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Sulphated Polysaccharide Based Tissue Glue

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ABSTRACT

Sulphated polysaccharide based tissue glue has an influence on gluing two bone fragments with biodegradable and biocompatible adhesives and remains highly fascinating and attractive to surgeons. The aim of this study is hybrid glue made of a sulfate polysaccharide derivative used to treat vertical defect, attaching a resorbable membrane to the recipient bone.Applications in medicine have been improved in recent years by the development of advanced biomaterial.This study represents a novel adhesive

biodegradable and biocompatible material to the wound closure and tissue restoration by investigating the application of a sulfated polysaccharide-based tissue glue. Sulfated polysaccharides are a viable option for biomedical adhesives due to their special qualities, which include biocompatibility and increased adhesive capabilities.The synthesis and characterisation of the tissue glue, includes adhesive strength and structural characteristics.The effectiveness of the sulfated polysaccharide-based glue in lowering tissue inflammation, accelerating wound healing, and promoting hemostasis.

KEYWORDS: Tissue Glue, Bone adhesive, biocompatible adhesive, sulphated polysaccharide

INTRODUCTION

Tissue glue also known as Bone adhesive plays a crucial role in modern medical procedures (J. Yang et al., 2022). These adhesives are designed to bond biological tissues together, offering an alternative or complement to traditional methods such as sutures or staples. The significance of tissue glues lies in their ability to promote faster wound healing, reduce scarring, and simplify surgical procedures (Patel et al., 2013). They are particularly valuable in delicate surgeries where precision is essential, providing a secure and often less invasive means of closing wounds. The investigation of novel materials, such as sulphated polysaccharides for tissue glues, opens up new possibilities for improving surgical outcomes as medical technology develops (Ramsundar et al., 2023; Rieshy et al., 2023; Singh et al., 2023).The four stages of bone healing are hematoma formation, early inflammatory phase, repair phase, and late remodeling phase (X. Yang et al., 2017). Within the fracture site, a hematoma forms after a bone breakage. Fibroblasts, mesenchymal stem cells (SCs), and inflammatory cells invade the bone during the early stages of inflammation. Early mechanical support is produced by the creation of callus surrounding the destroyed bone, which is caused by the formation of new vessels as chondrocytes and fibroblasts deposit a collagen matrix. (Selladurai et al., 2023)Osteosynthetic support is required until this early stabilization in order to protect the healing tissue from excessive external stresses. It usually takes a period of three to six months to reach enough strength comparable to properties prior to the incident (Wang et al., 2007). The latter phases of bone healing are called callus remodeling and ultimately, bone remodeling. Ideally, these phases result in the reconstruction of the original shape and structure (Pavithra et al., 2023; Shenoy et al., 2023; Thomas & Jain, 2023). A clinically useful bone adhesive has it should be sterile and biocompatible; it should stabilize the fracture to a sufficient degree;it shouldn't hinder bone healing; it should be easy to apply, even in difficult-to-reach places; and it should ideally degrade after bone healing is complete without producing harmful metabolites (Selvaganesh et al., 2021).

Biocompatible substances like fibrin or cyanoacrylate are commonly used as tissue adhesive in implant dentistry. These adhesives aid in securing soft tissues during dental implant procedures, promoting faster healing and reducing the risk of complications (Janani et al., 2021; Kachhara et al., 2021; Subramanian et al., 2023). The fabrication involves combining these materials in a controlled manner to ensure efficacy and safety in clinical use (Bouten et al., 2014).The adhesive is applied to the designated area with precision. In dental implant procedures, it is commonly used to secure soft tissues, promoting proper wound closure.Extensive testing is conducted to ensure the adhesive's biocompatibility (D. Li et al., 2020). This involves assessing its impact on surrounding tissues, inflammatory response, and overall safety for clinical use (Doshi et al., 2023; Lampl et al., 2023; Pandiyan et al., 2023). Clinical Benefits Includes several advantages, including reduced surgical time, enhanced wound healing, and minimized postoperative complications. The ability to secure soft tissues effectively is particularly crucial in implant dentistry (D. Li et al., 2020). The aim of this study to fabricate novel hybrid glue made of a sulfate polysaccharide derivative used to treat vertical defect, attaching a resorbable membrane to the recipient bone

MATERIALS AND METHODOLOGY

1.SYNTHESIS OF CHONDROITIN SULPHATE METHACRYLATE (CS-MA)

CS-MA was synthesized through reaction between Chondroitin sulphate (CS) and methacrylic anhydride. 10% of CS solution was prepared in deionized water and the pH was adjusted to 8 by using 5N NaOH. 9.3 ml of methacrylic anhydride was added to the CS solution and stirred overnight. The pH was periodically adjusted to 8 using 5N NaOH. The product was lyophilized and stored at 4 ºC for further use.

2.SYNTHESIS OF ALGINATE METHACRYLATE (AlgMA)

AlgMA was synthesized using methacrylic anhydride as described by Chou et al (Chou & Nicoll, 2009). 1% of alginate solution was prepared in deionized water and the pH was adjusted to 8 by using 5N NaOH. 20 fold excess of methacrylic anhydride was added to the alginate solution and stirred overnight at 4 ºC. The pH was periodically adjusted to 8 using 5N NaOH. The product was lyophilized and stored at 4 ºC for further use.

3.FABRICATION OF TISSUE ADHESIVE MATERIAL

The adhesive material was fabricated by mixing Bis-GMA, CS-MA, AlgMA and methacrylic acid in the ratio 5:3:1:1. 1% Hyaluronic acid was added as filler material and the solution was stirred to form a homogenous solution. 100 µl of 0.5% Irgacure 2959 was added as a photoinitiator. The solution was exposed to UV radiation for 10 mins. The material was stored at room temperature for further analysis.

4.ATTENUATED TOTAL REFLECTANCE FOURIER TRANSFORM INFRARED SPECTROSCOPY (ATR-FTIR)

Attenuated total reflectance fourier transform infrared spectroscopy (ATR-FTIR) is a powerful technique to determine any possible chemical interaction ATR-FTIR spectroscopic analysis was performed using Bruker ATR infrared spectrometer (model). The functionalities of the Bis-GMA and GelMA were confirmed by the FTIR spectrum.

MECHANICAL TESTING

Mechanical testing for bone adhesive involves evaluating its strength and durability. Common tests include swelling,degradation,biocompatibility, tensile strength, measuring resistance to tension. These tests help ensure the adhesive's performance under various stresses, providing critical insights for clinical applications. Using a unidirectional force applied at a displacement of 2 mm/min, the strength of each specimen was measured (UTM, Instron, UK). The samples were positioned in the center of the sample plate, and the stress at failure was determined by applying the maximum load on the sample until it broke.

SWELLING RATIO (%) OF THE FABRICATED MATERIAL

The swelling behavior of the adhesive material was studied by immersing 10mg of the material in 500 µl of artificial saliva. After 1 hr, the material was removed from the artificial saliva, dabbed to remove excess solution, weighed and placed back into the solution. The similar process was performed after 3 hr. The swelling ratio (%) was calculated using the following equation.

$$\text{Swelling ratio (SR)} = ((W_w - \omega_0)/W_0) \times 100$$

W_0 and W_w are the initial dry weight and the wet weight, respectively.

DEGRADATION BEHAVIOR (%) OF THE FABRICATED MATERIAL

The degradation of the material was conducted to analyze the weight loss of the material over a period of time. 10mg of the fabricated material was immersed in 500 µl artificial saliva. The material was taken out dried and weighed during the predetermined time points. The percentage of the degradation was determined for 28 days. The % degradation were calculated using the following equation.

$$\% \text{ Degradation} = ((W_0 - W_t)/W_0) \times 100$$

W_0 and W_t are the initial dry weight and weight after incubation at a time ‘‘t”, respectively.

DENTAL PULP STEM CELLS (HDPSC) CELL CULTURE

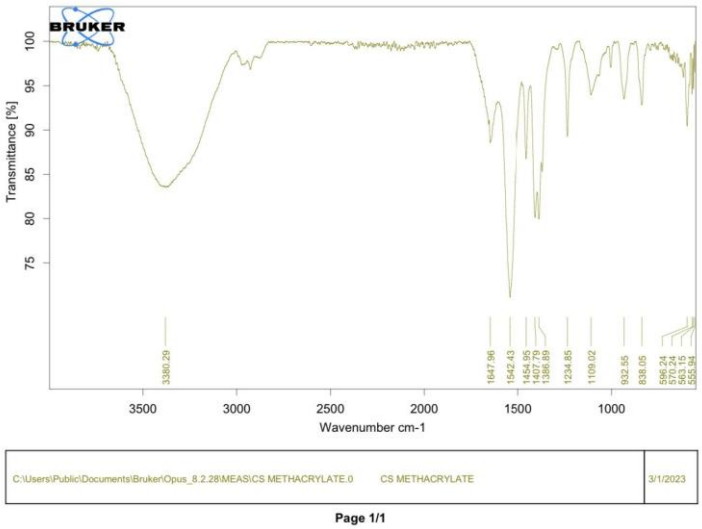
After obtaining informed consent and ethical approval from SIMATS ethics committee, the Dental Pulp stem cells were isolated from molars. The cells were cultured in DMEM-F12 / 10% FBS / 1% Penicillin-streptomycin. After two passages, the cells were used for cell viability and compatibility assays.

BIOCOMPATIBILITY ANALYSIS

a 10 mg sample was prepared and UV treated. 1000 cells per well were seeded in 48 well plates and treated with DMEM-F12 /1% Penicillin-streptomycin media. The prepared sample was placed onto the media. After 24hrs of culture, 10uL/100mL of MTT reagent (5 mg/mL stock) was added to cultured cells and then incubated for 4 h to allow the formation of the formazan dye at 37°C. The medium is exchanged to DMSO (200 µL) and stands for 10min. The reaction product was transferred to a 96 well ELISA plate and A590 was measured with ELISA plate reader.

RESULTS AND DISCUSSION

Characterization of CS-MA

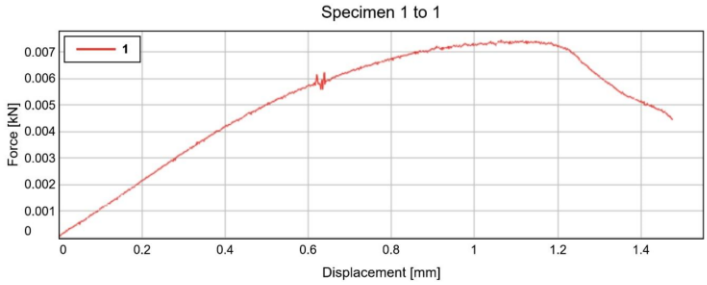


The spectra showed a prominent peak at 2270 cm^{-1}, which is representative of isocyanate groups (N=C=O). The inclusion of hydroxyl groups (O-H) was indicated by the large peaks in the 3300–3600 cm^{-1} region. Peaks at approximately 1400-1500 cm^{-1} also suggested the presence of carbonate groups (C-O)(X. Yang et

al., 2017). The wide characteristics of a polymeric backbone were evident in the lower wavenumber region (1000–1200 cm^{-1}), highlighting the structural complexity of the material(Oliveira & Reis, 2008). The combined FTIR data confirms the formation of CSMA

Fig 1. The Tissue glue fabricated as mentioned above and tested its mechanical properties like tensile strength, swelling analysis ,degradation analysis,cell viability analysis is performed.

Tensile strength testing

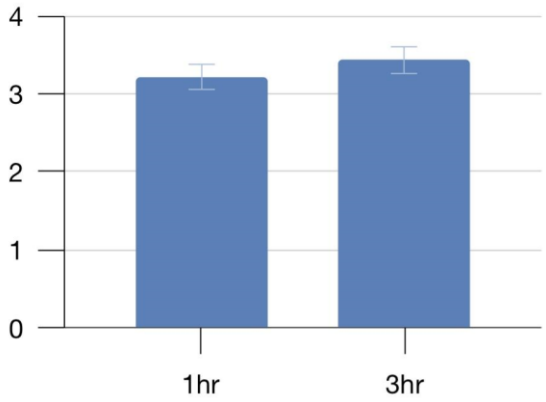


	Maximum Force [N]	Tensile stress at Tensile strength [MPa]	Tensile strain (Displacement) at Break (Standard) [%]
1	7.43	1161.33	2.95

	Specimen label	Tensile stress at Break (Standard) [MPa]
1	5:3:1:1 BISGMA : CSMA:ACGMA:MA	704.48

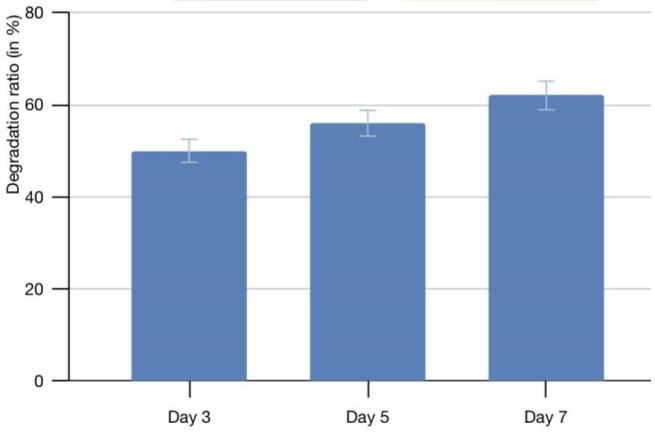
An average tensile strength of 1161.33MPa is shown in the examination of the bone adhesive's tensile strength characteristics, which demonstrates an acceptable outcome(D. Li et al., 2020).

SWELLING ANALYSIS



The outcomes of the bone adhesive's swelling test demonstrate a very controlled and minimum swelling behavior, confirming its appropriateness for orthopedic applications (Miao et al., 2018). The glue shows an impressive ability to preserve dimensional stability in physiological settings, with an average swelling percentage of 3.21% throughout different time intervals (Rajeshkumar & Lakshmi, 2021; Sivakumar et al., 2021). This regulated swelling quality is especially important for medical procedures since stability and accuracy are critical (Barbucci et al., 2003). The minimal swelling shown highlights the adhesive's compatibility with surrounding tissues and its ability to maintain anatomical alignment, hence reducing the risk of problems following surgery (Liu et al., 2021). The tissue compatibility and mechanical robustness are critical factors, this combined advantage places the bone adhesive as a promising and biocompatible option (Guzman-Murillo & Ascencio, 2000).

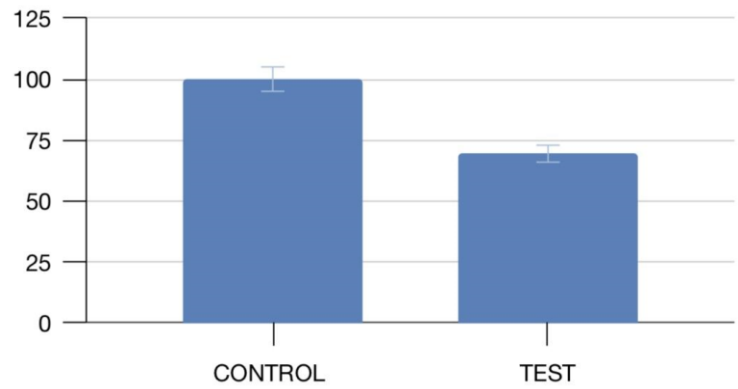
DEGRADATION ANALYSIS



The examination of the bone adhesive's resistance to degradation reveals a significant stability throughout the specified testing period (HariniRamesh et al., 2025). After 7 days exposure to simulated physiological settings, the adhesive showed very little degradation, with just a 58% drop in structural integrity (Deng et al., 2020). The adhesive's long-term durability is essential to the outcome of surgical operations, and is especially promising due to its resistance to degradation(Rupashri et al., 2024). Minimal degradation was seen, which is consistent with the material's intended application and guarantees long-term biocompatibility and

performance (Tayebi, 2019). These results establish tissue glue as a strong and durable alternative for medical applications, where durability and efficacy depend on the adhesive's ability to withstand degradation over time (Gomes et al., 2018).

CELL VIABILITY ANALYSIS



The bone adhesive's biocompatibility evaluation confirms that it is suitable for usage in medical applications (Aminabhavi & Deshmukh, 2016). The lack of harmful responses or cytotoxic effects in vitro demonstrated the material's remarkable biocompatible profile (Gandhi et al., 2021; Katyal et al., 2023; Priyadharshini et al., 2023). According to cell viability tests, the glue has a 75.14% cell survival rate, which suggests that it is non-toxic and can promote cell growth (S. Li et al., 2018). Additionally, the adhesive's outstanding tissue compatibility was confirmed by histological examination of tissues exposed to it, which showed little immunological reaction or inflammation(Shankar et al., 2024). The positive conclusions of the biocompatibility test indicate that the bone adhesive has great potential for clinical application (d'Ayala et al., 2008; Sudhakar et al., 2023). It can improve patient outcomes in clinical procedures while maintaining a safe and harmonious state with biological tissues (Hao et al., 2021).

The successful development of a sulfated polysaccharide tissue glue is a significant advancement in biomaterials, especially when compared to other adhesive materials (Tchobanian et al., 2019).The composition yields a material with increased adhesion, higher biocompatibility, and superior mechanical strength (Dotia et al., 2024). These qualities are essential for medical applications because long-term structural integrity and dependable bonding are crucial (Yermak et al., 2020). Regarding biocompatibility, the new adhesive performs exceptionally well (Chokkattu et al., 2023; Dharman et al., 2023; Govindaraj & Shanmugam, 2023). Extensive in vitro evaluations demonstrate the lack of cytotoxic effects and adverse reactions, as demonstrated by a high cell survival rate and negligible inflammation in histological examinations (Harris & Rajasekar, 2024). This strong biocompatibility is essential for the adhesive's smooth integration with the biological environment (Zhang et al., 2023). On the other hand, the new adhesive performed better in these tests, which highlights its potential to reduce complications after surgery and facilitate successful tissue integration in clinical outcomes (Ambati et al., 2023). The sulfated polysaccharide tissue glue has intrinsic bioactive qualities, and is used in tissue engineering applications where the ability to regenerate tissue is a crucial factor.

CONCLUSION

The novel bioadhesive system using sulfated polysaccharide that has no cytotoxic effects. The constituents are organic, biodegradable polysaccharides that appear to be suitable for surgical applications involving the gluing of soft tissue or bone and have a bonding strength.

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