# Development of decitabine nano objects for oral administration

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| Résumé en anglais | **Introduction:**<br>Currently decitabine (trade name Dacogen®) is only approved for acute myeloid leukemia in old patients and is administered via intra-venous (IV) route once a day for five days, every four weeks. It's a painful treatment with difficulties due to IV administration: pain, risk of infectious, nursing, hospitalization. Decitabine oral bioavailability is limited to 3.9 to 14% mainly due to the quick hydrolyse of the molecule in acidic conditions.<br>The aim of our study was to design new formulations to administer decitabine orally.<br>**Material and methods:**<br>Four different nano-object strategies, already published, have been adapted for decitabine encapsulation: lipid nanocapsules (LNC) with a Transcutol® HP core (1), lipid drug conjugate (LDC) (2), polymeric nanoparticles (NP) (3), and LNC loaded with reverse micelles (LNC-RM) (4). For each strategy, size, polydispersity index (PdI), and Zeta potential were monitored by dynamic light scattering on a Zetasizer® Nano series DTS 1060. Encapsulation efficiency and encapsulation yield were determined after an ultra-centrifugation of the formulation or by filtration associated to centrifugation depending on the nanoparticles formulated. An UPLC-UV method was developed to quantify decitabine.<br>Results and discussion:<br>Very different sizes of nanoparticles were obtained: 27.4±1.6 nm for LNC-RM, 38.7±7.0 nm for LNC, 34.3±4.5 nm for LDC and 145.2±0.9 for NP. PdI were found inferior to 0.2 for all the encapsulation strategies used. Encapsulation efficiency was not sufficient for LNC, LDC and NP (1.20±2.00%, 25.00±1.94% and 2.81±3.10% respectively) but promising for the LNC-RM (48.76±14.18%), corresponding to an encapsulation yield of 244.6±74.9µg/mL.<br>**Conclusion:**<br>All formulations were prepared with only GRAS excipients and without class 1 and 2 solvents. Analytical method were designed and validated in accordance with the international conference on harmonization. An interesting formulation based on LNC and reverse micelle were obtained. The stability of this formulation in simulated fluids and in vitro permeability across a caco-2 cells culture model are in progress.<br>**References:**<br>(1) Heurtault B., Saulnier P., Pech B., Proust J-E., B J-P. Pharmaceutical Research. 19(6), 875-880, 2002<br>(2) Neupane Y-R., Sabir M-D., Ahmad N., Ali M., Kohli K. Nanotechnology. 24, 1-11, 2013<br>(3) Gonzalo T., Lollo G., Garcia-Fuentes M., Torres D., Correa J., Riguera R., Fernandez-Megia E., Calvo P., Avilés P, Guillén M-J., Alonso M-J., Journal of Controlled Release. 169, 10–16, 2013<br>(4) Vrignaud S, Anton N, Gayet P, Benoit J-P., Saulnier P. European journal of pharmaceutics and biopharmaceutics. 79, 197-204, 2011 |
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