Title	**Sublingual Film of Salmon Calcitonin Loaded Hydroxyapatite Nanoparticles as a Non-Invasive Alternative to Parenteral Administration**
Keywords (up to 5)	Osteoporosis, Salmon Calcitonin, Hydroxyapatite, Film, Sublingual
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Abstract	Salmon Calcitonin(SCT) a peptide, is a drug of choice for Osteoporosis. It undergoes rapid enzymatic degradation and hence is administered as subcutaneous injection. In the present study we report a sublingual film of SCT loaded Hydroxyapatite nanoparticles(HAP-NP) as a non-invasive and patient friendly alternative to the subcutaneous injection. Surface stabilized spherical HAP-NP were prepared by aqueous precipitation at pH 12 using an anionic stabilizing agent. The HAP-NP were centrifuged washed, resuspended in pH 7.4 and SCT added to the dispersion. SCT being cationic at pH 7.4 was readily loaded onto HAP-NP by ionic interaction with high entrapment efficiency of >80%. The SCT-HAP-NP exhibited an average size ~100 nm, polydispersity index < 0.2 and zeta potential of < -25 mv. Fourier Transform Infra-Red(FTIR) spectra confirmed ionic interaction of cationic SCT with the negatively charged HAP-NP. DSC and XRD indicated amorphization of SCT. Physical stability of SCT was confirmed by Circular dichroism while HPLC analysis confirmed chemical stability over 3 months as per ICH guidelines. SCT-HAP-NP were dispersed in aqueous polymer solution, cast on a plastic liner on a Mathis Coater and immediately freeze dried to obtain a film wherein 20X20mm contained 200iu of SCT. The film was optimized by Box-Behnken design. Concentration of HPMC, PVA and propylene glycol were the independent variables while tensile strength(TS), disintegration time(DT) and particle size of HAP-NP were the dependent variables. Optimized batch exhibited TS ~4.5 N/mm^2 and DT<60 seconds. No change in size of HAP-NP was observed. Stability of SCT in the film was confirmed. A comparative in-vivo pharmacokinetic study in New Zealand rabbits of the SCT-HA-NP film with the subcutaneous Injection(~200iu/rabbit) revealed good bioavailability of 18.2% with the sublingual SCT-HAP-NP film. The sublingual SCT-HAP-NP film exhibits great promise as a non invasive delivery system for osteoporosis.
References	1) Dobrovolskaia MA et al., Nanoletters, 2008, 8: 2180–7 2) Zhengrong Cu et al., Pharmaceutical Research, 2002,19: 12