Taylor & Francis
Taylor & Francis Group

Cutaneous and Ocular Toxicology

ISSN: 1556-9527 (Print) 1556-9535 (Online) Journal homepage: http://www.tandfonline.com/loi/icot20

# The Safety and Efficacy of Diphoterine® for Ocular and Cutaneous Burns in Humans

Darren D Lynn MD, Leonid M. Zukin & Robert Dellavalle

**To cite this article:** Darren D Lynn MD, Leonid M. Zukin & Robert Dellavalle (2016): The Safety and Efficacy of Diphoterine® for Ocular and Cutaneous Burns in Humans, Cutaneous and Ocular Toxicology, DOI: 10.1080/15569527.2016.1217423

**To link to this article:** http://dx.doi.org/10.1080/15569527.2016.1217423

Accepted author version posted online: 03 Aug 2016.
Published online: 03 Aug 2016.

**TITLE**: **The Safety and Efficacy of** Diphoterine® for Ocular and Cutaneous Burns in Humans

**Abstract:**

**Context:** Diphoterine, developed by the French company Prevor, is a polyvalent, chelating, amphoteric and slightly hypertonic solution used in the management of chemical cutaneous and ocular burns. While used extensively in Europe and Canada, it is has not been approved by the United States Occupational Safety and Health Administration (OSHA) as an alternative to the water-rinse method due to a lack of evidence of its safety and efficacy on human subjects. An unbiased and extensive systematic review was undertaken in order to better understand Diphoterine's safety and efficaciousness on humans.

**Objective**: Review the safety and efficacy of Diphoterine for treating chemical burns of the skin and eyes in humans.

**Methods**:

*Data sources:* Information sources included Pubmed, the National Library of Medicine's Medline Database, and the "Publications" sections of the Prevor website. Search terms included Diphoterine, chemical burn, ocular burn, and cutaneous burn.

*Study Selection:* Any study type published through a peer-reviewed journal up to May 2016 were considered eligible. Published data must have included Diphoterine in the treatment of chemical burns on the skin or eyes as well as meet other specified criteria. Acceptable studies had to use either a quantitative (e.g. number of work days lost) or qualitative (e.g. level of erythema) approach when measuring cutaneous or ocular lesion outcomes.

*Data Extraction:* Independent assessment of article inclusion by 2 authors using predefined criteria.

**Results and Conclusion**: Diphoterine is safe and highly effective in improving healing time, healing sequelae, and pain management of chemical burns on the skin and eyes of humans. Outcomes are significantly improved when compared to water or a physiologic solution equivalent. We recommend that this product be readily available to emergency responders and

companies that expose their employees to hazardous chemical substances in order to improve healing sequelae, pain management, and lost work days from these type of burns.

**Introduction**

Chemical burns account for only a fraction of reported cutaneous and ocular injuries though are responsible for nearly 30% of all burn-related deaths (1). The agents responsible for these injuries, which vary immensely, are thought to act by coagulating the proteins on the surface of the skin or eyes via a variety of different mechanisms with the damage resulting in moderate-severe pain, poor scar formation, and increased loss of disability-adjust life years (2, 3). In the US, the current standard of care for the emergency treatment (set by OSHA regulations) of skin or eye chemical burns are immediately applying copious amounts of water, rinsing the site for 15 minutes and using mild soap if the chemical is fat soluble (4). Within an industrial or laboratory setting, this typically occurs in emergency eye wash stations or quick-drench water showers. Rinsing with water is a passive decontamination process, thought to act by diluting and rinsing the chemical off the surface of the cornea or skin; suppressing the inflammatory reaction by decreasing tissue metabolism; returning skin pH back to normal (in acid and alkali burns); and minimizing the hygroscopic effects of chemicals (2, 4). However, an exhaustive literature review of the value of this water-rinsing for these chemical burns revealed the poor effectiveness of this method (5)—Hall and Maibach arrive at a similar conclusion in their analyses (4). Alternative rinsing agents, such as Diphoterine, have exhibited significantly better outcomes than the water-rinse method using *in vitro* and animal models, suggesting a similar result is possible in humans. To better understand Diphoterine's effects, we critically review all known publications which specifically evaluate this its safety and efficacy on human subjects for chemically-induced ocular and cutaneous burns.

**Background**

Diphoterine is a polyvalent, chelating, amphoteric, and slightly hypertonic solution developed by Latoratoir, Prevor of Valmondois, France that is used for the neutralization, decontamination, and irrigation of chemical splashes to the skin or eyes (6). Currently, it is widely used by ambulance services and fire-fighters in Sweden and France as a first-line decontaminating agent for chemical burns (7). In Europe and Canada, it has been used for the management of chemical burns in hospitals with no adverse effects yet being reported in the company's post-market surveillance program (8, 9). Diphoterine has a large safety margin due to its hyperosmolarity in physiologic tissue and, thus, low absorbability into eyes and skin of chemical burn recipients. *In vitro* and animal studies have demonstrated Diphoterine's ability to improve wound healing and reduce pain by inhibiting substance P release or increasing β-endorphin concentration when comparison to controls (0.9% saline or calcium gluconate) (3). Despite these encouraging studies, there are few published human experiments with the quality methodology needed to definitively advocate Diphoterine's safety and effectiveness.

Testing chemical burns has made controlled research on humans particularly difficult on many levels. Methodologically, there are no pre-set standards for gauging burns or treatment outcomes in patients, forcing researchers to rely on their own quantitative or qualitative modes of measurement. Accordingly, the heterogeneity of data generated by human experiments has precluded any reasonable analysis or cross-examination of outcomes between publications. Even within the same publication it can be difficult to draw substantial conclusions, as the chemicals responsible are often diverse in nature and in concentration. Thus, our goal was to create a holistic, critical review of Diphoterine's safety and effectiveness in human subjects by compiling the pertinent data extracted from select publications and analyzing the findings.

## Methods

*Types of studies*. Any study type published up to May 2016 were considered eligible.

*Inclusion criteria.* Eligible studies must have incorporated all of the following elements in order to be considered:

- Diphoterine in the treatment of ocular or cutaneous chemical burns (either in monotherapy or in combination with water).
- Any method of assessing burns that used either a quantitative (e.g. – number of work days lost) or qualitative (e.g. – level of erythema) approach.
- Must have been published through a peer-reviewed journal.

*Exclusion criteria*. Studies having at least one these in their methodology were automatically excluded from the eligible population:

- *In vitro* or *ex vivo* studies.
- Experiments not using humans.
- Articles not able to be translated into English.
- Studies not meeting any one of the inclusion criteria.



## Search Strategies

Databases used included the Cochrane Library, Embase, the National Library of Medicine's (NLM) Medline Database, EBSCO, and OvidSP. To be as thorough as possible, two academic search engines with access to multiple and distinct databases, EBSCO and OvidSP, were included to find other potentially eligible articles. Boolean techniques were employed in all searches to find publications with the word "Diphoterine" in the text or the title. The sum off all search results were combined and de-duplicated. The "Publications" section of the Prevor website contains a thorough record of all publications from a variety of sources and article types that include Diphoterine either directly or indirectly (10). These publications were added to the list after

removing duplicates found from the combined search results. Two reviewers then independently examined each article to assess whether or not it met all required inclusion criteria. Eligible publications were then assessed to verify lack of all exclusion criteria. Remaining publications were included in our review. Any disagreement would be resolved by a third party. A flowchart of the search strategy results and finalized article selection can be found in Figure 1.

**Data Extraction and Synthesis**

Data from the included studies were extracted by one reviewer and checked by the other reviewer for accuracy. Data extraction was performed in order to make our analysis more transparent and objective to the reader. Categories selected were based on the possible common confounding factors that could affect a chemical burn study outcome in humans. A standardized table specifically developed for this systematic review was filled out for each article and included:

1. Initial time to rinse.
2. Chemical description responsible for burn.
3. Total area burned.
4. Burn outcome.
5. Intervention outcome.

Other factors, such as duration of eye irrigation or fluid flow rate, were also considered important, but were not included due to lack of data in eligible studies. Case-matching Diphoterine intervention to the water-rinsing method was heavily considered, but the degree of variability between these potentially confounding factors proved too great to control. Meta-analysis was not undertaken due to the heterogeneity of the initial inciting chemicals and the inconsistency of analogous outcome measurements. Hence, our findings are presented in a narrative summary.

**Overview of Included Studies**

### *Cutaneous burns*

Only 3 studies, with a total of 317 patients, qualified for our review of cutaneous burns. Of those burned, only 32 were due to acid chemicals with the remaining 285 being due to a variety of alkaline-based chemicals. The time to rinse with Diphoterine ranged from 30 seconds after chemical exposure to 11 minutes. All studies measured burn outcomes and subsequent intervention outcomes differently, using both qualitative and quantitative methods. This information is summarized in Table 1.

### *Ocular burns*

Four studies, with a total of 134 patients, qualified for our review on ocular chemical burns. Only 11 patients had chemical burns caused by acids with the remaining 123 being caused by alkaline substances. Time to Diphoterine administration ranged from "nearly immediate" to 193 minutes after chemical incident, as well as one study with prophylactic usage. Outcome measurements proved to be quite disparate and—similar to the cutaneous burn studies—included both qualitative and quantitative methods. This information is summarized in Table 2.



## Discussion of Diphoterine Efficacy on Cutaneous and Ocular Burns

The retrospective analysis done by Zack-Williams was designed as a comparative study of the delayed use of Diphoterine versus water-rinsing for chemical burns at an adult tertiary referral burn center (see Table 1) (7). Though the comparison is helpful, many significant differences made it challenging to delineate the true efficacy of Diphoterine to the standard OSHA protocol. For example, the time to presentation was statistically significant between the two methods, possible confounding results—the longer a chemical is allowed to stay on the skin, the longer it has to react and cause more damage. Despite this and the variations in patient presentation, intervention outcome (change in pH) proved to be significant ($p < 0.05$) with Diphoterine being superior to water-rinsing. Diphoterine changed an average of 1.076 units whereas water-rinsing

changed an average of 0.4 units, presumably towards the physiologic pH. This pH change would theoretically allow for less scar formation, less pain, or faster healing time and is an ideal clinical consequence for victims of chemical accidents.

In contrast to the former report of delayed application, A. Michael Donoghue documents the effects of Diphoterine versus water-rinsing at alumina factories in Australia after "nearly immediate" rinsing (see Table 1) (11). Victims were randomly assigned to either: 1.) the "Diphoterine-first" group, which either used Diphoterine first and then rinsed water or used Diphoterine only, or 2.) the "water-first" group, which rinsed with water first and then used Diphoterine. This methodology resulted in an anticipated significant difference in the time to rinse [with Diphoterine] values between the two groups ($p < 0.001$). No variation, though, existed between the chemical source (sodium hydroxide) and body surface area affected ($p = 0.233$). Intervention outcome was recorded via a pre-set qualitative scale of erythema and blistering, ranging from 1 (none) to 4 (severe erythema and blistering). The outcome measurement and lack of dissimilarity between treatment groups permits an adequate comparison of Diphoterine to the standard water-rinsing protocol with respect to its healing properties, despite not having initial burn data. The data is significant among grades 1 & 2, but is only significant in grades 3 & 4 when combined ($p < 0.001$). The comparatively large number of "Diphoterine-first" patients within grades 1 & 2 and small number of grades 3 & 4 patients strongly suggests rinsing with Diphoterine first enhances healing time and overall sequelue when compared to the alternative. This result authenticates the efficacy of Diphoterine in humans that was similarly seen in animals as well as *in vitro* experiments (3).

Research done by Nehles and collegues included diverse cases of both cutaneous (Table 1) and ocular burns (Table 2), recording the chemical composition, concentration, and location of lesion on the patient's body (2). Unfortunately, the authors chosen method of evaluation (amount of work days lost and patient sequelae) makes it difficult to extract meaningful differences, as no real

variation appears to exist between any cases of either cutaneous or ocular burns. One can only speculate, though, if the lack of dissimilarity is a consequence of Diphoterine's effectiveness or simply poor methodology.

Unlike cutaneous burns, ocular burns have a pre-defined criteria found in the literature which allow clinicians to quickly assess and categorize chemical burns known as the "Roper-Hall modification of the Hughes classification system" (12). This qualitative analysis organizes burns according to the relative damage done to the cornea and limbus (12). Progression of ocular healing is typically recorded as the time it takes to obtain total re-epithelialization of the cornea (12). Merle utilized this system and shed important clinical light on Diphoterine's ability to heal ocular burns when compared to a physiologic solution (13) (see Table 2). Consistently, the Diphoterine intervention outcome (measured by days to re-epithelialization) took at least half the time required by the physiologic solution for burns within the same Roper-Hall classification. Differences of corneal opacity and corneal perforation correspondingly demonstrated Diphoterine's superiority to the physiologic solution group but were not considered statistically significant. Interestingly, no differences were noted in the final visual acuity between the two groups; however, the most severe classification of burn, Grade IV, lacked patients who were treated with Diphoterine and may have confounded the ability to find substantial variances in this measurement. One case study done by Gerard and colleagues did, however, manage to record an example of a Grade IV ocular burns caused by an alkaline substance and rinsed with Diphoterine (see Table 2). Regrettably, it would be difficult to draw any conclusive inferences to the Merle study patients with Grade IV lesions treated with a physiologic solution because of the substantial differences between their initial times to rinse (Gerard – 1hr, Merle – 4.5hr average). Nevertheless, these studies confirm Diphoterine can likewise be used for ocular burns and improve healing time when compared to an alternative.

Finally, it is worth mentioning the research done by Viala that investigated the effects of Diphoterine when sprayed onto the face before and after police officers were exposed to tear gas (see Table 2) (14). The aforementioned groups along with a control group (no Diphoterine) used a 1-10 point scale to measure the amount of pain while within the tear gas cloud as well as the residual pain felt after the officers considered themselves "ready for action." The pre-exposed group had significantly less pain, time interval to "ready for action", and residual pain than any of the other groups ($p < 0.05$ for all measurements). The post-exposure group had analogous findings in their residual pain measurement ($p < 0.05$), signifying Diphoterine additionally helps alleviate pain in humans from chemical accidents when used either before or after exposures.

**Safety**

The toxicological characteristics of Diphoterine, such as the median lethal dose ($LD_{50}$) or the human irritancy equivalent (HIE), have been evaluated in a variety of laboratory models resulting in promising outcomes for human clinical trials (9). A review of the literature revealed at least two separate experiments that specifically addressed the safety aspects of Diphoterine in health human volunteers and confirm the data from past laboratory model findings. In one experiment, a single application of 0.02 mL of Diphoterine was applied to 55 normal volunteers and maintained with an occlusive patch for 48 hours in order to test patient tolerance of the decontamination solution (9). Blinded dermatologists then evaluated the skin for erythema, papules, vesicles, or blisters and rated the intensity of reaction on a four-point scale (4 being most severe). The average of these scores, known as the average irritation index (IIM), was found to be 0.00, meaning it had no observable irritant properties on the skin of these volunteers. In a separate experiment, skin sensitization properties were tested by applying 25 μL of Diphoterine to the skin under an occlusive patch 3 times per week at 48 hour intervals for a duration of 3 weeks (9 total applications) in 111 healthy human volunteers (9). Between the $6^{th}$ and $8^{th}$ applications, signs of sensitization became apparent. Yet, after the 3 week experiment, the IIM was calculated to be 0.09

for the volunteers, qualifying as “slightly irritating” according to the clinical criteria developed by the International Contact Dermatitis Group (ICDG) (15). Overall, the study classified Diphoterine as hypoallergenic and presenting minimal risk of contact dermal sensitivity; however, given the sensitivity of the cornea, one would expect these minor effects to be greatly multiplied in ocular tissue with this same experimental protocol. From a cutaneous standpoint, this finding is consistent with the lack of sensitization and sequelae seen from Diphoterine application groups in our selected studies.

Unlike cutaneous burns, the osmolarity of the rinsing solution plays a critically important role in determining favorable patient outcomes for ocular burns: hypoosmotic solutions (water) can rapidly penetrate the injured cornea, causing cell swelling, edema, and cell death (5, 16, 17). Diphoterine and other high osmolarity solutions avoid these consequences, enhancing healing time by mobilizing water and dissolved corrosives out of the damaged tissue. One study comparing Diphoterine to a phosphate buffer solution in 10 healthy human volunteers found both irrigation fluids to be equally safe and absent of any harmful effects (17). Moreover, data from the company’s post-market surveillance program have yet to report any adverse effects from the hospitals and fire-fighters where Diphoterine is currently used to manage chemical burns (8, 9). Notably, ocular studies testing safety were done under emergent conditions, obscuring the possible irritant effects Diphoterine has directly or indirectly (i.e., exothermic reaction from chemical neutralization).



**Conclusion**

Chemical splashes to the skin or eyes have become an unfortunate consequence to many working with hazardous materials. Many countries outside the US now require hospitals and fire-fighters to rinse these chemical mishaps with the solution Diphoterine instead of water (8, 9). While

Diphoterine's safety and efficacy has been proven in many *in vitro* and animal models, its safety and effectiveness have not been thoroughly evaluated in human subjects. Therefore, this systematic review was created to critically evaluate the available research of Diphoterine used specifically on humans in order to understand its applicable safety and efficacy. To our knowledge, this is the first review that examines this aspect.

The current available research of Diphoterine in humans is heavily criticized due to poor methodologies, small study populations, and heterogeneity of study measurements. This makes it difficult to use any one individual study outcome as a definitive evidence of this irrigation fluid's true safety and efficacy potential, however, the sum of these reports reveal consistent themes that are clinically valuable. For example, we found that despite most of the comparative studies lacked pre-treatment consistency in chemical compositions, concentrations, time to rinse, and burn locations, the groups treated with Diphoterine always fared better than the group treated with water (or physiological equivalent). Clinically, the heterogeneity in pre-treatment conditions is more realistic than a heavily controlled experiment and speaks to Diphoterine's flexibility in treating real-world chemical burn patients.



As a whole, our review found that Diphoterine is a safe product and appears to be highly effective in improving healing time, healing sequelae, and pain management of chemical burns on the skin and eyes of humans—especially when compared to rinsing with water or a physiologic equivalent. We recommend future studies wishing to compare the effectiveness of Diphoterine to alternative solutions follow a methodology exemplified by Merle's research and include: homogenous chemical substances, similar time to rinse, and, perhaps most importantly, graded qualitative measurements for both burn and intervention outcomes. Even before such a meticulous study can take place, we recommend that this product be readily available to emergency responders, hospitals, and companies that expose their employees to hazardous chemical substances in order to

improve victim healing sequelae, pain management, and work days lost from accidental burns to the skin or eyes. Further, based on the data presented, we submit that OSHA's current emergency protocol of managing chemical burns be revisited and reevaluated.

## Declarations of Interest

*Funding/Support*: The current study was unfunded. The Department of Veterans Affairs was not involved in the current study design, data acquisition and interpretation, or manuscript preparation or review.

*Financial Disclosure:* Robert Dellavalle is employed by the US Department of Veterans Affairs. D. Lynn and LM Zukin report no disclosures.

**References**


1. Hardwicke J, Hunter T, Staruch R, Moiemen N. Chemical burns--an historical comparison and review of the literature. Burns. 2012;38(3):383-7.

2. Nehles J, Hall AH, Blomet J, Mathieu L. Diphoterine for emergent decontamination of skin/eye chemical splashes: 24 cases. Cutan Ocul Toxicol. 2006;25(4):249-58.

3. Hall AH, Blomet J, Mathieu L. Diphoterine for emergent eye/skin chemical splash decontamination: a review. Vet Hum Toxicol. 2002;44(4):228-31.

4. Hall AH, Maibach HI. Water decontamination of chemical skin/eye splashes: a critical review. Cutan Ocul Toxicol. 2006;25(2):67-83.

5. Rihawi S, Frentz M, Schrage NF. Emergency treatment of eye burns: which rinsing solution should we choose? Graefes Arch Clin Exp Ophthalmol. 2006;244(7):845-54.

6. Donoghue AM. Diphoterine(R) for alkali splashes to the skin. Clin Toxicol (Phila). 2014;52(2):148.

7. S.D.L. Z-W. The clinical efficacy of Diphoterine® in the management of cutaneous chemical burns: a 2-year evaluation study. In: Z. A, editor.: Annals of Burns and Fire Disasters; 2015.

8. Mathieu L, Burgher F, Hall AH. Diphoterine chemical splash decontamination solution: skin sensitization study in the guinea pig. Cutan Ocul Toxicol. 2007;26(3):181-7.

9. Hall AH, Cavallini M, Mathieu L, Maibach HI. Safety of dermal diphoterine application: an active decontamination solution for chemical splash injuries. Cutan Ocul Toxicol. 2009;28(4):149-56.

10. Scientific publications, studies and articles on DIPHOTERINE® solution: Prevor.com; 2016 [Available from: http://www.prevor.com/en/scientific-publications-studies-and-articles-on-diphoterine-solution.

11. Donoghue AM. Diphoterine for alkali chemical splashes to the skin at alumina refineries. Int J Dermatol. 2010;49(8):894-900.

12. Dua H, King A, Joseph A. A new classification of ocular surface burns. The British Journal of Ophthalmology. 2001;85(11):1379-83.

13. Merle H, Donnio A, Ayeboua L, Michel F, Thomas F, Ketterle J, et al. Alkali ocular burns in Martinique (French West Indies) Evaluation of the use of an amphoteric solution as the rinsing product. Burns. 2005;31(2):205-11.

14. Viala B, Blomet J, Mathieu L, Hall AH. Prevention of CS "tear gas" eye and skin effects and active decontamination with Diphoterine: preliminary studies in 5 French Gendarmes. J Emerg Med. 2005;29(1):5-8.

15. Ivens U, Serup J, O'Goshi K. Allergy patch test reading from photographic images: disagreement on ICDRG grading but agreement on simplified tripartite reading. Skin Res Technol. 2007;13(1):110-3.

16. Kompa S, Schareck B, Tympner J, Wustemeyer H, Schrage NF. Comparison of emergency eye-wash products in burned porcine eyes. Graefes Arch Clin Exp Ophthalmol. 2002;240(4):308-13.

17. Langefeld S, Press UP, Frentz M, Kompa S, Schrage N. [Use of lavage fluid containing diphoterine for irrigation of eyes in first aid emergency treatment]. Ophthalmologe. 2003;100(9):727-31.

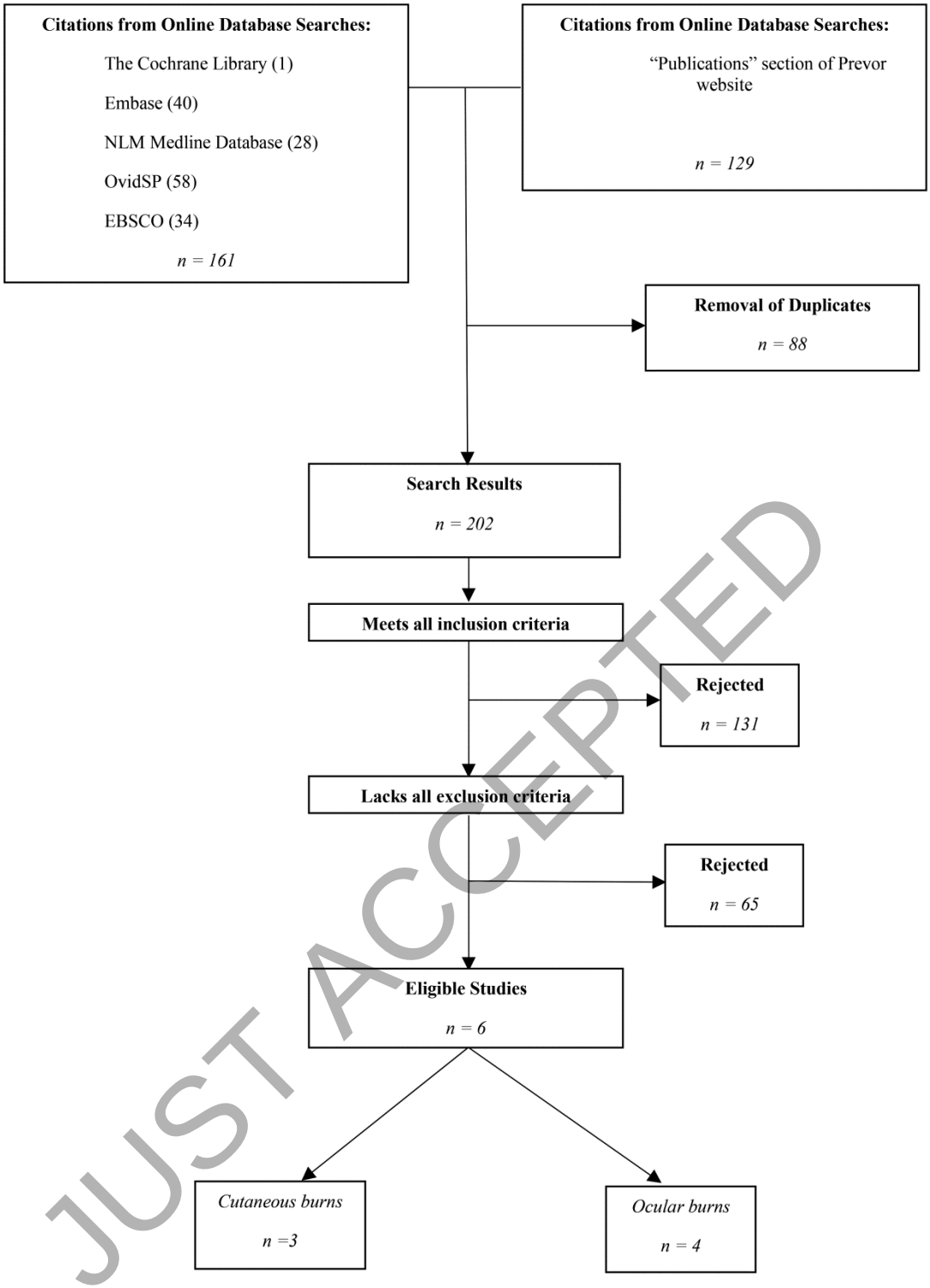




**Figure 2.** Flowchart of the search strategies and study selection.

## *CUTANEOUS BURN STUDIES*

| Title<br>*Author* | Study Type | Chemical | Time to rinse (minutes) | | Area burned | | | Burn outcome | | | Intervention Outcome | | | | Notes |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| The clinical efficacy of Diphoterine® in the management of cutaneous chemical burns: A 2-year evaluation study<br><br>*Zack-Williams* | Comparative Study | "Alkali burns"<br>n = 72 cases (55.0%) | Diphoterine (DAP) | Water ($H_2O$) | | DAP | $H_2O$ | | DAP | $H_2O$ | *Measured (Days)* | DAP | $H_2O$ | P-value | The Diphoterine-treated patients were significantly younger (mean 37.7 vs 43.2 years, $p = 0.044$) than those treated without. Patients who received Diphoterine presented to the hospital significantly earlier than those who did not receive it (0.5 vs 2.55 days $p = 0.006$) |
| | | "Acids"<br>n = 24 cases (18.3%) | 0.57 | 2.15 | TBSA(%) | 1.76 | 1.25 | Mean Pre-irrigation pH | 8.07 | 7.77 | Injury to surgery | 3.50 | 5.00 | 0.067** | |
| | | | n = 47 | n = 84 | | | | | | | Injury to heal time | 9.00 | 7.00 | 0.258 | |
| | | "Other chemicals"<br>n = 35 cases (26.7%) | *p = 0.004** | | | *p = 0.203* | | | *p = 0.369* | | Injury to discharge | 2.0 | 2.0 | 0.469 | |
| | | | | | | | | | | | Mean ΔpH | 1.076 | 0.4 | *<0.05** | |
| Diphoterine® for alkali chemical splashes to the skin at alumina refineries<br><br>*Donoghue* | Comparative Study | "…strong alkali solutions (primarily sodium hydroxide)" | DAP first | $H_2O$ first, then DAP | | DAP | $H_2O$ | Severity was recorded by medical personnel in the initial assessment. These results were not published with the article. | | | *Severity* | DAP | $H_2O$ | | "Time to rinse" is measuring the time to rinse *with Diphoterine* in both treatment groups. |
| | | | 2.9 | 11 | Body Surface Area (%) | 1.6 | 2.9 | | | | 1 (no signs) | 73 cases | 9 cases | | |
| | | | n = 135 | n = 42 | | | | | | | 2 (erythema) | 54 cases | 23 cases | | |
| | | | *p = 0.001** | | | *p = 0.233* | | | | | 3 (blisters) | 10 cases | 8 cases | | |
| | | | | | | | | | | | 4 (more severe) | 1 case | 2 cases | | |
| | | | | | | | | | | | | n = 138 | n = 42 | | |
| Diphoterine® for Emergent Decontamination of Skin/Eye Chemical Splashes: 24 Cases<br><br>*Nehles* | Case Series | **ACIDS** | | | | | | | | | No sequelae in any case. | | | | |
| | | $HNO_3$ (53%) | "…nearly immediate (within the first 30–120 seconds after exposure)" | | Head | | | Lost work days | 0 | | | | | | |
| | | $H_2SO_4$(20%) | | | Right cheek | | | | 0 | | | | | | |
| | | $H_2SO_4$(20%) | | | Thorax | | | | 0 | | | | | | |
| | | $H_3PO_4$(16%) | | | Left forearm | | | | 0 | | | | | | |
| | | $H_2SO_4$(20%) | | | Face | | | | 0 | | | | | | |
| | | $H_3PO_4$(15%) | | | Right hand | | | | 0 | | | | | | |
| | | $H_3PO_4$(75%) | | | Thorax, genitals | | | | 0 | | | | | | |
| | | $H_2SO_4$(20%) | | | Right hand | | | | 0 | | | | | | |
| | | **BASES** | | | | | | | | | | | | | |
| | | NaOH (45%) | (same as acids) | | Knee | | | | 0 | | | | | | |

* statistically significant

** approaching statistical significance

TBSA – Total Body Surface Area

DAP – Diphoterine

## *OCULAR BURN STUDIES*

| Title<br>*Author* | Study Type | Chemical | Time to rinse<br>(minutes unless otherwise listed) | Area burned | Burn outcome | Intervention Outcome | Notes |
|---|---|---|---|---|---|---|---|
| Diphoterine® for emergent decontamination of skin/eye chemical splashes: 24 cases.<br>*Nehles* | Case Study | **ACIDS** | | | | No sequelae in any case. | |
| | | $H_3PO_4/HNO_3$ (5/30-35%) | "…nearly immediate (within the first 30–120 seconds after exposure)" | Left eye (L) | Lost work days: 0 | | |
| | | $H_2SO_4$ (20%) | | Right eye (R) | 0 | | |
| | | NH2SO3H (Powder) | | R | 0 | | |
| | | H2SO4 (20%) | | Not reported | 0 | | |
| | | NH2SO3H (Powder) | | Not reported | 0 | | |
| | | H2SO4 (20%) | | R | 1 | | |
| | | $H_3PO_4/HNO_3$ (5/35%) | | L | 1 | | |
| | | H2SO4 (20%) | | L | 0 | | |
| | | H2SO4/HNO3 (5/35%) | | L | 1 | | |
| | | $H_2SO_4$ (20%) | | R | 0 | | |
| | | $H_2SO_4$ (20%) | | L | 0 | | |
| | | **BASES** | | | | | |
| | | NaOH (30%) | | R | 0 | | |
| | | "Basic Solution" (30%) | | R | 0 | | |
| | | Quicklime (CaO) | | R | 0 | | |
| | | Quicklime (CaO) | | L | 0 | | |
| Martinique (French West Indies) Evaluation of the use of an amphoteric solution as the rinsing product.<br>*Merle H* | Comparative Study | Alkali<br>n= 32 (48.5%) | *Roper-Hall Modification of the Hughes Classification System* | Grade I | DAP: 15 ± 48; Phys.: 25.6 ± 58; *p = 0.49*; DAP *n* = 35; Phys. *n* = 17; *Specific eye not recorded* | • Corneal epithelial damage<br>• No limbal ischemia<br>• Good prognosis | Time to Re-epithelialization (days): DAP 1.9 ± 1; Phys. 11.1 ± 1.4; p = $10^{-7}$* | Injuries were first irrigated with their respective solution at an average of the times listed (units in minutes). A second irrigation occurred 5 hours after the accident (5.1 ± 4.3 h). No significant differences existed between DAP and Phys. Solutions for any Grade.<br><br>All Grade IV injuries were rinsed with the physiologic solution and were therefore not included in this table. |
| | | DAP: 9 (25%); Phys.: 23 (76.7%)<br>*p <0.0001** | | Grade II | DAP: 22.2 ± 60; Phys.: 17.3 ± 45; *p = 0.79*; DAP *n* = 16; Phys. *n* = 16; *Specific eye not recorded* | • Corneal haze, iris details visible<br>• <1/3 limbal ischemia<br>• Good prognosis | DAP: 5.6 ± 4.9; Phys.: 10 ± 9.2; p = 0.02* | |
| | | Javel[1]<br>n = 10 (15.1%)<br>DAP: 7 (19.4%); Phys.: 3 (10%)<br>*No p-value reported* | | Grade III | DAP: 193 ± 262; Phys.: 120 ± 264; *p = 0.64*; DAP n = 5; Phys. n = 7; *Specific eye not recorded* | • Total epithelial loss, stromal haze, iris details obscured<br>• 1/3–½ limbal ischemia<br>• Poor prognosis | DAP: 20 ± 14.1; Phys.: 45.2 ± 23; p = 0.21 | |
| | | "Other"[2]<br>n = 24 (36.4%)<br>DAP: 20 (55.6%); Phys.: 4 (13.3%)<br>*No p-value reported* | | | | | | |

| Title<br>*Author* | Study Type | Chemical | Time to rinse<br>(minutes unless otherwise listed) | Area burned | Burn outcome | Intervention Outcome | | Notes |
|---|---|---|---|---|---|---|---|---|
| An amphoteric rinse used in the emergency treatment of a serious ocular burn<br>*Gerard* | Case Study | Ammonia (Alcali®): 15.3%, pH: 12.8 | "…1 hour after the accident." | Right eye | Grade IV<br>*Roper-Hall Classification*<br>• Cornea opaque, iris and pupil obscured<br>• >½ limbal ischaemia<br>• Poor prognosis | Time to Re-epithelialization (days)<br>"Progression to healing [began at]": 21<br>"Total re-epithelializtion": 180 | | Rinsing was enhanced by instillation of local anaesthesia with oxybuprocaine eye drops. |
| | | | | | Visual acuity 2/20 | 4/20 | 14/20 | |

| Title<br>*Author* | Study Type | Chemical | Experimental groups | | Pain level<br>(inside CS cloud) | **Time Interval** between CS exposure and arrival…<br>…at the 'ready-for-action' checkpoint | **Residual Pain…** | Notes |
|---|---|---|---|---|---|---|---|---|
| Prevention of CS "Tear Gas" eye and skin effects and active decontamination with Diphoterine®<br>*Viala* | Comparative Study | Chlorobenzylidene malononitrile (CS) tear gas | CS group<br>n = 6 | Exposed to only CS. | 9.7±0.5 | 2:28±0:25 | 2.3±0.5 | Pain was scored according to a 10-point scale.<br><br>A control group with 200ml low-pressure spray containers filled with water were prepared; however, the but officers refused to use water sprays due to their previous bad experiences with water decontamination after CS exposure. |
| | | | Pre-exposure group<br>n = 8 | Faces sprayed with Diphoterine (200mL) just before CS exposure. | 5.6±1.1* | 1:26±0:44* | 1.1±0.4* | |
| | | | Post-exposure group<br>n = 8 | Faces sprayed with Diphoterine (200mL) immediately after CS exposure. | 9.1±0.4 | 2:30±0:48 | 1.4±0.7* | |

* statistically significant ($p < 0.05$)

** approaching statistical significance

TBSA – Total Body Surface Area

DAP – Diphoterine solution used

Phys. – Physiologic solution used

[1] Javel contains 6.8% sodium hypochlorite and has a pH of 11.5.

[2] "Others" are soda-based cleansers and detergents, lime, and cement.