An automated method for accelerated prediction of new micellar nanomedicines

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Background: Approximately 70% of currently available active pharmaceutical ingredients (APIs) are considered poorly water soluble, which often results in significant challenges in drug development and formulation. Surfactant micellar systems have been extensively studied for their ability to increase the amount of dissolved API, however less than 3% of marketed nanomedicines are micellar. Additionally, the conventional trial-and-error methods of designing solubility-enhancing formulations are laborious and time-consuming. Subsequently, an automated solubility screen has been developed with the view of exploiting machine learning (ML) to inform more efficient, automated formulation of micellar systems.

Methods: A method for automated small-volume solubility studies was developed using an Opentrons OT2 liquid handling robot (OT2) and plate readers commonly found in pharmaceutical laboratories. Curcumin (CUR) was employed as a model hydrophobic nutraceutical and the FDA's Inactive Ingredients Database was used to identify a range of surfactants approved for parenteral use. Following automated formulation of single-surfactant micellar formulations in well plates, the concentration of solubilised CUR was determined spectrophotometrically, whereas size and polydispersity of micellar particles were analysed using dynamic light scattering. The solubilisation power of pharmaceutical surfactants polysorbate 80 and polysorbate 20 was expressed as the mass solubilisation ratio, defined as the weight of CUR solubilised by the unit mass of surfactant above its critical micelle concentration.

Results: It was found that in the examined CUR micellar formulations, polysorbate 80 provided a higher mass solubilisation ratio compared to polysorbate 20.

Conclusions: An automated method for preparation of micellar systems has been developed, and it will further be utilised to examine the solubilisation power of a library of surfactants against a library of poorly soluble drugs, with the view of investigating multi-surfactant systems, and curating an extensive data collection for development of an ML model for prediction of novel micellar formulations.