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Synthesis and biological evaluation of new carbaisoflavonoids with anti-HCV activity

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Isoflavanoids have being used in our laboratory as inspiration for the preparation of new compounds with antiviral, antiparasitic and antineoplastic activities. Several new 1-carbaisoflavanones, designed as analogues of bioactive natural isoflavanones, were prepared in environmentally appropriate conditions, by palladium catalyzed α-arylation of α-tetralones with o-bromoalkoxyphenols. Compound LQB-314 exhibited the best profile for HCV inhibition, being active in both replicon reporter cells (IC_{50} 1.8 μM, SI > 111 in Huh7/Rep-Feo1b and IC_{50} 4.3 μM, SI> 46 in Huh7.5-FGR-JC1-Rluc2A). Compound LQB-307 was the more potent and selective in Huh7.5-FGR-JC1-Rluc2A replicon reporter cells (IC_{50} 1.5 μM, SI>101.4). Both compounds presented high bioselective index. Several of these substances have been converted in high yields into the corresponding 5-carbapterocarpens (total or partial demethylation of methoxy groups, followed by cyclization in a single step). These pterocarpens also showed potent anti-HCV activity. The best profile in Huh7/Rep-Feo1b replicon reporter cells was observed with LQB-359 (EC_{50} 5.5 μM/SI 20), while LQB-418 was the most active in Huh7.5-FGR-JC1-Rluc2A replicon reporter cells (EC_{50} 1.5 μM/SI 70). Hydroxy groups at A- and D-rings are essential for anti-HCV activity, and substitutions in the A-ring at positions 3 and 4 resulted in enhanced activity of the compounds.

Biography

Paulo Roberto Ribeiro Costa obtained his Post-doctoral studies at Université Joseph-Fourier (1984) and Université Paris-Sud (1988). He is Full Professor of Organic Chemistry at the Federal University of Rio de Janeiro since 1996 and has published more than 110 papers in reputed journals. He collaborated with several laboratories of the biological area in projects aiming the discovery of new bioactive compounds, especially isoflavonoid analogues with antiviral, antiparasitic and antineoplasic properties.

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