New lipid nanocapsules for decitabine encapsulation

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Auteur	Briot, Thomas [1], Roger, Emilie [2], Lautram, Nolwenn [3], Lagarce, Frédéric [4]
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Résumé en anglais	Introduction: Currently decitabine, an antimetabolite agent is approved for acute myeloid leukemia in old patients and is administered via intra-venous (IV) route. It is a harsh treatment characterized by side effects mainly related with the IV administration as pain, risk of infectious, nursing and hospitalization. Oral route may represent a valid alternative route to IV administration because patient convenience and compliance. Due to the quick hydrolyze of the molecule in acidic conditions, decitabine oral bioavailability is very low, it ranges from 3.9 to 14%. The objective of this work was to design and develop a novel formulation to administer the decitabine per os. Material and method: Firstly, decitabine was solubilized in a reverse micelle (RM) formulation based on a mixture of Transcutol® HP and Tween® 80. RM were then incorporated into lipid nanocapsules (LNC-RM) (1).The formulation was then freeze dried and the stability after the freeze drying process was evaluated by comparing the size, the polydispersity index and the zeta potential to the initial values obtained before the freeze drying. The drug paylaod and encapsulation efficiency were determined after an ultracentrifugation to collect the free decitabine and the decitabine loaded in LNC-RM in two different fractions. In vitro release behavior of decitabine from LNC-RM in PBS medium (pH 7.4, 37°C) was evaluated using a dialysis method (Float a Lyzer 100kDa) and compared with the free drug solution. The drug was quantified using LC-MS/MS method. Finally, in vitro permeability study of decitabine-loaded LNC-RM was assessed in a Caco-2 cell model (2). Results and discussion: After freeze drying LNC-RM were stables showing an average size of around 30nm, with a low polydispersity index and a neutral zeta potential. The decitabine payload was 216±57µg/mL, with an encapsulation efficiency of 45±8%. The in vitro release results showed that, after 90min, almost 5% of decitabine was released from the LNC-RM, while the 45% was released from decitabine solution. The apparent permeability was increased when decitabine is encapsulated as compared to the free drug solution in the Caco-2 model after a contact of four hours. Conclusion: Here we presented a new formulation for the oral administration of decitabine. Further studies will be developed to assed the stability of the system in simulated gastro-intestinal media. References: (1) Heurtault B., et al. Pharm Research. 19(6), 2002 (2) Roger E., et al. Eur J Pharm Biopharm. 79(1), 2011
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