

UNREVEALING LA MAGIE DE CYANOACRYLATE: A REVIEW

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ABSTRACT

Cyanoacrylate has been used in different surgical and dental specialties as a medical adhesive from last six decades. Owing to their unique properties, including bacteriostatic effect; hemostatic effect; biodegradation; biocompatibility, easy manipulation and reduced surgical time, they are now well accepted for wound closure. One of its advantages is that it has an excellent immunological response. In view of aesthetic needs, cyanoacrylate has been applied with satisfactory results, when compared with sutures. It presents a better approximation of edges of cutaneous and mucosal lesions, smaller residual scars, and biocompatibility. This article reviewed literature with the aim of revealing the uses of cyanoacrylates in different dental and medical fields.

Keywords: Cyanoacrylates, Sutures, Wound closure, Dental

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INTRODUCTION

Cyanoacrylates or acrylic adhesives are groups of materials that are widely used nowadays for various clinical applications. Cyanoacrylate also has been used successfully as a tissue adhesive in various wound-repair procedures and to control haemorrhage. In the past many years, many useful properties of cyanoacrylate-based adhesives have been discovered like biocompatibility, ease of handling, and slow biodegradability to ensure its stability during the process of healing. As cyanoacrylates are in liquid form they can reach the irregular tissue, surface easily and helps in tissue approximation. Cyanoacrylate are polymerized in few seconds when in contact with water and surfaces such as endothelium, mucosa, skin, blood, and bone [1]. In dentistry they are mainly used to cover biopsy sites on the palate, palate, lip, cheek and interdental papilla, as post-extraction dressings, as a protective covering over aphthous ulcers, an approximation of periodontal flaps and in gingival grafting procedures. In the medical field, the uses of cyanoacrylates range from repair of organs, closure of lacerations, skin and mucosal grafting procedures, ophthalmic surgery, to anastomose blood vessels, close nephrotomies, and neurosurgery.

History

In 1949, Ardis [2] synthesized and introduced the cyanoacrylates. Coover et al.[3] in 1950's at the laboratories of Tennessee Eastman Company by chance discovered their unique adhesive properties and proposed their application in surgical procedures in early 1960's. In 1958, the first commercial cyanoacrylate adhesive Eastman 910@ (methyl-2-cyanoacrylate) was introduced but was found to be toxic during medical uses. Later, other higher homologues were discovered and used in various surgical procedures successfully due to their inherited property to polymerize on the moist surface [4].

Chemical structure

The general formula of alkyl-2-cyanoacrylate is $\text{CH}_2=\text{C}(\text{CN})-\text{COOR}$; here R represents the side chain which can be replaced by methyl-, ethyl-, propyl-, butyl-, hexyl-, heptyl-, and octyl groups. The higher homologues like butyl cyanoacrylate are more biocompatible as it contains four alkyl groups in its side chain [5].

Synthesis

The synthesis of alkyl-2-cyanoacrylate occurs in 2 step reaction. The first step is a base catalyst polymerization reaction which involves the condensation of formaldehyde and cyanoacetate esterified with alcohol resulting in poly (alkyl-2-cyanoacrylate) formation. The second

step involves depolymerization which occurs by application of heat to this material yielding alkyl-2-cyanoacrylate monomer (fig. 1) [6].

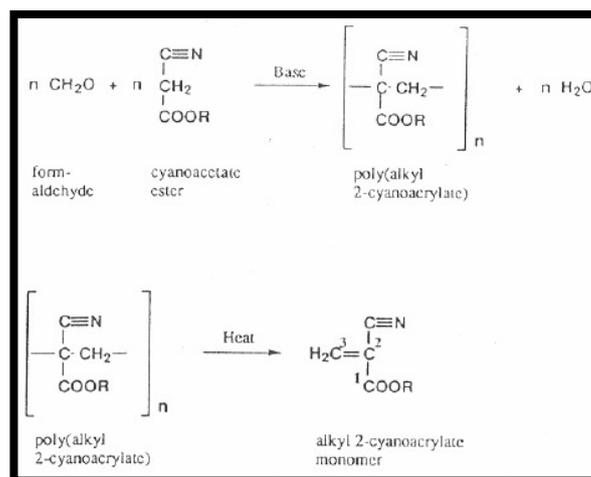


Fig. 1: Synthesis of alkyl-2-cyanoacrylate

Polymerization and bonding

The bonding action of cyanoacrylates occurs by anionic polymerization which is exothermic and rapidly occurs within seconds to minutes even at room temperature.

The cyanoacrylates function as adhesive by molecular attraction with the smooth, dense surface as well as mechanical adhesion caused by the interlocking of the set adhesive in the surface irregularities [7]. Upon application to tissues, the monomer undergoes hydroxylation reaction that results in the glue setting. The speed of polymerization depends upon the function of alkyl side chain as cyanoacrylate with, 4 or 6 carbons polymerize within seconds of contacting tissues [6].

Pharmacokinetics

Cyanoacrylates are biodegradable, in general, readily absorbed from the skin and mucous and excreted through urine and faeces its products are not considered carcinogenic [8, 9].

Degradation

Alkyl-2-cyanoacrylate degradation mainly occurs chemically or enzymatically. In aqueous solutions, the chemical degradation involves an initial attack by hydroxyl ions leading to a reverse Knoevenagel reaction [7,10], which results in cleavage of carbon-to-carbon backbone leading to the formation of formaldehyde and ultimately alkyl cyanoacetate. The degradation is enhanced by alkaline solution and heat. The degradation rate is generally directly proportional to the length of the side chain. It also depends upon polymer surface, particle size, polymer molecular weight, and molecular weight distribution [11, 12].

Medical applications

Cyanoacrylates have been used extensively in the medical field for the approximation of lacerated wounds. As an ear, eye, and nose adhesive to restore the receptors of eyes and the ear, is a delicate process and successfully aided by cyanoacrylates. These can be used to seal corneal or sclera fistulas to prevent oozing optical fluids. Cyanoacrylates have been used to rejoin bones of middle ear during mastoid surgery [13, 14], to stop nose bleeding and to seal haemorrhoids [15]. Cyanoacrylates are also widely used to close skin incisions and demonstrate a higher tensile strength sutured control wounds after 24 h* but less after 4 w. They are found to produce less inflammation, edema, and granulation when compared to sutures and mainly ethyl, propyl and octyl cyanoacrylates are used for these purposes [16]. When used as a surgical adhesive, they are used to seal fistulae e. g. corneal, cerebrospinal fluid, intestinal and urinary. In some of the medical problems cyanoacrylates are found uniquely useful is sutureless surgery, rejoining veins, arteries, and intestines. They are also useful in sealing and reinforcing suture lines.

In cosmetic surgery, cyanoacrylates use replaces or supplements sutures to a great extent by reducing scarring. Bleeding ulcers could be sealed to provide protection from stomach acids. Repair of soft organs, lungs lesions can be easily performed by the use of cyanoacrylates, mesh fixation in hernia repair.

The major indication includes its use in a patient whose bleeding can't be stopped with conventional means in life-threatening situations [17].

Other uses include

1. In Orthopaedics, used for fracture osteosynthesis [17].
2. Oesophagus varix treatment [18]
3. Pancreatic fistulae
4. GI tract fistulae
5. For fixation of implants
6. Skin graft fixation
7. Nail paint adhesive
8. Wound closure in full-thickness skin graft donor area.
9. Transient otoplasty in neonates
10. In elective breast and cosmetic surgery
11. To treat arteriovenous malformations
12. In contaminated wound model, a higher rate of infection found when closed with sutures. As cyanoacrylates have an antibacterial effect and also there is a lack of foreign material in the wound [19].

Dental applications

With the advent of higher homologues with better biocompatibility cyanoacrylates found a wide range of applications in the field of dentistry.

In Periodontal Surgery, the cyanoacrylate tissue adhesives are used for immobilization of periodontal flaps, by Binnie and Forrest [20] in 1974 and sutureless free gingival grafts (FGG) stabilization introduced by Hoxter [21] in 1978, as cyanoacrylate achieves

immobilization, asepsis, and homeostasis, which is considered a prime requisite for successful grafting procedure. Reatzke [22] in 1985 (p) used cyanoacrylate adhesive to cover the localized root exposure with palatal connective tissue graft with envelope technique.

The cyanoacrylates are also used as

1. A periodontal dressing after surgical procedure like:
 - Following gingival depigmentation procedures.
 - After harvesting gingival biopsies from interdental gingiva,
 - After taking a free gingival graft from the palatal region.
2. For stabilization of semilunar coronally repositioned flap and free gingival grafting [23] used for the treatment of gingival recession.
3. Deep pocket tetracycline fibre fixation.
4. Membrane fixation in periodontal defects.
5. When used in free gingival grafting procedures they show a significant reduction in horizontal and vertical direction.
6. In treating dental hypersensitivity in teeth with exposed roots.
7. Over a large area of mucosal ulcerations in recurrent aphthae and leukemia to provide transitory relief from pain and discomfort.
8. Used as a bioactive filling material composed of Hydroxyapatite/ β -tricalcium phosphate for stabilizing the graft material in bone defects.
9. In spray form to cover the biopsy site [24].

In endodontics, they are used

1. Pulp capping
2. To seal remaining dentin in endodontically treated teeth to control microleakage of oral fluid at tooth restoration interface [25].
3. Desensitizing teeth
4. Retrograde filling material in endodontic surgeries,
5. Cervical plug for pulpless teeth bleaching.
6. As a dental filling material, cyanoacrylate is mixed with inert hardening filler.
7. Infiltration of porosities in early caries tissue [26].

In preventive dentistry

1. Cyanoacrylates are used for pit and fissure sealant [27].

In oral and maxillofacial surgery, they are used as

1. Repair unilateral and bilateral cleft.
2. Dressing for extraction sites, as it provides immediate haemostasis, prevents entry of food debris, act as a protective layer over a socket, prevents secondary inflammation.
3. For osteosynthesis: these tissue adhesives were used to fix osteotomized cranial bone fragments [28].

In orthodontics

1. Used for bonding orthodontics brackets [29]

In prosthodontics

1. Used for repair of dentures [30].

Advantages [5, 23, 24]

1. Safe for topical application.
2. Easy to apply
3. Polymerize rapidly i.e. shorter operative time.
4. Polymerization in the presence of moisture and even blood.

5. Good bonding properties support the approximated skin edge and maintain its eversion.
6. Sufficient tensile strength
7. Forms its own protective barrier (no bandage or dressings required).
8. Eliminate the need for suture removal (no suture removal anxiety)
9. Slower degradation rate i.e. less inflammation
10. Hemostatic properties
11. Bacteriostatic, serve as a barrier against microorganism penetration.
12. Do not require local anaesthesia for closure procedure.
13. Repair of laceration was faster and less painful
14. Reduced post-operative pain.
15. Promotes faster healing
16. Elimination of dead space
17. Minimal scarring
18. Viscous forms have gap filling properties.
19. Patient's comfort
20. Less operative time.
21. Excellent cosmetic outcome.
22. Considerable cost-benefit

23. Suitable for elderly, disabled and those with busy work schedules.

24. Minimize the rate of transmission of bacterial and viral haematological infections e. g. Hepatitis and HIV to the clinician.

Disadvantages

1. Low tensile strength
2. After polymerization, the cyanoacrylate becomes brittle and can fragment over a joint crease.
3. There are chances of adherence to the surrounding non-operated to adhere.
4. Delayed healing occurs in foreign body reaction if become embedded under the tissue.

Histotoxicity

Toxicity of cyanoacrylates is related with the speed of degradation and size of chain i.e. larger the side chain slower the degradation speed and histotoxicity, and also the larger the lateral chain, longer the curing time. The methyl, ethyl, and alkyl homologues have been reported to be cytotoxic. It was observed that methyl-cyanoacrylate has highest grade of cytotoxicity causing edema, and tissue necrosis and not used these days clinically. Studies have shown that higher groups of cyanoacrylates are more tissue compatible than lower ones. The histotoxicity is mainly associated with heat produced during polymerization reaction and because of unreacted monomer [31].

The Local tissue responses show histiocytic proliferation and giant cell proliferation. When cyanoacrylate is placed deep in an extraction socket or under the tissue/mucosal flaps when compared with placed superficial, the foreign body cell responses are more pronounced. Miller [32] *et al.* (1974) noted some bone resorption which may be due to heat released during polymerization. However, these adhesives delay wound healing by preventing the proliferation of fibroblasts and microcirculation. Histotoxicity is characterized by inflammation, tissue necrosis, granuloma formation, and wound breakdown. Ellis and Shakick in 1990 concluded n-butyl-2-cyanoacrylate is an ideal tissue adhesive tissue material to close skin surface concerning safety, reliability, effectiveness of pulling resistance and cost [33].

Handling and storage

The cyanoacrylate should be protected from light, heat and to be stored at room temperature.

Trade names

MediBond, Medicroyl, PeriAcryl, GluStich, Xoin, Gesika, VetGlu, Vet Bond, LiquiVet, Indermil, LiquiBand, Histoacryl and others

CONCLUSION

The use of cyanoacrylates has increased in recent years owing to their unique combination of chemical and physical properties like; they cure rapidly at ambient temperature within 5-10 seconds and forms strong bond with a variety of living tissues without the addition of a catalyst and can be applied manually or with the help of automatic equipment. It has good bonding properties and has enough strength to hold the tissue margin together. Cyanoacrylate is an effective tissue adhesive which is hemostatic and bacteriostatic and with the invention of higher nontoxic homologues they can be considered an alternative to conventional sutures in soft tissue surgery and may be used for wound synthesis, lacerations, and healing of wound ranging from 0.5 to 50 cm in length. Research indicates that the use of cyanoacrylates should be restricted to the superficial application.

CONFLICT OF INTERESTS

Declared none

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