NASAL NANOCARRIER DELIVERY SYSTEM FOR THE TREATMENT OF OSTEOPOROSIS

Chapter 6

Conclusion and Summary
The present study aimed to develop nanoparticles of selective estrogen receptor modulator for the treatment of osteoporosis. Intranasal delivery system comprising of raloxifene loaded nanoparticulate suspension were developed for the treatment of osteoporosis.

The study can be summarized as follows:

1. Physicochemical characterization and identification of procured raloxifene HCl was done on the basis of organoleptic properties, solubility, loss on drying, partition coefficient, IR spectroscopy, XRD and differential scanning calorimetry.

2. An analytical method using RP-HPLC was developed and validated for determining drug entrapment efficiency, drug loading and in vitro release.

3. RP-UPLC method was developed and validated for the analysis of nanoparticulate formulations during stability studies.

4. LC-MS/MS method was developed and validated for the quantification of raloxifene HCl in plasma and tissue homogenates during in vivo studies.

5. The chitosan nanoparticulate formulations for intranasal delivery were developed successfully to satisfactory levels in terms of particle size, particle shape, particle size distribution, zeta potential, drug entrapment, drug loading and drug release.

6. The in vitro release of raloxifene from chitosan nanoparticulate suspension was found to be $98.11 \pm 0.55\%$ and the release followed Higuchi release kinetics.

7. The pharmacokinetic parameters after intranasal administration of chitosan nanoparticulate suspension were, $t_{\text{max}} = 0.17$ h, $C_{\text{max}} = 124.4 \pm 10.45$ ng/mL, $AUC_{0-t} = 407.1795 \pm 15.43$ h.ng./mL, and $AUC_{0-\text{inf}} = 529.0589 \pm 17.23$ h.ng/mL in plasma.

8. The biodistribution of drug administered via intranasal route was compared with of drug given orally. From the biodistribution data of drug loaded nanoparticulate system administered via intranasal route it was observed that nanoparticulate formulation resulted in a higher concentration of drug in blood as compared to the oral route this was because of avoidance of first pass metabolism.

9. The IVIVC showed the linear model for in vitro in vivo correlation ($R^2 = 0.933$) which indicates sufficient degree of correlation.
10. Stability studies revealed no significant change in the particle size, zeta potential and drug loading of chitosan nanoparticulate formulation after time intervals of 0, 1, 2, 4, and 6 months (p > 0.05) indicating stability of the formulation. The shelf life of raloxifene loaded chitosan nanoparticulate formulation was found to be 18.07 months when determined as per ICH guidelines. Shelf life determined using Arrhenius plot was found to be 15.45 months.

In conclusion raloxifene loaded chitosan nanoparticulate formulation was developed for intranasal delivery. This provided a non-invasive route for rapid and efficient delivery of raloxifene to systemic circulation for treatment of osteoporosis. The delivery system is useful to avoid first pass metabolism associated with the oral delivery of drug which is the most important cause of low concentration of drug. Overall, the research work highlighted the usefulness of intranasal delivery of raloxifene loaded polymeric nanoparticles for systemic delivery.