Enhancing Delivery Of Biopharmaceutics Classification System Class II Drugs Through a Novel Alginate/Carrageenan/Oleogel Matrix: A Case Study On Praziquantel for Improved Therapeutic Efficacy

Nsanzubuhoro, C. N. & Tai, S. L.

Introduction

Schistosomiasis is a waterborne and neglected tropical disease prevalent in Sub-Saharan Africa and South-East Asia. Limitations of the oral administration of the biopharmaceutics classification system (BCS) class II drug, praziquantel (PZQ), include its bitter taste, limited efficacy against juvenile worms, and low bioavailability due to its lipophilicity. In an effort to enhance the efficacy of PZQ, a novel drug delivery system composed of alginate, AG, carrageenan, CG, and a wax-based oleogel will be developed. The study will employ analytical methods including differential scanning calorimetry (DSC) for thermal behaviour analysis, confocal light microscopy for material morphology observations, fourier-transform infrared spectroscopy (FTIR) for understanding release mechanisms, high-performance liquid chromatography (HPLC) for quantifying release material concentration, and the Instron instrument for determining the Young modulus. Additionally, release kinetics will be investigated through dissolution studies using the United States Pharmacopeia (USP) 1 basket method.

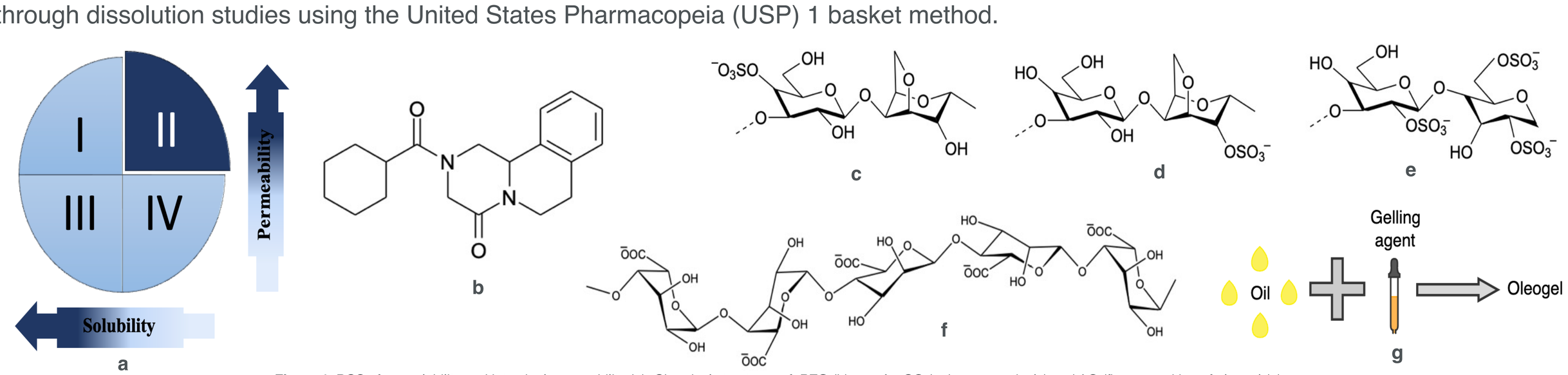

Figure 1: BCS of aq. solubility and intestinal permeability (a); Chemical structures of PZQ (b); ι,κ, λ –CG (c,d,e, respectively) and AG (f); composition of oleogel (g)

Alginate/Carrageenan/Oleogel

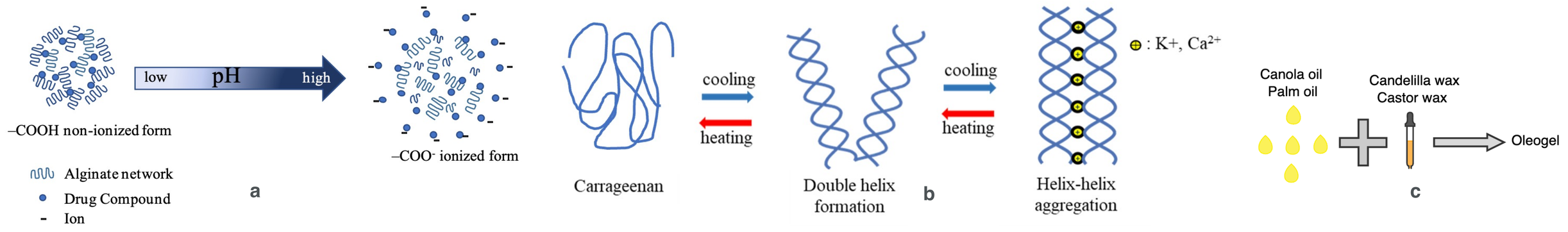

Figure 2: Schematic of the pH-responsive behaviour of drug-loaded alginate (adapted from Agüero *et al.*, 2017, a) ; The potential gelling mechanism of ι,κ-CG (adapted from Cunha and Grenha, 2016, b); composition of wax-based oleogel used In the study (c)

Aims and Objectives

Aim: To develop a ternary drug delivery system using natural polymers (alginate and carrageenan) and oleogel to enhance drug absorption by improving bioavailability through sustained release of PZQ, and ultimately enhance drug efficacy for the treatment of schistosomiasis.

Objectives:

- To investigate the structural, physical and dissolution behaviour of the i) AG/CG hybrid gel (without oleogel) by varying AG:CG ratios; ii) pure oleogel with varying oil and gelling agents of different melting points; iii) AG:CG:oleogel gel bead by varying the AG:CG to oleogel ratios.
- To study the time release of AG, CG and oleogel of the AG/CG/oleogel gel bead under simulated stomach and intestinal gastrointestinal environments.
- To investigate and to apply design of experiments (e.g. surface response methodology or factorial design) in understanding the release behaviour of praziquantel within the AG/CG/oleogel bead in comparison to free PZQ.

Study Justification

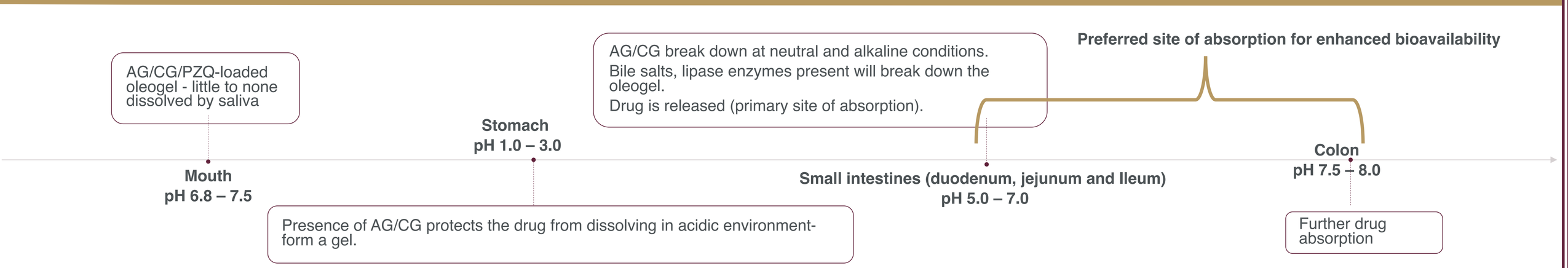

Figure 3:The proposed mechanism of the AG/CG/Oleogel matrix

Methodology

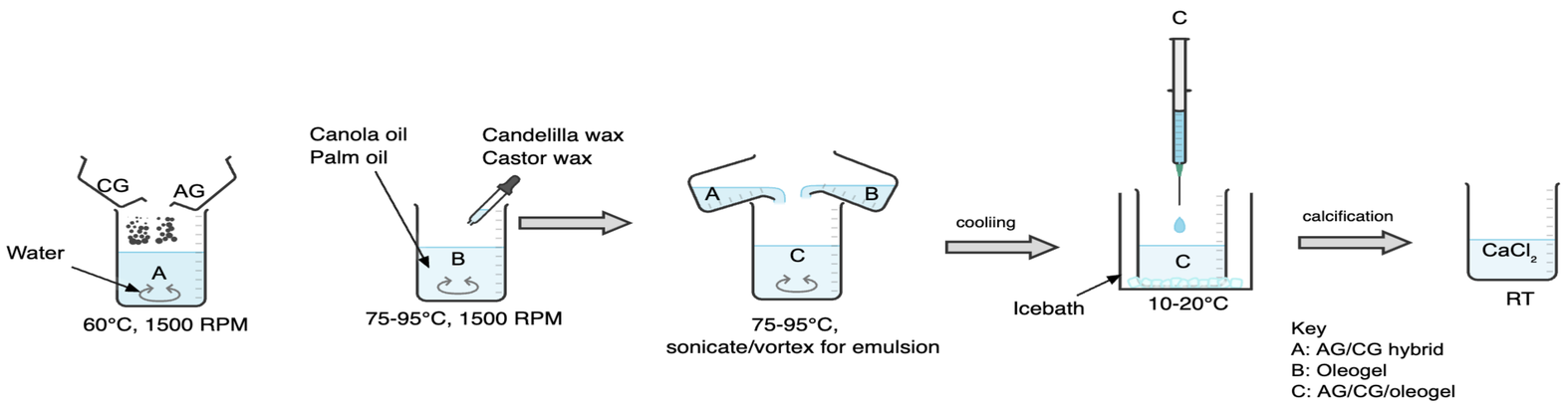

Figure 4: Schematic of methodology (created with Chemix 2023)

Characterization:

- DSC
- Light microscopy
- FTIR
- HPLC
- Dissolution test USP 1 basket (pH 1-8)
- Instron instrument

References

- Agüero, L., Zaldivar-Silva, D., Peña, L. & Dias, M. 2017. Alginate microparticles as oral colon drug delivery device: A review. Elsevier Ltd. DOI: 10.1016/j.carbpol.2017.03.033.
- Cunha, L. & Grenha, A. 2016. Sulfated seaweed polysaccharides as multifunctional materials in drug delivery applications. MDPI AG. DOI: 10.3390/md14030042.