British Journal of Pharmacy

https://doi.org/10.5920/bjpharm.1409

British Journal of Pharmacy

www.bjpharm.hud.ac.uk

Proceedings of the 14th APS International PharmSci 2023

Impact of molecular weight of polyethylene glycol on physicochemical characteristics of polymeric nanoparticles encapsulating pimozide.

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ARTICLE INFO

Received: 31/07/2023
Accepted: 08/08/2023
Published: 30/12/2023

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KEYWORDS: PEG, PEGlyation, PLGA-PEG, Nanoparticles.

SUMMARY

The aim of the study is to examine the effect of the molecular weight of Polyethylene glycol (PEG) on the properties of nanoparticles. PEGlyation of nanoparticles is a promising approach to extend the circulation time and protect nanoparticles from opsonisation and macrophage. However, PEG molecular weight has a significant effect on key parameters of nanoparticles such as Size and encapsulation efficiency. In this study, PLGA-PEG nanoparticles with Pimozide were prepared using a microfluidic technique using two different molecular weights of PEG. Physicochemical characterizations were undertaken including Encapsulation efficiency and Fourier transform infrared spectroscopy (FTIR). Results were compared for these two formulations to understand how the weight variation of PEG impacts on physicochemical properties of nanoparticles.

INTRODUCTION

Nanotechnology brings a big revolution in the diagnosis of cancerous cells, targeted delivery and conquering limitations of traditional chemotherapies (Sutradhar and Amin, 2014). Polymeric nanoparticles are one of the novel formulations used as targeted drug delivery approach for various cancer treatments. Polylactic-co-glycolic acid (PLGA) nanoparticles (PLGA NPs) are used on a bigger scale for encapsulating multiple drugs such as peptide drugs and vaccines (El- Sherbiny, El-Baz and Mohamed, 2015). Pimozide showed promising results in various cancer treatments such as glioblastoma.

The main problem of polymeric nanoparticles is the opsonisation and clearance by the macrophage. Nanoparticles leak into tumours compared to normal tissue because of enhanced permeability and retention effect. It leads to limiting the time of nanoparticles in blood circulation (Yoo, Chambers and Mitragotri, 2010).

The surface modification of nanoparticles is required to reduce the trap of nanoparticles by the reticuloendothelial system (RES) and to achieve the practical therapeutic effect of the nanoparticle by increasing the EPR effect (Kobayashi, Watanabe and Choyke, 2014). Polyethlene glycol (PEG) is used to overcome this issue. The process is called PEGylation, where polymeric nanoparticles are coated with PEG. It helps to prolong the circulation time and longer half-life of nanoparticles (El- Sherbiny, El-Baz and Mohamed, 2015) (Jokers et al.,2011).

MATERIALS AND METHODS

PLGA (Resomer 502 H) with a ratio of 50:50 of Lactide: glycolide (MW 7000-17000) were purchased from Sigma Aldrich UK. PEG 2000 and PEG 4000 were purchased from Sigma Aldrich UK. Acetonitrile was HPLC grade and other reagents were of analytical grade or higher. PLGA-PEG nanoparticles were formulated by using the microfluidic method.

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Malvern Zetasizer (Malvern Instruments) measured particle size and zeta potential. A transmission electron microscope (TEM) is used for morphological study. Chemical interaction was analysed by FTIR (Shimadzu FTIR, UK). Encapsulation efficiency (EE) of pimozide was calculated by analysis of HPLC results. All measurements were performed in triplicate.

RESULTS AND DISCUSSION

This study was carried out to analyse the impact of the molecular weight of PEG on key four parameters of polymeric nanoparticles.

TEM images (fig 1) confirmed the size variation in both formulations.

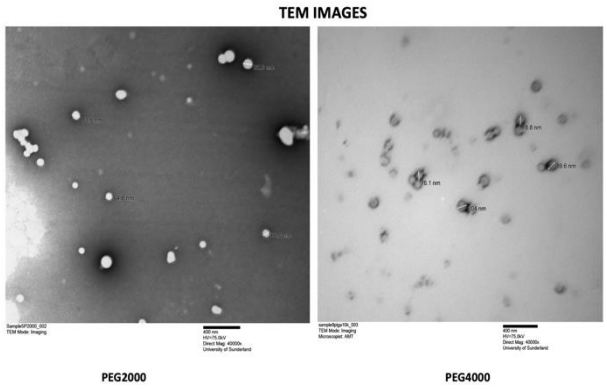

Fig. 1. *TEM images of PEG 2000 and 4000 nanoparticles.*

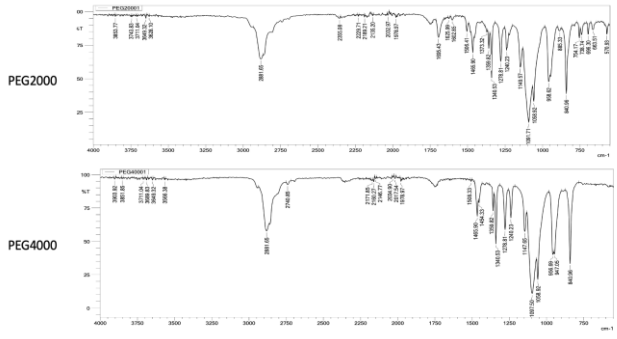

Fig. 2. *FTIR images of PEG 2000 and 4000 nanoparticles.*

FTIR was preformed to confirm the PEG attachment to the NPs. When compared with the PLGA-PEG-Pimozide spectrum for both PEG 2000 and 4000, it showed variation in the spectrum. It also clearly stated that there was an absorption of PEG on the surface of nanoparticles.

The particle size of PEG 2000 is smaller compared to PEG 4000. Encapsulation efficiency (EE) is much higher for PEG 2000 against PEG4000. The surface charge for both formulations has a diminutive difference (Table 1).

Table 1. *Physicochemical properties of PLGA-PEG nanoparticles.*

Formulations	Size(nm)	Zeta Potential (mV)	EE (%)
PEG 2000	71.63	-17.3	76.97
PEG 4000	80.01	-12.2	52.61

CONCLUSIONS

The current study and results indicated that lower molecular weight PEG-containing nanoparticles have an ideal particle size, charge and chemical interactions and encapsulation efficiency for targeted drug delivery systems. Lower molecular weight PEG showed promising results for developing future nanoparticles with distinctive properties.

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