Skin permeation studies of Pioglitazone from different dosage forms

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Introduction

Pioglitazone (PGZ) is an agonist of peroxisome proliferator-activated receptors (PPARs) from the nuclear receptor superfamily that regulate lipid, glucose, and amino acid metabolism. More recently, PPARs and corresponding ligands have been shown in skin and other organs to regulate important cellular functions, including cell proliferation and differentiation, as well as inflammatory responses. The main goal of this work was the association of PGZ to poly (D,L-lactide-co-glycolide) poly(ethylene glycol) (PLGA-PEG) nanospheres (NSs), for the treatment of skin disorders.

Methods

Nanoparticles preparation and characterization

PGZ-NPs were prepared using the solvent displacement technique (Fig. 1).

Morphometric parameters (average particle size and polydispersity index (PI)) were determined by dynamic light scattering (DLS) and zeta potential (ZP) by electrophoretic mobility. Morphology was determined by transmission electron microscopy (TEM) and Entrapment efficiency (EE%) of PGZ by HPLC.

$$EE\ (\%) = \frac{Total\ amount\ of\ PGZ - Free\ PGZ}{Total\ amount\ of\ PGZ} \cdot 100 \quad (Equation\ 1)$$

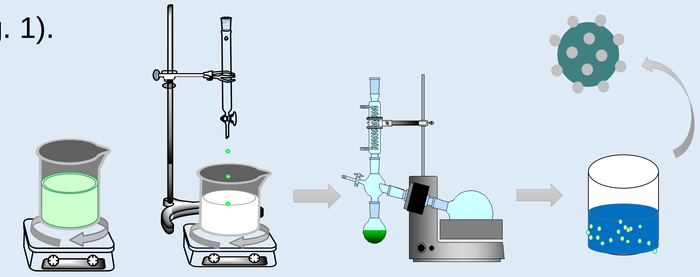
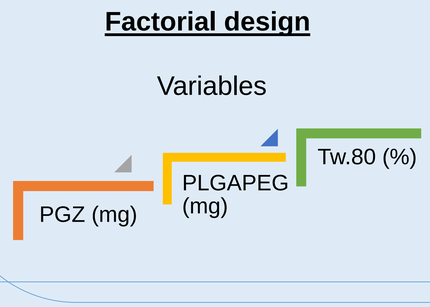


Fig. 1 : Elaboration method of PGZ-NPs

Factorial design



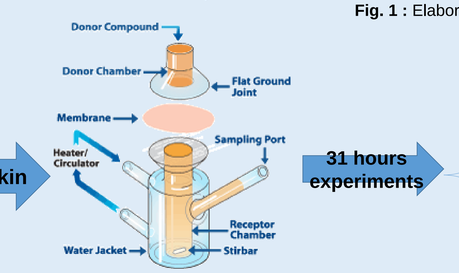


Fig.2.: Franz´s cell

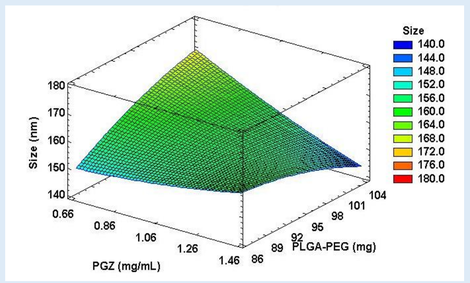
Assay

- Different Promoters of permeation
- PGZ- NPs
- Free drug

Results and Conclusions

Factorial design and Caracterization

a)



b)

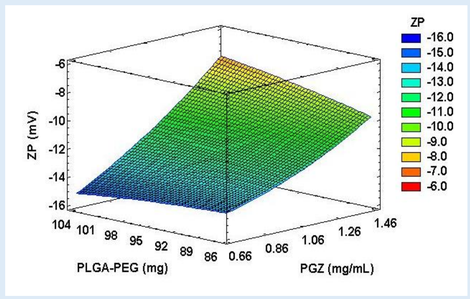


Fig.2: Factorial Design - Response Surface Tween 80 2% (a) size and b) ZP

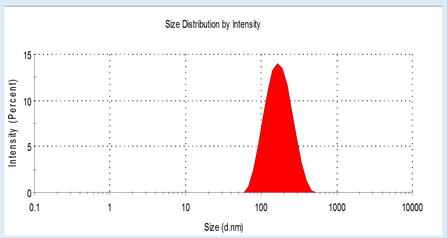


Fig.3.: Size by Zetasizer Nano ZS

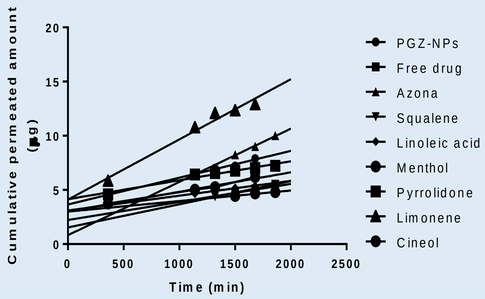


Fig. 4: Analysis of flows permeation

Table 1.: Amount of drug retained

Tested Formulations	Drug retained (µg/g skin/ cm²)	Kp (cm/h)
PGZ-NPs	14.55	8.9E-05
Free drug	42.60	4.9E-05
Azona	8.42	1.2E-04
Squalene	53.61	3.6E-05
Linoleic acid	14.84	3.2E-05
Menthol	101.82	2.3E-05
Limonene	207.65	1.3E-04
Cineol	94.74	2.5E-05
Pyrrolidone	18.04	4.2E-05

Conclusions

In view of these results all formulations tested are safe for possible application in inflammatory diseases of the skin and should be contrasted therapeutic efficacy *in vivo* skin test.

References

Bongartz, T., Coras, B., Vogt, T., Scholmerichand, J., Muller-Ladner, U. (2005). Treatment of active psoriatic arthritis with the PPAR ligand pioglitazone: an open-label pilot study. Rheumatology. 44(1):126-129.

Chawla, A., Barak, Y., Nagy, L., Liao, D., Tontonoz, P., Evans, R.M. (2001) PPAR-gamma dependent and independent effects on macrophage-gene expression in lipid metabolism and inflammation. Nat. Med. 7(1), 48-52.

Takayama, K., Nagai, T. (2008). Limonene and related compounds as potential skin penetration promoters. Drug Development and Industrial Pharmacy, 20 (4): 677-684.

Taylor, S.C. (2002). Skin of color: Biology, structure, function, and implications for dermatologic disease. J. Am. Acad. Dermatol, 46: 41-62.

Acknowledgements

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