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Antigingivitis effect of Coenzyme Q10 on plaque induced chronic gingivitis

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Abstract
CoQ10 is of nutritional nature and is an intracellular antioxidant which is widely distributed in the tissues of the human body. A deficiency of CoQ10 at gingival sites may exist independently of and /or because of periodontal disease.
Aims: The present study was designed with the aim to evaluate the antigingivitis effect of coenzyme Q10 on plaque induced gingivitis
Methods and material: A total 40 systemically healthy gingivitis subjects aged 16-64 years, were divided into 2 groups randomly, control group (A):-20 subjects with gingivitis were treated with scaling, test group (B):-20 subjects with gingivitis were treated with scaling and topical application of Perio Q gel for a period of 28 days.Statistical analysis. Repeated two way analysis of variance (ANOVA) followed by post hoc tukey test for intergroup comparisons.
Results. There was statistically significant reduction in plaque index scores, gingival scores and sulcular bleeding scores in the control group but in the test group showed a gradual reduction in sulcular bleeding index. There was a clinical improvement in both the tests and controls Conclusion Topical application of PerioQ gel along with mechanical debridement has improved clinical parameters. Further long term clinical trials in larger sample sizes with long term revaluation are needed for their use in routine supportive periodontal therapy.

Keywords: coenzyme q10, plaque induced gingivitis, plaque index, sulcular bleeding index, antioxidants

Introduction
Coenzyme Q10 was discovered by Fred Crane and his colleagues in 1957 in beef heart mitochondria at the University of Wisconsin. Because of its ubiquitous presence in nature and its quinone structure (similar to that of vitamin K), it is also known as ubiquinone [2]. It is as a cofactor in the electron-transport chain and helps in the synthesis of ATP thus it is essential for the health of virtually all human tissues and organs [4]. CoQ10 deficiency appears to be greatest in cells that are metabolically active (such as those in the heart, immune system, gingiva, and gastric mucosa. Since oral administration of CoQ10 can increase tissue levels of the nutrient, it is possible to correct CoQ10 deficiency [3].
Periodontal disease is an infectious disease causing inflammation of supporting tissues of teeth such as gingiva, periodontal ligament, cementum and alveolar bone leading to tissue destruction and tooth loss. A deficiency of CoQ10 at gingival sites may exist independently of and /or because of periodontal disease. In such patients' dental treatment and oral hygiene could correct plaque and calculus but not that part of deficiency of CoQ10 due to systemic cause. Thus periodontal therapy with CoQ10 can be included for an overall improvement of gingival health in periodontal disease. The present study was designed with the aim to evaluate the antigingivitis effect of coenzyme Q10 on plaque induced gingivitis.

Materials and Method
A total 40 systemically healthy gingivitis subjects aged 16-64 years attending Department of Periodontology, Yenepoya dental college, Mangalore, were divided into 2 groups randomly. A detailed systemic and family history were recorded. Clinical periodontal findings were also recorded. All the participants had received verbal explanation of the nature of the study, and written informed consent were taken**.** The groups were randomly distributed into Control group (A):-20 subjects with gingivitis were treated with scaling. Test group (B):-20 subjects with gingivitis were treated with scaling and topical application of Perio Qgel. Individuals who were systemically healthy individuals with a minimum of 20 teeth having 3 posterior teeth in all three quadrants and gingival index scores GI≥1were included in the study. Patients with any systemic diseases and smokers and who had taken anti-inflammatory drugs or antibiotics for the past 3 months, pregnant or lactating mothers were excluded in the study.

Procedure
Baseline examinations were recorded. Clinical parameters was assessed at 7th, 14th, 21st and 28th day. Clinical parameters which were recorded are the plaque index (PI; Silness and Loe 1964), gingival bleeding index (Muhlemann 1975), and gingival index (GI; Loe and Silness, 1963).
Patients were motivated and standard oral hygiene instructions were given. On the 8th day subjects were recalled and scaling was performed in control group (A) and topical application of the gel along with scaling were done in the test group (B).
Perio-Q gel (Coenzyme Q10 gel manufactured by PERIOQ INC, Manchester, USA), supplied as a pack of gel, containing

a mixture of coenzyme Q10 and vegetable glycerin base in a ratio of 1:9. The gel should preferably be used within 48 months from the date of manufacture and stored in a dry area away from sources of light and heat.It does not have to be stored in the refrigerator. However, when kept in the refrigerator at a temperature between 4- -80C, its shelf-life would be maintained. (fig 1(A). Topical application was used with the tip of the applicator completely soaked in gel and applied to the sites (test group) (fig 1(B).Technique for gel application was demonstrated to all the subjects using cotton roll stick and were instructed to do the same at night. The subjects were followed for a period of 28 days (fig 2). Plaque, gingival and bleeding index were recorded at 0th, 8th, 14th, 21st and 28th day as summarized in fig 1.Any untoward reaction after using the gel were recorded and appropriate measures were taken. Such subjects were excluded from the study. The results expressed as mean±SD and proportions as percentages. Repeated two way analysis of variance (ANOVA) followed by post hoc tukey test for intergroup comparisons at 5% level of significance and 95% confidence limit were carried out. p value equal to and less than 0.05 was considered statistically significant.

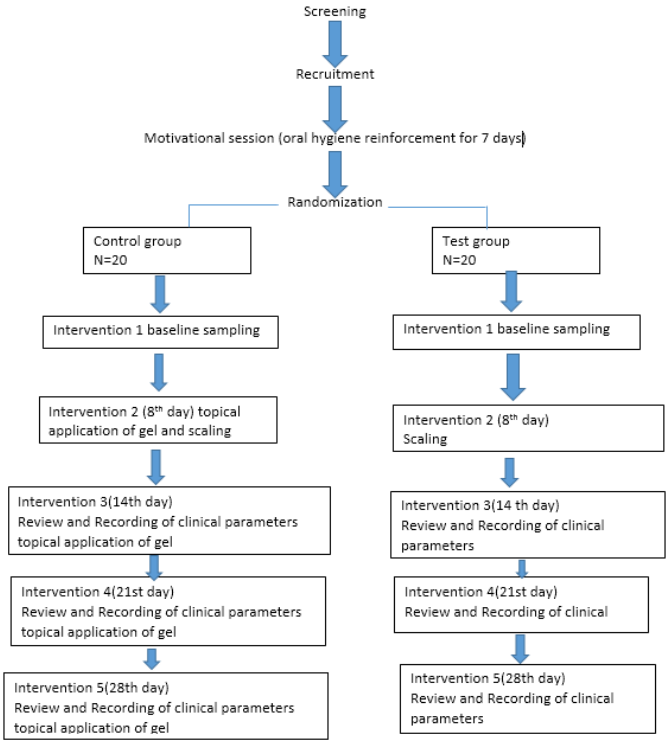

Fig 1: Flowchart depicting participant enrolment and measurements

Fig 1(A): Perio-Q gel

Fig 1(B): Topical application of perioQ gel at tests site in 8th day

Fig 2: Reevaluation done at the end of 28 days

Results

Repeated measures ANOVA test was employed for plaque index, gingival index, sulcular bleeding index.

Gingival Index

Repeated measures ANOVA test is done to compare the values of GI between tests and controls in four time periods. The mean values are denoted in the Table 1. The values constantly go down from 8th day to the 28thday.There was a gradual improvement in the scores from baseline to 28th day. In the test group scores reduced from 1.427000+/- 0.13 to 0.996+/- 0.15 (P<0.000).In the control group scores reduced from 1.576400+/-0.27 to 0.865680+/-0.297 (P<0.002). Fig 3 depicts that both tests and control shows a gradual reduction in scores, the orange line represents the tests and the blue line control. Table 2 shows there is significant difference seen in the time period in each group separately as well as there is difference in the groups.

Table 1: Repeated measures ANOVA for GI

Descriptive Statistics				
	Group	**Mean**	**Std. Deviation**	**N**
8TH Day GI	Control	1.576400	.2765689	20
	Tests	1.427000	.1394010	20
	Total	1.501700	.2290303	40
14TH Day GI	Control	1.295450	.2022610	20
	Tests	1.270750	.1720566	20
	Total	1.283100	.1857657	40
21ST Day GI	Control	1.112050	.2400010	20
	Tests	1.234050	.1452933	20
	Total	1.173050	.2053354	40
28TH Day GI	Control	.865680	.2978283	20
	Tests	.996750	.1596895	20
	Total	.931215	.2450348	40

Table 2: Tests of Within-Subjects Effects Measure: Measure_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME	Huynh-Feldt	6.757	2.857	2.365	67.733	.000
TIME * GROUP	Huynh-Feldt	.534	2.857	.187	5.357	.002

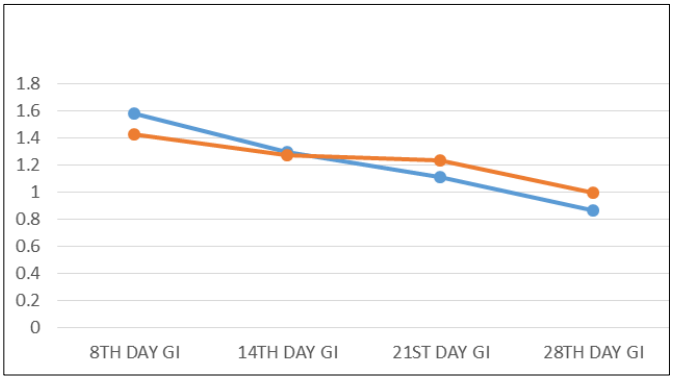

Fig 3: Repeated Measures ANOVA for GI

Plaque Index

There was statistically significant improvement in the plaque index from 8th day to 28th day. Table 3 depicts in the tests group, the plaque scores were reduced from 1.4869+/-0.3807277 to 0.65770+/-0.3027151 (P < 0.00). In the control group, scores were reduced from 1.492+/-0.277 to 1.0038+/-0.382 (P<0.004). Table 4 shows the difference in time as well as the group is seen. Table 4 shows on intergroup comparison of PI statistically significant results were found in the test group. The drop was more in the test group and there was significant difference in value over time. Fig 4 shows a gradual decrease in plaque scores in the tests and controls, the orange line represents the tests

Table 3: Repeated measures ANOVA for PI

Descriptive Statistics				
	Group	Mean	Std. Deviation	N
8TH Day PI	Control	1.492000	.2778265	20
	Tests	1.486900	.3807277	20
	Total	1.489450	.3289822	40
14TH Day PI	Control	1.258600	.1946131	20
	Tests	1.183350	.2740538	20
	Total	1.220975	.2376833	40
21ST Day PI	Control	1.178750	.1877134	20
	Tests	.939250	.2926390	20
	Total	1.059000	.2712840	40
28TH Day PI	Control	1.003800	.3821578	20
	Tests	.657700	.3027151	20
	Total	.830750	.3827629	40

Table 4: Tests of Within-Subjects Effects Measure: Measure_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
Time	Huynh-Feldt	9.219	2.765	3.334	48.957	.000
Time * group	Huynh-Feldt	.720	2.765	.260	3.822	.014

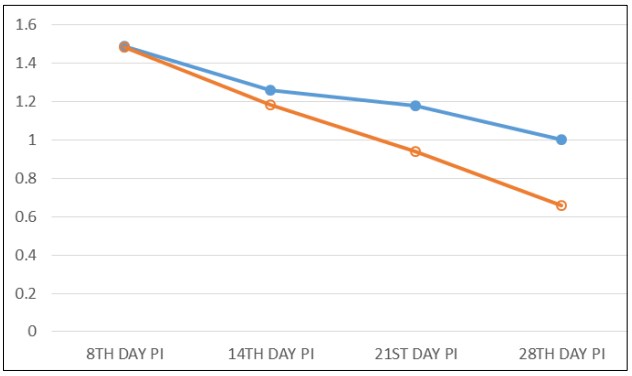

Fig 4: Repeated measures ANOVA for PI

Sulcular Bleeding Index

In the test group the bleeding scores showed improvement from 1.50 +/- 0.19 to 0.86300+/-0.203 (P<0.015) which is depicted in Table 5. There was significant difference seen in the time period in each group separately as well as there is difference in the groups shown in Table 6.

In Fig 5 the orange line represents the tests group which shows a gradual improvements from baseline to 28th day compared to control. Tests have significant drop in PI but GI and SBI is better dropped in controls. Based on the Students T test in table 7, the differences in GI, PI and SBI was calculated between 28 days and the baseline and the assessment of this difference is done between the two groups.

As shown in Fig 6, we see that the difference is higher in the control than the tests in tests of GI and SBI but PI is dropped more in test represented by the orange bar. Differences in Gingival index test 0.43+/-0.216(p value =0.001) control 0.677+/-0.212(p=0.001) Differences in plaque index tests 0.8142+/-0.43 (p value=0.003) control 0.44+/-0.29 (p value =0.003) Differences in sulcular bleeding index tests 0.63+/-0.26(p value =0.37) control 0.7+/-0.4(p value =0.373).

There was a clinical improvement in the test sites in the test group as shown in Fig 2 at the end of 28 days.

An intergroup comparison was done between age and gender, there is no statistical significance in the distribution of gender and age

Table 5: Repeated measures ANOVA for SBI

Descriptive Statistics				
	Group	Mean	Std. Deviation	N
8TH Day SBI	Control	1.574150	.4307667	20
	Tests	1.508550	.1907778	20
	Total	1.541350	.3305085	40
14TH Day SBI	Control	1.217950	.2482360	20
	Tests	1.295250	.1698157	20
	Total	1.256600	.2135454	40
21ST Day SBI	Control	.964050	.2714868	20
	Tests	1.245900	.1799924	20
	Total	1.104975	.2684399	40
28TH Day SBI	Control	.843150	.2836448	20
	Tests	.876300	.2031958	20
	Total	.859725	.2441156	40

Table 6: Tests of Within-Subjects Effects Measure: Measure_1

Source		Type III Sum of Squares	df	Mean Square	F	Sig.
TIME	Huynh-Feldt	9.768	2.118	4.611	65.228	.000
Time * Group	Huynh-Feldt	.641	2.118	.303	4.283	.015

Table 7: Students T test for comparison of the differences from base line to 28 days

	Group	N	Mean	Std. Deviation	T	df	P value
DIFF in GI	Tests	20	0.4302	0.21625	-3.648	38	0.001
	Control	20	0.6777	0.21279			
DIFF in PI	Tests	20	0.8142	0.43194	3.167	38	0.003
	Control	20	0.4442	0.29382			
DIFF in SBI	Tests	20	0.6323	0.26273	-0.905	30.76	0.373
	Control	20	0.737	0.44623			

Table 8: Age and Gender distribution

		Group							
		Control				Tests			
		Mean	Standard Deviation	Count	Column N %	Mean	Standard Deviation	Count	Column N %
Age		28.5	7.8			27.4	8.5		
Gender	Female			10	50.0%			11	55.0%
	Male			10	50.0%			9	45.0%

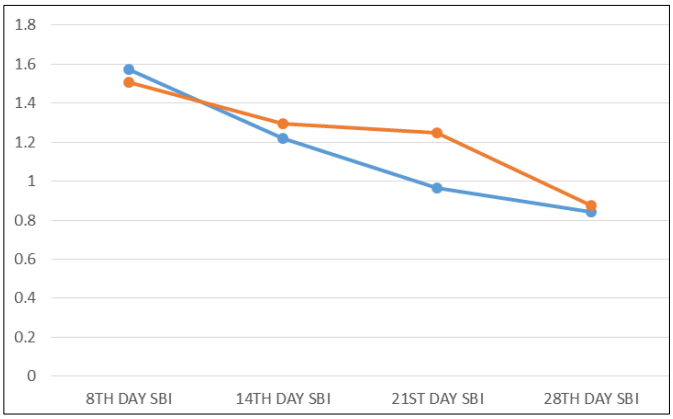

Fig 5: Repeated measures ANOVA for SBI

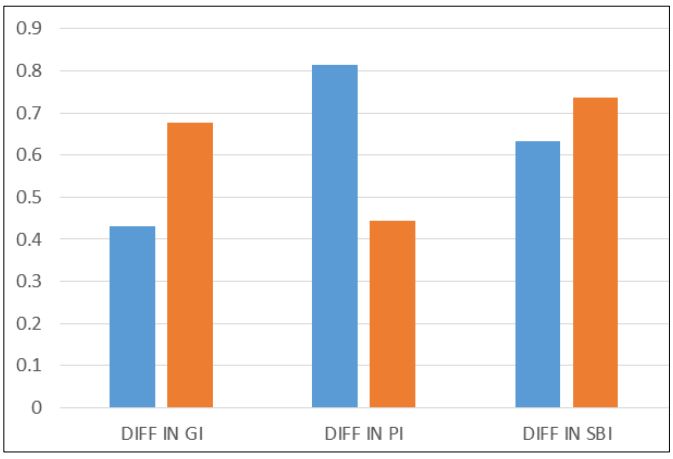

Fig 6: Comparison of the differences from baseline to 28 days

Discussion

The concept of antioxidant therapy in the treatment of numerous diseases including inflammatory periodontal disease exists in the literature. Because of its function CoQ10 has received much research attention in a medical literature in the last several years.

Bliznakov *et al.* [1] used CoQ10 to treat mice susceptible to tumors and observed that there was reduction in tumor size or number of those mice that developed tumors. He also investigated a parasitic model which consisted of mice that had been infected with malarial organism and found that CoQ10 potentiated the effectiveness of chloroquin and increased survivors.

Langsjoen *et al.* [7] demonstrated that CoQ10 enhanced the host defense mechanism in patients with AIDS and AIDS related complex.

However there is a dearth of new information regarding CoQ10, in the treatment of periodontal conditions.

Hanoika *et al.* [8] suggested that the needed oxygen supply to inflamed gingiva may be increased with oral administration of CoQ10 with a decrease in gingival index and pocket depth during a 2-month trial. Kinane *et al.* [9] found depressed T4/T8 ratios in early inset forms of periodontitis

Hanoika *et al.* [10] had demonstrated an increase in T4/T8 ratios with an oral administration of 100mg CoQ10 per day for 2 months. Listgarden *et al.* [11] had demonstrated decrease in motility of rods and improves periodontal health. Healing and repair of periodontal tissues depends on the adequate supply of coenzyme Q10 for efficient energy production and metabolic functions of periodontal tissues.

According to Nakamura and Littaru [12], a deficiency of coenzyme Q10 have been found in the gingiva of patients with periodontal disease. Gingival biopsies from patients with inflamed periodontal tissues showed a deficiency of CoQ10, in contrast to patients with normal periodontal tissues

In our study, there was significant reduction in plaque index scores, gingival scores and sulcular bleeding scores in the control group and in the test group there was significant reduction in both plaque scores and gingival index scores but a gradual reduction in sulcular bleeding index. There was a clinical improvement in both the test and control

In a study conducted by Brzozowska *et al.* [4] showed that Coenzyme Q10 with vitamin E has a beneficial effect on the periodontal tissue.

A split mouth trial conducted by Hanioka *et al.* [6] demonstrated improved periodontal scores along with gingival scores when coenzyme Q10 was applied alone or as an adjunct to scaling and root planning.

A study conducted by Figuero *et al.* [13] evaluated the potential oxidant/antioxidant interactions of nicotine with antioxidant coenzyme Q10 in smokers who were diagnosed with periodontitis and suggested that the catabolic effects of nicotine could be reversed by the addition of antioxidants such as Coenzyme Q10.

A study conducted by Manthena *et al.* [14] concluded that the use of coenzyme Q10 supplements as an adjunct to scaling and root planing showed significant reduction in gingival inflammation

This study shows some limitation that includes small sample size and the substantivity of the gel was not known. It was neither a sustained release nor controlled release formulation.

Topical application of the gel in chronic gingivitis resulted in significant reduction in plaque scores and gingival index scores but not in sulcular bleeding index in 28th days. The results are not similar to the earlier studies. Recently the use of tooth pastes and mouthwashes containing COQ10 allow contact of gingival tissues. Babbush *et al.* [15] conducted a double blind study that tested a commercially available fluoride toothpaste with CoQ10 β-cyclodextrin inclusion complex (Micron Active CoQ10) and found that it was significantly reduced gingivitis.

Conclusion

Topical application of Perio Qgel along with mechanical debridement has improved clinical parameters. In our research, there was significant reduction in plaque index scores, gingival scores but a gradual reduction in sulcular bleeding index. There was a clinical improvement.

Thus further long term clinical trials of Perio Q gel in larger sample sizes with long term revaluation along with other antioxidants are needed for their use in routine supportive periodontal therapy.

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