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BISPHOSPHONATE CONJUGATION FOR BONE SPECIFIC DRUG TARGETING

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ABSTRACT

Bones provide essential functions and are sites of unique biochemistry and specialized cells, but can also be sites of disease. The treatment of bone disorders and neoplasia has presented difficulties in the past, and improved delivery of drugs to bone remains an important goal for achieving effective treatments. Drug targeting strategies have improved drug localization to bone by taking advantage of the high mineral concentration unique to the bone hydroxyapatite matrix, as well as tissue-specific cell types. The bisphosphonate molecule class binds specifically to hydroxyapatite and inhibits osteoclast resorption of bone, providing direct treatment for degenerative bone disorders, and as emerging evidence suggests, cancer. These bone-binding molecules also provide the opportunity to deliver other drugs specifically to bone by bisphosphonate conjugation. Bisphosphonate bone-targeted therapies have been successful in treatment of osteoporosis, primary and metastatic neoplasms of the bone, and other bone disorders, as well as refining bone imaging. In this review, we focus upon the use of bisphosphonate conjugates with antineoplastic agents, and overview bisphosphonate based imaging agents, nanoparticles, and other drugs. We also discuss linker design potential and the current state of bisphosphonate conjugate research progress. Ongoing investigations continue to expand the possibilities for bone-targeted therapeutics and for extending their reach into clinical practice.

Keywords

Bisphosphonates, Bone-targeting, Drug conjugates, Cancer Induced Bone Disease, Infection, Osteomyelitis

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