Can a Soy Diet Mimic the Effects of Estrogen?

Cody Gouyer, Emily Humphries, Jonah Hottinger, and Kelly Tarmon
Longwood University, Department of Biological and Environmental Sciences
Biology 404-Immunology, Dr. Amorette Barber

Background

- Cancer: The body's cells not acting correctly
  - Myeloid-derived suppressor cells (MDSCs): protect cancer from the immune system, make tumors resistant against immunotherapy, & allow the tumor to be strong as it weakens its host
- Estrogen: enhances the immune system & the way MDSCs weaken the immune system.[2]
- Xenoestrogens: estrogen-mimicking substances that can be found in many foods we consume such as soy.[3]
- Isoflavones: specific category of xenoestrogens, considered one of the most multipurpose xenoestrogens naturally produced.[3]

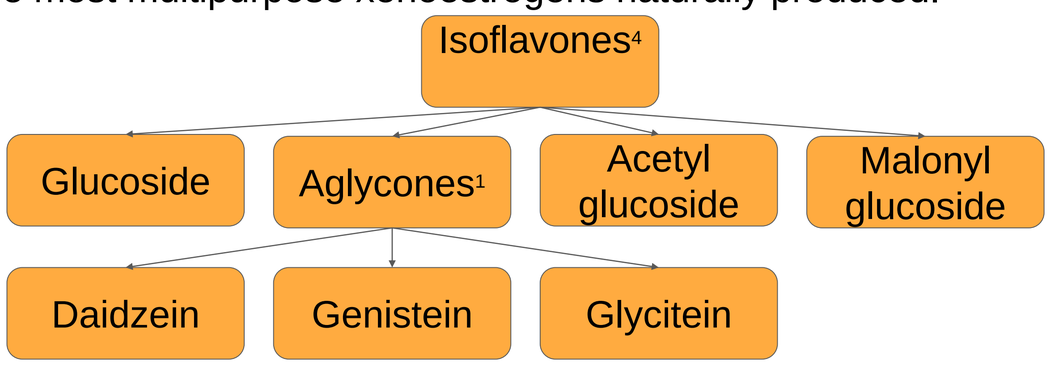
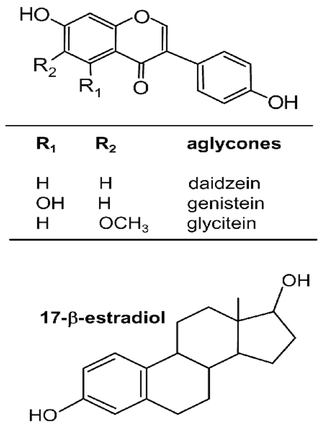


Figure 1. *Categories of Isoflavones in Specifics to the Ones we Experimented With. Isoflavones have four different categories each of which have three different subcategories. The aglycones of daidzein, genistein, and glycitein are the ones we experimented with.*

- Xenoestrogens mimic estrogen closely in structure (Fig. 2) & chemical function.[5,6]



R_1	R_2	aglycones
H	H	daidzein
OH	H	genistein
H	OCH_3	glycitein

Figure 2. *Comparison Between Structure of Aglycones and Estradiol.* These two structures are similar in that they contain some of the same properties, structure, and function when introduced into the body.

- Once the isoflavones enter the body, they find and bind to the same chemical receptors that estrogen binds to.

Hypothesis

As estrogen mimicking compounds, these three xenoestrogens will be statistically similar to estrogen. If they are similar to estrogen, they will enhance MDSC function as estrogen does.

Methods

1. Culture of Dendritic Cells
2. Flow Cytometry for expression of MHC II and CD80
3. T cell Isolation and Cell Culture
4. MTT Proliferation to assess cell viability
5. ELISA for comparison of IL-4 and IFN-g
6. Statistical Analysis

Results

CD80 expression showed similarities in estrogen and glycitein.
IFNγ secretion showed similarities between estrogen and daidzein.

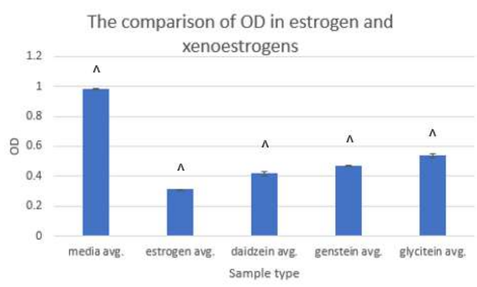


Figure 3 (left). *MTT Proliferation Data*. Two tailed t-tests were used to compare OD in the media, estrogen and xenoestrogens. Significant differences were shown between all. ^(P<0.05)

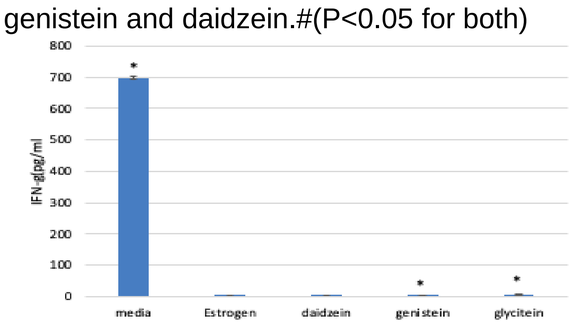


Figure 4 (right). *Flow Cytometry Data.* Flow cytometry was used to test the levels of CD80 and MHCII when stimulated with media, estrogen, daidzein, genistein, and glycitein.For MHC II, all stimulants were significantly different except for estrogen-daidzein, estrogen-genistein, and daidzein-genistein @. For CD80, significant results were shown between all stimulants but genistein and daidzein.#(P<0.05 for both)

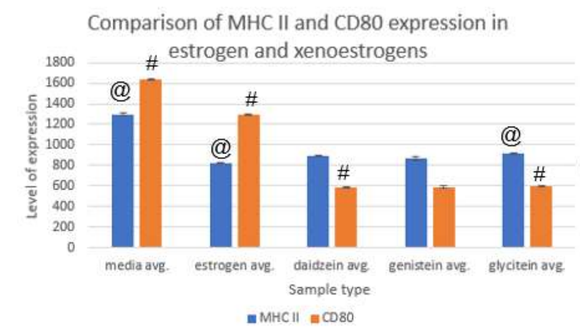


Figure 5 (left). *ELISA IFNγ Secretion Data.* ELISA was run to determine the picogram/mL values of each of our media, estrogen, and xenoestrogens. The graph shows these values. Significant differences were shown between all except estrogen and daidzein. *(P<0.05)

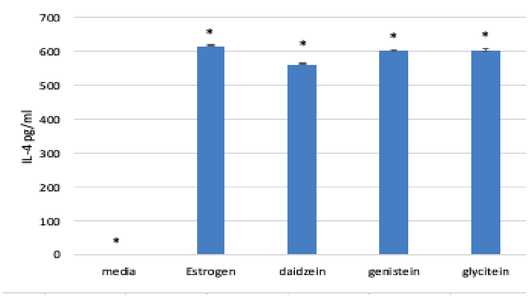


Figure 6 (right). *ELISA IL-4 Secretion Data.* ELISA was run to determine the picogram/mL values of each of our media, estrogen, and xenoestrogens. Significant differences were shown between all. *(P<0.05)

Conclusions/Future Directions

We found few statistically significant similarities between estrogen and our xenoestrogens. Therefore, we cannot conclude that these xenoestrogens enhance MDSC function. Many believe these xenoestrogens are mimics of estrogen, but what makes them mimics? There was not enough evidence to show that they effect MDSC function, but maybe they affect a different function estrogen also affects.

References

[1]Izumi, T., Piskula, M. K., Osawa, S., Obata, A., Tobe, K., Saito, M., … Kikuchi, M. (2000). Soy Isoflavone Aglycones Are Absorbed Faster and in Higher Amounts than Their Glucosides in Humans. *The Journal of Nutrition*, *130*(7), 1695–1699.
[2]Ozerova, M., & Nefedova, Y. (2019). Estrogen promotes multiple myeloma through enhancing the immunosuppressive activity of MDSC. *Leuk Lymphoma,* 60(6), 1557-1562. doi: 10.1080/10428194.2018.1538511
[2]Setchell, K. D. (1998). Phytoestrogens: the biochemistry, physiology, and implications for human health of soy isoflavones. *The American Journal of Clinical Nutrition*, *68*(6).
[3]Song, T. T., Hendrich, S., & Murphy, P. A. (2002). Estrogenic Activity of Glycitein, a Soy Isoflavone. *Journal of Agricultural and Food Chemistry*, *50*(8), 2470–2470.
[4]Vacek, J., Klejdus, B., Lojkova, L., & Kubáň, V. (2008). Current trends in isolation, separation, determination and identification of isoflavones: A review. *Journal of separation science*. 31. 2054-2067.
[5]Vitale, D. C., Piazza, C., Melilli, B., Drago, F., & Salamone, S. (2013). Isoflavones: estrogenic activity, biological effect and bioavailability. *European Journal of Drug Metabolism and Pharmokinetics*, *38*(1), 15–25.
[6]Tesi, R. J. (2019). MDSC; the Most Important Cell You Have Never Heard Of. *Trends in Pharmacological Science,* 40(1), 4-7. doi: https://doi.org/10.1016/j.tips.2018.10.008
Lastly, we would like to thank Dr. Barber for all of her help and guidance. We truly could not have completed this research without her.