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Comparative Evaluation of Porcine-Derived Barrier Membranes for Alveolar Bone Regeneration in a Canine Model

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Abstract: ***This study compares the physicochemical and osteogenic properties of two porcine-derived absorbable membranes—small intestinal submucosa (Chenggu Kuai®) and porcine peritoneum (Lando®)—in the context of alveolar bone regeneration. Using a beagle dog model, bilateral mandibular extraction sockets were filled with identical bone graft materials and covered with the respective membranes. Key measurements included pH levels, mechanical strength, bone dimensions, and bone volume using Micro-CT and histological analysis. Results showed that both membranes supported bone regeneration without significant differences in bone volume or healing response. However, the Chenggu Kuai® Oral Collagen Membrane exhibited better mechanical properties and a more neutral pH, indicating greater biocompatibility and potential for clinical application.***

Keywords: Collagen membrane, Guided bone regeneration, Porcine biomaterials, Alveolar bone, Animal study

1. Introduction

Tooth loss can directly affect a patient's chewing function and speech clarity. Whether it is the loss of a single tooth or multiple teeth, it can accelerate the resorption of the alveolar bone beneath the missing tooth or teeth, thereby compromising the outcome of subsequent dental restoration [1]. Guided Bone Regeneration (GBR) technology, which isolates soft tissues and promotes the migration of bone cells through the use of a barrier membrane, has become a core approach for addressing insufficient bone volume. Currently, the commonly used barrier membranes in clinical practice include two categories: absorbable and non-absorbable. Among them, absorbable membranes have garnered significant attention due to the elimination of the need for a secondary surgical procedure. Both Chenggu Kuai® Oral Collagen Membrane and Lando® membrane (derived from porcine peritoneum) are porcine-derived absorbable materials. However, differences in their sources and structures may affect their performance. This study systematically compared the bone regeneration effects of two types of membranes through physicochemical testing and animal experiments, providing a basis for clinical selection.The primary purpose of this study is to evaluate and compare the osteogenic potential and physicochemical properties of Chenggu Kuai® and Lando® oral barrier membranes in guided bone regeneration using a canine model.

2. Materials and Methods

2.1 General Information

1) Experimental Materials

Barrier membranes: Chenggu Kuai® Oral Collagen Membrane (Xiling Medical), Lando® Oral Absorbable Barrier Membrane (Shenzhen Landu Biology).

Bone filling material: Xinkang Chen's same bone implant material (Beijing Xinkang Chen).
Experimental animals: 12 healthy Beagle dogs (8-15 months old, weighing 10-15 kg), purchased from Beijing Fuhao Experimental Animal Breeding Center.

2) Physical and chemical property testing

pH value

Ten samples (each measuring 20mm×30mm) were taken from each of the two types of absorbable membranes. These samples were cut into small pieces and subjected to extraction using normal saline as the extraction medium, following the extraction method outlined in Table 1. The extraction was carried out in a sealed container at 37℃±1℃ for 24 hours. The pH of the resulting solution was then measured using a pH meter.

Table 1: Standard Surface Area and Extraction Solution Volume

Thickness (mm)	Extraction ratio (calculated by the area on both sides)
＜0.5	6cm^2/ml
0.5~1.0	3cm^2/ml

2.2 Mechanical properties

Tensile strength: Five samples with a width of no less than 10 mm were taken from each of the two types of absorbable membranes. The width (b) and thickness (h) of each sample were measured within 5 mm from each end of the gauge length at the middle part of the specimen. The width (b) was measured to an accuracy of 0.1 mm, and the thickness (h) to an accuracy of 0.02 mm.

Record the maximum and minimum values of the width and thickness for each specimen to ensure that they fall within the tolerance range specified in the corresponding material standard.

Place the specimen into a single-column benchtop testing machine and stretch it at a rate of 100 mm/min until it fractures. Ensure that the long axis of the specimen is aligned in a straight line with the axis of the testing machine, and record the maximum force value.

Calculate the stress according to the formula: The stress value is calculated based on the original cross-sectional area of the specimen using formula (1).

$$\sigma = \frac{F}{A} \qquad \text{----------} \quad (1)$$

In the formula:
σ ------- Tensile stress, with the unit being megapascals (MPa)
F -------- The corresponding measured load, with the unit being newtons (N)
A -------- The original cross-sectional area of the specimen, with the unit being square millimeters (mm^2)

Tear force: Cut the sample into a strip shape (10 mm × 25 mm) (refer to Figure 1). After saturating it with water in purified water, thread a suture through it and secure it to the testing machine. Stretch it at the same speed (100 mm/min) until it tears. Take the average value from five tests.

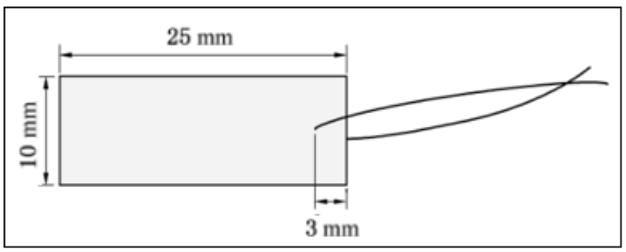


Figure 1: Schematic Diagram for Measuring the Tear Force of a Suture

2.3 Animal experiments

1) Grouping: Using a block randomization method, one randomly selected side of the bilateral premolars (P3-P4) in each dog was assigned to the experimental group (Chenggu Kuai® Oral Collagen Membrane), while the other side was assigned to the control group (Lando® Membrane).
2) Surgical procedure: After acclimatizing the 12 experimental beagle dogs for 1 week, general anesthesia was induced by intramuscular injection of xylazine hydrochloride injection (200 μL per dog). After administering general anesthesia, the surgical area was disinfected with a 5 g/L iodophor solution and 75% alcohol. An incision was made through the mucoperiosteal flaps in the bilateral premolar regions (P3-P4) of the mandible to fully expose the bone surface. The teeth in the bilateral premolar regions (P3-P4) of the mandible were then extracted, resulting in the formation of extraction sockets. The extraction sockets were filled with human demineralized bone matrix material (produced by Beijing Xinkangchen Medical Science and Technology Development Co., Ltd.) without compression, ensuring that the bone graft material was flush with the alveolar ridge crest.
3) The barrier membrane materials for either the experimental or control group were trimmed and placed in a straddling manner over the homologous bone graft material (one piece of barrier membrane covered each extraction socket). Subsequently, the gingiva was sutured without tension. Postoperatively, the dogs received an injection of ceftiofur sodium for one week (40,000 U/kg per day).

2.4 Observation indicators

Radiographic evaluation: Micro-CT scans were performed at 1, 3, and 6 months postoperatively to measure the buccal-lingual bone height, bone width (at 1/2/3 mm below the alveolar ridge crest), and bone volume to tissue volume ratio (BV/TV).

Histological analysis: HE staining was employed to observe material degradation, inflammatory response, and trabecular bone structure, with grading conducted according to the YY/T0127.4-2009 standard.

Incision healing: Redness, swelling, infection, and necrosis were recorded at 1 and 2 weeks postoperatively.

1) Physicochemical properties. Including the pH value, tensile strength, and tear resistance of the two types of barrier membranes.
2) Bone height and bone width. Micro-CT scans were performed on beagle dogs euthanized at 1 month, 3 months, and 6 months postoperatively. Bone height was measured individually, along with the bone width at 1 mm, 2 mm, and 3 mm below the alveolar ridge crest of the extraction sockets. The average values were calculated, and the similarities and differences between the experimental and control groups were analyzed and compared.
3) Bone volume to total volume ratio (BV/TV). The BIOQUANT bone morphometric analysis system was employed to measure and analyze the ratio of bone formation volume to total volume within the extraction sockets of beagle dogs euthanized at 1 month, 3 months, and 6 months postoperatively.
4) Incision healing status. Observations were made on the oral healing conditions of beagle dogs during the first and second weeks postoperatively, including the health status of the gums, suture condition, edema, infection, and necrosis. The suture removal time did not exceed

14 days.

5) Histological observation, material degradation, and barrier effect. Tissue blocks containing samples were excised from beagle dogs euthanized at 1 month, 3 months, and 6 months postoperatively. These samples were fixed in 10% neutral buffered formalin, dehydrated, processed through paraffin embedding, sectioned, and stained with HE. Microscopic analysis was conducted to evaluate the tissue response, material degradation, and the ingrowth of connective tissue. The samples were graded according to the histological response evaluation grading scale outlined in the industry standard YY/T0127.4-2009 《 Biological Evaluation of Medical Devices for Dentistry - Part 2: Bone Implantation Tests》

3. Results

3.1 Basic properties

The pH value of the barrier membrane in the experimental group was closer to neutral, and the experimental group exhibited superior mechanical properties compared to the control group. For detailed information, please refer to Table 2.

Table 2: Comparison of pH Value and Mechanical Properties

Group	Acidity or alkalinity	Tensile strength /MPa	Tear force /N
Experimental group	6.28	56.94	36.36
Control group	4.97	17.04	27.69

3.2 Height of the buccal-lingual lateral bone

The post-operative trends in buccal bone height and lingual bone height were similar between the experimental group and the control group, both showing a gradual increase. There were no significant differences observed between the two groups. For detailed information, please refer to Table 3.

Table 3: Comparison of Buccal and Lingual Height Data

Measure time	Buccal Bone Height (mm)		Lingual bone height /mm	
	Control group	Experimental group	Control group	Experimental group
One month after the operation	7.23	7.67	6.53	6.55
Three months after the operation	7.48	7.82	7.56	7.64
Six months after the operation	7.33	7.87	7.54	7.52

3.4 Bone Width

According to the collected data, there was no significant difference in the overall trend of bone width at 1mm, 2mm, and 3mm below the ridge top of the tooth extraction socket between the experimental group and the control group at 1 month, 3 months, and 6 months after the operation. For details, please refer to Table 4.

Table 4: Comparison of Bone Width Data at 1mm, 2mm, and 3mm Below the Crest of the Alveolar Socket after Tooth Extraction

Measure time	Bone width at 1mm /mm		Bone width at 2mm /mm		Bone width at 3mm /mm	
	Control group	Experimental group	Control group	Experimental group	Control group	Experimental group
One month after the operation	1.54	1.61	2.07	2.32	1.91	1.88
Three months after the operation	2.78	3.04	3.43	3.10	4.03	3.93
Six months after the operation	2.53	2.88	3.11	3.38	3.74	3.66

3.5 Bone volume/Total volume

According to the collected data, the bone volume/total volume of the tooth extraction socket in the experimental group and the control group at 1 month, 3 months and 6 months after the operation showed an overall upward trend, and there was no significant difference between the two. For details, please refer to Table 5.

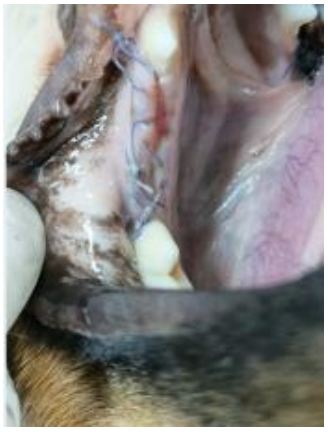
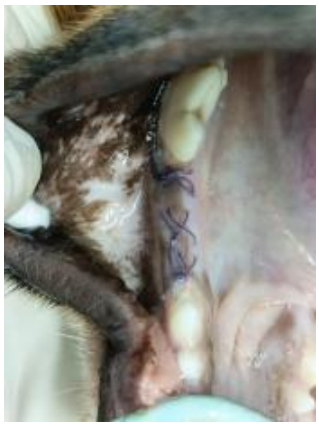
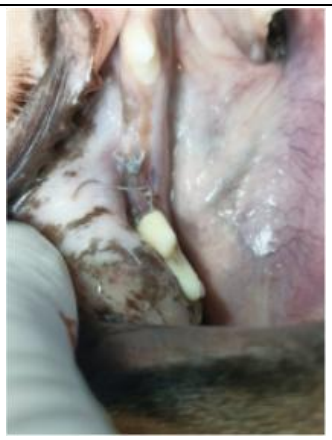
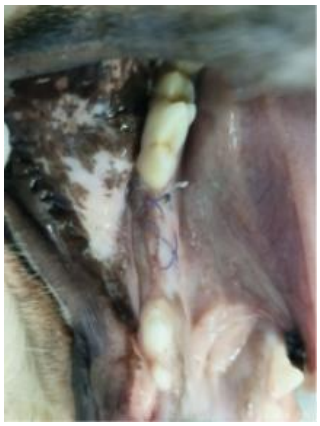
Table 5: Comparison of bone volume/total Volume data

Measure time	Bone volume/total volume	
	Control group	Experimental group
One month after the operation	0.687	0.719
Three months after the operation	0.838	0.838
Six months after the operation	0.797	0.839

3.6 Incision healing condition

One week after the surgery, sutures and incisions were visible in the surgical area. The sutures were largely intact, and the incisions were clearly discernible. Granulation tissue hyperplasia and scar epidermis were observed, with no obvious signs of redness, swelling, edema, or inflammatory symptoms, and no necrosis was noted.There were no significant differences between the control group and the experimental group. Two weeks after the surgery, the incisions had basically healed, with redness, swelling, and inflammation disappearing. Residual sutures and incision marks were visible, and again, there were no significant differences between the control group and the experimental group. For detailed information, please refer to Table 6.

Table 6: Comparison of incision healing conditions

Incision healing condition			
One week after the operation		Two weeks after the operation	
			

3.7 Histological observation, material degradation and barrier effect

Based on the data collection of histological observations and material degradation in the experimental group and the control group at 1 month, 3 months, and 6 months post-surgery, the following observations can be made:

No significant differences were observed in histological examinations between the experimental group and the control group. No obvious inflammatory responses were detected at the tooth extraction sites in either the control group or the experimental group. At the 3-month post-surgery observation, a small amount of residual barrier membrane was visible in both the experimental and control groups. However, no barrier membrane material was observed at the 6-month mark, indicating that the degradation period for both groups was between 3 to 6 months. For detailed information, please refer to Tables 7-1, 7-2, and 7-3.

Table 7.1: Table of Tissue Response and Material Degradation Conditions

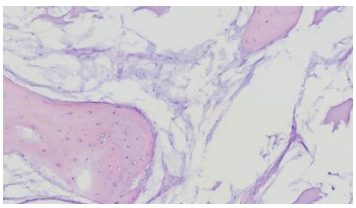
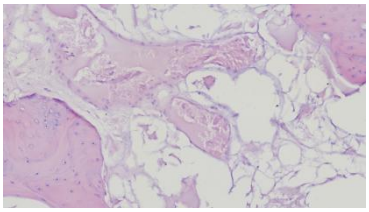
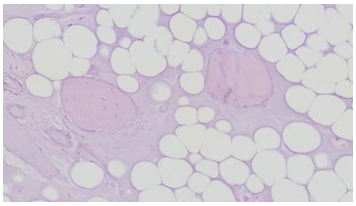
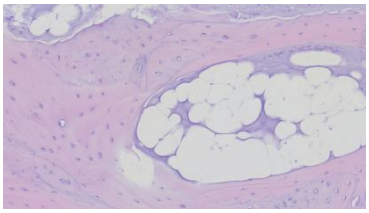
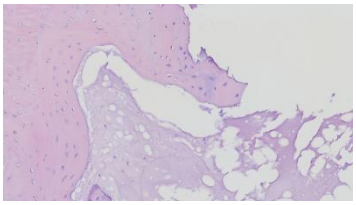
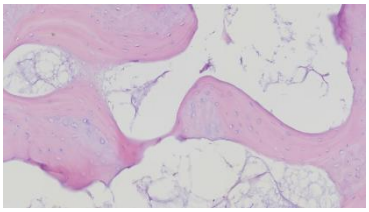
Observation time point	Experimental group	Control group
One month	Pore-like structures can be observed within the bone trabeculae 	The pore-like structures within the bone trabeculae have basically disappeared 
Three months	The bone trabecular structure is intact 	The bone trabecular structure is intact 
Six months	The bone trabecular structure is intact and occupies a large area within the tooth extraction socket. 	The bone trabecular structure is intact and occupies a large area within the tooth extraction socket. 

Table 7.2: Histological Observation Results Table

Reaction type	One month after the operation		Remarks	
	Control group (individuals)	Experimental group(individuals)	Control group (individuals)	Experimental group(individuals)
Fibrosis	2	1	/	/
Degree of inflammation	3	3	Three at Level 1	Three at Level 1
Degeneration (histomorphological changes)	0	0	/	/
Inflammatory cell types at the material/tissue interface	Lymphocyte	Lymphocyte	/	/
Tissue necrosis/vascular rupture	0	0	/	/
Neovascularization	0	0	/	/
Fat infiltration	0	0	/	/
Granuloma	0	0	/	/
New bone formation	2	1	/	/
Material fragments/chips	7	8	A large amount of materials	A large amount of materials
Reaction type	Three months after the operation		Remarks	
	Control group (individuals)	Experimental group(individuals)	Control group (individuals)	Experimental group(individuals)
Fibrosis	0	0	/	/
Degree of inflammation	0	0	/	/
Degeneration (histomorphological changes)	0	0	/	/
Inflammatory cell types at the material/tissue interface	0	0	/	/
Tissue necrosis/vascular rupture	0	0	/	/
Neovascularization	0	0	/	/
Fat infiltration	0	0	/	/
Granuloma	0	3	/	/
New bone formation	4	3	Bone formation	Bone formation
Material fragments/chips	3	2	A small amount of material	A small amount of material
Reaction type	Six months after the operation		Remarks	
	Control group (individuals)	Experimental group(individuals)	Control group (individuals)	Experimental group(individuals)
Fibrosis	0	0	/	/
Degree of inflammation	0	0	/	/
Degeneration (histomorphological changes)	0	0	/	/
Inflammatory cell types at the material/tissue interface	0	0	/	/
Tissue necrosis/vascular rupture	0	0	/	/
Neovascularization	0	0	/	/
Fat infiltration	0	0	/	/
Granuloma	0	0	/	/
New bone formation	8	7	Bone formation	Bone formation
Material fragments/chips	0	0	No materials seen	No materials seen

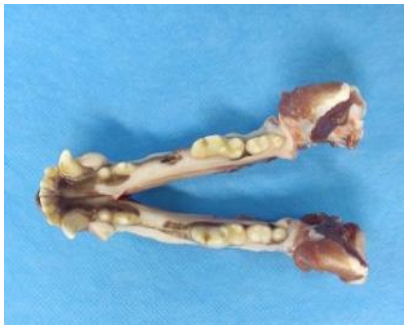
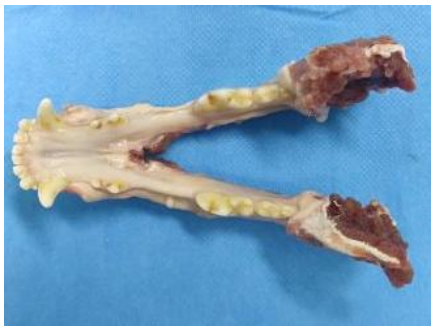
Table 7.3: Evaluation of Tissue Response - Cell Type Response

Grouping	Classification				
	0	1	2	3	4
One month after the operation					
Experimental group	1	3	0	0	0
Control group	2	3	0	0	0
Three months after the operation					
Experimental group	5	0	0	0	0
Control group	6	0	0	0	0
Six months after the operation					
Experimental group	6	0	0	0	0
Control group	6	0	0	0	0

3.8 General condition of the lower jaw

There was no significant difference between the experimental group and the control group. One month after the surgery, the oral incisions had basically healed, and there was no clear demarcation between the soft tissues in the surgical area and the normal tissues. Three months and six months postoperatively, based on the gross structural observation, the gingiva had largely returned to normal, with no visible injured wound surfaces observed. Detailed information is provided in Table 8.

Table 8: Observation of the mandibular condition after the operation

Postoperative mandibular condition		
One month after the operation	Three months after the operation	Six months after the operation
		

4. Discussion

This study holds clinical significance as it contributes to the ongoing search for effective and biocompatible absorbable membranes for use in guided bone regeneration, potentially guiding material selection in dental implantology. The healing of the tooth extraction socket is a complex biological process that involves the formation of a blood clot, proliferation of granulation tissue, re-epithelialization, maturation of connective tissue, and ultimately, bone formation. Studies conducted by Mauricio G. [2] and others have demonstrated that within the initial six months following tooth extraction, there is approximately 3.79 mm of horizontal alveolar bone resorption and 1.24 mm of vertical alveolar bone resorption. Alveolar bone resorption after tooth extraction is inevitable. Guided tissue regeneration (GBR), through the application of a barrier membrane, effectively isolates soft tissue ingrowth, maintains the space for bone regeneration, and enriches bone growth factors. It has become a crucial technique for addressing insufficient bone volume in implant therapy, significantly expanding the indications for dental implantation [3].

There are diverse types of barrier membranes, which can be categorized based on their degradability into absorbable and non-absorbable types, and based on their sources into allogeneic and xenogenic materials. This study focuses on two types of absorbable xenogenic barrier membranes: the Chenggu Kuai® Oral Collagen Membrane derived from porcine small intestinal submucosa (SIS membrane) and the Lando® Oral Absorbable Barrier Membrane derived from porcine peritoneum.

From a histological perspective, although both the SIS membrane and porcine peritoneum are porcine-derived materials, their structures exhibit differences. The raw material of the SIS membrane is composed of decellularized submucosa, which retains a natural three-dimensional collagen fiber network. It has the advantages of a wide source and low cost for raw material acquisition [4], facilitating large-scale production to meet the clinical demand for a stable supply of biomaterials [5].This structural characteristic enables the thickness of the SIS membrane to be adjusted by stacking layers to accommodate different clinical requirements. In contrast, porcine peritoneum is composed of a single layer of mesothelial cells and the underlying loose connective tissue. Regarding biosafety, the SIS membrane can effectively reduce immunogenicity due to the properties of its source tissue and the thorough decellularization process it undergoes.

Key characteristics of the SIS membrane and its application potential in Guided Bone Regeneration (GBR):

Biocompatibility and Low Immunogenicity: The SIS membrane is primarily composed of extracellular matrix (ECM), with a structure similar to that of human tissue matrix. Its decellularization treatment further reduces immunogenicity [6-11]. This provides a suitable microenvironment for host cell adhesion, proliferation, and differentiation, serving as the foundation for tissue repair materials.

Three-dimensional Structure and Bioactivity: The SIS membrane possesses a loose and porous three-dimensional structure [6, 12], which facilitates cell migration, nutrient exchange, and vascular ingrowth [13]. Meanwhile, the endogenous growth factors it retains (such as TGF-β, VEGF, FGF) and signaling molecules (such as fibronectin, laminin) [14,15,16,17] may be involved in regulating the repair process, promoting tissue regeneration and vascularization.

Mechanical Properties: The collagen components in the SIS membrane endow it with certain mechanical strength and toughness [18], which is crucial for the stable placement of the membrane during Guided Bone Regeneration (GBR) surgery, maintaining the space for bone regeneration, and resisting the pressure from soft tissues.

Biodegradability: The SIS membrane can be gradually degraded and absorbed in vivo. Theoretically, its degradation rate needs to match the rate of new bone formation to avoid a secondary surgical procedure [14,19], which is an important attribute of the SIS membrane as an absorbable membrane.

Guided Bone Regeneration (GBR) technology places multifaceted demands on the performance of barrier membranes. Excellent biocompatibility and low immunogenicity serve as fundamental prerequisites. Adequate mechanical strength is beneficial for intraoperative handling (such as trimming and stretching) and postoperative space maintenance. An appropriate barrier

function is essential to prevent the infiltration of non-osteogenic cells. A suitable degradation timeline should be synchronized with the rate of new bone formation. Additionally, the potential three-dimensional structure and bioactivity of the membrane may facilitate the repair process.

This study experimentally evaluated the key performance indicators of the SIS membrane (Chenggu Kuai®) and porcine peritoneal membrane (Lando®), as well as their roles in new bone formation. ① Physicochemical properties: The test results indicated that the Chenggu Kuai® group showed a pH closer to neutrality, indicating fewer residual chemical reagents.In terms of mechanical properties, the Chenggu Kuai® group exhibited relatively higher tensile strength and tear resistance. ② In vivo bone regeneration effects (animal experiments):At the key postoperative intervals of 1, 3, and 6 months, the two membrane groups demonstrated a high degree of consistency in promoting bone regeneration. Specifically, there were no significant differences in the changes of buccal and lingual bone heights; no significant differences were observed in the changes of bone widths at 1mm, 2mm, and 3mm below the crest of the extraction socket; and the trends in bone volume/total volume (BV/TV) changes were similar. Overall, throughout the 6-month experimental period, the SIS-based Chenggu Kuai® membrane achieved effects comparable to those of the Lando® porcine peritoneal membrane in maintaining alveolar bone dimensions (height and width) and promoting bone mass (BV/TV) accumulation. Moreover, both groups showed an upward trend in bone regeneration indicators.

5. Conclusion

The findings of this study demonstrate that, as a barrier membrane, the Chenggu Kuai® Oral Collagen Membrane has a pH closer to neutral, indicating good biocompatibility. It also exhibits superior mechanical properties compared to the Lando® Oral Absorbable Barrier Membrane, making it more capable of handling clinical situations that require greater supportive strength. During its degradation cycle, its morphological structure can meet the requirements for guided bone regeneration, showing no significant differences from the Lando® Oral Absorbable Barrier Membrane, and thus it can achieve similar functional effects. However, this study has limitations. For instance, the limited number of animal models may make it difficult to comprehensively reflect complex physiological conditions; the relatively short observation window results in insufficiently thorough evaluation of the long-term effects, safety, and potential long-term impacts of Chenggu Kuai® Oral Collagen Membrane. Nevertheless, Combining the material characteristics and clinical application advantages of the SIS membrane, the Chenggu Kuai® Oral Collagen Membrane demonstrates greater application potential as a new-generation biological barrier material, providing robust support for clinical use.

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