Medical Devices: Evidence and Research

Dovepress
Taylor & Francis Group

Open Access Full Text Article

ORIGINAL RESEARCH

Preclinical Performance Evaluation of an Oxidized Regenerated Cellulose Hemostat: Antibacterial Activity and Wound Healing Outcomes

Piyush G Patel[1], Bhavin Trivedi[2], Shahid N Karatela[3]

[1]Quality and R&D, Aegis Lifesciences Private Ltd., Ahmedabad, GJ, India; [2]Regulatory Affairs, Aegis Lifesciences Private Ltd., Ahmedabad, GJ, India; [3]Regulatory Affairs and Quality Assurance, Aegis Lifesciences Private Ltd., Ahmedabad, GJ, India

Correspondence: Piyush G Patel, Quality and R&D, Aegis Lifesciences Private Ltd., Ahmedabad, GJ, 382213, India, Tel +91 9898791189, Email qc@aegis-lifesciences.com

Purpose: Antimicrobial resistance (AMR) complicates surgical site infections (SSI), making it important to address surgical bleeding and bacterial bioburden. Oxidized regenerated cellulose (ORC) is a topical hemostat that generates a localized acidic microenvironment hostile to the survival of microbes. The present study evaluated the intrinsic antibacterial action and wound healing results of a commercial ORC-based hemostat in an infected wound environment.

Methods: In vitro and in vivo experimental designs were used to evaluate the antibacterial activity. An in vitro experiment was designed to show inhibition zones against 32 Gram-positive and Gram-negative bacterial strains, including antibiotic-resistant pathogens, compared to the negative control. In vivo efficacy was tested in a Wistar rat excisional wound model (n = 42), in which polymicrobial inoculation was performed with the same bacterial strains, and animals allocated to specific groups were monitored for hemostasis time, wound contraction, clinical observations, and histopathology over 28 days.

Results: Using an agar diffusion method, ORC hemostat exhibited in vitro antibacterial activity against all the 32 tested strains. In vivo, hemostasis time was significantly reduced in the test groups compared to that in the disease control group (adjusted $p < 0.001$), achieving hemostasis within 42.2–54 seconds. Similarly, wound healing was statistically significant for the test specimens, achieving up to 88.5% wound closure by day 28 (adjusted $p < 0.001$). Histopathological analysis after 28 days revealed complete re-epithelialization of the wound bed and reduced inflammatory infiltration.

Conclusion: Within the study limitations, the commercial ORC-based hemostat (Surgi-ORC®) exhibited inherent antibacterial potential against various pathogens including antimicrobial-resistant organisms and provided rapid hemostatic action. These preclinical findings suggest that ORC may help reduce microbial burden, support wound healing along with tissue regeneration. Further clinical studies are warranted to establish the relevance of these observations in surgical practice.

Keywords: oxidized regenerated cellulose, ORC, antibacterial activity, wound healing, topical hemostat, antibiotic resistance, tissue regeneration

Introduction

Microbial contamination is an important factor that interferes with the healing of surgical and traumatic wounds. It disrupts the normal repair processes and increases the risk of complications. This slows down tissue regeneration and prolongs inflammation and recovery. If it spreads from the wound and becomes uncontrolled, serious systemic problems such as sepsis can occur.[1,2] According to the World Health Organization (WHO), surgical site infections (SSIs) are the most common healthcare-associated infections globally. Their occurrence is reported to be differed by type of surgical procedures but generally more pronounced in low- and middle-income countries.[2,3] This burden is driven, in part, by the pathogens frequently involved in wound infections, such as *Staphylococcus aureus, Acinetobacter baumannii* and *Pseudomonas aeruginosa*, which use specialized virulence factors to facilitate adherence, invasion, and persistence.[4–6]

https://doi.org/10.2147/MDER.S610024
Received: 25 March 2026
Accepted: 9 July 2026
Published: 23 July 2026

In line with these underlying pathophysiological mechanisms, SSIs attributable to AMR organisms continue to be a recurrent and clinically meaningful problem that significantly increases morbidity, mortality, and healthcare costs.[7–11]

Wound healing occurs in a biological complex of tissue dynamics; therefore, objective assessments must be performed using clinical, biochemical, and histological parameters. Histology incorporates key repair processes including angiogenesis, inflammatory cell infiltration, fibroplasia, collagen deposition, wound contraction and remodeling as well as epithelialization and tissue differentiation.[12–14] Effective haemostasis and infection control are closely interconnected. Uncontrolled bleeding can lead to the formation of a protein-rich hematoma, creating a favorable environment for bacterial growth and potentially increasing the risk of surgical site infections. Against this background, topical hemostatic agents which are commonly employed in the treatment of bleeding that can simultaneously control hemorrhage and reduce bacterial burden may offer additional benefits in contaminated surgical environments.[4]

ORC-based hemostats have been well-characterized for their ability to control hemorrhage. Their mechanism of action is linked to the oxidation of cellulose, which creates a localized acidic environment that promotes clot formation through vasoconstriction, protein denaturation, restricted local blood flow and red blood cell lysis.[15–17] This localized acidic microenvironment generated upon application, confers intrinsic antibacterial properties through a non-specific, pH-mediated mechanism which in turn inhibit the growth of both susceptible and antibiotic resistant organisms, rendering conventional resistant mechanisms less effective.[18] Previous studies have reported that ORC exhibits antibacterial activity against several clinically important resistant pathogens, including *methicillin-resistant Staphylococcus aureus* (MRSA), *vancomycin-resistant Enterococcus* (VRE), and *penicillin-resistant Streptococcus pneumoniae* (PRSP), under in vitro conditions.[8] In addition to its haemostatic and antibacterial properties, ORC has been reported to support primary wound healing by promoting re-epithelialization and reducing post-hemostatic fibrosis.[19–22] Although the antibacterial properties of ORC have been previously documented, most published studies have evaluated a limited number of bacterial species, focused primarily on in vitro testing, or assessed antimicrobial activity and wound-healing outcomes separately. Additional evidence evaluating ORC against a clinically relevant pathogens, including antimicrobial-resistant pathogens, together with biological validation in vivo with wound healing analysis, would further strengthen the understanding of its potential role in contaminated surgical environments.

Therefore, the present study was designed as an extension and validation of previous findings regarding the antibacterial activity of ORC. Using a combined in vitro and in vivo preclinical approach, we evaluated a commercially available ORC-based hemostat (Surgi-ORC) against 32 clinically relevant bacterial strains, including AMR strains commonly associated with SSIs. The in vitro phase employed an agar diffusion assay, a validated method for assessing antibacterial activity of solid textile biomaterials. In the in vivo phase, we investigated whether the observed antibacterial activity was associated with favorable wound-healing outcomes, including wound contraction, re-epithelialization, histopathological characteristics, and hemostatic performance in an infected animal wound model. By integrating microbiological and biological assessments, this study aims to provide additional preclinical evidence supporting the multifunctional role of Surgi-ORC as a hemostatic material with antibacterial activity and favourable wound healing effects in contaminated wound environments.

Materials and Methods

A: In-vitro

This test was performed using commercial bacterial strains and did not need ethical approval. The microorganisms used in this study were obtained from the American Type Culture Collection (ATCC) and National Collection of Type Cultures (NCTC). The ORC-based hemostat (Surgi-ORC Original/Standard – manufactured by Aegis Lifesciences Private Ltd.) was used as test specimens and Trulene polypropylene synthetic fabric [Sterile Non-Absorbable Surgical Polypropylene Mesh, from Healthium Medtech Ltd.] was used as negative control (Figure 1).

Method Description

To evaluate the antibacterial efficiency, a total thirty-two bacterial strains were categorized into Groups A, B, C and D (Table 1), and ORC samples were challenged against these microorganisms over a period of 24 h. A double-layer agar

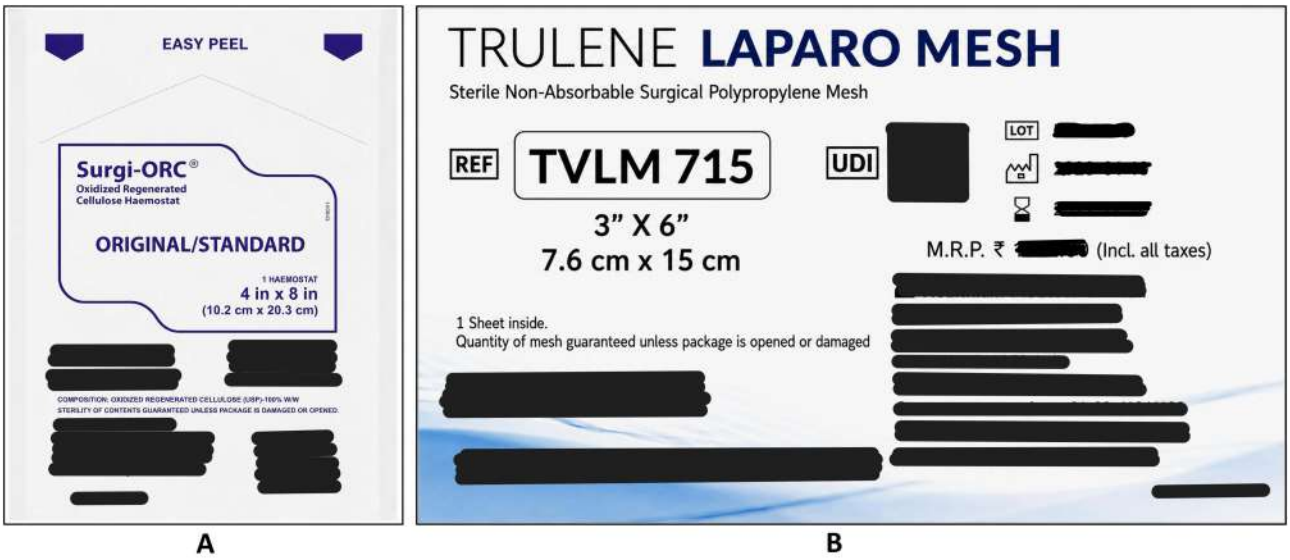

Figure 1 Products used for the in-vitro antibacterial evaluation. (**A**) An absorbable oxidized regenerated cellulose (ORC) hemostat (test material) manufactured by Aegis Lifesciences Private Ltd., and (**B**) a sterile non-absorbable polypropylene surgical mesh (negative control) manufactured by Healthium Medtech Ltd.

diffusion method[23,24] was employed for testing, where sterile agar was prepared for the lower layer and 10 ± 0.1 mL was poured into each sterilized petri plate and allowed to solidify. For the upper layer, 15–20 mL of sterile molten agar was prepared and cooled to 45 ± 1°C in a water bath, after which 1 ± 0.1 mL of bacterial working culture (1–5 × 10^8 CFU/mL) was inoculated into 150 mL of agar and mixed thoroughly to ensure uniform bacterial distribution. Approximately 5 ± 0.1 mL of the inoculated agar was poured onto each plate and allowed to congeal. The test specimens were aseptically cut into circular shapes with a diameter of (25 ± 5) mm, placed on the agar surface, and gently pressed to ensure complete contact with the medium throughout the incubation period. The plate was incubated at 30–35°C for 18–24 h immediately after specimen placement. After incubation, the plates were visually inspected for the presence or absence of bacterial growth zones around the test specimens as well as for the eventual appearance of an inhibition zone around the specimen. When a clear inhibition zone was present, its width was calculated by using following formula and the results were expressed in millimeters (mm) (Table 2).

Table 1 Groups of Microorganisms Used for Infection Creation

Sr. No.	Group	Microorganisms	Strain No.	Gram Staining	Morphology
1	A	*Staphylococcus aureus*	ATCC 6538	+Ve	Cocci (Cluster)
2		*Staphylococcus epidermidis*	ATCC 35984	+Ve	Cocci (Cluster)
3		*Micrococcus yunnanensis*	ATCC 7468	+Ve	Coccoid or cocci
4		*Streptococcus pyogenes*	ATCC 12384	+Ve	Round-to-ovoid cocci
5		*Streptococcus agalactiae*	ATCC 12386	+Ve	Round-to-ovoid cocci
6		*Streptococcus salivarius*	ATCC 13419	+Ve	Cocci
7		*Enterococcus faecium*	ATCC 6057	+Ve	Ovoid cocci
8		*Streptococcus pneumoniae*	ATCC 6303	+Ve	Cocci

(*Continued*)

Table 1 (Continued).

Sr. No.	Group	Microorganisms	Strain No.	Gram Staining	Morphology
9	B	*Lactobacillus johnsonii*	ATCC 11506	+Ve	Rod
10		*Bacillus spizizenii*	ATCC 6633	+Ve	Rod
11		*Corynebacterium xerosis*	ATCC 373	+Ve	Rod
12		*Microbacterium testaceum*	ATCC 15829	+Ve	Rod
13		*Clostridium bifermentans*	ATCC 638	+Ve	Rod
14		*Clostridium perfringens*	ATCC 13124	+Ve	Rod
15	C	*Moraxella catarrhalis*	ATCC 23246	-Ve	Diplococci
16		*Escherichia coli*	ATCC 8739	-Ve	Rod
17		*Klebsiella aerogenes*	ATCC 13048	-Ve	Rod
18		*Salmonella enteritidis*	ATCC 13076	-Ve	Rod
19		*Serratia marcescens*	ATCC 14041	-Ve	Rod
20		*Proteus vulgaris*	ATCC 33420	-Ve	Rod
21		*Bacteroides fragilis*	ATCC 25285	-Ve	Rod
22		*Enterobacter cloacae*	ATCC 13047	-Ve	Rod
23		*Pseudomonas aeruginosa*	ATCC 9027	-Ve	Rod
24		*Pseudomonas stutzeri*	ATCC 17588	-Ve	Rod
25		*Proteus mirabilis*	ATCC 12453	-Ve	Rod
26		*Shigella dysenteriae*	ATCC 13313	-Ve	Rod
27	D	*Methicillin-resistant Staphylococcus aureus*	ATCC 33591	+Ve	Cocci
28		*Vancomycin-resistant Enterococcus*	ATCC 51299	+Ve	Cocci
29		*Carbapenem-resistant Acinetobacter baumannii*	NCTC 13304	-Ve	Spherical, rod-shaped
30		*Extended-spectrum beta-lactamase-producing bacteria*	NCTC 13351	-Ve	Rod
31		*Plasmid-mediated Fluoroquinolone Resistance*	NCTC 13439	-Ve	Rod
32		*SHV β-lactamase*	ATCC 700603	-Ve	Rod

$$H = D - d/2$$

where H is the inhibition zone in millimeters, D is the total diameter of the specimen and inhibition zone in millimeters, and d is the diameter of the specimen in millimeters.

The inhibition zone values reported in this study represent the radial width of the clear zone (distance from the edge of the specimen to the edge of visible bacterial growth) rather than the total inhibition diameter.

B: In vivo

Animals

This animal study was conducted at Ribosome Research Centre Pvt. Ltd. (Registration No. 2078/PO/RcBi/S/2019/CCSEA) following the recommendations and ethical practices as laid down in the Committee for the Control and Supervision of Experiments on Animals (CCSEA) guidelines. The animal study protocol was reviewed and approved by

Table 2 Inhibition Zones of Bacterial Strains Exposed to ORC Hemostat After 24 H

S. No.	Microorganisms	Diameter of Specimen (mm)	Diameter of Specimen and Inhibition Zone (mm)
Group A			
1	*Staphylococcus aureus*	23.00	27.87
2	*Staphylococcus epidermidis*	23.00	26.97
3	*Micrococcus yunnanensis*	23.00	24.42
4	*Streptococcus pyogenes*	23.00	31.63
5	*Streptococcus agalactiae*	23.00	27.40
6	*Streptococcus salivarius*	23.00	34.17
7	*Enterococcus faecium*	23.00	28.14
8	*Streptococcus pneumoniae*	23.00	27.94
Group B			
9	*Lactobacillus johnsonii*	23.00	30.79
10	*Bacillus spizizenii*	23.00	25.32
11	*Corynebacterium xerosis*	23.00	43.47
12	*Microbacterium testaceum*	23.00	28.11
13	*Clostridium bifermentans*	23.00	28.89
14	*Clostridium perfringens*	23.00	32.28
Group C			
15	*Moraxella catarrhalis*	23.00	41.49
16	*Escherichia coli*	23.00	26.42
17	*Klebsiella aerogenes*	23.00	24.82
18	*Salmonella enteritidis*	23.00	24.75
19	*Serratia marcescens*	23.00	23.92
20	*Proteus vulgaris*	23.00	25.45
21	*Bacteroides fragilis*	23.00	28.54
22	*Enterobacter cloacae*	23.00	27.22
23	*Pseudomonas aeruginosa*	23.00	25.75
24	*Pseudomonas stutzeri*	23.00	30.66
25	*Proteus mirabilis*	23.00	27.67
26	*Shigella dysenteriae*	23.00	30.12
Group D			
27	*Methicillin-resistant Staphylococcus aureus*	23.00	27.49
28	*Vancomycin-resistant Enterococcus*	23.00	27.00
29	*Carbapenem-resistant Acinetobacter baumannii*	23.00	23.62
30	*Extended-spectrum beta-lactamase-producing bacteria*	23.00	27.02
31	*Plasmid-mediated Fluoroquinolone Resistance*	23.00	23.86
32	*SHV β-lactamase*	23.00	26.48

the Institutional Animal Ethics Committee (IAEC) of Ribosome Research Centre Pvt. Ltd. (Approval No. RRC/IAEC/13/2024/066; approved on 15 October 2024). A total of 42 male Wistar rats (Rattus norvegicus), aged less than 12 weeks, with mean body weight of 255.3 ± 18.3 g and were randomly assigned to seven experimental groups (Table 3). Only male animals were selected to avoid hormonal variability associated with the estrous cycle in female rats, which can influence wound healing measurements. At the end of the study, all surviving animals were humanely euthanized using carbon dioxide (CO_2) inhalation with gradual fill method, in accordance with CCSEA guidelines which are consistent with the American Veterinary Medical Association (AVMA) Guidelines for the Euthanasia of Animals.

Table 3 In vivo Experimental Design

Group	Animal Numbers	Treatment
G1	1–6	Normal Control (Animals not operated for wound creation and not treated with anything)
G2	7–12	Disease Control (Group A + B + C + D and not treated with anything)
G3	13–18	Group A + Test Item
G4	19–24	Group B + Test Item
G5	25–30	Group C + Test Item
G6	31–36	Group D + Test Item
G7	37–42	Positive Control (Group A + B + C + D and treated daily with framycetin sulfate 1% w/w cream until 85% wound closure)

Notes: Group A: Gram +ve organisms (Cocci morphology); Group B: Gram +ve organisms (Rod morphology); Group C: Gram -ve organism (Cocci and Rod morphology); Group D: Antibiotic-resistant organisms (Cocci and Rod morphology).

Preparation of Microbial Consortium

The microbial consortium was prepared, and 10^8 CFU was estimated using the serial dilution technique. Culture suspensions were prepared up to -10^{-10} dilution. From each dilution, 0.1 mL was inoculated into a sterile Petri dish in duplicate. Then, 15–20 mL of sterile soybean casein digest agar (SCDA) was poured into each Petri dish allowed to solidify and then transferred to incubator at 32.5°C for 24–48 h. For obligate anaerobic organisms, including *Clostridium* spp. and *Bacteroides* spp., cultures were incubated under anaerobic conditions using an anaerobic culture system to ensure optimal growth and viability prior to preparation of the microbial consortium.

Treatment Procedure

All animals were anesthetized with suitable anesthetic agents, except those in Group G1. All animals were shaved and the selected area was sterilized with 70% ethanol. Animals from groups G2 to G7 were placed on the lateral side, and the dimensions of the wound (approximately 2.5 × 2.5 cm) were made on the dorsum cervical region, using infected straight surgical scissors/blade and tissue forceps with a culture of microorganisms. Different groups of microbial consortia (eg Group A/B/C/D) were applied to the scalpel or surgical blade before wound creation in all the animals of different groups. Animals from Group G1 were kept without wounds. For animals in group G2, all four groups of microorganism strains (32 strains) were applied to the wound area without any treatment. Animals from groups G3–G6 were assigned to the respective groups of microbial organisms along with the test item after wound creation, as per the experimental design. Animals from group G7 were infected with all 32 bacterial strains and subsequently treated with the positive control, Soframycin® cream (framycetin sulfate 1% w/w in a cream base; Sanofi India Ltd). Test items were applied on day 1, and the positive control was applied for up to 85% wound contraction according to their intended clinical use. The test and reference items were applied in such a way that the treated area of the wound was covered. Bandage was applied (applicable group) for at least 6 h to prevent the loss of test items.

Observations

During the course of the study, observations were made are as below;

1. Mortality/morbidity was checked twice daily throughout the study period.
2. General clinical signs were observed once daily throughout the study period.
3. The body weight of each animal was recorded on day 1 before dosing and weekly thereafter.
4. The wound area was measured on days 1, 8, 15, 22, and 28 using digital planimetry with the software "imitoMeasure".[25]
5. At the end of the experiment, swab samples were collected to identify the microbial strains using the VITEK 2 automated system.[26] The isolated organisms were inoculated into identification cards containing specific biochemical substrates. The system monitored microbial growth by detecting the optical changes within the microwells.

These reaction patterns were then analyzed and compared with the reference database to determine the identity of the organism and its antimicrobial susceptibility profile.

6. Duration of hemostasis was determined on day 0 after treatment.
7. Wound skin samples were collected and fixed in 10% neutral buffered formalin. After fixation, tissues were processed using a tissue processor. After processing, tissues were embedded in paraffin to create blocks. Sections were cut from these blocks using a semi-automated rotary microtome to prepare slides. Finally, the slides were stained with Hematoxylin and Eosin (H&E) for microscopic examination.
8. Histopathological examination was performed on the preserved organs (skin) of all animals. In addition, all gross lesions from all animals were examined microscopically. Tissues selected for histopathological evaluation were processed, embedded, and sectioned for further processing and microscopic examination. Data were compiled based on the incidence and severity of the changes.

Above all measurements were performed by trained operators of Ribosome Research Centre Pvt. Ltd, a third-party contract research organization and investigators (authors) were blinded to treatment allocation during wound measurements or histopathological analysis.

Statistical Analysis

Data are presented as mean ± standard deviation (SD). Normality was assessed using the Shapiro-Wilk test, and homogeneity of variances was verified with Levene's test. One-way analysis of variance (ANOVA) was performed for hemostasis time and wound area on day 28. When ANOVA was significant ($p < 0.05$), pairwise comparisons were conducted using Tukey's HSD post-hoc test to control the family-wise Type I error rate. As a sensitivity analysis, non-parametric Kruskal-Wallis and Wilcoxon rank-sum tests with Bonferroni correction were also applied to confirm the robustness of the findings. All statistical analyses were performed using R version 4.3.2. A corrected p-value <0.05 was considered statistically significant. No a priori power analysis was conducted; the sample size of n = 6 per group was based on previously published similar preclinical studies evaluating wound healing and antimicrobial activity in rodent excisional/superficial wound models.[27,28] This sample size is also consistent with the principles of ISO 10993–2:2022 (Animal Welfare Requirements) and the 3Rs concept, ensuring that the minimum number of animals is used.[29]

Results

In-vitro Antibacterial Efficacy

Following a 24-hour exposure period, the negative control showed no clear zone, whereas the Surgi-ORC exhibited a clear zone against all tested Gram-positive and Gram-negative bacterial strains, indicating effective antibacterial activity. The 23 mm test specimens consistently prevented bacterial colonization, which is demonstrated by total inhibition diameters ranging from 23.62 mm to 43.47 mm. Among the tested groups, the maximum inhibition zones were observed as follows: Group A, *Streptococcus salivarius* (5.6 mm); Group B, *Corynebacterium xerosis* (10.2 mm); Group C, *Moraxella catarrhalis* (9.2 mm); and Group D, MRSA (2.2 mm). The zone of inhibition was more pronounced against Gram-positive bacteria, such as *Corynebacterium xerosis* and *Moraxella catarrhalis* demonstrating a stronger bacteriostatic effect on these species. Figures 2 and 3 represent the zones of inhibition for all microbial strains, including antibiotic-resistant microbes.

In vivo Safety and Pathology Observations

Throughout the 28-day observation period, no morbidity, mortality, or adverse clinical signs were observed in either the vehicle or treatment groups. All animals had normal body weights within the expected parameters. Furthermore, gross necropsy revealed no macroscopic lesions in any of the terminally sacrificed animals. These results demonstrate the safety of the tested specimens.

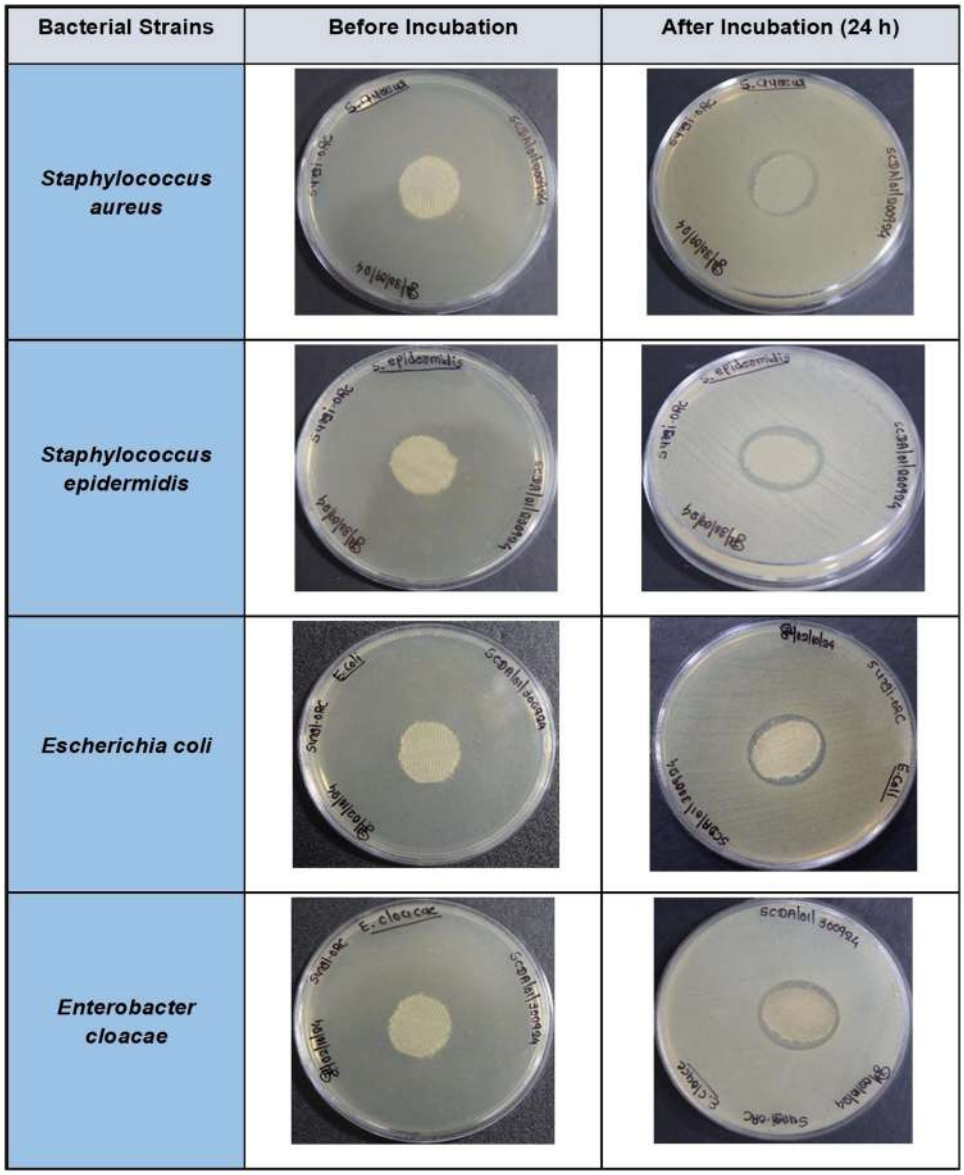

Figure 2 Inhibition zone analysis showing the antibacterial activity of ORC against pathogenic and antibiotic-resistant bacterial strains.

In vivo Hemostasis Kinetics

Following wound creation on day 0, animals treated with ORC-based hemostat exhibited reduced hemostasis times (42.2–54 s) compared with the untreated disease control group (66.7 s) and were comparable with the positive control (36 s) group, indicating effective bleeding control. As shown in the Figure 4A, hemostasis time was significantly reduced in all ORC-treated groups compared with the disease control group (adjusted $p < 0.001$ for all groups). Groups A, B, C, D and positive control group demonstrated shorter hemostasis times, with the shortest times observed in Group D and the positive control group. The mean haemostasis time for individual groups is mentioned in Table 4.

In vivo Wound Contraction and Pathogen Clearance

Table 5 provides details about the wound contraction in groups of animals over the 28-day study period. The disease control group exhibited only a relatively small reduction in mean wound areas, decreasing only from 2.31 cm^2 to 1.36 cm^2 by day 28. In contrast, test cohorts demonstrated progressive wound closure, with mean wound areas declining from 1.89 to 0.36 cm^2 (Group A), 1.60 to 0.24 cm^2 (Group B), 1.44 to 0.14 cm^2 (Group C), and 1.42 to 0.77 cm^2 (Group

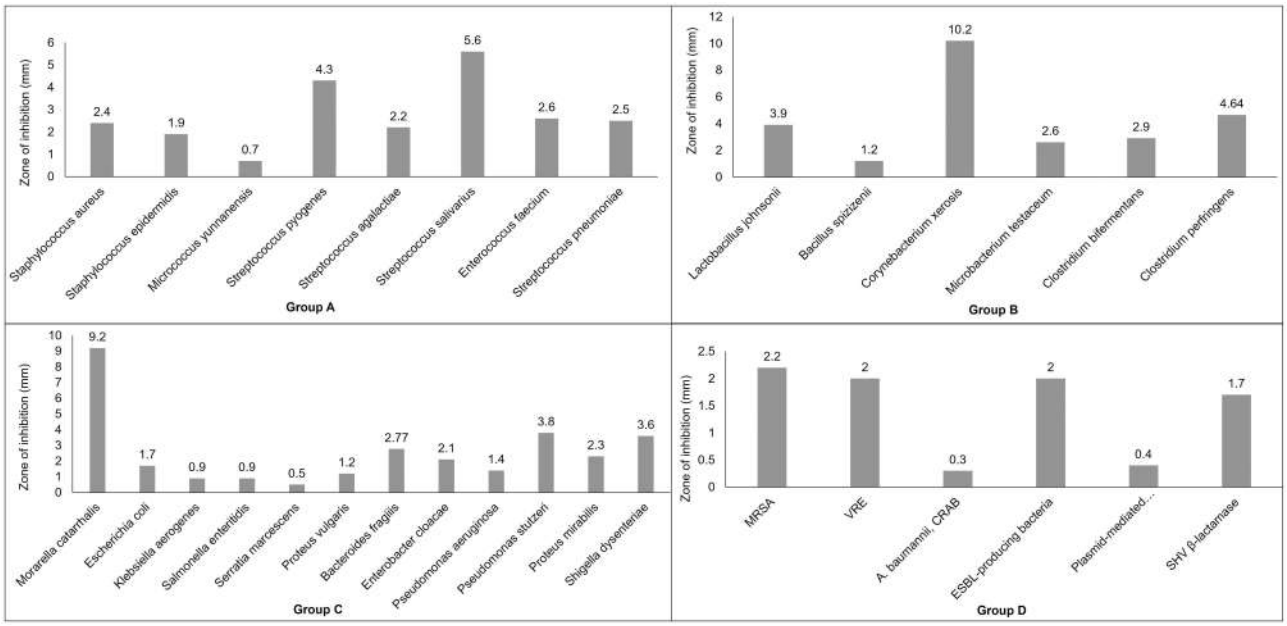

Figure 3 Group-wise inhibition zones of bacterial strains after 24 h exposure to ORC.
Notes: Group (**A**) Inhibition zones of Gram +ve organisms (Cocci morphology); Group (**B**) Inhibition zones of Gram +ve organisms (Rod morphology); Group (**C**) Inhibition zones of Gram -ve organism (Cocci and Rod morphology); Group (**D**) Inhibition zones of antibiotic-resistant organisms (Cocci and Rod morphology).

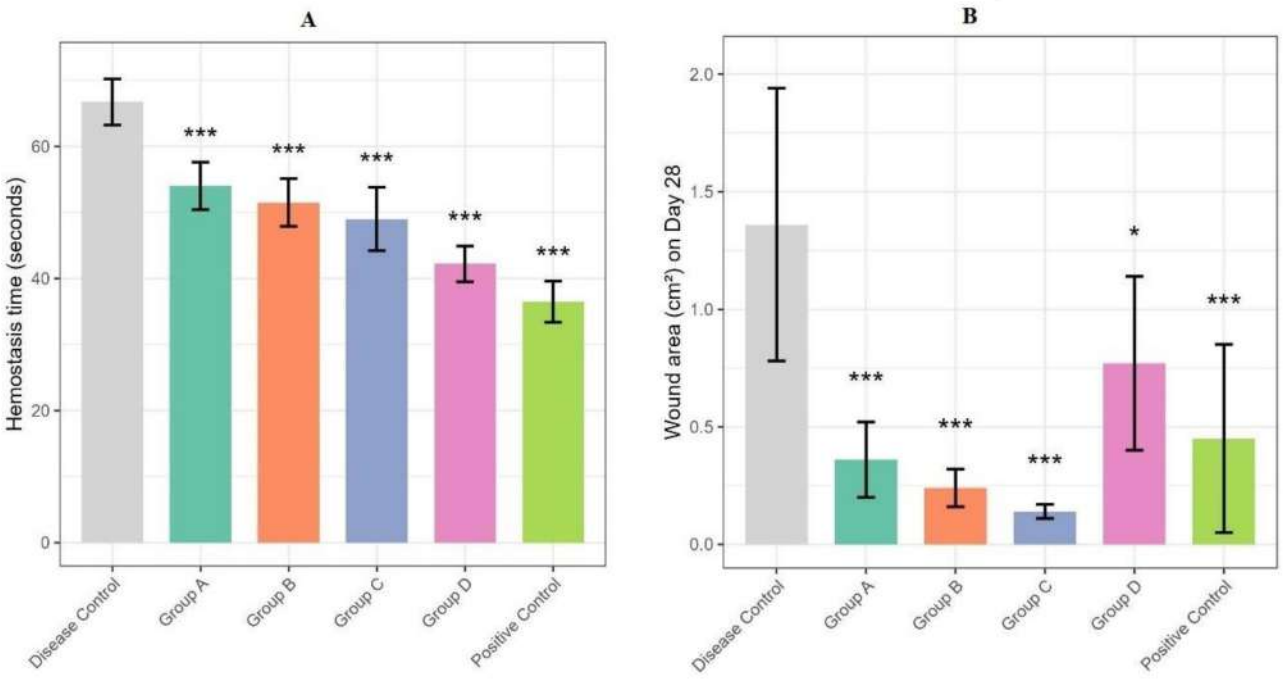

Figure 4 Effect of ORC hemostat on (**A**) hemostasis time and (**B**) wound area on day 28. Data are presented as mean ± SD. Significance asterisks indicate Tukey-adjusted p-values compared to the disease control group: *** p adjusted < 0.001, * p adjusted < 0.05. Colors represent different treatment groups.

D). The positive control group showed a reduction from 2.73 to 0.45 cm^2 over the same period. By Day 28. All treatment groups showed smaller residual wound areas than the disease control group (Figure 4B). Significant reductions in wound area were observed in Groups A, B, C, and the positive control group (adjusted $p < 0.001$), while Group D (resistant organisms) demonstrated a smaller though statistically significant, improvement in wound area (adjusted $p < 0.047$).

https://doi.org/10.2147/MDER.S610024

Table 4 Effect of ORC Hemostat on Hemostasis Time

Group	Hemostasis Time (s), Mean ± SD
Disease Control (A + B + C + D), (n = 6)	66.7 ± 3.5
Group A + Test Item, (n = 6)	54.0 ± 3.6
Group B + Test Item, (n = 6)	51.5 ± 3.6
Group C + Test Item, (n = 6)	49.0 ± 4.8
Group D + Test Item, (n = 6)	42.2 ± 2.7
Positive Control (A + B + C + D), (n = 6)	36.5 ± 3.1

Notes: Group A: Gram +ve organisms (Cocci morphology); Group B: Gram +ve organisms (Rod morphology); Group C: Gram -ve organism (Cocci and Rod morphology); Group D: Antibiotic-resistant organisms (Cocci and Rod morphology).

Table 5 Effect of ORC Hemostat on Wound Contraction (%) in Terms of Area

Group	Day 1	Day 8	Day 15	Day 22	Day 28	Mean % Wound Closure Achieved	p Value (vs Disease Control) *	p Value (vs Positive Control) †
Disease Control (A + B + C + D), (n = 6)	2.31 ± 0.52	1.79 ± 0.76	1.67 ± 0.70	1.53 ± 0.66	1.36 ± 0.58	42.8	–	–
Group A + Test Item, (n = 6)	1.89 ± 0.35	1.13 ± 0.59	0.57 ± 0.23	0.47 ± 0.20	0.36 ± 0.16	80.3	**0.00017**	0.996
Group B + Test Item, (n = 6)	1.60 ± 0.30	0.96 ± 0.17	0.38 ± 0.12	0.32 ± 0.11	0.24 ± 0.08	83.6	**0.00003**	0.879
Group C + Test Item, (n = 6)	1.44 ± 0.67	0.98 ± 0.50	0.23 ± 0.06	0.18 ± 0.05	0.14 ± 0.03	88.5	**0.000008**	0.611
Group D + Test Item, (n = 6)	1.42 ± 0.68	1.05 ± 0.38	1.00 ± 0.37	0.92 ± 0.35	0.77 ± 0.37	49.8	**0.04699**	0.545
Positive Control (A + B + C + D), (n = 6)	2.73 ± 0.63	1.39 ± 0.51	0.66 ± 0.50	0.56 ± 0.44	0.45 ± 0.40	83.5	–	–

Notes: Data are presented as mean ± SD, wound contraction (%) in terms of area (cm^2). * p value from one-way ANOVA followed by Tukey's HSD post-hoc test (disease control as reference). † p value from Tukey's HSD comparing each test group to positive control. All p-values are adjusted for multiple comparisons. Statistically significant differences ($p < 0.05$) are shown in bold. Group A: Gram +ve organisms (Cocci morphology); Group B: Gram +ve organisms (Rod morphology); Group C: Gram -ve organism (Cocci and Rod morphology); Group D: Antibiotic-resistant organisms (Cocci and Rod morphology).

Among the ORC-treated groups, Group C exhibited the smallest residual wound area. Non-parametric analyses (Kruskal-Wallis and Wilcoxon with Bonferroni) confirmed these findings, with consistent significance for Groups A–C. Overall, wound closure in the treatment groups reached up to 88.5% by Day 28.

Furthermore, microbial identification using the VITEK system on day 28 revealed that pathogen clearance was not uniform across test groups. The disease control group remained colonized by multiple pathogenic organisms, while the test groups (G3–G6) exhibited a substantial reduction in the pathogen load, although complete elimination of pathogens was not achieved. In contrast, complete pathogen clearance was observed in the positive control group (G7). These results suggest that Surgi-ORC's antibacterial efficacy may be varied by organism category, with greatest efficacy against Group B (Gram-positive rods) and more limited activity against Group C (Gram-negative) and Group D (antibiotic-resistant) organisms. The findings of VITEK system are summarized in Table 6. The entire wound healing process, from full-thickness wound creation, material application, achievement of hemostasis to complete wound closure, and lack of visible inflammation by day 28, is illustrated with the graphical images of Wistar rats in Figure 5.

Histopathological Evaluation

Histopathological evaluation revealed no abnormalities in the control group, whereas the treatment groups showed varying degrees of inflammation and progressive healing. Re-epithelialization was observed in most test groups, with complete healing in the higher groups. Histopathological analysis suggested that Surgi-ORC promoted tissue regeneration and reduced the inflammatory response compared with the disease control group (Table 7).

Table 6 Identification of Organism Strain by VITEK Method

Group	Identified Microorganisms
G3 (Group A+ Test item)	*Staphylococcus aureus*
G4 (Group B + Test item)	*Bacillus spizizenii*
G5 (Group C + Test item)	*Klebsiella aerogenes*
	Shigella group
	Escherichia coli
G6 (Group D + Test item)	*Acinetobacter baumannii complex*
	Enterococcus faecalis
G7 (Positive Control (A + B + C + D) with Soframycin)	Not detected

Notes: Group A: Gram +ve organisms (Cocci morphology); Group B: Gram +ve organisms (Rod morphology); Group C: Gram -ve organism (Cocci and Rod morphology); Group D: Antibiotic-resistant organisms (Cocci and Rod morphology).

Discussion

Contamination of wounds and post-operative infections is still a clinical overburden, especially in surgical procedures where exposure to multiple bacteria as well as antimicrobial-resistant (AMR) pathogens creates difficulties in management strategies. In this context, local hemostatic materials with intrinsic antibacterial properties are theoretically advantageous for providing concomitant control of hemorrhage while reducing the microbial burden at the surgical site. Traditionally, the effectiveness of ORC has been tested mainly in isolated situations using microbiological tests or in a single in vivo surgical model. The current study extends existing evidence on ORC by employing dual experimental design proceeded in a step-wise manner, starting with controlled in vitro evaluation against 32 bacterial strains, including antimicrobial resistant organisms, and followed by in vivo assessment of hemostatic performance and wound-healing outcomes of a commercial ORC matrix in an infected wound model. The 32 different bacterial strains studied were prevalent in contaminated environments and hospital settings, representing a key source of exposure. They confer an enhanced risk of nosocomial infection with complications, including systemic infection, sepsis, delayed wound healing, and progressive tissue necrosis.[2,30,31]

ORC promotes hemostasis via a combination of biochemical and physical effects. Upon contact with blood, it transforms into a brownish or black gelatinous mass, which facilitates platelet adhesion and aggregation, leading to the formation of a platelet-fibrin plug.[32] Oxidation converts the cellulose hydroxyl groups into carboxyl groups to form polyuronic acids. This modification creates an acidic microenvironment that enhances clot formation by promoting

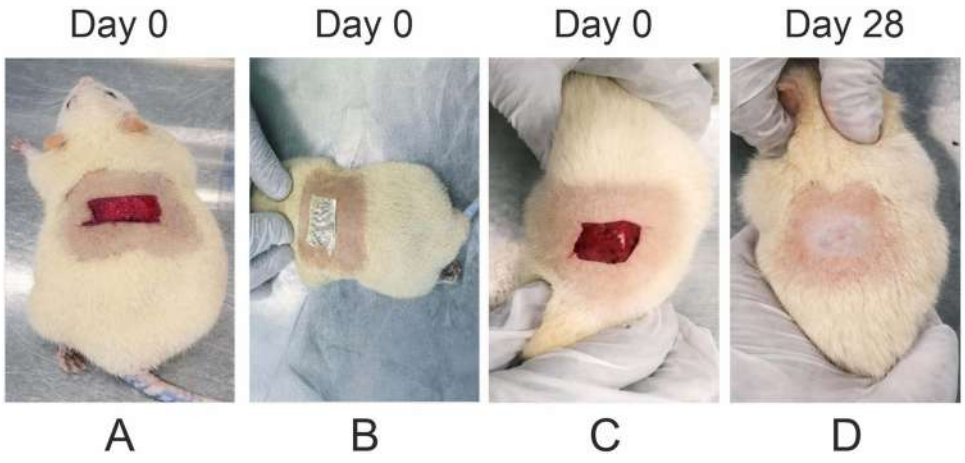

Figure 5 Representative photographs of hemostasis and wound healing in a Group C animal following ORC application: (**A**) Full-thickness excisional wound immediately after wound creation (Day 0), (**B**) ORC test item applied to the wound bed (Day 0), (**C**) Wound appearance after achieving hemostasis (Day 0), (**D**) Complete wound closure with re-epithelialization (Day 28). Photographs are shown for illustration only; wound area measurements were performed independently using calibrated digital planimetry (imitoMeasure), as described in Methods.

Table 7 Summary of Severity-Wise Histopathological (Microscopic) Observations

Group	Animals ID	Organ/Tissue	Microscopic Observations
G1	1-6	Skin	No abnormality detected in epidermis or dermis
G2	7-12	Skin	Presence of inflammatory cells in the epidermis; pustule formation observed in some animals
G3	13-18	Skin	Mild inflammatory cells present in some animals; Re-epithelialization observed, indicating healing
G4	19-24	Skin	Inflammatory cells present in some animals; Re-epithelialization observed, indicating healing
G5	25-30	Skin	Complete Re-epithelialization observed, indicating healing
G6	31-36	Skin	Inflammatory cells present in some animals; Re-epithelialization observed, indicating healing
G7	37-42	Skin	Complete Re-epithelialization observed, indicating healing

Notes: G1; Normal control; G2: Disease control (All 32 organisms) + non-treated; G3: Group A organisms + Test item; G4: Group B organisms + Test item; G5: Group C organisms + Test item; G6: Group D: Antibiotic-resistant organisms + Test item; G7: Positive control (All 32 organisms) + Soframycin treatment.

vasoconstriction, protein denaturation, restriction of local blood flow, and red blood cell lysis, while simultaneously inhibiting bacterial growth.[15,16] As a bioabsorbable hemostatic material, in vivo ORC undergoes degradation and resorption gradually through hydrolytic and cellular processes.[33,34] Although degradation kinetics and local wound pH were not directly evaluated in the present study, previous reports have shown that acidic effect is meant to diminish over time as the material is progressively absorbed and loses its structural integrity after implantation with resorption expected within approximately 7 to 14 days of application.[21,35] Consequently, the antibacterial activity associated with ORC may be most pronounced during the early post-application period, while the continued wound-healing progression observed through Day 28 probably represents combined effects of early bacterial burden reduction, rapid hemostasis and subsequent host-mediated tissue repair processes (Supplementary Figure 1).

While ORC have an established safety profile, some potential adverse effects reported in literature should be discussed. The acidic microenvironment generated by ORC has been reported to induce localized tissue irritation and cytotoxicity particularly in neuronal and fibroblast cell lines.[35] In addition, foreign-body reactions and granuloma formation resulted from chronic inflammatory response to retained ORC material have been occasionally reported in confined anatomical spaces and may mimic tumor recurrence on post-operative imaging.[36,37] Although ORC is typically absorbed within 2–8 weeks, delayed or incomplete absorption has also been described in isolated cases and may present diagnostic challenges during postoperative follow-up.[38] None of these adverse effects were observed in the present animal model with 28-day observation period, consistent with generally favourable tolerability of ORC in superficial wound environments, although further studies evaluating ORC in enclosed surgical compartments would provide additional insight into its safety profile.

In vitro study demonstrated antibacterial activity against a comprehensive panel of Gram-positive and Gram-negative bacteria, including antibiotic-resistant pathogens. These results were based on inhibition-zone assays, indicating contact-mediated antibacterial properties linked to its known acidic microenvironment mechanism. Spangler et al demonstrated that the low pH of ORC affects a wide range of bacteria through a nonspecific mechanism; even antibiotic-resistant strains remain susceptible to the antimicrobial effect of ORC. In their study, three ORC variants were tested against nine bacterial strains, including four antibiotic-resistant isolates of MRSA, *methicillin-resistant Staphylococcus epidermidis*, VRE and PRSP, where three-log or greater reductions were observed at 24-h exposure.[18] In another study, Alhetheel AF and others have reported that ORC and its variants (standard, knit, fibril, and non-woven) effectively inhibited the growth of 32 distinct bacterial strains, with inhibition rates ranging from 40% to 100%. Notably, this included resistant pathogens, such as MRSA, VRE, and PRSP.[8]

In vivo findings suggest that ORC may contribute to reducing bacterial burden while simultaneously supports hemostasis and wound healing in contaminated wounds. While interpreting comparative wound healing outcomes, the difference in dosing frequency of test groups and positive control should be considered. Treatment with ORC resulted in faster control of bleeding across all groups compared with the disease control group, confirming its hemostatic performance (adjusted $p < 0.001$). Furthermore, animals in Groups G3, G4, and G5 showed enhanced wound healing, achieving wound closure rates of 80.3%, 83.6%, and 88.5%, respectively, which were significantly higher than those observed in the disease control group. However, Group G6 (antimicrobial-resistant organisms) showed comparatively

lower wound closure rate (49.8%), suggesting that ORC produced a smaller, but still statistically significant improvement against antibiotic-resistant organisms (adjusted $p = 0.047$). These in vivo findings indicate that in vitro antibacterial activity does not necessarily translate into complete pathogen elimination in vivo, particularly against highly resistant organisms.[39,40] This may be attributed to factors not present in agar diffusion method, such as buffering of the acidic pH environment by wound exudate, biofilm formation by MRSA and *Acinetobacter baumannii*, and the inherent resistance mechanisms of Group D organisms. Similar animal studies have proven ORC's capability to control hemorrhage. Khoshmohabat et al assessed 20 rats with liver lacerations and noted that ORC led to a reduction in total blood loss and more frequent clot formation relative to gauze packing ($p < 0.001$), facilitating its use in management of traumatic hemorrhage.[41] Furthermore, an exploratory study from J. Velázquez-Aviña et al showed that ORC can successfully reduce bleeding in gastric mucosal resection lesions in anticoagulated rabbits. Closed-pore ORC was significantly faster than open-pore ORC in achieving hemostasis (24.5 vs 66.5 seconds; $p < 0.001$), and no rebleeding, complication, or mortality occurred.[42] Clinical case reports have demonstrated that ORC provides rapid and effective haemostasis across diverse surgical settings. In myomectomy and ENT procedures, achieved haemostasis within approximately 1 to 2.1 minutes, with no reported adverse events or treatment-related complications.[43,44]

Histopathological analysis further supported the favourable wound healing results, revealing tissue re-epithelialization and reduced inflammation. These findings are supported by Liu et al, who reported that esophagotomy wounds showed good healing outcomes on post-operative day 10, and microscopic analysis on day 5 demonstrated significantly reduced inflammatory cell infiltration in ORC-treated wounds compared with those without ORC.[45] Similarly, Kang et al reported that ORC (Surgicel) resulted in milder inflammation and better healing than gelatin (Spongostan), which causes severe tissue reactions and delayed wound healing. These findings indicate that ORC-based hemostatic materials may provide advantages over gelatin in supporting favorable wound healing.[46] Furthermore, our VITEK analysis presented reduction in inoculated pathogens compared with the disease control group, although complete pathogen clearance was not uniform across all test groups, particularly in G6 (Group D organisms).

Overall, dual assessment approach study provides preliminary preclinical evidence that evaluated ORC-based hemostatic material (Surgi-ORC) possesses antibacterial activity against clinically relevant microorganisms including AMR pathogens while supporting hemostasis and wound healing. These observations may be relevant in contaminated surgical fields where reducing early microbial burden is desirable. Although promising, the results will need further mechanistic and controlled clinical studies before its efficacy and expanded clinical application for antibacterial activity can be determined.

Study Limitations

First key limitation of present study design is the non-equivalent bacterial inoculation burden between test groups and control groups. The G3 to G6 test groups were challenged with individual bacterial groups (8 strains each), whereas control groups received the full polymicrobial inoculum (total 32 strains); therefore, data from G3–G6 groups should be interpreted primarily as evidence of within-group wound healing progression in a specific bacterial context, rather than as superiority evidence relative to the control groups. Second limitation is for the in vitro design, where antibacterial activity was evaluated using an agar inhibition zone method, which is standard for solid biomaterials but does not provide Minimum Inhibitory Concentration (MIC) or Minimum Bactericidal Concentration (MBC) values. Third, quantitative histopathological scoring including semi-quantitative inflammation grading, collagen deposition scoring, angiogenesis assessment and epithelial thickness measurements was not performed. These all together would significantly strengthen the conclusions and should be incorporated in future studies.

Conclusion

The present preclinical findings support the antibacterial potential of evaluated ORC-based hemostat (Surgi-ORC), a property predominantly mediated by the characteristic low pH microenvironment of the material. The in-vitro study established effectiveness of ORC against a variety of Gram-positive, Gram-negative and antimicrobial resistant pathogenic strains, thus supporting a hypothesis that ORC hemostat may contribute to reducing microbial colonization at

wound site. In vivo observations further demonstrated faster haemostasis, favourable wound healing progression and improved histopathological outcomes compared with the untreated disease control group.

Considering degree of response varied among microbial challenge groups, particularly those having antimicrobial-resistant organisms, these preliminary data suggest that the tested Surgi-ORC may function as a multifunctional surgical aid that not only covers the traditional hemostatic role but also contributes to reducing bacterial burden during the early stages of wound healing. However, confirmation of its effectiveness in preventing SSIs requires well-controlled clinical trials on humans.

Abbreviations

ATCC, American Type Culture Collection; CCSEA, Committee for Control and Supervision of Experiments on Animals; CRAB, Carbapenem-resistant *Acinetobacter baumannii*; ESBL, Extended-spectrum beta-lactamase-producing bacteria; IAEC, Institutional Animal Ethics Committee; MRSA, Methicillin-resistant *Staphylococcus aureus*; ORC, Oxidized regenerated cellulose; PRSP, Penicillin-resistant *Streptococcus pneumoniae*; SHV, Sulfhydryl variable beta-lactamases; SSI, Surgical site infections; VRE, Vancomycin-resistant Enterococcus.

Data Sharing Statement

Data supporting the findings of this study are available upon reasonable request from the corresponding author. The data were not publicly available due to privacy or ethical restrictions.

Ethics

The animal study was conducted in accordance with the guidelines of the Committee for the Control and Supervision of Experiments on Animals (CCSEA) the Government of India. The experimental protocol was reviewed and approved by the Institutional Animal Ethics Committee (IAEC) of the Ribosome Research Centre Pvt. Ltd. (CPCSEA Registration No. 2078/PO/RcBi/S/2019/CCSEA). Approval Number: (RRC/IAEC/13/2024/066); Date of Approval: (15 October 2024).

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This research received no external funding.

Disclosure

Piyush G Patel, Bhavin Trivedi, and Shahid N. Karatela declare a potential competing interest as employees of Aegis Lifesciences Private Ltd., the manufacturer of the evaluated ORC hemostat. However, the authors state that standard, predetermined protocols were strictly followed throughout the data collection, analysis and reporting to ensure compliance and data integrity. ln vivo experimental procedures were conducted at an independent, contract research organization (Ribosome Research Centre Pvt. Ltd.) and data were collected under independent laboratory conditions. The authors declare no other competing interests in this work.

References

1. Rezaei AR, Zienkiewicz D, Rezaei AR. Surgical site infections: a comprehensive review. *Journal of Trauma and Injury*. 2025;38(2):71–81. doi:10.20408/jti.2025.0019
2. Bowler PG, Duerden BI, Armstrong DG. Wound microbiology and associated approaches to wound management. *Clin Microbiol Rev*. 2001;14 (2):244–269. doi:10.1128/CMR.14.2.244-269.2001
3. Mengistu DA, Alemu A, Abdukadir AA, et al. Global incidence of surgical site infection among patients: systematic review and meta-analysis. *Inquiry*. 2023;60:469580231162549. doi:10.1177/00469580231162549

4. Uberoi A, McCready-Vangi A, Grice EA. The wound microbiota: microbial mechanisms of impaired wound healing and infection. *Nat Rev Microbiol*. 2024;22(8):489–503. doi:10.1038/s41579-024-01035-z
5. Serra R, Grande R, Butrico L, et al. Chronic wound infections: the role of *Pseudomonas aeruginosa* and *Staphylococcus aureus*. *Expert Rev Anti Infect Ther*. 2015;13(5):605–613. doi:10.1586/14787210.2015.1023291
6. Kaushik A, Kest H, Sood M, Steussy BW, Thieman C, Gupta S. Biofilm producing methicillin-resistant *Staphylococcus aureus* (MRSA) infections in humans: clinical implications and management. *Pathogens*. 2024;13(1):76. doi:10.3390/pathogens13010076
7. Jones V, Grey JE, Harding KG. Wound dressings. *BMJ*. 2006;332(7544):777–780. doi:10.1136/bmj.332.7544.777
8. Alhetheel AF, Alrfaei BM, Mujamammi AH, et al. REGECEL (an oxidized regenerated cellulose) provides superior bioactivity effect on microorganisms. *Infect Drug Resist*. 2024;17:3353–3365. doi:10.2147/IDR.S454539
9. Wu S, Applewhite AJ, Niezgoda J, et al. Oxidized regenerated cellulose/collagen dressings: review of evidence and recommendations. *Adv Skin Wound Care*. 2017;30(11 Suppl):S1–S8. doi:10.1097/01.ASW.0000525951.20270.6C
10. Monk EJM, Jones TPW, Bongomin F, et al. Antimicrobial resistance in bacterial wound, skin, soft tissue and surgical site infections in Central, Eastern, Southern and Western Africa: a systematic review and meta-analysis. *PLOS Global Public Health*. 2024;4(4):e0003077. doi:10.1371/journal.pgph.0003077
11. Ching PR. Care bundles in surgical site infection prevention: a narrative review. *Curr Infect Dis Rep*. 2024;26. doi:10.1007/s11908-024-00837-9
12. Huded P. Wound healing: a narrative review of cellular mechanisms, regulatory factors, and clinical implications. *Int J Sci Res*. 2026;15(1):1672–1674. doi:10.21275/SR26128222251
13. de Moura Estevão LR, Cassini-Vieira P, Leite AGB, et al. Morphological evaluation of wound healing events in the excisional wound healing model in rats. *Biol Protoc*. 2019;9(13):e3285. doi:10.21769/BioProtoc.3285
14. Chowdhry SA. Use of oxidized regenerated cellulose (ORC)/collagen/silver-ORC dressings to help manage skin graft donor site wounds. *JPRAS Open*. 2019;22:33–40. doi:10.1016/j.jpra.2019.08.001
15. Kanagal D, Rao K, Gathoga P, et al. Biomaterial-based hemostasis: a review of the clinical and functional versatility of oxidized regenerated cellulose. *Cureus*. 2025;17(10):e94602. doi:10.7759/cureus.94602
16. Lewis KM, Spazierer D, Urban MD, Lin L, Redl H, Goppelt A. Comparison of regenerated and non-regenerated oxidized cellulose hemostatic agents. *Eur Surg*. 2013;45(4):213–220. doi:10.1007/s10353-013-0222-z
17. Rinnovati R, D'Angelo P, Peli A, Ralletti MV, Meistro F. Considerations about the antimicrobial activity of oxidized cellulose and oxidized regenerated cellulose and their potential application in veterinary surgery. *Vet Sci*. 2026;13(4):349. doi:10.3390/vetsci13040349
18. Spangler D, Rothenburger S, Nguyen K, Jampani H, Weiss S, Bhende S. In vitro antimicrobial activity of oxidized regenerated cellulose against antibiotic-resistant microorganisms. *Surg Infect*. 2003;4(3):255–262. doi:10.1089/109629603322419599
19. Ezer M, Doğantekin E, Çaydere M, Koç A, Öktem Ç, Hücümenoğlu S. The impact of absorbable hemostatic agents on wound healing in an experimental penile fracture rat model. *BMC Urol*. 2025;25(1):13. doi:10.1186/s12894-025-01697-8
20. Jeschke MG, Sandmann G, Schubert T, Klein D. Effect of oxidized regenerated cellulose/collagen matrix on dermal and epidermal healing and growth factors in an acute wound. *Wound Repair Regen*. 2005;13(3):324–331. doi:10.1111/j.1067-1927.2005.130316.x
21. Wagenhäuser MU, Mulorz J, Ibing W, et al. Oxidized (non)-regenerated cellulose affects fundamental cellular processes of wound healing. *Sci Rep*. 2016;6:32238. doi:10.1038/srep32238
22. Ströthoff HHI, Shabes P, Beckamp KH, et al. Comparative effects of cellulose- and gelatin-based hemostatic biomaterials on the early stage of wound healing: an in vivo study. *J Funct Biomater*. 2026;17(2):64. doi:10.3390/jfb17020064
23. International Organization for Standardization. ISO 20645:2004. *Textile Fabrics—Determination of Antibacterial Activity—Agar Diffusion Plate Test*. Geneva, Switzerland: International Organization for Standardization; 2004.
24. Orasugh JT, Temane LT, Pillai SK, Ray SS. Advancements in antimicrobial textiles: fabrication, mechanisms of action, and applications. *ACS Omega*. doi:10.1021/acsomega.4c11356
25. Khan S, Banu SA, Mamachan M, et al. Comparative assessment of smartphone-based digital planimetry for wound area measurement. *Narra J*. 2025;5(2):e1987. doi:10.52225/narra.v5i2.1987
26. Joyanes P, Del Carmen Conejo M, Martinez-Martinez L, Perea EJ. Evaluation of the VITEK 2 system for the identification and susceptibility testing of three species of nonfermenting gram-negative rods frequently isolated from clinical samples. *J Clin Microbiol*. 2001;39(9):3247–3253. doi:10.1128/JCM.39.9.3247-3253.2001
27. Tyeb S, Kumar N, Kumar A, Verma V. Agar-iodine transdermal patches for infected diabetic wounds. *ACS Appl Bio Mater*. 2020;3(11):7515–7530. doi:10.1021/acsabm.0c00722
28. Mohammad H, Cushman M, Seleem MN. Antibacterial evaluation of synthetic thiazole compounds in vitro and in vivo in a methicillin-resistant *Staphylococcus aureus* (MRSA) skin infection mouse model. *PLoS One*. 2015;10(11):e0142321. doi:10.1371/journal.pone.0142321
29. International Organization for Standardization. ISO 10993-2:2022. *Biological Evaluation of Medical Devices—Part 2: Animal Welfare Requirements*. Geneva, Switzerland: International Organization for Standardization; 2022.
30. Swain B, Samal D, Agrawal SN. Microorganisms causing wound infection and their antibiotic susceptibility pattern. *Int J Res Med Sci*. 2022;10(11):2617–2621. doi:10.18203/2320-6012.ijrms20222869
31. Puca V, Marulli RZ, Grande R, et al. Microbial species isolated from infected wounds and antimicrobial resistance analysis: data emerging from a three-years retrospective study. *Antibiotics*. 2021;10(10):1162. doi:10.3390/antibiotics10101162
32. Patel P, Sharma D, Trivedi B, Karatela S. Real-world evaluation of the safety and efficacy of Surgi-ORC® in orthopedic surgeries: a multicenter prospective study. *Cureus*. 2025;17(2):e78616. doi:10.7759/cureus.78616
33. Dimitrijevich SD, Tatarko M, Gracy RW, Linsky CB, Olsen C. Biodegradation of oxidized regenerated cellulose. *Carbohydr Res*. 1990;195(2):247–256. doi:10.1016/0008-6215(90)84169-U
34. Dimitrijevich SD, Tatarko M, Gracy RW, et al. In vivo degradation of oxidized regenerated cellulose. *Carbohydr Res*. 1990;198(2):331–341. doi:10.1016/0008-6215(90)84303-C
35. Kleine J, Leisz S, Ghadban C, et al. Variants of oxidized regenerated cellulose and their distinct effects on neuronal tissue. *Int J Mol Sci*. 2021;22(21):11467. doi:10.3390/ijms222111467
36. Alameer E. Surgicel® granuloma mimicking recurrent thyroid tumor after thyroidectomy: a case report and literature review. *Cureus*. 2023;15(10):e46587. doi:10.7759/cureus.46587

37. Wang H, Chen P. Surgicel® (oxidized regenerated cellulose) granuloma mimicking local recurrent gastrointestinal stromal tumor: a case report. *Oncol Lett*. 2013;5(5):1497–1500. doi:10.3892/ol.2013.1218
38. Puckett Y, Doubleday K, Olson M, Long K, Doubleday A. Delayed absorption of oxidized cellulose (Surgicel®) mimicking residual tumor in post-thyroidectomy patients. *ACS Case Rev Surg*. 2024;4(7):33–38.
39. Nazeer RR, Askenasy I, Swain JEV, Welch M. Contribution of the infection ecosystem and biogeography to antibiotic failure in vivo. *Npj Antimicrob Resist*. 2024;2(1). doi:10.1038/s44259-024-00063-2
40. Põhako-Palu K, Preem L, Randmäe K, et al. Development of rapid and economic in vitro assay and biorelevant ex vivo biofilm inhibition wound model to test the antibacterial efficacy of wound dressings. *Wound Repair Regen*. 2025;33(4):e70080. doi:10.1111/wrr.70080
41. Khoshmohabat H, Paydar S, Karami MY, et al. SURGICEL compared with simple gauze packing in grade IV liver injury: an experimental study. *Comp Clin Pathol*. 2019;28(2):467–471. doi:10.1007/s00580-018-2880-5
42. Velázquez-Aviña J, Mönkemüller K, Sakai P, et al. Hemostatic effect of oxidized regenerated cellulose in an experimental gastric mucosal resection model. *Endoscopy*. 2014;46(10):878–882. doi:10.1055/s-0034-1365494
43. Sharma D, Mate V, Trivedi B, Karatela SN, Patel P. Evaluation of haemostatic efficacy and safety of Surgi-ORC® in myomectomy procedures. *Int J Clin Stud Med Case Rep*. 2024;41:001007. doi:10.46998/IJCMCR.2024.41.001007
44. Patel P, Sharma D, Trivedi B, Karatela SN, Bhatnagar A. Real-world case series on Surgi-ORC® in ENT surgery. *Cureus*. 2025;17:e95539. doi:10.7759/cureus.95539
45. Liu SA, Cheng CC, Chen JS, Hung YW, Chen FJ, Chiu YT. Effect of oxidized regenerated cellulose on the healing of pharyngeal wound: an experimental animal study. *J Chin Med Assoc*. 2012;75(4):176–182. doi:10.1016/j.jcma.2012.03.007
46. Kang BS, Na YC, Jin YW. Comparison of the wound healing effect of cellulose and gelatin: an in vivo study. *Arch Plast Surg*. 2012;39(4):317–321. doi:10.5999/aps.2012.39.4.317