co-treatment of LAQ824 increased Gleevec®-induced apoptosis of CML-BC cells. LAQ824 also down-regulated levels of mutant Bcr-Abl, relevant to blast crisis, and induced apoptosis of Gleevec®-resistant primary CML-BC cells, suggesting that LAQ824 might be a promising agent in the treatment of Gleevec®-sensitive or -refractory CML.

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Molecules

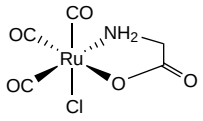
Carbon monoxide-releasing metal carbonyls: a new class of pharmaceuticals?

Carbon monoxide (CO) is produced naturally in humans at a rate of between 3 and 6 cm^3 per day, and this rate is increased in certain inflammatory states and pathological conditions that are associated with red blood cell haemolysis and oxidant-mediated stress. This endogenous CO is derived from the degradation of intracellular haem by a family of constitutive (HO-2) and inducible (HO-1) haem oxygenase enzymes.

Over the past ten years, interest in the biological effects of CO has greatly increased and CO is now regarded as a versatile signaling molecule, having essential regulatory roles in a variety of physiological and pathophysiological processes that take place within the cardiovascular, nervous and immune systems.

Research into the biological effects of CO and its potential therapeutic exploitation has been hampered by the practical inconvenience and danger involved in administering low doses of the toxic gas. However, a group of scientists from the Northwick Park Institute for Medical Research and the University of Sheffield (http://www.shef.ac.uk) have developed a family of compounds that overcomes these problems.

Initially, it was shown that certain transition metal carbonyls reported in the literature were able to liberate CO and mimic the effects of CO gas in biological systems [1]. Subsequently, novel forms of 'CO-RMs' (carbon monoxide-releasing molecules) have been developed. As a prototype of this class of compounds, $[Ru(CO)_3Cl(glycinate)]$ or CORM-3 (**i**) is a stable, solid, water-soluble Ru(II) complex, which liberates CO by ligand exchange [2]. This compound is able to induce a range of functions that are described for CO gas, and has been evaluated in a model of ischaemic reperfusion damage, where its presence during



(i)

reperfusion enhances heart function and reduces muscle infarction [3].

Ruthenium-centered organometallic compounds are also undergoing intense development as anti-cancer agents [4]. The successful development of marketed drugs from this class of compound should open up a floodgate of interest in the whole field of bioorganometallic chemistry, turning it into a mature subject to be taken seriously by the pharmaceutical industry.

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