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

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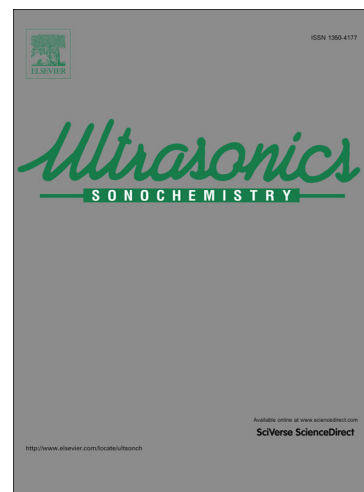
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Ultrasound-promoted copper-catalyzed synthesis of bis-arylselanyl chrysin derivatives with boosted antioxidant and anticancer activities

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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 μ M) and ABTS⁺ (IC_{50} : 6.5 μ M) radicals. Similarly, in the Reactive Species (RS) assay, **3b** showed high antioxidant activity in mice cortex (IC_{50} : 5.67 μ M), whereas 6,8-bis(*p*-anisoylselanyl)-chrysin **3c** was the more active in the hippocampus (IC_{50} : 5.63 μ M). The Se-chrysin derivatives were effective in prevention of lipid peroxidation, highlighting 6,8-bis(*p*-fluorophenylselanyl)-chrysin **3d** in cortex (IC_{50} : 0.54 μ M) and **3b** in hippocampus (IC_{50} : 0.27 μ M). In addition, **3d** was effective in inhibiting human lung adenocarcinoma (A549) cells growth, with a IC_{50} of 19.9 μ M 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 μ M).

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