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New Tactics for the Design of Drugs Targeted to Bone

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The use of bisphosphonates for the design of bone-targeted drugs has continued to receive attention in our laboratories over the last few years.[1] While the bisphosphonate moiety, with its high inherent affinity for calcium phosphate minerals, appears to be an ideal drug carrier, some design hurdles have required custom syntheses of bisphosphonates with selective properties and linkers to drugs that offer a "target and release" feature. We have demonstrated promising in vivo results, with pharmacologically inactive bisphosphonates as drug carriers utilizing linking moieties with adequate serum stability and useful lability at the bone surface to locally release drugs. The linkers include carbamates such as HBCX and BCT, hydrazones, and the very unique bortezomib-derived boronate ester BP-BTZ in Figure 1 [2,3]. Useful drug leads include efficacy in animal models of osteomyelitis, multiple myeloma, and bone loss. New analogs and synthetic methods are under development to capitalize on our initial proof of concept bisphosphonate – drug conjugates.

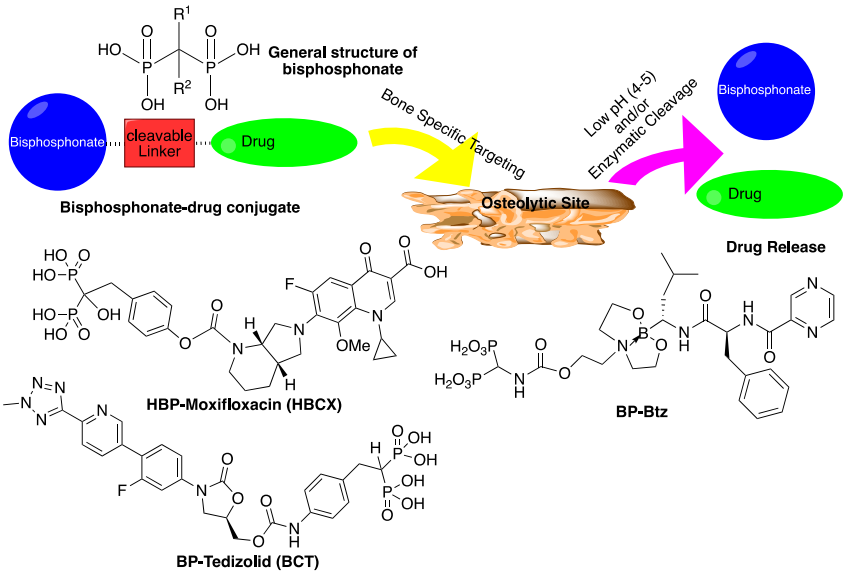

Figure 1. Bone targeted drug design and examples.

References

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