A Comparative Study of BioMend® and BioMend® Extend™ Membranes Made at Two Different Manufacturing Facilities

Authors

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Introduction

BioMend Membrane was the first collagen-based membrane released in the United States for guided tissue and bone regeneration surgeries in 1995.

It is manufactured from type I collagen fibers purified from bovine tendon. It has been marketed by ZimVie for more than 15 years. BioMend Membrane is biodegradable in vivo via enzymatic pathways (collagenases and proteases). It has a resorption time of about 8 weeks and moderate conformability and is suitable for periodontal and dental implant surgeries. BioMend Extend Membrane was released in the United States in 1999 to supplement BioMend Membrane with an extended in vivo stability (about 18 weeks) and stronger mechanical properties for use in oral surgeries that require these enhanced properties (e.g., ridge augmentation).

The object of the present study was to compare key functional parameters of BioMend and BioMend Extend Membranes made at two different manufacturing facilities with the specific aim that the membranes will function equally in clinical dental surgery practices.

Materials

BioMend and BioMend Extend Membranes from original manufacturing facility A (A-BM and A-BME, respectively, Part Numbers 0107 and 0142).

BioMend and BioMend Extend Membranes from manufacturing facility B (B-BM and B-BME, respectively, Part Numbers 0107Z and 0142Z).

All membranes utilized were manufactured from purified type I collagen fibers derived from bovine tendon. A-BM and A-BME membranes were manufactured in a facility utilized historically for the manufacture of BioMend and BioMend Extend Membranes. B-BM and B-BME were prepared in a newly-identified facility following procedures similar to those of US patent number 7,807,192 [1]. Briefly, the purified type I collagen fibers were dispersed in an acidic media (pH 2.5), homogenized, filtered, reconstituted, dehydrated, compressed, freeze dried, crosslinked, sized, packaged and sterilized. Representative Scanning Electron Micrographs (SEMs) for A-BM, B-BM, A-BME and B-BME membranes are shown in Figures 1-4, respectively.

Methods

A series of function-related parameters were evaluated in vitro to define the characteristics of the membranes. Tests were performed under identical conditions such that results can be analyzed and compared without introducing systematic error factors. Ten membranes from each of three separate lots of A-BM, A-BME, B-BM and B-BME membranes were used in the study. The following describes the tests conducted and methods utilized.

Density

Density relates to the permeability (pore structure) of the membrane. Density is defined as the weight of collagen fibers per unit volume of the membrane in unit of g/cm3. The membrane was dried over P2O5 for 24 hours and the dry weight was recorded in grams. The volume was determined by measuring the width (W), length (L) and the thickness (T) of the membrane using a caliper, and it is expressed as W x L x T in cm3.

Hydrothermal Shrinkage Temperature

Hydrothermal shrinkage temperature is defined as the onset temperature of phase transition from triple helix to random coil of collagen molecules in fibers. Hydrothermal shrinkage temperature measured in vitro correlates with in vivo stability of the membrane [2].

Generally, if all things are equal, the higher the hydrothermal shrinkage temperature, the more stable the membrane will be in vivo or the slower the rate of membrane degradation in vivo.

Hydrothermal shrinkage temperature was determined using a differential scanning calorimeter (Mettler/Toledo Polymer DSC, Mettler-Toledo Inc., Columbus, Ohio). Briefly, for each membrane, a disc 2.5 mm in diameter was punched out, hydrated in phosphate buffered saline (PBS), placed in an aluminum crucible, and sealed. The sample was then placed into a furnace of the DSC and heated at a rate of 5°C per minute for ten minutes.

SEMs of A-BM

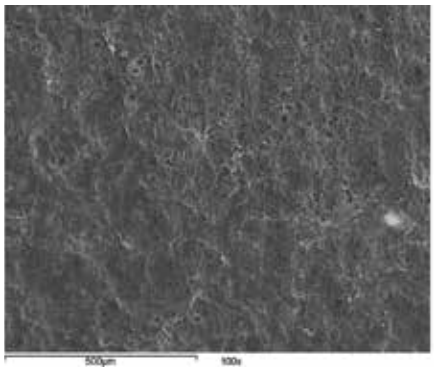


Figure 1a: A-BM, Side A (100X)

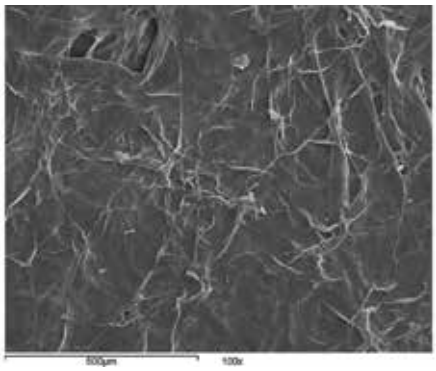


Figure 1b: A-BM, Side B (100X)

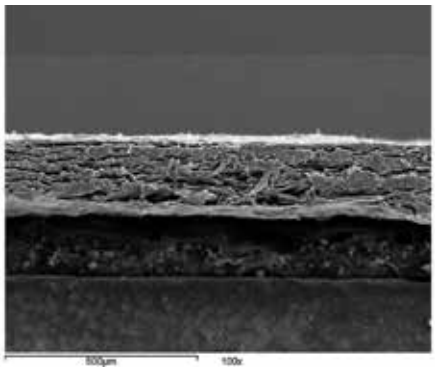


Figure 1c: A-BM, Cross Section (100X)

SEMs of B-BM

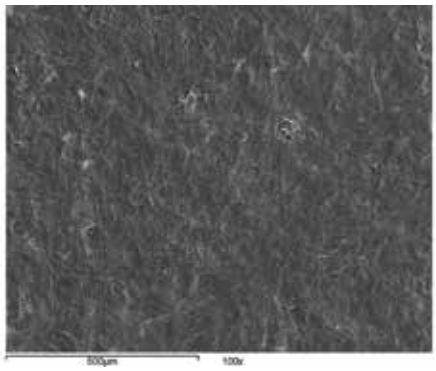


Figure 2a: B-BM, Side A (100X)

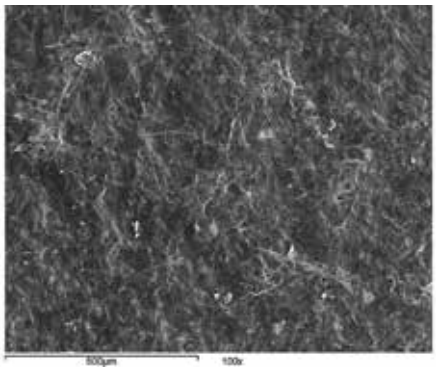


Figure 2b: B-BM, Side B (100X)

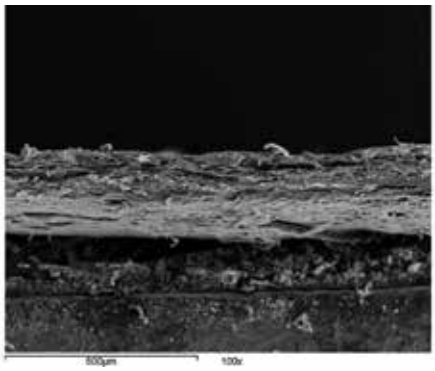


Figure 2c: B-BM, Cross Section (100X)

SEMs of A-BME Membrane

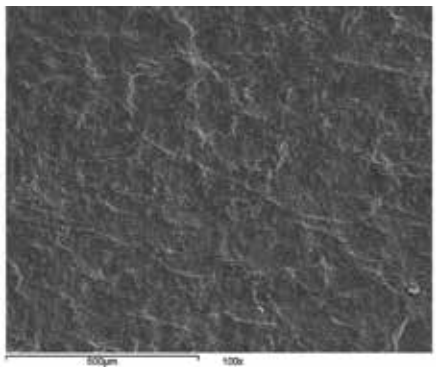


Figure 3a: A-BME, Side A (100X)

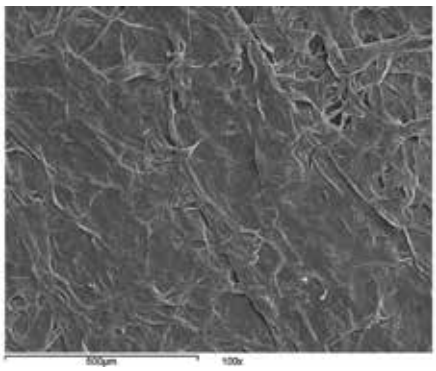


Figure 3b: A-BME, Side B (100X)

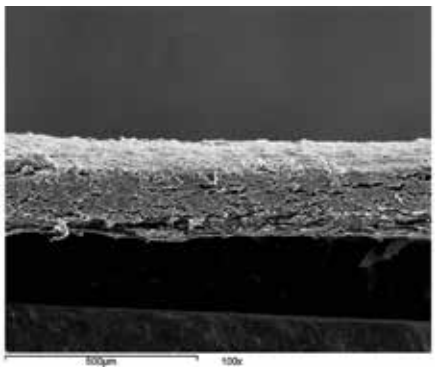


Figure 3c: A-BME, Cross Section (100X)

SEMs of B-BME

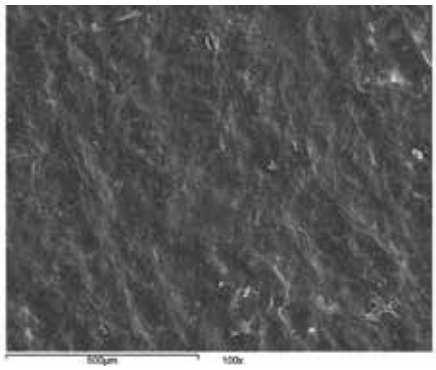


Figure 4a: B-BME, Side A (100X)

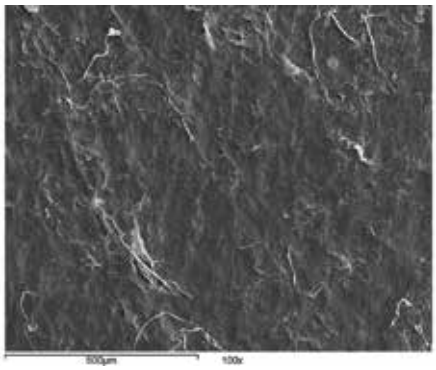


Figure 4b: B-BME, Side B (100X)

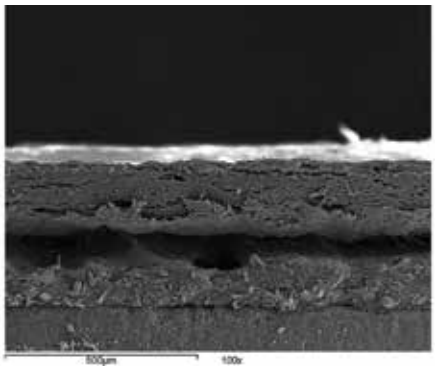


Figure 4c: B-BME, Cross Section (100X)

Mechanical Properties

Suture pullout strength, tensile strength and tear strength were determined for both product lines. The suture pullout strength measures the amount of pulling force the membrane can withstand until tearing. Tensile strength measures the ultimate stress strength or ultimate force needed to break the membrane in the stress direction. The tear strength measures the strength of the membrane under shear stress conditions. Various techniques are described below.

Suture Pullout Strength

The suture pullout strength was determined using a mechanical tester (Lloyd Instruments LF Plus, Ametek, Largo, FL). The membrane was cut to a size of 1.5 cm x 2 cm and hydrated in purified water at 25°C for about 2 minutes. A 3-0 silk suture was passed through the long axis (2 cm) side of membrane at approximately 3 mm from the edge and secured to a hook adapter of the mechanical tester. The membrane was then secured with a clamp at the opposite side of the suture. The suture was pulled at a speed of 2.5 cm/min until the membrane was pulled apart. The suture pull out strength was recorded as kilograms.

Tensile Strength

A sample was cut into a dumbbell shape by a die punch and hydrated in purified water at 25°C for about 5 minutes. It was then secured to a clamp fixture at both ends, and pulled at a speed of 2.5 cm/min by a mechanical tester (Lloyd Instruments LF Plus, Ametek, Largo, FL) until the membrane was pulled apart. The tensile strength was recorded as kg/cm2.

Tear Strength

A membrane was cut to a size of 0.5 cm wide and 1 cm long. A 1 mm hole was punched in the membrane so that the center of the hole is 0.4 cm away from the nearest end and is in line with a slit that is cut down the middle of the sample. The sample was hydrated in purified water at 25°C for about 5 minutes. Each tongue of the test specimen was then secured to a clamp fixture, and pulled at a speed of 0.25 cm/min by a mechanical tester (Lloyd Instruments LF Plus, Ametek, Largo, FL) until the membrane was completely torn and the tear strength was recorded in kilograms.

Conformability

Conformability of a membrane is defined as the adaptability of the membrane to the dental bone grafting site. The requirement of the degree of conformability is dependent

upon the type of dental surgery. A less conformable membrane can provide stronger compression resistance making it more suitable in procedures such as ridge augmentation where the bone grafting material can be maintained in place (e.g., height and width of the grafting material). On the other hand, a more conformable membrane may be more suitable for small periodontal defects where the membrane can be easily adapted to the bone graft surface to prevent epithelial cells from growing into the defect site (e.g., periodontal surgery and socket ridge preservation procedures).

The conformability of a membrane is determined by measuring the angle of drapeability. A sample (1.5 cm x 2.0 cm) was hydrated in purified water for about 5 minutes, and the excess surface water removed. The wet sample was then placed over a rectangular block in such a manner that half of the length of the membrane was allowed to drape along the edge of the block. The degree of conformability was measured by measuring the angle (°α) formed between the membrane on the horizontal plane of the block and the free membrane that draped from the edge of the block.

Collagenase Degradation

Collagen molecules are degraded in vivo via enzymatic pathways. Mammalian and bacterial collagenases, both found in the oral cavity in pathogenic conditions, can cleave collagen molecules. Once the molecule is cleaved by the collagenase enzyme, the short triple helical segments become unstable at body temperature and the denatured peptides are further degraded by proteases. The degraded peptides are metabolized or secreted.

Bacterial collagenase was used in this study. Briefly, each sample was dried in a vacuum oven, weighed, and incubated in 2 ml of bacterial collagenase solution (US Biological, Flemington, NJ) (5 units/ml in 0.025 M PBS, 0.36 mM CaCl2) at 37°C. At pre-determined time points, the residual samples were removed and dried. The initial and final dry weights were used to calculate the percent mass remaining.

TABLE 1: Summary of Characteristic Testing of A-BM, B-BM, A-BME and B-BME Membranes

Products	Density* (g/cm3)	Hydrothermal Shrinkage Temperature* (°C)	Suture Pull Strength* (kg)	Tensile Strength* (kg/cm^2)	Tear Strength* (kg)	Conformability* (°)
A-BM	0.749±0.058	56.5±1.7	0.212±0.102	89.2±24.4	0.035±0.008	162±8
B-BM	0.716±0.035	56.4±1.7	0.400±0.043	82.8±7.4	0.115±0.029	153±4
A-BME	0.798±0.083	64.6±4.0	0.309±0.057	91.0±27.8	0.065±0.018	178±2
B-BME	0.790±0.147	62.1±1.2	0.410±0.050	95.6±12.6	0.157±0.057	162±5

**AVG±SD of 30 samples tested*

Results

SEM micrographs A-BM, B-BM, A-BME and B-BME membranes shown in Figure 1-4 indicated that both families of membrane products are dense collagen fibers with rough fiber surfaces. There were no major differences in overall gross morphology of the surfaces and cross sections of A-BM compared to B-BM and A-BME compared to B-BME.

Table 1 summarizes the results of the study. Each number in the table represents the mean of 30 samples and associated standard deviation of the mean from three separate lots with the exception of the permeability and enzyme degradation study where 5 samples from each lot were used in the study. We will discuss the results of each of the tests below.

Density

The density for B-BM is similar to that of A-BM. The density of B-BME was similar to that of A-BME. The difference between each comparison group of products is not statistically significant: $p=0.15$ for B-BM vs. A-BM and $p=0.68$ for B-BME vs. A-BME, respectively.

Hydrothermal Shrinkage Temperature

The hydrothermal shrinkage temperature of B-BM is indistinguishable from A-BM ($P=0.97$) and the hydrothermal shrinkage temperature of B-BME is slightly higher than that of A-BME ($P<0.05$). It is noted that there is a significant overlap of hydrothermal shrinkage temperature between B-BME and A-BME.

Mechanical Properties

Suture Pullout Strength: Sufficient suture pull-out strength is required if the membrane is to be sutured with the adjacent tissue for stability. Generally, a suture pullout strength of 150 grams or higher is needed to serve this function, and all samples tested exceeded this requirement. The suture pullout strength for B-BM is consistently higher than the A-BM membrane ($P<0.05$). The variability of suture pullout strength for A-BM is high indicating that the suture pullout strength of A-BM is not as reproducible as B-BM. It is noted that the suture pullout strength for A-BME is lower as compared to B-BME ($p<0.05$) and that the suture pullout strength of A-BME is more consistent than that of A-BM within the lots tested. It should be emphasized that the consistency and higher suture pullout strength is important in dental surgeries when suturing or tacking is required for the stabilization of the membrane in situ.

Tensile Strength: The overall tensile strength was similar for both families of products. It is noted that the standard deviations for A-BM and A-BME are significantly higher than B-BM and B-BME, indicating that the sample to sample variation is significantly higher for membranes manufactured at facility A. However, the overall tensile strength for membranes made at the A facility are not significantly different from those made at the B facility: P=0.17 and P=0.42 for B-BM vs. A-BM and B-BME vs. A-BME, respectively.

Tear Strength: Tear strength is another mechanical property that is often required to minimize suture tear of the membrane due to the shear effect of the suturing process. Consistent with other mechanical properties, the tear strength for membranes made at the B facility are consistently higher than those made at the A facility ($P<0.05$ for both groups).

Figure 5a: Collagenase Degradation Profile of B-BM vs. A-BM

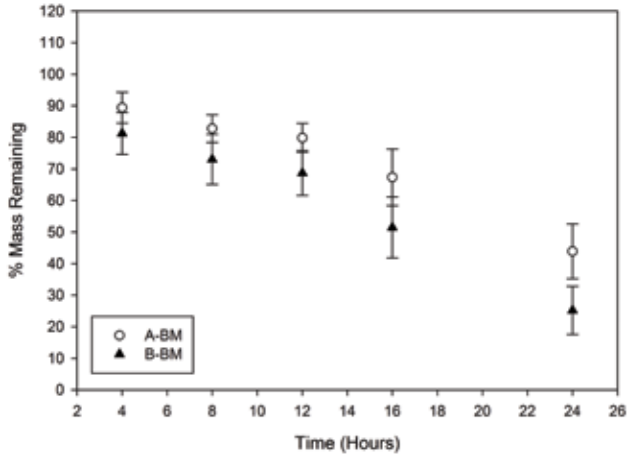
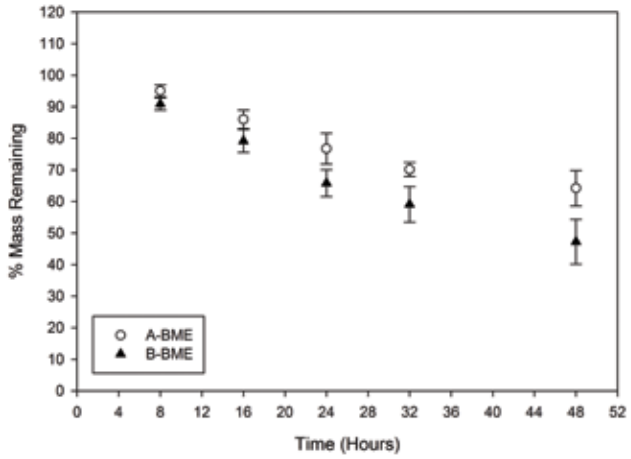


Figure 5b: Collagenase Degradation Profile of B-BME vs. A-BME



Conformability

Conformability is an important handling parameter in using membranes for guided tissue regeneration. B-BM and B-BME are moderately more conformable than A-BM and A-BME ($p<0.05$ for both product lines), based on the drapability test. As will be discussed in the next section, conformability is a parameter that is more difficult to define from surgery to surgery. Often the conformability requirement is based on the subjective determination of the clinician.

Collagenase Degradation

Figure 5 summarizes the kinetics of in vitro collagenase degradation study of the membranes evaluated. The percent weight of residual membrane remaining is plotted as a function of the time of degradation. It is of interest to note that both product lines degraded approximately linearly with time and that B-BM and B-BME degraded at a rate slightly faster than A-BM and A-BME. It is worth mentioning that the extent of new tissue deposition over time observed in vivo could not be simulated in the current study. Based on the similar characteristics of the two product lines, the resorption rate as well as the rate of new tissue deposition in vivo are anticipated to be comparable [3].

Discussion

The use of barrier membranes in guided tissue regeneration and guided bone regeneration in dental surgeries has become a standard of care. Initially, membranes were developed for periodontal surgery applications for guided tissue and bone regeneration as a barrier to prevent epithelium down growth such that bone growth, cementum regeneration followed by periodontal ligament attachment, can occur during the wound healing period of the surgery [4]. As the science and technology of implantology progressed in the 1990s, the applications of membranes have rapidly expanded to include ridge augmentation (mandible), sinus floor elevation (maxilla) and tooth socket preservation procedures. Each of these procedures requires a somewhat different characteristic of the membrane. For example, in the ridge augmentation procedure, various bone grafting materials are used to produce a three dimensional scaffold for bone growth. The common bone grafting materials used in dental surgery include autograft, allograft, natural and synthetic calcium phosphate ceramics and collagen-mineral composites utilized in particulate form of various sizes. It is common to augment the vertical ridge height by several millimeters above the base-line of the existing bone of the patient. As such, a more rigid membrane like BioMend Extend Membrane or a metal (titanium) supported membrane is required to maintain the bone graft implant height for bone growth. On the other hand, in periodontal defect surgery, a conformable membrane like BioMend Membrane may be easier to adapt to the surface of the grafted defect than the rigid membrane for the purpose of preventing epithelium

down growth into the wound site. Thus, at present, a number of dental membranes with different characteristics are on the market to meet the needs of various dental surgeries.

BioMend Membrane (A-BM and B-BM) has the characteristics that are useful for most of the periodontal and implant surgeries that do not require extensive rigidity and long in vivo stability. It has been used in dental surgeries since 1995 with acceptable results. In order to provide longer in vivo stability of the membrane, ZimVie also markets BioMend Extend Membrane to compliment the BioMend Membrane in surgeries that require enhanced mechanical properties and in vivo stability. The BioMend Extend Membrane is generally utilized in procedures where a longer-lasting membrane is required, as in the augmentation of a large bony defect in ridge construction where maintaining ridge height is important. However, a segment of dental clinicians prefers more conformable membranes in many dental bony defect procedures. As a result, membranes like CopiOs® Pericardium (ZimVie, Palm Beach Gardens, FL) and Bio-Gide (Ed. Geistlich Soehne AG, Wolhusen, Switzerland) have increasingly been used clinically in recent years.

Conclusion

BioMend and BioMend Extend Membranes manufactured at facility B (B-BM and B-BME) are type I collagen-based dental membranes that have characteristics comparable to BioMend and BioMend Extend Membranes manufactured at the original manufacturing facility A (A-BM, A-BME). A wider sample to sample variation was observed in membranes manufactured at facility A than facility B, indicating that some of the functional parameters studied are not as reproducible by facility A, and that a more consistent product is anticipated from facility B. A careful comparison of the membranes made at different facilities indicated that B-BM and B-BME can be used as replacements for A-BM and A-BME respectively in dental surgeries and are expected to perform essentially equivalent clinically.

References

1. Li, ST, et al., Biopolymeric Membranes. Patent assigned to Collagen Matrix Inc. U.S. Pat. No. 7,807,192, 2010.
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3. Data on file at Collagen Matrix, Inc.
4. Bunyaratavej P and Wang HL. Collagen Membranes: A Review. J Periodontal. 72: 215-229, 2001.

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