

# Design and optimization of Teriparatide loaded PHBV/PLGA blend nanoparticles

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## ABSTRACT SUMMARY

The main purpose of this study was to design and evaluate PHBV/PLGA blend nanoparticles with the potential to serve nanoparticulate system for Teriparatide used in treatment of patients suffering from severe osteoporosis. In order to obtain the most desirable nanoparticles that possess the uttermost loading, superlative entrapment efficiency with acceptable size and size distribution, the effect of formulation variables such as PVA concentration, peptide concentration and PHBV/PLGA ratio were studied, using Box- Behnken response surface methodology. Spherical nanoparticles with rough surface that possess 234 nm in diameter with narrow size distribution (PDI=0.18) were obtained. The entrapment efficiency (EE) and loading were 86% and 4.9% in optimized nanoparticles, respectively. The release profile of Teriparatide from fabricated nanoparticles will be studied in near future.

## INTRODUCTION

Teriparatide, which has an identical sequence to the 34 N-terminal aminoacids of the full length of human parathyroid hormone, is indicated for treatment of severe osteoporosis particularly for those with high risk of fracture. The considerable point is that Teriparatide is the only FDA-approved drug, which causes bone formation through stimulation of osteoblasts compare to other antiosteoporotic drugs such as bone resorption inhibitors, which only inhibit osteoclasts. Generally, it is administrated 20 mcg once a day for a long period of time (up to 2 years) (1).

Poly (3-hydroxybutyrate-co-3-hydroxyvalerate) (PHBV) is a linear aliphatic polyester.

Similar to PLGA, PHBV is biocompatible, biodegradable and non-toxic polymer. It undergoes hydrolysis within the body to

generate its primary monomers. Since the degradation rate of PHBV is slower than PLGA, the concern about creating an acidic environment around biomaterials attributed to high degradation rate of PLGA is entirely resolved (2).

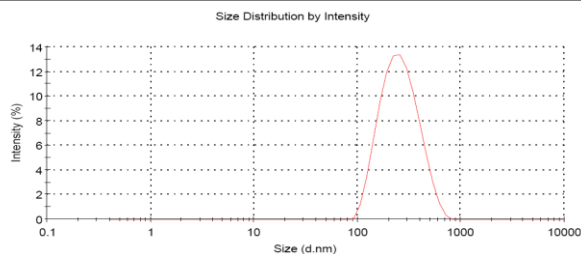
## EXPERIMENTAL METHODS

In the present article, parental Teriparatide nanoparticles were prepared by double emulsion solvent evaporation technique (w/o/w) using a mixture of two polymers, PHBV and PLGA (3). Dynamic light scattering (DLS), scanning electron microscope (SEM) and transmission electron microscope (TEM) were employed to characterize the fabricated nanoparticles for size, size distribution, surface morphology and distribution of two polymers. Circular dichroism (CD) was applied to confirm the bioactivity of peptide after processing. The entrapment efficiency and loading were investigated using HPLC method.

## RESULTS AND DISCUSSION

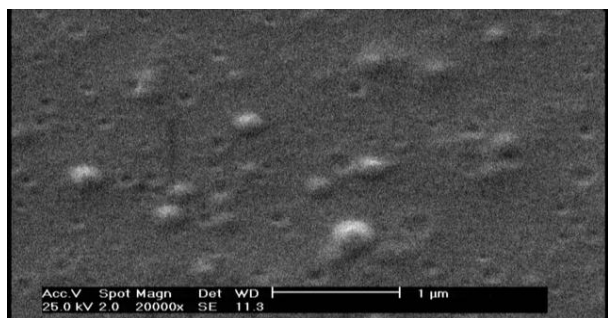
Both PVA concentration and ratio of polymers were effective parameters in size; whereas peptide concentration had no significant effect on size of nanoparticles.

Optimized spherical nanoparticles with rough surface that possess 234 nm in diameter with narrow size distribution (PDI=0.18) were obtained, as shown in Fig 1.



**Fig 1.** Size distribution of PHBV/PLGA blend nanoparticles.

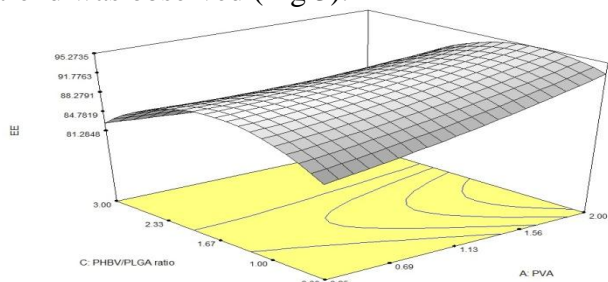
Fig 2 shows spherical PHBV/PLGA blend nanoparticles. The surface of PHBV/PLGA blend nanoparticles was rough which was in accordance with other fabricated nanoparticles in previous studies (3).



**Fig 2.** SEM image of PHBV/PLGA blend nanoparticles.

The entrapment efficiency (EE) and loading were 86% and 4.9% in optimized nanoparticles, respectively.

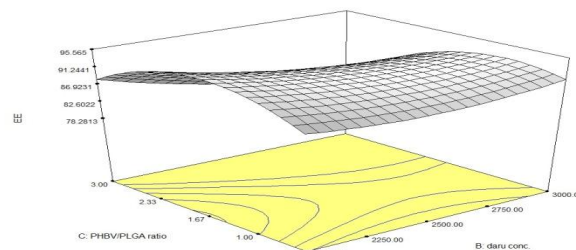
The high hydrophobic shell which was substantially made from PHBV prevented Teriparatide from leaking resulted in high entrapment efficiency. It can be concluded that major part of peptide incorporated into particles or adsorbed on the surface of target nanoparticles unlike other previous works in which a dominant portion of hydrophilic drugs remained in solution during phase separation(3). Response surface plots displayed that an increase in ratio of PHBV/PLGA resulted in significant increase in entrapment efficiency up to intermediate point and after that descending trend was observed (Fig 3).



**Fig 3.** Three-Dimensional Plot for the effect of PHBV/PLGA ratio and PVA concentration on entrapment efficiency.

Drug concentration had an antagonist effect on E.E. In polymer ratio lower than intermediate point an increase in drug concentration resulted in slight increase in E.E but in polymer ratio higher than intermediate point an increase in

drug concentration led to decrease in E.E. This phenomenon can be due to the concentration gradient which was created in high drug concentration (Fig 4).



**Fig 4.** Three-Dimensional Plot for the effect of PHBV/PLGA ratio and Drug concentration on entrapment efficiency.

TEM image and CD spectroscopy confirmed the core-shell structure of nanoparticles and the bioactivity of peptide, respectively.

## CONCLUSION

Final optimized nanoparticles in this study possess the size of 234nm, PDI of 0.18, entrapment efficiency of 86% and loading of 4.9%. The higher loading and entrapment efficiency of nanoparticles in this study were attributed to the specific structure of nanoparticles. As noted, the more hydrophobic polymer with higher molecular weight, PHBV, distributed mainly in the shell of nanoparticles prevented peptide leaking. The proposed system can be a promising candidate for preparing efficient controlled release formulation of Teriparatide which is aimed for further studies.

## REFERENCES

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