From Bench to Bedside: The Development & Evaluation of Orodispersible Films for Paediatric Drug Delivery

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Introduction

Orodispersible Films (ODFs) that have been shown to be a child-friendly dosage form for young patients. As such, ODFs represent a breakthrough in paediatric drug delivery, particularly in managing and improving the treatment of chemotherapy-induced nausea and vomiting (CINV) in paediatric oncology patients.

I aim to:

1. Carry out laboratory characterisation to measure the structure and stability of ODFs to ensure quality and efficacy.
2. Understand experiences with CINV and current antiemetic treatments and management strategies to understand effective approaches and limitations.
3. Evaluate the use of ODFs and if they're an acceptable child-friendly alternative.

Orodispersible Films (ODFs)

Injections/infusions are the chosen method of administration but they're invasive, can be painful, and require hospitalisation to be administered. Alternative dosage forms would simplify drug administration and allow drug delivery at home, which would be much more comfortable for the patient and their caregiver(s).

ODFs are thin, polymeric sheets *(Figure 1)* that dissolve rapidly in the mouth and release active pharmaceutical ingredients (APIs) that are quickly absorbed into the bloodstream. ODFs are formulated using a polymer solution containing the API and excipients.

Electrospinning

ODFs are created using electrospinning which "spins" a polymer solution into ultrafine fibres by applying electricity *(Figure 2)*. The API is evenly distributed throughout, ensuring consistent dosing and a large surface area-to-volume ratio. This allows rapid disintegration, leading to fast drug release, and absorption, and a rapid onset of action. This is ideal when paediatric patients require rapid relief from CINV.

Chemotherapy-Induced Nausea & Vomiting (CINV)

Chemotherapy comes with side effects like CINV. It's a significant concern in paediatric cancer care due to its impact on patients' quality of life (dehydration and malnutrition), treatment adherence, and overall clinical outcomes (delayed recovery).

CINV can be classified into three main types: anticipatory CINV, acute CINV, and delayed CINV.

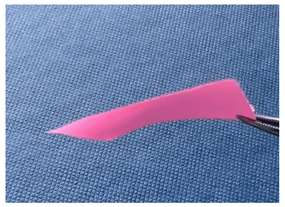

Figure 1: A thin polymetric film consisting of a polymer solution combined with rhodamine (an artificial dye).

Figure 2: The Electrospinning machine at the UCL School of Pharmacy.

Laboratory Research

ODFs were characterised with:

1. TGA: measured thermal stability and moisture loss, which tells me how stable ODFs are under heat and how they'll break down.
2. DSC: measures a sample's heat flow to identify physical and chemical changes like melting or crystallisation (phase changes)
3. PXRD: analyses material composition, purity, and crystallinity determination (if a material is crystalline or amorphous), which influences solubility and stability.
4. SEM: creates high-resolution images of a sample's surface at a microscopic level to analyse morphology and topology.

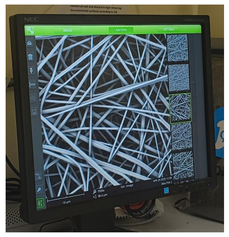

Figure 3: A scanning electron microscopy (SEM) image of crystalline structure found in a prototype ODF.

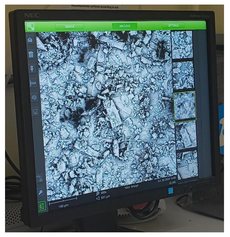

Figure 4: A scanning electron microscopy (SEM) image of amorphous structure found in a prototype ODF.

SEM analysis revealed that one ODF sample retained a crystalline API structure *(Figure 3)*, indicating improved physical stability and longer shelf life - beneficial for the long-term management of CINV. The other sample *(Figure 4)* showed an amorphous structure, suggesting the API underwent structural changes during formulation.

5. UV-Vis: measures the absorbance of light by a sample to determine drug concentrations and drug release profiles.

Absorbance of light changes with wavelength for each concentration (7–25 µg/mL), where there's an increase in absorbance with concentration. There's a strong linear relationship between absorbance and concentration for the standard drug solutions ranging from 7–25 µg/mL in *Figure 5*, supported by the R^2 value of 0.997. This indicates a very low level of variance in the absorbance data set. *Figure 7* could be used to determine the concentration of drug released from ODFs during dissolution studies, which tells me whether ODFs can achieve therapeutic concentrations rapidly enough to prevent or treat acute CINV, and whether sustained release characteristics may manage delayed CINV.

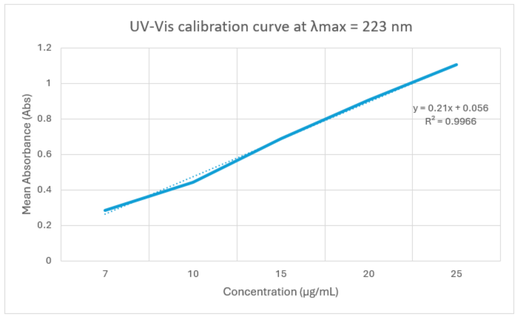

Figure 5: UV-Vis calibration curve at λmax.

Clinical Research

I used the survey that the previous Laidlaw Scholar designed and edited it by adding more questions to gain a better understanding of 3 key areas:

1. Frequency and Severity of Nausea and Vomiting
2. Current Management Strategies
3. Treatment Experiences and Expectations

Overall, 19 caregivers of paediatric oncology patients in the Oncology and Haematology Department at Great Ormand Street Hospital (GOSH) participated.

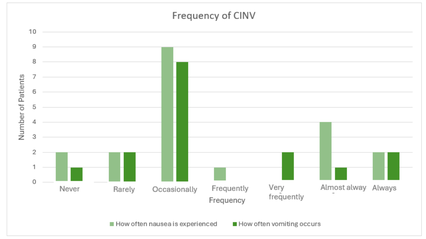

Figure 6: Bar chart displaying the reported frequency of CINV.

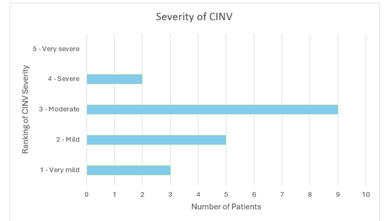

Figure 7: Bar chart displaying the reported severity of CINV.

Chemotherapy timing and food were common triggers of CINV. Duration varied: six families experienced short (<30 min) episodes, another six reported 1–2 hour durations, and five described symptoms lasting over two hours—some for half a day or longer.

Open-ended responses described extensive physical, emotional, and social impacts. Many patients expressed anxiety and distress around chemotherapy, developing anticipatory CINV.

Oral solutions were the most common dosage form - poor taste and swallowing difficulties were frequently cited problems. Infusions are effective but invasive and anxiety-inducing. Tablets were rarely used. Families often used multiple dosage forms due to setting (home vs hospital) or dosage form changes.

Most families reported receiving no non-drug advice from healthcare professionals. Only a few mentioned using distractions (TV, music) or aromatherapy to ease symptoms.

Participants were unfamiliar with ODFs initially, but responded positively once informed, appreciating their ease of use, portability, and minimal risk of being vomited. Tablets and dispersible tablets were the least favoured due to bitterness, size, and difficulty administering during nausea.

Conclusion, Evaluation, & Reflections

- Laboratory analysis showed that prototype ODFs possessed desirable structural stability and uniformity, supporting their potential for therapeutic effectiveness.
- Clinical findings from caregivers and patients at GOSH revealed that current antiemetic formulations, especially syrups and tablets, are poorly tolerated due to taste, swallowing difficulty, and emotional distress, highlighting the need for more acceptable alternatives.
- Participants responded positively to ODFs.
- This project has been one of the most rewarding and eye-opening experiences of my academic journey.
- My motivation, as a pharmacy student, to pursue innovations that combine science with empathy to improve real-world healthcare outcomes has developed.

Supervisors: Dr Karolina Dziemidowicz & Dr Diba Keyhanfar