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Remineralization Potential Of Grape Seed Extract - ASystematic Review

P.Priyanka [1] , Bharathwaj [2] , S Shreelakshmi [3], Sindhu [4], Prabu D [5], Dinesh [6] And Rajmohan [7]

[1]bachelor Of Dental Surgery, [2] *S*enior Lecturer, [3] Senior Lecturer, [4] *S*enior Lecturer [5] Hod *And* Professor[6]reader, [7]reader. Department Of Public Health Dentistry, Srm Dental College And Hospital, *Srm Institute Of Science And Technology*, Ramapuram, Chennai- 600089.

Abstract

Background: Promoting Remineralization Is The Ultimate Goal Of Prevention Of Caries Lesion. Natural Products Have Long Been Used To Prevent And Treat Oral Diseases Such As Dental Caries. Grape Seed Extract Is Known To Have A PositiveEffect On Remineralization Of Caries Lesions.

Aim: The Present Study Aimed To Assess The Remineralization Potential Of GrapeSeed Extract.

Study Design: A Systematic Review Of In Vitro Studies And Clinical Trials Were Per-Formed. Various Scientific Electronic Databases Were Searched And A Total Of 58 Articles Were Obtained, Of Which 53 Were Screened And Among Which 9 Were In- Cluded In This Study. The Intervention And Outcomes Were Assessed.

Results: 9 Studies Were Included In This Systematic Review. These Studies Showed That The Gse Group Significantly Increased The Micro Hardness Of The Le-Sions And Promotes Remineralization

Conclusion: Gse Enhanced The Remineralization Process Of Caries Lesions And Also Prevents Demineralization And Thus Might Be Considered As An Effective Nat-Ural Agent In Non-Invasive Dentistry

Keywords: Remineralization, Grape Seed Extract, Dentistry, Randomized ControlTrials.

Introduction

Natural Products Can Be Used To Prevent And Treat Dental Caries Which Is The Most Prevalent Oral Disease Though The Use Of Antimicrobial Agents Such As Chlorhexidine Or Sodium FluorideLimit The Growth And Biofilm Formation Of Cariogenic Microorganisms, These Have Some Limitations And Have Not Been Recommended For Regular Caries Prevention. Grape Seeds Are Gaining A Lot Of Importance Because Of The Proanthocyanidins Present In Them Which Have Excellent Antibacterial,Anticariogenic And Remineraliz-Ing Properties [1].Grape Seed Extract(Gse) Is A Naturally Occurring Plant Me- Tabolite Which Is A Rich Source Of Proanthocyanidin(Pa) Which Is Widely Available In Fruits,Vegetables,Nuts,Seeds,Flowers And Barks That Has Been Reported To Strengthen Collagen-Based Tissues By Increasing Collagen Cross-Links[2]. Gse May Interact With The Organic Portion Of Enamel Through Pa-Collagen Inter- Action, Thereby Stabilizing The Exposed Collagen Matrix [3]. The Gse Investigated Here Is A Flavonoid Obtained From The Seeds Of Vitis Vinifera. It Is Known To Have A Positive Effect On Remineralization Of Artificial Caries Lesions [4]. Grape Seed Extract Has Been Found To Be A Promising Remineralizing Agent For Treatment Of Demineralized Tooth [3].

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Remineralization Is A Process Where Calcium And Phosphate Ions Are Supplied From A External Source To The Tooth, Thereby Resulting In Mineral Gain [2].Reminer-Alization May Stop Or Reverse Early Tooth Decay. Despite Its Promising Properties,A Comprehensive Study Review On Whether GrapeSeed Extract Can Promote Remineralization Is Necessary Before Gse's Recom- Mendation Can Be Made By Health Care Professionals. The Present Study Was Designed To Assess Whether Gse Can Effectively Influ- Ence The Remineralization Of Artificial Caries.Therefore, The Aim Of This Study Is ToDetermine The Remineralization Potential Of The Grape Seed Extract.

Objectives

To Assess The Remineralization Potential Of Grape Seed Extract

Materials And Methods

A Systematic Review About Clinical Trials Showing The Remineralization Potential OfGrape Seed Extract.

Eligibility Criteria :

Inclusion Criteria

1. Publications Of Studies In English With Full Text Articles Were Included.
2. Compulsory Inclusion Of Grape Seed Extract As One Of The Treatment Modali-Ties.
3. Publication From All Years Was Included.4.Clinical Trial Studies.
4. Articles Showing Remineralization Potential Of Grape Seed Extract.6.In-Vitro Studies.

Exclusion Criteria

1. Articles Published In Other Languages.
2. Studies Which Do Not Use Grape Seed Extract As One Of The Treatment Modali-Ties Were Excluded.
3. Conditions Limiting Abilities Of Patients To Participate In The Study.4.Review Articles
4. Unrelated Articles 6.Only Abstract Available

Search Strategy :

The Following Electronic Databases Were Used To Find Published Articles On Rem-Ineralization Potential Of Grape Seed Extract : Pubmed, Google Scholar, Cochrane Library, Science Direct, Lilacs.

Each Database Was Searched To Obtain The Articles By Using The Keywords "Rem-Ineralization And Grape Seed Extract" And In Google Scholar The Keywords Used Were "Remineralization Potential" With "Grape Seed Extract" And "Dentistry" And "Randomized Control Trials". After The Search, A Total Of 58 Articles Were ObtainedAmong Which 9 Articles Were Finalized For Further Scrutinization.

Search Words :

Specific Keywords Used For Each Electronic Database Is Shown In Table 1

Table 1 : Database And Search Terms

S.No	Database	Search Terms	Articles
1	Pubmed	Remineralization And Grape Seed Extract	17

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2	Google Scholar	"Remineralization Potential" With "Grape Seed Extract" And "Dentistry" And "Randomized Control Trials"	26
3	Cochrane	Remineralization And Grape Seed Extract	5
4	Science Direct	Remineralization And Grape Seed Extract	9
5	Lilacs	Remineralization And Grape Seed Extract	1

Result

The Search Yielded 58 Articles, And 53 Were Screened Which Were Independently Assessed. 44 Articles Were Eliminated Based On Titl
Es And Abstract (Based On Title = 29 And Based On Abstract = 15) And 9 Articles Were Included In Qualitative Synthesis. Figure 1 Shows The Flow Diagram Of The Re- Ports That Were Identified, Screened, Assessed For Eligibility, Excluded And Includ- Ed In The Review.

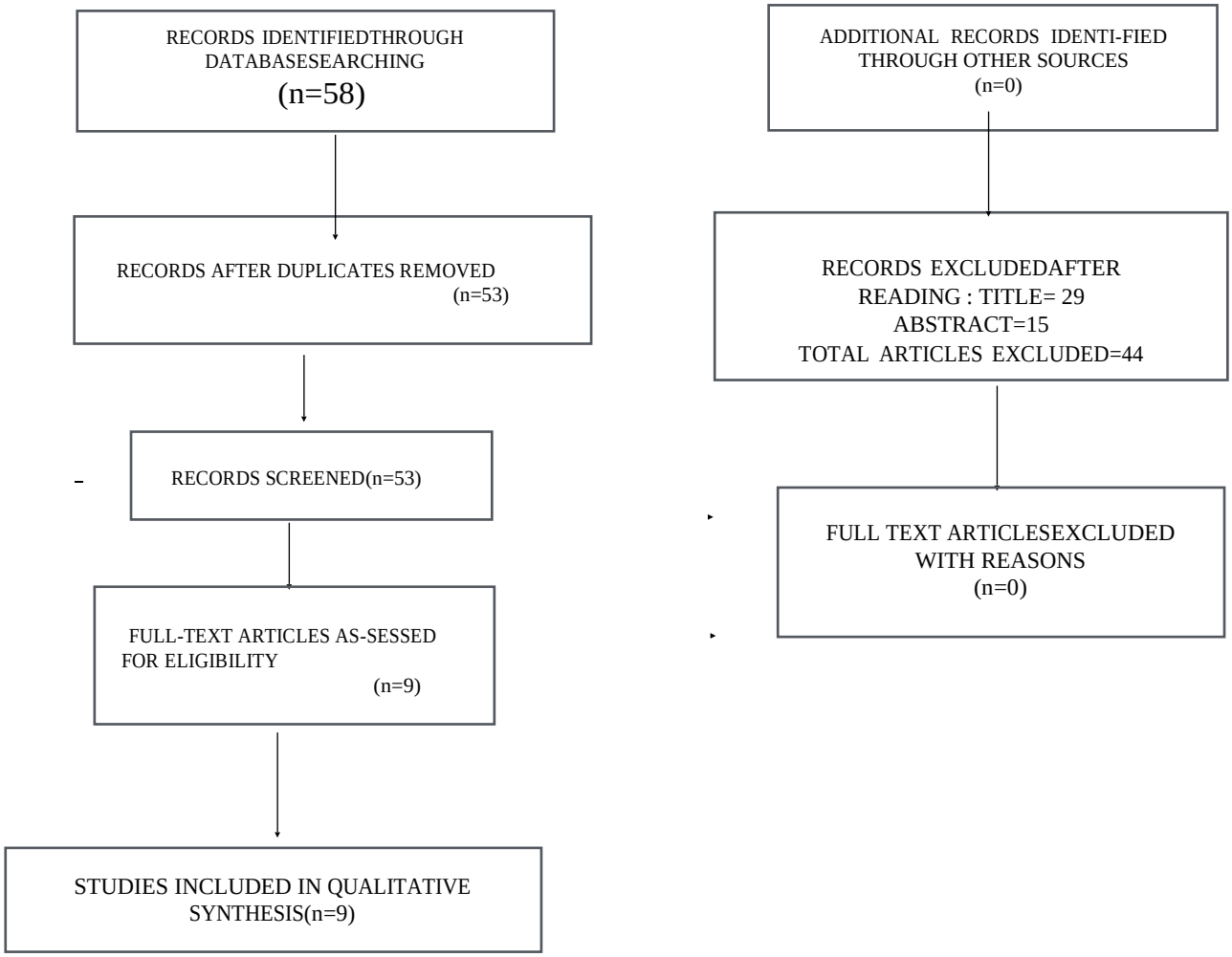

Figure 1: Prisma Flowchart

S.No.	Author Name	Journal Name	Volum E	Issue	Year	Page No.
1	Rubel M, Prashant Gm, Naveen Kumar Pg, Sushanth Vh, Mohamed Imranulla, Ipshita Potlia, Swati Mallick	Asian Journal Of Pharmac Eutical And Clinical Research	9	5	2016	174-176
2	Ketaki DinkarJawale, Sharad Basavraj Kamat , Jayakumar Appasaheb Patil, Girish Shankar Nanjannawar, Rutuja VijayChopade	Journal Of Conserva Tive Dentistry	20	6	2017	415–418.
3		ClinicalTrials Registry				
4	Cheng-FangTang, Ming Fang , Rui-Rui Liu , Qi Dou , Zhi-Guo Chai , Yu-HongXiao , Ji-Hua Chen	Archives Of Oral Biology	58		2013	1769-1776

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5	Mahkameh Mirkarimi Solmauz Eskandarion Majid Bargrizan Abbas Delazar Mohammad Javad Kharazifard	Journal Of Dental Research, Dental Clinics,Den Tal Prospects	7	4	2013	206-210
6	S. Pavan Q. Xie A.T. Hara A.K. Bedran-Russo	Caries Research	45		2011	443-447
7	Qian Xie, Ana Karina Bedran-Russo, Christine D.Wu	Journal Of Dentistry	36	11	2008	900-906
8	Shaymaa M.Nagi , Shahinaz N.Hassan , Sameh H. Abd El-Alim, Mostafa M.Elmissiry	Journal Of Clinical And Experime Ntal Dentistry	11	5	2019	401–407.
9		Clinicaltrials.Gov				

Aim	**Metho Ology**	**D-GrouPs**	**Statis Ti-Cal Tests**	**Interv-Ention**	**Sam Size**	**PleResUlt**	**Stat Isti-Cal Sig NificAnc E**

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To Investigate The Effect Of Grape Seed Extract On Artificial Enamel Caries In Human Teeth	The Teeth Were Cleaned And Were Immerse D In A Deminer Alizing Solution For 96 Hrs At 37°C And 50% Relative Humidity To Create Artificial Lesions.	The Samples Were Randomly Divided Into: 2 Groups Of 25 Each. Half In Gse Solution(Te St) Other Half In Saline (Control)	Independ Ent T-Test And Paired T-Test	2 Groups Of 25 Each: Half Of The Samples Were Immersed In The Gse Solution (Test) And The Other Half In Saline (Control), Respectivel Y, For 8 Days. The Samples Were Measured By Microhard Ness Tester To Obtain Values In Vickers Hardness Scale.	50 Sound Extracte D Premola Rs Were Extracte D From Patients Undergo Ing Orthodo Ntic Treatme Nt	Gse Group Significan Tly Increased The Micro Hardness Of The Lesions (P≤ 0.001)	Yes (P≤ 0.001)
To Determine Remineralizi nG Potential Of Grape Seed Extract (Gse) Compared To Casein Phosphopep Tide-Amorphous Calcium Phosphate (Cpp-Acp) And Calcium Glycerophos Phate (Cagp) Through Ph-Cycling Model And Subsequent Evaluation Using Polarized Light Microscope (Plm).							

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To Evaluate The Remineralizing Efficacy Of Grape Seed Extract Oil Vs Fluoride Mouthwash In Management Of Post-Orthodontic White Spot Lesions	Patients Are Asked To Rinse Mouth With Grape Seed Extract Mouthwash And Sodium Fluoride Mouthwash	2 Groups : Experimental : Grape Seed Extract Mouth Wash 15% Concentration Active Comparator : Sodium Fluoride Mouthwash 1000 Ppm	Independent T-Test And Paired T-Test	1.Grape Seed Extract Mouth Wash 2.Sodium Fluoride MouthwaSh	40 Participants	Gse Group Significantly Increased The Microhardness Of The Lesions (P≤0.001).	Yes (P ≤ 0.001).
To Investigate Whether Biomodification Of Caries-Like Acid-Etched Demineralized Dentine, Using Proanthocyanidins-Rich Gse, Would Promote Its Remineralization Potential.	Dentine Specimens Were Acid-Etched For 30 S, Then Biomodified Using Proantho-Cyanidin-Based Preconditioners (At Different Concentrations And Ph Values) For 2 Min, Followed By A 15-Day Artificial Remineralization Regimen.	All Specimens, With Or Without Embedment, Were Randomly Divided Into Nine Groups : Group A,B,C,D,E,F,G,H(Empty Control),I(Negative Control).	One Way Anova And Lsd Tests	Groups A, B And C Exhibited Steady Increases In Vhn Values.However, The Micro-Hardness-Promoting Effect Was Somewhat Compromised In Groups D, E And F, They Were Subsequently Subjected To Microhardness Measurements,Microm Orphological Evaluation And X-Ray Diffraction Analyses.	45 Extracted Intact Human Third Molars Were Collected	A Concentration-Dependent Increase Was Observed In The Microhardness Of The Specimens That Were Biomodified Using Gse Preconditioners,	Yes (P < 0.05)

To Investigate The Effect Of Grape Seed Extract (Gse) On Artificial Enamel Caries In Primary Human Teeth.	Primary Incisors Were Sectioned Mesiodistally. The Tooth Slices Were Placed In A Demineralizing Solution For 96 Hours At 37oc And 50% Relative Humidity To Create Lesions.	The Demineralized Fragments Of Each Tooth Were Randomly Divided Into: 2 Case And Control Groups.	Independent *T*-Test.	Groups : 2 Case (Immersed In Gse Solution In Phosphate Buffer For 8 Days) And Control (Immersed In Distilled Water) . The Samples Were Subsequently Evaluated Using A Scanning Electron Microscope And A Micro-Hardness Tester.	17 Human Sound Primary Incisors Were Collected	Grape Seed Extract Significantly Increased The Micro-Hardness Of The Lesions (P=0.03)	Yes (P=0.03)
To Evaluate The Effects Of A Proanthocyanidin-Rich Grape Seed Extract (Gse) On The In Vitro De-Mineralization Of Root Dentine	Samples Were Treated Daily For 30 Min And Subjected To A Ph Cycling Artificial Caries Protocol Using Demineralization Cycles For 6 H And Remineralization Cycles For 17.5 H.	The Fragments Were Randomly Assigned To Different Treatments Solutions: Gse, Fluoride (F), Gse +F And Distilled Water (Control)	One-Way Anova And Post-Hoc Fisher's Plsd Tests	Gse Was Able To Minimize Mineral Loss And Lesion Depth Compared With The Control Group (P<0.0001). The Gse+F And F Groups Showed The Lowest Values (P <0.05), With No Statistically Significant Differences Between Them. Mineral Loss	Twelve Extracted Sound Human Third Molars Were Used In This Study.	Gse Treatment Was Able To Minimize Mineral Loss And Lesion Depth When Compared To The Control Group (P < 0.0001)	Yes(P < 0.0001)

				And Lesion Depth Were Deter- Mined After 18 Days Of Ph Cycling, By Transverse Microradiography			
To Evaluate The Effect Of Gse On The Reminerali Zation Of Artificial Root Caries	Sound Human Teeth Fragments Obtained From The Cervical Portion Of The Root Were Stored In A Deminerali Zation Solution For 96 Hr At 37°C To Induce Artificial Root Caries Lesions.	Divided Into 3 Treatment Groups : 6.5% Gse, 1,000 Ppm Fluoride (Naf), And A Control (No Treatment)	Anova And Fisher's Tests	The Demineralized Samples Were Ph-Cycled Through Treatment Solutions, Acidic Buffer And Neutral Buffer For 8 Days At 6 Cycles Per Day. The Samples Were Subsequently Evaluated Using A Microhardness Tester; Polarized Light Microscopy (Plm) And Confocal Laser Scanning Microscopy (Clsm).	25 Extracted Sound Human Third Molars Were Obtained	Gse And Fluoride Significa Ntly Increase D The Microhar Dness Of The Lesions ($P<0.05$) When Compared To A Control Group.	Yes ($P<0.05$)

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To Evaluate The Remineralizati On Effectiveness Of Experimental Y Prepared Grape Seed Extract Hydrogels (Gse) Compared To Fluoride Gel On Bleached Enamel.	3 Tested Reminerali Zing Agents Were Applied To The Labial Surfaces And Left For10 Minutes. Then Specimens Were Rinsed And Stored In Artificial Saliva Until Testing.	Divided Into 3 Groups (10/Group) According To The Reminerali Zing Agents Tested: [Gse 6%, Gse 10%, Or Fluoride Gel].	Kolmogorov- Smirnov And Shapiro-Wilk Tests One-Way Anova Test Tukey's Hsd Post-Hoc Test Dependent T-Test	Group A (N=10): Specimens Received Gse 6% ; Group B (N=10): Specimens Received Gse 10% ; Group C (N=10) : Specimens Received Fluoride Gel. Micro-Hardness And Energy-Dispersive X-Ray And Ultra-Morphologic Al Evaluation Were Tested At Baseline	30 Extracted Maxillary Incisors Were Bleached.	Statistical Significant Decrease On Mean Micro-Hardness Values Had Resulted After Bleaching Procedure Compared To Baseline, Followed By A Significant Increase In Gse (10%) And Fluoride Groups.	Yes($P \leq 0.05$)
To Assess The Effectiveness Of Applying Grape Seed Extract (Gse) Gel Versus Cpp- Acp Paste On Remineraliza Tion Of White Spot Lesion (Wsls) In Post Orthodontic Patients.	Every Week The Grape Seeds Extract (Gel) Is Put Into The Tray And Applied To The Upper Teeth Of The Participant. Cpp-Acp Paste Is Applied To The Teeth Twice Daily.	2 Groups : Experimental : Grape Seeds Extract Active Comparator: Cpp-Acp	One Way Anova And Scheffe Post Hoc Comparis On Test	1. Grape Seeds Extract Powder Cpp-Acp Paste	24 Particip Ants	Plm Data Revealed A Significantly Thicker Mineral Precipitati On Band On The Surface Layer Of The Gse-Treated Lesions Compared To Cpp-Acp	Yes ($P < 0.001$)

Discussion

Grape Seed Extract Is A Rich Source Of Proanthocyanidin (Pa) Which Is A Naturally Occurring Plant Metabolite. It Should Be Noted That Pa Has A Chelating Mechanism With Calcium Ions, Which Enhances Mineral Deposition On The Surface Of Dentin.

The Pa-Treated Collagen Matrices Are Non-Toxic And Inhibit The Enzymatic Activity Of Glucosyltransferase, F-Atpase And Amylase Glucosyltransferases, Which Are Produced By Streptococcus Mutans And Polymerize The Glucosyl Moiety From Su- Crose And Starch Carbohydrates Into Glucans. This Is The Basis Of The Sucrose-De- Pendent Pathway Of Streptococcus Mutans And Is Critical For Plaque Formation And Development Of Caries.

This Grape Seed Extract Is Known To Have Antibacterial And Remineralizing Proper- Ties. Grape Seed Extract Has Been Found To Be A Promising Remineralizing Agent For Treatment Of Demineralized Tooth .[3]

Remineralization Is A Process Whereby Calcium And Phosphate Ions Are Supplied From An External Source To The Tooth, Thereby Converting Ion Deposition Into Crys- Tal Voids In Demineralized Enamel, Hence Producing Net Mineral Gain. [2] Based On The Data Obtained From These Studies, Gse May Positively Affect The Remineralization Process Through 2 Distinct Mechanisms. First, It May Contribute To Mineral Deposition On The Superficial Layer Of The Lesion. Secondly, Gse May Interact With The Organic Portion Of The Root Dentin Through Pa-Collagen Interac- Tion,Thereby Stabilizing The Exposed Collagen Matrix.[7] With This, We Can Come To A Conclusion That Gse Inhibits Demineralization And Promotes Remineralization Of Artificial Carious Lesions.

Conclusion

Based On The Data Obtained, It Can Be Concluded That Grape Seed Extract Is A Po- Tential Remineralizing Agent Which Not Only Promotes Remineralization Of Artificial Carious Lesions But Also Inhibits Demineralization.

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