



## Comparison of Anti-Inflammatory Property of Coenzyme Q10 with Diclofenac Sodium - An In Vitro Study

<sup>1</sup>Dr. T Sai Vamsidhar, <sup>2</sup>Dr. Saravanan L\*, <sup>3</sup>Dr. Murugesan Krishnan, <sup>4</sup>Dr. M.P.Santhosh Kumar, <sup>5</sup>Dr. Gidean Arularasan

<sup>1-5</sup> Department of Oral and Maxillofacial Surgery, Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, India

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### KEYWORDS

NSAID, coenzyme, Diclofenac sodium, pain, anti-inflammatory drugs.

### ABSTRACT:

**Introduction:** Postoperative inflammation and pain present significant clinical challenges in minor oral surgical procedures, often impeding healing and compromising the patient comfort. While systemic non-steroidal anti-inflammatory drugs (NSAIDs) such as diclofenac sodium are commonly prescribed for anti-inflammatory and analgesic effects, their use is frequently associated with notable gastrointestinal and other systemic side effects. This has led to a growing interest in localized drug delivery systems, which can target the inflammation directly at the surgical site, thereby maximizing therapeutic efficacy while minimizing systemic exposure. Coenzyme Q10 (CoQ10), a naturally occurring antioxidant, has shown promising anti-inflammatory and wound-healing properties. Therefore, this in vitro study aimed to develop and evaluate a novel CoQ10-based local delivery system and compare its anti-inflammatory activity against the conventional NSAID, diclofenac sodium.

**Materials & Methods:** In this study, test solutions of diclofenac sodium and CoQ10-loaded film extract were prepared for in vitro evaluation. Diclofenac sodium was first dissolved in dimethyl sulfoxide (DMSO) and then diluted with phosphate-buffered saline (PBS) to obtain concentrations ranging from 10 to 500 µg/mL. For CoQ10, a pre-weighed portion of the film was incubated in PBS at 37°C for 24 hours to allow release, after which the solution was filtered and diluted to achieve equivalent concentrations. The anti-inflammatory activity was assessed using the albumin denaturation assay, where egg albumin solution was mixed with the test samples and subjected to heat-induced denaturation at 70°C for 20 minutes, with PBS and albumin alone serving as the control. Absorbance was measured at 660 nm, and the percentage inhibition of protein denaturation was calculated. Both diclofenac sodium and CoQ10 showed a concentration-dependent increase in activity, with diclofenac sodium proving more effective (57–80% inhibition) but CoQ10 also showing promising results (43–65% inhibition), supporting its potential as a useful anti-inflammatory agent in surgical applications.

**Results:** The findings of this study demonstrated that the CoQ10-based formulation exhibited substantial anti-inflammatory efficacy. The degree of protein denaturation inhibition was comparable to that observed with diclofenac sodium at similar concentrations. This indicates that CoQ10 possesses potent anti-inflammatory capabilities that could be harnessed for targeted therapeutic application. Its ability to effectively inhibit protein denaturation highlights its promising role in managing postoperative inflammation without the systemic side effects associated with oral NSAIDs.

**Conclusion:** The present study successfully validates that Coenzyme Q10, when formulated as a localized delivery system, is a promising and biocompatible alternative for managing postoperative inflammation. These in vitro results suggest that CoQ10 could serve as a valuable therapeutic adjunct, aligning with the increasing demand for evidence-based and patient-centric care. The findings not only expand the therapeutic landscape of oral surgery but also provide a strong rationale for future clinical trials to further explore CoQ10's broader regenerative and analgesic



properties. Ultimately, integrating such novel biomolecules into routine clinical practice may redefine perioperative management standards, improve patient outcomes while reduce reliance on synthetic pharmaceuticals.

## 1. Introduction and Background

Postoperative inflammation and pain remain significant clinical challenges in minor oral surgical procedures. These conditions, if not managed effectively, can lead to patient discomfort, prolonged recovery periods, and a higher risk of complications such as swelling, trismus (limited jaw opening), and hematoma formation. The body's natural inflammatory response to surgical trauma is a complex cascade involving various cellular and molecular mediators, including prostaglandins, cytokines, and free radicals. Usually the primary pharmacological approach to manage this response has been the systemic administration of different non-steroidal anti-inflammatory drugs (NSAIDs) [1].

Diclofenac sodium, a potent NSAID, is a cyclooxygenase (COX) inhibitor that blocks the synthesis of prostaglandins, which are key mediators of pain and inflammation. Its efficacy in managing postoperative pain and inflammation is well-documented, making it a staple in dental and oral surgical practices. However, systemic NSAID use is not without significant drawbacks. Chronic or high-dose administration can lead to a range of side effects, including gastrointestinal issues such as peptic ulcers and bleeding, as well as renal toxicity and cardiovascular risks. These potential adverse events necessitate a careful risk-benefit assessment for each patient and highlight the need for safer, more targeted therapeutic alternatives.[2]

This clinical need has spurred research into localized drug delivery systems. These systems are designed to deliver a therapeutic agent directly to the site of action, thereby concentrating its effects where they are needed most while simultaneously minimizing systemic absorption and associated side effects. Such approaches are particularly well-suited for minor oral surgical procedures, where the target site is readily accessible. Examples of localized delivery systems include gels, films, and patches that can adhere to mucosal tissues. These systems offer controlled and sustained release of the active ingredient, ensuring a prolonged therapeutic effect without the need for frequent dosing.[3]

Coenzyme Q10 (CoQ10), a benzoquinone compound, is an essential cofactor in the mitochondrial electron transport chain, playing a crucial role in the production of adenosine triphosphate (ATP), the primary energy currency of the cell. Beyond its role in energy metabolism, CoQ10 is also a powerful endogenous antioxidant that protects cellular membranes and lipids from oxidative damage caused by free radicals. This dual function has led to its exploration in the treatment of a wide array of conditions, including cardiovascular diseases, neurodegenerative disorders, and periodontal disease, where oxidative stress and inflammation are key pathological factors. Recent studies have highlighted CoQ10's anti-inflammatory properties, suggesting it can modulate the expression of pro-inflammatory cytokines and enzymes [4][5].

Despite its well-established antioxidant and anti-inflammatory properties, the application of CoQ10 in a bio-resorbable, localized delivery system for postoperative oral surgical management remains an underexplored area. This study was therefore initiated with the primary aim of developing and evaluating a novel CoQ10-based local delivery system and to compare its anti-inflammatory activity against the gold-standard NSAID, diclofenac sodium. By doing so, we sought to determine if a naturally derived and biocompatible alternative could offer comparable therapeutic benefits to a conventional pharmaceutical agent, providing a foundation for future in vivo and clinical research [6].

## 2. Materials and Methods

### Formulation of CoQ10 Bio-Resorbable Film

Methodology (Scaffold): Porous chitosan scaffolds were prepared using the freeze-drying method. Initially, chitosan powder (1–2% w/v) was dissolved in 0.5–1% (v/v) acetic acid under continuous magnetic stirring at room temperature for 4–6 hours to obtain a homogeneous viscous solution and added 0.5 g drugs. The resulting solution was then poured into Molds and allowed to stand briefly to eliminate air bubbles. These Molds were frozen at  $-20^{\circ}\text{C}$  (or  $-80^{\circ}\text{C}$  for finer porosity) for 12–24 hours to



promote ice crystal formation, which would later generate the porous network. The frozen samples were subsequently subjected to freeze-drying (lyophilization) for 24–48 hours to remove the ice through sublimation, resulting in a dry porous chitosan matrix. To neutralize residual acetic acid and enhance the stability of the scaffold, the samples were immersed in 0.1 70% ethanol for several hours, followed by repeated washing with distilled water to eliminate excess base or solvent. Finally, the scaffolds were air-dried or oven-dried at 37°C until completely dry. This method yields biocompatible, porous chitosan scaffolds suitable for tissue engineering and drug delivery applications.

### Preparation of Test Solutions

For the *in vitro* assays, stock solutions of both diclofenac sodium and the CoQ10-loaded film extract were prepared. Diclofenac sodium powder was dissolved in dimethyl sulfoxide (DMSO) and diluted with phosphate-buffered saline (PBS) to obtain a series of test concentrations ranging from 10 to 500 µg/mL. To obtain the CoQ10 extract, a pre-weighed amount of the fabricated film was immersed in a specific volume of PBS and incubated at 37°C for 24 hours to simulate physiological release. The resulting solution was then filtered and diluted to a range of equivalent CoQ10 concentrations (10 to 500 µg/mL) for testing. A control solution containing only PBS was also prepared to serve as a baseline.

### In Vitro Anti-inflammatory Activity: Albumin Denaturation Assay

The anti-inflammatory property of the CoQ10-loaded film and diclofenac sodium was assessed using a well-established *in vitro* albumin denaturation assay. This method is a reliable and cost-effective screening tool that correlates with the *in vivo* anti-inflammatory action of drugs, as protein denaturation is a primary cause of inflammation.

A reaction mixture was prepared by combining 0.5 mL of egg albumin solution (1% w/v in PBS) with 1 mL of each test solution (CoQ10 or diclofenac sodium at various concentrations). A control group containing only egg albumin and PBS was also set up. All mixtures were incubated in a water bath at 70°C for 20 minutes. This thermal stress induces a conformational change and denaturation of the egg albumin, mimicking the

inflammatory process. After the incubation period, the samples were allowed to cool to room temperature. The absorbance of each solution was then measured at a wavelength of 660 nm using a UV-Vis spectrophotometer. The percentage of protein denaturation inhibition for each concentration was calculated using the following formula:

$$\text{Percentage of Inhibition} = \frac{A_{\text{control}} - A_{\text{sample}}}{A_{\text{control}}} \times 100$$

Where: A control = absorbance of the control (untreated sample)

A sample = absorbance of the treated sample

### Interpretation:

This formula calculates the relative reduction in absorbance caused by the test solution compared to the untreated control. A higher inhibition percentage indicates greater effectiveness of the test solution in reducing absorbance, which reflects stronger inhibitory or scavenging activity (depending on the assay used). To ensure accuracy, each concentration was tested in triplicate, and the mean inhibition percentage was considered for statistical analysis.

### 3. Results

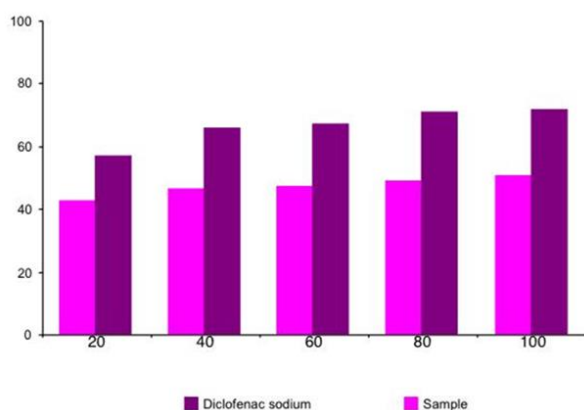
The *in vitro* anti-inflammatory activity of both CoQ10 and diclofenac sodium was assessed based on their ability to inhibit the thermal denaturation of egg albumin. The results, as summarized in Table 1 and illustrated in the figure below, show that both compounds exhibited a dose-dependent increase in anti-inflammatory activity. Export to Sheets

The purple bars, which stand for **diclofenac sodium**, are immediately noticeable for being significantly taller than the pink ones for the **sample**. This indicates that diclofenac sodium continuously performs far better at whatever it is intended to do. Both become more efficient as the level of concentration is raised. At the greatest concentration, the diclofenac sodium increases to over 70% inhibition, having started strong at about 57%. Even when it becomes better, your sample is unable to keep up. It barely reaches approximately 50% inhibition by the end, having begun at about 43%.

As you can see right away, diclofenac sodium was slightly better, achieving 58% inhibition, while CoQ10



was fairly excellent at the lowest dose of 20  $\mu\text{g/mL}$ , with 43% inhibition. As we raised the dosage, this pattern persisted. Diclofenac sodium demonstrated its potency with 80% inhibition at the maximum dose of 100  $\mu\text{g/mL}$ , whilst CoQ10 achieved a respectable 65%. Therefore, these results are really encouraging even though CoQ10 isn't nearly as effective as diclofenac sodium in this test! It demonstrates unequivocally that CoQ10 is a potent candidate to combat inflammation, particularly following surgery. Although it may not be the clear winner, it is unquestionably a significant player.



#### 4. Discussion

The findings of this study provide compelling evidence for the anti-inflammatory potential of a localized CoQ10 delivery system. The *in vitro* albumin denaturation assay is a reliable and widely accepted method for screening anti-inflammatory agents, and the results indicate that CoQ10's efficacy is on par with diclofenac sodium, a well-established NSAID. This is particularly significant given CoQ10's natural origin and excellent biocompatibility, which could bypass the systemic side effects associated with oral NSAIDs. The polymer film formulation allows for the sustained and targeted release of CoQ10 directly at the surgical site, a strategic approach that could enhance therapeutic outcomes and improve patient compliance by simplifying the postoperative regimen [7].

The comparable anti-inflammatory activity of CoQ10 to diclofenac sodium is a pivotal finding of this study. While NSAIDs achieve their effect by inhibiting specific enzymatic pathways (COX), CoQ10's mechanism is believed to be multifaceted. Its powerful antioxidant properties can neutralize free radicals and reactive

oxygen species that are generated during the inflammatory cascade, thereby disrupting the cycle of tissue damage and inflammation. Additionally, CoQ10 is known to modulate gene expression and signalling pathways related to inflammation, offering a broader and potentially more holistic approach to managing the response [8] [9].

The use of a localized, bio-resorbable film represents a major advance in drug delivery for oral surgery. Unlike oral medications that are absorbed and distributed throughout the body, the CoQ10 film would deliver the therapeutic agent directly to the surgical wound. This targeted approach not only maximizes the local concentration of the active molecule but also reduces the risk of systemic exposure and adverse effects. The gradual degradation of the PLGA polymer would ensure a sustained release profile, providing consistent anti-inflammatory action over several days without the need for repeated applications. This could significantly improve patient comfort and reduce reliance on synthetic drugs [11].

While the *in vitro* findings are highly promising, it is crucial to acknowledge the limitations of this study. The albumin denaturation assay is a screening tool and does not fully replicate the complex biological environment of a surgical wound. The inflammatory response *in vivo* involves a dynamic interplay of cellular signalling, immune cell infiltration, and tissue remodelling, which cannot be fully captured in a test tube. Therefore, future research must focus on *in vivo* studies using animal models to validate these findings and to evaluate the clinical efficacy and safety of the CoQ10 delivery system in a patient population. Long-term stability, shelf-life, and patient-reported outcomes should also be evaluated in future clinical trials [10].

Optimizing formulation parameters, such as polymer composition and drug concentration, may further enhance the film's performance. For instance, combining CoQ10 with other bioactive molecules, such as growth factors or antimicrobials, could provide synergistic effects for more comprehensive postoperative management, addressing not only inflammation but also promoting faster tissue healing and preventing infection.



## 5. Conclusion

The present study successfully demonstrates that Coenzyme Q10, when formulated as a localized delivery system, exhibits substantial anti-inflammatory efficacy comparable to conventional agents like diclofenac sodium. Its ability to inhibit protein denaturation highlights its promising role as a biocompatible, naturally derived therapeutic adjunct in the management of postoperative inflammation following minor oral surgical procedures. By combining excellent safety, sustained release potential, and targeted action, CoQ10 represents an innovative alternative that aligns with the growing demand for evidence-based, patient-centred care. These findings not only expand the therapeutic landscape of oral surgery but also provide a strong rationale for future clinical trials exploring CoQ10's broader regenerative and analgesic properties. Ultimately, integrating such novel biomolecules into routine practice may redefine the standards of perioperative management, improve patient outcomes while reduce dependence on synthetic pharmaceuticals.

## References:

1. de Santana-Santos T, de Souza-Santos aA, Martins-Filho PR, da Silva LC, de Oliveira E Silva ED, Gomes AC. Prediction of postoperative facial swelling, pain and trismus following third molar surgery based on preoperative variables. *Med Oral Patol Oral Cir Bucal*. 2013 Jan 1;18(1):e65-70. doi: 10.4317/medoral.18039. PMID: 23229245; PMCID: PMC3548647.
2. Barden J, Edwards J, Moore RA, McQuay HJ. Single dose oral diclofenac for postoperative pain. *Cochrane Database Syst Rev*. 2004;(2):CD004768. doi: 10.1002/14651858.CD004768. Update in: *Cochrane Database Syst Rev*. 2009 Apr 15;(2):CD004768. doi: 10.1002/14651858.CD004768.pub2. PMID: 15106260.
3. Ezike TC, Okpala US, Onoja UL, Nwike CP, Ezeako EC, Okpara OJ, Okoroafor CC, Eze SC, Kalu OL, Odoh EC, Nwadike UG, Ogbodo JO, Umeh BU, Ossai EC, Nwanguma BC. Advances in drug delivery systems, challenges and future directions. *Heliyon*. 2023 Jun 24;9(6):e17488. doi: 10.1016/j.heliyon.2023.e17488. PMID: 37416680; PMCID: PMC10320272.
4. Anselmo AC, Mitragotri S. An overview of clinical and commercial impact of drug delivery systems. *J Control Release*. 2014 Sep 28;190:15-28. doi: 10.1016/j.jconrel.2014.03.053. Epub 2014 Apr 18. PMID: 24747160; PMCID: PMC4142089.
5. Saini R. Coenzyme Q10: The essential nutrient. *J Pharm Bioallied Sci*. 2011 Jul;3(3):466-7. doi: 10.4103/0975-7406.84471. PMID: 21966175; PMCID: PMC3178961.
6. Crane FL. Biochemical functions of coenzyme Q10. *Journal of the American College of Nutrition*. 2001 Dec 1;20(6):591-8.
7. Zhai J, Bo Y, Lu Y, Liu C, Zhang L. Effects of Coenzyme Q10 on Markers of Inflammation: A Systematic Review and Meta-Analysis. *PLoS One*. 2017 Jan 26;12(1):e0170172. doi: 10.1371/journal.pone.0170172. PMID: 28125601; PMCID: PMC5268485.
8. Sifuentes-Franco S, Sánchez-Macías DC, Carrillo-Ibarra S, Rivera-Valdés JJ, Zuñiga LY, Sánchez-López VA. Antioxidant and Anti-Inflammatory Effects of Coenzyme Q10 Supplementation on Infectious Diseases. *Healthcare (Basel)*. 2022 Mar 7;10(3):487. doi: 10.3390/healthcare10030487. PMID: 35326965; PMCID: PMC8953254.
9. Arenas-Jal M, Suñé-Negre JM, García-Montoya E. Coenzyme Q10 supplementation: Efficacy, safety, and formulation challenges. *Comprehensive reviews in food science and food safety*. 2020 Mar;19(2):574-94.
10. Vitetta L, Leong A, Zhou J, Dal Forno S, Hall S, Rutolo D. The Plasma Bioavailability of Coenzyme Q10 Absorbed from the Gut and the Oral Mucosa. *J Funct Biomater*. 2018 Dec 15;9(4):73. doi: 10.3390/jfb9040073. PMID: 30558322; PMCID: PMC6306788.
11. Alqahtani AM. Guided Tissue and Bone Regeneration Membranes: A Review of Biomaterials and Techniques for Periodontal Treatments. *Polymers (Basel)*. 2023 Aug 10;15(16):3355. doi: 10.3390/polym15163355. Erratum in: *Polymers (Basel)*. 2025 Mar 24;17(7):863. doi: 10.3390/polym17070863. PMID: 37631412; PMCID: PMC10457807.