

# Durability of the Continuous Subcutaneous Insulin Infusion (CSII) Patch Adhesive

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## Summary

Diabetes, a serious global epidemic growing at a tremendous rate, affects about 26 million people in the United States. Diabetes occurs when the pancreas cannot produce sufficient insulin or use that insulin to regulate blood-sugar level. Thus, most diabetics need to inject insulin into their bodies. In recent years, many diabetics are using Continuous Subcutaneous Insulin Infusion (CSII), also known as the 'insulin pump', to minimize hyperglycemia and hypoglycemia. Patients have indicated that using the CSII is more comfortable than the traditional treatment, which requires multiple daily injections. However, one of the most significant challenges with the CSII is the low durability of the patch adhesive, which leads to dislodgement of the cannula (a small plastic insulin delivery tube) from the skin. The purpose of this study was to compare the durability of the current CSII adhesive to an octyl cyanoacrylate-based adhesive. Four experimental plates and a jig with a ratchet were constructed. Adhesive was placed on synthetic skin and gauze was placed over each adhesive. By operating the ratchet, the gauze was ripped off the synthetic skin, and a data-collection program attached to a computerized gauge recorded the force over time. For half of the experiment, artificial sweat was sprayed onto the gauze and adhesive before operating the ratchet. The steps were repeated for 80 experiments. Using an Analysis of Variance (ANOVA) statistical test, we showed that the octyl cyanoacrylate-based adhesive is significantly ( $F(3,79)=76.3$ ,  $p<0.001$ ) stronger than the current CSII adhesive, both with and without the presence of artificial sweat.

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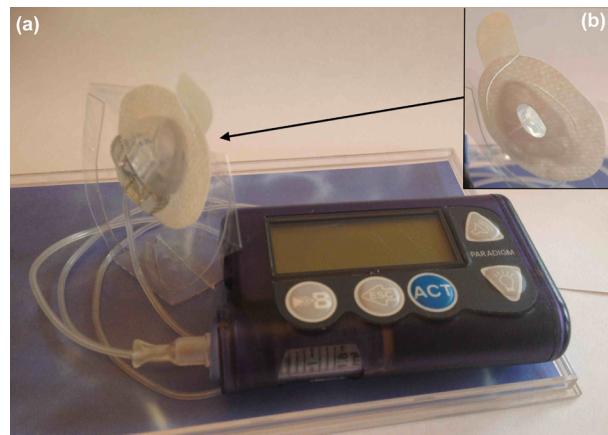
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## Introduction

Diabetes is a growing global epidemic that continues to affect new Americans of all ages every year. According to the American Diabetes Association, over 8% of the population (or 25.8 million people) in the United States has diabetes (1). Diabetes is a disorder in which the blood-sugar level is not regulated due to the failure of the pancreas to produce adequate amounts of insulin or the failure of the body to use that insulin (2). Insulin is

a hormone that is responsible for signaling to cells to take up glucose from the blood following the digestion of foods, such as starches and sugars, that elevate blood glucose levels (3, 4). The body needs to maintain certain levels of glucose in the blood in order to properly function (3, 4). There are three main types of diabetes: (i) Type 1 (T1D), (ii) Type 2 (T2D), and (iii) gestational diabetes (5). T1D, also called 'juvenile diabetes,' can start as early as childhood or begin later during the teenage or young adolescent years. T2D, which is the most common type, can be developed at any age. T1D and T2D both require a lifetime of treatment and management, and are associated with numerous risks (6). While some individuals suffering from T2D can maintain a steady insulin level in their blood with oral medication, most T1D and significant numbers of T2D patients depend on insulin injections to artificially maintain proper blood insulin levels (7). Gestational diabetes is less common and affects some women during pregnancy (5). Some patients with gestational diabetes also require insulin injections.

One of the biggest challenges for a diabetic patient is that the amount of insulin needed to regulate the blood-glucose level in their body fluctuates throughout the day (8, 9). Although many diabetics inject insulin using a syringe, some use an alternative insulin delivery method called Continuous Subcutaneous Insulin Infusion (CSII), or the 'insulin pump' (10, 11). The CSII looks like a small battery powered device, the size of a cell phone, with a miniature pump and an insulin cartridge (8). Moreover, CSII includes a tube connecting the pump on one end and the infusion set on the other. The infusion set includes a plastic piece with an adhesive patch and a cannula that injects insulin through the skin and into the body (12, 13) (Figures 1a, 1b). Current medical knowledge advocates that



**Figure 1:** Continuous subcutaneous insulin infusion (CSII) (a) and the infusion set (b).

intensive insulin therapy should be done in conjunction with regular glucose monitoring. In order to determine the appropriate insulin dosage, finger-prick blood tests are needed, which many patients find both inconvenient and painful (6). Studies have shown that the CSII is a better treatment for intensive therapy than the current method (finger-prick blood tests and insulin injection via syringe) and that it minimizes hyperglycemia (a high level of blood sugar) and hypoglycemia (a low level of blood sugar) (6). Moreover, patients have indicated that using the CSII is more comfortable than the traditional treatment requiring multiple daily injections (14).

While the CSII has many benefits over multiple daily injections, including continuous insulin injection when the patient is sleeping, exercising, or just doing their daily routine, it also has some disadvantages (13). One of the key disadvantages of the CSII is the dislodgment of the cannula from the body (8). Such dislodgment is mainly due to low durability of the adhesive on the adhesive patch. The cannula can come out of the body when sweating, swimming, showering, and when wearing certain clothes, like jeans (12). When the cannula dislodges, the patient does not receive the insulin needed. This event can be life threatening because it increases the potential for stroke and other lethal complications (11).

The adhesive used on the current CSII patch is a polymer-based adhesive, similar to the one used in Band-Aid™, commonly used in the medical and veterinary fields. There are other topical adhesives used in the medical profession, but these are less well known and rarely used due to their price. Many adhesives are based on ingredients from the cyanoacrylate class (14). Of this adhesive class, the most commonly used cyanoacrylate adhesive in the medical field is octyl cyanoacrylate, because it supplies rapid wound closure, prevents the growth of bacteria, and is typically painless (16). Most

importantly, adhesives from the cyanoacrylate class are known for their strength (17). For example, cyanoacrylate adhesives are the basis for household adhesives such as Superglue™ and KrazyGlue™.

Cyanoacrylate adhesives have been used by surgeons in the private industry and the military to aid in suture closures and/or other skin attachments (17). One octyl cyanoacrylate adhesive used in such medical applications is the Octylseal Topical Skin Adhesive. While cyanoacrylate adhesives have been used for medical purposes, they do not appear to have been used in the context of CSII adhesive patches. Therefore, this study aimed to compare the durability of an octyl cyanoacrylate adhesive and the current polymer-based CSII patch adhesive. We hypothesized that the durability of the current CSII patch adhesive will be significantly less than that of the octyl cyanoacrylate-based adhesive with and without the presence of artificial sweat. The argument behind the need for investigation was that an octyl cyanoacrylate-based adhesive is stronger than a polymer-based adhesive.

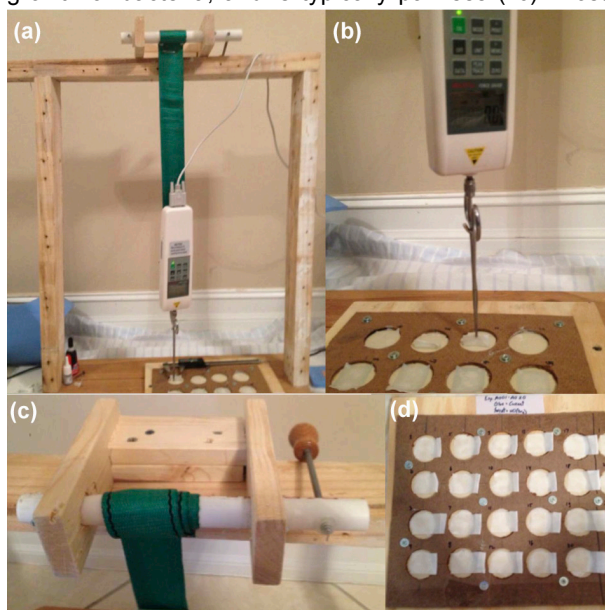
## Results

This study's aim was to compare the durability of the current CSII patch adhesive to that of the octyl cyanoacrylate-based adhesive with and without the presence of artificial sweat. The two independent or manipulated variables were: (i) adhesive type (current CSII patch adhesive vs. Octylseal) and (ii) artificial sweat level (no artificial sweat vs. with artificial sweat). The dependent or responding variable was the durability of the adhesive as measured by the impulse (J). Durability was measured using a computerized gauge that recorded the force and the time every 8 milliseconds (msec). The durability was computed by a combination of the amount of force that the adhesive patch resisted and the amount of time it could resist until the adhesive patch was dislodged (18). This combination is known as the 'impulse' or 'impulse of force' (noted as J), which is the integral (area under the graph) of average force exerted over time (19) (Equation 1). Considering that the study tested the durability of adhesives (J), the control or constant variables in this study were the humidity in the room, the room temperature, the synthetic skin, the digital force gauge meter, the experimental jig, and the medical gauze (mimicking current CSII patch).

$$\text{Durability} = \text{Impulse (J)} = \int_{t=0}^{t=T_{Exp}} (\text{Calibrated } F \cdot dt)$$

**Equation 1.** The calculation used to determine the Impulse (J), the durability of the adhesives.

In this study, we designed and constructed a special jig with a ratchet (Figure 2) and a digital push-pull force gauge. Moreover, we designed and constructed experimental plates that included sheets of synthetic skin attached to wood planks. Polymer-based adhesive (the current CSII patch adhesive) and octyl cyanoacrylate adhesive were applied to small gauzes attached to the sheets of synthetic skin on the experimental plates.



**Figure 2.** The jig constructed and used in the experiment (a); a surgical clamp and gauze (b); the ratchet (c); the experimental plates (d).

		Adhesive Type	
		Current CSII Patch Adhesive	Octylseal
Sweat Level	No Sweat	20 Experiments A0	20 Experiments B0
	With Artificial Sweat (0.9g NaCl/lit H <sub>2</sub> O)	20 Experiments A1	20 Experiments B1

Figure 3. The 2x2 experimental factorial research design.

Following the connection to a surgical clamp, the gauzes were pulled from the synthetic skin by the pulling of the ratchet, which also activated the reading on the digital push-pull force gauge.

An Analysis of Variance (ANOVA) statistical test was conducted to investigate the durability as measured by impulse (J) differences between the current polymer-based CSII patch adhesive and an octyl cyanoacrylate-based adhesive with or without the presence of artificial sweat. In total, 80 experiments were conducted: 40 experiments without artificial sweat and 40 experiments with artificial sweat. In each set of experiments, two types of glues were used, providing 20 experiments for each type and level of artificial sweat, including (A0) current CSII patch adhesive without artificial sweat, (A1) current CSII patch adhesive with artificial sweat, (B0) octyl cyanoacrylate-based adhesive without artificial sweat, and (B1) octyl cyanoacrylate-based adhesive with artificial sweat (Figure 3).

The area of adhesive applied to the artificial skin and gauze varies between experiments. In order to reduce the effect of the variations in adhesive area on the measured durability, the force was calibrated. A variation in the adhesive area would impact the durability. For example, a larger adhesive area (with all other variables remaining constant) would make the adhesive more durable. However, the purpose of this study was to compare the durability of the adhesive itself, not the durability of the amount of adhesive area. Therefore, the adhesive force was calibrated by adjusting the force with a normalized area. The normalized area was calculated using the mean area of all experimental adhesive areas divided by the specific experimental adhesive area to ensure that the force is calibrated for that specific experimental area (Equation 2).

The ANOVA post hoc comparison using the Tukey HSD test for the 40 experiments without artificial sweat (A0=1-20 & B0=1-20 – Figure 4) indicated that the mean impulse score for an octyl cyanoacrylate-based adhesive (B0) (M=511.17, SD=214.56) was significantly higher (p<0.001) than the current CSII patch adhesive (A0) (M=87.27, SD=32.43). Moreover, for the 40 experiments with artificial sweat (A1=1-20 & B1=1-20 – Figure 4), the results indicated that the mean

$$Calibrated\ F = \left( \frac{\bar{A}}{A_{Exp}} \right) \cdot F$$

Equation 2. The equation used to calculate the Calibrated Force

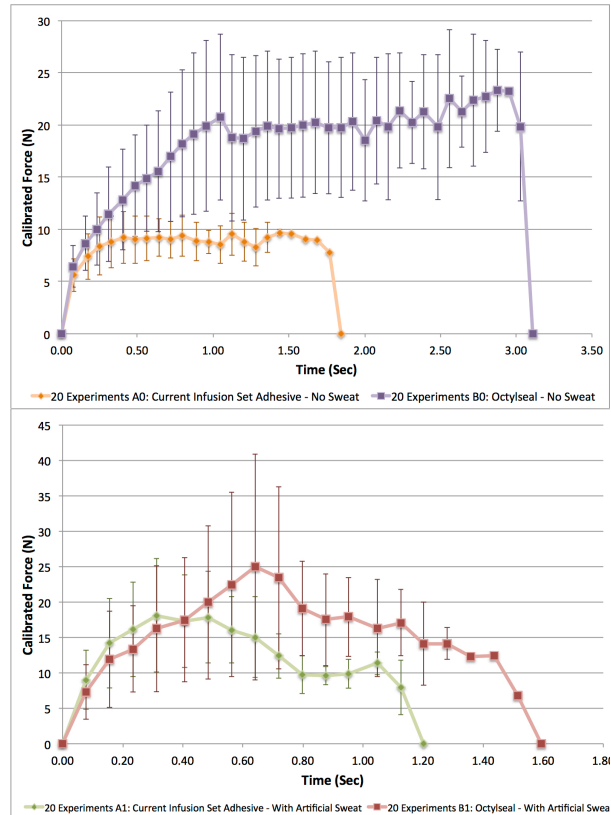


Figure 4. Calibrated force (F) vs. time of A0 and B0 experiments (top) and A1 and B1 experiments (bottom).

impulse for an octyl cyanoacrylate-based adhesive (B1) (M=127.77, SD=24.91) was significantly higher (p<0.05) than the current CSII patch adhesive (A1) (M=50.19, SD=13.49). Therefore, the results revealed that the octyl cyanoacrylate-based adhesive is statistically more durable than the current CSII patch adhesive both with the presence of artificial sweat and without (Figures 5 & 6).

### Discussion

The results of this experiment show that the octyl cyanoacrylate-based adhesive is statistically more durable than the current polymer-based CSII patch adhesive, both with the presence of artificial sweat and without. It appears that the biggest challenge with the CSII is that the adhesive on the patch is not durable enough to withstand the comfortable daily life of many diabetic patients (9, 22). This experimental research study shows that by switching the adhesive on the CSII patch from the traditional polymer-based adhesive to the octyl cyanoacrylate-based adhesive, the CSII patch adhesive should be more durable and the quality of life of the patient could be higher. One of the biggest goals in the field of endocrinology is developing an artificial, closed-loop (not relying on the patient) pancreas (6). Switching the current CSII patch adhesive to an octyl cyanoacrylate-based adhesive will potentially improve the patch adhesive and bring the CSII one step closer

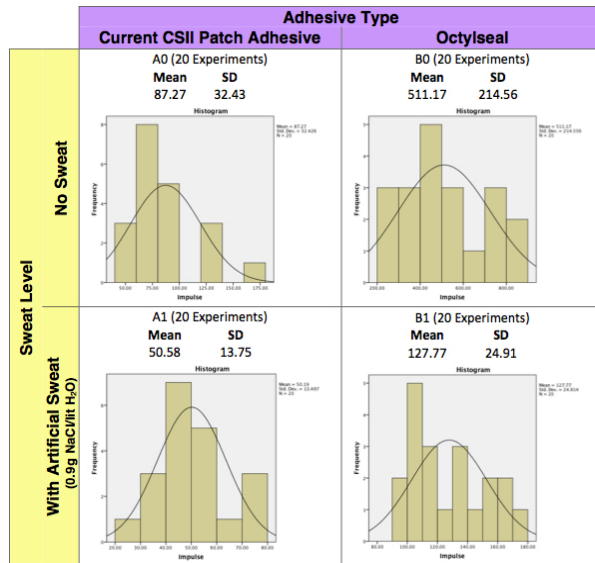


Figure 5. Statistical distributions of mean scores for research experiments.

to this goal.

The results of this study did support the hypothesis set for this investigation. Specifically, the durability of the current polymer-based CSII patch adhesive was significantly less than that of the octyl cyanoacrylate-based adhesive with and without the presence of artificial sweat. It is evident that the octyl cyanoacrylate-based adhesive is much more durable than a polymer-based adhesive (used as the current CSII patch adhesive).

There were a few limitations to this experimental study. The first limitation of this study was that it focused on comparing only two types of commercially available adhesives. Future research might find interesting results when comparing additional types of adhesives. Another limitation of this study relates to the use of synthetic skin. While synthetic skin was used in this study, using real skin probably would have impacted the results. An earlier experiment on real skin provided similar, but slightly higher durability results, as the gauze on the real skin resisted slightly more than on the synthetic skin.

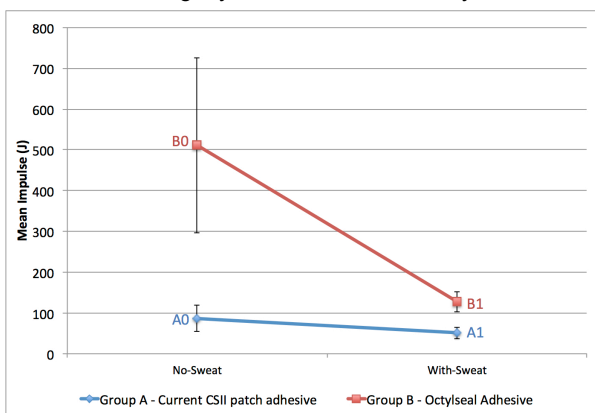


Figure 6. SPSS ANOVA statistical means results of durability vs. two artificial sweat levels.

Repeating this experiment with people might also be a direction for future research. If the octyl cyanoacrylate were used as the improved CSII patch adhesive, it would have also required additional training on patch removal. Removing a patch with octyl cyanoacrylate would require water, soap, and a bit of scrubbing. However, removing the current CSII patch would only require adding water and ripping the patch off the body. An additional limitation of this study is related to the rate at which the ratchet handle was moved. While the researcher attempted to ensure that the rate of movement was as consistent between trials as possible, using an electric motor to pull the gauge could improve the accuracy of the experimental measures.

An issue related to the widespread adoption of the results from this study relates to the cost of production. Given that the octyl cyanoacrylate-based adhesive is relatively expensive compared to the traditional current CSII patch adhesive, it might discourage many CSII manufacturers from producing the patch adhesive with the octyl cyanoacrylate-based adhesive. However, considering the danger that dislodgment can bring to patents, such investment appears warranted.

Future research could expand on the results found in this research by testing more types of adhesives with varied levels of sweat, different skin types, and different areas of the body that the infusion set may sit on. Furthermore, while the gauze used is similar to the composition of the CSII patch, it is not exactly the same; thus, additional work may explore the use of the same chemical composition of the CSII patch to ensure the accuracy of the adhesive durability. Also, there is a significant amount of research currently being conducted on the topic of a non-invasive Continuous Glucose Monitor (CGM). These CGM's may measure glucose in the body by sweat, breath, ear cartilage, or tear analysis. Devices like these may couple with the CSII to form an ex-vivo artificial pancreas, ideal for diabetic patients. However, ensuring that the adhesive is durable enough for continuous daily use is essential to the widespread adoption of this ex-vivo artificial pancreas.

## Methods

Before the experiment was conducted, a jig and experimental plates were constructed. The jig was constructed from three wood planks and eight screws (Figure 2a) with an electrical drill. The ratchet and gauge were constructed using three wood planks, a plastic pipe, a handle and knob, a belt, the Digital 500N Push-Pull Force Gauge Tester Meter HF-500 (Measures the force, F, every 8 millisecond), and 12 screws (Figure 2c). The ratchet and gauge were attached to the jig using the drill.

There are several types of artificial skins including ones that are entirely man-made (synthetic skin) or a blend of natural and synthetic materials (bioartificial or biosynthetic), both of which feel similar to human skin (20). Synthetic skin has good thermal stability and mechanical properties, including adequate properties to mimic human skin in the biomedical field (20). The

synthetic skin sheets used in this study were obtained from Amazon.com and are high-quality blends of man-made polymers made for tattoo practice.

The procedure for constructing the experimental plates included first laying a sheet of synthetic skin on a wood plank, and cutting out circles from a Masonite plank using a circular saw connected to an electric drill (Figure 2d). The Masonite plank was laid over the synthetic skin, and four screws were screwed in to keep the experimental plate together. This research used four experimental plates labeled: (i) A001-20, (ii) B001-20, (iii) A101-20, and (iv) B101-20 (four sheets of synthetic skin & 16 screws were used in total). Using scissors, 20 pieces of gauze were cut from a roll of medical gauze (mimicking the current CSII patch). The edge of the gauze was folded, and about 12x12 millimeters of polymer-based adhesive (the current CSII patch adhesive) was applied to the first circle. The cut piece of gauze was laid onto the adhesive and pressed gently in a process similar to the one that a diabetic patient would use to attach his/her CSII patch. These actions were repeated for all remaining 19 circles on experimental plate A001-20.

While waiting two minutes for the adhesive to dry, the HF-500 Digital Gauge Force Meter application for PC, titled "Multiple Force Gauges Testing System," was opened on a computer. A RS232 data cable was used to connect the gauge to the computer. We verified that the computer was synced with the digital gauge via the HF-500 Digital Gauge application. Then, experimental plate A001-20 was screwed into the jig with A001 directly under the gauge. A surgical clamp was attached to the folded edge ( $\frac{1}{4}$ " ) of the gauze and to the hook end of the digital gauge (Figure 2b). Following that, counterclockwise movement of the ratchet handle pulled the digital gauge upwards, which activated the data recording process until the experimental gauze came off the skin.

The data for A001-20 were collected by operating the ratchet 19 more times. During each experiment, the gauze resisted but eventually came off the skin. After the gauze gave away, the application was paused, and the length and width of the adhesive area were measured with a digital caliber. The plate was then unscrewed from the jig, the used gauze removed from the clamp, and the steps repeated for A002-20, B001-20, A101-20, and B101-20.

The experimental plates were readied with adhesive and gauze, and the data were collected for B001-20 and B101-20 in the same procedure; however, the adhesive used in the 'B' experiments was octyl cyanoacrylate, not the polymer-based adhesive (noted as 'A' experiments). In regards to the artificial sweat solution used in experiments A101-20 and B101-20, it was a solution of table salt (NaCl) and water (H<sub>2</sub>O) that, when sprayed onto the artificial skin, served as a substitute for skin surface perspiration. The artificial sweat was made by mixing 0.9 grams of table salt (NaCl) and a liter of water (H<sub>2</sub>O) in a mixer. It was then sprayed twice before the ratchet was operated. Later, the data were analyzed in an ANOVA test using Statistical Package for Social

Sciences (SPSS) version 21. The experiment used 40ml of the OSTO BOND Latex Adhesive (mimicking the current polymer-based CSII patch adhesive) and 40ml of the Octylseal Topical Skin Adhesive (the octyl cyanoacrylate adhesive).

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