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Fabrication and physicochemical characterisation of novel pimozide loaded PLGA nanoparticles

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SUMMARY

Cancer has always been a big concern for human health. There is always an increased need for fabrication of newer drugs or repurposing existing drugs to treat cancer. Apart from being an antipsychotic agent, pimozide has already shown its anticancer activity against various cancers in several studies. The aim of the present study was to fabricate pimozide loaded PLGA nanoparticles and characterise them. Single emulsion and microfluidic techniques were used to prepare nanoparticles. Physicochemical properties such as particle size, shape, surface charge and encapsulation efficiency were investigated. Results showed that the nanoparticles had an average size distribution of 200-300 nm, were spherical in shape and negatively charged. Additionally, a high encapsulation efficiency (50-89%) makes these nanoparticles potential drug delivery systems to target cancer cells.

INTRODUCTION

According to WHO, cancer is the second leading cause of death worldwide reporting 8.8 million deaths in 2015, accounting for approximately 1 in 6 deaths (World Cancer Report, 2014). Although many treatment options exist, there is always an increased need for fabrication of newer drugs or repurposing existing drugs. Pimozide is an antipsychotic drug indicated for Tourette Syndrome and schizophrenia. However, several studies have found significant anticancer activity with pimozide. It inhibits the growth of breast cancer cells, prostate cancer cells and glioblastoma cells (Lee *et al.*, 2016). The delivery of pimozide to the targeted cancer cells is challenging because only 40-50% pimozide (oral administration) is bioavailable after first-pass metabolism in the liver. Moreover, overdose of pimozide causes severe extrapyramidal symptoms, hypotension, sedation, QT interval prolongation and ventricular arrhythmias (Fako *et al.*, 2016). To solve this problem, biodegradable nanoparticles could be employed as pimozide delivery systems which might provide enhanced biocompatibility, less or no systemic toxicity, increased encapsulation efficiency, and very convenient release profile. Poly-D-L-lactic-co-glycolic acid (PLGA) is one of the most extensively used, US FDA and European Medicine Agency (EMA) approved biodegradable polymers for therapeutic use in humans as many anticancer drugs including paclitaxel and doxorubicin have been successfully loaded in PLGA nanoparticles (Danhier *et al.*, 2012). We prepared pimozide loaded PLGA nanoparticles by using two techniques. This work aimed to investigate the physicochemical properties of the prepared nanoparticles.

MATERIALS AND METHODS

Pimozide, both ester terminated PLGA (Resomer® RG 503, MW 24 kDa-38 kDa) and acid terminated PLGA (MW 30 kDa-60 kDa) having 50:50 lactic: glycolic ratio,

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dichloromethane (Chromasolv®, ≥99.8%) which was analytical grade and poly (vinyl alcohol) (PVA, 87-89% hydrolysed, MW 31 kDa-50 kDa) were purchased from Sigma Aldrich company. Polysorbate 80 (polyoxyethylene sorbitan monooleate/ TWEEN® 80, product of Switzerland) was purchased from Fluka Analytical. Acetonitrile (Pierce®, LC-MS grade) and ethanol (HPLC grade) were purchased from Thermo Fisher Scientific. Single emulsion-solvent evaporation and microfluidic techniques have been used to prepare nanoparticles. Pimozide encapsulation efficiency (EE) was analysed by a reverse-phase high performance liquid chromatography (RP-HPLC) method. Fourier Transform Infrared Spectroscopy (FTIR) confirmed the degree of interaction between drug and polymer. Particle size and zeta potential were measured by dynamic light scattering (DLS) technique. The surface morphology was studied by scanning electron microscopy (SEM).

RESULTS AND DISCUSSION

Results obtained (Table 1) show that nanoparticle size distribution was in the range of 200-300 nm regardless of the PLGA types and preparation techniques.

Table 1. *Physicochemical properties of prepared nanoparticles*

Formulation	Size (nm)	PDI	Zeta potential (mV)	EE (%)
AF1.SE	236.3±51	0.221±0.14	-4.34±2.7	89
AF2.SE	227.4±17	0.199±0.08	-5.53±0.9	83
EF1.SE	262.1±10	0.328±0.05	-5.15±2.3	70
EF2.SE	234.2±68	0.324±0.07	-8.66±1.3	76
AF1.MF	224.9±13	0.172±0.05	-25.1±1.1	79
AF2.MF	225.9±20	0.136±0.04	-22.2±1.7	108
EF1.MF	229.2±58	0.201±0.13	-25.4±2.6	50
EF2.MF	202.1±22	0.095±0.01	-21.5±1.6	83

A – Acid terminated PLGA, E – ester terminated PLGA, F1 – formulation containing 2.5% pimozide, F2 – formulation containing 5% pimozide, SE – Single emulsion, MF – microfluidic, EE – encapsulation efficiency, PDI – polydispersity index

The microfluidic technique produced nanoparticles having a narrower polydispersity index (≈0.2) and higher negative zeta potential (-20 to -25 mV) than those from the single emulsion technique. This can be explained by the surface properties of PLGA/PVA nanoparticles (single emulsion) and PLGA/Tween® 80 nanoparticles (microfluidic).

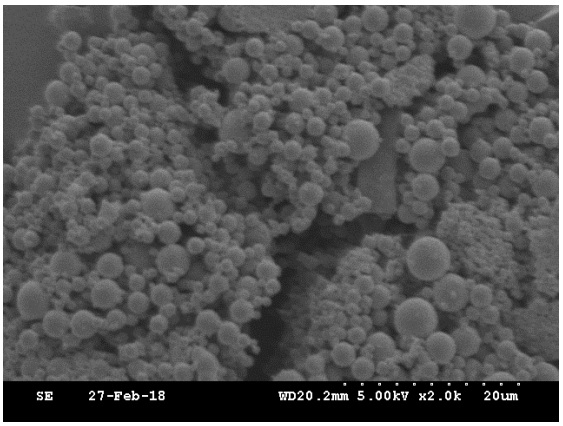

Fig. 1. *Scanning electron microscopy (SEM) image of prepared nanoparticles*

A high pimozide encapsulation efficiency (50-89%) was observed by both techniques, thus, making current formulations a potential therapeutic option to work on for cancer treatment.

CONCLUSIONS

For the first time, pimozide loaded PLGA nanoparticles were successfully prepared and characterised. Optimising the EE, size, and charge, while preserving stability and biological activity during fabrication can be achieved through adjustment of process variables. Future works on drug release, addition of surfactants and targeting ligands on nanoparticles, and in vitro studies on cancer cell lines will determine the superior formulation.

REFERENCES

Danhier, F. *et al*., 2012. PLGA-based nanoparticles: An overview of biomedical applications. J.Con.Rel., 161,505-522.

Fako, V. *et al*., 2016. Inhibition of wnt/β-catenin Signaling in Hepatocellular Carcinoma by an Antipsychotic Drug Pimozide. Int. J. Biol. Sci, 12, 768–775.

Haggag, Y. *et al*., 2016. Preparation and in vivo evaluation of insulin-loaded biodegradable nanoparticles prepared from diblock copolymers of PLGA and PEG. I.J.Pharm., 499, 236-246.

Lee, J K. *et al*., 2016. Repurposing antipsychotics as glioblastoma therapeutics: Potentials and challenges (Review). Oncol. Lett. 11, 1281–1286.

World Cancer Report 2014. World Health Organization. 2014. pp. Chapter 1.1. ISBN 9283204298. Archived from the original on 12 July 2017.