Advances in Bone-Targeted Drug Delivery Systems: A Review of Bisphosphonates, Nanoparticles, Liposomes, Nanocarriers, and Radiopharmaceuticals




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Abstract:
This review article highlights the latest advancements in bone-targeted drug delivery systems, including bisphosphonates, calcium phosphate nanoparticles, liposomes, nanocarriers, and radiopharmaceuticals. These drug delivery systems have been extensively explored for the treatment of various bone diseases, such as osteoporosis and bone cancer. This paper will review the current bone-targeted delivery systems and future prospects of bone-targeted drug delivery systems. The article also discusses the potential of these systems in the delivery of gene therapy agents and small interfering RNA (siRNA) for the treatment of bone diseases.

1.Introduction:

Bone-targeted drug delivery systems have become an emerging field of research due to their potential to improve the treatment of various bone diseases such as osteoporosis, bone metastasis, and bone cancer. These systems are designed to selectively deliver drugs to bone tissue, which can improve drug efficacy, reduce toxicity, and minimize off-target effects. Various approaches have been developed to target drugs to bone tissue, including bisphosphonates, calcium phosphate nanoparticles, targeted liposomes, targeted nanocarriers, and bone-seeking radiopharmaceuticals. These bone-targeted delivery systems offer unique advantages in terms of their specificity, biocompatibility, and biodegradability. As such, they represent a promising avenue for the development of novel and effective treatments for bone diseases. Here is a review of some of the bone-targeted delivery systems and their applications.

Bisphosphonates: Bisphosphonates are a class of drugs commonly used for the treatment of osteoporosis. They have a high affinity for bone tissue and bind strongly to the hydroxyapatite crystals in bone (1). This property allows them to accumulate selectively in bone tissue, making them an effective bone-targeted drug delivery system. Bisphosphonates have been used as carriers for the delivery of various drugs, including anticancer agents. Bisphosphonates have also been shown to enhance bone regeneration when combined with growth factors (2, 3). Bisphosphonates work by inhibiting the activity of osteoclasts, the cells responsible for breaking down bone tissue. This leads to a reduction in bone resorption and an increase in bone density.

Bisphosphonates are taken up by osteoclasts through an active transport mechanism, as they are structurally similar to pyrophosphate. Once inside the osteoclast, they bind to and inhibit the enzyme farnesyl pyrophosphate synthase (FPPS), which is involved in the synthesis of several molecules necessary for osteoclast function. Inhibiting FPPS also leads to a reduction in the prenylation of small GTPases such as Ras and Rho, which are important for osteoclast function. This ultimately induces osteoclast apoptosis, leading to a decrease in bone resorption and an increase in bone density. Therefore, the mechanism of action of bisphosphonates involves uptake by osteoclasts, inhibition of FPPS, inhibition of prenylation, and induction of apoptosis.

Calcium phosphate nanoparticles: Calcium phosphate nanoparticles (CaP NPs) are biocompatible and biodegradable, and have been used as bone-targeted drug delivery systems. Recent studies have explored their potential in the delivery of small interfering RNA (siRNA) for the treatment of bone diseases such as osteoporosis and bone metastasis. Calcium phosphate nanoparticles have also been used to deliver antibiotics and growth factors to promote bone regeneration (4, 5). These nanoparticles have a high affinity for bone tissue and can be loaded with drugs, such as antibiotics, growth factors, and anticancer agents. They have been shown to improve drug efficacy and reduce toxicity (6).

CaP NPs have a high affinity for bone tissue and can be loaded with antibiotics or growth factors through adsorption, encapsulation, or co-precipitation. Once bound to bone tissue, the agents can be released in a controlled manner through diffusion or degradation of the CaP NPs. Growth factors released from CaP NPs stimulate osteoblast activity, promoting bone formation. Antibiotics released from CaP NPs inhibit bacterial growth and prevent infection. CaP NPs are biocompatible and biodegradable, ensuring their safety and eventual elimination from the body. Overall, CaP NPs offer a promising approach to delivering agents for bone regeneration.

Targeted liposomes: Liposomes are spherical vesicles composed of a lipid bilayer that can encapsulate drugs. Targeted liposomes have been developed to selectively deliver drugs to bone tissue. These liposomes are functionalized with bone-targeting ligands, such as bisphosphonates, and can encapsulate a variety of drugs, including antibiotics and anticancer agents (7-9).

Targeted liposomes can deliver drugs specifically to bone tissue by attaching a targeting ligand to the surface of the liposome, such as bisphosphonate, which has a high affinity for bone tissue. The liposomes bind to receptors on bone cells, are internalized by endocytosis, and release drugs inside the bone cells. This leads to a localized drug effect, reducing systemic side effects and increasing treatment efficacy. Targeted liposomes offer a promising approach to delivering drugs to bone tissue.

Targeted nanocarriers: Targeted nanocarriers are nanoparticles that can encapsulate drugs and deliver them to target tissues. Recent studies have explored the use of targeted nanocarriers for the delivery of small molecules and gene therapy agents for the treatment

3.2 of bone diseases (10, 11). Targeted nanocarriers can be functionalized with bone-targeting ligands, such as bisphosphonates, to enhance their bone-targeting properties (12).
Targeted nanocarriers are an effective drug delivery system for treating bone diseases, as they deliver small molecules and gene therapy agents specifically to bone tissue. The mechanism involves targeting the bone tissue with a ligand, interacting with the bone cells, being internalized by the cells, and delivering the drugs to the nucleus for localized effect. By minimizing systemic side effects and enhancing the efficacy of the treatment, targeted nanocarriers offer a promising approach for treating bone diseases.

Bone-seeking radiopharmaceuticals: Bone-seeking radiopharmaceuticals are used for the diagnosis and treatment of bone cancer. These radiopharmaceuticals are selectively taken up by bone tissue and emit radiation that can be detected by imaging techniques. They can be used for targeted delivery of radiation to bone tissue, which can be effective in the treatment of bone cancer (13, 14). Recent studies have shown that bone-seeking radiopharmaceuticals can also be used for the treatment of bone metastasis from various types of cancer (15).
Bone-seeking radiopharmaceuticals are used to target bone tumors due to their high affinity for bone tissue. They are administered intravenously and localize to areas of high bone turnover, such as bone tumors. They emit gamma rays for imaging and beta particles for radiation therapy, which primarily target the bone tissue and bone tumors while sparing healthy tissue. This approach offers a promising solution for the diagnosis and treatment of bone cancer.

2.Future prospects:
Bone-targeted drug delivery systems have demonstrated significant potential in the treatment of various bone diseases. These systems offer numerous advantages, such as improved drug efficacy, reduced toxicity, and enhanced bone regeneration. Future prospects for bone-targeted drug delivery systems are diverse and exciting, including the development of more specific and efficient bone-targeting ligands, combination with other therapies, personalized medicine approaches, and the use of advanced imaging techniques for real-time monitoring. Further research and development in this field could lead to the development of novel and effective treatments for bone diseases, benefiting patients in the future.

3.Conclusion:
In conclusion, bone-targeted drug delivery systems have shown great potential for the treatment of various bone diseases, including osteoporosis, bone metastasis, and bone cancer. Bisphosphonates, calcium phosphate nanoparticles, targeted liposomes, targeted nanocarriers, and bone-seeking radiopharmaceuticals are among the most promising bone-targeted drug delivery systems. These systems can selectively deliver drugs to bone tissue, improving drug efficacy and reducing toxicity. Further research and development of bone-targeted drug delivery systems are needed to improve their effectiveness and expand their clinical applications in the treatment of bone diseases.

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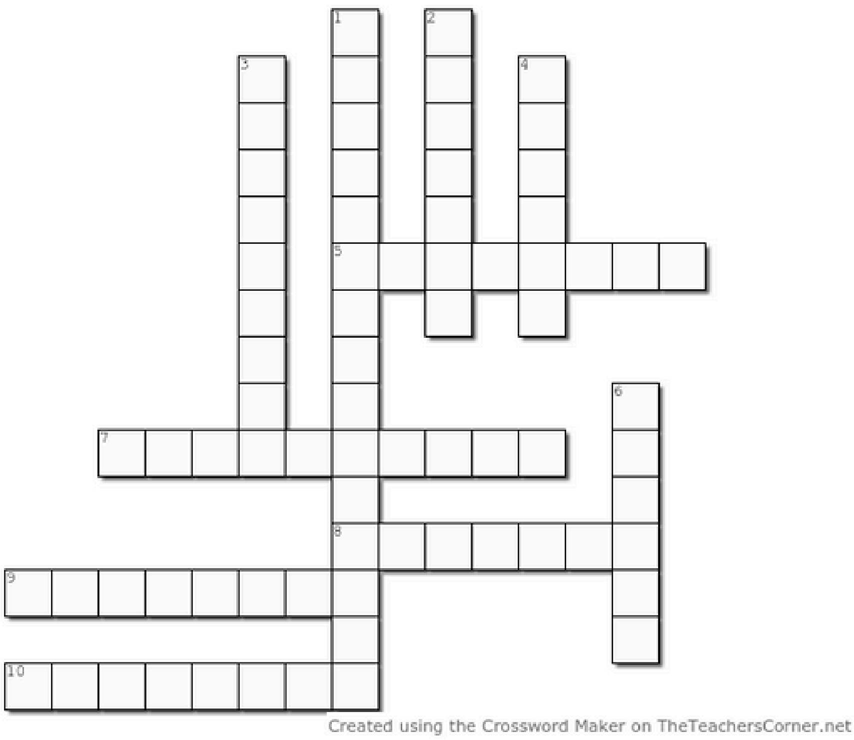
Fun & frolic - Crossword



Across

5. Commercial Allogeneic-derived Scaffold
7. Calcium cement-based product
8. Commercial collagen/tricalcium phosphate scaffolds
9. Medical Device
10. Silica-based biomaterial used for synthetic bone grafts

Down

1. Agents targeting hydroxyapatite
2. FDA approved bone-building humanized monoclonal antibody
3. Commercial biohybrid graft
4. Marketed collagen/hydroxyapatite composite
6. Bioceramic glue

Solution on page 13