Drug loading levels affect \textit{in vitro} release of vinorelbine from thermosensitive liposomes

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Triggered drug release from thermosensitive liposomes (TSL) has been proposed as a strategy to address limitations associated with conventional liposomal drug delivery: heterogenous drug uptake and distribution as well as limited drug release at the target site. Ongoing clinical studies with a TSL formulation of doxorubicin are highlighting the potential of this treatment and delivery approach. Many other drugs would benefit from the same localized and targeted delivery strategy as it can result in significant improvements in therapeutic index. Our lab has developed TSLs loaded with cisplatin, alvespimicycin and the vinca alkaloid vinorelbine (VRL) [1,2]. Here we aimed to understand how formulation parameters (e.g. drug loading level, internal/external buffer) influence the performance (e.g. drug release, stability) of a TSL formulation encapsulating VRL (Figure 1).

Lyso-lipid containing TSLs were loaded with varied amounts of drug and heat-triggered release over a temperature range of 37 to 42°C was measured in protein containing release media. Differential scanning calorimetry (DSC) was used to evaluate the effect of formulation preparation and drug loading on the formulation’s thermal properties to predict their \textit{in vitro} release behaviour. Cryogenic transmission electron microscopy (cryo-TEM) images were obtained and image gray values were determined to assess the degree of drug precipitation (if any) within the liposomes. The \textit{in vitro} release behaviour is assessed in the absence and presence of protein.

The current studies demonstrate the importance of thorough \textit{in vitro} characterization during development of a TSL formulation. The results highlight that previously determined formulation characteristics and their influence on a formulation’s performance cannot be easily translated from non-thermosensitive liposomes to their thermosensitive counterparts.
