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FIRST APPROACH OF A PROTOCOL FOR TEST BONE ADHESIVES

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INTRODUCTION

Despite its origins in the mid-1950s with a bone adhesive called Ostamer [1], the development of bone adhesives is still in its early stages and is not a mature field. There lacks a consensus on aspects of adhesive performance and bond strength measurement. As a result, there are not standard tests for quantifying and evaluating the adhesive strength at the interface between the bone tissue and biomaterial [2-4]. The purpose of this study is to design and standardize a protocol capable of measuring the bond strength of bone adhesives. The protocol consists of mechanically evaluated different formulations of adhesives based on chitosan and alginate, selected based on their individual potential as bone adhesives [5]. Three mechanical tests were implemented. The first and second methods are tensile tests with a controlled fracture at 90º (TT90) or 45° (TT45) relative to the load direction along a constant transverse section of 10 mmx10 mm. The third test is a three point flexural test (3PFT), where the deflection of cancellous bone sheets is tested with and without adhesive reinforcement. In order to propose a methodology to apply the adhesive in bone specimens, a dental adhesive Adper Single Bond (3M Espe) was used. Finally, the results from the mechanical characterization were analyzed using ANOVA ($p<0.05$) and pos hoc Tukey tests to compare the bond strength of each formulation against Kryptonite® (Doctor´s Research Group, Inc.,), a commercial bone cement with adhesive properties that has shown promising *in vivo* results and has FDA approval [6].

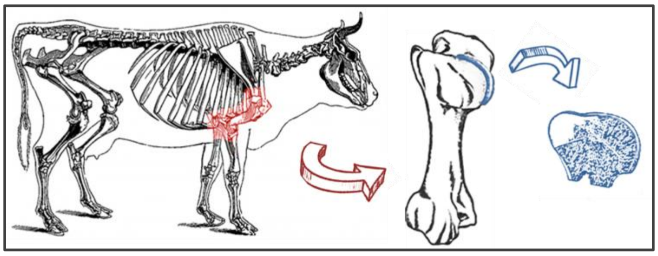

Figure 1. Cancellous bone extracted from bovine proximal humerus bone. Adapted from [7].

Currently, formulations of adhesives capable of fixing small fragments of bones are in development at Universidad de los Andes. Six different adhesives, three based on chitosan, three based on alginate, and each one mixed with calcium carbonate ($CaCO_3$) and hydroxyapatite (HA) at different concentrations. (C1: chitosan + $CaCO_3$ (low), C2: chitosan + $CaCO_3$ (low) + HA (low), C3: chitosan + CaCO3 (high) + HA (high), A1: alginate+$CaCO_3$, A2: alginate+CaCO3 (low) + HA (low) and A3: alginate + $CaCO_3$ (high) + HA (high)), were tested using the protocol proposed. We hypothesized that formulations with high concentration of $CaCO_3$ and HA improve adhesive stiffness.

METHODS

Materials

Cancellous bone, extracted from bovine proximal humerus bone, is used because it plays an important role in the transmission and distribution of loads in large bones like the humerus and femur [8,9] (Figure 1). Cancellous bone is also well characterized from a materials perspective as a composite, anisotropic, and open porous cellular solid material.

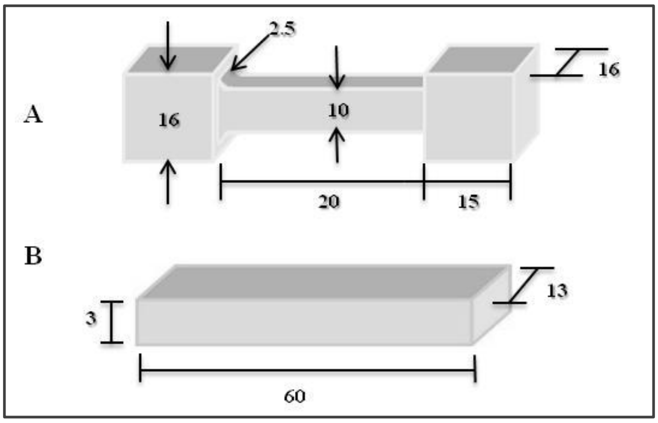

Figure 2. Specimens of A) TT90 and TT45 and, B) 3PFT. All measurements are in mm.

The geometry of TT90 and TT45 specimens was selected from the control test without fracture. The specimens have cross sectional area of 10 mm x 10 mm (Figure 2A.). For 3PFT, specimens were manufactured (60 mm x 12.7 mm x 3 mm). All tests were conducted on a universal testing machine Instron Model 3367 at a strain rate of 1 mm/min for TT90 and TT45 and 0.1 mm/mm / min and 48 mm of space between pivots for 3PFT.

Mechanical tests

The TT90 quantifies the lower limit of strength of the adhesive-bone interface, as this is a peeling stress test. The

TT45 characterizes the shear behavior of the adhesive, and 3PFT is used to evaluate how well the adhesive reinforces the bone under a flexural load.

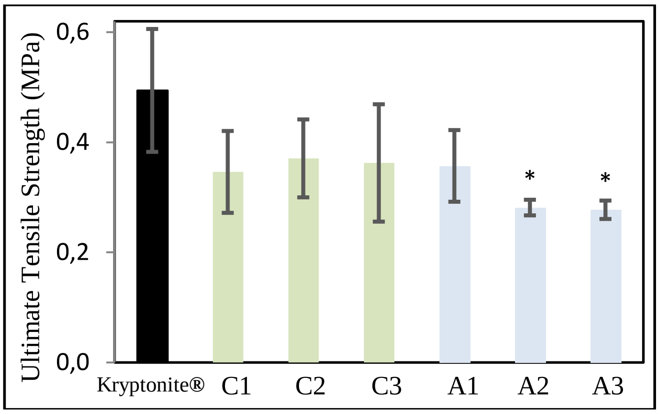

Figure 3. Results for TT90 for adhesive based on chitosan and alginate compared with Kryptonite®, Significance difference (*p<0.05). Error bars of one standard deviation.

In order to select the geometry of the specimens used for TT90 and TT45, two different control tests without fracture were conducted (n=10), aiming to measure the ultimate tensile strength in order to compare it to previously reported data [10,11]. In order to identify the best method to apply the adhesives, Adper Single Bond dental adhesive was used as a standard (n=7). Adper Single Bond was selected as the control adhesive due to its versatility in different physiological environments, photopolymerization properties and high stiffness [12]. The last control test aimed to compare our formulations to Kryptonite ® (n=7). Finally each bone adhesive were tested at TT90 (n>5) with mass (0.18 g) controlled.

The test specimen for the 3PFT consists of a cancellous bone sheet with a layer of adhesive on its lower surface, thereby obtaining a single adhesive-bone interface. This arrangement reinforces the bone sheets if the adhesive is sufficiently rigid.

RESULTS AND DISCUSSION

Preliminary results show C1, C2, C3 and A1 presented better results at TT90, showing no statistical difference compared to Kryptonite® ($p<0.05$); A2 and A3 did show lower bond strength than Kryptonite® after Tukey´s test (Figure 3).

For 3PFT, C1 was the only one that showed an increase in flexural strength when comparing reinforced and non-reinforced test data ($p<0.05$). Currently, TT45 tests are in development and we hypothesize that all formulations support more stress than in TT90, based on prior knowledge that adhesives behaved more rigid under shear than tensile loads. It is expected that C3 and C2 formulations give betters results because of the contribution of HA and $CaCO_3$ in the composite structures.

CONCLUSIONS

TT90 has been proposed as a standard experimental methodology for comparing the bond strength of different formulations of bone adhesives. And thanks to that its clear now that HA plays an important role in formulations, as tendencies show it decreases mechanical resistance in alginate based adhesives, but increases it in chitosan ones.

At this time, we are developing more data in order to show more precise analysis and conclusions with TT45 and 3PFT in order to select the best adhesive of chitosan and alginate, which will be used in an animal model with the aim to study its behavior in an *in vivo* experiment.

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