Journal of Critical Reviews

ISSN- 2394-5125 Vol 3, Issue 2, 2016

Review Article

UNREVEALING LA MAGIE DE CYANOACRYLATE: A REVIEW

YOGENDER SINGH[1], HIMANSHU DESWAL[2], HARPREET SINGH GROVER[3], AMIT BHARDWAJ[4], SHALU VERMA[5]

[1, 2] Department of Periodontology, [3]Department of Periodontology, [4]Department of Periodontology, [5]Department of Paediatric & Preventive Dentistry, Faculty of Dental Sciences, SGT University, Gurgaon.
Email: deswal706@gmail.com

Received: 12 Jan 2016 Revised and Accepted: 27 Mar 2016

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

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 CH_2=C(CN)-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].

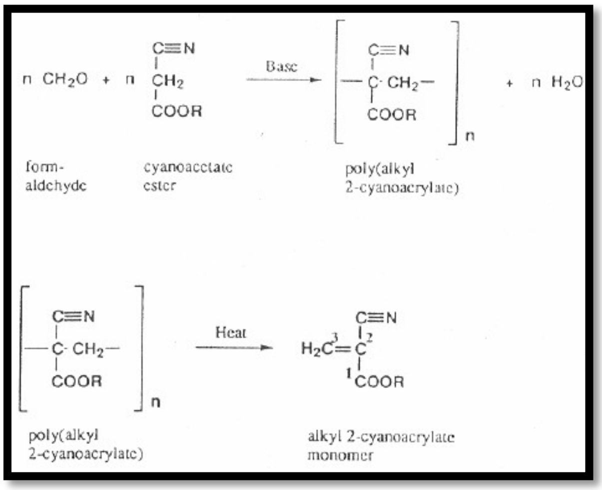

Fig. 1: Synthesis of alkyl-2-cyanoacrylate

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 endodotically 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 unreached 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, Medicryl, 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

REFERENCES

1. Giray CB, Sungur A, Atasever A, Araz K. Comparison of silk sutures and n-butyl-2-cyanoacrylate on the healing of skin wounds. A pilot study. Aust Dent J. 1995;40:43-5.
2. Ardis AE. U. S. Preparation of monomeric alkyl alpha-cyano-acrylates. Patents No. 2467926 and 2467927; 1949.
3. Coover H, Joyner F, Shearer N. Chemistry, and performance of cyanoacrylate adhesive. J Soc Plast Surg Eng 1959;15;413-7.
4. Coover HW. Cyanoacrylate adhesives. A day of serendipity, a decade of hard work. J Coat Technol 1983;706:59-61.
5. Verma D, Ahluwalia TPS. Cyanoacrylate tissue adhesives in oral and maxillofacial surgery. J Indian Dent Assoc 2002;73:171-4.
6. Coover HW, Joiner FD, Shearer NH, Wicker TH. Chemistry and performance of cyanoacrylate adhesives. Soc Plastics Eng J 1959;15:413-7.
7. Leonard F. The n-alkyl alpha cyanoacrylate tissue adhesive. Ann NY Acad Sci 1968;146:203-13.
8. Cameron J. The degradation of cyanoacrylate tissue adhesives. J Surg 1956;98:424.
9. Mori S. Comparative studies of cyanoacrylate derivatives *in vivo*. J Biomed Res 1967;1:55.
10. Leonard F, Hodge JW, Houston S, Ousterhout DK. α-Cyanoacrylate adhesive bond strength with proteinaceous and non-proteinaceous substances. J Biomed Mater Res 1968;2:173-8.
11. Tseng YC, Hyon SH, Ikada Y. Modification of synthesis and investigation of properties for two cyanoacrylates. Biomaterials 1990;11:73-9.
12. Vezin WR, Florence AT. In vitro heterogeneous degradation of poly(n-alkyl a-cyanoacrylates). J Biomed Mater Res 1980;14:93-106.
13. Watanabe S. Application of tetoron mesh-adhesive. Nagoya J Med Sci 1968;31:191-205.
14. McKelvie P. A trial of adhesives in reconstructive middle-ear surgery. J Laryngol 1969;83:1105–9.
15. Matsumoto T**,** Soloway HB**,** Cutright DE**,** Hamit HF. Tissue adhesive and wound healing. Arch Surg 1969;98:266-71.
16. Bhaskar SN**,** Cutright DE. Healing of skin wounds with butyl cyanoacrylate. J Dent Res 1969**;**48:294-7.
17. Capasso G, Bentivoglio G, Testa V, Maffulli N. osteosynthesis with an adhesive in skeletal fractures: an experimental study. Arch Putti Chir Organi Mov 1991;39:309-14.
18. D'Imperio N, Piemontese A, Baroncini D, Billi P, Borioni D, Dal Monte PP, *et al.* Evaluation of undiluted n-butyl-2-cyanoacrylate in the endoscopic treatment of upper gastrointestinal tract varises. Endoscopy 1996;28:239-43.

19. Magee WP, Ajkay N, Githae B, Rosenblum RS. Use of octyl-2-cyanoacrylate in cleft lip repair. Ann Plast Surg 2003;50:1-5.
20. Binnie WH, Forrest JO. A study to tissue response to cyanoacrylate adhesive in periodontal surgery. J Periodontal 1974;45:619-25.
21. Hoxter DL. The sutureless free gingival graft. J Periodontol 1979;50;75-8.
22. Reatzke PB. Covering localized the area of root exposure employing the envelope technique. J Periodontol 1985;56:397-402.
23. Paknejad M, Shayesteh YS, Esmaielieh A. Free gingival grafting; epiglu vs silk thread suturing: a comparative study. J Dentistry Tehran University Med Sci 2004;1:39-44.
24. Bhaskar SN, Frisch J, Margetis PM, Leonard F. Application of new chemical adhesives in periodontics and oral surgery. Oral Surgery 1966;22:526-35.
25. Lage-Marques JL, Conti R, Antoniazzi JH. The use of histoacryl in endontics. Braz Dent J 1993;3:95-8.
26. Robison C, Brookes SJ, Kirkham J, Wood SR, Shore RC. *In vitro* studies of the penetration of adhesive resins into artificial caries-like lesions. Caries Res 2001;35:136-41.
27. Ripa LW. Sealants revisited: an update of the effectiveness of pit and fissure sealants. Caries Res 1993;27:77-82.
28. Ahn DK, Sims CD, Randolpf MA, O'Connor D, Butler PEM, Amarante MTJ, *et al.* Craniofacial skeletal fixation using biodegradable plates and cyanoacrylate glue. Plast Reconstr Surg 1997;99:1508-15.
29. Bishara SE, Von Wald L, Laffoon JF, Warren JJ. Effect of using a new cyanoacrylate adhesive on the shear bond strength of orthodontic brackets. Angle Orthod 2001;71:466-9.
30. Clancy JM, Dixon DL. Cyanoacrylate home repair denture: the problem and a solution. J Prosthet Dent 1989;62:487-9.
31. Montanro L, Arciola CR, Cenni E, Ciapetti G, Savioli F, Filippini F, et al. cytotoxicity, blood compatibility and antimicrobial activity of two cyanoacrylate glues for surgical use. Biomaterials 2001;22:59-66.
32. Miller GM, Dannenbaum R, Cohen WD. A preliminary histologic study of the wound healing of mucogingival flaps when secured with cyanoacrylate tissue adhesives. J Periodontol 1974;45:608-18.
33. Saska S, Gaspar AMM, Hochuli-Vieira E. Cyanoacrylate adhesives for the synthesis of soft tissue. An Bras Dermatol 2009;84:585-92.