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S-triazine based biocompatible hyperbranched epoxy adhesive with antibacterial attribute for suture less surgical sealing

Shaswat Barua\textsuperscript{a}, Pronobesh Chattopadhyay\textsuperscript{b} and Niranjan Karak*\textsuperscript{a}

\textsuperscript{a}Advanced Polymer and Nanomaterial Laboratory, Centre for Polymer Science and Technology, Department of Chemical Sciences, Tezpur University, Napaam-784028, Assam, India

\textsuperscript{b}Defence Research Laboratory, Tezpur, Assam, India

Abstract

Endeavors have been made from last few decades to relieve mankind from painful suturing during surgery, especially in case of pediatrics. A few surgical sealants or tissue adhesives were designed; but biocompatibility and degradation are the major concerns which limit their use. Here, a S-triazine based hyperbranched epoxy along with a poly(amido amine) hardener is used to develop a highly biocompatible surgical sealant. The epoxy can be crosslinked up to 62\% at room temperature. Further, the sealant exhibited antibacterial activity against \textit{Staphylococcus aureus}, the most notorious microorganism that causes surgical site infections. The sealant was degradable under body conditions and degraded products are non-toxic. Thus, here we show the major merits of the present sealant such as high mechanical stability, optimum balance between strength and flexibility, biocompatibility and degradability.

Keywords: Hyperbranched epoxy; surgical sealant; antibacterial; biodegradable; biocompatible.

*Corresponding author: karaniranj@gmail.com, Tel: +91-3712-267009. Fax: +913712267006.
Introduction

Surgical suturing has been a longstanding problem associated with medical science. Surgical site infection due to suturing is another disastrous crisis, which leads to mortality in severe cases. Despite such inconvenience, this is the mostly adopted mean for closing of surgical incisions. For last few decades, some topical skin adhesives (TSA) were fabricated to develop sutureless wound closing materials. Most of these are either acrylate based or fibrin based. Cyanoacrylate based TSA were popular because of their fast curing, strength and flexibility.\(^1\) However, the by-products were found to be highly toxic to L-929 cells, lymphocytes, and human oral fibroblasts.\(^2\) Another class of TSA used extensively is of fibrin origin. Again, human origin of fibrin and thrombin allow viral transmission.\(^3\) Therefore, an ideal tissue adhesive or sealant is desired to possess optimum strength and stability, adequate biocompatibility and its degradation products should be compatible to the host body.

Due to the aforementioned causes, a sudden halt is observed in the commercialization process of surgical sealants. Adhesion ability of epoxy is well known to the scientific community.\(^4\) So, we tried to utilize this property of epoxy to bind skin tissues in a surgical incision. Hyperbranched epoxy (HE) resin would be considered for the purpose because of its higher tensile and adhesive strength as well as better flexibility as compared to the conventional linear analogs.\(^5\) In 1999, Louis et al. witnessed several fold increment of toughness of commercial linear epoxy upon incorporation of only 5 wt\% of hyperbranched epoxy resin, although the tensile strength decreased to some extent.\(^6\) However, in 2006, Zhang and co-workers reported low viscosity hyperbranched epoxies which not only increased the toughness of commercial epoxy but the tensile and flexural strengths increased considerably.\(^7,8\) Further, properly designed hyperbranched thermosets many cases reported to exhibit superior mechanical
properties that their linear analogs.\textsuperscript{5,9} Ease of processability is another merit of hyperbranched polymers. In case of HE, high surface functionalities and reactivity helps in forming a rigid network when reacted with an efficient crosslinker.\textsuperscript{9} HE to hardener ratio and their reactivity governs the crosslinking conditions.\textsuperscript{10} A room temperature cured epoxy system is therefore desired for the present target. This may trigger the utility of this two component system as a surgical sealant which would be able to seal incisions at body temperature. The vital criterion of a surgical sealant is its compatibility to the host system.\textsuperscript{11} Thus, non-toxic HE may provide a biocompatible matrix which could be sufficiently strong to form a stable interface between tissues. At the same time this should be flexible enough to withstand body movements. Moreover, the matrix is desired to be degradable under body conditions and the degraded product must not lead to any toxicological influence to the body system.

Thus, in the present investigation, a two component sealant system is investigated which is comprised of a triazine based hyperbranched epoxy and a poly (amido amine) hardener.

**Materials and methods**

**Materials**

Bisphenol-A (BPA) and cyanuric chloride (CYC, Merck, India) were recrystalized from toluene and chloroform respectively. Sodium metal, sodium hydroxide, N,N-dimethylacetamide (DMAc), dichlormethane, acetone, chloroform, toluene, tetrahydrofuran and epichlorohydrin (Merck, Mumbai, India) were used as obtained.
Synthesis of hyperbranched epoxy resin

Sodium salt of BPA was prepared by treating BPA with sodium methoxide in super dry methanol according to a reported method. Hyperbranched polyol (HP) core was synthesized by following the same method.

Hyperbranched epoxy resin was synthesized by the polycondensation of HP and BPA with epichlorohydrine (1:2 mol ratio with respect to the total hydroxyl groups of HP and BPA). The reaction temperature was maintained at 110°C. A 5N aqueous solution of NaOH (equivalent to the hydroxyl groups) was added very slowly to the reaction mixture by a pressure equalizing funnel. The reaction was carried out for 4 h. Synthesized resin was extracted from the reaction mixture by dichloromethane and washed with distilled water. The viscous and transparent resin thus obtained was dried under vacuum at 70°C for 48 h. Similarly three resins were synthesized by altering the percentage of the polyol core. They were coded as HE1, HE2 and HE3 according to the incorporation of the amount of HP (10, 20 and 30 wt%).

Characterization

FTIR spectra of the resin and the thermoset were recorded in a FTIR spectrophotometer (Impact-410, Nicolet, USA) using KBr pellet. ¹H and ¹³C NMR spectra of HE2 (as a representative one) were recorded in a JEOL 400 MHz FTNMR spectrometer using CDCl₃ as the solvent and TMS as the internal standard. Different physical properties such as hydroxyl value, epoxy equivalent, drying time and viscosity of the synthesized resin were determined by the standard methods.

Curing study and mechanical performance

Prepared resins were cured by reacting with poly(amido amine) hardener by taking equimolar amount to the epoxy equivalent of the resins. The mixture was cast on steel plates with
dimension of 150 mm × 100 mm × 1.44 mm and the plates were kept at room temperature to note the touch free time. Swelling test was performed to determine the extent of crosslinking by immersing weighed amount of the cured films in sufficient amount of THF. After 24 h, the weight of the swollen film was taken. The swelling value (%) was determined from the weight of dry and swelled films, using the following equation.

\[ \text{Swelling (\%) = } \left( \frac{W_s - W_d}{W_d} \right) \times 100 \]

where, \( W_s \) and \( W_d \) are the weights of the swelled and dry films respectively.

Mechanical properties and adhesive strength of the thermosets were tested with the help of a Universal Testing Machine (UTM, WDW10, Jinan, China, loadcell=10 kN, crosshead speed=50 mm min\(^{-1}\)) as according to our previous report.\(^{14}\)

**In vitro biocompatibility assessment**

Liver and heart of wistar rat were isolated and were flushed out, centrifuged and re-suspended in William medium and low-glucose Dulbecco’s modified Eagle medium (DMEM, Sigma-Alrich, Germany) respectively and were supplemented with 10% fetal bovine serum (FBS). Prepared thermosets were sterilized by 75% alcohol and rinsed in phosphate buffer saline (PBS). Cells were cultured in 96 well plates in presence and absence of the HE2 films for 72 h at 37 ºC in a 5% CO\(_2\) incubator and proliferation was estimated by MTT assay. The plates were read in an ELISA plate reader (Eppendorf, Germany) at 540 nm. All the experiments were performed in triplicates and average was recorded as cell-viability percentage in comparison with the control, while untreated controls were considered as 100% viable.\(^{15}\)

**Skin irritation index (SII) and application of the sealant**

Experiments involving animals were carried out as per the Principles of Laboratory Animal Care (NIH publication 85-23, revised 1985) with approval from the Institutional Animal Ethics
Committee. A total of 15 wistar rats weighing 250-300 g were used in this experiment. The animals were acclimatized 7 days prior to experimentation and given a standard rodent diet. They were anesthetized by injecting sodium phenobarbitone peritoneally by placing on a surgical table with a water-heating pad and prepped with Betadine surgical skin prep. A 70% alcohol solution was used to remove the residual iodine. Two small dorsal portions on both sides of the spine of rats were shaved well and the resin was applied with an applicator on one side and the cured film was sticked on the other side. SII was calculated at 24, 48 and 72 h, by following the protocol described by Draize et al. Skin sensitization was recorded by scoring visually as per the OECD Guideline 406.

For testing the performance of the sealant, a 3 cm dorsal incision was made on each of the test animals. Just after the surgery, the resin (HE2) with 50 phr of poly(amido amine) was applied gently to the skin of the wound portion of the rats. The skin sides were joined simply by finger press and hold for 3 min. Wound closing times were recorded. After the rats were sacrificed, the resulting skin samples were tested for the tensile strength to judge their wound stability. Efficiency of the sealant was evaluated by scanning electron microscopy (JSM-6390LV). The toxicity accord was analyzed thoroughly by analyzing the hematological and histopathological parameters after 15 days of surgery according to reported protocol.

Antimicrobial potency

Zones of inhibition for HE2 resin, hardener and the combined system were tested against S. aureus (ATCC 11632). The strain was cultured in nutrient broth (HiMedia, India) for 24 h. The materials were dissolved in 1% DMSO (HiMedia, India). Then, 50 µL of each sample were added to the wells of 8 mm diameter on the solidified agar plates. The plates were incubated for 24 h at 37 °C. Zones of inhibition were measured by a zone scale (HiMedia, India).
In vitro degradation study

Degradation of the HE2 thermosets were studied in vitro according to standard method (ASTM F 1635-04). A solution of 0.1 M PBS with pH of 7.4±0.2 was used as the degradation medium. The films were incubated at 37 ºC in an oven under static mode. Degradation was evaluated by taking out the films from the media after 15, 30, 45 and 60 days of incubation. The films were washed with de ionized water and dried under vacuum for 36 h at 40 ºC to determine the retention of weight. SEM images were taken to investigate the occurrence of any morphological change during the degradation period.

The degradation medium (after 60 days) was assessed for checking the in vitro toxicity, by the same procedure as mentioned above.

Results and discussion

Preparation of hyperbranched epoxy resin

The synthetic protocol involves the polycondensation of a multifunctional HP core and BPA with epichlorohydrin by following the slow addition and high dilution technique. This prevents the probability of crosslinking of the product during the reaction time. The reaction scheme is presented in Fig. 1. Optimum reaction conditions were observed to be 4 h at 110° C in context of low viscosity, high yield, low curing time, low hydroxyl value and high epoxy equivalents (Table1).

Characterization

Chemical functionalities present in the structure of HE2 resin and its thermoset were characterized by FTIR spectroscopy. The bands for asymmetric vibrations for epoxy ring appeared at 912 and 832 cm\(^{-1}\) in the resin, while their absence in the thermoset vouched for the successful crosslinking with the amine hardener (Fig. 2). A strong absorption band at 1034 cm\(^{-1}\)
confirmed the presence of alkyl-aryl ether groups in the structure of the epoxy. Similarly, a sharp absorption band was observed at 1240 cm\(^{-1}\) for aryl ether linkage in the resin. The -C=C-stretching vibrations associated with the BPA moiety were observed at around 1605 cm\(^{-1}\). Bands at 2965-2876 cm\(^{-1}\) and 3051 cm\(^{-1}\) confirmed the presence of aliphatic and aromatic -C-H stretchings respectively. The -O-H stretching vibration was evident from the band at 3421 cm\(^{-1}\).

Structural feature of HE2 was monitored by the \(^1\)H NMR spectrum (Fig 3, a). Chemical shift value at \(\delta\) 1.62 ppm was due to the methyl protons of the BPA moieties. Presence of the oxirane protons were confirmed by the signals at \(\delta\) 2.2, 2.7 and 2.92 ppm. The -CH\(_2\) protons attached with the ether linkages of aliphatic and aromatic units were observed at \(\delta\) 3.3-4.09 ppm. The peak at \(\delta\) 4.18 ppm was due to the –OH groups. Two types of phenyl protons associated with the BPA moieties were observed at \(\delta\) 6.81 and 7.13 ppm.

Similarly, the carbons with different chemical atmospheres present in the structure of HE2 were analyzed from the \(^{13}\)C NMR spectrum (Fig 3, b). Signals at \(\delta\) 39.6 and 44.1 ppm were due the methyl and the quarternary carbons of BPA respectively. The characteristic signals for the oxirane ring carbons were observed at \(\delta\) 48.2 and 54.0 ppm. Carbons attached directly to the aliphatic and aromatic –O– linkage was confirmed by the signal at \(\delta\) 141.2 ppm. Peaks at \(\delta\) 116.8, 123.9 and 144.2 ppm were due to the different carbons of the BPA moieties.

Three signals were observed for the carbons of the triazine rings, (enlarged in Fig. 3, b) at 171.6, 171.9 and 173.5 ppm for the linear (L), terminal (T) and dendritic (D) units of the HE2 resin. This confirmed that the synthesized epoxy resin possesses a hyperbranched architecture, with degree of branching 0.83.
Physical properties and curing study

Physical properties of the HE resins are given in Table 1. HE2 has the lowest epoxy equivalent and the shortest curing time amongst the studied resins. In the curing process, the HE thermoset was prepared by the chemical crosslinking of the liquid resins with poly(amido amine) hardener. The oxirane ring of the resin is highly strained and readily opens up in presence of an active amine group.\(^9\) It is quite fascinating to notice that HE2 could be cured up to 62% at room temperature within 30 min (Table 1). Room temperature curing is a vital feature for a surgical sealant. However, the plates were kept for 24 h to record the mechanical performance.

Performance

Performance characteristics of the cured resins are provided in Table 2. HE2 showed the highest tensile and adhesive strengths amongst the three systems. Optimum crosslinking of HE2 aided to this fact. With increase in amount of the polyol, flexibility got decreased as evident from the elongation value of HE3. Moreover, to judge the adhesion ability of the materials with biological system, a preliminary test was carried out by applying the two component systems on the overlapping surfaces of two wood substrates. The observation ascertained the efficient adhesion strength of the materials.

In vitro biocompatibility assessment

MTT assay was carried out to evaluate the in vitro biocompatibility of the epoxy thermoset (prepared by homogeneously mixing HE2 with poly(amido amine) hardener). Cell viabilities were 95.74% and 99.7% respectively for liver and heart cells of wistar rat (Fig. 4). CYC is regarded as a toxic reagent for its corrosive nature.\(^{23}\) Again, BPA shows toxicity, because in its
free state it can mimic the structure of the hormone, estrogen and binds to the estrogen receptors. However, in the present case, the –OH groups of BPA and the Cl groups of CYC were eliminated during the course of the reaction, which greatly influenced the biocompatibility profile of the thermoset with the tested cell lines.

**Skin irritation index (SII) and application of the sealant**

The present study aims on the application of the material as a surgical sealant. Therefore, the compatibility of the material was also tested upon wistar rat through skin irritation index of both the resin and the thermoset. No mortality of animals was witnessed during the experiment time. Further, food consumption and locomotion were quite normal after the application of the materials to the skin of rats. Possible edema or erythema was noted during the course of the experiment. Data provided in Tables 3 and 4 confirmed that no skin irritation or sensitization occurred for the treated rats which were in contact with the sealant as well as the thermoset film. From Fig. 5, the observation is abundantly clear. This emphasized the use of the present material as a non-toxic, derma-friendly surgical sealant.

The wounds created by surgery were sealed with the application of the homogeneous mixture of HE2 and poly(amido amine) hardener (Fig. 6). The main constituents of the mammalian stratum corneum are sphingolipids, glycosphingolipids, ceramides etc., which possess lots of chemical functionalities. These help in forming a crosslinked HE2 bridge to join the torn sides of the skin. Many acrylate or fibrin based surgical sealants have been applied to mammalian hosts. A solid observation was made by Shamiyeh et al. that suturing is advantageous over tapping or using tissue adhesive in regard of cost, time and compatibility. Contrarily, tissue adhesives were used by a few researchers for fast healing of surgical incision. However, cost and compatibility issues could not be addressed by them. Thus, the present
sealant is better in terms of compatibility and processability. Though the crosslinking time is high in the present case, but this could be admissible for minor surgeries using anesthesia.

The wound bursting strength was determined by measuring the tensile strength of the skin containing the surgical wound (Fig. 7, a) after treatment with the sealant. Measurements were done after seven and fifteen days from the surgery. Tensile strength was also determined for the skin of a sutured group of animals for comparative study (Table 5). Observation confirmed that the strength of the sealant treated rats was quite comparable to the sutured ones. As reported by Yang et al., tensile strength of sutured rats lies within 6 MPa, which is close to the obtained values.\textsuperscript{30}

The rat skin obtained for tensile strength testing was characterized additionally for toxicity and stability of the applied material over the wound crack and histomorphology of wound healing by scanning electron microscopy (Fig. 7, b). After fifteen days of surgery, formation of stable dermabond bridging was observed.\textsuperscript{1} No toxic interaction of the thermoset material with the tissues was noticed. Sufficient mechanical bridging of the material by scarred skin lesions was observed and beginning of organization with connective tissue structures was confirmed.

\textbf{In vivo biocompatibility assessment}

To ensure \textit{in vivo} compatibility of the material, hematological parameters of the treated rats were evaluated and the data were compared with the control. The data in Table 6 demonstrated that all the parameters are within normal range for the treated group and no sign of hematological toxicity was induced on application of the sealant.

This affirmation was further supported by the histopathological examination of skin sections of the rats, which were subjected to application of the sealant. Fig. 8 shows the
comparative microscopic images of skin tissues of the control and the treated animals after 15 days. Regular cellular organization was observed for the treated animal, which was quite comparable to the control.\(^{31}\)

**Antimicrobial potency**

Antibacterial activity of HE2, poly(amido amine) and the combined system was determined against *S. aureus*, the most infectious bacteria found in surgical microflora. Zone inhibition assay revealed (Fig. 9) that the combined system (HE) showed better efficacy to that of HE2 (E) and the hardener (H). This may be due to the synergistic effect of the combined system. Antimicrobial activity of s-triazine derived compounds is well known to the scientific community.\(^{32}\) This moiety in the structure of HE2 is primely responsible for inhibiting *S. aureus*. Thus, the present sealant has an inbuilt infection resisting capacity to the pathogenic bacteria of surgical microflora, which could restrict the use of an additional antibacterial agent. Surgical sealant with such activity may be a good alternative to the painful suturing, which have high chance of infection without the use of antibiotic.

**In vitro degradation study**

*In vitro* degradation of a biomaterial is an essential criterion to avoid repeated surgery. Here, retention of weight (%) of HE2 was recorded against incubation time in PBS at 37 °C. Decrement of weight with time is shown in Fig. 10, a. The progressive weight loss profile demonstrated the possibility of degradation of the material under *in vivo* conditions. Surface erosion of the HE2 film was evident from the SEM micrographs within 30 days of incubation (Fig. 10, b-c). Physiological fluids, which include water, enzymes and different salts are mainly
responsible for degradation. Trypsin, esterase, papain etc. are some of the enzymes which help in the degradation process of polymeric biomaterials.\textsuperscript{33}

Further, to assure the non-toxicity of the degraded products, MTT assay was carried out for the extract (PBS medium used for degradation) after 60 days of incubation (Fig. 10, d). Excellent cell survival rate was noted in this case, which ascertained that the sealant would not impart any kind of toxicity to the host even after degradation of the matrix within the host body.

**Conclusion**

A synthetic hyperbranched epoxy based surgical sealant has been reported, which showed optimum balance between strength and flexibility. The epoxy can be crosslinked up to 62\% at room temperature with 50 phr of poly(amido amine) hardener. The material was compatible to mammalian (wistar rat) liver and cardiac cell lines. Further, it can inhibit the most notorious microorganism found in surgical microflora. The sealant showed excellent adhesion when tested on the dorsal surgical incision of wistar rat. This showed possible degradation of the matrix under physiological conditions. Interestingly, the degradation products were found to be compatible with mammalian cells. Thus, the present material may be an apt alternative to the painful surgical suturing. However, critical clinical trial is a prerequisite before applying to higher animals.

**Acknowledgment**

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Note

Parts of the results in this manuscript are patented as an Indian patent, Application no. 211/KOL/2014

Reference


Figure captions

Fig. 1: Schematic representation of the synthetic protocol for the hyperbranched epoxy resin.

Fig. 2: FTIR spectra of HE2 resin and thermoset.

Fig. 3: (a) $^1$H NMR spectrum and (b) $^{13}$C NMR spectrum of HE2; onset: magnification of the peaks, describing the linear, dendritic and terminal units of the hyperbranched epoxy resin.

Fig. 4: In vitro biocompatibility assessment via MTT assay using wistar rat primary liver and cardiac cell lines.

Fig. 5: Skin irritation study.

Fig. 6: Creation of surgical incision and application of the sealant.

Fig. 7: (a) Skin sample for tensile strength test and (b) SEM micrograph showing the formation of dermabond after application of the sealant.

Fig. 8: Histopathological sections of skins for (a) control and (b) sealant treated rats.

Fig. 9: Zone inhibition assay against S. aureus.

Fig. 10: (a) In vitro degradation of HE2 (weight loss profile), (b) SEM micrographs of control and (c) HE2 thermoset after 60 days of incubation and (d) cytocompatibility of the degraded products.
Fig. 1
Fig. 2
Fig. 3
Fig. 5
Fig. 6
Fig. 7
Fig. 10
Table 1: Average yield and physical property of the resins along with the curing time and swelling value of their thermosets

<table>
<thead>
<tr>
<th>Property</th>
<th>HE1</th>
<th>HE2</th>
<th>HE3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Curing time (min) at room temperature</td>
<td>80</td>
<td>30</td>
<td>45</td>
</tr>
<tr>
<td>Swelling (%)</td>
<td>48.92</td>
<td>38.21</td>
<td>31.45</td>
</tr>
<tr>
<td>Yield (%)</td>
<td>92</td>
<td>91</td>
<td>88</td>
</tr>
<tr>
<td>Viscosity, $\eta_{inh} , (g , dL^{-1})$</td>
<td>0.023</td>
<td>0.041</td>
<td>0.07</td>
</tr>
<tr>
<td>Hydroxyl value (mg KOH/g)</td>
<td>106.95</td>
<td>130.84</td>
<td>156.78</td>
</tr>
<tr>
<td>Epoxy equivalent (g/ eq.)</td>
<td>334.67</td>
<td>281.09</td>
<td>302.22</td>
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Table 2: Performance of the HE thermosets

<table>
<thead>
<tr>
<th>Resins</th>
<th>Tensile strength (MPa)</th>
<th>Elongation (%)</th>
<th>Adhesive strength (MPa) W-W</th>
<th>Bending (mm)</th>
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</thead>
<tbody>
<tr>
<td>HE1</td>
<td>15.31</td>
<td>43.51</td>
<td>1270</td>
<td>1</td>
</tr>
<tr>
<td>HE2</td>
<td>22.22</td>
<td>37.23</td>
<td>2507</td>
<td>1</td>
</tr>
<tr>
<td>HE3</td>
<td>19.34</td>
<td>32.12</td>
<td>1980</td>
<td>1</td>
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</table>
Table 3: Skin irritation analysis

<table>
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<tr>
<th>Skin reaction</th>
<th>Erythema</th>
<th>Edema</th>
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<tr>
<td>Observation time (h)</td>
<td>24 48 72</td>
<td>24 48 72</td>
</tr>
<tr>
<td>Groups</td>
<td>C T C T C T C T</td>
<td>C T C T C T C T</td>
</tr>
<tr>
<td>Total score</td>
<td>0 0 0 0 0 0</td>
<td>0 0 0 0 0 0</td>
</tr>
<tr>
<td>Mean score&lt;sup&gt;x&lt;/sup&gt;</td>
<td>0 0 0 0 0 0</td>
<td>0 0 0 0 0 0</td>
</tr>
<tr>
<td>Total mean score</td>
<td>0 0 0</td>
<td>0 0 0</td>
</tr>
<tr>
<td>Primary irritation index&lt;sup&gt;y&lt;/sup&gt;</td>
<td>0 0 0</td>
<td>0 0 0</td>
</tr>
<tr>
<td>Remark</td>
<td>Non irritating</td>
<td>Non irritating</td>
</tr>
</tbody>
</table>

<sup>x</sup>Mean score=(total erythema score + total edema score)/3

<sup>y</sup>Irritation index (primary)=mean score at (24 + 48 + 72 )h/3
Table 4: Skin sensitization study

<table>
<thead>
<tr>
<th>Group</th>
<th>Sensitization (%)</th>
<th>Sensitization grade</th>
<th>Sensitization classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>0</td>
<td>I</td>
<td>Weak</td>
</tr>
<tr>
<td>T</td>
<td>0</td>
<td>I</td>
<td>Weak</td>
</tr>
</tbody>
</table>
Table 5: Average tensile strength of the skin samples of wistar rats

<table>
<thead>
<tr>
<th>Samples</th>
<th>Days</th>
<th>Tensile strength (MPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin control</td>
<td>7</td>
<td>4.38</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>4.38</td>
</tr>
<tr>
<td>Skin (Sutured)</td>
<td>7</td>
<td>3.33</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>4.28</td>
</tr>
<tr>
<td>Skin (HE2 treated)</td>
<td>7</td>
<td>4.16</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>4.91</td>
</tr>
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</table>
Table 6: Hematological parameters in control and treated wistar rats

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control rat</th>
<th>Treated rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>White Blood Cell (M/Mm$^3$)</td>
<td>11.25</td>
<td>10.95</td>
</tr>
<tr>
<td>Lymphocyte (%)</td>
<td>41.7</td>
<td>44.1</td>
</tr>
<tr>
<td>Monocyte (%)</td>
<td>9.9</td>
<td>9.0</td>
</tr>
<tr>
<td>Neutrophil (%)</td>
<td>45.2</td>
<td>59.4</td>
</tr>
<tr>
<td>Eosinophil (%)</td>
<td>2.9</td>
<td>3.8</td>
</tr>
<tr>
<td>Basophil (%)</td>
<td>0.3</td>
<td>0.7</td>
</tr>
<tr>
<td>Red Blood Cell (m/mm$^3$)</td>
<td>7.67</td>
<td>7.71</td>
</tr>
<tr>
<td>Mean Corpuscular Volume (fL)</td>
<td>53.6</td>
<td>52.3</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>40.8</td>
<td>40.3</td>
</tr>
<tr>
<td>Mean Corpuscular Hemoglobin (pg)</td>
<td>15.2</td>
<td>15.4</td>
</tr>
<tr>
<td>Mean Corpuscular Hemoglobin Concentration (MCHC) (g/dL)</td>
<td>28.6</td>
<td>29.5</td>
</tr>
<tr>
<td>Hemoglobin (g/dL)</td>
<td>11.7</td>
<td>11.9</td>
</tr>
<tr>
<td>Platelet (%)</td>
<td>1.12</td>
<td>1.14</td>
</tr>
</tbody>
</table>
S-triazine based biocompatible hyperbranched epoxy adhesive with antibacterial attribute for suture less surgical sealing

Shaswat Barua\textsuperscript{a}, Pronobesh Chattopadhyay\textsuperscript{b} and Niranjan Karak*\textsuperscript{a}

Hyperbranched epoxy based antimicrobial, biodegradable and non-toxic surgical sealant