

Research and Testing Results on the Ability of Certain Compounds to Reduce CS Gas Skin Irritation in Rabbits

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Received: 05 Mar 2026,

Received in revised form: 08 Apr 2026,

Accepted: 11 Apr 2026,

Available online: 14 Apr 2026

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Keywords— CS gas, Dermal irritation, GHS 2025, In vivo testing.

Abstract— This study employs in vivo testing on rabbit skin to evaluate the toxicity and detoxification efficacy of CS gas (o-chlorobenzylidene malononitrile) based on the GHS 2025 standards (Globally Harmonized System of Classification and Labelling of Chemicals, Eleventh revised edition). Test samples were applied via direct dermal permeation to monitor the progression of erythema and edema at fixed intervals of 24, 48, and 72 hours. The research combines experimental tear gas irritation models with simple irritation tests to accurately determine safety profiles and injury recovery capabilities. Results were determined through a standardized scoring system, allowing for the classification of chemical hazard levels according to international categories. The test samples demonstrated significant effectiveness in reducing acute irritation symptoms caused by CS gas in rabbit skin models. By monitoring erythema and edema indices, the irritation-reducing active ingredients significantly shortened epithelial recovery time compared to the control group. Observations at 24, 48, and 72 hours evidenced the ability to soothe the skin, prevent widespread inflammation, and limit deep lesions such as hyperkeratosis or alopecia. Comparison with GHS 2025 scales confirmed that these test samples could lower irritation levels from Category 2 to Category 3 or to a non-irritating status. This provides an important scientific basis for confirming the practical application of these compounds in the safe and effective treatment of lachrymatory agents. The research offers high practical value by establishing a scientific and objective evaluation process for irritation reduction in animal models. Strict application of the latest international standards from GHS 2025 not only ensures accuracy in irritation classification but also enhances the legal validity and reliability of testing results in Vietnam. The efficacy of the test samples was clearly proven through the rapid reduction of inflammatory reactions, erythema, and edema, opening great prospects for developing specialized medical support products. This serves as an important prerequisite for practical applications aimed at protecting human health against potent irritants.

I. INTRODUCTION

CS gas was first synthesized in 1928 and saw extensive use by the U.S. military during the conflict in Vietnam,

with volumes reaching approximately 9,000 tons [2]. Currently, in addition to environmental residues from buried munitions in various regions, CS is utilized by

public security forces in the form of tear gas sprays for maintaining security and order. However, it is an extremely potent irritant capable of causing skin burns, corneal damage, and respiratory issues, with high concentrations posing severe health risks. The dermal impact of CS often results in congestion and blistering [1]. Consequently, researching solutions and detoxification compounds is necessary to protect health from these toxic effects.

The substance causes intense irritation through direct chemical interaction with TRPA1 sensory nerve receptors. Upon contact, CS forms stable covalent bonds with the thiol groups of proteins, causing ion channels to open and inducing membrane depolarization. This process transmits acute burning pain signals to the brain and activates TRPV1 receptors, which are sensitive to heat and capsaicin, prolonging the sensation [3]. This dual impact on the pain receptor system necessitates specialized measures to interrupt the chemical reaction chain.

Current detoxification research focuses on multi-layered mechanisms. Amphoteric properties play a role in neutralizing irritation, while chelating capabilities help prevent the formation of covalent bonds with nerve receptors. Hypertonic characteristics assist in drawing chemical molecules from the epithelium to the surface, and lipid membrane solubility helps remove adhering particles. Combining these mechanisms aims to soothe immediate sensations and prevent inflammatory complications.

This study investigates specific chemicals capable of neutralizing skin irritation caused by CS. A comprehensive evaluation of safety and epithelial recovery is conducted on experimental models to ensure practical applicability. These results provide a scientific basis for selecting optimal components for health protection compounds.

II. RESEARCH CONTENT

2.1. Materials and Equipment

2.1.1. Equipment

- Biomedical digital camera (high resolution, standardized lighting)
- Skinfold thickness gauge (or mini ultrasound device)
- Corneometer (for skin hydration measurement)
- Skin surface pH meter
- Handheld dermatoscope (dermatological microscope)

2.1.2. Chemicals

- CS agent (USA)
- Ammonia; Ethanol; PEG - 400; NaHCO₃ (Sodium bicarbonate)

2.1.3. Experimental Models

Tests were conducted on three healthy rabbits in accordance with OECD 404 guidelines and GHS 2025 classification. The skin on both flanks was shaved 24 hours prior to the procedure. Five specific sites were marked: a control site, a site for the irritant spray (CS), and three sites for the irritant spray combined with different irritation-reducing samples. The samples were applied in their original form, sprayed from a distance of 10 cm in three 1-second bursts. Immediately following the irritant application, the reduction samples were applied to their respective sites. After 4 hours, the skin areas were gently cleaned. Dermal reactions were monitored at 1, 24, 48, and 72 hours. The degree of irritation was scored based on erythema and edema (on a scale of 0 to 4) to calculate the mean score and classify the irritation level [4,5].

Table 1. Evaluation Scores of Dermal Irritation in Rabbits

No.	Dermal Reaction	Score
Erythema and Eschar Formation		
1	No erythema	0
2	Very slight erythema (barely perceptible)	1
3	Well-defined erythema	2
4	Moderate to severe erythema	3
5	Severe erythema (beet redness) to eschar formation preventing grading of erythema	4
Edema Formation		
1	No edema	0
2	Very slight edema (barely perceptible)	1
3	Slight edema (edges of area well defined by definite raising)	2
4	Moderate edema (raised approximately 1 mm)	3
5	Severe edema (raised more than 1 mm and extending beyond area of exposure)	4

Table 2. Classification Scale for Dermal Irritation Severity in Rabbits

Reaction Category	Mean Irritation Score (MIS)
Non-irritating	0
Negligible irritant	> 0 - 0,4
Slight irritant	0,5 - 1,9
Moderate irritant	2,0 - 4,9
Severe irritant	5,0 - 8,0

III. RESULTS AND DISCUSSION

3.1. Dermal Irritation Test Results for CS Agent

In the group exposed to the CS agent, erythema appeared 1 hour after skin cleansing. Two subjects showed well-defined reactions, while one showed only very slight effects, indicating individual biological variation within the slight-to-moderate irritation range. After 24 hours, erythema persisted and became more uniform across all three subjects, reflecting an acute transient inflammatory response. By 48 hours, erythema significantly subsided to very slight levels, with no signs of severe damage such as edema, excoriation, or necrosis. After 72 hours, the skin of all subjects returned to normal. These results demonstrate that the CS agent causes temporary dermal irritation, primarily characterized by erythema typical of lachrymatory agents, without causing long-term injury.

3.2. Irritation Reduction Results for Test Sample 1 (Containing Ammonia)

Ammonia (NH₃) reduces the irritant effects of CS by creating a mildly alkaline environment that promotes CS decomposition and diminishes sensory receptor activation. Additionally, NH₃ helps mitigate local inflammation and increases fluid secretion, aiding in the rinsing of CS from the contact surface. Results showed that in the Ammonia-treated group, erythema was very slight immediately after cleansing and subsided rapidly. By 24 hours, irritation remained only at a slight level with no strong inflammatory response. Most subjects recovered by 48 hours, and all achieved full recovery by 72 hours. Compared to the control group, Sample 1 significantly reduced both the intensity and duration of the CS-induced reaction.

3.3. Irritation Reduction Results for Test Sample 2 (Containing Sodium Bicarbonate)

Sodium bicarbonate (NaHCO₃) mitigates CS irritation by providing a mild alkaline buffer that accelerates decomposition and reduces the stimulatory activity of CS on the skin surface. Simultaneously, NaHCO₃ neutralizes local inflammatory responses and assists in dissolving and washing away CS, rapidly alleviating burning sensations. Results for Sample 2 showed very slight to nearly no irritation immediately after cleansing. Within 1 hour, most subjects returned to a normal skin state; by 24 hours, only one subject exhibited very slight erythema. At 48 and 72 hours, all subjects were completely normal with no delayed inflammation or residual irritation. Sample 2 demonstrated superior efficacy and high safety compared to the control group.

3.4. Irritation Reduction Results for Test Sample 3 (Containing Sodium Bicarbonate and Polyethylene Glycol)

The combination of Sodium bicarbonate (NaHCO₃) and Polyethylene glycol (PEG) reduces CS irritation through a synergy of chemical and physical mechanisms. While NaHCO₃ neutralizes the agent and local inflammation, PEG acts as a solvent and carrier, effectively dissolving and lifting CS from the skin while forming a moisturizing barrier to prevent secondary irritation. Testing showed that immediately after cleansing (approximately 4 hours), the skin of all three subjects was completely normal with no recorded erythema or irritation, whereas the control group still showed well-defined erythema. At the 1, 24, 48, and 72-hour marks, the skin remained stable with no signs of delayed inflammatory reactions or residual irritation.

3.5. Dermal Scoring Results According to OECD Guidelines

Table 3. Mean Skin Reaction Score in Rabbits

Sample	Rabbit		Mean Skin Reaction Score	
	No.	Sex	Erythema score	Edema score
CS toxicant sample	1	♂	1,0	0,0
	2	♂	1,0	0,0
	3	♀	1,0	0,0
Sample 1	1	♂	0,3	0,0
	2	♂	0,7	0,0
	3	♀	0,7	0,0
Sample 2	1	♂	0,0	0,0
	2	♂	0,0	0,0
	3	♀	0,3	0,0
Sample 3	1	♂	0,0	0,0
	2	♂	0,0	0,0
	3	♀	0,0	0,0

Compared to the control group and other test samples, sample No. 3 demonstrated superior anti-irritant efficacy, not only reducing but completely eliminating the symptoms of irritation caused by the CS agent. These results prove that the NaHCO₃/PEG mixture possesses high anti-irritant effectiveness, safety, and good skin tolerance, providing an important scientific basis for further research and practical application.

IV. CONCLUSION

The research results initially identified several compounds capable of reducing skin irritation caused by the CS agent on rabbit models, among which Sodium bicarbonate and the Sodium bicarbonate/Polyethylene glycol mixture showed significant efficacy. Tests conducted on rabbit skin models following OECD guidelines demonstrated that the test samples could rapidly reduce erythema levels, shorten the duration of inflammatory responses, and prevent prolonged skin damage. Notably, the NaHCO₃/PEG mixture exhibited the highest anti-irritant effect with a mean irritation score of 0, proving excellent tolerance and high safety. These findings help clarify the scientific basis for selecting CS irritant neutralizers while providing critical experimental data for the development of skin decontamination compounds. Furthermore, the study opens up potential applications in chemical safety and the management of tear gas-related incidents in practice.

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