H₂S-based drug development and delivery

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More than a toxin generated in chemistry industry and from environmental pollution, hydrogen sulfide (H₂S) is also produced in our bodies with L-cysteine and homocysteine as the endogenous substrate. Over the last decade, the physiological importance of H₂S has been demonstrated in numerous human body systems, including the cardiovascular and respiratory, neuronal, endocrinal, gastrointestinal, reproductive, liver, kidney and urinary systems. Altered metabolism and functions of H₂S constitutes a critical factor for the pathogenesis of a number of human diseases, such as hypertension, atherosclerosis, heart failure and stroke, diabetes, asthma, neurodegenerative diseases, gastrointestinal inflammation, cancer, etc. In recent years, multiple lines of H₂S-based drugs (organic and inorganic H₂S-donors or hybrid molecules) have been developed for different clinical situations. Fast-releasing H₂S donors, such as NaHS and Na₂S, offer the tool to quickly correct H₂S deficiency under specific pathological conditions, e.g. ischemic/reperfusion heart failure. Slow-releasing H₂S donors, such as GYY4137, provide sustained protection against H₂S-related chronic diseases. Mitochondria-targeted H₂S donors, such as AP39, have the potential to directly optimize mitochondrial energy production and oxidant/antioxidant balance. These novel approaches have been successful in animal studies and being tested clinically at different trial stages. With improved delivery methods and organ- and cell type-specific releasing mechanism for H₂S release, H₂S-based drug development opens new horizon for improving the efficiency and potency, decreasing the side effect, minimizing the disturbance of system homeostasis of the next generation of drugs. (Supported by an operating grant from Canadian Institutes of Health Research)

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