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Polymeric Nanoparticles and Ionic Liquids hybrid systems for delivery of poorly soluble drugs

Introduction: Poor drug solubility and low permeation are two challenges when developing drug delivery systems. Nanotechnology may avoid these problems, by allowing a controlled or targeted delivery system [1]. Ionic liquids (ILs) are salts, liquid below 100 °C and have been used to increase drug solubility and permeation [2].
Our aim was to develop nanoparticle-IL hybrid systems to deliver a poorly soluble drug, Rutin.
Materials and Methods: Nanoparticles were produced using Poly(lactic-co-glucolic) Acid (PLGA) 50:50 or PLGA 75:25 by a modified solvent evaporation, w/o/w double emulsion technique[3]. The inner phase was an aqueous solution of 0.2 % (v/v) of IL, (2-hydroxyethyl)-trimethylammonium-L-phenylalaninate ([Cho][Phe]) or (2-hydroxyethyl)-trimethylammonium-L-glutamate ([Cho][Glu]) [2], dissolving rutin at its maximum solubility. The nanoparticles were also prepared with an inner phase at pH 6.7, the isoelectric point of rutin [4]. The association efficiency (AE) and the loading capacity (LC) were assessed by UV at 354 nm. The antioxidant activity was evaluated by DPPH assay.
Results and Discussion: The nanoparticles had a diameter in the range of 250-300 nm with a good PdI and colloidal stability (Figure 1). The AE of rutin, was around 70 % for the formulations with [Cho][Phe] and around 50 % for formulations with [Cho][Glu] (Table 1), representing a good improvement for a drug with poor solubility. There are no relevant differences between the two ratios of PLGA used. The LC of rutin showed that, for the same IL, results were similar for both ratios of PLGA (Table 1). However, when comparing both ILs, [Cho][Phe] showed a higher LC than [Cho][Glu]. The nanoparticles with the inner phase at pH 6.7, presented a significant increase in diameter (data not shown). The AE of rutin, only increased using [Cho][Glu], with an increase of about 8 % for both ratios of PLGA, while the LC presented the same tendency (data not shown).

Conclusion: This work showed the potential of nanoparticle-IL hybrid systems to deliver poorly soluble drugs, since they allow a higher loading of Rutin, compared with nanoparticles without IL. Stable and robust hybrid IL-nanosystems were obtained, regardless of the pH adjustment.
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References

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Figures

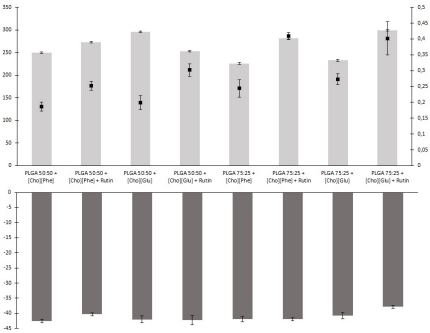

Figure 1: Diameter (nm), PdI and ZP (mV) of Rutin-loaded choline-based ILs PLGA nanoparticles hybrid systems. n=3, mean ± SD.

Table 1: AE (%) and LC (%) of Rutin-loaded ILs PLGA nanoparticles hybrid systems.n=3, mean ± SD.

Polymer	IL	AE (%)	LC (%)
PLGA 50:50	[Cho][Phe]	75.6 ± 1.0	1.0 ± 0.01
	[Cho][Glu]	53.8 ± 2.4	0.5 ± 0.04
PLGA 75:25	[Cho][Phe]	73.2 ± 0.9	1.0 ± 0.08
	[Cho][Glu]	51.3 ± 1.3	0.4 ± 0.03