Tissue adhesives in ophthalmic surgery

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لاصقات الأنسجة في جراحة العيون

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Contents

List of Abbreviations

CDVA	Corrected Distance Visual Acuity
DALK	Deep Anterior Lamellar Keratoplasty
G	Gauge
GDD	Glaucoma Drainage Device
IOL	Intra-Ocular Lens
IOP	Intra-Ocular Pressure
LASIK	Laser-Assisted In Situ Keratomileusis
PC	Posterior Chamber
PKP	Penetrating Keratoplasty
TSV	Transconjunctival Sutureless Vitrectomy
VISC	Vitreous Infusion Suction Cutter

List of Figures

Introduction

Suturing is a time consuming process for which surgeons are in search of an ideal alternative. An ideal suture is one which is easy to handle, non-allergenic, affordable and does not promote infection. Besides, none of the available sutures fulfill the requirements of an ideal suture. To overcome these shortcomings, tissue adhesives are being increasingly used. **(Forseth et al, 1992)**

Tissue adhesive sealants have been used as substitutes for sutures in ophthalmic surgery in recent years since the latter may cause irritation, inflammation and infection. Tissue adhesives were developed as suture adjuncts and alternatives for sealing wounded tissues. They are gaining popularity for their ease of use and postoperative comfort. **(Park et al, 2011)**

The application of tissue adhesives in ophthalmology started as early as the 19th century. The first surgical application of tissue adhesive was described by performing sutureless ocular surgery in rabbits using methyl-2-cyanoacrylate. Later, from the start of the 20th century, various other tissue adhesives were invented and used in ophthalmology. The drive towards the development of an adhesive comes from the complications associated with suturing. These include postoperative discomfort, prolonged

healing time, risk of infection as well as prolongation of surgical time, and scarring. **(Park et al, 2011)**

Tissue adhesives have a long history of use in almost all surgical disciplines, both as an alternative and a complement to sutures. Among the currently available adhesives, synthetic glues are mainly represented by cyanoacrylates and biologic glues by fibrin-based adhesives. Cyanoacrylate-based glues are especially useful for treating perforated or preperforated corneal ulcers and performing temporary tarsorrhaphy. Fibrin-based glues have the largest field of application, as they can be used in corneal perforations and are being widely used in pterygium surgery and conjunctival surgery. **(Vera et al, 2009)**

Properties of ideal tissue adhesives include postoperative comfort, cost-effectiveness, rapid setting time and transparency, high tensile strength by creating a strong bridge between wounded margins, easy application, biodegradable and biocompatible. Currently there are two main classes of tissue adhesives: synthetic (e.g., cyanoacrylate and acrylic-based polymers), and biological (e.g., fibrin glue). Each of these adhesives has their own advantages and disadvantages. **(Park et al, 2011)**

Aim of the work

To highlight the role of different types of tissue adhesives in ophthalmic practice.

Cyanoacrylate

Cyanoacrylates are esters (alkyl side chains) of cyanoacrylic acid. Figure 1 shows the chemical structure of Histoacryl (butyl-2-cyanoacrylate) with the active double bond with oxygen that plays the key role in polymerization (hardening). **(Vote et al, 2000)**

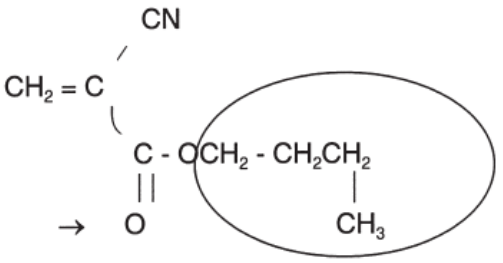

Figure 1. Chemical structure of butyl-2-cyanoacrylate (Histoacryl). Arrow, active double bond with oxygen; ellipse, alkyl (ester) side chain, in this case four carbon (butyl) ester. **(Vote et al, 2000)**

The alkyl side chain can be modified to produce cyanoacrylates with different bonding properties. As an ester chain increases from one carbon to higher numbers (e.g. 10C) the compound becomes more biocompatible. Shortchain esters (< 4C) are toxic either directly or through breakdown products. Early derivatives of cyanoacrylates had short side chains (methyl, ethyl) and degraded rapidly into cyanoacetate and formaldehyde. The degradation products accumulated in tissues and led to significant histotoxicity characterized by both acute and chronic inflammation. **(Trott, 1997)**

The longer alkyl chains of currently available glues (e.g. N-butyl-2-cyanoacrylate) slow degradation significantly, limiting accumulation of byproducts to amounts that can be effectively eliminated by tissues. Histotoxicity, however, depends on the vascularity of tissues, being greater in well-vascularized soft tissues. **(Trott, 1997)**

Cyanoacrylates are monomers that harden by polymerization, through contact with water or a weak base (such as cell membranes/tissue pH). Hydroxylation occurs through the exclusion of oxygen from the substances being bonded. **(Vote et al, 2000)**

In general, shear (side–side force) and compression /distraction strength is high once two surfaces are bonded; however, 'peel' strength is poor (hence you can slowly peel your fingers apart if they are inadvertently stuck together). **(Vote et al, 2000)**

Refojo and co-workers (1969) evaluated the bond strength of several cyanoacrylate adhesives from an ophthalmological perspective. They analysed bond strength between corneal stroma and PMMA, silicone and corneal stroma under different conditions (wet or dry, time of contact before bond stress). Considering only those derivatives currently used, they found that the tensile strength of N-butyl

cyanoacrylate derivatives (e.g. Histoacryl) to be greater than longer chain derivatives (e.g. octyl-cyanoacrylate/Dermabond) across the different bonded materials. Furthermore, for butyl derivatives polymerization occurs better in dry conditions than wet, with peak bond strength at 2 min. The longer chain derivatives (e.g. octyl-cyanoacrylate) were generally weaker whether applied wet or dry, although these had better bond strength in wet conditions (no predrying). The water provided enough initiator on both surfaces for rapid polymerization, whereas in dry conditions the glue polymerized well with tissue which had enough surface moisture, but poorly with the dry plastic.

Figure 2. 2-Octyl cyanoacrylate (Dermabond, Ethicon, Inc.)
(Shivamurthy et al, 2010)

Available preparations of cyanoacrylate:

• Indermil (butyl-2-cyanoacrylate; Sherwood, Davis and Geck, St Louis, MO, USA)

• Histoacryl (butyl-2-cyanoacrylate; BBraun, Melsungen, Germany)

• Histoacryl Blue (N-butyl-2-cyanoacrylate; BBraun)

• Nexacryl (N-butyl-cyanoacrylate; Closure Medical, Raleigh, NC, USA)

• Dermabond (2-octyl-cyanoacrylate; Closure Medical)(figure 2). **(Vote et al, 2000)**

Fibrin Glue

Fibrin glue is a biological tissue adhesive which imitates the final stages of the coagulation cascade when a solution of human fibrinogen is activated by thrombin (the two components of fibrin glue). Fibrin glue includes a fibrinogen component and a thrombin component, both prepared by processing plasma. **(Thompson et al, 1988)**

When human tissue is injured, bleeding ensues and then ceases due to formation of a blood clot. This is the initial mechanism of natural wound closure. Clot is formed as a product of the final common pathway of blood coagulation.

Fibrin glue mimics this coagulation cascade resulting in its adhesive capability. Once the coagulation cascade is triggered, activated factor X selectively hydrolyses prothrombin to thrombin (Figure 3). In the presence of thrombin, fibrinogen is converted to fibrin. Thrombin also activates factor XIII (present in the fibrinogen component of the glue), which stabilizes the clot, by promoting polymerization and cross linking of the fibrin chains to form long fibrin strands in the presence of calcium ions. This is the final common pathway for both the extrinsic and intrinsic pathways of coagulation in vivo, which is mimicked by fibrin glue to induce tissue adhesion. **(Thompson et al, 1988)**

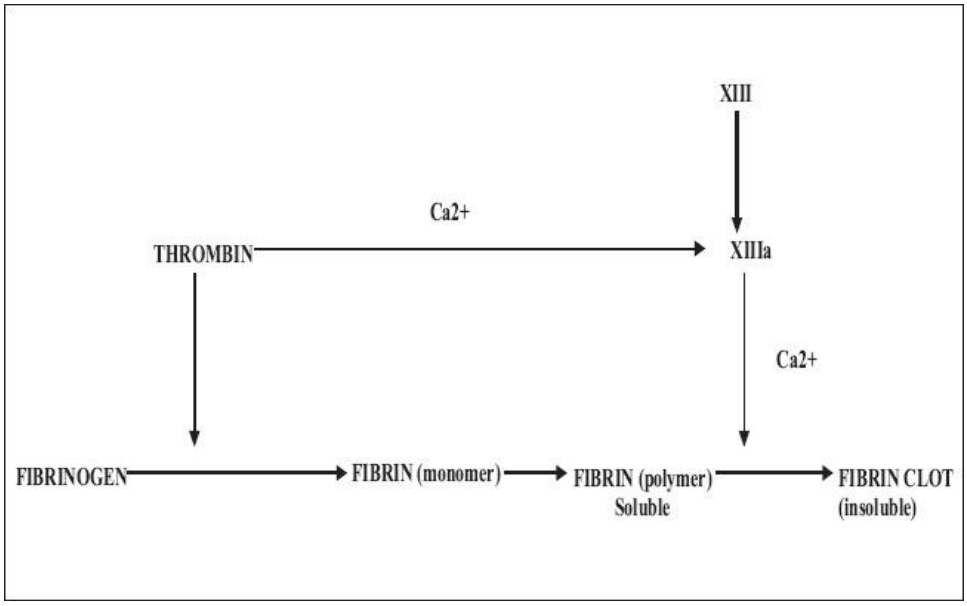

Figure 3. Final common pathway of coagulation cascade **(Panda et al, 2009)**