Magna Scientia Advanced Biology and Pharmacy
eISSN: 2582-8363
Cross Ref DOI: 10.30574/msabp
Journal homepage: https://magnascientiapub.com/journals/msabp/

(REVIEW ARTICLE)

Check for updates

p-Toluene sulfonic acid, C-DEB, and chronic ulcers: chemical, toxicological and clinical analysis and therapeutic prospects

Giampietro Bertasi [1,*] and Mariana Peroni [2]

[1] *Department of Biotechnology, University of Padua, Italy.*
[2] *Diabetology Unit, IRCCS Sacro Cuore, Negrar, Italy.*

Magna Scientia Advanced Biology and Pharmacy, 2025, 16(02), 026-033

Publication history: Received 21 October 2025; revised on 01 December 2025; accepted on 03 December 2025

Article DOI: https://doi.org/10.30574/msabp.2025.16.2.0073

Abstract

Theis paper analyzes the role of p-toluenesulfonic acid (p-TsOH) in the treatment of chronic ulcers, highlighting its ability to remove bacterial biofilm and promote wound healing.

Clinical and experimental studies show that topical application of p-TsOH is effective and safe, with minimal and transient side effects, especially when used according to validated protocols.

Despite the promising results, the document emphasizes the need for further research and controlled trials to confirm the role of p-TsOH compared to other debridement strategies.

Keywords: Chronic wound; p-toluenesulphonic acid; p-TsOH; CDEB; p-TsOH therapeutic prospects

1 Introduction

Chronic ulcers represent a major clinical challenge, both in terms of their impact on patients' quality of life and the healthcare costs associated with their management. The presence of bacterial biofilms, antibiotic resistance and the difficulty in promoting healing are key factors in the chronicity of skin lesions [1][2][3][4][5][6][7][8][9][10][11][18]. In recent years, interest in chemical agents capable of effectively removing biofilm and reactivating healing processes has grown considerably. Among these, p-toluenesulfonic acid (p-TsOH) has attracted attention for its desiccant and anti-biofilm properties, with emerging applications in the clinical field [12].

This report presents a comprehensive analysis of the association between p-toluenesulfonic acid and chronic ulcers, structuring the evaluation as follows:

- chemical and industrial overview of p-TsOH [13][17]
- toxicological and regulatory assessment [14][15]
- literature review on effects on human health and the gastrointestinal system.
- clinical and experimental evidence on topical use in chronic wounds [19][20][21][22][23][24]
- proposed biological mechanisms [12]
- comparison with similar agents [16]
- safety of use, guidelines and practical recommendations ¡19]

* Corresponding author: Giampietro Bertasi

2 Chemical overview of p-toluenesulfonic acid (p-TsOH)

2.1 Chemical structure and physical properties

P-toluenesulphonic acid (p-TsOH, CAS 104-15-4) is an organic compound classified as an arylsulphonic acid. Its structure features a benzene ring with a methyl group and a sulfonate group (-SO3H) in the para position. The molecular formula is $C_7H_8O_3S$, with a molecular weight of 172.2 g/mol for the anhydrous form and 190.22 g/mol for the monohydrate. Physically, p-TsOH is a white, highly hygroscopic solid that dissolves readily in water (over 600 g/L), alcohols, and other polar solvents. The melting point ranges from 105-107°C (anhydrous) to 38°C (monohydrate). This compound is a strong acid with a pKa between -2.8 and -1.3, and it is completely dissociated in aqueous solution.
P-Toluene sulfonic acid is one of the few strong organic acids available in solid form, a characteristic that facilitates its handling and weighing in laboratories and industrial settings.

Properties	Value
Molecular formula	C7H8O3S
Molecular weight	172.2 g/mol (anhydrous)
Melting point	105-107°C (anhydrous)
Solubility in water	>600 g/L
pKa	-2.8 / -1.3
Appearance	White, hygroscopic solid
Density	1.24 g/cm3

Figure 1 p-TsOH chemical structure

2.2 Synthesis and purity

Industrially, p-TsOH is made by sulphonating toluene with concentrated sulphuric acid, then purifying it through recrystallisation to remove impurities like benzene-sulphonic acid and leftover sulphuric acid. The commercial product typically has a purity of 90% to 98%, with higher grades available for pharmaceutical and fine chemical synthesis.

2.3 Industrial and pharmaceutical uses

P-toluenesulphonic acid serves as a widely utilized acid catalyst in organic synthesis, primarily in esterification, transesterification, and acetalisation reactions, as well as a protecting agent for hydroxyl groups [3]. Its applications span several industries and include:

- ▪ Epoxy and amino resin production (polymerization catalyst)
- ▪ Paints and coatings manufacturing (cross-linking agent)
- ▪ Adhesive and plastic formulation
- ▪ Pharmaceutical intermediates (including the synthesis of antibiotics such as amoxicillin and doxycycline)
- ▪ Cosmetics (as a pH regulator and catalyst in ingredient synthesis)
- ▪ Food additives (used as a precursor)
- ▪ Explosives (as a chemical precursor)

The global market for p-TsOH continues to expand, with demand primarily driven by the pharmaceutical (40%), specialty chemical (35%), resin (30%), and coating (25%) sectors. Major producers include Stepan, Nanjing Ningkang Chem, Henan Newland Pharma, and Zu-Lon Industrial.

3 Toxicological properties, safety and regulatory assessments

3.1 Toxicokinetic and acute toxicity

Studies in animal models (rats, dogs) show that p-TsOH is rapidly absorbed and almost completely excreted in the urine, with a plasma half-life of approximately 75 minutes. The oral LD50 in rats is between 1,410 and 2,480 mg/kg, indicating low acute systemic toxicity. [6] .Data on dermal exposure are limited, but analogues such as hydrotropic salts show no systemic effects up to 1,600-2,000 mg/kg/day.

3.2 Repeated dose toxicity and carcinogenicity

Subchronic toxicity studies in rats (28-90 days) showed no systemic adverse effects at doses up to 500-1,000 mg/kg/day; high doses only caused local irritation and diarrhea. Genotoxicity and carcinogenicity tests (including those on analogue salts) were negative.

3.3 Reproductive and developmental toxicity

Screening tests on analogue salts (sodium p-toluenesulphonate) showed no effects on fertility, embryonic development or offspring growth up to 1,000 mg/kg/day.

3.4 Ecotoxicological data

P-TsOH and its salts dissolve easily in water, do not bioaccumulate (logKow -0.6/-2.4), and biodegrade quickly. Acute toxicity tests show LC50/EC50 values above 500–1,000 mg/L for fish, daphnia, and algae, suggesting minimal ecological risk.

3.5 Regulatory assessment

Major international agencies (Canada, OECD, ECHA) classify p-TsOH as a low-risk substance for human health and the environment under typical exposure conditions. In Canada, p-TsOH does not meet CEPA hazard criteria and no additional restrictions are required. In Europe, no specific occupational exposure limits have been set, but the use of personal protective equipment is recommended when handling dusts or concentrated solutions

3.6 Safety data sheets (SDS) and recommendations

SDSs classify p-TsOH as corrosive to the skin and eyes, with a risk of respiratory irritation if dust is inhaled [6]. The use of nitrile gloves, protective eyewear and suitable clothing is recommended. In case of contact, wash thoroughly with water and consult a doctor.

4 Effects on human health and the gastrointestinal system

4.1 Systemic exposure and gastrointestinal risk

There are no clinical studies documenting systemic or gastrointestinal adverse effects in humans due to exposure to p-TsOH at typical concentrations of use. Accidental oral ingestion of significant amounts may cause mucosal irritation, nausea, vomiting and, in extreme cases, chemical burns to the gastrointestinal tract, similar to other strong acids. However, the risk is considered low for controlled topical use.

4.2 Skin and local exposure

Topical application of p-TsOH at low concentrations (≤2%) in cosmetic products (face lotions, hair dyes, conditioners) has not shown any significant systemic or local adverse effects in post-marketing surveillance data. Skin exposure to higher concentrations may cause irritation, burning and, in the case of concentrated solutions, chemical burns.

4.3 Inhalation exposure

p-TsOH has negligible volatility, so inhalation exposure is minimal except when handling powders or aerosolised concentrated solutions.

4.4 Considerations for vulnerable populations

Regulatory assessments have included vulnerable subpopulations (children, pregnant women, individuals with skin conditions) without highlighting any specific risks under typical conditions of use.

5 Clinical and experimental evidence on the topical use of p-TsOH in chronic ulcers

5.1 Clinical rationale: biofilm and chronicity of ulcers

Bacterial biofilm is recognised as one of the main obstacles to the healing of chronic ulcers, due to its ability to protect microorganisms from antibiotics and the immune system. Effective removal of biofilm is considered a priority in the management of difficult wounds.

5.2 Observational clinical studies on p-TsOH (C-DEB)

An observational study at a diabetic foot clinic assessed the efficacy of p-TsOH (C-DEB) for managing chronic lower limb ulcers. Fifty-two patients with ulcers persisting for at least four weeks received weekly topical applications of 1–2 ml p-TsOH for 10 seconds, followed by a saline rinse and standard dressing. The primary endpoints included achievement of 100% granulation tissue formation at 16 weeks and at least a 50% reduction in initial ulcer size.

These data suggest that the application of p-TsOH promotes granulation tissue formation and the transition from 'chronic' to 'active' ulcer, favoring closure of the lesion in the following weeks.

5.3 Case studies and clinical series

Other case reports and clinical series document the efficacy of p-TsOH (C-DEB) in removing biofilm and reactivating healing in arterial, venous, diabetic and traumatic ulcers.

5.3.1 In vitro and in vivo experimental studies

In vitro microbiological tests have shown that p-TsOH is able to rapidly remove biofilms formed by clinical strains of MRSA, Pseudomonas aeruginosa and Proteus mirabilis, with a non-species- specific antibiofilm effect and persistence of the effect up to 72 hours after application [14]. The effect is attributed to the denaturation and dehydration of the extracellular matrix of the biofilm.

5.4 Safety of topical use

In all available clinical studies, topical application of p-TsOH was well tolerated, with transient pain during application (intensity 1-5/10, duration 1-10 minutes) and no serious adverse reactions or damage to surrounding tissues. No sensitization or allergy phenomena were observed.

6 Proposed biological mechanisms

6.1 Desiccant and denaturing action

The mechanism of action of p-TsOH in chronic ulcers is mainly physical-chemical: thanks to its high hygroscopicity and acidity, the acid induces rapid dehydration of the biofilm and necrotic tissues, denaturing proteins and polysaccharides in the extracellular matrix. This process leads to coagulation and separation of the devitalized material from the wound bed, exposing the vital surface and promoting the formation of granulation tissue.

6.2 Biofilm removal and inflammation reduction

Complete removal of the biofilm reduces the bacterial load, interrupts the chronic stimulation of inflammatory mediators (e.g. interleukins, TNF-α, metalloproteases), and allows the resumption of cell proliferation and angiogenesis processes. The effect is independent of the bacterial species, as it acts on the matrix and not on the microorganisms themselves.

6.3 Respect for healthy tissues

Unlike many broad-spectrum antiseptics, low concentrations of p-TsOH applied for controlled periods seem to target only dead tissue and biofilm, while leaving healthy tissue unharmed. This lowers the risk of cell toxicity and helps support the healing process.

6.4 Comparison with other agents

Other dehydrating and acidic agents (methanesulphonic acid, phenolsulphonic acid, acetic acid) share similar mechanisms, but p-TsOH stands out for its efficacy, ease of use and favourable safety profile.

7 Comparison with similar agents and alternatives for biofilm removal

7.1 Strong and dehydrating acids

Methane sulfonic acid (MSA): It exhibits rapid desiccant properties, with sufficient energy production to destroy biochemical bonds in infected tissues.

Clinical studies document its effectiveness in removing biofilm and promoting granulation, with transient pain as the only significant adverse effect.

Phenolsulfonic acid: Studies in dentistry and chronic wounds suggest efficacy in removing biofilm, but with greater causticity than p-TsOH and MSA.

Acetic acid (1%): An alternative for resistant Pseudomonas aeruginosa infections, but associated with pain and risk of tissue necrosis.

7.2 Traditional antiseptics

Povidone-iodine, chlorhexidine, PHMB, hypochlorite: Widely used for wound cleansing, they have variable efficacy against biofilm and a risk of cytotoxicity to healthy tissue, especially at high concentrations or in cases of prolonged exposure.

Surfactants and chelating agents: Used to facilitate mechanical removal of biofilm, often in combination with other agents.

7.3 Advantages and limitations of p-TsOH

7.3.1 Advantages

- Fast-acting and non-species-specific.
- Proven effectiveness in removing biofilm and promoting granulation.
- Favorable safety profile when used correctly.
- Ease of application and standardizable protocol.

7.3.2 Limitations

- Transient pain during application
- Need for thorough washing and control of contact times
- Lack of large-scale randomized controlled trials

8 Safety of topical use: dosages, application times, local adverse effects

8.1 Application protocols

Apply 1–2 ml of p-TsOH (C-DEB) directly to the wound bed for 10–15 seconds, then rinse thoroughly with saline and remove dehydrated material with sterile gauze. If residue remains, perform additional mechanical debridement.

8.2 Local adverse effects

Transient discomfort during application is the most commonly observed adverse effect, with an intensity ranging from 1 to 5 out of 10 and duration between 1 and 10 minutes. The use of topical anesthesia decreases procedural discomfort and enhances contact time. There have been no documented cases of healthy tissue necrosis, allergic reactions, or sensitization.

8.3 Practical recommendations

- Use topical anesthesia when possible.
- Limit contact time to 10-15 seconds.
- Wash thoroughly after application.
- Monitor for pain, redness, signs of infection or necrosis.
- Monitor for pain, redness, signs of infection or necrosis.

8.4 Clinical guidelines, recommendations and future prospects

The primary guidelines suggest that removing biofilm should be a key goal in treating chronic ulcers. This can be done with mechanical, surgical, autolytic, enzymatic, or chemical debridement. Using chemical agents against biofilm is seen as a promising approach, particularly when standard treatments have not been successful.

8.5 Role of p-TsOH and analogues

P-TsOH and analogues such as MSA represent a new frontier in chemical debridement, thanks to their ability to rapidly remove biofilm and reactivate healing [15]. Current evidence, although limited to observational studies and case series, suggests a favourable efficacy and safety profile.

8.6 Practical recommendations for clinicians

- Consider the use of p-TsOH in refractory chronic ulcers, after assessing contraindications
- Supplement chemical treatment with mechanical debridement (WBP) and standard wound management (TIME framework).
- Inform the patient about possible side effects and obtain informed consent.
- Monitor clinical response and adjust the frequency of applications based on the evolution of the lesion.
- Follow validated and updated protocols, participating in controlled clinical trials when available.

8.7 Limitations of the literature and need for research

The quality of available studies is limited by small sample sizes, lack of control groups, and short-term follow-up. Large-scale randomized controlled trials are needed to confirm the efficacy and safety of p-TsOH compared to other debridement strategies.

8.8 Occupational and environmental risk assessment

The production and industrial use of p-TsOH are regulated by national and international regulations. Occupational risk is considered low if personal protective measures and safe handling procedures are adopted. Environmental risk is negligible due to rapid biodegradability and low bioaccumulation potential.

8.9 Commercial products and market prospects

Products based on p-TsOH and analogues are available for clinical use in Europe and other markets, with specific indications for the chemical debridement of chronic ulcers and biofilm [15]. The market is expanding, driven by demand for innovative solutions for the management of difficult wounds.

9 Conclusions

P-Toluene sulfonic acid is a promising agent for treating chronic ulcers due to its effective biofilm removal and granulation promotion. Evidence shows good efficacy and safety, especially when used with established protocols and wound care methods. However, research is limited and larger studies are needed to confirm its clinical role. Toxicological and regulatory reviews indicate low systemic and environmental risk, but pain management and local contraindications must be addressed for broader use.

9.1 Key take-home messages

- p-TsOH is a strong, solid, highly soluble and hygroscopic acid, widely used as a catalyst and chemical debridement agent
- Clinical evidence suggests efficacy in removing biofilm and promoting the healing of chronic ulcers, with a good local safety profile
- The mechanism of action is physical-chemical (dehydration, denaturation of the biofilm matrix), independent of the bacterial species
- Transient pain during application is the most common side effect, which can be managed with topical anesthetics and control of contact times.
- The literature is promising but limited; randomised controlled trials are needed to define the role of p-TsOH compared to other strategies
- Regulatory assessments support low systemic and environmental risk, with standard safety recommendations for topical use.

Compliance with ethical standards

Disclosure of conflict of interest

The Authors have no actual or potential conflict of interest in relation to this paper.

References

[1] Caroline Dowsett, Kimberly Bain, Christoffer Hoffmann, Mary R .Brennan, Alessandro Greco, Tonny Karlsmark, David Keast, Marcelo Ruettimann Liberato de Moura, Jose L. Lázaro-Martínez, Karl-Christian Münter, Terry Swanson, Hubert Vuagnat and Mark Bain"The Wound Care Pathway – an evidence-based and step-by-step approach towards wound healing"Wounds International 2021 | Vol 12 Issue 3 | ©Wounds International 2021 | www.woundsinternational.com

[2] Malone M. Bjarnsholt T, McBain AJ et al (2017) The prevalence of biofilms in chronic wounds: a systematic review and meta-analysis of published data. J Wound Care 26(1): 20–5

[3] Martinengo L, Olsson M, Bajpai R et al (2019)Prevalence of chronic wounds in the general population: systematic review and meta-analysis ofobservational studies. Ann Epidemiol 29: 8–15

[4] Annabel z. Shen, Mohamad Zhaka, Mahmoud Gannoum, Stephen K. Tyring Biofilms and Chronic Wounds: Pathogenesis and Treatment Options - MDPI. Clin. Med. 2025, 14(21), 7784; https://www.mdpi.com/2077-0383/14/21/7784

[5] Penesyan, A.; Paulsen, I.T.; Kjelleberg, S.; Gillings, M.R. Three faces of biofilms: A microbial lifestyle, a nascent multicellular organism, and an incubator for diversityNpj Biofilms Microbiomes 2021

[6] A Mendoza, R.; Hsieh, J.C.; D Galiano, R. The Impact of Biofilm Formation on Wound Healing. In Wound Healing—Current Perspectives; Dogan, H.K.Ed.; IntechOpen: London, UK, 2019; Available online: https://www.intechopen.com/books/wound-healing-current-perspectives/the-impact-of-biofilm-formation-on-wound-healing (accessed on 8 Nov 2025).

[7] Liu, Y.; Long, S.; Wang, H.; Wang, Y. Biofilm therapy for chronic wounds Int. Wound J. 2024, 21, e14667.

[8] Haesler, E.; Swanson, T.; Ousey, K.; Carville, K. Clinical indicators of wound infection and biofilm: Reaching international consensus J. Wound Care 2019, 28, s4–s12.

[9] Wu, Y.K.; Cheng, N.C.; Cheng, C.M. Biofilms in Chronic Wounds: Pathogenesis and Diagnosis. Trends Biotechnol. 2019, 37, 505–517

[10] Versey, Z.; da Cruz Nizer, W.S.; Russell, E.; Zigic, S.; DeZeeuw, K.G.; Marek, J.E.; Overhage, J.; Cassol, E. Biofilm-Innate Immune Interface: Contribution to Chronic Wound Formation. Front. Immunol. 2021, 12, 648554

[11] Gajula, B.; Munnamgi, S.; Basu, S. How bacterial biofilms affect chronic wound healing: A narrative review Int. J. Surg. Glob. Health 2020, 3, e16. Giampietro Bertasi The use of p-toluensolfonic acid to manage biofilm effectively https://doi.org/10.53430/ijsru.2022.4.2.0187

[12] p-Toluenesulfonic acid https://www.chemicalbook.com/ChemicalProductProperty_EN_CB1771154.htm

[13] Safety Data sheet Revision Date 02/07/2023 Version 8. https://www.sigmaaldrich.com/GB/en/sds/sigma/t3751

[14] p-toluensulfonoc acid 5043 https://www.cdc.gov/niosh/docs/2003-154/pdfs/5043.pdf

[15] Comparing methods of debridement for removing biofilm. https://www.woundcare-professional.com/content/research-article/comparing-methods-of-debridement-for- removing-biofilm

[16] P-Toluenesulfonic Acid Market Size & Trends 2025-2033. https://www.globalgrowthinsights.com/market-reports/p-toluenesulfonic-acid-market- 108176

[17] Therapeutic wound and skin cleansing: Clinical evidence and recommendations.Int'l Consensus Document, Wounds Internationalhttps://woundsinternational.com/wp-content/uploads/2025/03/IWII_2025_Wound-cleansing- web.pdf

[18] Mariana Peroni, Marlene Dall'Alda, Sergio Minervini, Ornella Pancheri, Francesca Baratto, Stefano Bonvini , Riccardo Pertile, Giampietro Bertasi and Francesco Fantin The use of p-toluenesulfonic acid in the removal of biofilm in chronic ulcersInternational Journal of Scientific Research Updates, 2024, 08(02), 077–089

[19] Giampietro BertasiThe use of p-toluensolfonic acid to manage biofilm effectively (C-deb) International Journal of Scientific Research Updates, 2022, 04(02), 201–206

[20] Mariana Peroni, Renzo Girardello, Ornella Pancheri, Stefano Bonvini and Giampietro BertasiHard-to-heal wounds: A new biofilm treatment with a novel desiccantMagna Scientia Advanced Biology and Pharmacy, 2021, 03(01), 058–063

[21] Giampietro Bertasi, Mariana Peroni and Lara Rugolotto The use of p-toluensulfonic acid (PTSA) to eradicate the biofilm in chronic ulcerMagna Scientia Advanced Biology and Pharmacy, 2025, 15(02), 089-094

[22] Cogo A. et Al.A desiccation compound as a biofilm- and necrosis-removing agent: a case seriesJournal of Wound Care, Vol 31, No 10, Oct 2022

[23] Various AuthorsA new option for chemical debridement Journal of Wound Care Vol 32, Issue 3 (Supp 4) , Mar 2023