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Synthesis and crystal structure of a new anticancer candidate: RPF151

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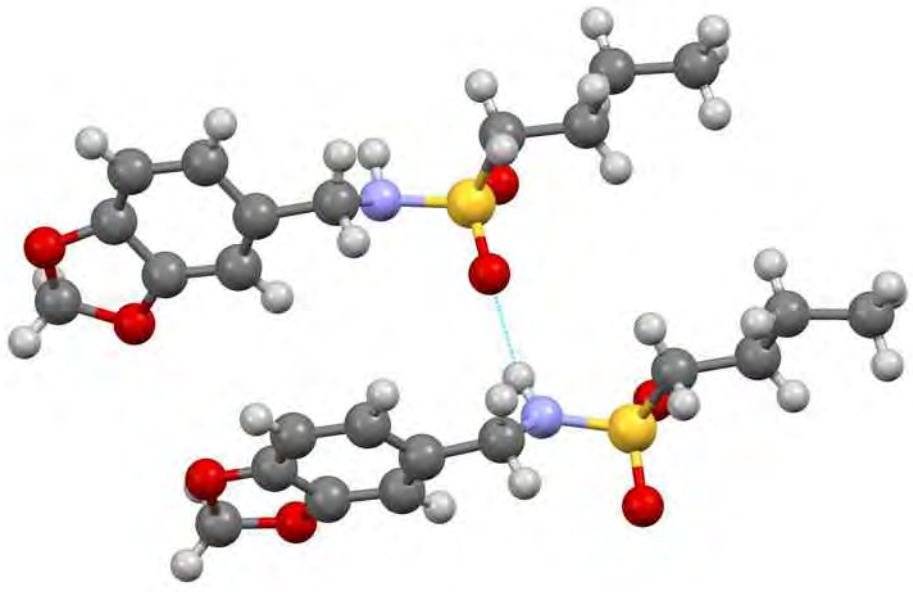
This work reports on the synthesis, crystal structural determination, conformational analysis and antiproliferative activity of an alkylsulfonamide analogue of capsaicin – RPF151 (N-(benzo[d][1,3]dioxol-5-ylmethyl)butane-1-sulfonamide). Capsaicin is the primary pungent and irritating natural product present in a variety of red chilli peppers of the genus Capsicum, and was reported to selectively inhibit the growth and to induce apoptosis in a wide variety of tumour cell lines.1-3 RPF151 was obtained by a simple reaction of 1-butanesulfonyl chloride with piperonylamine, in an anhydrous DCM (dichloromethane) and TEA (tetraethylammonium) mixture (Yield 70%). The crystal structure determination was carried out by means of an ab initio simulated annealing approach using X-ray powder diffraction data. RPF151 crystallized under a monoclinic system (P21/a) with final unit cell parameters refined using the Rietveld method: a = 29.0171(13) Å, b = 10.4745(3) Å, c = 9.1117(3) Å, β = 104.268(4)°, V = 2683.98(17) Å3, Z = 8, Z' = 2. The statistical parameter as well as R-factors were: χ2 = 1.11, Rwp = 0046, Rexp = 0.042 and RBragg = 0.010. The molecules are held together along the c-axis by hydrogen bonds involving the atoms N(37)–H(42)···O(4). Calculated elemental analysis for C12H17NO4S (271.09 g mol-1) shows C = 53.12, H = 6.32 and N = 5.16 while experimental values are C = 53.13, H = 6.39 and N = 5.14. The effects of RPF151 10 µM on human umbilical vein endothelial cells (HUVEC) proliferation was tested by flow cytometry. It was verified that RPF151 induced changes on cell morphology, a fact corroborated by HUVEC cell size and complexity. Furthermore, it caused a significant reduction on cell proliferation and evidenced no cytotoxic effects. Therefore, RPF151 could be developed as a candidate to an anti-angiogenic drug for the fighting against cancer. Acknowledgments: We are grateful to FAPESP (proc. nr.: 2013/18160-4, 2012/23233-8 and 2008/10537-3), CNPq (proc. nr. 305186/2012-4 and 477296/2011-4) and Provost's Office for Research of the University of São Paulo for financial support.

[1] *K. Ito, T. Nakazato, K. Yamato, et al., Cancer Res., 2004, 64, 1071-1078.,* ***[2]*** *S. P. Huang, J. C. Chen, C. C. Wu, et al., Anticancer Res., 2009, 29, 165-174.,* ***[3]*** *R. Maity, J. Sharma and N. R. Jana, J. Cell. Biochem., 2010, 109, 933-942.*



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