

C. ELEGANS STABILIZATION OF MICROTUBULES VIA TAXOL



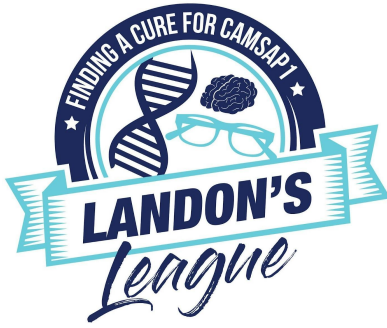
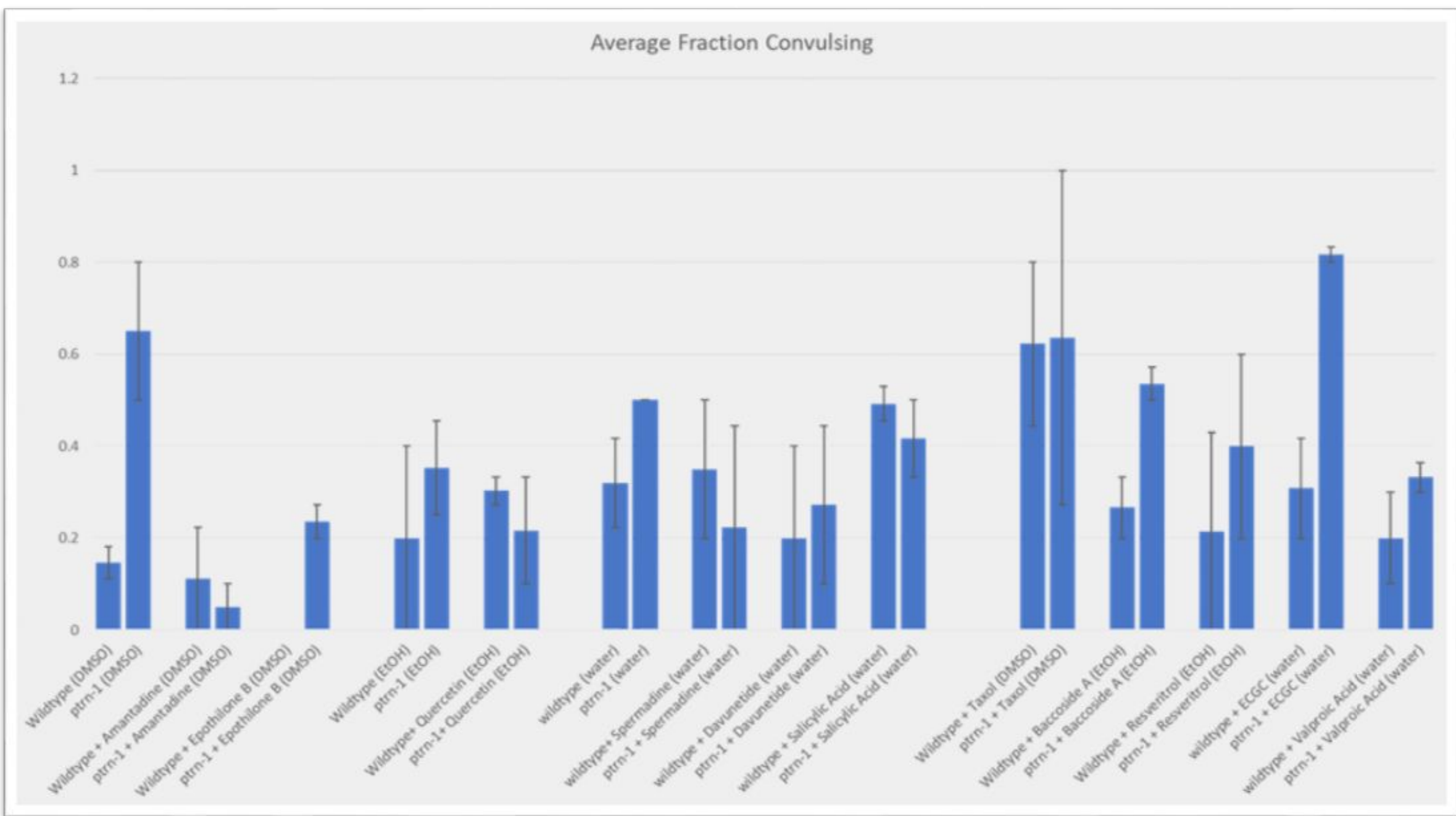
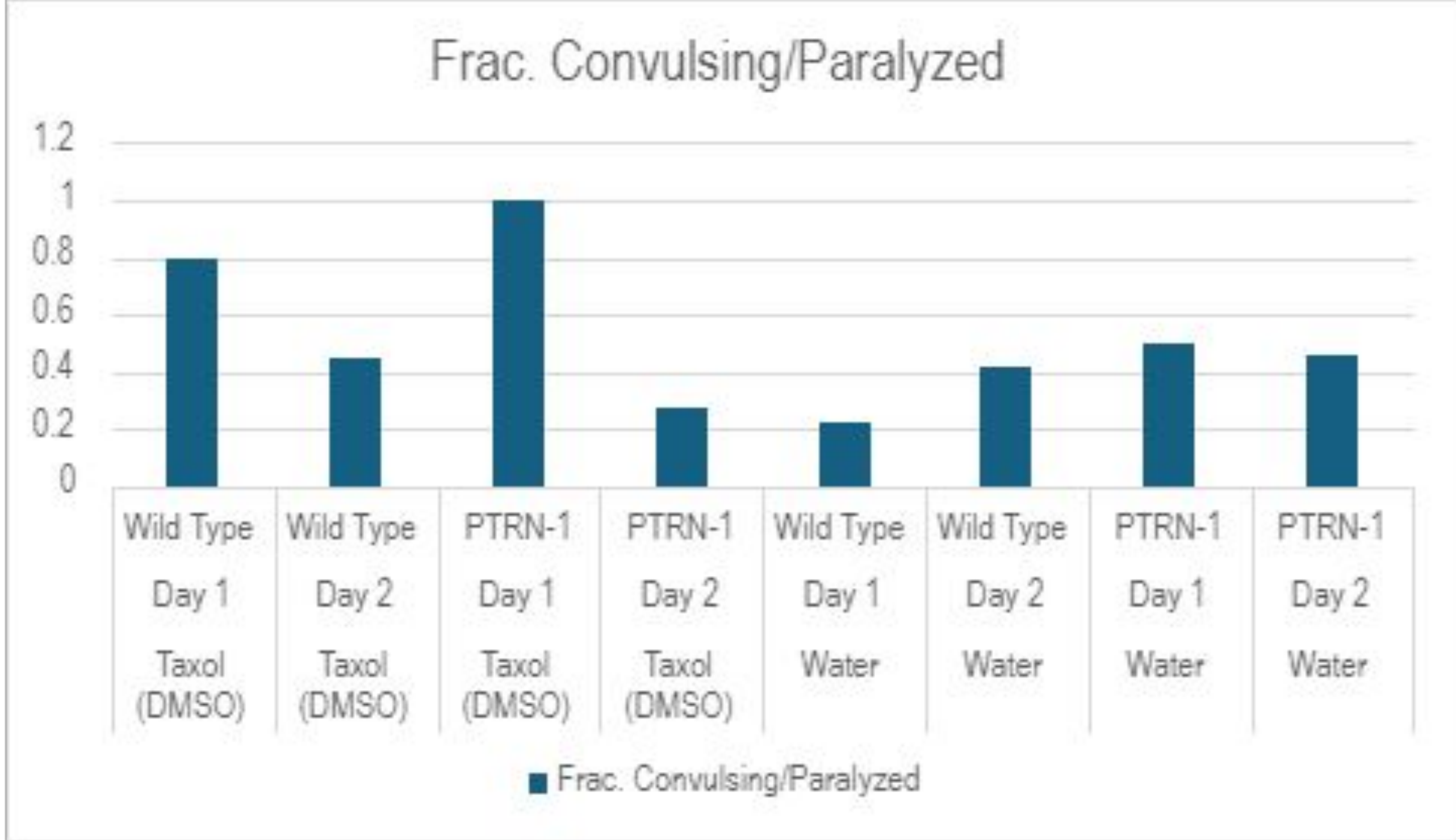
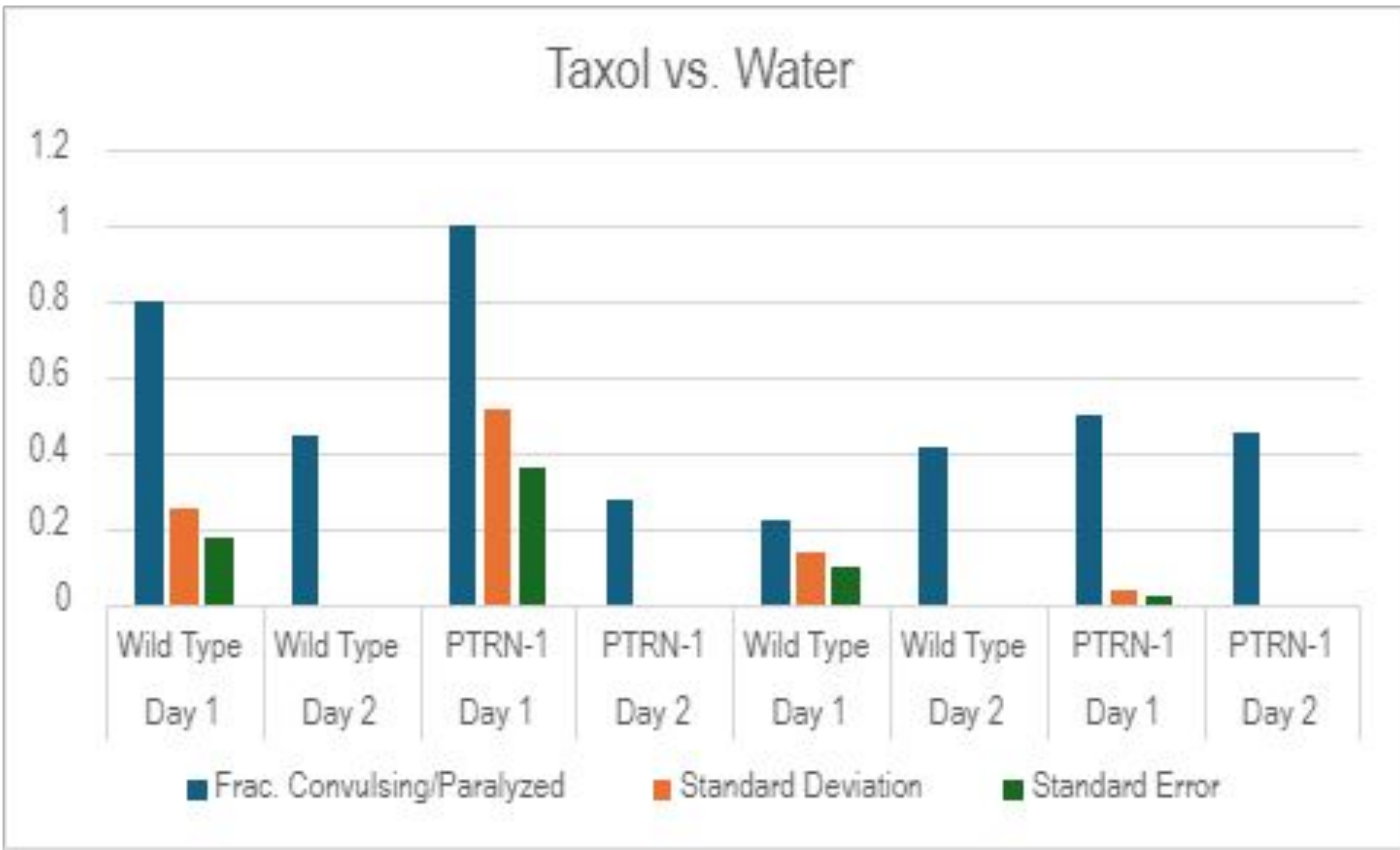
Epilepsy is a common brain condition causing frequent seizures, characterized by bursts of electrical activity. On the cellular level, unstable microtubules can disrupt cell function, seen in models like *C. elegans*, which mimic neurodegenerative diseases. Taxol, a drug aimed at stabilizing microtubules, is being applied to *C. elegans* to study its potential in cellular function restoration, with implications for broader microtubule stabilization throughout the body.



ABSTRACT

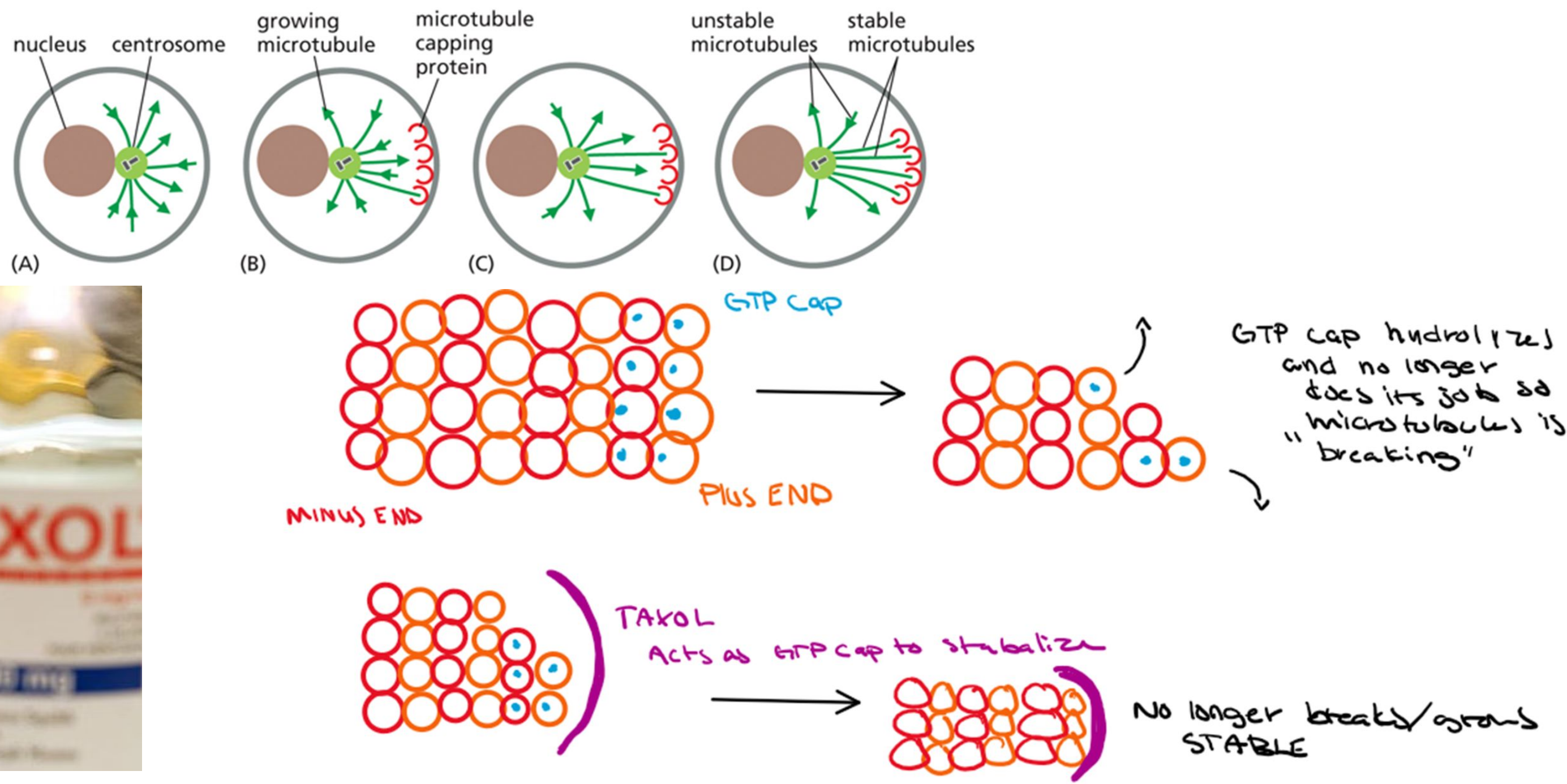
Recent discoveries have unveiled a mutation in the CAMSAP gene as a causative factor in a distinct form of epilepsy. CAMSAP's pivotal role in microtubule stabilization and cellular signaling underscores its significance in neuronal function. This experiment poses the answer to the question: Does the stabilization of microtubules stop the progression of convulsions for a specific type of epilepsy? Microtubules orchestrate the spatial organization within cells, essential for cellular integrity and function. Perturbations in microtubule dynamics, marked by instability and subsequent shrinkage due to GTP hydrolysis, can precipitate cellular dysfunction. To address this, we propose the application of Taxol, a renowned microtubule-stabilizing agent, in a *C. elegans* model. Leveraging the simplicity of *C. elegans'* nervous system, we aim to elucidate Taxol's potential in mitigating seizures induced by a specified solution. Through systematic observation at five and ten-minute intervals, we anticipate Taxol's intervention to stabilize microtubules and ameliorate convulsions. This research offers a promising avenue for understanding the molecular underpinnings of epilepsy and exploring therapeutic interventions targeting microtubule dynamics.

DATA



AUTHORS:
DR. JANA MARCETTE & MADELYNE ELBERT
MONTANA STATE UNIVERSITY BILLINGS

ACKNOWLEDGEMENTS
JOE WALSH AND LANDON'S LEAGUE FOUNDATION, INCLUDE THEIR LOGO ://LANDONSLEAGUE.COM/
ALEKSANDRA FOKSINSKA | PROGRAM MANAGER
UAB | THE UNIVERSITY OF ALABAMA AT BIRMINGHAM
THE UNDIAGNOSED DISEASE NETWORK AND THEIR LOGO IN THIS SECTION ://UNDIAGNOSEDISEASES.WUSTL.EDU/
THE CGC: * C. ELEGANS WORM STRAINS WERE PROVIDED BY THE CGC, WHICH IS FUNDED BY NIH OFFICE OF RESEARCH INFRASTRUCTURE PROGRAMS (P40 OD010440). ://CGC.UMN.EDU//



OBJECTIVE

The intention is to induce convulsions in *C. elegans* by exposing them to a specific solution. Subsequently, they will be transferred to a solution containing the convulsion-suppressing drug Taxol with the expectation that the convulsions will cease, allowing the worms to return to normal swimming activity.

METHODS + PROTOCOLS

C. elegans will be kept on calcium-free NGM plates. We'll have two groups of worms: one is the control group, and the other will interact with the drugs we're testing. Both groups of worms will be raised in an incubator at 25±4°C.

The drugs for our experiment will be prepared in concentrations suitable for their solubility. These concentrations will be added to the NGM plates along with about 8 drops of concentrated *E. coli* bacteria, which will act as a carrier to deliver the drugs to the *C. elegans*.

We will prepare a seizure buffer (made of 100mM NaCl + 50mM MgCl₂) where we will put the worms on separate NGM plates (still without calcium). Once the worms are in this buffer, we will gradually increase the temperature of the plates using a lamp, monitoring the temperature with a thermometer, adjusting within a range of 1-3°C.

Afterward, we will place the worms onto plates containing the drug concentrations and concentrated *E. coli*, introducing them to more seizure buffers. We will observe any convulsions the worms experience, recording the observations and using necessary technology to record our findings.

Based on the results, we will decide on the next steps or draw conclusions regarding the information we have gathered.

CONCLUSION

From our empirical findings, it has been discerned that Taxol exhibits inefficacy in mitigating seizures in the model organism *Caenorhabditis elegans* (*C. elegans*). Our experimentation encompassed subjecting the worms to various solutions, with water serving as the control group. Analysis of the gathered data illuminated that Taxol, in comparison to water, exerted a ruinous effect on the worms. Notably, our study employed two strains of *C. elegans*: PTRN, known to possess the CAMSAP gene implicated in seizure manifestation in humans, and the N2 (wild type) strain, the CAMSAP gene status of which remained indeterminate. Strikingly, Taxol induced seizures in all specimens, contrary to its anticipated antiepileptic properties. Rather than abating seizures, Taxol appeared to exacerbate them, even when contrasted against water. Consequently, Taxol's viability as a prospective antiepileptic agent targeting CAMSAP gene-induced seizures was effectively invalidated.

In summation, our investigation concludes that Taxol lacks efficacy in preventing seizures attributed to the CAMSAP gene. Despite its purported microtubule-stabilizing properties, our experimental outcomes suggest its inadequacy in this context. However, amidst the failure of Taxol, our study did identify a potential candidate in Amantadine, an antiviral and dopamine promoter utilized in the treatment of various neurodegenerative disorders. The modest success observed with Amantadine infuses a glimmer of optimism into our pursuit of therapeutic solutions for this form of epilepsy. Thus, despite setbacks, our endeavor advances us incrementally towards the eventual discovery of a remedy for CAMSAP gene-related seizures.