A Greener Approach to Fighting Cancer: α–Solanine's Potential against Glioblastoma

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A growing body of research shows that chemicals derived from natural sources can be used to treat a variety of diseases. Maltese researchers are currently investigating the effects of a molecule which may be extracted from plants such as potatoes to assess its potential against a specific type of brain cancer.

Cancers are devastating diseases, with nearly two million new cases diagnosed in the US alone since 2020. Several therapeutic approaches may be utilised depending on the particular presentation. However, not all current therapy is successful in curing the targeted cancer.

Glioblastoma multiforme is the most aggressive primary malignant brain cancer, and the success of conventional therapy is limited, with few patients surviving beyond two years since their diagnosis. Therefore, great efforts are being made to identify tentative alternative therapeutic approaches.

A growing body of literature is demonstrating the suitability of natural extracts and single molecules as putative anti-cancer agents. One emerging molecule is α-solanine, which may be extracted from crops such as potatoes and tomatoes. This molecule has traditionally been viewed as a poison, but contemporary research has described α-solanine as antipyretic, anti-diabetic, anti-allergic, anti-inflammatory, and more recently, also as a promising anti-cancer. With a multitude of anti-properties, this molecule has been tested against several types of cancer, but not brain tumours.

AN UNLIKELY SOURCE

'What I found very interesting about this chemical is that you can extract it from potatoes,' laughs Andrea Cuschieri, a medical student currently on a suspension of studies to pursue a Master of Science degree (supervised by Prof. Byron Baron). In Europe, potato industries face a serious problem with potato peel waste. As the fourth main crop worldwide (following rice, wheat, and maize), potato peel is a zero-value waste or sold at a very low cost. 'This means that with further research, potatoes may someday become a cheap source for cancer therapy, contributing to environmentally friendly treatments,' explains Cuschieri.

Chances are you've already seen α-solanine without realising it: specifically, that layer of green skin under the potato peel and sprouts (commonly known as eyes). The greening of the potato is caused by α-solanine, which is also a predominant chemical within the sprouts themselves. The interesting part is that 'you can literally use the potato peels, sprouts, or rotting potatoes to manufacture an anti-cancer drug,' explains

Cuschieri. It's environmentally friendly, almost like a renewable drug, and the potato production itself is also quite sustainable.

Sustainability is currently one of the major concerns worldwide. According to recent predictions, the world's population is expected to increase by nearly 2 billion in the next 30 years, reaching 10 billion in 2050. Therefore, it is now urgent to have the ability to meet our current needs without compromising the ability of future generations to do so.

The healthcare industry is one of the most significant contributors to climate change. However, several counteractive measures are being made to reduce waste, promote preventive care, and develop more efficient and environmentally friendly treatments. Maltese researchers and medical practitioners are currently working towards this common goal through the combination of a sustainable use of agriculture waste and greener anti-cancer drugs.

A-SOLANINE AND GLIOBLASTOMA

'This molecule has never been tested against glioblastoma, a specific type of brain cancer,' adds the researcher. There are over 100 different types of brain tumours, usually named after the type of cell they develop from. Glioblastoma originates from cells known as glial cells, which support neurons. 'The scientific community is not entirely sure what causes glioblastomas to occur,' explains Cuschieri, 'but it is dangerous and deadly. After being diagnosed, most people may unfortunately die within 15 months (on average). There is no cure.'

Surgery followed by chemoradiotherapy is still the gold-standard treatment used. As a result, Maltese researchers devised a proof-of-concept study to determine whether and how α-solanine works against this type of brain cancer. The first set of experiments is already finished.

Cuschieri's preliminary findings using cell cultures (cells grown and maintained outside of a living organism under controlled conditions) show that 'in the presence of α-solanine, the tumour becomes less aggressive.' But how did the researchers arrive at this interpretation?

'We performed different experiments to assess the effect of α-solanine on the cell's viability and metastatic properties,' explains the researcher. Cell viability assays

Right: **Slide 1: E**

Negative Control shows the three cell lines with no treatment
Positive control shows the three cell lines with a chemical known to produce a positive [killing] effect
Row 3 shows the three cell lines' response to α-solanine treatment
Row 4 shows the three cell lines' response to conventional treatment.

Image courtesy of Andrea Cuschieri

focused on understanding the effects of different concentrations of α-solenine on glioblastoma cell death. Interestingly, researchers discovered that the quantity of α-solenine needed to induce the same effect as chemotherapy was significantly lower. 'Our drug seems to work better than the standard of care in the in vitro conditions tested.' These results are highly important since exposing a person to higher drug concentrations can have a bigger negative impact in the body but not necessarily a better outcome.

Migration and invasion assays focused on understanding how α-solanine affects metastatic properties of glioblastoma cells. 'With our drug, cells migrated and invaded less.' How do we know that? To study cell migration, researchers created a scratch in a cell layer to simulate a wound. Then, they monitored if and how long it took the wound area to close. For invasion, they placed the cells in contact with a permeable membrane and observed whether the cells could invade the surroundings by travelling through the membrane. The researchers tested three conditions: the cancer cells alone, establishing the tumour's capability to invade surrounding tissues; cells exposed to current chemotherapy; and finally those exposed to α-solenine. These are the fundamental conditions for determining whether α-solenine can have a better outcome than the standard anti-cancer treatment. Closing these experiments, researchers are now working to understand the mechanism of cell death induced by α-solenine to obtain a better understanding of the anti-cancer mechanisms of this drug.

THE FUTURE?

'It is still early to state that these types of results can have a real medical application,' highlights Cuschieri. 'The discussed results were obtained in vitro, with cell cultures.' That means that the system complexity is non-existent. We don't know how and if other brain cells are contributing to the progression of glioblastoma. Therefore, there are still several steps needed to say with absolute certainty that α-solenine can be used against this specific brain cancer.

As a follow up, after testing the basis and showing α-solenine's potential, work should be done to replicate its findings using animal models. The success of this molecule against glioblastoma still needs to be evaluated considering a multitude of parameters.

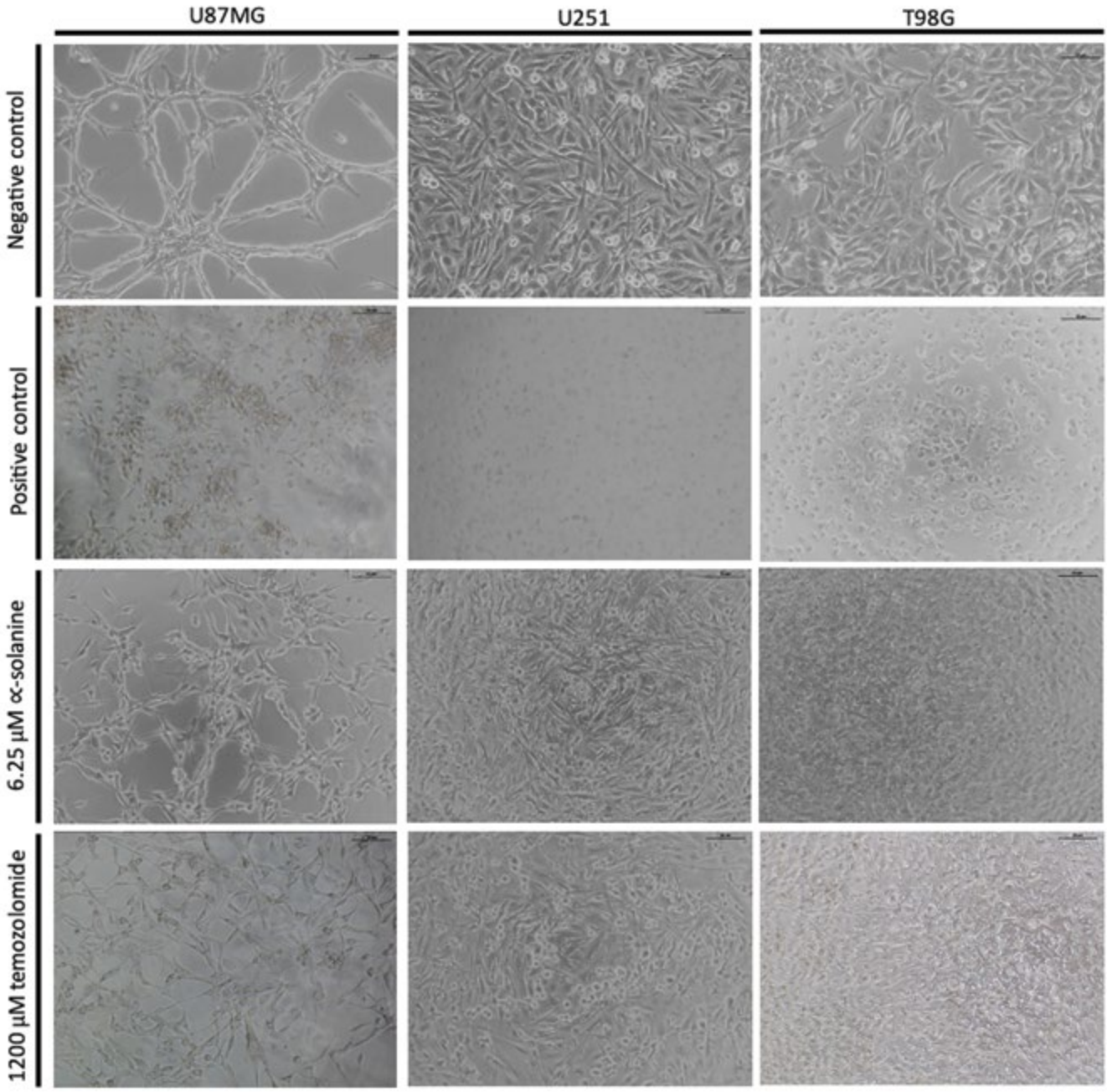
The major goal of this study was not to demonstrate with absolute certainty the α-solenine anti-cancer effect in glioblastoma. Rather, its aim was to 'grow current knowledge regarding potential treatments against a currently incurable disease, while better understanding the mechanisms governing α-solenine-induced cell death,' finalises Cuschieri. 'We are increasingly showing that chemicals derived from natural sources such as potatoes do not need to be viewed as ineffective or as alternative medicines. Instead, they can actually have modern day uses and applications.' T

Further Reading:

Susanne, A. (2022). Climate change and global health: What actions are healthcare leaders taking? https://www.weforum.org/agenda/2022/11/climate-change-global-health-actions-healthcare-leaders/

Emran, T. B., Shahriar, A., Mahmud, A. R., Rahman, T., Abir, M. H., Siddiquee, M. F. R., et al. (2022). Multidrug Resistance in Cancer: Understanding Molecular Mechanisms, Immunoprevention and Therapeutic Approaches. *Frontiers in Oncology, 12*, 891652. doi:https://doi.org/10.3389/fonc.2022.891652

Wu, D. (2016). Recycle Technology for Potato Peel Waste Processing: A Review. *Procedia Environmental Sciences, 31*, 103-107. doi:https://doi.org/10.1016/j.proenv.2016.02.014


U87MG
U251
T98G
Negative control
Positive control
6.25 µM α-solanine
1200 µM temozolomide