SYNTHESIS AND PROPERTIES OF NOVEL COENZYME-Q DERIVATIVES OBTAINED FROM COENZYME Q-0

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Coenzyme Q-0, 2,3-Dimethoxy-5-methyl-1,4-benzoquinone is an amphiphilic compound that is involved in the biosynthesis of Coenzyme Q-10.
As we know, Coenzyme Q-10 is one of the crucial compounds taking part in the synthesis of ATP in mitochondrial Electron transport chain. Its role is to transfer electrons between complexes I, II and III, while also transferring protons across inner mitochondrial membrane.
During the processes of oxidative phosphorylation, Coenzyme Q turns between two stable forms—**the oxidized Quinone** and the reduced **Quinol form**.

**QUINONE** (oxidized form)

\[ \text{2 e}^- + 2 \text{H}^+ \]

**QUINOL** (reduced form)
Next to its role as an electron&proton carrier, the **reduced form of Coenzyme Q-10** often acts as a radical scavenger for the **reactive oxygen species** generated during the processes of oxidative Phosphorilation.
Two years ago, a paper of Gulaboski, Mirceski et al. has been published in JACS, where the chemical properties of novel Coenzyme Q 10-derivatives synthesized in alkaline media have been reported.
Our aim was to study the chemical features of Novel Coenzyme Q-0 derivatives obtained by reaction of Coenzyme Q-0 in alkaline media, and to study its metal-binding and antioxidative properties.

Why $\text{Ca}^{2+}$?

$\text{Ca}^{2+}$ - are one of the most important secondary messengers in many physiological processes!!!
Coenzyme Q-0 dissolves nicely in neutral, slightly alkaline and acidic media while giving yellow-colored solutions.

The cyclic voltammograms of Coenzyme Q-0 in neutral media consist of a single reversible signal having features of diffusional controlled redox reaction.

Scan rate dependence of 0.1 mM Coenzyme Q-0 in pH of 7.00
One of our goals—to find whether native Coenzyme Q-0 can make complexes with \textit{Ca}^{2+} \textit{ions}

The voltammetric signal of native Coenzyme Q-0 is \textit{Insensitive to the concentration of Ca}^{2+} \textit{ions}= no complexation (same was true for other earth-alkaline cations)
When Coenzyme Q-0 is dissolved in alkaline media, there is quite fast conversion of the color from yellow to intensive red.

....this is a strong indication that chemical reaction takes place between Coenzyme Q-0 and the hydroxide OH- anions.
In cyclic voltammograms, one observes two signals of coenzyme Q-0 when it is dissolved in 0.1 M NaOH. While the signal of the native Coenzyme Q-0 (the peak assigned as “1” at more positive potentials) decreases with the time, the new signal (the peak assigned as “2” at more negative potentials) concomitantly gains in intensity.
Ratio of the peak II-peak I currents vs the time from SWV experiments of CoQ-0 in pH of 13
Upon re-titration from alkaline to neutral pH, the reaction between CoQ-0 and OH- ions can be quenched, while the color of solution in pH of 7.00 remains **RED**.
The products of the reaction of Coenzyme Q-0 and OH- anions have been identified by HPLC-MS.
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<th>Супстанца</th>
<th>$t_R$/min</th>
<th>UV max/nm</th>
<th>MW</th>
<th>[M+H]$^+$</th>
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HO
OCH$_3$
C
H$_3$C
3????? M = 176

HO
OCH$_3$
C
H$_3$C

HO
OCH$_3$
C
H$_3$C

HO
OCH$_3$
C
H$_3$C

HO
OCH$_3$
C
H$_3$C

HO
OCH$_3$
C
H$_3$C

HO
OCH$_3$
C
H$_3$C

HO
OCH$_3$
C
H$_3$C

HO
OCH$_3$
C
H$_3$C
One of the derivatives of CoQ-0 obtained in alkaline media makes complex with Ca$^{2+}$ cations in neutral solutions in stochiom. 1:2(L:M$^{2+}$)
The slope of the linear dependence of $E_{p,\text{mid}}$ vs $\log[c(\text{Ca}^{2+})]$ of 59mV implies formation of 1:2 (Ligand to Metal) Complex between the product of the electrochemical reaction and the Ca$^{2+}$ cations.

This slope implies that compound “2” is most probably the Ligand that binds Ca$^{2+}$ ions.
2,5-dihydroxy-3 methoxy-5-methyl-benzoquinone is the compound responsible for complexation with calcium cations.
To determine the antioxidative properties of the compounds created by reaction of Coenzyme Q-0 in alkaline media, we have used the ABTS assay as a reference standard.

ABTS undergoes stepwise two electron electrochemical oxidation while giving radical cation (in the first oxidation step), and double cation in the second oxidation step.
In presence of derivatives of CoQ-0 obtained in alkaline media, we observe *catalytic regenerative mechanisms* by both signals of ABTS.

Addition of

Reacted in 45 min in pH of 13, and afterwards Re-titrated to pH of 7.00
The catalytic increase of the current intensities in presence of the derivatives of Coenzyme Q-0 obtained in alkaline media is comparable to that observed of Vitamin C (same concentrations of Vit. C are used as in the experiment with Coenzyme Q-0 derivatives).

This comparison shows that the antioxidative capacity of the compounds obtained by alkaline reaction of Coenzyme Q-0 is similar to that of Vitamin C.
Conclusions

- There are many natural secondary metabolites with structures similar to that of Coenzyme Q-0 and its reported derivatives.

- Many of them can show similar features to those of derivatives obtained by alkaline reaction of CoQ-0.

- Metal-binding and antioxidative features of the CoQ-0 derivatives obtained in alkaline media are of fundamental importance for these classes of compounds.

... Isolation of the products is a task currently going on.
Literature:


