AMINO ACIDS-PEGYLATED CoQ10 ADDUCTS CONTROLLED RELEASE BEHAVIOUR AND ANTIOXIDANT ACTIVITY EVALUATION

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INTRODUCTION

Polyethylene glycol (PEG, HO-$(CH_2CH_2O)_n$-CH_2CH_2OH) is a polyether polymer easily available at low cost, soluble in both water and organic solvents and biocompatible. PEG is used as inert polymeric support in organic synthesis, as conjugating agent of bioactive molecules of pharmacological interest and its use is approved by FDA[1].

The ubiquinol (UBI), also considered the CoQ10 of next generation, is a raw material for food supplements with antioxidant activity; it plays a key role in energy production and in increasing body resistance[2]. In recent years nutraceuticals constituted by branched chain amino acids (Branch Chain Amino Acids, BCCA) have found increasing use as anti-fatigue active elements. The main objective of this work is to increase the water solubility and the ubiquinol stability through chemical modifications with polyethylene glycol (PEG) using spacer arms, consisting of specific amino acids, alanine, valine, isoleucine and leucine.

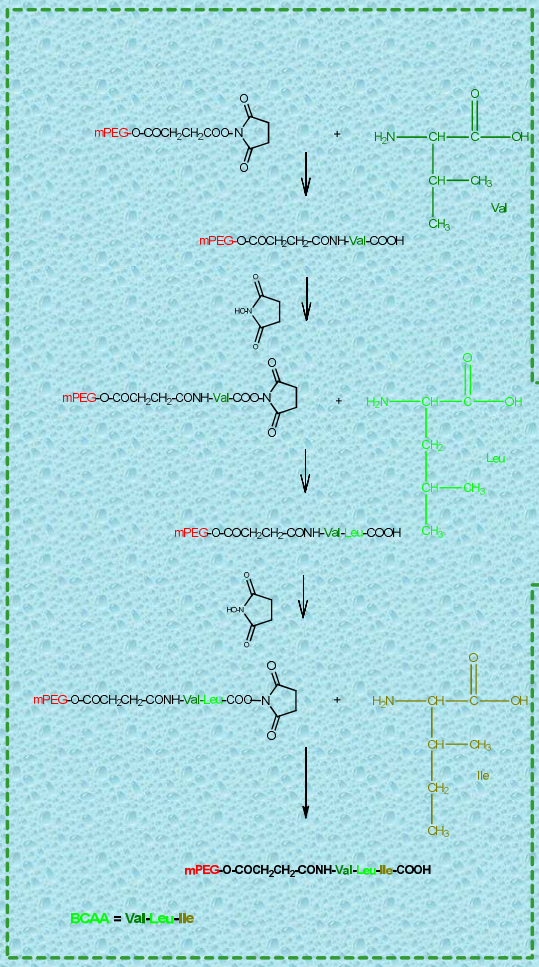
1. **Pasut, G., Veronese, F.M., State of the art in PEGylation: The great versatility achieved after forty years of research. J. Control. Rel. 2012,161, 461–472.**
2. **Novellino, E., Iadevaia V., Alimenti e nutraceutica; Edizioni Punto Effe Srl: Milano, 2012; pp. 75-78.**

RESULTS

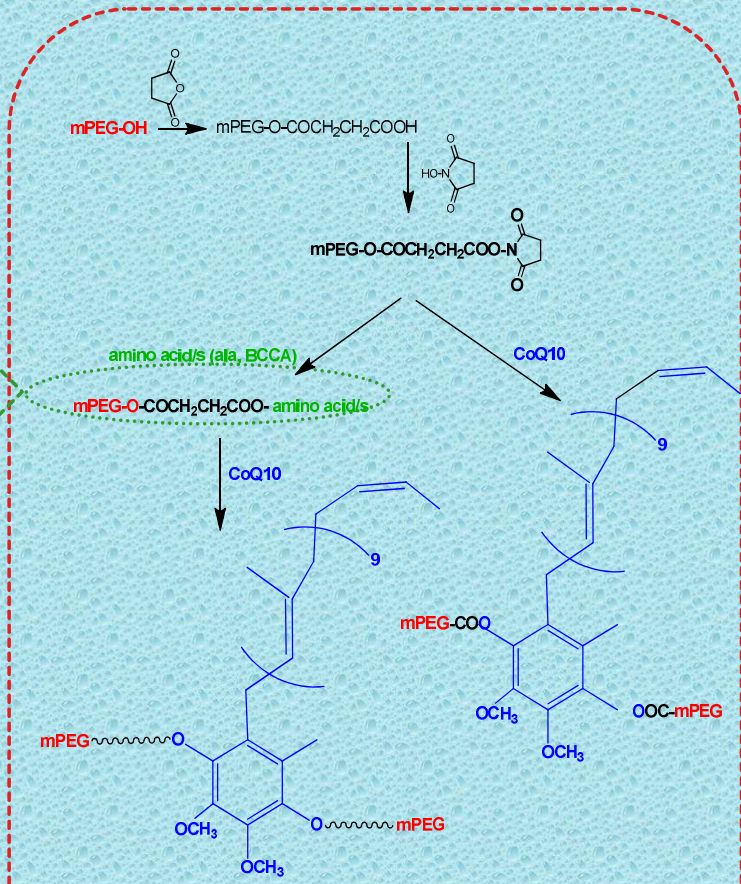
The aim of the present conjugation is to obtain an amphiphilic soluble mixed conjugates.

Pharmacokinetic studies *in vitro* show that the adducts deliver the corresponding beneficals amino acids together with ubiquinol giving a good antioxidant action.

Synthetic route of mPEG-amino acid-CoQ10 conjugates



Synthesis of mPEG-amino acids



Study *in vitro*

SAMPLE PREPARATION

Plasma + mobile phase + $FeCl_3$ 0.1%

⇩

Vortex

⇩

Centrifugation

⇩

Filtration (Millex-LH 0.22µm)

ANALYSIS

Mobile phase: H_2O, ACN, THF 5: 55: 40 (v/v)

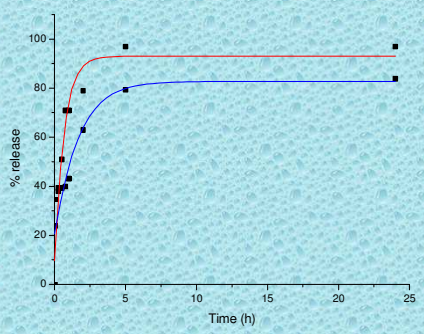
Column : RP C18 Gemini, 25 x 4 mm, 5µm, Supelco

Flow: 1 ml/min

λ: 275nm

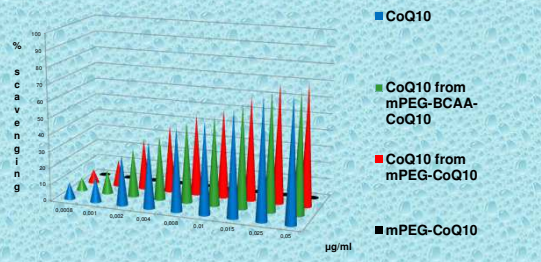
HPLC

The hydrolytic stability of the mPEG-conjugates was evaluated in mouse plasma



Release of CoQ10 from in plasma from adducts (mediated by esterase and amydase enzymes) at 37C (blu: mPEG-BCAA-CoQ10, red mPEG-CoQ10)

DPPH scavenging ability of CoQ10 when the assay was carried out in different samples of adducts



The scavenging activity is the some for standard CoQ10 and CoQ10 released from the adducts by enzymatic reactions in plasma. The scavenging activity was absent in the all adducts but gradually increases on the basis of drug delivery. mPEG-CoQ10 adducts does not present activity, because the phenolic group in eugenol is engaged in polymer bond

The radical scavenging activity was assayed spectrophotometrically by a loss of absorbance at 525nm.