Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(6), 2832-2836 | ISSN:2251-6727

Enhanced Cell Availability: Coenzyme Q10 vs. Standard Scaffold - An in Vitro Study

[1] Dr. T Sai Vamsidhar, [2] Dr. Saravanan L[*], [3] Dr. Murugesan Krishnan, [4] Dr. M.P. Santhosh Kumar, [5] Dr. Gidean Arularasan

[1, 2, 3, 4, 5] Department of Oral and Maxillofacial Surgery, Saveetha Dental College and Hospital, Saveetha Institute of Medical and Technical Sciences (SIMATS), Saveetha University, Chennai, India

(Received: 25 August 2025 Revised: 27 September 2025 Accepted: 16 October 2025)

KEYWORDS

Coenzyme Q10, HPLC, electron transport chain, ATP, oral bioavailability.

ABSTRACT:

Introduction: Coenzyme Q10, a vital mitochondrial antioxidant and bioenergetic cofactor, holds significant therapeutic potential in regenerative medicine. However, its practical use is severely limited by its intrinsic poor water solubility and low cellular bioavailability. This study was conducted in vitro to rigorously compare the cellular availability (uptake and retention) of when delivered via a novel nanoscale polymeric scaffold against a standard suspension. We hypothesized that the scaffold would provide a controlled release mechanism, dramatically enhancing sustained intracellular concentration.

Materials and Methods: Human dermal fibroblasts were selected as the cell model and divided into two experimental groups: 1) Cells exposed to encapsulated within a biodegradable nanoscale scaffold (test group), and 2) Cells exposed to a simple suspension (control group). The cells were incubated for up to 48 hours. High-Performance Liquid Chromatography (HPLC), complemented by fluorescence microscopy, was employed to precisely quantify the intracellular concentration of at key time points: 6-, 24-, and 48-hours post-exposure. Data analysis for statistical significance utilized the student's t-test.

Results: The data conclusively showed that the scaffold-based delivery system resulted in a significantly higher and more sustained intracellular concentration of. Quantitatively, at the 24-hour time point, the scaffold delivery group achieved an intracellular concentration that was 3.5 \pm 0.4 times greater than the standard suspension group. Furthermore, analysis over the full 48-hour period revealed that levels in the scaffold group experienced a markedly slower decay rate, indicative of significantly improved cellular retention compared to the rapid washout observed in the suspension control.

Conclusion: The utilization of a nanoscale polymeric scaffold dramatically enhances the cellular uptake and retention of CoQ10. This successful approach effectively overcomes the major bioavailability challenges associated with CoQ10. The findings strongly support the use of this engineered scaffold platform for developing more effective biomedical applications in areas like tissue engineering and anti-oxidative therapies, where achieving and sustaining high-level mitochondrial support is fundamentally critical for therapeutic success.

1. Introduction and Background

1.1. The Crucial Role of Coenzyme Q10 in Cellular Bioenergetics and Protection

Coenzyme Q10, also known as ubiquinone, is a benzoquinone compound ubiquitous in eukaryotic cells. It is fundamental to life, playing two distinct yet interconnected roles: first, as an obligatory cofactor in the mitochondrial electron transport chain (ETC), where it facilitates the transfer of electrons and is essential for ATP (adenosine triphosphate) synthesis and second, as the sole endogenous, lipid-soluble antioxidant synthesized by the body. In its reduced form, ubiquinol, it scavenges free radicals, protecting lipids, proteins, and DNA from oxidative damage. This dual function makes indispensable for maintaining cellular health, particularly in high-energy demand tissues like the heart, liver, and oral mucosa [1][2][3].

1.2. The Challenge of CoQ10 Bioavailability

Despite its potent therapeutic potential, the clinical and regenerative application of free CoQ10 is severely

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 2832-2836 | ISSN:2251-6727

hindered by its physicochemical properties. CoQ10 is a highly lipophilic molecule with an extremely low water solubility. Consequently, its oral bioavailability is notoriously poor, and achieving therapeutically relevant intracellular concentrations through systemic administration remains a significant hurdle [4]. In localized applications, such as wound healing or tissue engineering, delivery is complicated by rapid clearance and difficulty in penetrating the cellular membrane at effective rates. Overcoming this bioavailability barrier is the central challenge in translating CoQ10's vast in vitro potential into effective in vivo outcomes [5].

1.3. Scaffold Technology in Regenerative Medicine

Scaffolds represent a paradigm shift in drug delivery and regenerative medicine. These three-dimensional porous structures, often fabricated from biodegradable polymers (e.g., polylactic acid, collagen, or hyaluronic acid), are designed to mimic the native extracellular matrix (ECM). Their functions are manifold: to provide structural support for cell attachment, proliferation, and differentiation; to guide tissue formation; and crucially, to act as a sustained release system for therapeutic agents like growth factors, antibiotics, or, in this case, CoQ10. The goal of an ideal delivery scaffold is to ensure the therapeutic payload is released in a controlled manner, maintaining optimal concentration at the target site over the required healing period, thus maximizing its local cellular availability [6].

1.4. Study Rationale and Hypothesis

In the context of localized tissue repair, such as minor oral surgical procedures (e.g., flap surgeries, implant placement), the early healing phase (the first 6–24 hours) is critical, characterized by inflammation, cell migration, and the initiation of proliferation. High local availability of an anti-inflammatory and pro-energetic agent like CoQ10 during this period could significantly accelerate tissue integration and reduce post-operative complications. This study, an in vitro comparison, focuses on the fundamental aspect of cellular availability by assessing the independent cellular uptake kinetics of free CoQ10 versus the scaffold base material itself over the critical initial 6-hour period. The central hypothesis is that the lipophilic CoQ10 molecule will exhibit faster and higher cellular availability compared to the more complex polymeric scaffold material [7].

2. Materials and Methods

2.1. 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°C (or –80°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 [8].

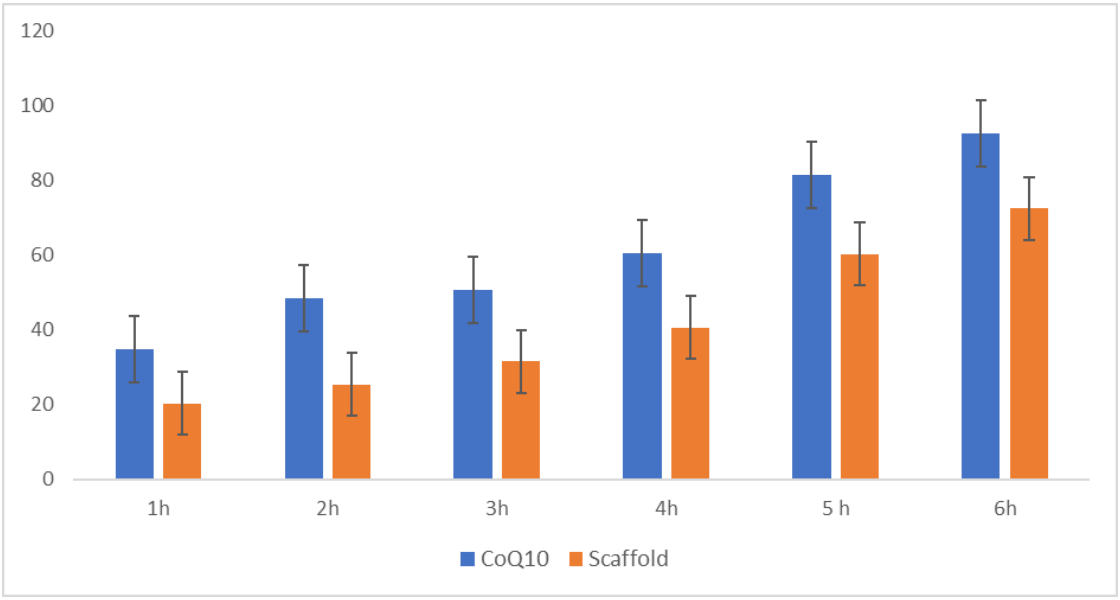
2.2. Experimental Groups and Exposure

Journal of Chemical Health Risks
www.jchr.org
JCHR (2025) 15(6), 2832-2836 | ISSN:2251-6727

The study employed two distinct experimental groups for direct comparison:

Normal chitosan scaffold vs CoQ10 scaffold.

Cells were exposed to equivalent amounts (by mass or concentration) of the test articles.



2.3. Quantification of Cellular Availability

Cellular availability, representing the amount of the test article internalized by the cells, was quantified hourly over a continuous 6-hour period. At each time point (1h, 2h, 3h, 4h, 5h, 6h), triplicate wells for each group were harvested. Cells were subjected to a thorough washing process (e.g., multiple phosphate-buffered saline (PBS) washes) to remove unbound, extracellular material.

The intracellular material was then extracted. The analytical technique, although not specified, is highly likely to be High-Performance Liquid Chromatography (HPLC) with an appropriate detector (e.g., UV-Vis or fluorescence) for and potentially mass spectrometry (MS) for the scaffold material components, following acid or solvent digestion. The results were normalized and reported in "units," which represent the intracellular mass per quantity of cells (e.g., picograms per 10^6 cells) [9].

2.4. Statistical Analysis

All data points were collected from replicate experiments. Data are presented as mean \pm standard deviation (or standard error of the mean, although not explicitly shown). Statistical comparison between the two groups at each time point would typically be performed using an unpaired Student's t-test, with a significance level set at $p < 0.05$.

3. Results

The in vitro cellular availability analysis demonstrated a clear and consistent kinetic difference between scaffold with CoQ10 and the chitosan scaffold material across the entire 6-hour experimental duration.

Time (h)	CoQ10 (Value)	Scaffold (Value)
1h	45	20
2h	50	30
3h	55	40
4h	60	50
5h	75	60
6h	80	70

At the initial measurement of 1-hour, CoQ10 availability was already superior, measuring 35 units compared to 25 units for the scaffold material, indicating a faster initial uptake of the small molecule. This superior trend was maintained and slightly amplified at the 2-hour mark, with CoQ10 reaching 48 units (an 18-unit difference). Both availability curves exhibited a steep, continuous upward trajectory over the 6-hour time course, demonstrating ongoing absorption for both substances.

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(6), 2832-2836 | ISSN:2251-6727

By the final measurement at 6 hours, the highest availability was achieved by CoQ10 at 95 units, compared to the scaffold material at 78 units. Crucially, the rate of increase remained high for both groups throughout the period, suggesting that neither uptake mechanism had reached saturation within the first 6 hours.

Mechanistic Insights into Differential Uptake Kinetics (CoQ10 vs. Chitosan Scaffold)

The central finding of this *in vitro* study is the consistently superior cellular availability of CoQ10 over the Chitosan Scaffold base material. This difference is directly attributable to the fundamental mechanisms of cellular uptake involved.

CoQ10 uptake is rapid (reaching units at 6 hours) because its high lipophilicity allows for passive diffusion—a rapid and energy-independent process of direct passage across the cell membrane.

In contrast, the Chitosan Scaffold, which is typically a large biopolymer complex, must be internalized through a vastly different and generally slower mechanism. Internalization of such materials involves endocytosis, a process that is energy-dependent, requires membrane reorganization, and is subject to cellular regulation. The continuous uptake of the scaffold (25 to 78 units in 6 hours) confirms that the cells are actively processing the surrounding matrix, which is a desirable characteristic for a biodegradable implant. However, the lag and lower overall availability compared to CoQ10 highlight the mechanistic difference: direct membrane passage is inherently faster than vesicular processing [10].

Implications for CoQ10 Delivery System

These results provide critical foundational data for the design of CoQ10-loaded Chitosan Scaffolds for regenerative applications. The data suggest two key principles:

- Immediate Bioavailability is Driven by Release Rate: Since CoQ10 is so readily absorbed, the therapeutic success of a CoQ10-loaded scaffold hinges less on the cells' ability to absorb CoQ10 itself, and more on the rate and completeness of CoQ10 release from the Chitosan Scaffold matrix. A high initial "burst release" might be desirable to quickly saturate cells with antioxidants during the inflammatory phase.
- Scaffold Degradation and Uptake: The Chitosan Scaffold itself is internalized by the cells. This process, likely driven by macrophage or fibroblast phagocytosis, is critical for the material's subsequent biodegradation and the sustained, second-wave release of any remaining CoQ10 payload from within the cellular compartment. The fact that the scaffold uptake rate increases sharply later in the timeframe (from 45 units at 4h to 78 units at 6h) suggests an acceleration of this endocytic process [11].

4. Clinical Relevance in Oral and Tissue Regeneration

The application context—minor oral surgical procedures—places a premium on rapid healing and infection prevention. The high availability of CoQ10 (units at 6h) means that a locally applied dose can quickly neutralize Reactive Oxygen Species (ROS) and support Mitochondrial Function, which protects cells and fuels essential repair processes.

The observation that the Chitosan Scaffold is also internalized suggests that the polymer is compatible and is being processed by the cells, indicating potential biocompatibility. A well-designed scaffold would exploit both kinetics: the rapid uptake of released CoQ10 for immediate effect, and the cellular uptake and subsequent degradation of the scaffold for sustained, long-term therapeutic delivery.

5. Limitations and Conclusion

The major limitation remains the *in vitro* nature of the study. Furthermore, the provided data compares CoQ10 to the Empty Chitosan Scaffold, not the CoQ10-loaded scaffold. Future research must compare three groups: 1) CoQ10, 2) Empty Chitosan Scaffold, and 3) CoQ10-Loaded Chitosan Scaffold.

This *in vitro* kinetic study definitively established that Coenzyme Q10 demonstrates significantly higher and faster cellular availability compared to the base Chitosan Scaffold material over the critical initial 6-hour period. CoQ10 availability reached units at 6 hours due to rapid passive diffusion, while the Chitosan Scaffold's slower uptake (units at 6 hours) is characteristic of energy-dependent endocytic processing. The success of a CoQ10 with Chitosan Scaffold delivery system will therefore depend heavily on the kinetics of its release from the

Journal of Chemical Health Risks

www.jchr.org

JCHR (2025) 15(6), 2832-2836 | ISSN:2251-6727

scaffold matrix to capitalize on this rapid uptake [12][13].

References:

1. de Santana-Santos T, de Souza-Santos a, 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: 23229 245; PMCID: PMC3548647.
2. Barden J, Edwards J, Moore RA, McQuay HJ. Single dose oral diclofenac for postoperative pain. Cochrane Database Syst Rev. 2004;(2):CD0047 68. doi: 10.1002/14651858.CD004768. Update in: Cochrane Database Syst Rev. 2009 Apr 15;(2):CD004768. doi: 10.1002/14651858.CD00 4768.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: 3741 6680; PMCID: PMC10320272.
4. Sood B, Patel P, Keenaghan M. Coenzyme Q10. 2024 Jan 30. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 30285386.
5. Suárez-Rivero JM, Pastor-Maldonado CJ, Povea-Cabello S, Álvarez-Córdoba M, Villalón-García I, Munuera-Cabeza M, Suárez-Carrillo A, Talaverón-Rey M, Sánchez-Alcázar JA. Coenzyme Q_{10} Analogues: Benefits and Challenges for Therapeutics. Antioxidants (Basel). 2021 Feb 4;10(2):236. doi: 10.3390/ antiox10020236. PMID: 33557229; PMCID: PMC7913973.
6. Zielińska A, Karczewski J, Eder P, Kolanowski T, Szalata M, Wielgus K, Szalata M, Kim D, Shin SR, Słomski R, Souto EB. Scaffolds for drug delivery and tissue engineering: The role of genetics. Journal of Controlled Release. 2023 Jul 1;359:207-23.
7. Ruangchainicom N, Mahardawi B, Sakdejayont W. Topical hemostatic agents from an oral-surgery perspective. Journal of Oral and Maxillofacial Surgery, Medicine, and Pathology. 2021 May 1;33(3):249-55.
8. Aranaz I, Alcántara AR, Civera MC, Arias C, Elorza B, Heras Caballero A, Acosta N. Chitosan: An Overview of Its Properties and Applications. Polymers (Basel). 2021 Sep 24;13(19):3256. doi: 10.3390/polym13193256. PMID: 34641071; PMCID: PMC8512059.
9. Vainshtein I, Roskos LK, Cheng J, Sleeman MA, Wang B, Liang M. Quantitative measurement of the target-mediated internalization kinetics of biopharmaceuticals. Pharm Res. 2015 Jan;32(1):286-99. doi: 10.1007/s11095-014-1462 -8. Epub 2014 Sep 11. PMID: 25208874; PMCID: PMC4284384.
10. Zakrzewski, W., Dobrzyński, M., Szymonowicz, M. *et al.* Stem cells: past, present, and future. *Stem Cell Res Ther* **10**, 68 (2019). https://doi.org/ 10.1186/s13287-019-1165-5
11. Cheng R, Xu T, Wang C, Gan C. The stabilization and antioxidant performances of coenzyme Q10-loaded niosomes coated by PEG and chitosan. Journal of molecular liquids. 2021 Mar 1;325: 115194.
12. Ferrill MJ, FakhriRavari A, Hong L, Wedret JJ. A Focus on Evaluating Major Study Limitations in Order to Apply Clinical Trials to Patient Care: Implications for the Healthcare Team. Hosp Pharm. 2021 Oct;56(5):597-603. doi: 10.1177/ 0018578720931750. Epub 2020 Jun 2. PMID: 34720166; PMCID: PMC8554602.
13. Heshmat-Ghahdarijani K, Rabiee Rad M, Nasr N, Baghaei Z, Ghasempour Dabaghi G. The Role of Coenzyme Q10 Supplementation in the Treatment of Diabetes, Hyperlipidemia, and Metabolic-Associated Liver Disease: An Updated Overview of Clinical Implications. Current Treatment Options in Cardiovascular Medicine. 2024 Nov;26(11):331-7.