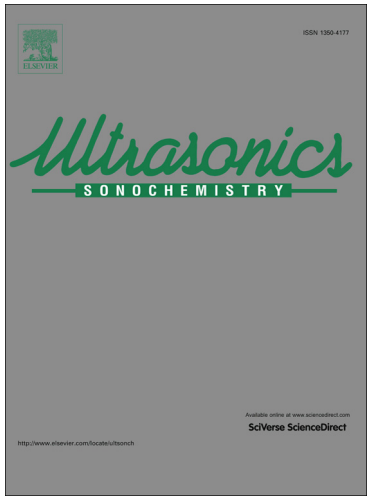

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PII: S1350-4177(17)30270-5
DOI: http://dx.doi.org/10.1016/j.ultsonch.2017.06.007
Reference: ULTSON 3730

To appear in: *Ultrasonics Sonochemistry*

Received Date: 11 March 2017
Revised Date: 8 June 2017
Accepted Date: 9 June 2017

Please cite this article as: S.F. Fonseca, N.B. Padilha, S. Thurow, J.A. Roehrs, L. Savegnago, M.N. de Souza, M.G. Fronza, T. Collares, J. Buss, F.K. Seixas, D. Alves, E.J. Lenardão, Ultrasound-promoted copper-catalyzed synthesis of bis-arylselanyl chrysin derivatives with boosted antioxidant and anticancer activities, *Ultrasonics Sonochemistry* (2017), doi: http://dx.doi.org/10.1016/j.ultsonch.2017.06.007

Ultrasound-promoted copper-catalyzed synthesis of bis-arylselanyl chrysin derivatives with boosted antioxidant and anticancer activities

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Abstract: Herein we report the use of ultrasonic irradiation (US) in the synthesis of six new semi-synthetic selenium-containing chrysin derivatives by a simple and effective methodology utilizing CuI as catalyst, in good to excellent yields (60-89%). It was observed that US accelerates the reaction compared to conventional heating with excellent selectivity for diselenylated products. Compounds were tested for their antioxidant and anticancer activities *in vitro* and it was observed that the presence of selenium in the A-ring of chrysin enhanced both antioxidant and anticancer properties. Semi-synthetic 6,8-bis(*o*-tolylselanyl)-chrysin **3b** has the best radical scavenging activity of DPPH (I_{max}: 39.79 µM) and $ABTS^+$ (IC_{50}: 6.5µM) radicals. Similarly, in the Reactive Species (RS) assay, **3b** showed high antioxidant activity in mice cortex (IC_{50}: 5.67 µM), whereas 6,8-bis(*p*-anisoylselanyl)-chrysin **3c** was the more active in the hippocampus (IC_{50}: 5.63 µM). The Se-chrysins were effective in prevention of lipid peroxidation, highlighting 6,8-bis(*p*-fluorophenylselanyl)-chrysin **3d** in cortex (IC_{50}: 0.54 µM) and **3b** in hippocampus (IC_{50}: 0.27 µM). In addition, **3d** was effective in inhibiting human lung adenocarcinoma (A549) cells growth, with a IC_{50} of 19.9 µM after 72 h of treatment, while 6,8-bis(*p*-anisoylselanyl)-chrysin **3c** presented the higher antiproliferative activity after 48 h of treatment (IC_{50} of 41.4 µM).