ABSTRACT
DEVELOPMENT AND CHARACTERIZATION OF A POLYMERIC NANOPARTICULATE DELIVERY SYSTEM FOR EXEMESTANE

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Keywords: Exemestane, Polymeric Nanoparticles, Poly (ɛ- Caprolactone), Nanoprecipitation, Spontaneous emulsification solvent diffusion, Poloxamer–188, Breast cancer, MTT Assay, MCF7 cell line, Vero cell line.

Background:
Exemestane is steroidal aromatase inhibitors used for treatment of ER-positive breast cancer. Conventional formulation has lots of drawbacks like hot flashes, arthralgias, insomnia, joint pain, fatigue and many more. This is due to non selective distribution of drug, frequent administration and drug resistance. To defeat the above problem biodegradable nanoparticles have been developed which can beat solubility problem of API. So far, research done on EXE NPs only one method solvent displacement has been used. We have used different methods for NPs preparation so we can compare and select best method for EXE NPs preparation.

Aim:
1. The aim of this investigation was to develop and evaluate biodegradable nanoparticles of Exemestane by different methods.
2. To check anticancer activity against MCF7 breast cancer cell line and Vero cell line.
Materials and Methods:
To achieve a desired objective Exemestane loaded Poly (ε–Caprolactone) nanoparticles were prepared by Nanoprecipitation and Spontaneous emulsification solvent diffusion methods using poloxamer 188 as stabilizer. Polymeric nanoparticles were characterized for physiochemical properties, particle size, drug loading and entrapment efficiency. The surface morphology was evaluated by SEM and TEM. Exemestane was quantitatively analyzed by RP–HPLC method with sun fire C\textsubscript{18} column and acetonitrile and water (90:10\% v/v) as mobile phase. The samples were detected by UV/Visible detector at 242 nm. In Vitro release study were performed using Shaker bath incubator maintained at 37ºC and 100 rpm. The cytotoxicity in MCF7 breast cancer cell line and Vero cell line were evaluated by MTT assay.

Results and Discussion:
FT–IR and DSC studies prove no any drug polymer interaction. From both the methods of nanoparticle preparation, Nanoprecipitation method found to be more superior then SESD method to achieve small size range from 37.81–319.9 nm, more recovery 63.99\%, high encapsulation efficiency of 76.39\%. All the particles carry overall negative surface charge. In vitro release shows 80.42\% and 76.90\% of drug release from method 1 and method 2 prepared NPs after 100 hours of study. For both the method it is found that as the percentage of drug increases from 10\% to 40\% in formulation particle size, drug loading, and drug release increases. The result of cytotoxicity by method 1 and method 2 prepared nanoparticle shows 95.22\% and 80.74\% cell growth inhibition of MCF7 cell line and 61.32\% and 55.56\% cell growth inhibition of Vero cell line after 96 hours.

Conclusions:
The nanoparticulate formulation of Exemestane loaded PCL NPs were successfully developed by Nanoprecipitation method. The formulation will have sustain release delivery so there will be improve in therapeutic window allowing lower doses and decrease in frequency of administration thus avoiding systemic toxicities. Formulation also shows significant improve in its cellular accumulation of drug and cytotoxicity.
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