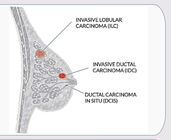
Saffron (Crocus sativus) extract has anticancer activity through inhibition of migration and invasion potential of breast cancer cells

Janelle Mecias, Meaghan McDonald, Savannah Bradley, Albina Mikhaylova, Ph.D , Fatima Rehman, Ph.D
Department of Biology, Material Science & Engineering Facility (MSERF), University of North Florida, Jacksonville, FL 3224

INTRODUCTION

Initial Diagnosis
- Mammography
- Ultrasound
- MRI



Standard Treatment Options
- Surgery
- Radiation
- Chemotherapy
- Hormone therapy
- Targeted therapy
- Immunotherapy

Negative Side Effects
- Nausea
- Pain
- Lethargy
- Hormone imbalance
- Decreased quality of life

Increased need for alternative cancer therapies

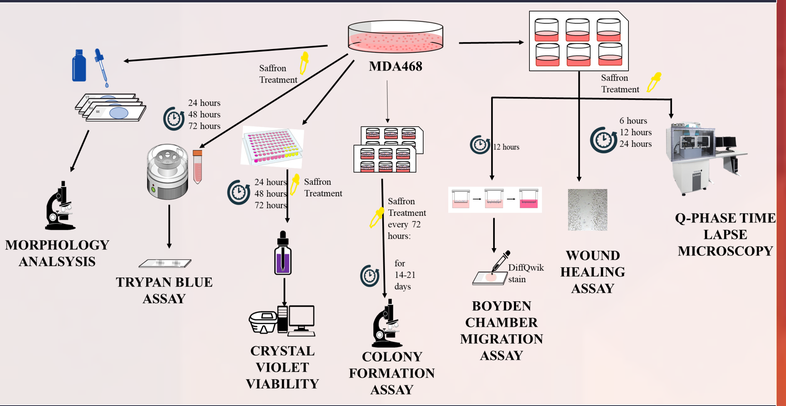
Saffron (Crocus sativus)

- Potential reduction of toxicity to patient
- Applications in adjuvant and neoadjuvant treatment
- Increase patient quality of life

HYPOTHESIS

Saffron was expected to have antitumor activity in MDA468 breast carcinoma cells

METHODS



Saffron inhibits growth of MDA468 cells in a dose dependent manner

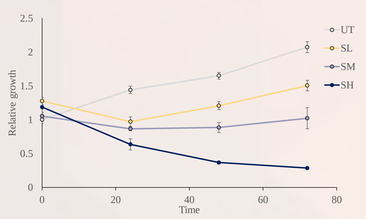


Figure 1. Comparison of relative growth as per crystal violet cell viability assay.
Table 1. Concentration of saffron in various treatment groups.

Treatment	Concentration
Untreated (UT)	0 ug/ mL
Saffron Low (SL)	100 ug/ mL
Saffron Medium (SM)	250 ug/mL
Saffron High (SL)	500 ug/ mL

Saffron decreases cell viability in a time and dose dependent manner

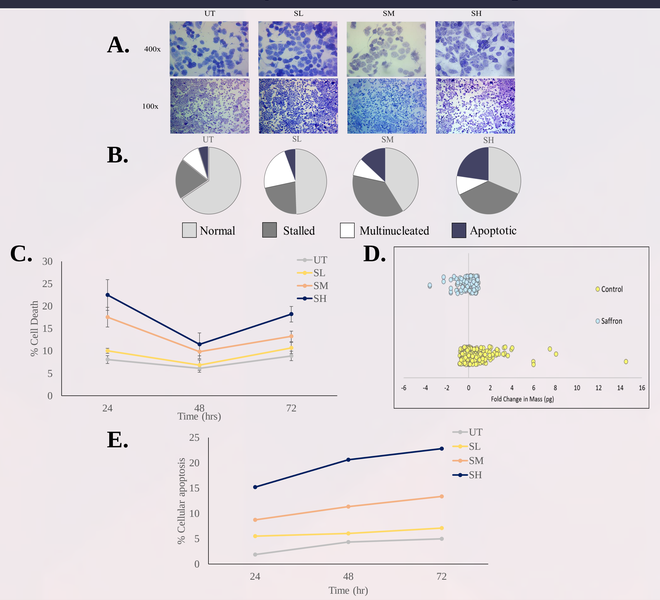


Figure 2A) Comparison of cell confluency at 100x and 400x magnification. **2B)** Percentage of normal, stalled, multinucleated, and apoptotic cells between 0-72 hours. **2C)** Percentage cell death calculated by trypan blue assay between 24-72 hours. **2D)** Percentage fold changes in mass in control and saffron groups as per Q-phase analysis. **2E)** Comparison of percentage cellular apoptosis between 24-72 hours.

Saffron induces marked reduction in tumorigenicity of MDA468 cells

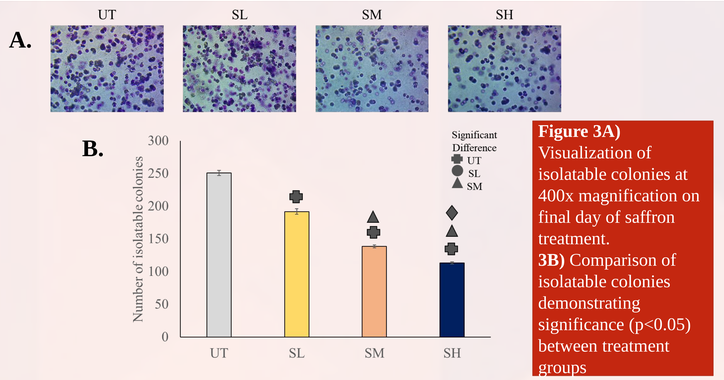


Figure 3A) Visualization of isolatable colonies at 400x magnification on final day of saffron treatment.
3B) Comparison of isolatable colonies demonstrating significance ($p<0.05$) between treatment groups

Increasing saffron concentration causes a decrease in breast cancer cell invasion potential

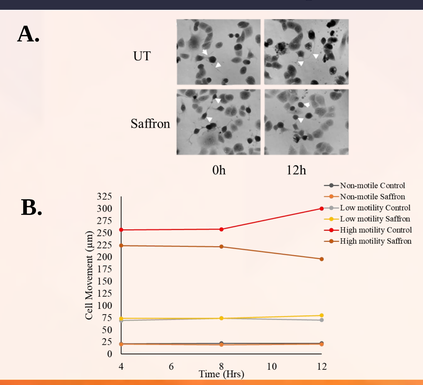


Figure 4A) Morphological comparison between control versus saffron treated MDA-MB-468 breast cancer cells at 0 and 12 - hour time periods. White arrows mark cell projections.

4B) Average distance traveled by cells over a 12-hour time period, as calculated by Q-Phase Analysis. Cells were split into three groups based on movement: Non-Motile (10-35µm), Low-Motile (35-150µm), and High-Motile (150-550µm).

Increasing saffron results in a decrease in cell motility and invasion potential

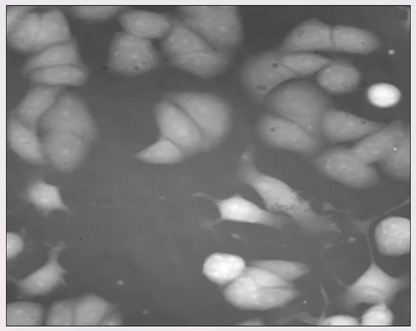


Figure 5A) The reduction of cell projections in a time dependent manner after the addition of Saffron as shown by video produced by Q-Phase.
5B) Comparison of cells migrated across Boyden chamber membrane with bovine serum albumin (BSA) ss a positive control after 12 hours of saffron treatment.
5C) Comparison of migration distance across scratch wound after 6 hours of treatment.

CONCLUSIONS

- Increasing concentrations of saffron cause a decrease in cell motility
- Cell viability decreases as saffron concentration increases.
- Cell invasion potential decreases as saffron concentrations increase.
- Saffron causes a decrease in tumorgenicity.

FUTURE DIRECTIONS

- Analysis of saffron's effectiveness against motility, cell viability, cell invasion potential, and tumorgenicity for increased duration of time.
- Further exploration of saffron as an alternative therapy for breast cancer carcinoma in an animal model.

REFERENCES

American Cancer Society. (2020). *Cancer Facts and Figures 2020*
Fariđi, N., Heidarzadeh, H., Mohagheghi, M.-A., & Bathaie, S. Z. (2019). BT-474 Breast Cancer Cell Apoptosis Induced by Crocin, a Saffron Carotenoid. *Basic & Clinical Cancer Research*, *11*(1), 5–15.
Hire, R. R., Srivastava, S., Davis, M.B., Konreddy, A. K., and Panda, D. (2017). "Antiproliferative Activity of Crocin Involves Targeting of Microtubules in Breast Cancer Cells." *Scientific Reports*. 7: 1-11.
Miller, M. E. (2018). Cancer. *Momentum Press.*
Mousavi, S. H., Tavakkol-Afshari, J., Brook, A., & Jafari-Anarkooli, I. (2009). Role of caspases and Bax protein in saffron-induced apoptosis in MCF-7 cells. *Food and Chemical Toxicology*, *47*(8), 1909–1913.
National Cancer Institute. (2020). *Cancer Stat Facts: Female Breast Cancer*. Surveillance, Epidemiology, and End Results (SEER).
Peart, O. *(2015).* Breast intervention and breast Cancer treatment options. *Radiologic Technology, 5.*
Ramani, K. V., Ramani, H., Alurkar, S., Ajaikumar, B. S., & Trivedi, R. G. (2017). Breast Cancer: Medical Treatment, Side Effects, and Complementary Therapies. *Momentum Press.*
Sajjadi, M., & Bathaie, Z. (2017). Comparative Study on The Preventive Effect of Saffron Carotenoids, Crocin and Crocetin, in NMU-Induced Breast Cancer in Rats. *Cell Journal (Yakhteh)*, *19*(1), 94–101.
Schneble, E., Jinga, D., & Peoples, G. (2015). Breast Cancer Immunotherapy. *Maedica- a Journal of Clinical Medicine*, 10(2), 185-191.
Siegel, R. L., Miller, K. D., & Jemal, A. (2020). Cancer statistics, 2020. *CA*, *1*, 7.
Tavakkol-Afshari, J., Brook, A., & Mousavi, S. H. (2008). Study of cytotoxic and apoptogenic properties of saffron extract in human cancer cell lines. *Food and Chemical Toxicology*, *46*(11), 3443–3447.
Vali, F., Changizi, V., & Safa, M. (2015). Synergistic Apoptotic Effect of Crocin and Paclitaxel or Crocin and Radiation on MCF-7 Cells, a Type of Breast Cancer Cell Line. *International Journal of Breast Cancer*, 1–7.

AKNOWLEDGMENTS

University of North Florida Biology Department, Material Science & Engineering Facility (MSERF), and a special thanks to Dr. Rehman for her collaboration and guidance in this project.