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Determining The Effects of Guarana and Nad+ On Ciliary Dysfunction of Dugesia Tigrina

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ABSTRACT

The purpose of this experiment is to see how two different stimulants affect Dugesia tigrina locomotion: Paullinia cupana and Nicotinamide adenine dinucleotide (NAD+). Because of its cilia-like hairs that allow it to move, Dugesia tigrina is an ideal specimen for locomotion research. The planarian body's abundance of cilia and remarkable accessibility make it an intriguing experimental model system for cilia biology. They move by secreting a mucous covering that coats their bodies and allows them to glide around submerged surfaces. Scientists have utilized these species to evaluate dependency since they have a genuine brain that can induce effects like neurological impairments in people. Paullinia cupana, a neurological stimulant, was employed in this investigation. Caffeine is primarily responsible for the stimulating effect of energy drinks. One of these components is Paullinia cupana. Paullinia cupana is a plant whose seeds have four times the caffeine content of coffee beans. Nicotinamide adenine dinucleotide is required for several cellular processes such as energy generation and repair. A reduction in motility produced by Paullinia cupana or NAD+ may suggest ciliary dysfunction. It was concluded that the Paullinia cupana stimulant increased the locomotion of Dugesia Tigrina, and therefore performed the best out of the experimental groups. The control group (natural spring water), however, proved to be the overall best solution for mobility. The knowledge gathered from the experiment can be used to bring deeper insight into the field of neurodegenerative studies in translational medicine.

Introduction

Caffeine is the primary stimulant in energy drinks, with sugars and additional ingredients like Paullinia cupana, taurine, and ginseng, as well as vitamin combinations, being added to create diverse blends. Energy drinks have gained popularity to boost cognitive capacity, memory, alertness, physical performance, and cardiovascular output. Although the addition of Paullinia cupana and other plant-based materials can boost the caffeine level and overall stimulant characteristics of these beverages, these plant-based additions are not subject to the same reporting requirements as sugars and caffeine since they are considered herbal supplements.

Guarana (Paullinia cupana) is an Amazonian climbing plant that is used as an antioxidant, traditional medicine, and potent stimulant. Guarana seeds, which may be more than four times the quantity found in coffee beans depending on how the extract is processed, are the major components of Paullinia cupana credited with these therapeutic effects. Despite the dearth of studies on the associative effects of plant-based extracts with other nutritional supplements, medicines, and stimulants, herbal items such as Paullinia cupana offer an appealing component to the producers of many popular energy drink compositions. Nicotinamide Adenine Dinucleotide (NAD+) is a coenzyme central to metabolism. An increase in NAD+ boosts energy production and upregulates cellular repair (which in short, increases the metabolism). As a result, increasing the NAD+ in *Dugesia Tigrina* will result in better physical movement and cognition as the metabolism increases. Putting this into context, neurological illnesses like Parkinson's and Huntington's disease have a detrimental influence on locomotive activity.

Huntington's disease and Parkinson's disease both affect mobility and mental function. Motor abilities and mental clarity deteriorate as the illness progresses. A bi-lobed brain and a pair of nerve cords that flow ventrally from the head make up *Dugesia Tigrina's* central nervous system. Paullinia cupana is a purine alkaloid that works by antagonizing adenosine receptors to increase dopamine transmission in the brain.

When the quantity of dopamine in the brain is raised, the central nervous system's metabolism is boosted, and in the *Dugesia Tigrina* model, dopamine improves the speed and amount of movement. Similarly, when the quantity of NAD+ in the body is raised, the central nervous system's metabolism is boosted, and in the *Dugesia Tigrina model*, increased metabolism increases cognition function and movement. Because the *Dugesia Tigrina* reacts to their surroundings, data on their movement may be obtained to measure the impact of the treatments. This study will look at NAD+ and Paullinia cupana as a coenzyme and a neurological stimulant that elevates metabolism levels in *Dugesia Tigrina* to determine whether this excess may assist in speeding up the locomotive process, which might be utilized to cure motor dysfunction in people and improve overall health.

Literature Review

In the study *Effects of Nicotinamide Adenine Dinucleotide on regional brain glucose metabolism in humans*: Relationship to dopamine D2 receptors.: Semantic scholar. NAD+ has been used to boost brain metabolism. The results of the connection between the stimulant and metabolic rates in eight participants showed an increase in six subjects and a reduction in two. Volkow (2017) and Wang (2017) conducted a meta-analysis study to obtain conclusions by carefully evaluating the outcomes of prior studies. However, if the researchers had looked into assessing D2 receptors in ADHD, it would have been possible to see whether there were any alterations that could assist predict drug responsiveness. Volkow (2017) and Wang (2017) discovered that NAD+ increased cerebellar metabolism consistently and significantly, while its effects on other brain regions varied substantially between people.

The fact that NAD+-induced metabolic changes in the frontal and temporal cortices, as well as the cerebellum, were correlated with D_2 measures suggests that they partially reflect dopamine concentration changes and that NAD+ response variability is due to differences in D2 receptor availability. $D_{2\ \text{availability}}$ was strongly associated with regional metabolic alterations in the cerebellum and frontal and temporal cortices. Those with high D2 receptors had higher frontal and temporal metabolism, while subjects with low D2 receptors had lower frontal and temporal metabolism. However, because correlations do not indicate causation, more research is needed to determine the role of dopamine in the function of these brain areas. Volkow (2017) and Wang (2017). Nonetheless, there was no possible bias in this experiment, and it was carried out appropriately. As previously said, adding outstanding material might potentially improve most of this research.

In the study, *Paullinia cupana Provides Additional Stimulation over Caffeine Alone in the Dugesia Tigrina Model*, Guarna at different concentrations when exposed to the *Dugesia Tigrina*, increased locomotive abilities over regular caffeine and glucose (Dimitrios Moustakas et al.). Paullinia cupana is a purine alkaloid that works by antagonizing adenosine receptors to increase dopamine transmission in the brain. When the quantity of dopamine in the brain is raised, the central nervous system's metabolism is boosted. Dimitrios Moustakas et al. (2015) studied how the *Dugesia Tigrina* would increase or decrease its motility based on different concentrations of Paullinia cupana. The *Dugesia Tigrinans* were exposed to concentrations of 0.001, 0.003, 0.01, 0.03, 0.1, 0.3, 1.0, 3.0, and 10 mM, and were observed during a two-minute incubation period. Dimitrios Moustakas et al. (2015) found that there was an increase in motility at 0.01 mM. The results confirmed that purified caffeine provides for a noticeable, albeit insignificant stimulation in *Dugesia Tigrina* locomotion at the concentrations tested. Their findings suggested that Paullinia cupana provides an additional level of stimulation above that provided by caffeine alone. This continues to build insight into how stimulants can increase the locomotive abilities of *Dugesia Tigrina.*

The study, *Herb-Drug Interaction of Paullinia cupana (Paullinia cupana) Seed Extract on the Pharmacokinetics of Amiodarone in Rats*, illustrates that a decrease in amiodarone plasma concentrations was also accomplished by a significant reduction in the tissue concentrations of amiodarone and MDEA, particularly in the heart (therapeutic target organ or biophase). Márcio Rodrigues et al. (2016) studied how Paullinia cupana combined with amiodarone (narrow therapeutic index drug) and how it affects the peak of plasma concentration. In rats, Paullinia cupana extract and amiodarone (a medication with a restricted therapeutic index) were tested. In one pharmacokinetic research, rats were given a single dosage of Paullinia cupana (821 mg/kg, p.o.) and amiodarone (50 mg/kg, p.o.) at the same time, while in a second investigation, rats were given Paullinia cupana (821 mg/kg/day, p.o.) for 14 days before getting amiodarone (50 mg/kg, p.o.) on the 15th The control rats were given the same amount of vehicle as to the experimental rats. Blood samples were taken at various times following amiodarone administration, and numerous tissues were extracted at the conclusion of the study (24 hours after the dosage).

Amiodarone and its main metabolite (mono-N-desethylamiodarone) concentrations in plasma and tissues were tested and analyzed (Rodrigues et al.). As a result, in rats treated concurrently with Paullinia cupana and amiodarone, there was a considerable reduction in peak plasma concentration (73.2%) and the amount of systemic exposure (57.8%), as well as a drop in tissue concentrations. This is the first report of a herb-drug interaction between Paullinia cupana extract and amiodarone in rats, which found a significant reduction in amiodarone bioavailability. This adds to our understanding of how medications can either boost motility movements too much or too little, as well as the repercussions for the rats.

This study, *Cognitive and mood improvements of caffeine in habitual consumers and habitual non-consumers of caffeine*, studies how caffeine can either increase or decrease cognition and mood improvements for humans. Crystal F. Haskell et al. studied the acute cognitive and mood effects of caffeine in habitual users and habitual non-users of caffeine. Following a 48-hour caffeine withdrawal period, 24 habitual caffeine consumers (mean=217 mg/day) and 24 habitual non-consumers (20 mg/day) were given a 150 ml drink containing either 75 or 150 mg of caffeine or a matched placebo. Cognitive and mood tests were performed at baseline and 30 minutes after the drink. The Cognitive Drug Research computerized test battery was used, as well as two serial subtraction tasks, a phrase verification task, and subjective visual analog mood scales. Results showed that There were no variations in mood or performance between the groups at the start (Crystal F. Haskell et al.) There were substantial improvements in simple response time, digit vigilance reaction time, numeric working memory reaction time, and phrase verification accuracy after coffee, regardless of group. Caffeine tended to benefit consumers' moods more while improving performance more in the non-consumers. This contributes to our knowledge of what caffeine can do to strengthen or impair our brain functions, and it can be used to show on a *Dugesia Tigrina* model whether it will continue to move or coil up and get distracted.

This study, *Paullinia cupana: Revisiting a highly caffeinated plant from the Amazon,* explains the chemical makeup of Paullinia cupana. Paullinia cupana (Paullinia cupana Kunth var. sorbilis (Mart.) Ducke) has been eaten by Amazonian indigenous peoples for centuries. It is regarded mostly for its stimulant properties due to its high caffeine concentration, which may reach up to 6% in the seeds. Paullinia cupana is largely grown in the Brazilian states of Amazonas and Bahia, with the soft drink and energy drink industries accounting for over 70% of total output (Flávia CamilaSchimpl et al.). The remaining 30% is used to make Paullinia cupana powder for capsules or water dilution, or it is used as a raw material in the pharmaceutical and cosmetics industries. Paullinia cupana has numerous medicinal benefits, in addition to its stimulating effects, that have piqued the scientific community's curiosity. This review demonstrates that further Paullinia cupana qualities may be investigated, as well as the scarcity of agronomic, plant pathology, physiology, and breeding research (Flávia CamilaSchimpl et al.). Caffeine has been the primary motivation for studying Paullinia cupana, and it will continue to do so because of the high demand for this alkaloid in the food and pharmaceutical industries, as well as a rapidly developing market for beauty goods.

This study, *Caffeine and Parkinson's Disease: Multiple Benefits and Emerging Mechanisms,* explains how caffeine can prevent a person from getting Parkinson's disease. Xiangpeng Ren and Jiang-Fan Chen studied how increased caffeine consumption decreased the risk of developing Parkinson's disease. The motor benefit of caffeine was documented in a pilot open-label, 6-week dose-escalation study (Altman et al., 2011) and a 6-week randomized controlled trial of caffeine (200–400 mg daily) involving 61 PD patients (Postuma et al., 2012). These clinical studies suggest that caffeine improved objective motor deficits in PD with the reduced total Unified PD Rating Scale score and the objective motor component. Furthermore, coffee consumption (>336 mg/day) is associated with a reduced hazard ratio for the development of dyskinesia compared with subjects who consumed <112 mg/day in the Comparison of the Agonist Pramipexole with Levodopa on Motor Complications of Parkinson's Disease (CALM-PD) and CALM Cohort extension studies (Wills et al., 2013). Based on these positive findings, caffeine was recently investigated for motor and disease-modification involving 121 PD patients PD in phase 3, 5-years (planned), two-arm, double-blind RCT, with a primary outcome focused on motor symptoms and disease-modification as a secondary outcome1. Unfortunately, with the primary outcome analysis after 6 months demonstrating no significant symptomatic benefit of caffeine (200 mg twice daily) (Postuma et al., 2017), the study was terminated earlier than planned. Based on the concentrated expression of A2AR in the striatum and the A2AR is the key molecular target of caffeine, caffeine (and A2AR antagonists) has been proposed to improve motor activity in PD. This contributes to our knowledge that there is a modest but obvious shift in human movements when caffeine levels rise.

This study, *Nicotinamide adenine dinucleotide (NADH)--a new therapeutic approach to Parkinson's disease*. A comparison of oral and parenteral applications illustrates how an increase in NAD+ in humans might benefit younger individuals more than elderly people in terms of movement production. J G Birkmayer et al. explains that the coenzyme NAD+ has been used as medication in 855 parkinsonian patients. NADH was given to around half of the patients as an intravenous infusion and the other half as pills. A positive clinical benefit was reported in roughly 80% of the patients: A very excellent (30-50 percent) improvement in disability was seen in 19.3% of the patients, whereas a moderate (10-30 percent) improvement was seen in 58.8%. 21.8 percent of people did not react to NADH (J G Birkmayer et al.). The following findings were discovered after statistical analysis of the improvement in relation to the disability before therapy, the length of the condition, and the age of the patients: All three variables have a meaningful, if little, impact on the improvement. A positive regression coefficient (t value 0.01) exists for the impairment prior to therapy. The orally administered version of NADH resulted in a disability improvement that was equivalent to the parenterally administered type. This expands on our understanding, which has been applied to a *Dugesia Tigrina* model, that an increase in NAD+ leads to an improvement in motility. The issue remains as to how long mobility will be enhanced.

The study, *Daytime sleepiness, circadian preference, caffeine consumption, and use of other stimulants among Thai college students* illustrates the prevalence of daytime sleepiness and evening chronotype and assesses the extent to which both are associated with the use of caffeinated stimulants among Thai college students. Jason Tran et al. conducted a study in which 3,000 Thai college students were used. The Epworth Sleepiness Scale and the Horne and OstbergMorningness-Eveningness Questionnaire were used to evaluate the prevalence of daytime sleepiness and circadian preference. Multivariable logistic regression models were used to evaluate the association between sleep habits and consumption of caffeinated beverages. Overall, the prevalence of daytime sleepiness was 27.9% (95% CI: 26.2 to 29.5%) while the prevalence of evening chronotype was 13.0% (95% CI: 11.8 to 14.2%). Students who use energy drinks were more likely to be evening types. For instance, the use of M100/M150 energy drinks was associated with a more than 3-fold increased odds of evening chronotype (OR 3.50; 95% CI 1.90 to 6.44), while Red Bull users were more than twice as likely to have evening chronotype (OR 2.39; 95% CI 1.02 to 5.58) (Jason Tran et al.). Additionally, those who consumed any energy drinks were more likely to be daytime sleepers. For example, Red Bull (OR 1.72; 95% CI 1.08 to 2.75) or M100/M150 (OR 1.52; 95% CI 1.10 to 2.11) consumption was associated with increased odds of daytime sleepiness. Their findings highlight the necessity of establishing educational and preventative programs aimed

at improving sleep hygiene and lowering energy drink intake among young individuals. This can be linked to *Dugesia Tigrina's* attentiveness and if they become distracted and coil up or shrink up and stop moving.

This study was about the *death of a young man after the overuse of an energy drink*. SemaAvcıMD et al. explain that energy drinks often contain caffeine, with or without added vitamins, taurine, yerba mate, and Paullinia cupana, the latter two of which also contain caffeine. Seven of the fatal case reports reported death after consuming 10 g of caffeine (Holmgren et al., 2004; Jabbar and Hanly, 2013; Poussel et al., 2013; Rudolph and Knudsen, 2010; Thelander et al., 2010) or more (Holmgren et al., 2004; Jabbar and Hanly, 2013; Poussel et al., 2013; Rudolph and Knudsen (Yamamoto et al., 2015). There was just one death reported at a dosage lower than 10 g. According to Avci et al. (2013), a dose of 240 mg was linked to cardiac arrest. This demonstrates how critical it is to select a *Dugesia Tigrina*-survivable concentration prior to conducting the experiment; if the concentration is too high, the *Dugesia Tigrina* will die.

Materials

- 45 Brown *Dugesia Tigrina*
- 100 mg Nicotinamide Adenine Dinucleotide (30 capsules) (0.000001 M in each 15-petri dish)
- 8-ounce (1 pack) Paullinia cupana Powder (0.001M in each 15 Petris dishes)
- Poland spring water (Water source for *Dugesia Tigrina*, will be mixed with solutes to form liquids)-
- 4-5 pipettes (used for precise measuring)
- 45 Petri Dishes
- Safety goggles
- 2 50 mL Beakers- To make the extract (liquid) of Nicotinamide Adenine Dinucleotide and Paullinia cupana
- Standard Notebook (additional observations)
- 1 Weighing Scale Machine
- 2 Weigh boats
- Pacon 3-Hole Punched Essay and Composition Paper 11" x 8-1/2", 1/4" Quad Ruling without Margin
- Light Microscope
- 2 Stirring rods
- 2 Funnel
- 6-7 Filter paper

Procedure

Preliminary Experiment

In brief, *Dugesia Tigrinan*s were exposed to five different concentrations for each experimental group (Paullinia cupana and NAD+) to identify a survivable concentration for them to move about in; while being alive. The concentrations that were tested were 0.1 M, 0.001 M, 0.0001 M, 0.00001 M, and 0.000001 M. Paullinia cupana was first pulverized and then turned into a liquid with the use of natural spring water and a standard filtration procedure. The NAD+ was likewise in a powdered form, and it was made into a liquid solution by mixing it with natural spring water and filtering it. Measuring 0.001M of Paullinia Cupana solution using the formula M1V1=M2V2. M1 would be the desired amount (0.001 M) and V1 would be the approximate amount of solution (100mL), M2 would equal 0.4 moles because we are originally starting with 8 grams and then dividing by 194.19. Using basic algebra V2 can be solved for, which would be equal to 25 mL of solution extract needed for that specific petri dish. Measuring 0.1M of Nicotinamide Adenine Dinucleotide solution using the formula

M1V1=M2V2. M1 would be the desired amount of concentration (0.1M) and V1 would be the approximate amount of solution (100mL), M2 would equal the mass of all pills crushed divided by the molar mass of Nicotinamide Adenine Dinucleotide (663.43g/mol) since the final desired amount of pill mashed equal 300 mg (0.3g). M2 should equal 0.3 moles. and V2 would be equal to the 33 ml approximately extracted solution needed for that specific petri dish.

Repeat this process with all the necessary amounts of concentration needed for each experiment (substance). Following that, a total of 10 Petri dishes were spread out on a black tabletop (5 for the Paullinia cupana solution and 5 for the NAD+ solution), and a single *Dugesia Tigrina* was inserted into each petri dish, as well as the 5 specific concentrations which was converted into milliliters for convenience, for each experimental group. For 30 minutes, the *Dugesia Tigrina* were observed to identify the optimal concentration. It was concluded that for the Paullinia cupana solution the best concentration was 0.001 M and for NAD+ it was 0.000001 M

Main Experiment

For the main experiment, 45 *Dugesia Tigrina* were used with a total of 45 Petri dishes (15 for each experimental group (2), and 15 for the control group). Based on the preliminary results, the concentrations that will be used for each experimental group Petri dish are 0.000001 M NAD+ and 0.001 M Paullinia cupana. Eight grams of Paullinia cupana (Paullinia cupana) were measured out on a weight boat and placed into a beaker, natural spring water was then added to the beaker to turn the powder into a liquid form.

The solution was then filtered three times, and the same procedure was repeated for the NAD+, but with a measured mass of 100 mg. Each of the forty-five Petri dishes received one *Dugesia Tigrina,* and 0.001 M was placed in each of the fifteen Petri dishes for the Paullinia cupana solution, 0.000001 M was placed in each of the fifteen Petri dishes for the NAD+ solution, and five milliliters of natural spring water was placed in each of the fifteen Petri dishes for the spring water control solution. One sheet of grid paper was placed beneath the light of the microscope lens, and each petri dish was placed one at a time on top of the grid paper and timed for five, ten, and fifteen minutes. The number of blocks traveled by the *Dugesia Tigrina* at each time was recorded on a spreadsheet. This procedure was carried out for each of the forty-five Petri dishes.

Results

The purpose of this experiment is to see how two different stimulants affect *Dugesia tigrina* locomotion: *Paullinia cupana* and Nicotinamide adenine dinucleotide, as well as how quickly the *Dugesia Tigrina* moves when exposed to a survivable concentration. The concentration for *Paullinia cupana* was 0.01 M and for Nicotinamide adenine dinucleotide it was 0.001M. Both the coenzyme and the stimulant increased the motility of the *Dugesia Tigrina.* The *Paullinia cupana* increased motility the fastest, then the Nicotinamide adenine dinucleotide. Throughout the experiment, there was a consistent pattern that after the 10-minute interval the *Dugesia Tigrina* would begin to coil up more and not move through the graph paper as quickly. The *Paullinia cupana* for 5min, 10min, and 15 min had means of 14.26, 23.66, and 15.6 respectively. The Nicotinamide adenine dinucleotide for 5min, 10min, and 15 min had means of 9.033, 9.42, and 10.77 respectively. Spring water for 5 min, 10min, and 15 min had means of 17.34, 22.2, and 25.83 respectively. This proves that overall, the stimulants did produce an increase in locomotion of the *Dugesia Tigrina.*

An ANOVA test was run on the finalized data. The p-value for each experimental group and control group was <0.001 which showed extreme significance. The mobility rate for *Dugesia Tigrina* under a 0.01 M concentration for *Paullinia cupana*, showed an increase in motility of 17.84% as compared to the control value which had an increased motility rate of 21.79%. This slight increase does suggest that the stimulant did provide

more cilia movement. The mobility rate for *Dugesia Tigrina* for 0.001M concentration for Nicotinamide adenine dinucleotide, showed an increased locomotion rate of 9.741% as compared to the control group, this increase is not as significant as was the *Paullinia cupana* group. Regression analysis is used due to the many variables present.

The means of the experimental group were significantly different. The combined experimental group's mean was 13.79 while the control group's mean was 21.79. The alternative hypothesis was accepted. The stimulants (*Paullinia cupana* and Nicotinamide adenine dinucleotide). The One-way Analysis of Variance (ANOVA) showed significant findings. The p-value for all groups is <0.0001, which is considered extremely significant. The variation among column means is significantly greater than expected by chance. (Shown in Table-1)

Graph 1. The effect of time on the mean value of mobility

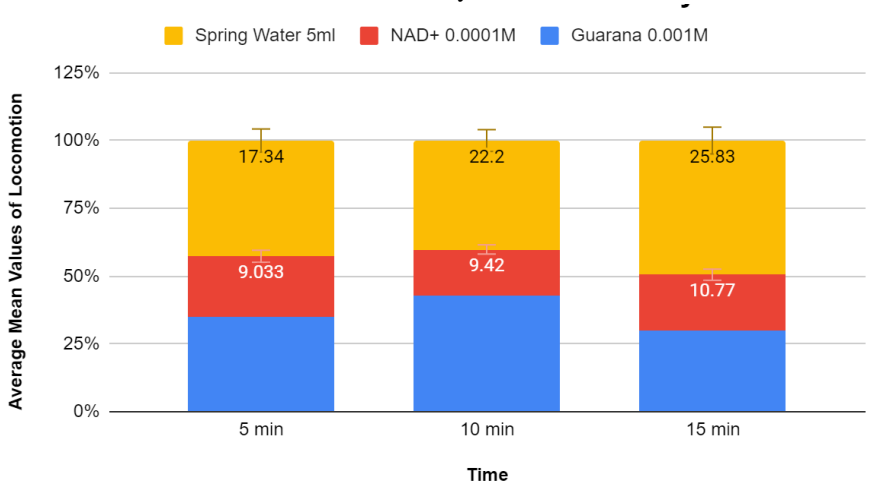

Table 1. Combined average ciliary function motility percentage of all time trials

Paullinia Cupana **Group A**	**Nicotinamide adenine dinucleotide Group B**	**Spring Water Group C**
17.84%	9.741%	21.79%

Table 1 (shown above) shows the mean total % of motility for both experimental groups (Groups A & B) and the control group (Group C). The percentages shown for Groups A & B both show an increase in motility as compared to the control (Group C). This proves that *Dugesia Tigrina* thrived in spring water. In the experimental groups, there was a significant increase in motility with *Paullinia cupana* at a 17.84% increase, but for the Nicotinamide adenine dinucleotide, there was very little significant increase in locomotion as compared to the spring water.

Mean and Standard Deviation

Tukey-Kramer Multiple Comparison Test

If the value of q is greater than 3.958 then the P-value is less than 0.05 (Shown in Table 2)

Table 2. P-values

Comparison	P-Value
5 minutes: Paullinia cupana vs NAD+	**P<0.001**
5 minutes: Paullinia cupana vs Spring Water	**P<0.05**
5 minutes: NAD+ vs Spring Water	**P<0.001**
10 minutes: Paullinia cupana vs NAD+	**P<0.001**
10 minutes: Paullinia cupana vs Spring Water	**P>0.05**
10 minutes: NAD+ vs Spring Water	**P<0.001**
15 minutes: Paullinia cupana vs NAD+	**P<0.05**
15 minutes: Paullinia cupana vs Spring Water	**P<0.001**
15 minutes: NAD+ vs Spring Water	**P<0.001**

Table two shows the p-value for each stimulant, and time interval showed there was extreme significance within each group.

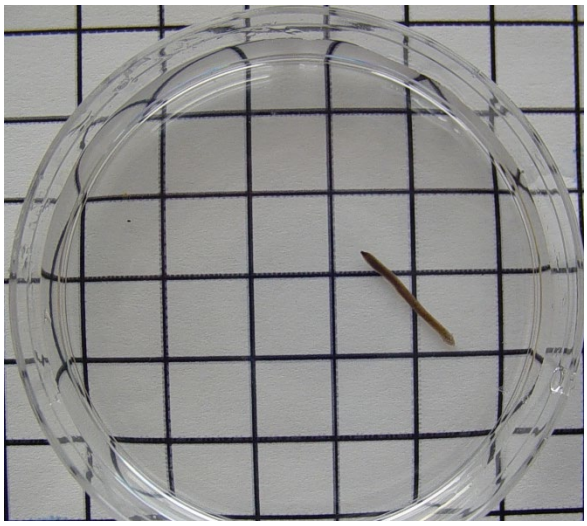

Figure 1. Picture of the *Dugesia Tigrina* on grid paper for pLmV Test

Figure 1 depicts a brown planaria in a control water petri dish. This was the setup utilized for the pLmV test. The grid paper made it easy to calculate how much the planaria traveled throughout the time intervals of five, ten, and fifteen minutes.

Discussion

Stimulants are essentially drugs that increase the activity of the central nervous system and the body. Scientists frequently employ these invertebrates to assess reliance because they have a functioning brain that can create similar effects to those caused by neurological medications in people. Movement and mental functioning issues are caused by degeneration. In the final stages of dementia, the person is likely to have a significant physical impact. They may lose their ability to walk, stand, or get out of a chair or bed over time.

They can also be more prone to falling. *Paullinia cupana* is a plant whose seeds have four times the caffeine content of coffee beans. Nicotinamide adenine dinucleotide is required for several cellular processes such as energy generation and repair. A reduction in motility produced by *Paullinia cupana* or Nicotinamide adenine dinucleotide may suggest ciliary dysfunction. If the cilia don't work well for *Dugesia Tigrina*, that

causes dysfunction to their movements, and for humans, if our cilia were malfunctioning our skeletal movements would be dysfunctional. If in fact, these stimulants did produce a large increase, then the hypothesis would show that if humans take *Paullinia cupana* or Nicotinamide adenine dinucleotide, then those stimulants would increase the ATP in humans, and therefore, increase the cilia movement in skeletal muscles which would improve overall human health.

The stimulant solutions provided a little increase in locomotion to the *Dugesia Tigrina,* but not as much as the control had with the locomotion. *Paullinia cupana* had the second greatest percent of increased locomotion, with an average fairly like the control percent. Therefore, the *Paullinia cupana* performed the best. This could further be tested by testing other stimulants or coenzymes with *Dugesia Tigrina* that will increase metabolic rates. These findings could lead to an increase in cilia movement resulting in overall better health for humans by improving human movement.

Conclusion

In conclusion, the hypothesis was proven and supported by the data collected. The p-value was $p<0.05$. The *Paullinia cupana* stimulant increased the locomotion of *Dugesia Tigrina,* and therefore performed the best. The control group (natural spring water) proved to be the best solution for *Dugesia Tigrina* to thrive in mobility. Although not as significant as *Paullinia cupana* the Nicotinamide adenine dinucleotide also increased the mobility of the *Dugesia Tigrina*. It was found constantly that for all the solutions, the 10-minute interval proved to have sparked the most mobility for the *Dugesia Tigrina.* Further research can be conducted in the future, such as using different concentrations of the two solutions or using different stimulants to test the mobility of *Dugesia Tigrina.*

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