Microbial barrier properties of LiquiBand® LIQUISEAL: an *in vitro* study

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Background

Cyanoacrylate skin adhesives are used throughout the world for their wound closure properties. In addition to their proven use as wound closure devices, cyanoacrylate skin adhesives are also increasingly used post-operatively as surgical site microbial barriers to protect the closed wound from microbial contamination after primary closure. LiquiBand® LiquiSeal is indicated for use as a protective microbial barrier dressing of surgical incisions after the skin has been closed using conventional closure techniques.

The use of cyanoacrylates as an adjunct to conventional sutures, that is, application of a cyanoacrylate skin adhesive layer on top of wounds primarily closed with sutures has been reported to reduce infection rates. Souza et al\(^1\) reported a reduction in infection rates for cardiovascular surgery patients from 4.9% down to 2.1%, and, consequently, a reduction in median length of postoperative hospital stays when comparing patients wounds closed with conventional sutures to those whose wounds were closed with conventional sutures plus topical skin adhesive.

Surgical Site Infections

It is difficult to quantify the levels of microorganisms found within the skin’s natural flora, however, a study by Larson et al\(^2\) found the mean number of colony forming units (cfu’s) on patient’s skin was 229.4 on the sternum. Quantitatively, it has been demonstrated that if a surgical site is contaminated with 100,000 microorganisms per gram of tissue (>10⁵), the risk of Surgical Site Infection (SSI) is markedly increased\(^3\). This may be much lower when foreign material (i.e. sutures, contaminated dressings) is present at the site\(^3,4\). MacLeod\(^5\) reported that just 100 staphylococci per gram of tissue introduced on silk sutures were capable of inducing infection.

Microbial contamination of the surgical site is a necessary precursor of SSI. Surgical site infections (SSI’s) are estimated to account for at least 20% of all hospital acquired infections\(^6\). It is also estimated that over 2% of all patients admitted for a surgical procedure will develop a surgical site infection\(^6\). As a result of these infections, patient hospitalization time is extended and the overall cost of care increases by up to 2.9 times\(^7\). These infections also significantly increase the risk of more serious complications and potential death of the patient. It follows that any device or practice which may provide a barrier to microorganism entry into the surgical site should be utilized to not only improve patient recovery outcomes, but also reduce the financial burden placed upon care facilities.

Objective

The purpose of this study was to demonstrate that LiquiBand® LiquiSeal is an effective barrier against the penetration of microorganisms.
Test Methodology

In order to prove that LiquiBand® LiquiSeal provides a microbial barrier, a strike through test was conducted against common organisms known to cause surgical site infections (*Candida albicans*, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, *Pseudomonas aeruginosa*, and MRSA).

In order to replicate use in the clinical environment, a thin layer of LiquiBand® LiquiSeal was applied to a number of agar plates containing a pH sensitive dye and allowed to polymerise. 10µL of challenge microorganism was pipetted onto the centre of each of the polymerised films. The plates were incubated at 30-35°C for seven days and were observed for microbial growth and colour change at 24 hours, 48 hours, 72 hours and 6 and 7 days. A total of 100 test challenges were conducted for each of the six microorganisms tested (600 total test challenges). Assessment of the thickness of the polymerized LiquiBand® LiquiSeal was also conducted using scanning electron microscopy techniques.

As a result of the pH sensitive dye within the agar plate, a color change from purple to yellow would indicate penetration of the LiquiBand® LiquiSeal by either the challenge organism or acidic metabolic by-products. A color change was recorded as a positive result, no color change as a negative. Sensitivity control plates were also produced to demonstrate that after an incubation period of 24-48 hours just one colony forming unit (cfu) of each microorganism challenge could be detected. A negative control plate was run at the same time with 10 one drop applications to demonstrate that no extraneous contamination was introduced during preparation of the plates and loading of the LiquiBand® LiquiSeal.

Test Results

<table>
<thead>
<tr>
<th>Microbe</th>
<th>ATCC</th>
<th>Challenge (CFU)</th>
<th>% maintaining microbial barrier properties (n = 100 tests)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>3 day time point 7 day time point</td>
</tr>
<tr>
<td><em>Staphylococcus aureus</em> #6538</td>
<td>1.28 x 10⁶</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td><em>Staphylococcus epidermidis</em> #12228</td>
<td>1.03 x 10⁶</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td><em>Candida albicans</em> #10231</td>
<td>6.8 x 10⁵</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td><em>Escherichia coli</em> #8739</td>
<td>1.1 x 10⁷</td>
<td>99%</td>
<td>99%</td>
</tr>
<tr>
<td><em>Pseudomonas aeruginosa</em> #9027</td>
<td>1.88 x 10⁶</td>
<td>100%</td>
<td>95%</td>
</tr>
<tr>
<td>MRSA #43300</td>
<td>1.21 x 10⁶</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

*Figure 1*
The results of this in-vitro experiment demonstrate that LiquiBand® LiquiSeal is an effective microbial barrier to a range of gram-positive and gram-negative motile and non-motile species as well as Candida albicans which is a fungus. Of the 600 individual test challenges, 599 LiquiBand® LiquiSeal films maintained 100% patency after 72 hours. After seven days of incubation, 99% of LiquiBand® LiquiSeal films prevented penetration of microorganisms into the agar. LiquiBand® LiquiSeal provided a 100% microbial barrier against S. aureus, C. albicans, S.epidermidis and MRSA for the entire duration of the challenge (7 days).

Of the one hundred films challenged with Ps. aeruginosa none were penetrated after 3 days of the test period. At the 7 day time point 5 films showed a positive result. It was considered likely that these positive results resulted from the migration of the inoculums droplet to and over the edge of the film and not from penetration of the film, as Pseudomonas exhibits a characteristic motility and product of extracellular polysaccharide during its growth cycle, which is not a feature of any of the other challenge organisms.

One of the one hundred films challenged with E. coli was penetrated. Microscopic examination (x100 magnification), however, revealed a hole in the film which compromised its integrity and allowed the passage of the motile cells of E. coli. Microscopic examination also showed that the edges of the hole were smooth and rounded indicating that this was formed as a result of error during application of sample and not due to the polymerization of the adhesive. Therefore, this is not considered an artifact of the product itself.

Discussion

This in vitro study was developed to prove the hypothesis that LiquiBand® LiquiSeal would prevent the passage of microorganisms. Even at very high microbial challenge levels, at least 2950 times greater than that of normal skin flora levels, and at least 6 times greater than the number of microorganisms known to lead to infection, LiquiBand® LiquiSeal proved to be an effective microbial barrier.

The study’s findings are similar to those of both Bhende et al and Brown who examined the microbial barrier properties of two topical skin adhesive products; Dermabond® 2-octyl cyanoacrylate (Ethicon Inc.), and Indermil™ n-butyl cyanoacrylate (Tyco Healthcare) respectively. All three products have demonstrated microbial barrier properties. In comparison to Bhende’s methodology, LiquiBand® LiquiSeal was challenged for a longer duration of time and with higher microbial challenge levels (7 days, >10^6 cfu/mL).

Community associated MRSA has become the most frequent cause of skin and soft tissue infections presenting to emergency departments. In the hospital setting, MRSA infections are associated with longer lengths of hospital stay, higher mortality, and increased cost. Hence, LiquiBand® LiquiSeal, with its ability to provide a barrier to penetration of this potentially dangerous and costly microbe into the surgical site, may play an important role in the fight against infection and financial burden.
A recent animal study by Karatepe et al.\textsuperscript{10} investigating the usefulness of cyanoacrylate in preventing early wound contamination demonstrated that maintaining skin integrity and providing a barrier to microbe entry for the first twenty-four hours is critical to prevent infection after skin closure. It also demonstrated that after this period the natural tissue healing process has commenced, and therefore the skin starts to provide its own microbial barrier function. In the control group (sutures) all the hernia grafts were infected after being subjected to a microbial challenge within 24 hours of closure. In the study arm (cyanoacrylate) no graft infections were noted after microbial challenge within 24 hours of closure. After 24 hours, the microbial challenge was repeated and there was no difference between the number of infections between those closed with sutures, and those closed with cyanoacrylate. These findings are in line with the CDC guidelines on preventing surgical site infections which recommend that a surgical wound be protected with a sterile dressing for 24 to 48 hours postoperatively following primary closure\textsuperscript{6}. Hence, it is within the first 24-48 hours that the microbial barrier properties of LiquiBand\textsuperscript{®} LiquiSeal are most critical. The above in-vitro microbial barrier findings (Figure 1) highlight how effectively LiquiBand\textsuperscript{®} LiquiSeal protects against microbial contamination during this critical time.

**Conclusion**

The results of this *in-vitro* experiment demonstrate that LiquiBand\textsuperscript{®} LiquiSeal is an effective microbial barrier to high titre ($10^5-10^6$ cfu) challenge of gram-positive and gram-negative motile and non-motile species as well as *Candida albicans*.

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Tests were performed for and on behalf of MedLogic Global Ltd by Agenda 1 Analytical Services Ltd, Leeds UK.
References:


