



## Thematic Evolution of Biomaterials in Wound Healing: An NLP-Based Topic Modeling of Research from 1990 to 2024

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This study aimed to examine thematic shifts in biomaterials research related to wound healing and to evaluate the emerging role of marine-derived materials. A total of 4,316 Web of Science publications (1990–2024) were analyzed using Latent Dirichlet Allocation. Topic modeling revealed a transition from pre-2008 focus on scaffold structure and in vitro cellular interactions toward post-2008 themes emphasizing in vivo evaluation, functional hydrogels, antimicrobial systems, and regenerative tissue engineering. Marine-derived collagens, particularly fish collagen, have gained increasing attention due to their biocompatibility, biodegradability, and ethical advantages; however, they remain underrepresented compared with mammalian sources. For transparency, the token 'marine' appeared in 34 abstracts overall (0.79% of the corpus). When stratified by period, it appeared in 0/297 abstracts before 2008 (0.0%) and in 34/4019 abstracts between 2008–2024 (0.85%), indicating an increase in explicit mention after 2008, while remaining a low-frequency signal. Therefore, 'marine' was interpreted as a secondary, qualitative signal rather than a dominant topic-forming term. Standardized extraction methods, interspecies comparative studies, and long-term in vivo safety assessments are needed to support their translational use. Strengthening interdisciplinary collaborations will accelerate their integration into clinical and veterinary practice.

**Key Words:** Wound healing, biomaterials, natural language processing (NLP), latent dirichlet allocation (LDA), marine collagen

### Yara İyileşmesinde Biyomalzemelerin Tematik Evrimi: 1990-2024 Arası Araştırmaların NLP Tabanlı Konu Modellemesi

Bu çalışma, yara iyileşmesi ile ilgili biyomalzeme araştırmalarındaki tematik değişimleri incelemek ve deniz kaynaklı malzemelerin ortaya çıkan rolünü değerlendirmek amacıyla yapılmıştır. Toplam 4.316 Web of Science yayını (1990–2024) Latent Dirichlet Allocation kullanılarak analiz edilmiştir. Konu modellemesi, 2008 öncesinde iskele yapısı ve in vitro hücresel etkileşimlere odaklanılmasından, 2008 sonrasında in vivo değerlendirme, fonksiyonel hidrojel, antimikrobiyal sistemler ve rejeneratif doku mühendisliğini vurgulayan temalara geçiş olduğunu ortaya koymuştur. Deniz kaynaklı kollajenler, özellikle balık kollajeni, biyoyumlulukları, biyolojik olarak parçalanabilirlikleri ve etik avantajları nedeniyle giderek daha fazla ilgi görmektedir; ancak memeli kaynaklarına kıyasla hala yeterince temsil edilmemektedirler. Şeffaflık açısından, "deniz" kelimesi toplam 34 özetinde (korpusun %0.79'u) geçmektedir. Dönemlere göre sınıflandırıldığında, 2008 öncesinde 0/297 özetinde (0.0%) ve 2008–2024 arasında 34/4019 özetinde (%0.85) yer almıştır, bu da 2008'den sonra açıkça bahsedilme sıklığının arttığını, ancak yine de düşük sıklıkta bir sinyal olduğunu göstermektedir. Bu nedenle, "deniz" kelimesi, baskın bir konu oluşturan terimden ziyade ikincil, nitel bir sinyal olarak yorumlanmıştır. Standartlaştırılmış ekstraksiyon yöntemleri, türler arası karşılaştırmalı çalışmalar ve uzun vadeli in vivo güvenlik değerlendirmeleri, bunların translaşyonel kullanımını desteklemek için gereklidir. Disiplinler arası işbirliğinin güçlendirilmesi, bunların klinik ve veterinerlik uygulamalarına entegrasyonunu hızlandıracaktır.

**Anahtar Kelimeler:** Yara iyileşmesi, biyomalzemeler, doğal dil işleme (NLP), latent dirichlet allocation (LDA), deniz kollajeni

### Introduction

The integration of artificial intelligence (AI) technologies in the field of healthcare enables more effective analysis of complex biological processes such as wound healing. Especially with advances in machine learning, image processing and natural language processing (NLP), both clinical decision support systems and literature analysis-based modeling have become increasingly meaningful and predictive (1, 2). In this scope, the Latent Dirichlet Allocation (LDA) algorithm stands out as an effective text mining method for identifying thematic trends in literature. Studies conducted in this perspective have analyzed artificial intelligence applications in the field of medicine with LDA and revealed that the main themes of wound healing are concentrated around concepts such as 'biomaterial development', 'infection control' and 'epithelisation' (3). Using LDA to track topic evolution in health research, prior studies have examined how AI-related themes align with clinical decision-making in wound healing (4). Image processing-based approaches also play an important role in wound healing. Recent studies have used support vector machines (SVM) and decision trees to analyze wound images and have shown that these methods can speed up medical decision-making about the healing phase (5). The hybrid neural network and decision tree model

developed by Kolli et al. (6) focused on optimising the timing of clinical interventions by predicting the healing time from wound images.

Wound healing (WH) is a complex and dynamic process that usually occurs in four basic phases: haemostasis, inflammation, proliferation and remodelling. Wounds are classified as acute and chronic according to their healing time. Acute wounds usually heal within a certain period of time, whereas chronic wounds are lesions that do not close for more than six weeks, often including examples such as diabetic foot ulcers, pressure sores and venous ulcers. Chronic wounds both reduce individual quality of life and create a significant economic burden on the health system (2). The main challenges encountered in wound treatment include the risk of infection, inadequate blood flow, nutritional disorders and chronic diseases such as diabetes. Modern treatment approaches developed in this context include wound dressings that provide a moist environment, negative pressure wound therapy, hyperbaric oxygen therapy, growth factors, electrical stimulation, ultrasound, laser and larval therapy. Especially wound dressings stand out thanks to their ease of application and usability in different wound types (7).

Innovative research has focused on biomaterial-based development of these products. The literature reveals a shift in the focus on biomaterials between the pre-2008 and post-2008 periods. In the pre-2008 period, cell-based tissue engineering and fibrin-based materials were prominent; after 2008, interest in antibacterial effect, growth factors, controlled release systems, and natural biopolymer-based hydrogel wound dressings increased. Especially marine-derived materials, such as fish collagen, have potential due to their biocompatible properties (4).

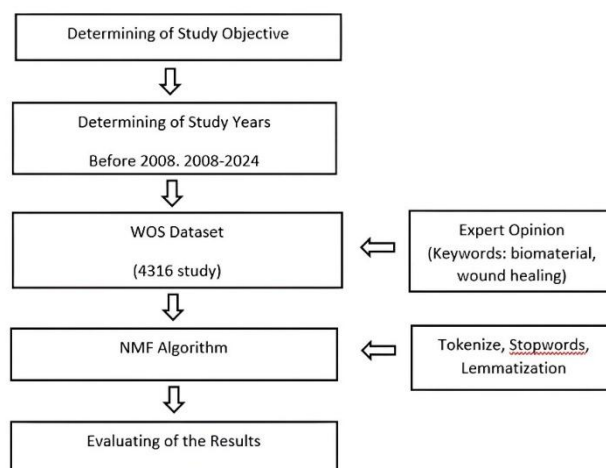
The primary aim of this study was to identify the temporal trends in the literature on wound healing and biomaterial-based approaches and to analyze the role of marine biomaterials in wound healing. As a result of LDA-based analyses, the limited emphasis on marine biomaterials points to an important research gap in this field. Accordingly, this study aims to contextualize marine biomaterials (e.g., fish collagen) within the evolving wound-healing biomaterials literature, highlighting their relative underrepresentation and outlining translational research needs.

## Materials and Methods

**Research Methodology:** This section provides information about the LDA algorithm, which is one of the NLP techniques used in this study. Figure 1 shows the methodological framework of the study.

The preprocessing, analyses, and visualization were carried out with the high programming language Python. The LDA model was implemented using the Gensim library in Python. Separate models were created for each time to observe thematic changes over time. To address sensitivity to random initialization, we fixed the

random seed for all final models to ensure reproducibility. In addition, we performed repeated runs using multiple random seeds and observed that the resulting topic structures were qualitatively stable (i.e., dominant topic labels and high-weight terms remained consistent across runs).



**Figure 1.** The methodological framework of the study

The optimal number of topics (K) for each period was selected by evaluating topic coherence across candidate K values and then confirming interpretability via manual inspection of the top terms and representative documents. Specifically, we evaluated  $K = [2-8]$  (step = 1) for each period and computed coherence using the UMass metric (Gensim CoherenceModel). The final K was selected as the solution that provided the best balance between coherence and semantic interpretability, avoiding redundant topic splitting at higher K values. We report the coherence-based selection procedure to improve reproducibility, while retaining expert-driven labeling for semantic clarity. Dominant keywords per topic were extracted, and each topic was manually labeled based on semantic interpretation.

For transparency, topic coherence was also calculated for the final models (UMass coherence): -1.25 for the pre-2008 model (K=3) and -1.23 for the 2008–2024 model (K=4), supporting the internal consistency of the selected topic solutions.

**Datasets:** This study is based on a corpus of 4316 peer-reviewed scientific articles retrieved from the Web of Science (WoS) Core Collection database. The search strategy included the keywords 'biomaterial' and 'wound healing' in article titles, abstracts, and keywords. The time period of interest ranged from the early 1990s to 2024, and publications were limited to English-language journal articles. The dataset was divided into two periods for comparative analysis: pre-2008 and 2008–2024. In this framework, the abstracts of these articles in WoS were analyzed with the LDA algorithm.

To enable an interpretable temporal comparison, we selected a single split year rather than multiple

arbitrary intervals. Using annual publication counts from the retrieved WoS records, we examined whether the growth trajectory exhibited a structural change and applied a segmented (piecewise) regression framework with an unknown breakpoint. The estimated breakpoint occurred around 2008, aligning with the onset of sustained acceleration in publication volume. Accordingly, the corpus was divided into pre-2008 and 2008–2024 subsets, and separate LDA models were trained for each period (8).

**Preprocessing:** Article abstracts were extracted and subjected to a text preprocessing pipeline. This included:

- i. Lowercasing all text
- ii. Removing stopwords and punctuation
- iii. Tokenization
- iv. Lemmatization (using spaCy and NLTK libraries)
- v. Filtering words with low frequency and overly common generic terms (e.g., “study,” “result”)

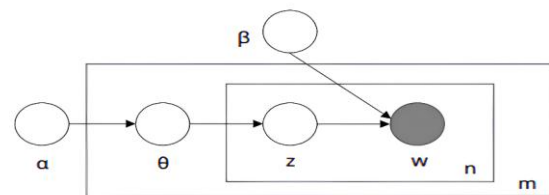
Only the abstract text was used for topic modeling to maintain consistency and reduce noise from full-text variability.

#### Natural Language Processing: LDA Algorithm:

Computational methods are used in NLP to learn, understand, and produce knowledge in human languages. Automating the study of the linguistic structure of language and building basic technologies such as machine translation, speech recognition, and speech synthesis were the main goals of early computational approaches to language research. Today, researchers are developing and applying these techniques in practical ways, developing speech-to-speech translation engines and spoken dialogue systems, searching social media for financial or health-related information, and detecting attitudes and sentiments towards goods and services (9).

Social media's growth has completely changed the kinds and quantity of information that NLP researchers can now access. Studying the connections between social contact, language use, and demography is made possible by data from websites like Facebook, YouTube, Twitter, blogs, and discussion forums. Using web scraping tools, researchers can acquire previously unthinkable volumes and types of data, frequently via website application program interfaces. Through the use of statistical and machine learning methods, they are able to predict the spread of disease from symptoms or food-related illnesses mentioned in tweets, detect deception in fake reviews, identify social networks of people interacting together online, track trending topics and popular sentiments, identify opinions and beliefs about politicians and products, and identify demographic information (like age and gender) from language (10).

NLP provides a thorough examination of methods for extracting features from text. One of the NLP approaches, LDA, may pinpoint the primary subjects in the text and extract detailed information about each one. To determine latent subjects that are likely to generate such words, LDA treats text as a collection of words. It makes the assumption that each document covers various subjects and that each word in the text has a connection to a certain subject. Finding these hidden topics and estimating topic proportions for every text are the objectives of the LDA algorithm (11). Figure 2 illustrates the LDA model:



**Figure 2.** LDA graphical model

Formula for the LDA model is as follows:

$$p(\theta, z, w | \alpha, \beta) = p(\theta | \alpha) \times \prod_{(n=1 \text{ to } N)} [ p(z_n | \theta) \times p(w_n | z_n, \beta) ]$$

In the model given in Figure 2, the parameter  $m$  represents the number of documents to be produced;  $\alpha$  represents the topic distribution;  $z$  represents a topic;  $\theta$  represents the topic distribution for a given document; and represents words. The figure reveals three levels of LDA representation. In the process of building a corpus, the parameters  $\alpha$  and  $\beta$  are assumed to be sampled once. The parameter  $\theta$  is sampled separately for each document (12).

LDA assumes that the corpus contains topics and that each document may be represented as a distribution that includes these topics. Simultaneously, LDA represents each topic as a distribution across all the languages in the corpus. To efficiently simulate these distributions, LDA makes use of Dirichlet priors.

The following succinctly describes the generating process:

For each unique document:

1. Choose a probability distribution from a Dirichlet distribution for various themes.
2. For every word that appears in the text:
  - a. From the previously selected distribution among several themes, pick a specific topic.
  - b. Pick a word from the list of terms related to the selected subject.

Finding out which latent topic distributions are responsible for producing the recorded observations is the main goal of LDA. This is accomplished by probabilistic inference, which frequently uses techniques like Gibbs sampling and variational inference. Following training, LDA can be used to assign topics to new documents and identify the most likely topics found in a particular document (13).

## Results

A total of 4316 articles indexed in the WoS database were analyzed using the LDA algorithm. The most frequently occurring keywords were clustered based on their co-occurrence patterns, and each cluster was thematically titled by researchers and subject-matter experts according to word frequency and contextual relevance. Of the total, 297 articles were published before 2008, while 4019 articles were published between 2008 and 2024. This division allowed for temporal comparison of thematic evolution within the field. Given the substantial imbalance in corpus size between periods (297 vs 4019 abstracts), cross-period differences in topic prevalence should be interpreted as descriptive patterns rather than statistically inferred changes. Accordingly, we did not perform inferential hypothesis testing on topic proportions across periods.

A review of the studies published before 2008 using the LDA algorithm showed that the articles mainly focused on three main themes. These were classified as Cellular Interactions–Tissue Formation (33.8%), Collagen–Matrix-Based Regeneration (31.3%), and Surface Properties–Controlled Drug Release (34.8%). The extracted keywords were clustered under these

thematic headings, indicating that research in this period predominantly focused on structural characteristics and their interplay with biological responses (Table 1).

The word cloud visualization of keywords from publications prior to 2008 is presented in Figure 3.

Between 2008 and 2024, analysis of the article corpus revealed four predominant thematic clusters: Infection Control–Wound Healing (22.8%), Functional Hydrogels–Tissue Engineering (25.1%), Therapeutic–Controlled Release Systems (24.8%), and Mechanical Properties–Structural Functionality (27.3%). The keywords associated with the publications during this period were systematically grouped under these thematic categories (Table 2).

The visualization of the words belonging to the studies between 2008–2024 with word cloud analysis is given in Figure 4.

In addition, the keywords were analyzed and presented graphically for both the studies before 2008 and those between 2008 and 2024 (Figure 5).

For transparency, the token ‘marine’ appeared in 34 abstracts overall (0.79% of the corpus). When stratified by period, it was absent pre-2008 (0/297; 0%) and occurred in 34/4019 abstracts post-2008 (0.85%). Therefore, it was interpreted as a secondary, qualitative signal rather than a dominant topic-forming term. These percentage distributions are reported for exploratory description only; we did not compute confidence intervals, effect sizes, or perform hypothesis testing, and therefore the results should not be interpreted as statistically significant differences.

**Table 1.** Identification of themes and keywords with LDA before 2008

Cellular Interactions–Tissue Formation	Weight (%33.8)	Collagen–Matrix Based Regeneration	Weight (%31.3)	Surface Properties–Controlled Drug Release	Weight (%34.8)
cell(s)	2130	collagen	1295	surface(s)	1315
tissue	1200	materials	665	tissue	570
fibrin	545	matrix	600	biomaterials	570
rights	520	growth	595	showed	550
material	475	response	575	days	525
treated	460	bone	545	reserved	520
release	455	chitosan	540	implants	495
vivo	445	human	480	skin	480
beta	410	implant	445	cell	465
properties	410	vitro	445	control	440
model	400	process	395	activity	350
effect	400	proliferation	365	found	345
culture	360	regeneration	340	matrices	335
weeks	340	inflammatory	330	type	300
dressing	335	significantly	315	membrane	295
acid	335	effects	315	evaluated	290
containing	325	based	300	Science	280
using	310	implantation	285	analysis	270

**Note:** ‘Weight’ denotes the absolute token frequency (raw count) of each keyword in the period-specific, preprocessed abstract corpus (not a topic–word probability). Certain high-weight tokens may reflect database export artifacts (e.g., publisher/copyright-related strings). A sensitivity run removing these tokens yielded stable topics and did not alter the main conclusions.



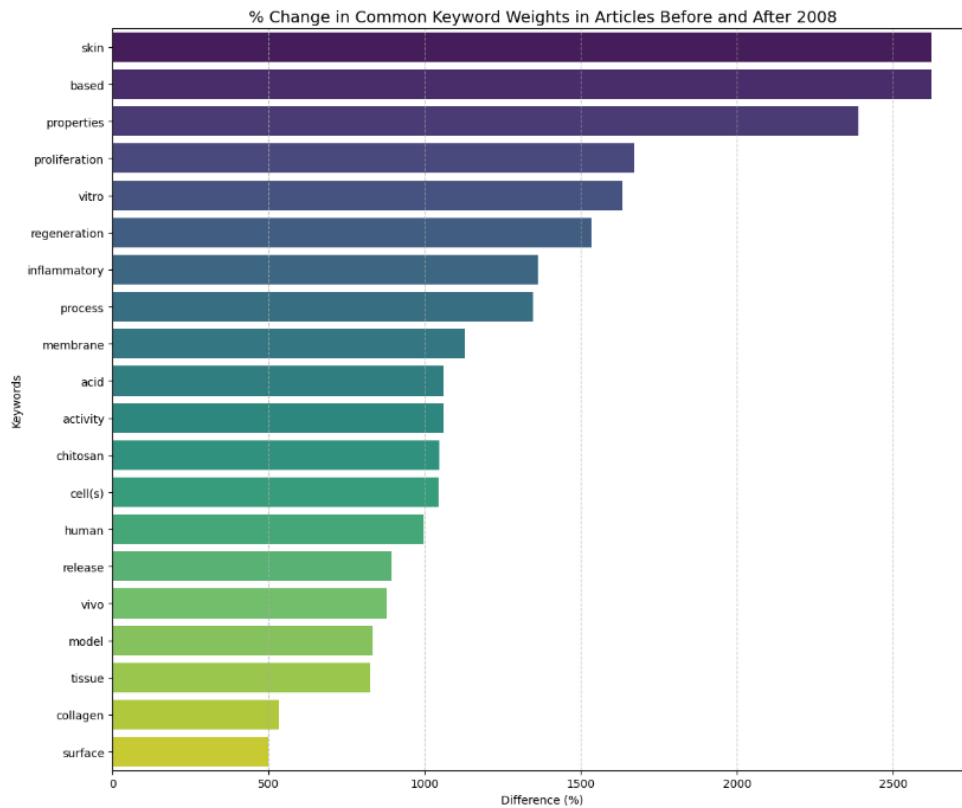
**Figure 3.** Word cloud visualization of frequently occurring words in publications prior to 2008. The visualization includes keywords identified in themes. The size of each term reflects its relative frequency in the literature before 2008. **Note:** Word clouds are provided for descriptive and illustrative visualization only and should not be interpreted as statistical evidence

**Table 2.** Identification of themes and keywords with LDA between 2008-2024

Infection Control-Wound Healing	Weight (%22.8)	Functional Hydrogels-Tissue Engineering	Weight (%25.1)	Therapeutic-Controlled Release Systems	Weight (%24.8)	Mechanical Properties-Structural Functionality	Weight (%27.3)
antibacterial	7710	hydrogel	12890	cell(s)	16655	skin	8915
growth	5715	tissue	12125	collagen	8195	hydrogels	8825
inflammatory	4825	properties	10200	based	8165	proliferation	6465
vivo	4355	scaffolds	6520	potential	7770	chitosan	6190
tissue	4275	cell	6085	treatment	5990	significantly	6160
healing	4260	dressing	5120	biomaterials	5835	cell	5885
promising	4225	diabetic	5060	regeneration	5550	mechanical	5755
skin	4155	dressings	4700	effect	5290	process	5710
fibroblasts	4145	increased	4645	release	4530	wounds	5550
repair	4135	vitro	4375	control	4405	demonstrated	5325
activity	4060	promote	4355	migration	4300	surface	5285
application	3990	engineering	4350	factor	4175	human	5270
formation	3945	loaded	4195	prepared	4130	biocompatibility	4840
biomaterial	3625	time	4015	bacterial	4075	composite	4335
delivery	3490	ability	3720	analysis	3925	matrix	4305
vitro	3340	material	3685	significant	3820	cells	4300
good	3325	membrane	3625	anti	3780	clinical	4250
excellent	3260	nanofibers	3515	rate	3565	acid	3890
expression	3165	beta	3480	therapeutic	3540	model	3735



**Figure 4.** Word cloud visualization of frequently occurring words in publications between 2008 and 2024. The visualization includes keywords identified in the themes. The size of each term reflects the relative frequency of the literature between the years indicated. **Note:** Word clouds are provided for descriptive and illustrative visualization only and should not be interpreted as statistical evidence.



**Figure 5.** Percentage change graph of the words that were common in the studies before 2008 and between 2008 and 2024

**Discussion**

Prior to 2008, components such as collagen and matrix in biomaterial research were primarily addressed in terms of their structural properties and biocompatibility. During this period, collagen was especially evaluated in the context of osteogenic

applications and cellular responses (14). However, after 2008, there has been a notable shift toward therapeutic applications in collagen-based biomaterial research. Notably, collagens from marine sources (like fish skin, jellyfish, and sponges) have become more popular because they cause fewer immune reactions, are more

sustainable, and offer ethical benefits (15, 16). This evolution marks a significant advancement toward clinical applications in biomaterials research, with marine-derived collagens offering promising new opportunities in wound healing and regenerative therapies due to their sustainability and biocompatibility advantages. Our findings are consistent with the growing interest in marine-derived collagen reported in recent biomaterials and wound-healing reviews; accordingly, we discuss marine-derived collagens as an emerging, qualitative sub-trend rather than as a primary driver of the LDA topics (17-19).

In support of this, the LDA analysis revealed the co-occurrence of the term "collagen" with concepts such as "therapeutic" and "regenerative," reinforcing the thematic transition observed in the field. In particular, the theme labeled as "Collagen-Matrix Based Regeneration," where collagen is prominently represented, highlights the therapeutic use of collagen-based biomaterials. Within this theme, collagen-based biomaterials are prominently represented; marine-derived collagens are therefore discussed here as a literature-supported sub-trend within the broader collagen landscape rather than as a distinct LDA-driven topic (16, 20). Furthermore, these biomaterials exhibit therapeutic potential in advanced applications, including controlled release systems and the design of biocompatible scaffolds (16, 21). Marine-sourced biomaterials may offer practical advantages (e.g., acceptability and supply sustainability) and are increasingly discussed in recent reviews; however, in our corpus they remained a secondary signal and were not a dominant driver of the LDA topics. Therefore, we frame marine-derived collagen as an emerging, literature-supported sub-trend that warrants targeted future work (e.g., standardized extraction/quality control and long-term in vivo safety studies) before stronger corpus-level claims can be made.

Expanding on the broader thematic trends, the findings also reveal distinct differences in biomaterials research before and after 2008. Studies prior to 2008 primarily focused on structural parameters, particularly surface properties and controlled drug release. The theme "Surface Properties-Controlled Drug Release" was dominant, representing 34.8% of that period's content. This focus reflected efforts to understand how physicochemical properties of biomaterials influenced cellular behavior. However, after 2008, a clear transition toward functional biomaterials became evident. During this newer period, themes such as "Mechanical Properties-Structural Functionality" (27.3%) and "Functional Hydrogels-Tissue Engineering" (25.1%) emerged, suggesting that biomaterials were increasingly being designed to perform biological roles, not just structural support. Among these, nanofiber-based wound dressings (particularly those produced via electrospinning) have shown promise in enhancing wound healing and minimizing scar formation (22). Functional hydrogels have similarly become central, given their high-water content, biocompatibility, and versatility in regenerative medicine. The expanding use

of such hydrogels, especially in personalized disease modeling, reflects a broader trend toward more active and regenerative roles for biomaterials (23).

This progression underscores a paradigmatic shift—from passive, structural materials to dynamic, bioactive systems. Our findings are consistent with this evolution, as reflected by the post-2008 prominence of topics centered on functional hydrogels, infection control, and regenerative tissue engineering in the LDA output. These advances pave the way for disease-specific, patient-tailored therapies with enhanced clinical efficacy, particularly for complex wound types such as diabetic foot ulcers, burns, and postoperative lesions.

As this thematic transformation unfolds, it is bringing biomaterials research closer to real-world clinical application. Innovations are now targeting specific medical challenges, including diabetic wounds, antimicrobial resistance, and host biocompatibility. Nanofiber and hydrogel-based biomaterials, in particular, are well positioned to meet these demands (24). Moreover, while wound healing did not appear as a clearly defined thematic category prior to 2008, the emergence of the "Infection Control-Wound Healing" theme post-2008 (though relatively lower in prevalence) indicates a growing clinical relevance. This evolution suggests that earlier studies were largely confined to laboratory environments, focusing on in vitro experiments. Supporting this, literature from the early 2000s often concentrated on cellular responses to material surfaces rather than holistic biological contexts (25, 26).

Clinically, the post-2008 emergence of 'Infection Control-Wound Healing' is plausibly linked to the rising emphasis on antimicrobial resistance and on local bioburden management in both chronic and postoperative wounds. This has accelerated interest in antimicrobial dressings and multifunctional biomaterials that combine barrier function with active antimicrobial or antibiofilm mechanisms. Examples include silver- and nanoparticle-containing systems, honey-based dressings and hydrogels, and plant-derived bioactives incorporated into films/hydrogels for antioxidant and antimicrobial effects. In this context, the infection-control signal captured by topic modeling can be interpreted as reflecting a broader convergence of biomaterials engineering with antimicrobial stewardship needs (27-29).

Importantly, part of this translational trajectory is reflected in veterinary wound management, where biomaterial dressings are frequently evaluated in clinically realistic contexts (contaminated wounds, large tissue loss, and challenging anatomic sites). In companion animals, biomaterial-based dressings and biologic grafts have been reported to support healing after wide excisions and complex soft-tissue defects. In equine surgery, distal limb wounds represent a well-known clinical challenge characterized by delayed granulation and higher complication risk, making them a relevant model for testing hydrogel- and antimicrobial-dressing strategies. We therefore interpret the

veterinary-oriented subset as complementary evidence that helps bridge laboratory innovation with real-world wound environments (30-32).

From a field-utility perspective, veterinary patients provide clinically realistic wound environments (contamination, motion, distal limb ischemia, large tissue loss) where biomaterial dressings are stress-tested under conditions similar to complex human wounds. Marine-origin dressings are particularly relevant here: acellular fish-skin xenografts and marine collagen matrices have been increasingly reported in companion animal soft-tissue reconstruction and in equine distal limb wounds, which are known for delayed granulation and higher complication rates. These applications strengthen the translational interpretation of the post-2008 'infection control' and 'functional hydrogel' themes by illustrating where and why clinicians adopt bioactive scaffolds and antimicrobial dressings outside controlled laboratory settings (33, 34).

In contrast, the post-2008 period has witnessed increasing attention to *in vivo* relevance and translational potential. For example, the emergence of functional wound healing themes corresponds with rising interest in direct biomaterial-tissue interactions. This shift has opened doors to translational research, leading to more clinically grounded strategies (35, 36). Notably, the increase in *in vivo* research reflects a demand for biomaterials that perform reliably in dynamic, real-world environments. Developments in dual-function biomaterials (those combining antimicrobial and regenerative capabilities) have played a role in improving success rates *in vivo* (37, 38).

Beyond simple term-frequency shifts, the post-2008 vocabulary increasingly reflects engineering-driven formulation strategies. The rise of '-based' is best interpreted not as an informative keyword *per se*, but as a linguistic marker of more specific material descriptors (e.g., collagen-based, hydrogel-based). In parallel, the field has moved toward composite and hybrid scaffolds (particularly fiber-hydrogel and nanofiber-enhanced hydrogel composites) that aim to combine ECM-mimicking architecture with tunable mechanics, moisture management, and controlled delivery of therapeutics. This composite design paradigm provides a more mechanistically meaningful interpretation of the lexical shift than the standalone token 'based' (39-41).

In parallel with these developments, the literature increasingly explores marine-derived collagens as alternatives to mammalian sources, motivated by biocompatibility, sustainability, and ethical considerations. Traditionally, collagen is derived from mammals like pigs, cattle, and rodents. However, concerns related to zoonotic transmission and religious acceptability have prompted increased exploration of marine organisms (including fish, jellyfish, and sponges) as safer alternatives (21, 42). Marine-sourced collagens, gelatins, and chitosan offer compelling advantages, including lower immunogenicity, ethical acceptability, and potential for sustainable production (15, 43-45).

A further driver of the shift toward non-mammalian collagen sources is biosafety. Mammalian-derived collagens (bovine/porcine) have historically raised concerns regarding zoonotic contamination and, although tightly regulated, a theoretical risk related to transmissible spongiform encephalopathies (e.g., prion/BSE) is frequently cited in the biomaterials safety literature. Marine-derived collagen avoids several mammalian-specific pathogen concerns and can offer advantages in acceptability and supply sustainability; nevertheless, marine sources introduce their own safety-control requirements (e.g., heavy metals, endotoxin burden, batch variability), making standardized extraction and quality-control pipelines essential for translational adoption (46, 47).

These considerations are presented here as contextual evidence from the broader literature rather than as a direct output of our LDA results. While marine-derived materials are discussed in reviews in relation to sustainability, acceptability, and biosafety, our corpus-level signal remained low (i.e., a secondary, qualitative signal rather than a dominant topic driver). Accordingly, we interpret ethical/ecological arguments and quality-control challenges (batch variability, interspecies differences, potential contaminants such as heavy metals and endotoxin, and standardization needs) as literature-informed translational considerations that warrant targeted future work, rather than as findings emerging from the topic model itself.

A methodological limitation relates to the search query. By using 'biomaterial' AND 'wound healing' as required terms, the corpus may undercapture studies that primarily use specific material family labels (e.g., hydrogel, scaffold, nanofiber, electrospun mat) without explicitly using the umbrella term 'biomaterial'. While this choice improved precision and reproducibility, it may reduce recall. Future work could incorporate an expanded query set (e.g., adding major material-family keywords) and compare topic stability via sensitivity analyses.

Additional limitations include reliance on a single database (WoS Core Collection), English-language records, and abstract-only modeling, which may omit full-text nuance and non-indexed literature. In addition, the pre-2008 and post-2008 subsets were markedly unequal in size (297 vs 4,019), which may influence estimated topic prevalence; therefore, temporal contrasts are reported descriptively. As an unsupervised approach, LDA provides thematic structure rather than causal inference; therefore, findings should be interpreted as descriptive trends.

When examined comprehensively, marine-sourced biomaterials clearly present compelling advantages. Their inherent antibacterial properties, biodegradability, environmental sustainability, and compatibility with cellular systems make them particularly well-suited for next-generation wound care and regenerative solutions (48). These considerations are discussed here as literature-based translational context; however, consistent with the low corpus-level frequency of marine-

related terms, marine collagens should be interpreted as an emerging, literature-supported sub-trend rather than a dominant LDA-driven finding.

This study provides a comprehensive overview of the evolving research landscape in wound healing and highlights the growing importance of marine-derived collagen as a sustainable, biocompatible, and immunologically safe alternative to traditional biomaterials. Topic modeling of over two decades of literature revealed a clear thematic shift from structure-

focused and in vitro studies toward functionality-driven applications such as controlled drug delivery, infection prevention, and tissue regeneration. Based on these trends, future research is expected to emphasize the development of biomaterials with enhanced mechanical and functional performance, integrated into smart systems that actively support the healing process. Marine collagen-based hydrogels and scaffolds, when combined with emerging technologies like 3D bioprinting and nanotechnology, may offer promising pathways toward personalized and translational wound therapies.

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