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| **Towards the development of pulsatile release systems for teriparatide** |
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| **Background:** Teriparatide is the N-terminal fragment of human parathyroid hormone (hPTH) and currently one of the only approved anabolic treatments for osteoporosis. The peptide is administered as a daily subcutaneous injection, but clinical use is limited by the invasiveness of the administration route and thus poor patient adherence. The anabolic effect of treatment is only achieved when administered intermittently, whereas continuous exposure of the peptide will result in bone resorption. Controlled release formulations must therefore produce a pulsatile release profile resulting in a brief plasma spike in teriparatide approximately every 24 h. Smart materials respond to an external stimulus (e.g. temperature). The development of peptide formulations employing such materials may therefore allow active control over the release of the therapeutic. |
| **Methods:** A range of thermo-responsive liposomes with different transition temperatures (Tc) were prepared by varying ratios of dipalmitoylphosphatidylcholine (DPPC) and distearoylphosphatidylcholine (DSPC). Liposome production methods and composition were optimised to yield small (< 200 nm) size vesicles while maximising teriparatide loading. The release profile of teriparatide was determined at temperatures below and above the Tc. |
| **Results:** Varying the composition of phospholipids allowed production of liposomes with different transition temperatures. At an 8:2 molar ratio of DPPC:DSPC, liposomes with a Tc of 43 °C were obtained. The inclusion of oleic acid within the liposomes resulted in an increase of teriparatide in the purified liposome fraction from 4% to 79% (of the theoretical loading, 0.2 mg/mL) and only slightly decreased the transition temperature (40 °C). |
| **Conclusions:** Exploiting the properties of thermo-responsive materials is a promising approach to actively control the release of therapeutics. Thermo-responsive liposomes with transition temperatures between 40 – 43 °C were successfully prepared and loaded with teriparatide. Peptide loading was improved 4.5-fold upon inclusion of oleic acid within the liposomes. |