Testing Novel Biopolymer Adhesives for Drug Delivery in the Treatment of Skin Disorders

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Abstract:

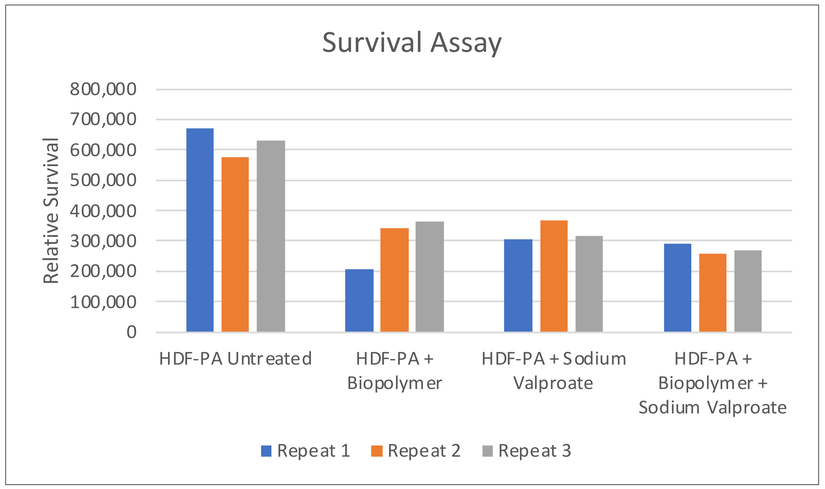
Keloids are non-cancerous fibroproliferative skin tumors that form due to aberrant wound healing. They are caused by excess collagen production and overproliferation of fibroblasts. Treatments include topical corticosteroids and a variety of other drugs used empirically to block keloid growth, although these show highly variable efficacy and high recurrence rates. Additionally, patient compliance with the long-term application of drugs remains a big challenge in the treatment of many skin conditions. In collaboration with the FSU College of Engineering, we are testing novel biopolymer adhesives for drug delivery through the skin. Here, we have tested the polymer neutral poly-2-acrylamido-2-methylpropane sulfonic acid (neutral AMPS) for the topical application of drugs to treat keloids and other skin diseases. In my research, I studied the effect of the biopolymer with and without the drug sodium valproate on human dermal fibroblasts (HDF) in culture to determine their effect on healthy skin cells. My preliminary results show that the polymer can release the drug but the polymer itself results in some cytotoxicity. However, since human skin has layers of dead cells protecting the underlying live cells, it is possible that this biopolymer maybe safe to use in low concentrations for drug delivery through human skin.

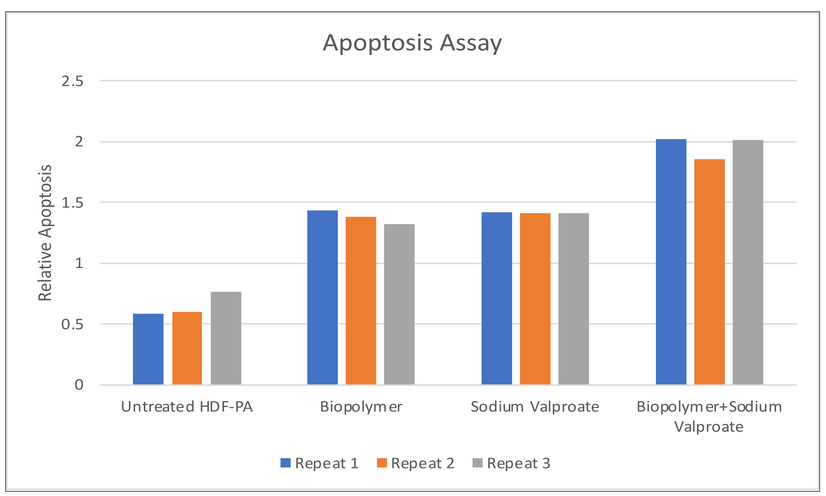
Methods:

- I separated my cells into two groups. The first group would undergo a senescence assay and the second group would undergo an apoptosis / necrosis assay.
- Next, I treated normal primary human dermal fibroblasts (skin cells) with sodium valproate, biopolymer, and a combination of the two. I left one row of cells untreated as a control.
- I incubated the cells for a week; I imaged the cells over the incubation period to keep an eye on cell death.
- After the incubation period, I counted the cells to determine cell survival, as well as perform senescence, apoptosis, and necrosis assays
- Finally, I finished imaging the cells and conducted a quantitative analysis of the images.

Hypothesis:

- The cells treated with sodium valproate alone and the cells treated with biopolymer alone will have more cell death than the untreated cells.
- The cells treated with both sodium valproate and biopolymer will have the most cell death.

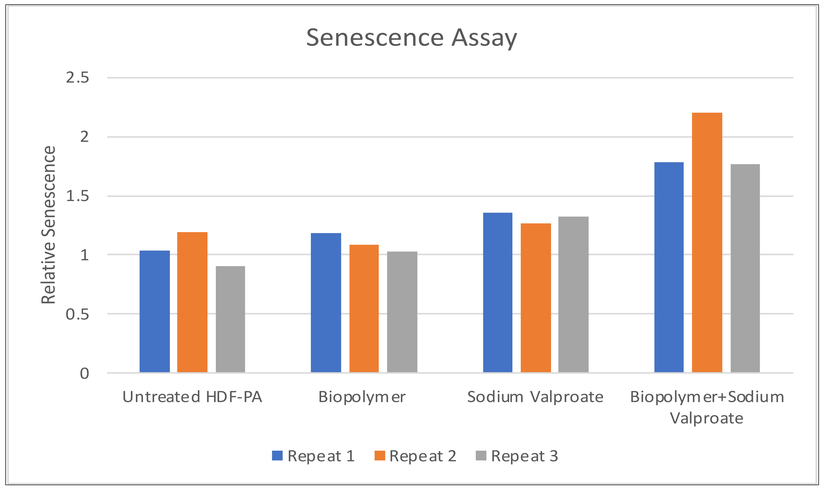




References:

Burks, S.; Spotnitz, W., "Safety and Usability of Hemostats, Sealants, and Adhesives." Assoc Oper Room Nurs 2014, 100 (2), 160-17

Andrews, J.P., Marttala, J., Macarak, E., Rosenbloom, J., and Uitto, J. "Keloids: The paradigm of skin fibrosis - Pathomechanisms and treatment." Matrix Biology 2016, 51, 37-46.



Results:

- Survival assays show that the introduction of the biopolymer alone resulted in a ~50% decrease in the overall cell count.
- The cell death observed upon biopolymer treatment was mostly due to apoptosis, although senescence did contribute some to cell death when the biopolymer was combined with the drug.
- Necrosis did not appear to be a contributor to cell death.

Conclusions:

- The biopolymer does result in cytotoxicity primarily due to apoptosis, especially when used with the drug sodium valproate.
- However, the biopolymer may be safe to use in low concentrations since human skin provides the live cells with layers of dead skin cells as a barrier against external factors.

Future Directions:

- This project will continue to test the neutral AMPS biopolymer to ensure that it is safe for commercial healthcare use.
- In the future, I will test the biopolymer on fresh pig skin, which closely resembles human skin, and mice to determine which concentrations of the biopolymer are safe and most effective.