Application of Nanocellulose in Nasal Spray Formulations.

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Introduction

The research aim was to provide evidence that crystalline nanocellulose (CNC) could potentially be used as an excipient in nasal spray formulations as a tailorable thickener. This could improve drug delivery as well as patient compliance. This was explored using a design of experiment (DOE) approach with chosen parameters; percentage concentration, blending time and blending speed. Measurement outputs were Spray area, viscosity and drip length on Carbopol polymer (to mimic effect on mucus). Statistics performed on output data to determine significant formulation parameters. Material characterisation was also performed on extracted samples using Eutectic solvents to determine their potential use as extraction medium.

Research Methodology

- **DOE** – Collection of measurements of viscosity, drip weight on polymer and spray areas (thermal analysis).
- **Extraction** – Material characterisation of extracted sample through PSD, zeta potential, FTIR and SEM.
- **Application of DOE** – Use of data solver to determine optimum formulation parameters for CNC with comparison to extracted sample.

DOE Parameters

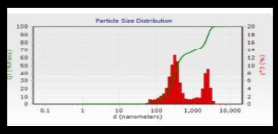
Experiment	Concentration	Time (min)	Speed (rpm)
1	6%	5	13500
2	6%	1	13500
3	0.6%	1	8000
4	0.6%	5	8000
5	6%	5	8000
6	0.6%	1	13500
7	6%	1	8000
8	0.6%	5	13500

Determined significant factors (Spray area)

	Coefficients	t Stat	P-value
Intercept	50.09	29.4	2.35×10^{-15}
Concentration	-10.95	-6.43	8.32×10^{-06}
Blending Speed	-5.34	-3.14	0.01
Time x Speed	-5.93	-3.48	0.00

Results and Discussion

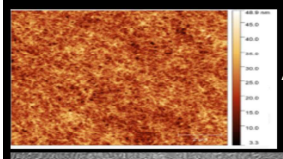
Material Characterisation



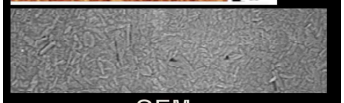
Particle Size Distribution

All samples showed evidence of Microparticles

Eutectic solvents not strong enough to extract nanoparticles on their own



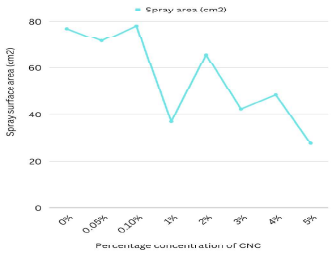
AFM



SEM

Research suggests original mode of extraction with sulfuric acid remains to be the best mode of extracting nanocellulose

Scoping trials of nanocellulose spray areas indicated an interesting phenomenon around the 1% concentration which led to the decision to concentrate on a wide concentration range in the DOE. This result could also have been influenced by the particular device used and visualisation difficulties.



Early research indicates a possible tailorable element to spray area in relation to CNC % concentration

SPRAY SURFACE AREA

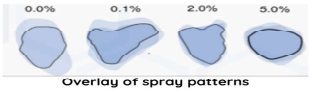
Concept

Addition of certain concentrations of nanocellulose to nasal spray formulations could potentially control the spray surface area of plume geometry

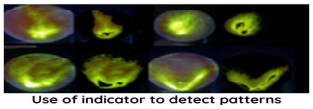
Methodology

Could not measure dynamic spray area so developed method of defining spray area from spray outlines on paper, to using indicators like Fluorescein sodium and finally the use of a thermal heat camera. ImageJ software used to calculate areas.

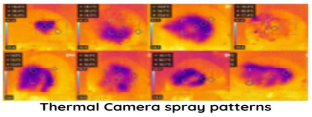
Results



Overlay of spray patterns



Use of indicator to detect patterns



Thermal Camera spray patterns

Conclusions

Research determined a potential for tailoring nasal spray formulations in relation to spray area by varying percentage concentrations of nanocellulose excipient as well as other formulation parameters such as blending speed, suggesting optimization is possible. A green extraction of nanocellulose was attempted using eutectic solvents but was determined unsuccessful due to large proportion of microparticles present. Future research needed on nasal spray formulations to utilise full potential of drug route.