ET-CORMs

Enzyme-triggered CO releasing molecules for therapeutic use

Invention

Carbon monoxide (CO), which is endogenously produced mainly in the course of heme degradation, was recently recognized as a powerful cytoprotective and homeostatic agent. For instance, CO was shown to ameliorate experimental cardiac, lung and vascular injuries and protect against numerous inflammatory states. While the clinical use of CO gas is associated with severe safety problems, a controlled delivery of CO to specific target sites by means of CO-releasing molecules appears to be a most promising solution. In this context, the invention comprises a novel class of iron carbonyl complexes, which release their CO load only after enzymatic activation. The powerful CO-releasing properties and the structural variability form a promising basis for the development of safe and pharmacologically useful CO-releasing molecules (CORMs). Biological tests (using different cell lines) have proven the chemical concept and confirmed the intracellular CO-release. Moreover, structural variation revealed pronounced structure-activity relationships. The clear-cut chemical concept and the developed synthetic schemes (opening short and efficient entries both to compound libraries and to larger amounts of individual complexes) provide excellent pre-conditions for structural optimization. Some initial results have been published.

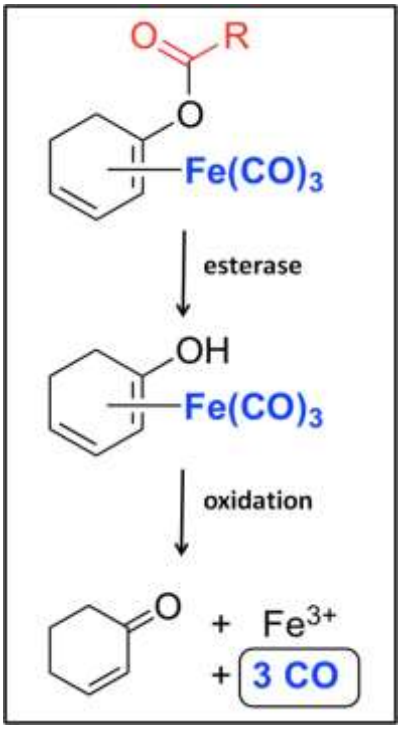

Figure 1: Enzymatically triggered CO release

Commercial Opportunities

CO-releasing molecules have the potential to become an important new class of drugs in the future. First generation CORMs reported in the literature do not meet the required pharmacological properties. However, the enzyme-triggered compounds (representing prodrugs) have a unique potential. The delivery of small amounts of CO to tissues can widen blood vessels, increase blood flow, prevent unwanted blood clotting, reduce inflammation and even suppress immune responses and the activity of cells and macrophages which attack transplanted organs.

Current Status

On behalf of the Universities of Cologne and Regensburg, PROvendis offers a patent license as well as a research collaboration with licensing option to innovative companies. In case of interest we will be pleased to inform you about the patent status.

Relevant Publications

Romanski, S.; et al.; Angew. Chem., Int. Ed. 2011, 50, 2392-96.
Romanski, S.; et al.; Dalton Trans. 2012, 41, 13862-75.
Romanski, S.; et al.; Organometallics 2012, 31, 5800-09.
Botov, S.; et al.; Organometallics 2013, 32, 3587-94.
Romanski, S.; et al.; Free Radical Bio. Med. 2013, 65, 78-88.
Wegiel, B.; et al.; Trends in Molecular Medicine 2013 19, 3-11.

An invention of the Universities Regensburg and Cologne.

Competitive Advantages

- Acyl-oxydiene-Fe(CO)3 complexes are an innovative class of ET-CORMs allowing for the first time a controlled intracellular and potentially tissue-specific CO-release
- First water-soluble enzyme-triggered CO-releasing molecules
- ET-CORMs open new perspectives for the prevention and cure of diseases involving inflammatory, infectious, thrombotic or proliferative processes

Technology Readiness Level

1 2 3 4 5 6 7 8 9

Technology concept formulated

Industries

- Biotechnology Industry
- Chemical Industry

Ref. No.

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