Wound Adhesive from Cyanoacrylate: Synthesis and Characterization

Rajangam Vinodh, Cadiam Mohan Babu, Aziz Abidov, Ramaswamy Ravikumar, Muthiahpillai Palanichamy, Eun Young Choi and Hyun Tae Jang

Abstract. 1-octyl cyanoacrylate is a main component of medical cyanoacrylate glues. As it rapidly polymerizes with water as an initiator, there are practical difficulties in designing simple synthetic routes. Any synthetic routes that evolve free nucleophilic products cannot, therefore be successful. Its synthesis too has not been reported in the open literature so far. Synthetic methods, which involve esterification of cyanoacetic acid with a chosen alcohol, polymerization by knevenagel condensation and subsequent depolymerization, are applied to the synthesis of lower membered alkyl cyanoacrylates in which the alkyl groups carry less than 8 carbons. We have synthesized 1-octyl cyanoacetate by a usual method involving p-toluene sulphonic acid as the catalyst. Its conversion to poly (1-octyl cyanoacrylate) is effected with 1, 3, 5-trioxane in a solvent free route, although paraformaldehyde has been suggested in few patents. Its FTIR spectrum confirmed its functional groups: Its $-\text{OH}$ stretching yielded a broad band around 3400 cm$^{-1}$. Its depolymerization to high yield of 1-octyl cyanoacrylate is under progress: during depolymerization $p$-toluene sulphonic acid, hydroquinone and phosphorous pentoxide are tried. We have avoided high temperature pyrolysis, as it is verified to degrade long alkyl chain.

Keywords: 1-octyl cyanoacrylate; Wound adhesive; Medical glue; $p$-toluene sulphonic acid

1 Introduction

Presently, wound closure techniques have evolved from the earliest development of suturing materials to resources that include synthetic absorbable sutures, staples, tapes, and adhesive compounds. The creation of natural glues, surgical staples and tapes to substitute sutures has supplemented the armamentarium of wound closure techniques. The use of tissue adhesives has long appealed to surgeons and they have been extensively studied for nearly four decades for diverse applications including tissue adhesion, wound closure, hemostasis, and closure of cerebrospinal fluid (CSF) leaks, vascular embolization and application of skin grafts [1].

The ideal method of laceration and incision closure should be simple, safe, rapid, inexpensive, painless, bactericidal, and result in optimal cosmetic appearance of the scar. The cyanoacrylate tissue adhesives offer many of these characteristics. Developed in 1949, the cyanoacrylate adhesives are applied topically to the outermost skin layer. The cyanoacrylates
are supplied as monomers in a liquid form. On contact with tissue anions, they polymerize forming a strong bond that holds the apposed wound edges together. The cyanoacrylate adhesives usually slough off with wound re-epithelialization within 5–10 days and do not require removal.

The use of cyanoacrylates has increased significantly in recent years owing to their unique combination of chemical and physical properties, namely: (1) they cure rapidly at room temperature; (2) they form strong bonds with a wide variety of different materials without the addition of a catalyst; (3) they can be easily and safely applied either manually or by automatic equipment; and (4) they are ready to use without mixing or using a primer [2]. These unique materials were discovered in 1951 in the course of applied research directed towards the characterization of stronger, tougher and more heat-resistant acrylate polymers for jet plane canopies [3].

Sutures have conventionally been the method of approximating wound edges due to their high tensile strength and favorable cosmetic outcomes. Sutures do, however, have some downfalls in that they require increased time and a skilled individual to accomplish good cosmetic outcomes. Over the past four decades, advances have seen other forms of wound closure methods emerge that address some of the disadvantages of sutures [4-10].

2 Experimental

2.1 Materials

1-octyl cyanoacrylate, cyano acetic acid and p-toluene sulphonlic acid were purchased from Sigma Aldrich, USA. All the other chemicals and solvents bought from Daejung Chemical, South Korea.

2.2 Preparation of 1-octyl cyanoacrylate

It involves three stages, (i) Preparation of 1-octyl cyano acetate; (ii) Preparation of poly (1-octyl cyano acrylate) and (iii) Preparation of 1-octyl cyano acrylate.

2.3 Synthesis of 1-octyl cyano acetate

8 g cyano acetic acid, 13 g 1-octanol, 1.0 g p-toluene sulphonlic acid and 50 mL toluene were taken in a 100mL RB flask. It is attached to a Dean-stark trap which in turn attached to a water condenser. The contents of the flask were heated to 130 °C under stirring for 12 h. Water formed in this esterification was removed by forming azeotrope with toluene in order to complete esterification. The total amount of water collected in the trap was equal to 3 g. The round bottom flask was cooled and toluene in it vacuum evaporated. The light red liquid in the flask was transferred to a 250 mL separating funnel. The trace of residual cyano acetic acid and p-toluene sulphonlic acid were removed by extraction with 20 mL portions of saturated sodium bicarbonate solution two times. The liquid was then finally washed with 20 mL portions of water two times, and the liquid transferred to a clean 100 mL beaker. 2 g of anhydrous magnesium sulphate was added to it, shaken well and allowed to stand for 5h. Then the clear liquid was transferred to a 100 mL round bottom flask and vacuum evaporated.
2.4 Synthesis of poly (1-octyl cyano acrylate)

4 g of 1-octyl cyano acrylate was taken in a 100 mL round bottom flask. 1.4 g of para formaldehyde, 1.0 g of magnesium acetate and 3 mL acetic acid were added to it. The flask was attached to a reflux condenser and the contents were vigorously stirred at 90 °C for 24 h. On cooling the flask a thick gel of poly (1-octyl cyano acrylate) was obtained. 20 mL ethyl acetate was added to the flask to dissolve poly (1-octyl cyano acrylate). The solution was transferred to a 250 mL separating funnel. Its acetic acid is removed by extraction with 20 mL portions of saturated sodium bicarbonate solution. Then the ester layer was washed 2 times with 20 mL portion of water. The ester layer was transferred to a 100 mL beaker, and 4g of anhydrous magnesium sulphate added to it, shaken well and allowed to stand for 5 h. The clear liquid was then transferred to a clean, dry RB flask and vacuum evaporated. The viscous liquid that remained in the flask was transferred to a bottle and FTIR analyzed. The schematic representation of wound healing illustrated in figure 1.

![Adhesive Cyanoacrylate glue container](image)

**Fig. 1.** Schematic illustration of synthesized adhesive to cure skin wound healing

3 Results and Discussion

3.1 Fourier Transform Infra Red Spectroscopy

Figure 2 shows the FTIR spectrum of 1-octyl cyanoacetate obtained by the reaction of 1-octanol and cyanoacetic acid. The alkyl –CH₂- stretching vibrations yielded intense peaks at 2929 and 2857 cm⁻¹. The –CN stretching occurred at 2265 cm⁻¹. The intense sharp peak at 1749 cm⁻¹ is due to C=O stretch. The –CH₂- bending vibrations showed peaks at 1395 and 1467 cm⁻¹. The group of peaks at 1335, 1266 and 1187 cm⁻¹ are due to ester –COO- vibrations. The peak at 1007 cm⁻¹ is due to –O-C vibration. The –CH₂- wagging occurred at 724 cm⁻¹.
3.2 Thermogravimetric Analysis

Fig. 2. FTIR spectrum of 1-octyl cyanoacetate

Fig. 3. TGA of 1-octyl cyanoacrylate
The results of TGA of poly (1-octyl cyanoacrylate) are illustrated in Fig. 3. The thermogram showed absence of weight loss below 150 °C illustrating absence of any entrapped solvent. The weight loss between 150 and 225 °C is assigned to residual 1-octyl cyanoacetate. The steady weight loss between 225 and 300 °C is due to degradation of the polymer into monomer. As the decomposition occurred in one stage without leaving any residue, the decomposition evidently rejects random degradation. The polymer is proved to be formed by addition rather than condensation. The present thermogram depicts the same features as that obtained by piperidine. Hence, both the polymers are verified to be formed by addition, though their molecular weights are different. Piperidine is miscible with 1-octyl cyanoacetate; formation of 1-octyl cyanoacrylate might be more rapid than its polymerization. It accounts for formation of high molecular weight polymer with piperidine. In contrast potassium carbonate is immiscible with 1-octyl cyanoacetate, so the rate of formation of polymer sight be lower than the rate of formation of 1-octyl cyanoacrylate.

4 Conclusions

1-Octanol and 2-cyanoacetic acid were esterified in the presence of p-toluene sulphonic acid to form 1-octyl-2-cyanoacetate. The ester was subjected to the Knoevenagel condensation with formaldehyde to form poly(1-octyl-2-cyanoacetate) using potassium carbonate or piperidine as initiators. The polymer was depolymerized using poly phosphoric acid catalyst under vacuum to obtain the monomer. A simple method of obtaining monomer was also attempted by the reaction of 1-octyl-2-cyanoacetate and diiodomethane in the presence of potassium carbonate. This process directly yields the monomer. The second method looks better than the others, and it can be applied to any type of alcohols.

Acknowledgments. This research was supported by the Korea Association of University Research Institute and Industry program funded by the Small and medium Business Administration (C0330026, 2015).

References


