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Joseph Camm[1], Hendrik Versteeg[2]

[1]School of Engineering, Technology and Design, Canterbury Christ Church University, North Holmes Road, Canterbury, Kent, CT1 1QU, UK

[2]Wolfson School of Mechanical, Electrical and Manufacturing Engineering, Loughborough University, Epinal Way, Loughborough, Leicestershire, LE11 3TU, UK

The Kigali amendment to Montreal protocol sets the timetable for phasing out of pMDI propellants HFA134a and HFA227ea, creating a requirement for green propellants to take their place. To assist this transition, accurate prediction of thermophysical properties that control aerosol generation of new formulations is crucial. A relevant challenge is how to predict property data such as saturated vapour pressure, surface tension and viscosity of propellant/excipient/drug mixtures using the smallest possible programme of physical testing. It is proposed to use a thermodynamic framework based on activity coefficients to model intermolecular forces between constituents, which are known to control multi-component thermophysical property behaviour. It is proposed to use the UNIFAC method, which is based on detailed physical understanding of molecular functional groups and their interactions, with the ability to capture azeotropic behaviour. Surface tension, viscosity and vapour pressure measurements of mixtures of HFA134a with ethanol at 20°C have been studied to validate the technique.

Utilizing UNIFAC parameter fitting to the experimental dataset with non-linear least-squares optimization, a root mean square deviation (RMSD) of 7% in predicted surface tension, 6% in predicted viscosity and 2% in predicted vapour pressure was obtained. Previously unavailable UNIFAC interaction parameters for HFA-alcohol mixtures were created.

The capability is highly versatile, accepting various thermophysical property data and giving good agreement with measured values for existing formulation mixtures. The framework can be readily applied to mixtures of green propellants such as HFA152a to extend experimental data when available and support insights into thermophysical properties and aerosol generation.