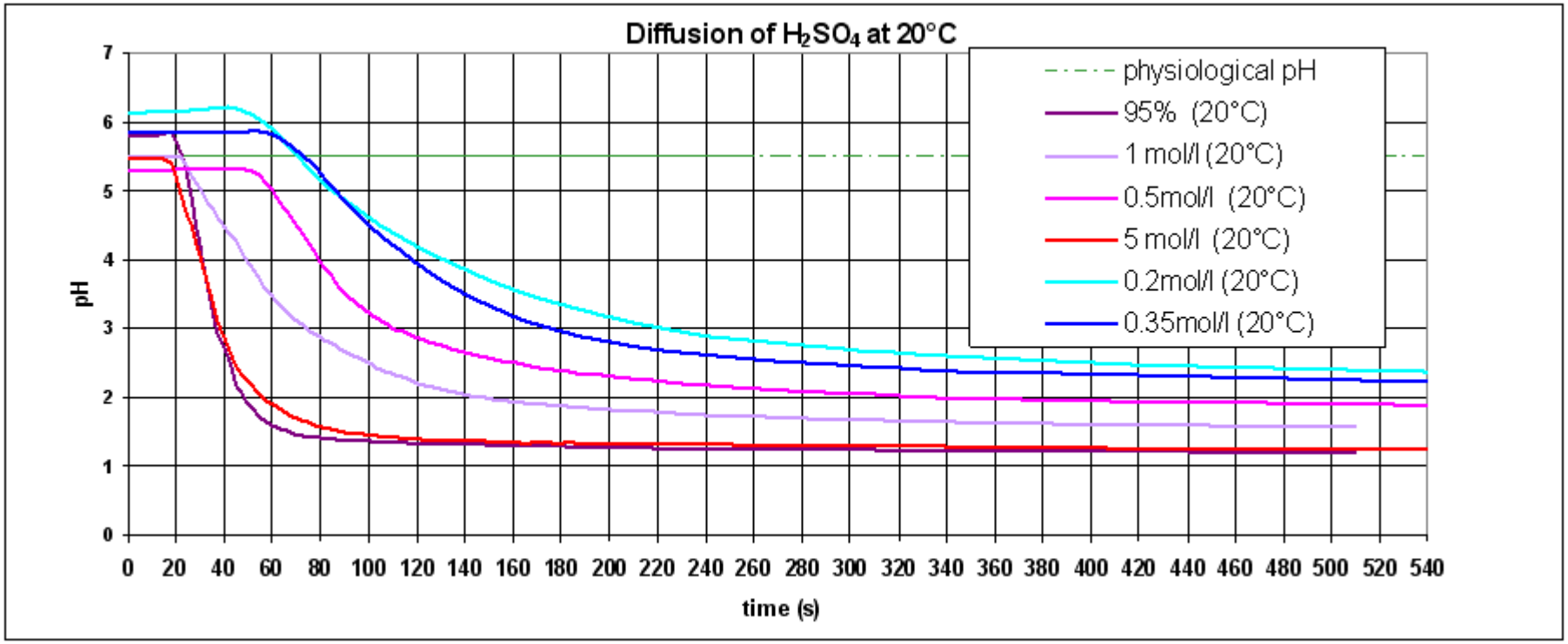
Belliard B, Hall AH, to be published

In vitro diffusion of 95% H_2SO_4

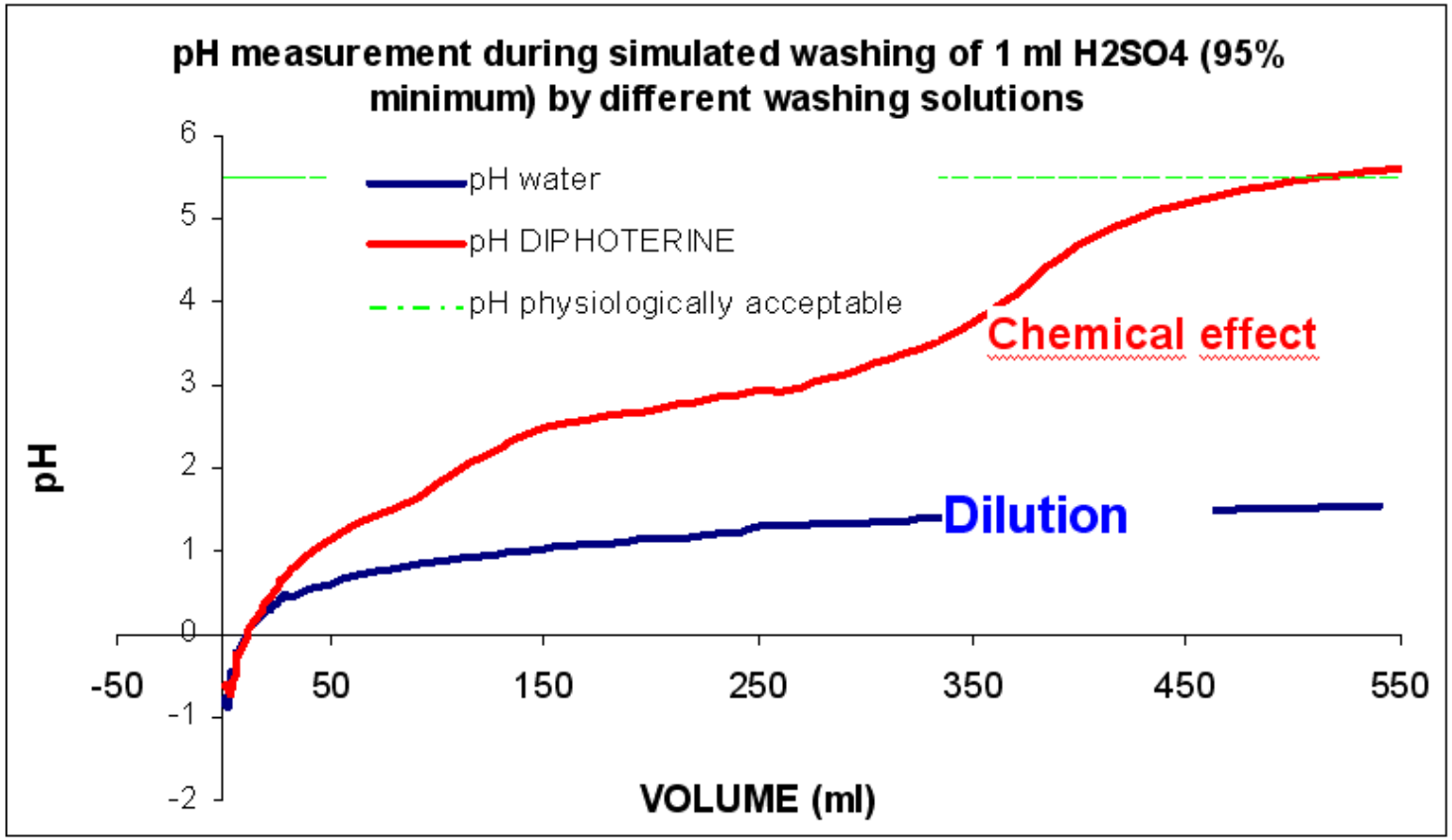


Diffusion of sulfuric acid is observed within the first minute

for concentration from 5M to 95% as we observed in the skin explant model.



Dilution and chemical effect



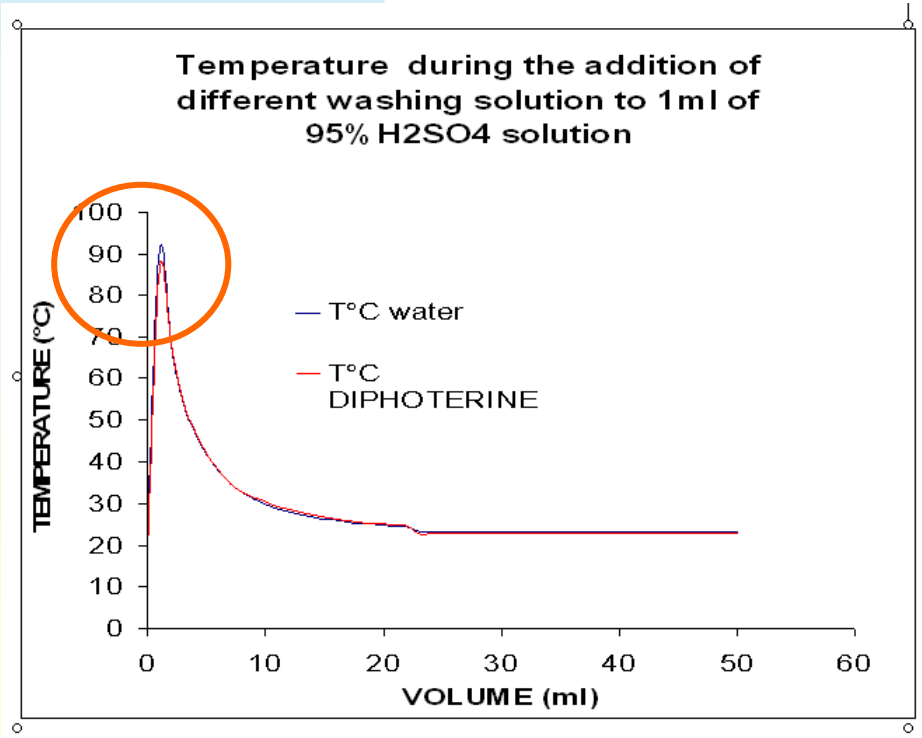
Dilution is a weak effect of the washing as the pH remains very low and corrosive.

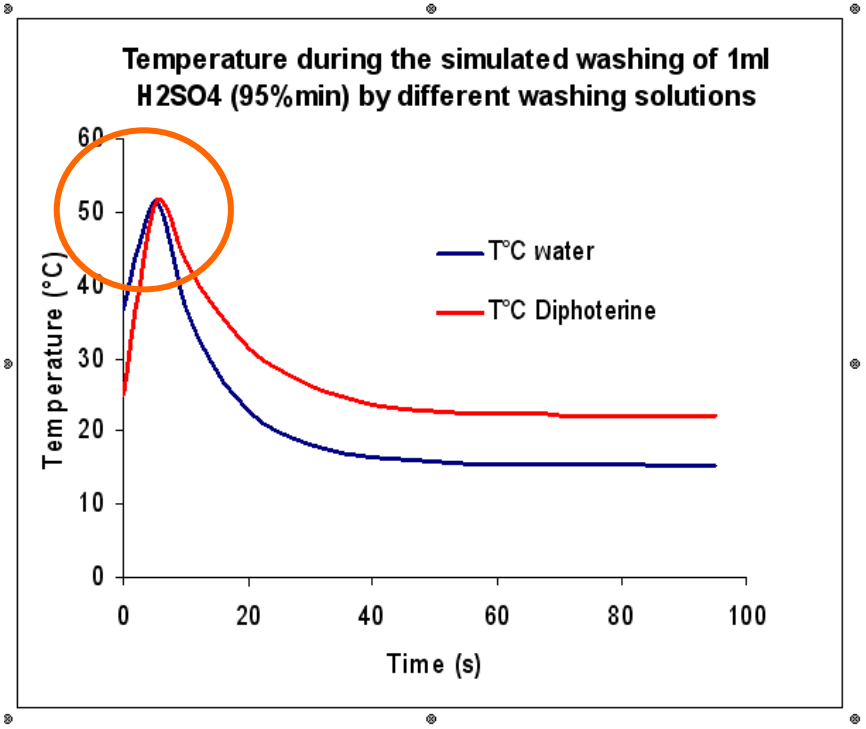
With the same volume, the chemical effect with an amphoteric agent such as Diphoterine® can rapidly increase the pH towards neutral value.

Heat release of H_2SO_4

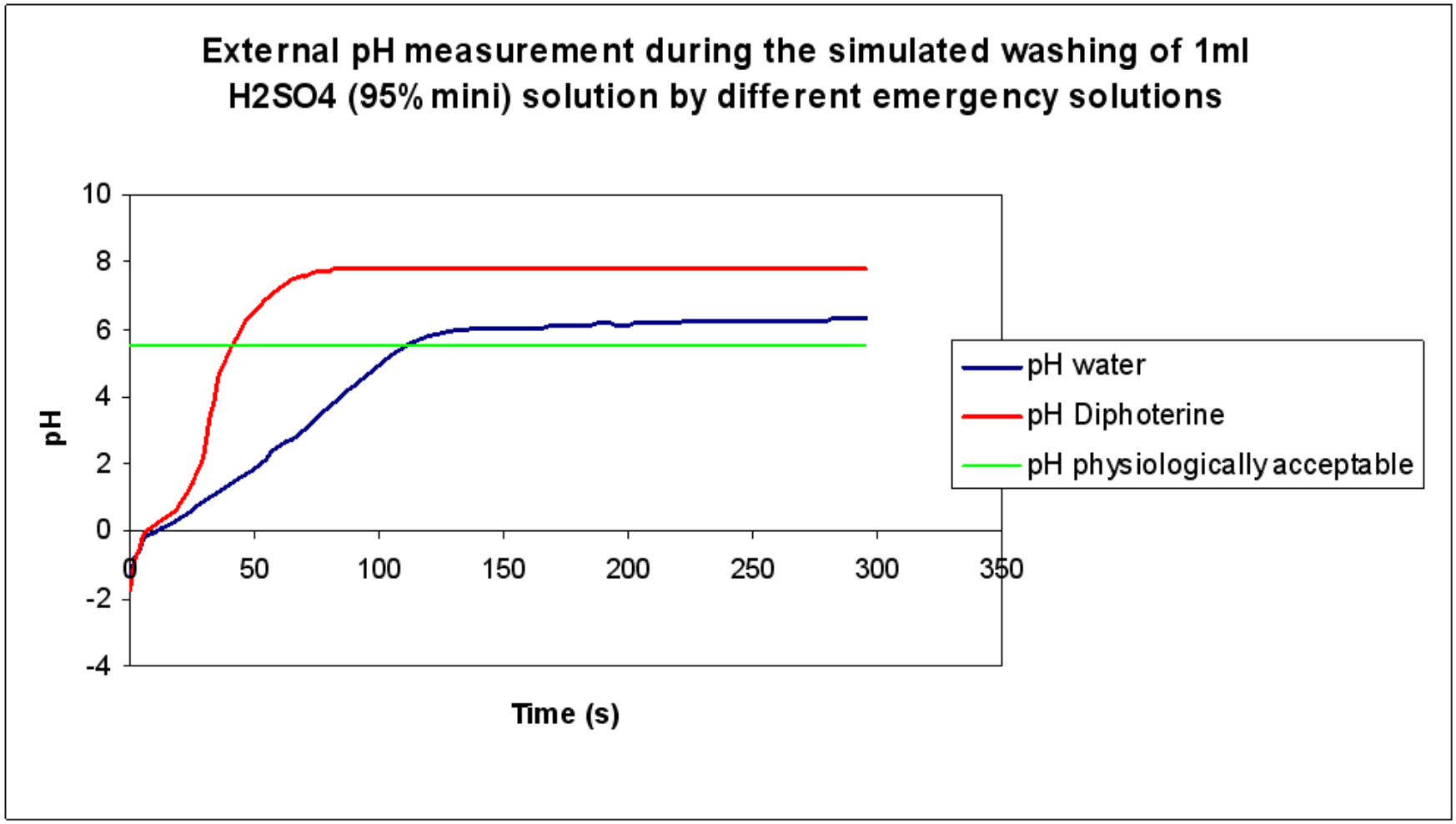
When an aqueous solution is added in a beaker, the temperature raises about 90°C.

When washing, the temperature rises only about 50°C and rapidly decreases.





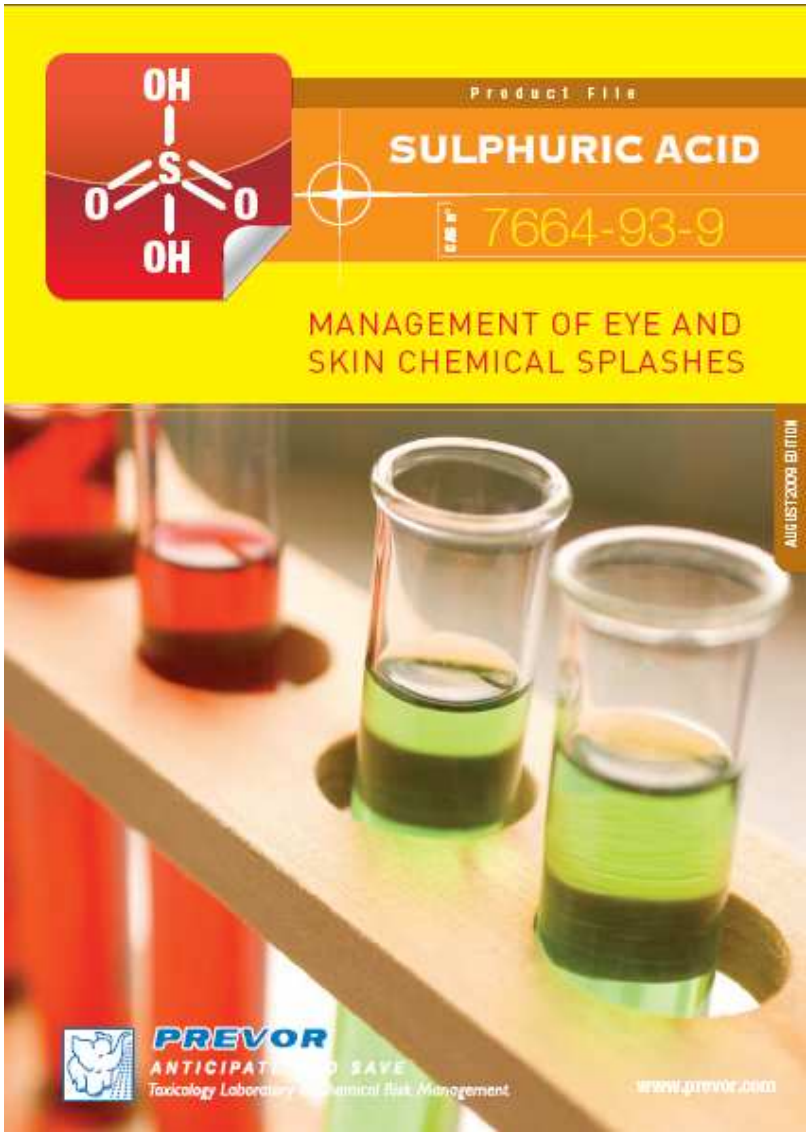
External washing of 95% H_2SO_4



Conclusion

- Never delay washing.
- Decontamination must be performed in an emergency, the best is within the first minute following the splash.
- Active decontamination with amphoteric compounds can secure the efficacy of the washing even for concentrated sulfuric acid.
- Theoreitical evaluation of contamination and decontamination of corrosives can be verified with simple models such as semi-permeable membrane.
- *Ex vivo* models such as human skin explants will bring us precise data about the mechanism of destruction at a biochemical level and can help us to improve decontamination protocols .

Thank you


OH
S
O
O
OH
Product File
SULPHURIC ACID
7664-93-9
MANAGEMENT OF EYE AND
SKIN CHEMICAL SPLASHES
PREVOR
www.prevor.com