Volume - 14 | Issue - 06 | June - 2024 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Surgery

FERACRYLUM FOR WOUND HEALING: A REVIEW

Dr. Sandeep Tiwari	HOD, Trauma, King George's Medical University, Lucknow, India.
Dr. Sudhir Dikshit	HOD, Dept of Surgery, V.N. Desai Hospital, Mumbai, Maharashtra, India.
Dr. Ritu Nandanikar	Senior Consulting Surgeon, V.N.Desai Hospital, Mumbai, Maharashtra, India.
Dr. Suresh Menon	Medical Director, Medical Affairs, Themis Medicare Ltd.
Dr. Balaji More	Medical Affairs, Themis Medicare Ltd.
Dr. Smita Kamtane*	Medical Affairs, Themis Medicare Ltd. *Corresponding Author
Dr. Roheet Rathod	Medical Affairs, Themis Medicare Ltd.

ABSTRACT

Introduction: Our skin is constantly exposed to the environment and bears the brunt of external injuries as wounds. Wound bleeding and infection are the critical factors determining the prognosis of wound healing. Hemostatic agents, both local and systemic, play vital roles in controlling bleeding. Local agents like collagen, gelatin, cellulose, and thrombin directly target the bleeding site, promoting clot formation and platelet aggregation. Systemic agents, on the other hand, enhance the body's natural clotting mechanisms. Interventions such as wound dressings and antimicrobial agents support the body's healing processes. Feracrylum, a local hemostatic agent, not only controls bleeding but also exhibits antimicrobial properties and absorbs moisture, fostering an optimal healing environment. Its safety and tolerability further endorse its utility in promoting efficient skin regeneration. **Methods:** This review summarizes the preclinical and clinical evidence for feracrylum as a wound healing agent in diverse clinical settings. Data from *in vitro* experiments, animal models, and phase II and III clinical trials are integrated, providing a comprehensive analysis of feracrylum's effectiveness, safety, and tolerability across various wound types. Systematic searches of reputable databases like PubMed and Google Scholar ensured the inclusion of up-to-date and reliable literature. **Key Findings:** Feracrylum exhibits a unique blend of hemostatic, antimicrobial, and hygroscopic properties, positioning it a promising agent for wound healing in surgical and traumatic settings compared to conventional dressings. Its iron-polyacrylate complex promotes rapid hemostasis by triggering platelet aggregation and coagulation. The broad-spectrum antimicrobial activity effectively combats wound infections, while the hygroscopic nature optimizes the wound environment by absorbing exudate and facilitating granulation tissue formation. **Conclusion:** Feracrylum, with its iron-polyacrylate complex, represents a significant advancement in wound healing. Its multifaceted properties, including hemostatic, antimicrobial, and hygroscopic characteristics, make it a valuable tool across diverse clinical settings for wound management.

KEYWORDS : Burns, Feracrylum, Trauma, Wound healing

BACKGROUND

Wound And Its Healing Process

There are a variety of wounds that may cause traumatic bleeding such as incisions, lacerations, abrasions, hematomas, puncture wounds, contusions, and post-burn injuries. Hence, rapid hemostasis is required to avoid blood loss, infection; and to promote wound healing. During injury, the epidermal layer of skin gets ruptured and the underlying dermis is exposed to the atmosphere. Skin and soft tissue infections during wounds are the most common infections in humans. *Staphylococcus aureus*, *Streptococcus pyogenes,* and *Escherichia coli* are the main pathogens observed in chronic wounds (Bowler PG and Duerden BI 2001). Figure 1 illustrates the interconnected phases of wound healing: hemostasis (clot formation), inflammation (immune response), proliferation (tissue regeneration), and remodeling/ maturation (scar formation) (Naseri E 2022).

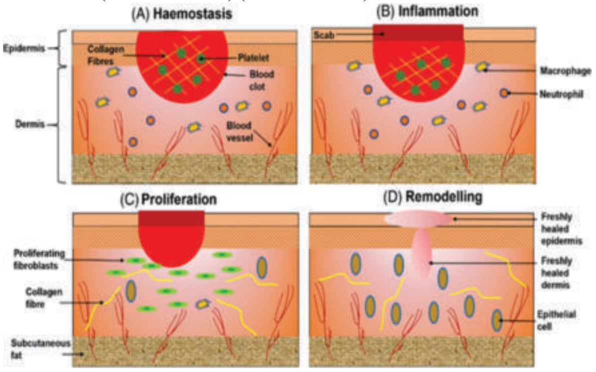

Figure 1: Schematic representation of the cutaneous wound healing (Deng X et al 2022)

Drugs Used In Wound Healing

Hemostatic agents: Hemostasis is the body's natural mechanism for stopping blood loss after injury. It involves a complex interplay of vascular constriction, platelet aggregation, and clot formation. When this process is impaired or insufficient, hemostatic agents play a crucial role in controlling bleeding and promoting wound healing. A diverse range of hemostatic agents are available, which include gelatin sponges, collagens, fibrin sealants, and active thrombin preparations, etc., each with its own strengths and weaknesses.

Polymers: Naturally occurring polymers offer numerous advantages for wound dressing applications. Their biocompatibility, biodegradability, and diverse therapeutic properties hold significant potential for improved wound healing and infection control. Studies suggest effectiveness of chitosan in controlling bacteria and promoting wound healing, particularly in burn wounds (Deng X et al 2022). High absorbency and ability of alginate to form a gel create a moist environment promoting healing and reducing pain (Yu P and Zhong W 2021). Collagen is a naturally occurring polymer provides a scaffold for tissue regeneration and supports wound closure.

Antimicrobial agents: Broad-spectrum agents, like polyvinylpyrrolidone-iodine (PVP-I), are widely used due to their effectiveness against bacteria, fungi, and viruses. They release iodine slowly, providing sustained antimicrobial activity with minimal tissue irritation. Another broad-spectrum agent, chlorhexidine, has potent activity against bacteria and some fungi. It is often used pre-operatively and for skin decontamination due to its residual activity. A few other similar agents include octenidine, and polyhexanide, bisphenols triclosan and hexachlorophene, silver compounds, benzalkonium chloride, hydrogen peroxide, etc. (Bigliardi P et al 2017).

Among all these agents, feracrylum is one of the most frequently used hemostatic and antiseptic agent. Feracrylum is a water-soluble mixture of incomplete iron salt of polyacrylic acid. It is biocompatible, biodegradable, non-toxic and non-allergenic. It is not only hemostatic but also anti-infective against several gram-positive and gram-negative pathogenic bacterial and fungal strains thus decreasing the risk of wound infection (Table 1). It has a favorable safety profile as it has no systemic adverse effects and is economical (Feracrylum Prescribing information).

Table 1: Comparative Activity Of Topical Agents Used In The Management Of Wound Healing

Topical agents applied for wound healing	Anti-bacterial	Anti-fungal	Hemo static	Hygros copic
Povidone-Iodine	√	√	-	-
Feramycetin	√	-	-	-
Neomycin+ Polymyxin B sulphate + Zinc Bacitracin	√	√	-	-
Silver sulphadiazine	√	√	-	-
Feracrylum	√	√	√	√

Introduction Of Feracrylum

Ferric hydroxide colloid, with its demonstrated ability to promote clot formation and control bleeding, paved the way for the development of feracrylum in 1992. This hemostatic agent is specifically designed to aid in managing bleeding during surgical and medical procedures, and has been in use for over 25 years.

Mode Of Action

The hemostatic effect of feracrylum is due to the formation of a synthetic complex with plasma protein mainly albumin. This forms a whitish film-like structure. This whitish film creates a physical barrier that reduces oozing from the wound site and protects the wound from external contamination exerting a hemostatic action. Due to its high molecular weight, feracrylum is not absorbed systemically and has no adverse effects on the liver, kidney, adrenals, cardiovascular, and hemostatic systems. Based on various *in vitro* and clinical studies, feracrylum is also used as an antimicrobial agent reducing the risk of wound infection (Feracrylum Prescribing information).

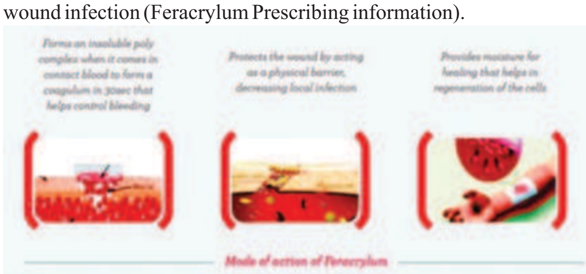

Figure 2: Mode Of Actions Of Feracrylum

An *in vitro* study was conducted to assess the mechanism of action (bactericidal activity) of 1% feracrylum against *E coli* and *S aureus*. The binding of feracrylum to protein creates a gelling effect. Aggregation of bacteria was observed due to the interaction of feracrylum with cell wall proteins. Thus, feracrylum affected the cell wall of *E coli.* A sporicidal activity was also noted with feracrylum (SPC-BKSC study report 2001).

Feracrylum Has Three Mechanisms Of Action For Wound Care

Hemostasis at the wound site is the prerequisite to initiating wound healing process. The wound infection caused by microorganisms is one of the common reasons for the occurrence of purulent septic complications delaying the wound healing process. Hence, any topical agent having hemostatic, antimicrobial, and hygroscopic properties is ideal for faster wound healing. Considering that feracrylum demonstrates the above three properties, it could be an excellent option for Surgeons like general surgeons, ENT surgeons, pediatric urologists, oncologic surgeons, dental surgeons, orthopedic surgeons, and even general practitioners to treat wounds in their daily clinical practice.

Hemostatic Action:

Feracrylum when in contact with blood albumin, forms a biodegradable water-insoluble synthetic complex creating a large rubbery clot that forms a physical barrier on the wound surface and stops capillary bleeding and oozing in 2-3 minutes. It is non-allergic with no systemic absorption (Feracrylum Prescribing information, Chauhan MK 2017). It does not interfere with the normal clotting process.

Antimicrobial Action:

Feracrylum is an anti-infective against many gram-positive, gram-negative pathogenic bacteria and fungi (Table 2) (Feracrylum Prescribing information, Chauhan MK 2017).

Table 2: Anti-microbial Activity Of Feracrylum

Gram-positive organisms	Gram-negative organisms	Fungi
Staphylococcus aureus	*E. coli*	*Microsporum*
Streptococcus pyogenes	*Shigella dysenteriae*	*Candida albicans*
Streptococcus haemolyticus	*Salmonella typhi*	*Trichoderma viride*
Pneumococcus Type-1	*Proteus vulgaris*	
Anthropoid bacillus or spores	*Pseudomonas aeruginosa*	
Corynebacterium diphtheria		

Hygroscopic Action:

It is well known that wound healing under moist wound conditions is more effective as it prevents dehydration, and enhances angiogenesis and collagen formation (Field FK and Kerstein MD 1994). Feracrylum is hygroscopic and prevents dehydration of the wound, which in turn promotes quicker wound healing. In addition, its hygroscopic property facilitates easy removal of dressings (Feracrylum Prescribing information, Chauhan MK 2017).

Feracrylum Formulations

Optimizing wound healing requires appropriate dosage forms and formulations that deliver essential therapeutic agents and create a conducive environment for tissue regeneration. Common types of formulations include solid formulations like powders and dressings; semisolid formulations like gels, ointments, and creams which offer better wound contact and sustained release of medications; and solutions used for irrigation and debridement of the wound, removing debris and in turn helps in preventing infection.

Gels, possess specific properties beneficial for wound healing like high water content, exudate absorption, cooling sensation, and ease of application and removal. Gels are usually non-oily and can be spread easily. This makes them easier to apply and causes less pain when removing them. (Saghazadeh S et al 2018, Sarabahi S 2012, FDA 2016).

Non-clinical Experience

Spectrum Of Activity

In Vitro Studies

A number of *in vitro* studies have been conducted to assess the antimicrobial and anti-fungal properties of feracrylum.

An *in vitro* comparative study assessed the minimum inhibitory concentration (MIC), bacteriostatic, bactericidal, fungistatic, and fungicidal concentrations of feracrylum and povidone-iodine against *S. aureus*, *S. pyogenes, C. diphtheriae, S. typhi*, *S. dysenteriae*, *P. aeruginosa, P. vulgaris, E. coli, T. viridae* and *C. albicans.* Feracrylum exhibited a lower MIC, indicating superior bacteriostatic and bactericidal activity, against *S. aureus, S. pyogenes, and C. diphtheriae* compared to povidone-iodine. For *S. typhi, S. dysenteriae, P. aeruginosa, P. vulgaris, E. coli, T. viridae, and C. albicans*, the MICs of both feracrylum and povidone-iodine were comparable, demonstrating similar antimicrobial efficacy.

While povidone-iodine remains a well-established antimicrobial agent, feracrylum demonstrates comparable or even enhanced efficacy against some key bacterial pathogens, highlighting its potential as an alternative or complementary antimicrobial (CBPRC report 1999a). Another *in vitro* study was conducted where *P. aeruginosa* cultures were exposed to either 1% feracrylum or 1% povidone-iodine for 7 and 15 days. Both feracrylum and povidone-iodine demonstrated bactericidal activity against *P. aeruginosa* at day 7, significantly reducing bacterial viability. After 15 days, feracrylum maintained its bactericidal effect, while povidone-iodine shifted to a bacteriostatic effect. This suggests potentially lower persistence of antibacterial activity for povidone-iodine over longer durations. Furthermore, iodine sublimation from povidone-iodine may affect its sustained antibacterial efficacy (CBPRC report 1999b).

In vitro cultures of *P. acnes* and *S. epidermidis* were exposed to varying concentrations of feracrylum (0.02% to 2%) and povidone-iodine (0.1% to 2%) using the direct contact method. Bacterial viability was then evaluated to determine the minimum bactericidal concentration (MBC), the lowest concentration at which bacterial killing occurs. The MBC of feracrylum against *P. acnes* was significantly lower than povidone-iodine, at 0.06% compared to 0.4%. Both feracrylum and povidone-iodine demonstrated similar potency against *S. epidermidis*, with MBCs of 0.04% for feracrylum and 0.1% for povidone-iodine. These findings suggest potential advantages of feracrylum for topical applications targeting *P. acnes*-related skin conditions. (CBPRC report on skin bacteria). In another experiment a culture of *E. coli* was incubated for 5 days and then exposed to a 1% feracrylum solution after which, the extent of bacterial lysis was determined. This resulted in the lysis of 95% of the *E. coli* population. This indicates significant bactericidal activity of feracrylum against this common Gram-negative pathogen (CCMB study report 1999). Similar results were obtained where the bactericidal activity of 1% feracrylum was assessed against *E coli*. Feracrylum affects the cell wall of *E coli.* Additionally, in this study, a sporicidal activity was noted with feracrylum (SPC-BKSC study report 2001).

In a study, feracrylum's activity was assessed against a range of both Gram-positive and Gram-negative bacterial strains, as well as two fungal species. The study likely employed quantitative methods like MIC determination or bacterial/fungal viability assays to evaluate the efficacy of feracrylum and povidone-iodine. Feracrylum demonstrated efficacy against the bacterial strains, suggesting its potential for diverse antibacterial applications. Feracrylum exhibited fungistatic activity against *Candida albicans* and *Trichophyton viridae.* This study suggests that feracrylum possesses broad-spectrum antibacterial and fungistatic activity, comparable to povidone-iodine in overall efficacy. This highlights its potential as an alternative or complementary antimicrobial agent with potential applications across various fields (Bhagwat AM 2001).

An *in vitro* study was conducted where cultures of *S. aureus, S. epidermidis, E. coli, P. aeruginosa, P. mirabilis and C. albicans* were exposed to a range of feracrylum concentrations (0.5% to 2.0%). The MIC was then determined for each microorganism, representing the lowest concentration at which bacterial growth was inhibited (bacteriostatic) or completely stopped (bactericidal). Feracrylum exhibited activity against all six tested microorganisms, showcasing its potential as a broad-spectrum antimicrobial agent. At concentrations between 0.5% and 1.0%, feracrylum primarily displayed bacteriostatic activity, Higher concentrations (0.5% to 2.0%) demonstrated bactericidal effects, (TCL-FA study report 1999). A similar *in vitro* study explored the lowest concentration of feracrylum that can inhibit fungal growth (fungistatic), and its minimum fungicidal concentration (MFC) against *C. albicans*, *Aspergillus brasiliensis*, *Trichophyton rubrum*, and *Trichophyton verrucossum.* Feracrylum exhibited the lowest MIC and MFC values (1.25% and 2.25%, respectively) against *C. albicans*, suggesting high susceptibility and potential effectiveness in combating candidiasis. The higher MIC and MFC values (2.25% and 3.00%, respectively) for *A. brasiliensis* indicate a slightly lower susceptibility compared to *C. albicans*. Both *T. rubrum* and *T. verrucossum* showed similar susceptibility patterns, with MICs of 1.25% and 1.50% and MFCs of 2.25% and 2.50%, respectively. This study demonstrates the promising fungicidal efficacy of feracrylum against diverse fungal pathogens, with variations in susceptibility observed across different species (ARI Report-2018).

Toxicity In Animals

In acute toxicity studies (14 Days), feracrylum did not show skin reaction or mortality in animals. In this study, the lethal dose of feracrylum was greater than 2000 mg/kg body weight. Other acute toxicity studies conducted on mice and rats did not show death in study animals. In this study, the lethal dose was greater than 3500 mg/kg body weight. These studies concluded that feracrylum has good tissue tolerability, for human application. In subacute studies (6 months), daily application of feracrylum did not lead to any skin toxicity or other side effects. The daily intra-peritoneal injection did not alter the condition of internal organs, develop tumors, or show significant changes in liver function. During this study, urine tests did not show any change in urine parameters. Neither did it show a local irritant effect after intra-abdominal and local application, nor affect hematological parameters. These findings suggest that feracrylum possesses good tissue tolerability and may be safe for human application (Feracrylum Prescribing Information).

Efficacy And Safety In Animals

Several animal studies have investigated the effect of feracrylum on wounds. Nivaskar *et al* investigated the wound healing efficacy of 3% feracrylum gel compared to povidone-iodine in a Sprague Dawley rat model over 24 days. Feracrylum-treated wounds displayed significantly faster and greater reductions in wound area. Microscopic examination of tissue sections supported the macroscopic observations. Rats treated with feracrylum gel exhibited greater cellular proliferation, collagen deposition, and granulation tissue formation, indicating accelerated wound healing processes. This study suggests that 3% feracrylum gel has superior wound healing activity compared to povidone-iodine in a rat model (Nivaskar M *et al* 2006).

Sinulingga S *et al* compared the hemostatic activity of an ethanol extract of Piper betle leaves (with ethanol) and a 1% feracrylum solution in a male mouse model. Male mice were subjected to a standardized tail-transection method to induce bleeding. Mice were then randomly assigned to receive either the Piper betle extract or the feracrylum solution at the designated site of injury. Bleeding time, a key indicator of hemostatic efficacy, was measured and compared between the two groups. The study suggests that both an ethanol extract of Piper betle leaves and a 1% feracrylum solution exhibit similar hemostatic effects in a male mouse model (Sinulingga S *et al* 2017).

Tsamarah A *et al* evaluated the dose-dependent effectiveness of feracrylum (1% and 4%) in controlling bleeding after gingival incisions in Wistar rats compared to a control group. Notably, the 4% feracrylum group exhibited a significantly faster cessation of bleeding (50 seconds) compared to the 1% feracrylum group (103 seconds). This suggests a dose-dependent hemostatic effect of feracrylum within the tested range. The average bleeding time in the control group without hemostatic agents was 221 seconds, highlighting the substantial hemostatic efficacy of both feracrylum concentrations. These findings suggest potential clinical applications of feracrylum in dental procedures requiring effective blood control (Tsamarah A *et al* 2022).

Ramachandra S *et al* compared the efficacy of carbazachrome salicylate, snake venom, and feracrylum in reducing hemorrhage associated with hemorrhagic enteritis in bonnet monkeys (*Macaca radiata*). In this study, carbazachrome salicylate (1 ml/5 kg body weight, intramuscularly, twice daily); snake venom (1 ml/5 kg body weight, intramuscularly, twice daily); and feracrylum (2 ml/kg orally, twice daily) was given to 60 bonnet monkeys (n=20 each). Study suggests that all three hemostatic agents effectively reduce hemorrhage in monkeys. Feracrylum demonstrated the most significant reduction (90%), followed by snake venom (50%) and carbazachrome salicylate (40%). In another study by Ramachandra S *et al* with a similar design, the reduction in hemorrhage was 100% after 18 h in monkeys given 2 or 3 ml feracrylum/kg. Feracrylum at 2 ml/kg body weight was an effective treatment for hemorrhagic enteritis in bonnet monkeys (Ramachandra S *et al* 2000).

Clinical Evidence

Feracrylum in acute wounds

Acute wounds are sudden disruptions in skin integrity caused by traumatic events. These events can manifest as various types, including cuts, abrasions, lacerations, and punctures. Topical gels find application in the management of acute wounds by facilitating healing, minimizing infection risk, and maintaining a humid microenvironment, all of which are essential for optimal tissue regeneration.

Kantharia C *et al.* conducted a randomized, prospective, active-controlled, multicenter trial across India at three major institutions (GSMC & KEMH, Mumbai; LTMMC, Mumbai; and Safdarjung Hospital, New Delhi) to compare the efficacy of 1% feracrylum gel and 5% povidone iodine in the treatment of chronic non-healing wounds, post-operative infected wounds, and burns. The study included 274 patients and demonstrated superior outcomes with feracrylum gel. Patients treated with 1% feracrylum gel exhibited a significant decrease in wound discharge, decreased peripheral edema surrounding the wound and lowered the bacterial count compared to povidone iodine 5%. Due to the hygroscopic properties of feracrylum gel, a moist wound environment is maintained conducive to healing. Also, the absence of systemic or local adverse events suggests excellent tolerability (Kantharia C *et al* 2008).

A nationwide post-marketing surveillance study by Rao AM and Patel RV evaluated the safety and efficacy of feracrylum gel in diverse wound types. This multi-center study involving 172 clinicians across India included 1204 patients with various acute and chronic wounds. Around 90% of patients achieved good to excellent wound healing within a 3-month period. This suggests that feracrylum gel effectively promotes tissue regeneration across a wide range of wound etiologies. No adverse local skin reactions were reported, indicating minimal or no irritation potential. The non-sticky and odorless properties of feracrylum gel were well-received by patients. Additionally, it did not cause discomfort during dressing changes, potentially leading to higher adherence to treatment protocols (Rao AM and Patel RV 2004).

Chaudhary MP conducted an open-label, multicenter, single-arm clinical trial enrolling 26 patients to assess the efficacy and safety of 3% feracrylum gel in treating lacerated wounds. At baseline, 50% of patients exhibited heavy to moderate wound discharge. Following feracrylum treatment for 2 weeks, discharge completely ceased in 88.5% of patients and remained absent in all cases by weeks 4 and 5. This improvement was statistically significant ($p < 0.05$). Bacterial counts demonstrably decreased in all patients from baseline to the end of the 5th week. No serious adverse events were reported and none of the patients required withdrawal due to adverse reactions. Feracrylum gel had higher compliance due to its suitability for wound and burn dressing (Feracrylum 3%w/w Clinical study report).

Feracrylum In Surgical Wounds

Major surgical procedures are often life-saving interventions, but the associated wounds carry increased risk of complications that can significantly impact patient outcomes.

Tonsillectomy is a very common procedure, associated with hemorrhage and pain. Tonsillectomy is associated with morbidity in terms of fever, poor oral intake and increased duration of hospitalization. Sathyaki D *et al*. demonstrated feracrylum, as a potential alternative for managing post-operative hemorrhage (POH) in tonsillectomy. They compared the effects of adrenaline and feracrylum in preventing primary POH (occurring within 24 hours) after tonsillectomy. Remarkably, the feracrylum group experienced no instances of primary hemorrhage, while the adrenaline group did ($p < 0.001$). In the adrenaline group, surgeons needed to ligate bleeding vessels in 12 cases, while no ligations were required in the feracrylum group ($p < 0.001$). This indicates feracrylum's superior ability to control capillary bleeding at the source. Additionally, feracrylum's antimicrobial properties may potentially reduce the incidence of secondary POH (occurring beyond 24 hours) due to bacterial infection in the healing wound (Sathyaki D *et al* 2017).

Similarly, Valse D *et al*. investigated the effects of 1% feracrylum on blood loss, surgery duration, and recovery in traditional cold steel tonsillectomy. Results indicate significant reduction in blood loss ($p < 0.001$) and shorter surgical times ($p < 0.001$) with feracrylum compared to controls. Patients treated with feracrylum recovered faster, returning to normal activities within 2-3 days vs. 3-5 days in the control group. This suggests feracrylum's potential in improving surgical outcomes and patient comfort without significant adverse effects. (Valse D *et al* 2021).

Oronasopharyngeal stricture, a narrowing of the passage between the mouth and nose, can significantly impact a child's breathing, swallowing, and speech. Surgery to correct this condition often involves manipulating delicate tissues, increasing the risk of bleeding. Excessive cautery, a common hemostatic technique in such surgeries, can inadvertently contribute to scar tissue formation and worsen the stricture. A recent study explored the potential of feracrylum gel 3% as a novel hemostatic agent in pediatric oronasopharyngeal stricture surgery. The results offer promising insights for improved surgical outcomes and reduced long-term complications. By minimizing tissue damage and potentially reducing scarring, this novel approach may contribute to better breathing, swallowing, and speech, leading to enhanced quality of life for these young patients (Shenoy VS et al 2023).

Feracrylum In Burn Wounds

Burns, ranging from superficial first-degree to deep fourth-degree involving underlying tissues, presents a spectrum of complex injuries demanding multifaceted management. Moenadjat *et al*. conducted an open-label, randomized, controlled study to investigate the efficacy and safety of feracrylum compared to silver sulfadiazine in second-degree burns involving both epidermis and dermis. They evaluated these topical agents applied to opposite sides of burned areas for 11 days. Compared to silver sulfadiazine, feracrylum demonstrated faster wound closure as evidenced by a reduced raw surface area on days 7 and 11, suggesting its superior re-epithelialization potential. During dressing changes, subjects in the feracrylum group reported significantly less pain compared to control group. This enhanced patient comfort could contribute to better treatment adherence and potentially faster recovery. Feracrylum was well-tolerated with no significant adverse events reported, indicating its safety for topical application in burn treatment (Moenadjat Y *et al* 2008).

Feracrylum In Chronic Wounds

Diabetic Foot Ulcers

Diabetic foot ulcers (DFU), a frequent and serious complication of diabetes, pose a significant challenge to both patients and healthcare systems. Priyankadevi *et al*. conducted a randomized controlled trial investigating the efficacy of feracrylum gel compared to conventional povidone-iodine dressing in DFU healing. Significantly faster wound healing was observed in the feracrylum group, complete healing occurred by the 3rd week in 14 (56%) patients, compared to only 6 (24%) in the povidone-iodine group. Patients treated with feracrylum gel had a shorter average hospital stay (approximately 25 days) compared to the povidone-iodine group (approximately 39 days). Feracrylum gel appeared to promote wound readiness for skin grafting, potentially speeding up the overall treatment process. Overall, this study provides promising evidence for the potential benefits of feracrylum gel in treating DFU. (Priyankadevi E *et al* 2023). Similarly, Bal A investigated the potential of feracrylum gel in managing DFU, classified as grade 2 or 3 according to the Wagner grading system. All patients experienced complete healing within 11 to 18 weeks. The study suggests longer healing times (16-18 weeks) may be expected for Wagner grade 4 wounds. Feracrylum gel was reported to be easy to apply and remove. The study suggests potential advantages of feracrylum gel compared to povidone-iodine, including faster healing times, shorter hospital stays, and reduced financial burden on the patient. Overall, the study provides a preliminary glimpse into the potential benefits of feracrylum gel for diabetic foot wound healing (Clinical study report 2001).

Dental Surgery/Tooth Extraction And Minor Oral Surgery

In the pulpotomy procedure infected pulp is removed from under the tooth's crown which leads to hemorrhage. To carry out this procedure smoothly, control of hemorrhage is a must. Prabhu NT and Munshi AK investigated the potential of 1% feracrylum as a hemostatic agent in pulpotomy procedures. This study assessed the efficacy and safety of feracrylum compared to conventional methods like pressure or cotton pellets for hemostasis during pulpotomy in primary teeth. Feracrylum gel, presents potential advantages due to its rapid hemostatic action to promote clotting and control bleeding quickly enhancing the efficiency. Also, being non-toxic and seemingly well-tolerated, it poses minimal risk to the remaining healthy pulp tissue (Prabhu NT and Munshi AK 1997).

Excessive bleeding during and after dental procedures or surgery is very common but could be more complicated in patients with bleeding disorders or patients taking anticoagulant drugs. In all such cases controlling bleeding is the main task for dentists. Rai S *et al*. conducted a comparative study to evaluate the efficacy and safety of feracrylum and tranexamic acid in controlling bleeding after tooth extraction in anticoagulated patients taking warfarin. Both feracrylum and tranexamic acid effectively controlled bleeding. Notably, no modifications to the patients' warfarin therapy were necessary to achieve effective hemostasis. Both agents were well-tolerated with minimal reported adverse events. This study provides encouraging evidence for the potential of both feracrylum and tranexamic acid as valuable tools for managing post-operative bleeding in anticoagulated patients undergoing tooth extraction, potentially allowing for uninterrupted anticoagulation therapy (Rai S *et al*. 2019). Mali S *et al.* presented a case report highlighting the use of feracrylum gel for achieving local hemostasis during a dental extraction procedure in a child with dyskeratosis congenita (DC). This brief report offers valuable insights into managing such procedures in children with this rare genetic condition. Hemostasis was successfully achieved after tooth extraction in their young patient with DC by applying a combination of pressure packs and feracrylum gel (Mali S et al 2018). Similarly, in another published case report on the management of patients with aphthous-like ulcers related to aplastic anemia, 1%

feracrylum mouthwash was prescribed to avoid spontaneous bleeding in the oral mucosa (Talahatu, L B *et al* 2022).

Bleeding during oral and maxillofacial surgery is common. Complications may arise in patients who are immunocompromised or on anti-platelet or anticoagulant treatment. Singh H *et al*. investigated the efficacy of feracrylum as a hemostatic agent in patients undergoing minor oral surgery while on antiplatelet therapy, specifically with an International Normalized Ratio (INR) below 3.5. Patients in the feracrylum group experienced significantly less bleeding compared to the saline gauze group across all time points evaluated, including immediately after surgery, 24 hours later, and on subsequent days. Importantly, no modifications to the patients' antiplatelet therapy were necessary to achieve effective hemostasis with feracrylum. Hence, they provide evidence that bleeding complications can be managed without modifying patients' essential medications. (Singh H *et al* 2022).

Jain P *et al.* presented a case series on managing dental bleeding in patients on antiplatelet and anticoagulant medications. Antiplatelet and anticoagulant medications are necessary for managing various cardiovascular conditions and can significantly prolong bleeding time during dental procedures. In patients on anticoagulant therapy, bleeding from the traumatized socket persisted for 6 hours. Conventional hemostatic methods like pressure packs alone failed to control prolonged post-procedural bleeding. The application of a pressure pack with feracrylum gel successfully arrested the bleeding, highlighting its potential in managing traumatic dental hemorrhage in anticoagulated patients. . Supplementation with feracrylum gel effectively controlled the hemorrhage, demonstrating its potential in managing persistent bleeding after dental procedures in patients on anti-coagulants (Jain P *et al* 2023).

Summary

Feracrylum is a topical hemostatic agent used to control bleeding, particularly in the field of medicine and surgery andis employed in various medical and dental procedures. Feracrylum is known for its ability to form a stable clot and helps in the quick cessation of capillary bleeding, without interfering with the normal clotting mechanism. When it interacts with blood, it forms an insoluble poly complex, which rapidly transforms into a coagulum within 30 seconds. This process aids in halting capillary bleeding. It's worth noting that the use of hemostatic agents like feracrylum is generally a part of standard medical practice offering various advantages over the conventional methods used to control capillary bleeding. Along with its hemostatic property, its antimicrobial effect against several gram-positive, gram-negative bacteria and fungi decreases the local wound infection. In addition, feracrylum's hygroscopic property provides moisture for healing and helps in the regeneration of new cells. Due to its unique wound healing properties, it is widely used clinically in the treatment of wounds and in different surgical settings like general surgery, ENT surgery, urological surgery, oncological surgery, dental surgery, orthopedic surgery, DFU management, etc.

Feracrylum - A Promising Option for Both Surgeons and Patients

Feracrylum emerges as a valuable hemostatic agent offering potential benefits for both surgeons and patients. Here's a summary of its key advantages:

For Surgeons:

Feracrylum is a versatile surgical aid with several key benefits. It effectively controls diffuse oozing and surface bleeding, which not only leads to a clearer surgical field but also potentially shortens procedure times due to its effective hemostasis. Unlike traditional methods like cauterization, Feracrylum minimizes tissue damage, which promotes faster healing and potentially results in fewer complications, thus reducing tissue damage. Furthermore, Feracrylum possesses inherent antimicrobial activity, which lowers the risk of post-surgery infection, providing an additional layer of protection. In addition, its application topically in various forms, offers flexibility during surgery. This combination of effective hemostasis, reduced tissue damage, antimicrobial properties, and ease of use makes Feracrylum a valuable tool in surgical procedures.

For Patients:

Feracrylum offers several significant advantages to the patients. Firstly, its effective bleeding control can lead to less blood loss during and after surgery, potentially enhancing recovery and reducing the need for blood transfusions. This can result in a smoother postoperative recovery process. Secondly, the reduced tissue damage and potential for lower infection rates can contribute to quicker wound healing, possibly leading to shorter hospital stays and a quicker return to normal life. Thirdly, Feracrylum, being a topical agent, avoids the need for invasive procedures like cauterization, which could potentially lessen patient discomfort and pain, making the surgical experience less daunting. Lastly, Feracrylum is considered a safer alternative with studies indicating a commendable safety profile with minimal side effects. This provides patients with added reassurance about their treatment, contributing to peace of mind during the recovery process.

In summary, Feracrylum's unique blend of hemostatic, antimicrobial, and hygroscopic properties make it a potential alternative to traditional methods, benefiting both surgeons and patients alike.

CONCLUSION

Feracrylum has revolutionized the field of hemostasis and has become a useful tool in various surgical procedures. Owing to its unique wound healing properties, mainly hemostatic, anti-bacterial and hygroscopic properties, feracrylum is widely used clinically in the treatment of acute and chronic wounds in various surgical settings. Chances of systemic adverse effects are less, as it does not get systemically absorbed because of its high molecular weight. Feracrylum simplifies wound care with its easy application and removal, no discomfort during dressing change, non-sticky and odorless properties, shorter hospital stays in chronic wound surgery, leading to higher patient adherence to treatment and reduced costs burden.

Conflicts Of Interest

The authors have no conflicts of interest to disclose.

Acknowledgement

The authors thank Nilesh Inamdar for providing medical writing assistance.

REFERENCES

1. Bowler, P.G., & Duerden, B.I. (2001). Wound microbiology and associated approaches to wound management. *Clin Microb Rev,* 14,244–69.
2. Naseri, E., & Ahmadi, A. (2022). A review on wound dressings: antimicrobial agents, biomaterials, fabrication techniques, and stimuli-responsive drug release. *Eur Polym J,* 173, 111293, 10.1016/j.eurpolymj.2022.111293
3. Deng, X., Gould, M., & Ali, M.A. (2022). A review of current advancements for wound healing: Biomaterial applications and medical devices. *J Biomed Mater Res B Appl Biomater,* 110(11), 2542-2573. doi:10.1002/jbm.b.35086
4. Yu, P., & Zhong, W. (2021). Hemostatic materials in wound care. *Burns Trauma*, 9:tkab019.. doi:10.1093/burnst/tkab019
5. Bigliardi, P., Langer, S., Cruz, J.J., Kim, S.W., Nair, H., & Srisawasdi, G. (2017). An Asian Perspective on Povidone Iodine in Wound Healing. *Dermatology*, 233(2-3),223-233. doi:10.1159/000479150
6. Feracrylum Prescribing information
7. SPC-BKSC study report 2001. Data on File
8. Chauhan, M.K., & Kumari, M. (2017). Feracrylum: An Effective and Safe Topical Haemostatic Agent. *World J Pharma Res,* 6(10),319-325.
9. Field, F.K., & Kerstein, M.D. (1994). Overview of wound healing in a moist environment. *Am J Surg,* 167(1A), 2S-6S. doi:10.1016/0002-9610(94)90002-7
10. Saghazadeh, S., Rinoldi, C., Schot, M., et al (2018). Drug delivery systems and materials for wound healing applications. *Adv Drug Deliv Rev,* 127,138-166. doi:10.1016/j.addr.2018.04.008
11. Sarabahi, S. (2012). Recent advances in topical wound care. *Indian J Plast Surg,* 45,379-387. doi:10.4103/0970-0358.101321
12. FDA executive summary: classification of wound dressings combined with drugs. In: Meeting of the General and Plastic Surgery Devices Advisory Panel 2016. p. 1-83
13. CBPRC report 1999a. Data on File
14. CBPRC report 1999b. Data on File
15. CBPRC report on skin bacteria. Data on File
16. CCMB study report 1999. Data on File
17. Bhagwat, A.M., Save, S., Burli, S. & Karki, S.G. (2001). A study to evaluate the antimicrobial activity of feracrylum and its comparison with povidone-iodine. *Indian J Pathol Microbiol*, 44(4), 431-433.
18. TCL-FA study report 1999. Data on File
19. ARI Report-2018. Data on File
20. Nivaskar, M., Banerjee, A., Shah, D., & Kurani, S.P (2006), Wound Healing Activity of Hemolok (Sepgard) Gel in Sprague Dawley Rats. *Adv Pharmacol Toxicol,* 7, 21-23.
21. Sinulingga, S., Kesumaputri, B.A., & Anggraini, G. (2017), Hemostatic Effect of Ethanol Extract of Piper betle, Linn Leaves to Male Mice. *Molekul*. 12(1), 23-29
22. Tsamarah, A., Rahman, E.F., & SriPraptiningsih, R. (2022). Comparison of the Effectiveness of Feracrylum 1% and Feracrylum 4% in Stoping Blooding after Gingiva Incision. *MEDALI Journal,* 4(2), 163-169
23. Ramachandra, S. G., Ramesh, V., & Krishnamurthy, H. N. (2000). Efficacy of different haemostatics for haemorrhagic enteritis in bonnet monkeys. *Indian Vet J,* 77(6), 508-512
24. Kantharia, C., Dharap, S., Mani, C., Gaikwad, S., Agarwal, B., & Kocharekar, M. (2008). Assessment of Efficacy of 1% Feracrylum (Sepgard) Gel in Wound Care. *Ind M Gaz,* 1-6.
25. Rao, A.M., & Patel, R.V. (2004). Sepgard Gel (Feracrylum 1%) in the Local Management of Wounds. *Ind M Gaz,* 518-521
26. Feracrylum 3%w/w Clinical study report. Data on File
27. Sathyaki, D.C., Roy, M.S., Mohan, M., Raghu, N., & Sheriff, R.M. (2017). Feracrylum Versus Topical Adrenaline for Hemostasis in Tonsillectomy. *Int J Sci Study,* 4(10),34-36
28. Valse, D., & Hosalli Kumaraswamy, N. (2021). To evaluate the role of Feracrylum (1%) as hemostatic agent in Tonsillectomy. Indian *J Otolaryngol Head Neck Surg*, 73(2),240-245. doi:10.1007/s12070-021-02515-x
29. Shenoy, V.S., Samanth, R., Parvathareddy, N., & Apoorva, K.V (2023). Pediatric

Oronasopharyngeal Stricture- A Rare Surgical Complication of Adeno-Tonsillectomy Abstract. *Indian J Otolaryngol Head Neck Surg*, 75(3),2352-2354. doi:10.1007/s12070-023-03694-5

30. Moenadjat, Y., Setiabudy, R., Astrawinata, D.A., & Gumay, S. (2008). The safety and efficacy of feracrylum as compared to silver sulfadiazine in the management of deep partial thickness burn: A clinical study report. *Med J Indones* [Internet]. 17(4),259-71.
31. Priyankadevi, E., Vinayagam, G., & Praveen, R.A (2023). The Effectiveness of Wound Healing in Diabetic Foot with Feracrylum over the Conventional Povidone Dressing - A Prospective Comparative Study. *EJMCM*, 10(5),312-321
32. Feracrylum Clinical study report 2001. Data on File
33. Prabhu, N.T., & Munshi, A.K. (1997). Clinical, radiographic and histological observations of the radicular pulp following "feracrylum" pulpotomy [published correction appears in J Clin Pediatr Dent 1997 Summer;21(4):356]. *J Clin Pediatr Dent*, 21(2),151-156
34. Rai, S., & Rattan, V. (2019). Efficacy of Feracrylum as Topical Hemostatic Agent in Therapeutically Anticoagulated Patients Undergoing Dental Extraction: A Comparative Study. *J Maxillofac Oral Surg*, 18(4),579-583. doi:10.1007/s12663-018-1156-6
35. Mali, S., Kundana, P.K., Singh, S., Khanchandani, S., Tullu, M.S., Agrawal, M., & Kakade A (2018). Platelet and blood transfusion in a child with dyskeratosis congenita for dental extraction – a case report. *RSBO,* 15(2),116-22
36. Talahatu, L. B., Kaban, B. E., Ayuningtyas, N. F., Brilyanti, I. N., Parmadiati, A. E., Radithia, D, & Pratiwi, A. S. (2022). Management of patients with aphthous-like ulcers related to aplastic anaemia in the COVID-19 pandemic era through teledentistry: A case report. *Dental Journal*, 55(1), 49–55. https://doi.org/10.20473/j.djmkg.v55.i1.p49-55
37. Singh, H., Khan, Z.A., Kishor, K., & Singh, A. To evaluate the efficacy of Feracrylum as a haemostatic agent following minor oral surgery. Preprint article. DOI: https://doi.org/10.21203/rs.3.rs-2652653/v1
38. Jain, P., Jain, A., Patidar, M., Banthia, R., & Batham, P. (2023). Dental Considerations in Patients on Antiplatelet and Anticoagulant Drugs – Clearing the Fog: A Case Series. *Journal of Datta Meghe Institute of Medical Sciences University*, 18(1),114-119. DOI: 10.4103/jdmimsu.jdmimsu_295_22.