

Ferric chloride for hemostasis of malignant neoplastic wounds: a scoping review

Cloreto férico para hemostasia de feridas neoplásicas malignas: uma revisão de escopo

Cloruro férico para la hemostasia de heridas neoplásicas malignas: una revisión de alcance

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ABSTRACT: Objective: To map the scientific evidence on the use of ferric chloride for hemostasis of bleeding malignant neoplastic wounds in adult patients within the healthcare context. **Method:** A scoping review conducted following the recommendations of the JBI. The electronic databases Medical Literature Analysis and Retrieval System Online (MEDLINE)/PubMed, Embase, Web of Science, Cumulative Index to Nursing and Allied Health Literature (CINAHL), EBSCO, *Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS)*, and gray literature sources were searched from inception to August 15, 2025. **Results:** A total of 31,952 records were identified, of which 17 were included. The studies addressed the use of ferric chloride in different formulations and concentrations across gynecology/obstetrics, dentistry, and dermatology, among surgical patients. No serious adverse events were reported following its use, and no study included patients with bleeding malignant neoplastic wounds. **Conclusion:** Ferric chloride has been used as a hemostatic agent in adults with various health conditions. However, the absence of specific evidence in bleeding neoplastic wounds highlights the need for further studies to investigate its effectiveness and safety in this patient population.

Keywords: Ferric chloride. Hemostasis. Wounds and injuries. Oncology nursing.

RESUMO: Objetivo: Mapear as evidências científicas sobre o uso de cloreto férico para hemostasia de feridas neoplásicas malignas sangrantes entre pacientes adultos no contexto da assistência à saúde. **Método:** Revisão de escopo conduzida conforme as recomendações do *Joanna Briggs Institute (JBI)*. Foram consultadas as bases de dados eletrônicas *Medical Literature Analysis and Retrieval System Online (MEDLINE)/PubMed*, Embase, *Web of Science*, *Cumulated Index to Nursing and Allied Health Literature (CINAHL)*, EBSCO, *Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS)* e bases de literatura cinza, desde sua criação até 15 de agosto de 2025. **Resultados:** Identificou-se 31.952 registros; destes, 17 foram incluídos. Os estudos contemplaram o emprego do cloreto férico, em diferentes apresentações e concentrações, nas áreas da ginecologia/obstetrícia, odontologia e dermatologia, entre pacientes cirúrgicos. Não foram reportados eventos adversos graves após o uso, e nenhum estudo incluiu pacientes com feridas neoplásicas malignas sangrantes. **Conclusão:** O cloreto férico tem sido empregado como hemostático em adultos com distintos agravos à saúde. Entretanto, a ausência de evidências específicas em feridas neoplásicas sangrantes aponta para a necessidade de novos estudos que investiguem sua efetividade e segurança nesta categoria de pacientes.

Palavras-chave: Cloreto férico. Hemostasia. Ferimentos e lesões. Enfermagem oncológica.

RESUMEN: Objetivo: Mapear la evidencia científica sobre el uso de cloruro férico para la hemostasia de heridas neoplásicas malignas sangrantes en pacientes adultos en el contexto de la atención en salud. **Método:** Revisión de alcance realizada según las recomendaciones del JBI. Se consultaron las bases de datos electrónicas *Medical Literature Analysis and Retrieval System Online (MEDLINE)/PubMed*, Embase, *Web of Science*, *Cumulated Index to Nursing and Allied Health Literature (CINAHL)*, EBSCO, *Literatura Latino-Americana e do Caribe em Ciências da Saúde (LILACS)* y bases de literatura gris, desde su creación

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hasta el 15 de agosto de 2025. **Resultados:** Se identificaron 31.952 registros; de estos, se incluyeron 17. Los estudios abordaron el uso de cloruro férrico en diferentes presentaciones y concentraciones, en las áreas de ginecología/obstetricia, odontología y dermatología, entre pacientes quirúrgicos. No se reportaron eventos adversos graves tras su uso, y ningún estudio incluyó pacientes con heridas neoplásicas malignas sangrantes. **Conclusión:** El cloruro férrico se ha utilizado como hemostático en adultos con diversas afecciones de salud. Sin embargo, la ausencia de evidencia específica en heridas neoplásicas sangrantes señala la necesidad de nuevos estudios que evalúen su efectividad y seguridad en esta categoría de pacientes.

Palabras clave: Cloruro férrico. Hemostasis. Heridas y lesiones. Enfermería oncológica.

INTRODUCTION

Cancer is considered the leading public health problem worldwide and is among the four main causes of premature death, defined as deaths occurring before the age of 70, in most countries. In 2018, 9.6 million cancer-related deaths were recorded globally, and approximately 70% of them occurred in countries classified as low- or middle-income¹⁻⁵.

Data published by the National Cancer Institute (*Instituto Nacional de Câncer – Inca*. Brazil) regarding estimates of new cancer cases in Brazil for each year of the 2023-2025 triennium indicate that approximately 704,000 new cases are expected annually, with the South and Southeast regions accounting for about 70% of the incidence. In total, the occurrence of 21 cancer types with the highest incidence in the country was estimated. Non-melanoma skin cancer is the most frequent, representing 31.3% of total cases, followed by breast cancer (10.5%), prostate cancer (10.2%), colon and rectum cancer (6.5%), lung cancer (4.6%), and stomach cancer (3.1%)⁴.

It has been observed that the more advanced the stage of breast cancer, the more frequent the complications, morbidity, and mortality. Furthermore, the physical and functional complications resulting from cancer interfere primarily with quality of life⁶. Among these complications are Malignant Neoplastic Wounds (MNW), which are formed by the invasion of neoplastic cells into the skin structure, leading to disruption of tissue integrity and impairment of local vascularization, ultimately resulting in tissue necrosis. Due to the uncontrolled cell proliferation, characteristic of carcinogenesis, the tumor wound rapidly progresses to an ulcerative and/or fungating lesion^{7,8}.

MNW can affect any part of the body; however, their incidence is significantly higher among patients with skin cancer, breast cancer, and head and neck cancer, with an estimated prevalence ranging from 5 to 10%⁷⁻⁹. Among the main complications experienced by patients with MNW, pain, malodor, and bleeding are particularly prominent⁹⁻¹¹. With regard to bleeding, it may occur in up to 72% of affected patients and can be associated with several factors, including trauma during

dressings removal, coagulation disorders related to cancer or its treatment, a bleeding-prone environment resulting from neovascularization, coagulopathy, thrombocytopenia, reduced fibroblast activity, and the fragility of newly formed blood vessels and capillaries^{7,9}.

In cases in which bleeding associated with MNW is more severe, surgical interventions or intravascular measures may be indicated. However, these procedures may present technical challenges due to the difficult location and control of bleeding vessels, particularly in the presence of large, friable, and highly vascularized tumor masses¹². Consequently, less invasive therapeutic approaches have been sought for bleeding control in MNW, including radiotherapy and topical treatments — such as dressings based on silver or calcium alginate and regenerated oxidized cellulose⁹⁻¹¹.

Among emerging alternatives, ferric chloride (FeCl_3) stands out. Its mechanism of action is based on the chemical reaction between ferric ions (Fe^{3+}) and plasma proteins, promoting protein denaturation and capillary occlusion through chemical hemostasis^{13,14}. In addition to this physicochemical effect, the acidic environment generated by the substance enhances vasoconstriction and local enzymatic inactivation, thereby contributing to bleeding control^{15,16}.

In dentistry, ferric chloride is used to control gingival bleeding and crevicular fluid during restorative and prosthetic procedures^{16,17}. In dermatology, it is employed for hemostasis after biopsy procedures and for the chemical cauterization of small skin lesions¹⁸. Furthermore, results from experimental animal studies have demonstrated that hemostasis time was significantly shorter with the use of ferric chloride in rat skin incisions when compared with traditional suturing^{19,20}.

OBJECTIVE

To map the scientific evidence on the use of ferric chloride for hemostasis of bleeding malignant neoplastic wounds in adult patients within the healthcare context.

METHODS

This scoping review was conducted in accordance with the recommendations established by the JBI^{21,22} and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Reviews (PRISMA-ScR)²³. The protocol for this scoping review was registered in the Open Science Framework (OSF) under DOI: <https://doi.org/10.17605/OSF.IO/BYT9N>.

Guiding question

The guiding question was structured according to the PCC (Participants, Concept, Context) acronym, commonly used in scoping reviews, and was formulated as follows: What evidence is available in the scientific literature regarding the use of ferric chloride for hemostasis of MNW, among adults, in the context of healthcare?

In defining the elements of PCC, Population (P) was established as individuals aged 18 years old or older; Concept (C) as the use of ferric chloride or similar substances, such as ferric subsulfate; and Context (C) as healthcare delivery settings (hospitals, specialized clinics, and physicians' offices).

Eligibility criteria

Inclusion criteria

Analytical observational studies (cross-sectional, case-control, and prospective or retrospective cohort studies); descriptive observational studies (case series, individual case reports, and descriptive cross-sectional studies); experimental and quasi-experimental studies (randomized and non-randomized controlled trials, before-and-after studies, and interrupted time series studies), conducted among adult patients were included, as well as technical guidelines issued by specialist societies and government agencies; and literature reviews published in English, Spanish, or Portuguese.

Exclusion criteria

Records involving animal studies and those that did not provide details on the use of ferric chloride or ferric subsulfate were excluded.

Data sources and search strategy

The electronic databases Medical Literature Analysis and Retrieval System Online (MEDLINE)/PubMed, Embase,

Web of Science, Cumulative Index to Nursing and Allied Health Literature (CINAHL), EBSCO, and Latin American and Caribbean Literature in Health Sciences (LILACS) were searched from their inception. The search strategies were developed with the assistance of a specialized librarian, based on combinations of descriptors and keywords — described in Supplement 1 — aligned with the PCC framework and corresponding to the first stage of the search, in accordance with the guidelines of the Peer Review of Electronic Search Strategies (PRESS) 2015 Statement²⁴.

The search strategies aimed to retrieve both published and unpublished records from the scientific literature (scientific manuscripts, theses, and dissertations). Therefore, a three-stage search was conducted, as follows:

First stage: limited to the electronic databases PubMed/MEDLINE, CINAHL, and Embase, with the aim of identifying keywords frequently used in the titles and abstracts of scientific studies. Second stage: a systematic search using all terms initially identified was conducted across the electronic databases selected for the review on August 15, 2025 (Supplement 1). Third stage: reference lists of the studies included in this scoping review were screened for additional relevant publications, as well as grey literature sources, including the Catalog of Theses and Dissertations of the Coordination for the Improvement of Higher Education Personnel (*Catálogo de Teses e Dissertações da Coordenação de Aperfeiçoamento de Pessoal de Nível Superior – CAPES, Brazil*), Open Access Theses and Dissertations (OATD), Google Scholar, and the Canadian Dissertation and Theses Portal. For this stage, the terms “ferric chloride” or “*cloreto férrico*” were used as search terms.

Selection of studies

For study selection, references retrieved from the electronic databases were imported into the Rayyan Intelligent Systematic Reviews[®] software. Manuscript selection followed the predefined eligibility criteria and was conducted in two stages. In the first stage, titles and abstracts were independently screened by two reviewers. Subsequently, the full texts of potentially eligible manuscripts were independently assessed by two reviewers, and any disagreements were resolved by a third reviewer.

Data extraction

After completion of the selection phase, two reviewers independently extracted data from the included studies using an

electronic form developed in Microsoft Excel for Mac®, based on the JBI template source of evidence details, characteristics, and results extraction instrument, complemented by an additional form designed to meet the objectives of this review. The extracted data comprised: authors, title, year of publication, study design, main results, principal limitations as reported by the authors, specialty, country of origin, formulation of ferric chloride/ferric subsulfate used, concentration, application site, contraindications, and occurrence of safety events. Discrepancies at this stage were resolved through discussion and consensus with a third reviewer.

Data summary

Based on the extracted data, summary tables were developed to present the most relevant information from the included manuscripts.

RESULTS

A total of 30,744 manuscripts were retrieved from the consulted databases. In the grey literature search, 1,208 records were identified, including 285 from the CAPES Thesis and Dissertation Catalog, 733 from OATD, 100 from Google Scholar, and 90 from the Canadian Dissertation and Theses Portal.

Duplicate records ($n = 5,969$) were removed prior to the screening process. After title and abstract screening, 24,324 records were excluded, and 451 studies were selected for full-text assessment. Reference lists of the selected manuscripts were also reviewed to identify additional records not retrieved through the database searches, resulting in the inclusion of eight further publications in the selection process. At the end of screening, 17 studies met the eligibility criteria, as illustrated in Figure 1.

The studies were published between 1986 and 2021, with the majority (13; 76.5%) conducted between 2005 and 2021²⁵⁻³⁶. Approximately one third of the investigations were carried out in Brazil (6; 35.3%)^{25-28,35}, followed by the United States of America (USA) (4; 23.5%)^{31,33,37,38} and the United Kingdom (3; 17.6%)^{29,34,39}; the remaining studies were conducted in Thailand³⁰, Serbia³², Canada⁴⁰, and Italy³⁵. Regarding study design, 6 (35.3%)^{30-32,35,36,38} were randomized controlled trials; 3 (17.6%) were cross-sectional observational studies^{25,26,41}; 2 (11.8%) were longitudinal studies^{27,28}; 3 (17.6%) were case reports^{33,34,40}; 2 (11.8%) were systematic literature reviews^{29,39}; and 1 (5.9%) was a narrative literature review³⁷.

The specialties in which the use of the product was reported included gynecology/obstetrics, with 11 (64.7%) investigations^{25-31,34,39-41}; dentistry^{32,35-37}, with 4 (23.5%) investigations; and dermatology^{33,38}, with 2 (11.8%) investigations.

In most studies (10; 59%)^{29-33,35-40}, the setting in which the hemostatic agent was employed was not reported. In six investigations^{25-28,30,41}, the procedure was performed on an outpatient basis, whereas in one study³⁴, due to the complexity of the obstetric procedure, it was conducted in the surgical unit. In 11 studies^{25-31,34,39-41}, only female participants were included. One study³⁶ enrolled participants of both genders, with a predominance of females (16; 66%). Another report³² included individuals of both genders but did not specify the number of participants in each group. In four investigations^{33,35,37,38}, the gender of the participants was not reported. In eight (47%) studies^{25,27-31,34,41}, information on the age range of participants was provided, indicating a predominance of women of reproductive age, as shown in Chart 1²⁵⁻⁴¹.

Regarding the results by specialty, in gynecology/obstetrics, the five observational cross-sectional and longitudinal studies (29.4%) did not include the analysis of ferric chloride as a study objective^{25-28,41}. In these studies, the use of the substance was described in the Methods section as part of the procedure following colposcopy-guided biopsy. Consequently, no outcome data related to the use of ferric chloride were available for analysis.

The findings of two literature reviews^{29,39} indicated that tamponade with Monsel's solution reduced perioperative blood loss compared with routine suturing. Additionally, two reports^{34,40} showed that a 20% ferric subsulfate solution promoted uterine hemostasis. The concomitant use of 20% ferric subsulfate with fulguration using a spherical electrode also appears to be effective as a hemostatic method following loop electrosurgical excision procedures for cervical tumors³⁰.

Studies conducted in dentistry have shown that the use of ferric chloride was associated with mild to severe inflammation^{32,35}; cold sensitivity³⁵; and a higher frequency of hemostasis in patients treated with an alternative hemostatic agent, calcium chloride³⁶. However, the findings of a literature review³⁷ described immediate hemostasis following endodontic microsurgery after the use of ferric subsulfate. In dermatology, one study reported that the application of ferric subsulfate solution was a simple, safe, and effective method for reducing postoperative bleeding from the pedicles of the paramedian frontal flap³³. Conversely, another report³⁸ found no differences in hemostatic outcomes when comparing the use of a collagen matrix with ferric subsulfate.

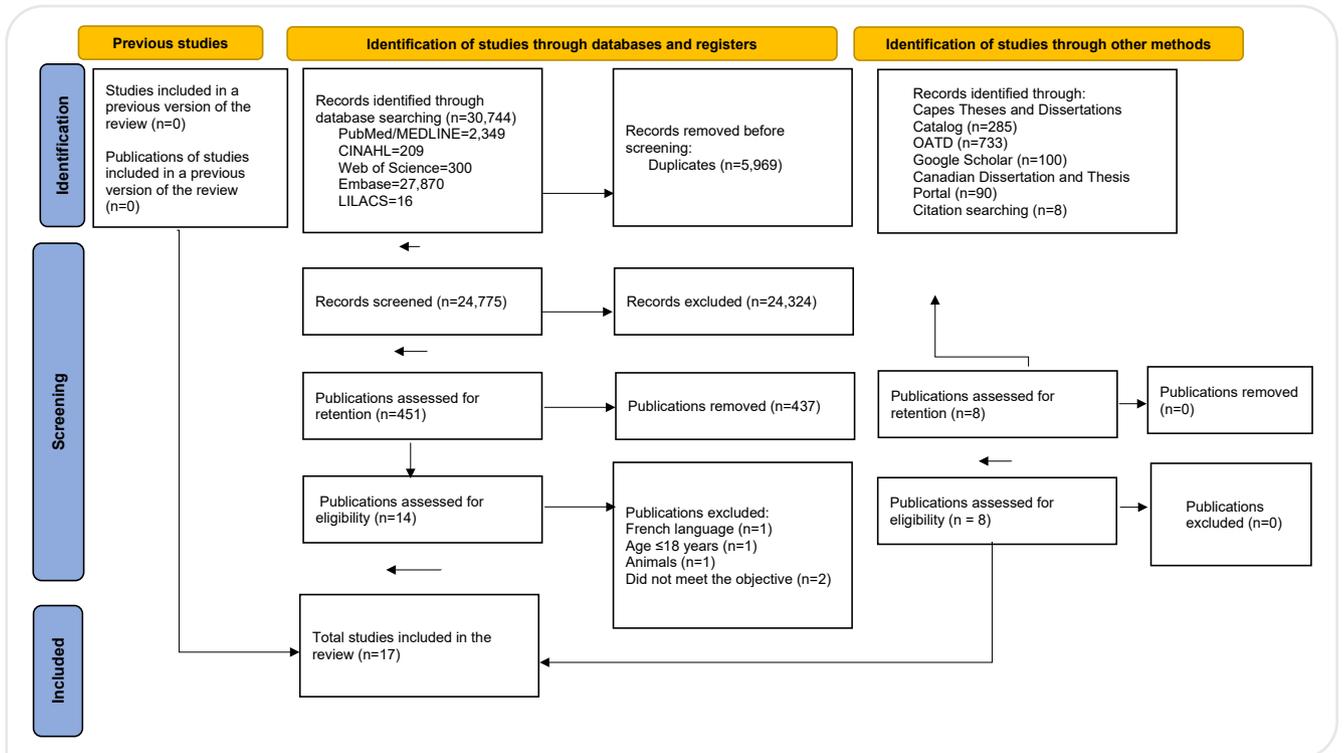


Figure 1. PRISMA-ScR flow diagram of the search and selection process of the studies included in the review. São Paulo, 2025.

Chart 1. Synthesis of scientific investigations on the effects of ferric chloride/subsulfate on wound hemostasis. São Paulo, 2025.

Author, design, n, baseline characteristics	Objective	Main results	Specialty (Setting)	Country
Guimarães ²⁵ Observational, analytical, cross-sectional study. Participants: 104 women. Mean age 36.08±11.62 years.	To determine the prevalence of high-risk human papillomavirus (HPV) infection and its respective genotypes, in single or multiple infections, correlating them with the degree of neoplasia diagnosed by cytology and histology.	Ferric chloride gel was used for hemostasis after tissue collection for histopathological analysis.	Gynecology (Outpatient)	Brazil
Pereira ²⁶ Observational, cross-sectional, retrospective study. Participants: 503 Indigenous women with a mean age of 30 years.	To describe and analyze cervical cancer prevention in the Xingu Indigenous Park, Mato Grosso, from 2005 to 2006.	Ferric perchloride gel was used for hemostasis after tissue collection for histopathological analysis.	Gynecology (Outpatient)	Brazil
Melli ²⁷ Prospective longitudinal observational study. Participants: 97 women. Divided into two groups, with 38 patients living with Human Immunodeficiency Virus (HIV) and 59 non-infected women. Group 1 mean age: 30 years; Group 2 mean age: 33 years.	To evaluate the effectiveness of High-Frequency Surgery (HFS) in the treatment of high-grade cervical intraepithelial lesions and the rate of late complications in patients with or without HIV; and to assess whether HIV infection favors persistence of high-grade cervical intraepithelial lesions after HFS.	Ferric perchloride solution was used for hemostasis after tissue collection for histopathological analysis.	Gynecology (Outpatient)	Brazil
Waisberg ²⁸ Prospective observational study. Participants: 50 women: 7 HPV+ (median age 43 (28-66)) 43 HPV- (median age 49 (18-74)).	To evaluate HPV and <i>Chlamydia trachomatis</i> infections in patients with rheumatoid arthritis before and after anti-TNF therapy.	Ferric perchloride gel was used for hemostasis after tissue collection for histopathological analysis.	Gynecology (Outpatient)	Brazil

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Chart 1. Continuation.

Author, design, n, baseline characteristics	Objective	Main results	Specialty (Setting)	Country
Bittencourt ⁴¹ Analytical, observational, retrospective cross-sectional study. Participants: 118 medical records of patients diagnosed with high-grade cervical lesions who underwent excision of the transformation zone. Mean age of 27.1 years.	To evaluate surgical specimens resulting from loop electrosurgical excision procedures in the treatment of high-grade cervical intraepithelial neoplasia.	Ferric perchloride paste was used for hemostasis after tissue collection for histopathological analysis.	Gynecology (Outpatient)	Brazil
Martin-Hirsch e Kitchener ³⁹ Systematic review with meta-analysis	To evaluate the efficacy and safety of interventions to prevent blood loss during treatment of cervical intraepithelial neoplasia.	Vaginal packing with 20% ferric subsulfate solution applied against the cervix appears to be significantly superior to routine suturing.	Gynecology (Not reported)	United Kingdom
Martin-Hirsch e Bryant ²⁹ Systematic review with meta-analysis	To evaluate the efficacy and safety of interventions to prevent blood loss during treatment of cervical intraepithelial neoplasia, particularly their effects on immediate, short-, and long-term morbidity.	Packing with 20% ferric subsulfate solution resulted in lower perioperative blood loss and reduced risk of dysmenorrhea, unsatisfactory colposcopy, and cervical stenosis compared with routine suturing.	Gynecology (Not reported)	United Kingdom
Kim e Rethnam ³⁷ Literature review	Not reported.	Hemostasis in a surgical procedure can be considered in three stages: preoperative, intraoperative, and postoperative. At the end of the surgical stage, small bleeding sites on bone may be brushed with ferric sulfate solution, achieving almost immediate hemostasis.	Dentistry (Not reported)	USA
Kietpeerakool et al. ³⁰ Prospective randomized controlled study. Participants: 297 women. Mean age (standard deviation) was 45.7 (9.4) years.	To determine the benefit of immediate application of Monsel's solution (ferric subsulfate) after loop electrosurgical excision procedure (HFS) of the cervix to prevent postoperative bleeding.	Immediate application of 20% ferric subsulfate solution after loop electrosurgical excision significantly reduced the duration of uncomplicated vaginal bleeding or the occurrence of persistent vaginal bleeding.	Gynecology (Outpatient)	Thailand
Lipscomb et al. ³¹ Randomized clinical trial. Participants: 100 women – Ball electrode group: n=53 (29.1; standard deviation 10.2 years). Monsel group: n=47 (29.7; standard deviation 9,7 years).	To compare the use of 20% ferric subsulfate paste with ball electrode fulguration for hemostasis after loop electrosurgical excision.	Twenty percent ferric subsulfate paste and ball electrode fulguration appeared to be equally effective as hemostatic agents after loop electrosurgical excision.	Gynecology (Not reported)	USA
Igic et al. ³² Non-randomized clinical trial. Participants: 60 individuals of both genders aged between 20 and 40 years.	To test the influence of the chemomechanical gingival retraction procedure on gingival bleeding index values and salivary MCP-1 concentration as indicators of inflammatory changes in the gingiva.	Gingival retraction agents showed significant effects on gingival bleeding index values. In both groups, the effect size was greater with aluminum chloride-based agents. Clinical changes were more pronounced after ferric sulfate use, although no statistically significant difference was found.	Dentistry (Not reported)	Serbia
Poletto et al. ³³ Case report	Not reported.	Application of 20% ferric subsulfate solution is a simple, safe, and effective method to reduce postoperative bleeding of paramedian forehead flap pedicles.	Dermatology (Not reported)	USA

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Chart 1. Continuation.

Author, design, n, baseline characteristics	Objective	Main results	Specialty (Setting)	Country
Disu et al. ³⁴ Case report Participant: one 30-year-old woman.	Not reported.	Severe bleeding after evacuation of retained products of conception with curettage. The uterus was packed with gauze soaked in 20% ferric subsulfate solution. Vaginal bleeding rapidly decreased and became minimal one hour after uterine packing.	Obstetrics and Gynecology (Operating room)	United Kingdom
Manca ⁴⁰ Case report Participant: female.	Not reported	Excessive and persistent bleeding after cervical biopsy or laser or loop excision. Cervical examination revealed an oozing wound site. Hemostasis was achieved by applying Monsel's solution (20% ferric subsulfate) to the cervix.	Gynecology (Not reported)	Canada
Accorinte et al. ³⁵ Randomized clinical trial. Participants: 25 healthy human premolars scheduled for extraction, aged 15–25 years.	To evaluate the response of human pulp capped with an adhesive agent after hemorrhage control using different hemostatic solutions.	The authors do not encourage professionals to use this solution for hemorrhage control, as this was the only group in which patients reported pain throughout the study.	Dentistry (Not reported)	Brazil
Scarano et al. ³⁶ Controlled trial. 31 teeth (12 mandibular, 19 maxillary) in 24 patients (16 women and 8 men) with a mean age of 44.6 years (standard deviation 13.2 years).	To describe a comparative study of hemostasis achieved using sodium chloride, gauze packing versus ferric sulfate during endodontic surgical procedures.	In Group I (sodium chloride), hemostasis was achieved in 11 cases. In Group II (gauze or cotton), adequate hemostasis was achieved in 3 of 10 cases. In Group III (ferric sulfate), adequate hemostasis was achieved in 6 of 10 cases.	Dentistry (Not reported)	Italy
Armstrong et al. ³⁸ Randomized controlled trial. Participants: 20.	To compare the effect of punch biopsy wound treatment using a collagen matrix or, as control, Monsel's solution (ferric subsulfate).	The collagen matrix and ferric subsulfate were equally effective in achieving hemostasis.	Dermatology (Not reported)	USA

The most frequently reported formulation across the studies was a ferric chloride solution with concentrations ranging from 15.5 to 20%. In gynecology/obstetrics investigations, ferric chloride formulations with concentrations between 25 and 80% were applied. The cervix was the primary site of application, with administration performed using cotton-tipped applicators, compresses, or gauze. Regarding contraindications, restrictions were identified in cases of uterine perforation, due to the risk of intestinal injury and necrosis; in situations where bleeding originated from within the cervical canal; and in cases of excessive hemorrhage^{34,40}. No safety events were reported in the included investigations^{25-30,34,36-41}.

In dentistry, the application sites of the hemostatic agent included the alveolar bone, gingival sulcus, pulp cavity, and root canal. Application was performed by brushing, using impregnated retraction cords, or with cotton pellets. Contraindications to the use of ferric formulations in soft tissues and in proximity to critical anatomical structures,

such as the mandibular or mental nerve, maxillary sinus, or nasal floor, were reported, along with warnings regarding the need for complete removal of the hemostatic agent to prevent delays in the healing process^{36,37}.

In dermatology, a 20% ferric subsulfate solution was used, with application to the pedicles of the paramedian frontal flap and to biopsy wounds in the forearm region, respectively^{33,38}. However, contact with the eyes is contraindicated due to the risk of ulceration³³. Some adverse effects were reported, including pigmentary discoloration of the tissue at the application site and the occurrence of inflammation, as described in Chart 2²⁵⁻⁴¹.

DISCUSSION

This scoping review identified 17 studies that used ferric chloride/subsulfate as a hemostatic agent. The findings

indicate that ferric chloride formulations have been widely employed for hemostatic purposes in dentistry, dermatology, and, most notably, gynecology. Women of reproductive age represented the primary population in which the product was used. The most common formulation was a solution with concentrations ranging from 15.5 to 20%. Reported adverse events included pain, irritation, and inflammation. Identified contraindications comprised use in soft tissues, cortical bone, and critical anatomical structures, such as the mandibular or mental nerve, maxillary sinus, and nasal floor.

A clinical trial involving 20 participants compared a collagen matrix with Monsel's solution in punch biopsy wounds of the forearm and demonstrated that both agents were effective in achieving hemostasis³⁸. Furthermore, in recent years, advances in biotechnology have led to the development of several topical hemostatic agents. In a literature review published in 2011²⁶, hemostatic agents were classified into three categories: absorbable agents, such as gelatins, microfibrillar collagen, and regenerated oxidized cellulose; biological agents, containing fibrin and thrombin; and synthetic agents, including glutaraldehyde and bovine albumin adhesive, cyanoacrylate, and polyethylene glycol. Given the wide variety of topical hemostatic agents available, selecting the most appropriate product and the optimal timing for its use can be challenging. Therefore, consideration of the characteristics of each agent and the specific needs of each patient is essential to optimize the selection process.

Topical hemostatic agents also appear to be used in the treatment of MNW. In a controlled clinical trial⁴², the hemostatic efficacy of oxidized regenerated cellulose (ORC) and calcium alginate (CA) dressings in controlling bleeding from MNW secondary to breast cancer was evaluated in 28 women; the results indicated no significant difference in the time required to achieve hemostasis between ORC and CA for the control of mild to moderate bleeding. In a review published in 2019⁴³, the use of topical hemostatic dressings to manage bleeding in MNW originating from tumors in the head and neck region was reported to be safe. In addition, the use of dressings composed of gelatin and CA was recommended.

Ferric chloride/subsulfate appears to be less expensive than most other hemostatic agents. The average cost of a 15 mL bottle of ferric chloride is approximately US\$2.50⁴⁴. In contrast, fluid combinations of biological derivatives may cost between US\$400 and US\$1,000 per application. Non-fluid matrices, such as ORC, collagen, microporous polysaccharide spheres, and single-agent biological derivatives (*e.g.*,

thrombin), present an intermediate cost compared with the other options⁴⁵.

In cases of severe bleeding associated with MNW, when locoregional measures are insufficient, surgical intervention may be indicated for selected patients, after careful consideration of risks and benefits. Surgical management may include ligation of larger vessels, excision of bleeding tissue, or therapeutic arterial embolization⁴⁶. A case report published in 2023⁴⁷ described the use of arterial embolization to control acute bleeding in a patient with MNW of the right breast. In this case, the endovascular approach proved effective and enabled patient stabilization when conventional treatments failed to achieve hemostasis or when bleeding was life-threatening⁴⁷.

Furthermore, as a cure is not expected for MNW, their management constitutes a clinical and predominantly palliative challenge, aimed at symptom relief, preservation of comfort, and maintenance of patients' quality of life⁴⁸. Consequently, the management of these conditions requires an interdisciplinary approach, with the objective of reducing suffering and restoring patient dignity. In this context, the nurse's role extends beyond the technical management of the wound, encompassing health education, active listening, and psychosocial support as essential components of comprehensive palliative care and of strategies to improve the quality of life of this patient population^{49,50}. Within this framework, the development and evaluation of new topical hemostatic agents, such as ferric chloride, may represent a strategy to optimize the management of MNW. The potential of ferric chloride lies in its rapid local action, low cost, and lack of requirement for complex infrastructure^{50,51}.

This scoping review provides a broad mapping of the scientific literature on the use of ferric chloride as a hemostatic agent. However, an important limitation is the lack of scientific evidence regarding its use in bleeding MNW. This scarcity limits the development of evidence-based care protocols for the management of bleeding in MNW, a complication frequently associated with the physical, emotional, and social suffering experienced by patients with cancer.

It is suggested that randomized clinical trials investigating the use of ferric chloride or ferric subsulfate, compared with other topical agents for achieving hemostasis in MNW, be conducted — assessing efficacy, safety, and cost-effectiveness —, adhering to the guidelines established by the Consolidated Standards of Reporting Trials (Consort). Furthermore, it would be appropriate to investigate the effects of different product concentrations with respect to efficacy, safety, and cost.

Chart 2. Synthesis of scientific investigations regarding study design and characteristics of ferric chloride/subsulfate use in wound hemostasis. São Paulo, 2025.

Reference	Study type	Formulation	Concentration	Application site	Method of application	Contraindications	Safety events
Guimarães ²⁵	Observational, analytical, cross-sectional study	Gel	48% ferric chloride	Cervix	Not reported	Not reported	Not reported
Pereira ²⁶	Observational, cross-sectional, retrospective study	Gel	50% ferric perchloride	Cervix	Not reported	Not reported	Not reported
Melli ²⁷	Prospective longitudinal observational study	Solution	80% ferric perchloride	Cervix	Not reported	Not reported	Not reported
Waisberg ²⁸	Prospective observational study	Gel	50% ferric perchloride	Cervix	Direct application	Not reported	Not reported
Bittencourt ⁴¹	Analytical, observational, retrospective cross-sectional study	Paste	25% ferric perchloride	Cervix	Not reported	Not reported	Not reported
Martin-Hirsch and Kitchener ³⁹	Systematic review with meta-analysis	Ferric subsulfate 20%	Ferric sulfate 20%	Cervical wound	Impregnated compress	Not reported	Not reported
Martin-Hirsch and Bryant ²⁹	Systematic review with meta-analysis	Ferric subsulfate 20%	Ferric sulfate 20%	Cervical wound	Impregnated compress	Not reported	Not reported
Kim and Rethnam ³⁷	Literature review	Ferric subsulfate 20%	Ferric sulfate 20%	Dental bone tissue	Brushing	Ferric sulfate damages bone and delays healing when used in maximum amounts and left <i>in situ</i> . Care should be taken to avoid contact with soft tissues	Not reported
Kietpeerakool et al. ³⁰	Prospective randomized controlled study	Paste	Ferric subsulfate 20%	Cervical bed = cervix	Cotton-tipped applicator	Paste application with a cotton swab and spreading only within the craters to minimize possible adverse effects	Not reported
Lipscomb et al. ³¹	Randomized clinical trial	Paste	Ferric subsulfate 20%	Cervix	Not reported	Not reported	Although pain was statistically lower with 20% ferric subsulfate paste, the difference was probably not clinically significant
Igic et al. ³²	Non-randomized clinical trial	Solution	Ferric sulfate 15.5%	Gingival sulcus	Retraction cord impregnated with ferric sulfate	Not reported	Inflammation

Continue...

Chart 2. Continuation.

Reference	Study type	Formulation	Concentration	Application site	Method of application	Contraindications	Safety events
Poletto et al. ³³	Case report	Solution	Ferric subsulfate 20%	Pedicle cut surfaces	Cotton-tipped applicator	Avoid contact with the eyes, as the solution may cause ulceration	Pigment staining or tissue tattooing at the site of application
Disu et al. ³⁴	Case report	Solution	Aqueous ferric subsulfate 20%	Uterus	Impregnated gauze	Uterine perforation must be excluded before using a 20% ferric subsulfate pack, as leakage into the peritoneal cavity may cause areas of intestinal injury and necrosis	Not reported
Manca ⁴⁰	Case report	Solution	Ferric subsulfate 20%	Cervix	Ring forceps with gauze soaked in 20% ferric subsulfate solution	Bleeding originating from within the cervical canal or when excessive hemorrhage requires additional intervention	Not reported
Accorinte et al. ³⁵	Randomized clinical trial	Solution	Ferric sulfate 15.5%	Pulp chamber	Sterile cotton pellets moistened with ferric sulfate and maintained for one minute. The cavity was then irrigated with saline solution	Not reported	Pain
Scarano et al. ³⁶	Clinical trial	Solution	Ferric sulfate 20%	Root canal cavity	Applied with moistened cotton pellets	In important anatomical structures such as the mandibular or mental nerve, maxillary sinus, or nasal floor; as well as cortical bone and soft tissues. After completion of the retrofilling procedure and before suturing, complete removal is essential to avoid delayed healing	Not reported
Armstrong et al. ³⁸	Clinical trial	Solution	Ferric subsulfate 20%	Forearm	Not reported	Not reported	Not reported

CONCLUSION

Ferric chloride has been used as a hemostatic agent in adult patients with various health conditions in the fields of gynecology/obstetrics, dentistry, and dermatology; in different formulations, such as liquid, gel, and paste; at concentrations ranging from 15.5% to 80%; and in diverse settings, including the operating room. However, no manuscripts were identified that reported its use in patients with MNW. Therefore, there is insufficient evidence to support the use of this substance for hemostasis in bleeding MNW. Accordingly, further studies are recommended to elucidate its effects, costs, and safety in this patient population.

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CONFLICT OF INTERESTS

The authors declare there is no conflict of interests.

AUTHORS' CONTRIBUTION

YRFCS: Project administration, Formal analysis, Conceptualization, Investigation, Writing – original draft, Validation, Visualization. EACP: Project administration, Formal analysis, Conceptualization, Methodology, Investigation, Writing – review & editing, Validation, Visualization. RAO: Project administration, Formal analysis, Conceptualization, Methodology, Investigation, Writing – review & editing, Supervision, Validation, Visualization.

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