

Development and Characterization of Bigels for Topical Applications

Joy Morrow¹, Jinsong Hao²

¹ Doctor of Pharmacy Candidate 2024, Campbell University College of Pharmacy & Health Sciences

² Campbell University College of Pharmacy & Health Sciences Department of Pharmaceutical & Clinical Sciences



INTRODUCTION

Wound healing is an intricate, modulated series of processes that maintain the integrity of the skin barrier. Diseases such as diabetes disrupt these processes involved in natural wound healing resulting in the development of a chronic wound.¹ To date, REGRANEX® Gel (becaplermin) remains the only FDA approved topical treatment for chronic wounds in the form of diabetic foot ulcers and only available in the United States.² Chronic wound healing remains an area of research interest and need for advancement. Our previous studies have demonstrated that digitoxigenin, a cardiotonic steroid, improved wound healing in a diabetic wound model by affecting many key events in a wound healing process, such as re-epithelialization and collagen deposition.² The studies also suggested the importance of olive oil and alginates in the formulations. In efforts to improve the formulation, we used a unique bigel as a platform to be able to load drugs of different physicochemical properties.

BACKGROUND

As this research was to develop a formulation platform for drug delivery, digitoxigenin was not utilized in this project. Instead, we used benzocaine and diclofenac sodium as the model drugs of different physicochemical properties. Benzocaine is relatively hydrophobic and diclofenac sodium is relatively hydrophilic. Bigels contain a hydrophobic organogel phase and a hydrophilic hydrogel phase. In this study, the organogel phase was 15% Span 60 in olive oil to load the hydrophobic drug and the hydrogel phase was 2% alginate in phosphate buffered saline (PBS) to load the hydrophilic drug.

OBJECTIVES

To develop and characterize the formulations for stability and in vitro release of model drugs using Franz diffusion cells.

FORMULATION

The hydrogel phase (A) and the organogel phase (O) were mixed at different ratios using a mortar and pestle to prepare the bigels with trituration method. The bigels were stored at room temperature for physical stability testing.



Figure 1. Bigels at five different phase ratios (left to right), A: O = 1:1, 1:3, 1:5, 3:1 and 5:1.

The bigel at 1:1 ratio was most stable (Fig. 1) and thus 10-gram batches of bigels were freshly prepared for release study of the two drugs, benzocaine and diclofenac, using a Franz diffusion cell apparatus (Fig. 2).

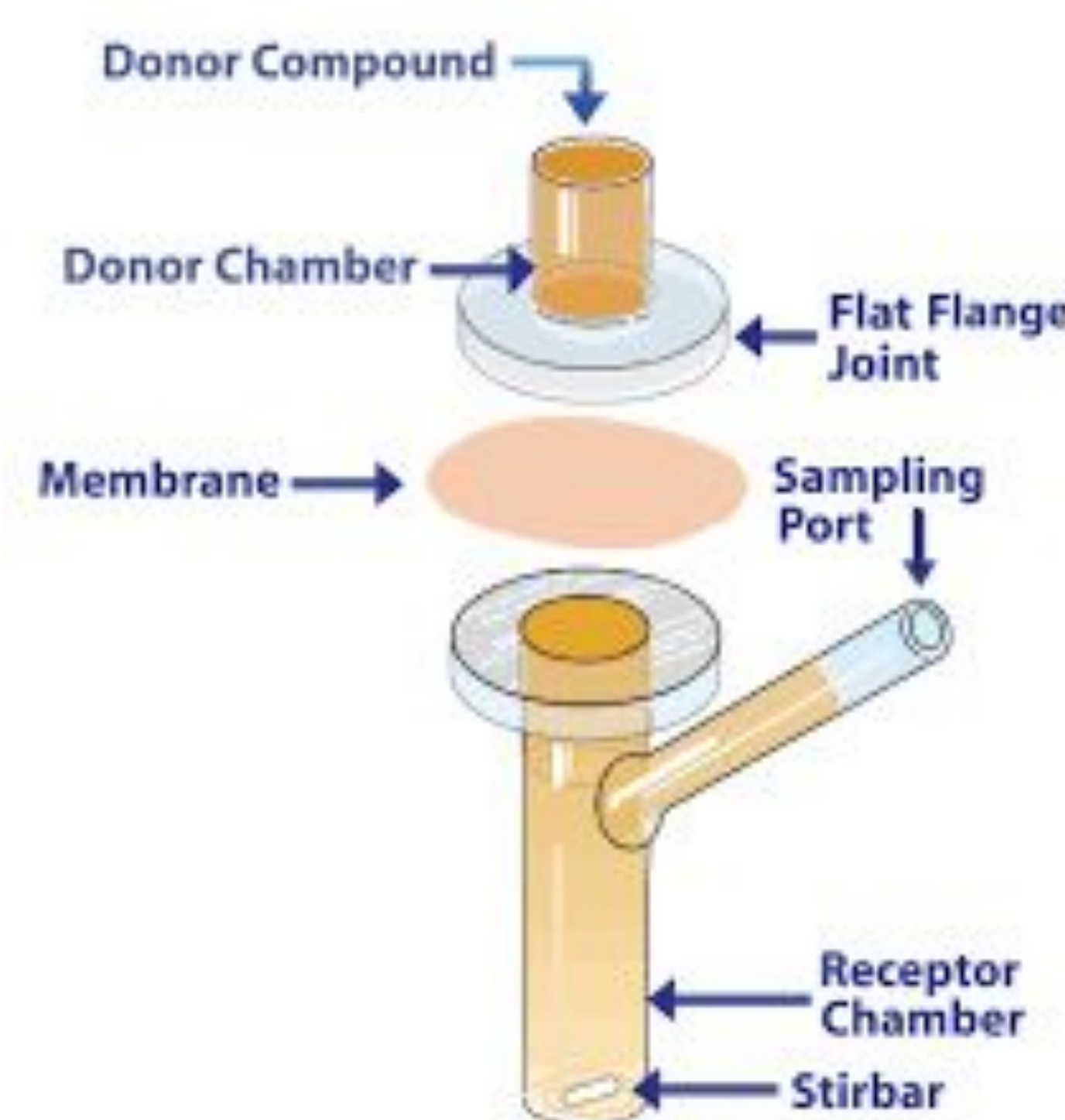


Figure 2. Unjacketed Franz Cell³

IN VITRO RELEASE STUDY

The Franz diffusion cell has a donor compartment and a receptor compartment. A 0.45 µm filter membrane was assembled between the donor and the receptor as a physical support to the bigel formulation that was loaded to the donor. PBS was added to the receptor as a receptor solution, which was magnetically stirred and maintained at 32°C. Samples of 2 mL was taken from the sampling port at 1, 2, 3, and 4 hours. The same volume of fresh PBS was added to the receptor to keep the volume of the receptor solution constant. The samples from the receptor were assayed for drug concentration. The cumulative amount of drug at different time points was plotted against time to obtain the release profiles. As shown in Figure 3, both drugs showed linear release from the bigel formulation.

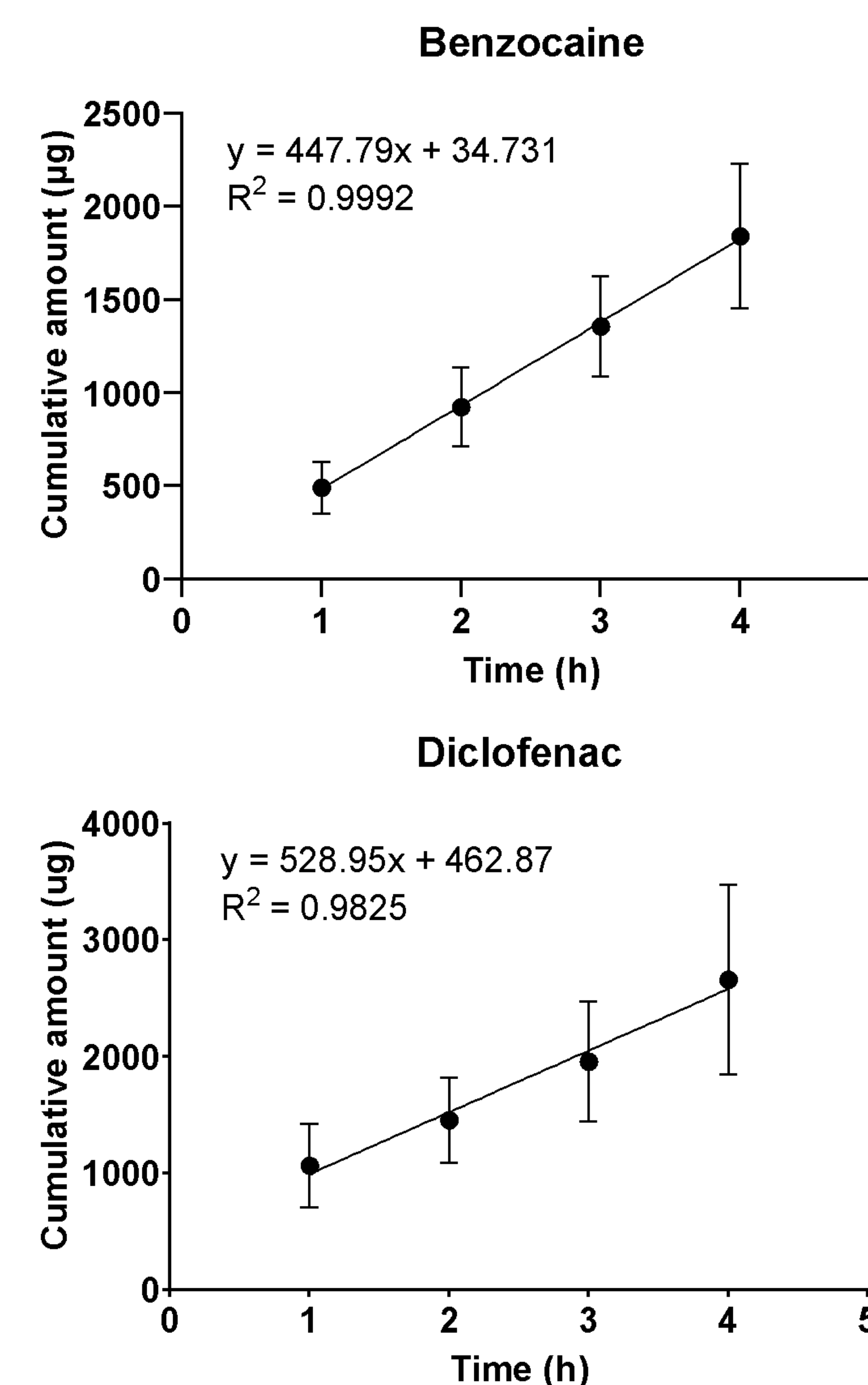


Figure 3. The release profiles for benzocaine and diclofenac. Data are presented as mean ± SD, n = 6-8.

DRUG ASSAY

A UV-Vis spectrophotometer was used to obtain the absorbance (AU) of the samples. A stock solution was prepared and diluted into a series of dilutions. The wavelengths used were 286 nm for benzocaine and 276 nm for diclofenac sodium. The calibration curve was first established as follows:

Benzocaine:

$$\text{Absorbance} = 0.1097 \times \text{Concentration } (\mu\text{g/mL}) + 0.0330 \quad (R^2 = 0.9989)$$

Diclofenac:

$$\text{Absorbance} = 0.0401 \times \text{Concentration } (\mu\text{g/mL}) + 0.0777 \quad (R^2 = 0.9872)$$

CONCLUSIONS

Based on the data, a bigel of both hydrophobic and hydrophilic properties can release a model drug at a constant rate.

ACKNOWLEDGEMENT

This research was supported by the Campbell University College of Pharmacy & Health Sciences Student Engagement in Research (SER) Grant.

REFERENCES

- Han G, Ceilley R. Chronic wound healing: A review of current management and treatments. *Advances in therapy*. <https://pubmed.ncbi.nlm.nih.gov/28108895/>. Published January 12, 2017. Accessed March 18, 2023.
- Feng X, Hao J. Identifying new pathways and targets for wound healing and therapeutics from natural sources. *Current Drug Delivery*. 2021;18(8):1064-1084. doi:10.2174/1567201818666210111101257
- Franz Cell- The Original. PermeGear. <https://permegear.com/franz-cells/>. Published 2019. Accessed March 18, 2023.