

Chemo-mechanical Caries Removal Agents: A systematic review and meta-analysis

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Abstract

Chemo-mechanical caries removal (CMCR) is a non-invasive approach that uses chemical agents to remove infected dentin. This method of caries removal which is based on “dissolution” (replacing drilling) using a chemical agent assisted by an atraumatic mechanical force to remove the remaining soft carious lesions. This methodology was introduced to dentistry as an alternative method of caries removal and was mainly indicated so as to benefit the patients from the inconvenience of sound of the handpiece and subjective use of local anesthesia which can be a major discomforting factor for a pediatric patient- further this methodology complies with the concept of minimal invasive dentistry (MID). Many advances in the field of cariology with the basic philosophy of MID have led to newer modalities replacing the conventional “drill and fill” dentistry which are anti-thetical to this concept. Various agents

and numerous techniques have been tried out for CMCR, but very few have been successful; to a name a few, carisolv has been one of the most successful till date, Papacarie and papain-based BRIX 3000 is the latest which also has produced substantial promising results on clinical use.

Keywords: Chemo-mechanical caries Removal (CMCR), Carisolv, Papacarie, Caridex, Infected dentin

Introduction

Dental caries is now regarded as one of the most prevalent chronic diseases. This condition involves localized disintegration and destruction of the calcified tooth tissues, as well as an infection of the dental pulp.¹ Usually, dentin caries could be recognized as two distinct successive layers, the outer layer (infected dentin) is highly decalcified, infected with bacteria, and could be selectively stained in vivo by caries detector dyes. Despite significant discoloration, the inner layer (affected dentin) is less decalcified, with intact collagen

fibers and no signs of bacterial invasion.² Furthermore, it is more resistant to proteolytic assault and carious lesion development. There is no need to keep preparing the tooth until the dentin is clear of stains in this case. But the ability to discriminate and remove only the diseased tissue remains as essential.³ In 1893, GV Black proposed his principle “extension for prevention”-The principle proposed the removal of sound tooth structure to help in minimizing the caries onset and progression. The fact is that Black’s principle was constrained by both the knowledge of disease process and restorative materials presented at that time, but the demand of removing sound enamel and dentin has been dramatically changed as a result of developing new adhesive restoratives and the alternative approaches for caries removal.⁴

The concept of the Chemo-mechanical approach of caries removal (CMCR) came from the research conducted in the 1970s by Goldman and Kronman in New Jersey, USA. Goldman, primarily an endodontist, invented the concept of chemo-mechanical caries eradication when eliminating organic debris from root canals using sodium hypochlorite (NaOCl). This chemical got the ability to dissolve carious dentine and since that time, the idea of removing caries was borne.⁵ they were studying the effect of sodium hypochlorite, which is a non-specific proteolytic agent, on the removal of carious dentine. Sodium hypochlorite itself was too corrosive for use on healthy tissue and so they decided to incorporate it into Sorensen’s buffer which resulted in a product which was more effective in the removal of carious dentine. This involved the chlorination of glycine to form N-monochloroglycine (NMG) and the reagent subsequently became known as GK-101. In subsequent studies, they discovered that replacing glycine with amino butyric acid improved the system's

effectiveness, producing N-monochloroaminobutyric acid (NMAB), also known as GK-101E. The NMAB method was first patented in the United States in 1975, and then again in 1987 by the National Patent Dental Corporation in New York. It was approved for use in the United States by the FDA in 1984, and it was commercialized as Caridex in the 1980s.⁶

However, Medi Team in Sweden continued to develop on the technology throughout this period, Carisolv made headlines in January 1998.

Carisolv's initial version required mixing two components/syringes prior to treatment, resulting in stable monochlorinated versions of these amino acids at pH 11. Hypochlorite's chlorine atom is transferred to the amino group of each amino acid, rendering it less reactive and hostile to healthy tissue. The alkaline pH prevents more reactive chlorine species such as dichlorinated amines and hypochlorous acid from forming. Furthermore, in an alkaline solution's reducing environment, chlorination rather than the oxidation of an organic molecule is preferred. By including the three chloro-aminoacids with different side-chain properties, positively and negatively charged and hydrophobic, it is ensured that they will electrostatically attract all three possible protein patches, not only collagen but also all proteins and large organic molecules.^{7,8}

The specificity towards proteins introduced by the amino acid chlorination gives the protection potential for the healthy dentin, which is largely non-proteinaceous and has as its major constituent the mineral hydroxyapatite. Also, the high pH stabilizes the mineral structure by decreasing its solubility.⁹ Many trials were conducted in order to solve the issues encountered when working with Carisolv-1 (long duration, lack of efficiency in some situations), culminating in Carisolv-2. The concentration of NaOCl has been raised in this version to improve the

gel's efficacy (i.e., antimicrobial and collagen-solving action). The red dye was discontinued because it was thought to be a visual impediment to determining the status of clean, healthy dentin.¹⁰

In 2003, a Brazilian research study resulted in the creation of a new, less expensive formula to universalize the use of chemo-mechanical caries removal technologies and promote their usage in public health. Papacarie was the commercial name for the new formula.¹¹ Bussadori introduced an enzyme-based CMCR its main action depends on the presence of papain enzyme which is a proteolytic enzyme that causes degradation of proteoglycans in the dentinal matrix. It is basically comprised of papain, chloramines, toluidine blue, salts, thickening vehicle, which together are responsible for the papacarie's bacteriocidal, bacteriostatic, and anti-inflammatory characteristics.¹²

In 2006, Clementino Luedemann evaluated BIOSOLV manufactured by 3M-ESPE AG, Seinfeld Germany, it consists of pepsin enzyme in phosphoric acid/ sodium biophosphate buffer this SFC-V solution compared to Carisolv was not found to be very effective.¹³ CARIE-CARE was manufactured by Uni-biotech Pharmaceuticals Pvt. Ltd, in 2010, it consists of papaya extract which breaks the peptide bonds in the denatured collagen and involves deprotonation from a molecule forming the conjugate base, which facilitates easy removal of carious tissue.¹⁴

In 2012, the BRIX-3000 was released, a chemical mechanical agent, also papain-base with a proteolytic enzyme obtained from leaves latex and fruits of green papaya (*Carica papaya*) that acts as a chemical debridant. The differential of this product according to manufacturers is the amount of papain used (3000 U/mg in a concentration of 10%) and the bioencapsulation thereof by EBE (Encapsulating Buffer Emulsion)

technology which gives the gel the ideal Ph to immobilize the enzymes and liberate them at the moment of exerting its proteolysis on the collagen.¹⁵

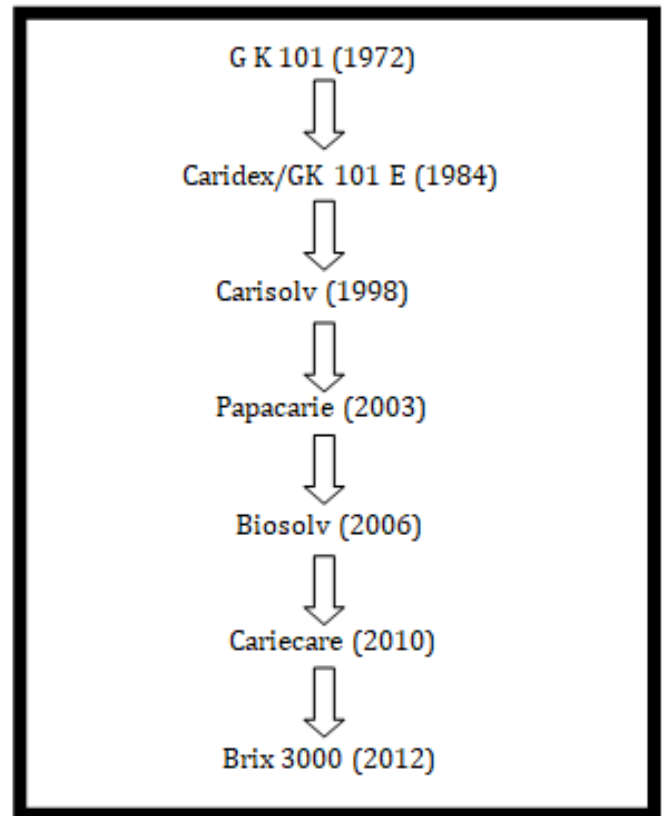


Figure 1: Evolution of CMCR

Methodology

A systematic search of original research articles, reviews, and clinical studies on chemomechanical techniques of caries removal was undertaken. Published studies on the topic comparison of techniques of caries removal were obtained based on a search of the Pubmed, the Cochrane central Register of controlled trials (CCTR93), Unbound Medline, Embase, and Metapress databases, using the search terms 'chemomechanical', caries removal, Carisolv, papacarie, cariecare and their related keywords and their combinations. The search was restricted to articles published till 2021 in the English Language by setting a language and period limitation during the search process.

Data on the type of study, with various performance parameters such as Completeness of Caries Removal\ Efficacy, Patients Perception, Anesthesia, Pain, treatment duration\efficiency, Shear bond strength, Microbiological Evaluation of Remaining Dentine, Adaptation of restoration, Microhardness, Survival\ longevity of Restoration were recorded and elaborated in Table 1 and table 2.

Discussion

One of the most important goals for removing dental caries is the efficacy of the treatment or the complete removal of caries to prevent further destruction of the healthy tooth. There have been many studies which have evaluated the efficacy of CMCR and complete caries removal was seen in a study done by munshi et al²⁴, whereas additional use of drill was used in some studies along with CMCR for complete removal of caries.^{31,40} Studies have been done which have compared the cariogenic flora and it was identified that the efficacy of CMCR of carious dentin was comparable to the conventional method in reducing the cariogenic flora^{10,80}. In fact, Lima et al evaluated CMCR to be more efficient in removing streptococcus mutans.⁷¹ The efficiency of the treatment or the time taken during the treatment has been evaluated by many authors and it was identified that CMCR is the most time-consuming method as compared to other conventional methods.^{31,36,38,41,42,49} Pain is identified as a significant barrier which prevents the patient from going for treatment, it was rated that the patients degree of pain was significantly lower in the CMCR group as compared to other conventional methods.^{36,38,49} whereas some pain was experienced in the CMCR group as compared to the conventional group but it was lower as compared to the conventional group.^{41,45}

During caries removal a situation comes where the anesthesia is required for caries removal, it is found that the need for anesthesia is lower in the CMCR group as compared to other conventional group.^{31,36,38,41} There have been many studies which have evaluated the patient's response and they identified that the CMCR treatment was accepted with high patient comfort, and when asked about which treatment would they preferred CMCR was identified as the treatment of choice.^{24,31,36,38} There has been only 1 study which states that the satisfaction and fear rate was more in the CMCR group.⁴⁴ The longevity of the restoration after caries removal with CMCR and other conventional methods, and the durability of fillings 6 months after treatment was equal in two groups.³⁸ Another study evaluated a better pulp survival rate of teeth excavated with CMCR as compared to conventional for a period of 2 years.⁹⁰ Microleakage is the escape of minute amounts of fluids, debris, and germs via the small gap between a dental restoration or its cement and the cavity preparation's adjacent surface. It can progress through the dentin and into the pulp, leading to the failure of the restoration. There have been studies done to compare the microleakage of composite restoration following caries removal with CMCR and conventional methods and no significant difference in microleakage between the two methods.^{68,83,89} There have been many studies done to evaluate the influence of CMCR on the shear bond strength of dentin bonding agents and it was evaluated that CMCR did not interfere in the adhesion to dentin.^{69,74,78,82} There has been a study which showed on radiographic evaluation that no secondary caries was seen after caries removal with CMCR.²⁴ There have been many studies done to check the dentinal microhardness and it was evaluated that CMCR does not produce any adverse side effects on dentinal microhardness.^{11,86} But a

study was done which stated that the hardness decreased in the CMCR group.⁸⁴

Conclusion

According to results of research, the following conclusions were made:

- Using Chemomechanical methods of caries removal the number of complaints of pain declined more than twice, which means that this method is less painful, less anxious and more efficient for soft carious dentin removal. High patient comfort is seen and none of the treated lesions showed the presence of secondary caries, with least dependence on local anaesthesia. It helps in reducing the cariogenic flora especially streptococcus mutans and did not interfere with the bond strength of adhesive system used in dentin and no change in microhardness.

Hence, in an environment in which “extraction is the rule rather than an exception” as in the developing countries, unconventional tooth preserving approaches such as the atraumatic restorative treatment have an opportunity to evolve. Application of this approach, which does not rely on electricity or dental equipment, makes it possible to provide an effective treatment for large population.

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Legend Tables

Table – 1 Studies selected for systematic review, their salient features (efficacy, patients Perception, Anesthesia, Pain and efficiency) and extracted data.

S.no	Author/Year	Completeness of Caries Removal \ Efficacy	Patients Perception	Anesthesia	Pain	Treatment Duration \ Efficiency
1	Anusavice et al ¹⁶ (1987)			Significantly greater number of patient requested for local anaesthesia in conventional method of caries removal as compared to CMCr method (p<0.05)	Higher level of pain (p<0.025) associated with the conventional treatment as compared to cmcr method.	
2	Zinck et al ¹⁷ (1988)	Complete caries removal -90-100%	93%-Patient preferred Carisolv treatment over drilling			Carisolv-4-10 times longer as compared to drilling
3	Ericsson et al ¹⁸ (1999)	Carisolv 106/1074 (99.06%) Drilling 19/20 (95%)	Treatment seemed faster with Carisolv, 74% found no discomfort, more pleasant with Carisolv	Offered Carisolv 3/104 Drilling 9/11	Less with Carisolv (P < 0.01)	Longer with Carisolv (P<0.01)
4	Cederlund et al ¹⁹ (1999)	After excavation with carisolv all dentin surfaces were caries free.				
5	Fure et al ²⁰ (2000)	Carisolv 34/34 (100%) Drilling 25/26 (96.15%)	23% faster with Carisolv, 76% found no discomfort, more pleasant with Carisolv	Offered Carisolv 3/34 (8.82%) Drilling 6/26 (23.07%)	Carisolv 0 Drilling 12/20 (60%)	Longer with Carisolv (P<0.05)
6	Banerjee et al ²¹ (2000)					Carisolv- excavation of caries was evaluated a slowest with this method.
7	Nandanovsky et al ²² (2001)	Cmcr- 7\66 Mechanical -4\66 Carisolv 59/66 (89.39%) Mechanical 63/66 (95.45%) P > 0.05	Chemicomechanical appeared to be more comfortable.	Cmcr-3% Mechanical- 8% Offered Carisolv 3/34 Drilling 6/26	Pain was experienced in Cmcr - 32% Mechanical-65% Less with Carisolv (P<0.01)	C m c r method-9.2±3.8 Mechanical-8.6 ±3.8 min
8	Maragakis et al ²³ (2001)	Carisolv 10/16 (62.5%) Drilling 16/16 (100%)	Children disliked drilling and preferred sitting for a longer duration for caries removal.	None in Carisolv All in drilling	62.5% reported having no trepidation with Carisolv	93.75% estimated Carisolv to have taken longer (P< 0.001) Cariolv 6min 46 sec-13 min 57sec
9	Munshi et al ²⁴ (2001)	Soft carious leion- 83.3% Arrested carious lesion-70%	No discomfort with Carisolv	None	None	Carisolv mean for arrested lesions = 6.10±1.04min 10Soft lesions = 4.56±0,58 min (no comparison group)
10	Rafique et al ²⁵ (2003)		More acceptable by patient as compared to other conventional methods.	Reduced need of local anesthesia.	No complain of pain	
11	Ansari et al ²⁶ (2003)		90 % patients' acceptance was seen.	Need of local anesthesia was removed \ eliminated.	No complain of pain	
12	Yazici et al ²⁷ (2003)	Carisolv-36% Drilling-93%				Carisolv -272 sec Drilling-116 sec
13	Beyth et al ²⁸ (2003)		This method is most comfortable for the patient.			
14	Chaussain et al ²⁹ (2003)	Carisolv -78.3%	99.2% patient were satisfied with the treatment.	Carisolv-60%treated without anesthesia.		Carisolv: 11.1±9.51 min

15	Lumbau et al ³⁰ (2003)	Carisolv is a valid alternative to traditional techniques.				
16	Kakaboura et al ³¹ (2003)	Carisolv 90% Drilling required 10%	82% found it to be more pleasant with Carisolv	Required in 8% during Carisolv & 40% during drilling (P < 0.05)	Less with Carisolv	Carisolv -12.2± 4.1 min Drilling 6.8 ±2.8 min
17	Lager et al ³² (2003)	Not Tested	Not mentioned	Not Mentioned	Not mentioned	Not mentioned
18	Fure, Lingstrom ³³ (2004)	100%	97% rated the gel treatment as pleasant	32/104 (30.76%) New Carisolv 30/98 (30.61%) Carisolv	39% some pain	Statistically different only for deep lesions
19	Kavvadia et al ³⁴ (2004)	100% Carisolv is effective in removal of caries in primary teeth.	Did not negatively affect children's cooperation. Patient cooperation did no differ	Administrated before caries removal in class I lesion with more than one third into dentin Class V : more need with conventional mechanical method (P < 0.05) Reduced need of local anesthesia.	Not mentioned	Working time was significantly increased with chemicomechanical method (p<0.001) Longer with Carisolv (P<0.01)
20	Fure et al ³⁵ (2004)		81% patient preferred chemicomechanical method to drilling.			Carisolv1- 7.6 ±4.2 min Carisolv 2- 6.7 ±4.1 min
21	Azrak et al ¹⁰ (2004)	100%	Not tested	Not Mentioned	Not mentioned	Not tested
22	Balciuniene et al ³⁶ (2005)	Carisolv-60% drilling required		Carisolv-3.3% Drilling-31%	Less painful	Carisolv-10.5 min Drilling- 5.9 min
23	Fluckiger et al ³⁷ (2005)	Conventional and hand excavation method both removed caries efficiently.				Carisolv method was more time consuming.
24	Bergmann et al ³⁸ (2005)	Carisolv 46/46 (100%) Drilling 45/46 (97.82%)	More patients rated Carisolv "Good/OK" compared with drilling	Before treatment 1 with carisolv 2 with drilling	Not mentioned (P > 0.05)	Longer with Carisolv (P<0.001)
25	Dammaschke et al ³⁹ (2005)	NaOCL-61.5% Carisolv-75.4%				
26	Peters et al ⁴⁰ (2006)	1 cycle-19.2% 2 cycle-30.8% 3 cycle- 7.7% Drilling was used in 42.3%		Carisolv-23.1% Drilling-16.7%		Carisolv- 934.96± 270.25 sec Drilling- 409.58 ± 169.61 sec
27	Lozano et al ⁴¹ (2006)		Carisolv was preferred by 71% Drilling was preferred by 1 %	Carisolv-0 Drilling- 2/40	Carisolv-17.5% Drilling- 40%	Carisolv-7.51 ± 2.10 min Drilling-2.47 ± 1.83 min
28	Magalhaes et al ⁴² (2006)					Carisolv-319 sec Drilling-173 sec
29	Meller et al ⁴³ (2006)					Carisolv 10.9 min
30	Inglehart et al ⁴⁴ (2007)		Carisolv-2.96 Drilling-3.46			Carisolv-604± 227.54 sec Drilling- 80.71 ± 83.99 sec
31	Kirzioglu et al ⁴⁵ (2007)			Carisolv- 7.1% Drilling- 35.7%		Carisolv-9.03± 4.14 min Drilling- 7.34± 3.14 min
32	Barata et al ⁴⁶ (2008)					Carisolv-11.6± 2.7 min Minimal Invasive 10.2± 3.1 min
33	Hosein et al ⁴⁷ (2008)	The difference between conventional and cmcr method of caries removal was statistically insignificant (p>0.005)				Carisolv-12.19 ± 3.7 Drilling-7.4 ± 3.21
34	Carrillo et al ⁴⁸ (2008)		Well, accepted by patient in all phases of treatment.			Papacarie-8 min per tooth.
35	Pandit et al ⁴⁹ (2009)	Hand instrument-1.26 Airotor-0.38 Carisolv-0.42			Hand instrument-1.280 Airotor-1.440 Carisolv-0.080	Hand instrument-424.60sec Airotor-257 sec Carisolv-534 sec

36	Peric et al ⁵⁰ (2009)	Complete caries removal -92% (p<0.05)	85% preferred carisolv 47% preferred rotary (p<0.05)	Reduced need for local anesthesia (p<0.001)		Carisolv-11.2±3.3 min Drilling -5.2±2.8 min
37	Kotb et al ⁵¹ (2009)	Papacarie was identified as efficient as the drill in caries removal.	Papacarie was more comfortable than the traditional methods.	Reduced need of local anesthesia.		There was no significant difference in the operating time.
38	Anegundi et al ⁵² (2012)	No statistical difference between both the groups.	No statistical difference in the preference for treatment.		In conventional treatment 50% experienced no pain as compared to papacaries-86.7% experienced no pain (p=0.01)	Conventional-4.7min Papacaries-17.96min (P<0.001)
39	Goomer et al ⁵³ (2013)				Pain perception is less in carisolv. Mean Value-0.82	In Carisolv more time was required as compared to handexcavation, and airotar. Least time was taken by airotar.
40	Motta et al ⁵⁴ (2014)					No statistical difference was seen in time required by both the group of treatment.
41	Boob AR et al ⁵⁵ (2014)					Time taken for CMCR excavation was more than hand excavation.
42	Divya et al ⁵⁶ (2015)					Time taken for stainless steel bur was least compared to carisolv which recorded the highest time taken.
43	Kumar et al ⁵⁷ (2016)		Cariecare more accepted by patient (P<0.05) compared to smart prep Burs.			Clinical set up- Cariecare was more time consuming compared to smart Prep burs. Community set up- cariecare was less time consuming and more efficient.
44	Sahana et al ¹⁴ (2016)	Papacarie more efficient than cariecare.				Mean time taken for cariecare was more than papacarie.
45	Sontake et al ⁵⁸ (2019)		CMCR More preferred and comfortable for children.			In CMCR mean time taken was more compared to conventional.
46	Katiyar et al ⁵⁹ (2021)		CMCR Enhances patient comfort.	CMCR Minimizes need for anesthesia.	Pain perception is less in CMCR.	Mean time taken is more for CMCR.

Table - 2 Studies selected for systematic review, their salient features (Shear bond strength, microbiological evaluation of remaining dentine, adaptation of restoration, micro hardness and longevity of restoration) and extracted data.

S.N	Author/Year	Shear bond strength	Microbiological Evaluation of Remaining Dentine	Adaptation of restoration	Microhardness	Restoration Survival\ longevity of restoration
1	Wolski et al60 (1989)	Bond strength appeared to enhance on specimen treated by CMCR.				
2	Burke et al61 (1994)	Mean bond strength for CMCR group was significantly greater than conventional method.				
3	Wennerberg et al62 (1999)				Carisolv increases surface restoration.	
4	Fure et al20 (2000)		Not tested			Carisolv 29/31 (93.54%) Drill 21/24 (87.5%) P > 0.05
5	Haak et al63 (2000)	Higher SBS in the carisolv group.				
6	Munshi et al24 (2001)					Arrested lesions = 11% Soft lesions = 53.6%
7	Sakoolnamarka et al64 (2002)	Carisolv may influence the longevity of bonds from adhesive restorative material				
8	Yazici et al65 (2002)				Few patent orifices of dentinal tubules were observed in dentin subjected to carisolv	
9	Lager et al32 (2003)		Both methods reduced cfu			Not mentioned
10	Burrow et al66 (2003)	Carisolv did not affect the adhesion of the adhesive restorative materials.				
11	Hossain et al67 (2003)				Carisolv does not produce any adverse side effects on dentinal compositions of the treated cavities.	
12	Fure, Lingstrom33 (2004)		Not tested			167/177 (94.35%)
13	Mousaivinasab et al68 (2004)			No significant difference in microleakage between conventional and CMCR method.		
14	Azrak et al10 (2004)		Both methods reduced cariogenic flora			Not tested
15	Erhardt et al69 (2004)	Carisolv did not interfere in the adhesion to dentin				
16	Bergmann et al38 (2005)		Not tested			40/46 (86.95%) in Carisolv group 42/45 (93.33%) in drilling group
17	El kholany et al70 (2005)	Higher (p>0.05) in carisolv treated dentin.				
18	Lima et al71 (2005)		Carisolv-95% reduction in streptococcus mutans Drilling-95% reduction in streptococcus mutans.			
19	Sakoolnamarka				Use of carisolv to	

	et al72 (2005)				excavate carious tissue can be as effective as rotary.	
20	Morrow et al73 (2005)				There was no difference in carisolv and bur treated dentin.	
21	Sonoda et al74 (2005)	Use of carisolv does not compromise bond strength to caries affected dentin.				
22	Hosoya et al75 (2005)	Carisolv decreased the SBS to primary dentin but did not influence SBS to permanent dentin.				
23	Roeleveld et al76 (2006)					ART-38% Conventional-50% Carisolv-35%
24	Peric et al77 (2007)		Carisolv-53% bacteria free Conventional- 87% bacteria free			
25	Lopes et al78 (2007)	There was no difference in the SBS between CMCR and conventional methods of caries removal.				
26	Li et al79 (2007)	CMCR benefits dentin adhesion.				
27	Correa et al11 (2007)				The microhardness of dentin remaining after removal with rotary and CMCR was similar.	
28	Subramaniam et al80 (2008)		92% reduction in cariogenic flora by both the methods.			
29	Barata et al81 (2008)					Both minimal invasive methods showed similar clinical performance after 12 months of follow up.
30	Tachibana et al82 (2008)	The highest bond strengths were observed with dentin treated with bur and carisolv as compared to laser.				
31	Yamada et al83 (2008)			Carisolv treated teeth facilitate good adaptation due to increase in surface roughness.		
32	Prabhakar et al84 (2009)				Carisolv treated dentin has less hardness number as compared to hand excavated method.	
33	Topaloglu et al85 (2009)					No significant difference of survival rate of restoration was seen between ART and CMCR group after 2 years.
34	Qasim et al86 (2009)				CMCR does not produce any adverse side effects on dentinal microhardness.	

35	Anegundi et al52 (2012)		No statistical difference seen in microbial growth, bacterial count and lactobacilli in both group (P=0.36)			
36	Juntavee et al87 (2013)			Mean microleakage level was lowest with CMCR method using Apacaries gel and highest with Er.YAG Laser.		
37	Motta et al54 (2014)					Success rate for a period of 18 months: CMCR-95% TM(traditional method-80%)
38	Boob et al55 (2014)				KHN of hand excavation method was more as compared to carisolv. Which signifies less amount of demineralised dentin.	
39	Pavuluri et al88 (2014)			No significant difference in microleakage between conventional and CMCR Method.		
40	Divya et al56 (2015)		Stainless steel bur caused more amount of dentinal tubule destruction compared to carisolv-which caused the least destruction.			
41	Nouzari et al89 (2016)			No significant difference between micro-leakage scores among conventional and CMCR method.		
42	Sahana et al14 (2016)		Dentinal tubule destruction was not evident in papacarie and carisolv.			
43	Ali AH et al90 2020					After 2 year statistically significant higher pulp survival rate of teeth excavated with CMCR as compared to conventional method.

Table 3: A comparison of CMCR agents

GK-101 [91,92,93]	CARIDEX/ GK-101E [91,92,93]	CARISOLV [91,92,93]	PAPACARIE [91,92,93]	BIOSOLV [91]	CARIE-CARE [91,92,93]	BRIX 300 [91]
<p>• Action-^[91]</p> <p>Conversion of hydroxyproline (essential factor of the stability of collagen) to pyrrole-2 carboxyglycine</p> <p>↓</p> <p>Chlorination of the denatured collagen</p> <p>↓</p> <p>Removal of carious tissue It necessitated the use of a specialised delivery device comprised of a reservoir (for warming the freshly produced solution to 41°C) and a pump (similar to a straight handpiece) connected to a 20-gauge needle delivery tip</p> <p><i>limitations</i>^[91,92] slow action Softened only the first layer, but not the second layer Need for special delivery equipment</p>	<p>• Two bottles system</p> <p>a) Solution I: 1% sodium hypochlorite (NaOCl)</p> <p>b) Solution II: Glycine, Aminobutyric acid, sodium chloride (NaCl) and sodium hydroxide (NaOH)</p> <p>The two solutions are mixed immediately before use to give the working reagent [pH 12] which is stable for 6 for 1 hour.</p> <p>• Action^[91,92] Exact mechanism is unclear Originally thought that</p> <p>GK-101E</p> <p>↓</p> <p>Conversion of hydroxyproline (essential factor of the stability of collagen) to pyrrole-2- carboxyglycine</p> <p>↓</p> <p>Chlorination of the denatured collagen</p> <p>↓</p> <p>Removal of carious tissue Further studies indicate</p> <p>GK-101E</p> <p>↓</p> <p>Cleavage by oxidation of glycine residues</p> <p>↓</p> <p>Disruption of the collagen fibrils which become more friable</p> <p>↓</p> <p>Easy removal of the damaged collagen fibrils</p> <p>• The delivery system comprises of a solution reservoir, a heater, and a pump that transfer the liquid through a tube to a hand piece and an applicator tip</p> <p>Limitations^[91,92]</p> <p>• Tissue or material other than damaged dentin collagen access to tiny or</p>	<p>• Medi Team in Sweden continued to work on the Caridex system, which resulted in the January 1998 release of Carisolv, a chemo-mechanical caries removal agent.</p> <p>• The primary difference between Carisolv and other products on the market at the time was the use of three amino acids – lysine, leucine, and glutamic acid – instead of the amino butyric acid.</p> <p>• Original gel (before 2004)</p> <p>Syringe A: carboxymethylcellulose-based gels, colouring agent and amino acids (glutamic, leucine and lysine)</p> <p>Syringe B: 0.25% NaOCl</p> <p>• Modified gel (after 2004) Multimix syringe the red coloring agent was removed, the amino acid concentration was reduced by half and the NaOCl concentration was increased to 0.475% New Carisolv System (2013)</p> <p>Incorporation of minimally invasive burs and special Carisolv caries detector dye to the modified Carisolv gel to shorten the caries excavation time</p> <p>Advantages</p> <p>• The Carisolv system is much easier to use than Caridex.</p> <p>• it involves a gel rather than a liquid, there is better contact with the carious lesion and the quantity required is very less which enhances precision placement.</p> <p>• Three amino acids are incorporated instead of one and different charges</p>	<p>The main action depends on the presence of the papain enzyme which is a proteolytic enzyme that causes degradation of proteoglycans in the dentinal matrix. Papacarie is a gel syringe that have 3 ml of solution</p> <p>Composition- Papain enzyme, chloramine, toluidine blue, salts, preservatives, a thickener, stabilizers and deionized water.</p> <p>• Action Degrades and eliminates the fibrin "mantle" formed by carious process</p> <p>↓</p> <p>Breaks the partially degraded collagen molecules</p> <p>↓</p> <p>By digesting the dead cell, causes breakdown of the collagen molecules</p> <p>↓</p> <p>Degraded collagen is chlorinated by chloramines</p> <p>↓</p> <p>Disturb the hydrogen bond and affects the secondary and quaternary structure</p> <p>↓</p> <p>Chemically soften the carious dentin and facilitating removal of caries tissue</p> <p>Advantages^[2]</p> <p>• Antibacterial biocompatible gel that avoids the need for anesthesia, removes just the damaged tissue, and maintains the healthy tissue better.</p> <p>• The formation of a smear layer is not observed after using the gel.</p> <p>• The gel combines an atraumatic approach with</p>	<p>• manufactured by 3M-ESPE AG, Seefeld, Germany.</p> <p>• Biosolv information is still scarce and primarily dependent on the manufacturer's claims. It is essentially, an experimental product.</p> <p>• Composition- consists of pepsin enzyme in phosphoric acid/sodium biophosphate buffer</p> <p>• Action^[1] Phosphoric acid in Biosolv</p> <p>↓</p> <p>Dissolve the inorganic components of caries infected dentine</p> <p>↓</p> <p>Permitting the pepsin to selectively disrupt the denatured collagen fibers</p> <p>↓</p> <p>The softened mass can then be easily removed by the specially designed plastics instruments without affecting sound tissue.</p> <p>Limitation^[91] not available commercially, it is an experimental product.</p>	<p>• manufactured by Uni-biotech Pharmaceuticals Pvt. Ltd., in 2010,</p> <p>• Composition- consists of papaya extract (papain) 100mg, clove oil 2mg, colored gel (blue), chloramines, sodium chloride, and sodium methyl paraben, with similar properties as that of Papacarie.</p> <p>• Manufacturer recommends using back of blunt spoon excavator.</p> <p>• Action^[91] Papaya extract in Carie-Care</p> <p>↓</p> <p>breaks peptide bonds in the denatured collagen and involves deprotonation</p> <p>↓</p> <p>Facilitates easy removal of carious tissue</p> <p>Advantages^[92] It is lower in cost as compared to papacarie. It is available commercially in India and is used in dental colleges widely.</p>	<p>• In 2012, the BRIX-3000 was released, a chemo mechanical agent, also papain-base, with a proteolytic enzyme obtained from latex and fruits of green papaya (Carica Papaya) that acts as a chemical debridant.^[91]</p> <p>• According to the manufacturers, the difference in this product is the amount of papain used (3,000 U/mg in a 10% concentration) and the bio encapsulation thereof by EBE (Encapsulating Buffer Emulsion) technology, which gives the gel the ideal pH to immobilize and liberate the enzymes at the moment of exerting its 22 proteolysis on the collagen.^[91]</p>

	<p>interproximal carious lesions may still require rotary or manual tools.</p> <ul style="list-style-type: none"> • system requires large volumes of solution 200-500ml and the procedure is slow and costly. • Minimal use because of time required, the large volumes of solution needed and the delivery system was no longer commercially available 	<p>have improved the interaction with the degraded collagen within the lesion, thus increasing efficiency.</p> <p>Limitations ^[91,92] Extensive training and customized instruments required, which increases the cost of the solution. Longer procedural time.</p>	<p>antibacterial characteristics while causing no pain and damage to healthy tissue.</p> <ul style="list-style-type: none"> • Papa carie was evaluated in vitro for cytotoxicity in fibroblasts culture at different concentrations (2, 4, 6, 8 and 10%) and was found to be safe and non-cytotoxic in vitro fibroblast culture. <p>Limitations ^[91] expensive procedure.</p>			
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