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Caprine Bone-Derived Biomaterials for Guided Bone Regeneration: A Comprehensive Review of Macroscopic and Histological Findings

Rafael Gerrard *, Evelyn Nathania Prasetyo, Alga Balqis Riyanlito, Anggraeni Endah Ningtyas, Zhalfa Zhahira Putri Agcanita, Hanindya Josephira, Salsabila Zahra Rasyidi, Fitriyas Nifah Pramesti and Adiesta Yusnia Prasetyawati

Undergraduate student, Faculty of Dental Medicine, Universitas Airlangga, Jl. Mayjen Prof. Dr. Moestopo No.47, Surabaya, East Java 60132, Indonesia.

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Abstract

Guided bone regeneration (GBR) is a key approach in oral and orthopedic reconstruction, relying on barrier membranes and graft materials to direct bone formation. While bovine and porcine xenografts dominate clinical use, caprine bone-derived biomaterials remain under-explored. This comprehensive review consolidates macroscopic and histological evidence on caprine bone-based grafts, focusing on demineralized bone matrix (DBM) and hydroxyapatite (HA) derivatives reported between 2019 and 2025. Database searches of PubMed, Scopus, and Web of Science identified relevant studies evaluating caprine materials' physicochemical properties, in vitro biocompatibility, in vivo bone formation, and systemic responses. Results show that caprine DBM and HA exhibit favorable osteoconductivity and biocompatibility, producing progressive bone formation with histological features comparable to autograft under optimized processing. Variability in bone volume outcomes was linked to differences in material preparation and defect models. Transient hematological responses indicate the need for standardized sterilization and safety monitoring. The review highlights methodological gaps, including inconsistent histomorphometry, limited GBR-specific models, and lack of unified reporting. Standardized processing, combined imaging-histology protocols, and GBR-oriented large-animal studies are recommended to advance clinical translation of caprine xenografts as cost-effective alternatives to conventional grafts.

Keywords: Caprine Bone; Demineralized Bone Matrix; Hydroxyapatite; Guided Bone Regeneration; Osteoconduction; Histology

1. Introduction

Guided bone regeneration (GBR) is a cornerstone technique in reconstructive dentistry and orthopaedics that relies on the combined use of barrier membranes and bone graft materials to direct selective bone formation while excluding soft tissue ingrowth. Successful GBR depends not only on the physical ability of a graft to maintain space and allow vascular invasion, but also on its biological property's biocompatibility, osteoconduction and, ideally, osteoinduction. A wide variety of graft sources have been employed clinically, including autografts, allografts, xenografts and synthetic substitutes, each with distinct advantages and limitations in terms of supply, morbidity and biological performance. Recent biomaterials research has emphasized both physicochemical optimization and biological enhancement of grafts to improve regeneration outcomes in challenging defects. Consequently, systematic assessment of candidate xenograft sources is needed to reliably compare their macroscopic performance and the histological quality of newly formed bone [1].

* Corresponding author: Rafael Gerrard

Xenogeneic bone substitutes derived from bovine and porcine sources are well established in clinical practice and preclinical research, providing widely available scaffolds with proven osteoconductive capacity. However, caprine-derived materials (goat/djia family) remain comparatively under-explored despite promising preliminary data that suggest caprine bone can be processed into hydroxyapatite (HA) and demineralized bone matrix (DBM) with suitable physicochemical characteristics. Several recent experimental studies have begun to evaluate caprine grafts in vivo, reporting acceptable biocompatibility and evidence of new bone formation in small animal defect models. These early efforts indicate that caprine-derived scaffolds may offer a feasible and locally-sourced alternative to conventional xenografts, but the evidence base is still fragmented with variable methods of processing, characterization and outcome reporting. A focused synthesis of macroscopic outcomes (radiographic and volumetric data) together with histological quality metrics is therefore timely to establish where caprine materials stand relative to established grafts [2,3].

Preclinical investigations have produced mixed but encouraging results: micro-CT studies of caprine demineralized bone matrix (DBMc) implanted in rabbit tibial defects have demonstrated progressive bone filling over time, although bone volume was sometimes lower than autologous controls (Santos et al., 2020). In contrast, histopathological evaluation of caprine DBM in a rabbit critical-size ulnar defect showed that caprine DBM produced bone tissue with histological features comparable to autograft at defined end points, suggesting that tissue quality can match the clinical gold standard under certain conditions. Systemic responses have also been documented transient hematological changes after caprine DBM implantation indicate the need for safety monitoring and standardized sterilization/deantigenation protocols. Furthermore, contemporary material-engineering approaches (for example, amino-acid enrichment or polymeric binders applied to ruminant-derived HA) demonstrate that physicochemical modification can enhance in vitro osteogenic signals and scaffold handling properties. Together, these findings underscore the necessity of integrating quantitative imaging, standardized histology and material characterization to judge clinical potential [3,4].

The aim of this review is to comprehensively consolidate and critically appraise published macroscopic and histological findings on caprine bone-derived biomaterials used for bone grafting and GBR between 2019 and 2025. By comparing study designs, processing methodologies, radiographic/micro-CT metrics and detailed histological endpoints (including matrix maturation, cellular composition and vascularization), we seek to identify reproducible signals of efficacy and the methodological gaps that impede translation. Particular emphasis will be placed on harmonizing outcome measures such as particle size, demineralization parameters, sterilization methods, and histomorphometric scoring—so that future preclinical and clinical studies can be more directly comparable. Finally, the review will highlight priority areas for future work, including standardized preclinical protocols, safety evaluations, and the potential for engineered caprine scaffolds to address regional supply and cost constraints in bone regenerative therapies [5].

2. Methods

We searched PubMed, Scopus, and Web of Science for articles published between January 2019 and May 2025 using the following Boolean string: ("caprine" OR "goat") AND ("bone graft" OR "bone grafting") AND ("guided bone regeneration" OR "bone regeneration") AND ("osteogenesis" OR "healing" OR "repair"). Inclusion criteria comprised original research, reviews, and proof-of-concept studies reporting physicochemical characterization, processing (e.g., demineralized bone matrix or hydroxyapatite), or in vitro/in vivo evaluation of caprine-derived materials for bone grafting or GBR with macroscopic, imaging, or histological data. Exclusion criteria included non-English articles, conference abstracts, editorials, studies not involving caprine bone as a primary material, and papers focused solely on non-GBR applications. Two independent reviewers screened titles/abstracts and full texts, removed duplicates, and extracted data using a pre-piloted form capturing material preparation, particle size, characterization (XRD/FT-IR/SEM), animal model and defect type, surgical protocol (including membrane use), follow-up times, quantitative imaging metrics (BV, BV/TV, Tb.N, Tb.Th, Tb.Sp), and histological endpoints (HandE, Masson's trichrome, TRAP, and immunohistochemistry where available). Study quality and risk of bias were assessed using SYRCLE's risk-of-bias tool for animal studies and an appropriate critical appraisal checklist for other designs, data were synthesized narratively with comparative tables.

3. Results and discussion

Table 1 Key Methodological Studies

Authors (year)	Country	Methods	Result
Koppaka R. *et al*. (2024) [4]	India (Chennai)	In-vitro: prepared ovine HA bone graft modified with L-leucine + hyaluronic acid; physicochemical and biological characterization SEM, XRD, FTIR, MTT (cell viability), Alizarin Red bone-formation assay; compared with commercial Bio-Oss.	L-leucine-modified HA graft showed interconnected porosity, HA crystalline peaks, good cell viability and higher bone-formation OD (≈61% vs Bio-Oss 58% and control 51%) suggesting improved osteoconductivity/biocompatibility.
Alimi O.A. *et al.* (2021) [2]	Nigeria	In vivo (rabbit xenograft): 24 male rabbits randomized to 3 groups (autograft, unfilled control, caprine DBM); blood sampled day 0, 28, 56, manual CBC and differential; two-way repeated measures ANOVA.	CDBM induced marked hematological changes (leukocytosis with neutrophilia/monocytosis by day-28) and significant differences in WBC, neutrophils, monocytes, RBC, Hb and PCV over time useful for monitoring graft response.
Alimi O.A. *et al.* (2022) [3]	Nigeria	In vivo (rabbit critical ulnar defect): 24 rabbits into 3 groups (ABG, CDBM, NC); radiographs at 0,14,28,42,56 days; euthanasia day-56 for histopathology (Emery score); radiographic + histo scoring; ANOVA and nonparametric tests.	Radiographic and histologic healing in CDBM was similar to autologous bone graft (no significant difference ABG vs CDBM), while unfilled control lagged CDBM shows comparable healing to ABG.
Santos F.R. *et al.* (2020) [5]	Brazil	In vivo (non-critical tibial defects, rabbits): DBMc implanted (left tibia) vs contralateral control; euthanasia at 15,30,60,90 days; micro-CT (SkyScan 1172) assessing BV, BV/TV, BS, Tb.N, Tb.Th, Tb.Sp; ANOVA + t-tests.	DBMc was safe/tolerable with no rejection; control often had higher early BV/BV-TV, but DBMc showed progressive bone formation authors conclude DBMc is a viable alternative when autograft is unavailable.

Caprine-derived bone material, principally demineralized bone matrix (DBM) and thermally processed hydroxyapatite (HA) demonstrate consistent biocompatibility and the capacity to support new bone formation in preclinical models. Macroscopically, implanted caprine grafts produced progressive defect filling on radiographic and micro-CT assessments, although the magnitude and speed of bone volume gain were variable between studies and generally lower than autologous controls in some non-critical defect models. Importantly, at least one study using a critical-size defect model reported histological outcomes for caprine DBM that were comparable to autograft at defined end points, suggesting that tissue quality can match the clinical gold standard under specific conditions. These mixed but encouraging findings support the notion that caprine materials are viable candidates for further development as xenografts, particularly where local availability and cost are important considerations. However, the variability in outcomes underscores the need to interpret efficacy in the context of material format, defect model, and study design [2,4,5].

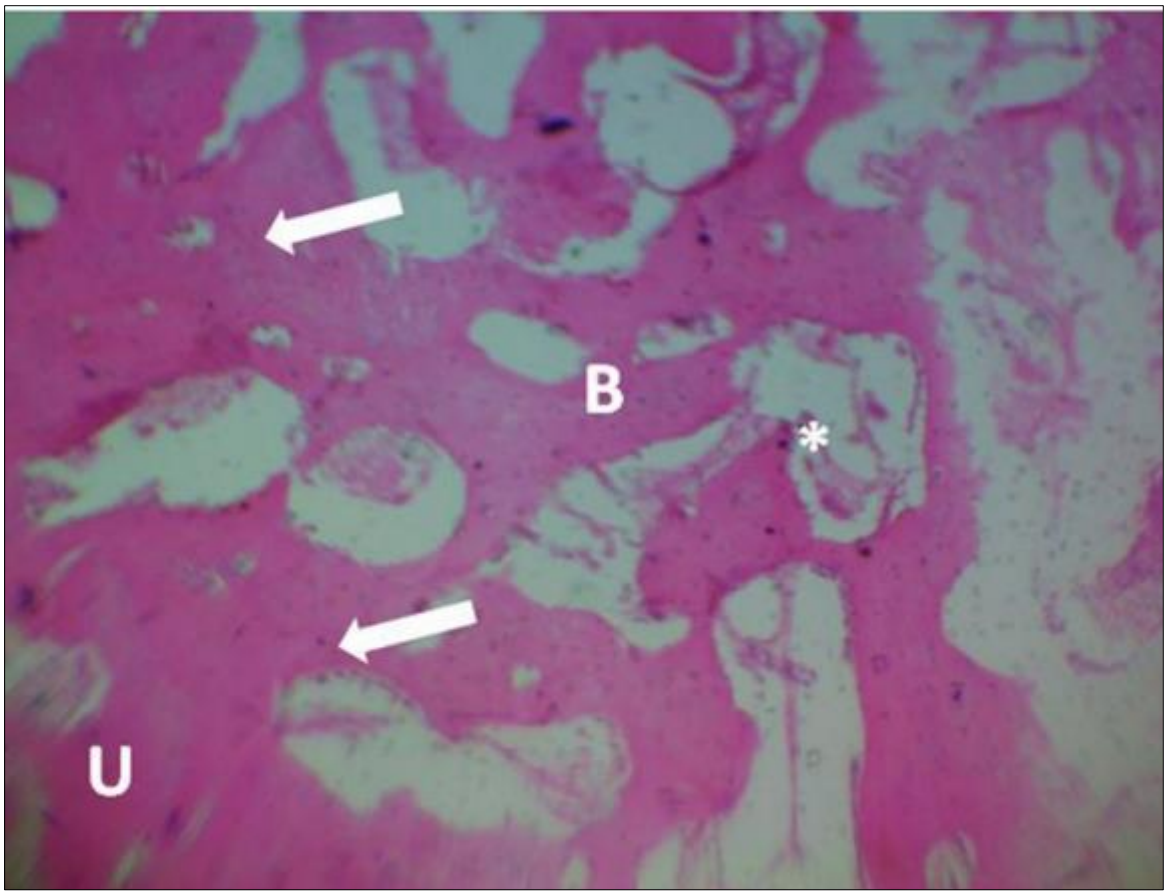

Figure 1 Histopathological photomicrograph of defect site (Caprine DBM); the defect is filled with normal bone tissue and has united with the unaffected part. Bone tissue at the defect site (B), point of union (white arrow), unaffected bone (U) and CDBM remnant (*). HE stain×100 [2]

Histological evidence emerging from the reviewed works shows that caprine DBM can give rise to mature bone tissue with normal histoarchitecture when processing and implantation conditions are appropriate. Where full histology was performed, investigators observed osteoid formation, cellular infiltration consistent with osteogenesis, and progressive mineralization comparable to autograft specimens at later time points, indicating functional remodeling rather than mere fibrous replacement. Conversely, studies that relied primarily on micro-CT metrics without detailed histology reported lower bone volume or slower filling, which raises the possibility that radiodensity alone may not capture qualitative maturation of new bone. Thus, combining quantitative imaging with standardized histomorphometry and immunohistochemistry (for markers such as osteocalcin, Runx2, and TRAP) is essential to conclusively determine whether caprine grafts promote fully mature, load-bearing bone. Without these complementary endpoints, assessments of caprine graft performance remain incomplete [6,7].

Material processing and physicochemical characteristics appear to be major determinants of biological performance and account for much of the interstudy variability. Parameters such as degree of demineralization, particle size distribution, residual organic content, calcination temperature for HA, and sterilization method influence porosity, surface chemistry, and the retention or loss of osteoinductive factors. Studies reviewed highlighted the importance of standardized granulometry and controlled deantigenation to optimize osteoconduction while minimizing adverse immune signaling; when these aspects were not harmonized, outcomes ranged from robust regeneration to merely modest bone deposition. Additionally, contemporary modifications such as incorporation of amino acids, polymeric binders, or trace-element doping show promise for improving handling, mechanical behavior, and in vitro osteogenic signals, but they require systematic in vivo validation. Therefore, developing consensus processing protocols and reporting standards would greatly enhance interstudy comparability and accelerate translational progress [2,7,8].

Safety and systemic responses to caprine xenografts were addressed in some studies, revealing generally favorable local tolerance but transient systemic hematological changes that warrant attention. Clinical observations reported no overt local rejection, infection, or flap complications attributable to the caprine material in the time frames studied,

supporting biocompatibility at the implantation site. Nevertheless, documented transient leukocytosis, neutrophilia, and other hematologic perturbations following implantation highlight the importance of rigorous sterilization, effective antigen removal, and perioperative monitoring in future preclinical and clinical protocols. These findings also suggest that standardized panels of systemic safety assays (hematology, acute-phase reactants, and relevant serology) should be incorporated into study designs rather than relying solely on local outcome measures. Addressing these safety endpoints early will be crucial to regulatory acceptance and to refining protocols that minimize systemic reactivity [9,10].

Translational relevance for guided bone regeneration specifically requires additional focus on the interaction between caprine grafts and barrier membranes, as space maintenance and soft-tissue management are fundamental to GBR success. Most reviewed caprine studies evaluated graft materials in isolation, often in contained defects, and thus did not fully model the mechanical and biological challenges of GBR—such as membrane exposure, flap tension, and the need to preserve a stable three-dimensional space for bone ingrowth. Future preclinical work should therefore test clinically realistic GBR constructs that pair caprine-derived granules or blocks with resorbable or non-resorbable membranes, and should include functional outcomes such as implant stability when relevant. Moreover, large-animal models that more closely approximate human craniofacial biomechanics and healing kinetics will strengthen the evidence base for clinical translation. Integrating such GBR-specific designs will clarify whether caprine materials can successfully replace or complement existing xenografts in everyday surgical practice [9,10,11].

4. Conclusion

In summary, the current body of evidence positions caprine bone–derived biomaterials as promising, locally accessible candidates for bone grafting and GBR, but critical knowledge gaps remain that limit immediate clinical adoption. Priority actions include adoption of standardized material processing and characterization, routine inclusion of combined micro-CT and quantitative histology with immunomarkers, rigorous systemic safety testing, and performance evaluation in GBR-specific large-animal models using clinically relevant membranes and fixation strategies. Coordinated reporting guidelines and multicenter preclinical studies would help overcome variability and allow meta-analytic comparisons across research groups. If these methodological improvements are implemented, caprine grafts have realistic potential to expand the pool of effective xenografts and to offer a cost-effective alternative in regions where bovine or porcine materials are limited or culturally constrained [11].

Compliance with ethical standards

Disclosure of conflict of interest

Authors declare that no conflict of interest

References

[1] Venkatesan, J., Anchan, R.V., Murugan, S.S., Anil, S. and Kim, S.K., 2024. Natural hydroxyapatite-based nanobiocomposites and their biomaterials-to-cell interaction for bone tissue engineering. Discover Nano, 19:169. doi:10.1186/s11671-024-04119-0.

[2] Alimi, O.A., Abdul Abubakar, A., Yakubu, A.S., Shehu, S.A. and Abdulkadir, S.Z., 2022a. Histopathological and radiographical evaluation of caprine demineralized bone matrix in a critical ulnar defect in a rabbit model. Journal of Orthopaedic Surgery and Research, 17, 561. doi:10.1186/s13018-022-03454-1.

[3] Alimi, O.A., Abubakar, A.A., Yakubu, A.S. et al., 2022b. Hematological changes after caprine demineralized bone matrix implantation in ulnar critical defect of rabbit model. Revista Brasileira de Ortopedia, 57(2), pp.218–222.

[4] Koppaka, R., Shah, K.K. and Maiti, S., 2024. Multifaceted enhancement of L-Leucine-enriched ovine bone graft: Physicochemical characteristics and osteogenic potential for improved guided bone regeneration. Cureus, 16(7): e64416. doi:10.7759/cureus.64416.

[5] Santos, F.R. dos et al., 2020. Caprine demineralized bone matrix (DBMc) in the repair of non-critical bone defects in rabbit tibias: A new bone xenograft. Acta Cirúrgica Brasileira, 35(8): e202000801.

[6] Luangphakdy, V., Elizabeth Pluhar, G., Piuzzi, N.S. et al. The Effect of Surgical Technique and Spacer Texture on Bone Regeneration: A Caprine Study Using the Masquelet Technique. Clin Orthop Relat Res 475, 2575–2585 (2017). https://doi.org/10.1007/s11999-017-5420-8

[7] Kardikadewi, A.W.V., Soesilawati, P. and Ariani, M.D. (2023) Demineralized dentin material sponge (DDMS) promotes RUNX2 expression in osteoblastogenesis. Malaysian Journal of Medicine and Health Sciences, 19(Suppl. 3), 172–176.

[8] Prabha, R.D., Ding, M., Bollen, P., Ditzel, N., Varma, H.K., Nair, P.D. and Kassem, M. (2020) Strontium ion reinforced bioceramic scaffold for load bearing bone regeneration. Materials Science and Engineering: C, 109, 110427. doi: 10.1016/j.msec.2019.110427.

[9] Soesilawati, P., Rizqiawan, A., Roestamadji, R.I., Arrosyad, A.R., Firdauzy, M.A.B. and Abu Kasim, N.H. (2021) In vitro cell proliferation assay of demineralized dentin material membrane in osteoblastic MC3T3-E1 cells. Clinical, Cosmetic and Investigational Dentistry, 13, 443–449. doi: 10.2147/CCIDE.S313184.

[10] Gerrard, R., Christie, K.V., Pribadi, R.H., Putri, A.M., Fadlilah, N., Pattinasarane, E.D., Luthfiani, B.L. and Hayuningtyas, D.E. 2025, 'Chewing on Change: How Fast Food Shapes Human Tooth Morphology and Oral Health', International Journal for Multidisciplinary Research (IJFMR), vol. 7, no. 4, pp. 1–9.

[11] Soesilawati, P., Zahra, A., Gerrard, R., Prasetyo, E.N., Simanjuntak, G.S.E. and Rahardjo, P.C.J. 2025, 'Evaluation of physical properties of demineralization dentine material membranes through tensile strength tests', World Journal of Advanced Research and Reviews, vol. 26, no. 3, pp. 362–365, doi:10.30574/wjarr.2025.26.3.2201.