

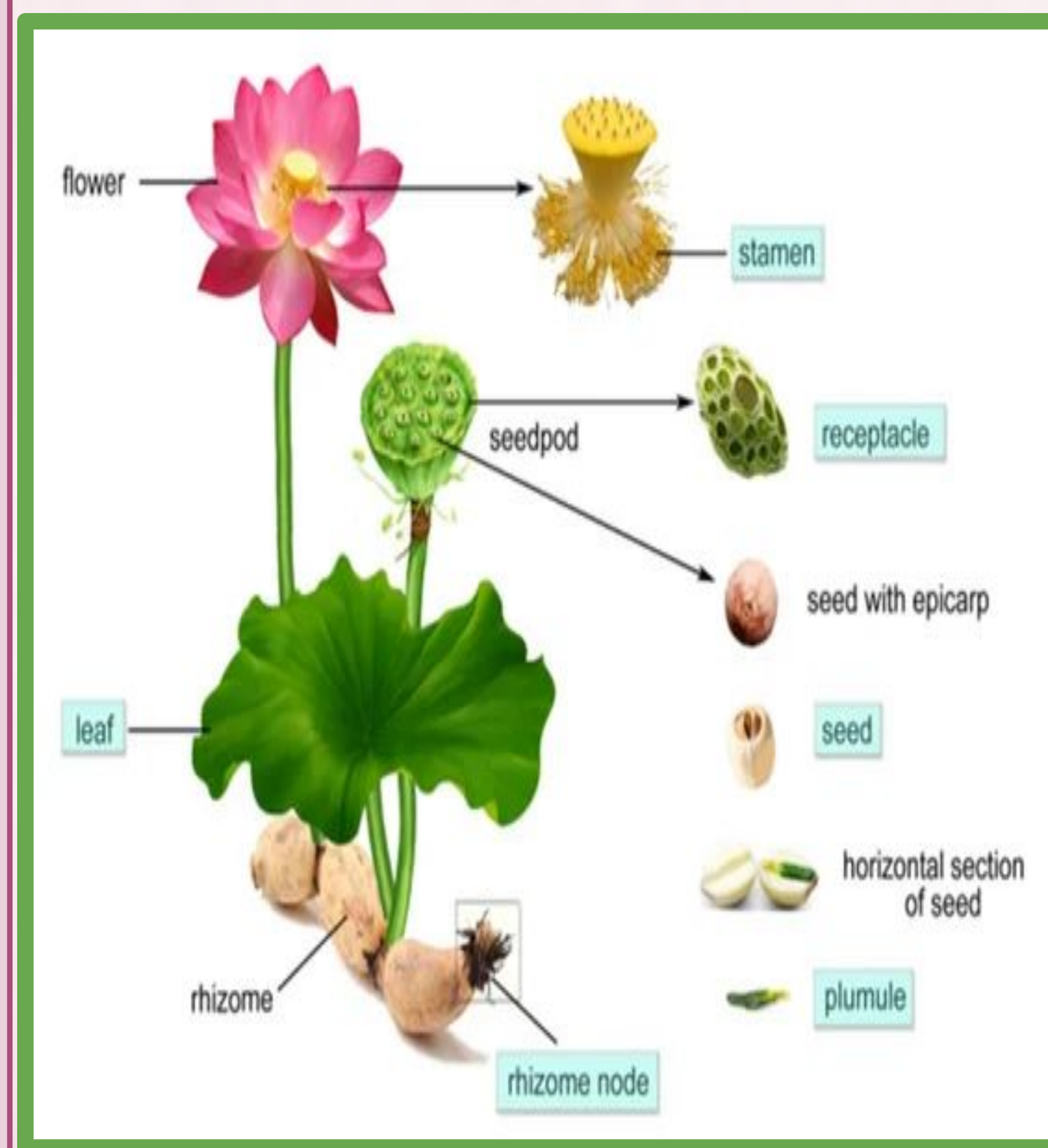


Lotus Plant Structures in Biotechnology: From Biomedicine to Material Science

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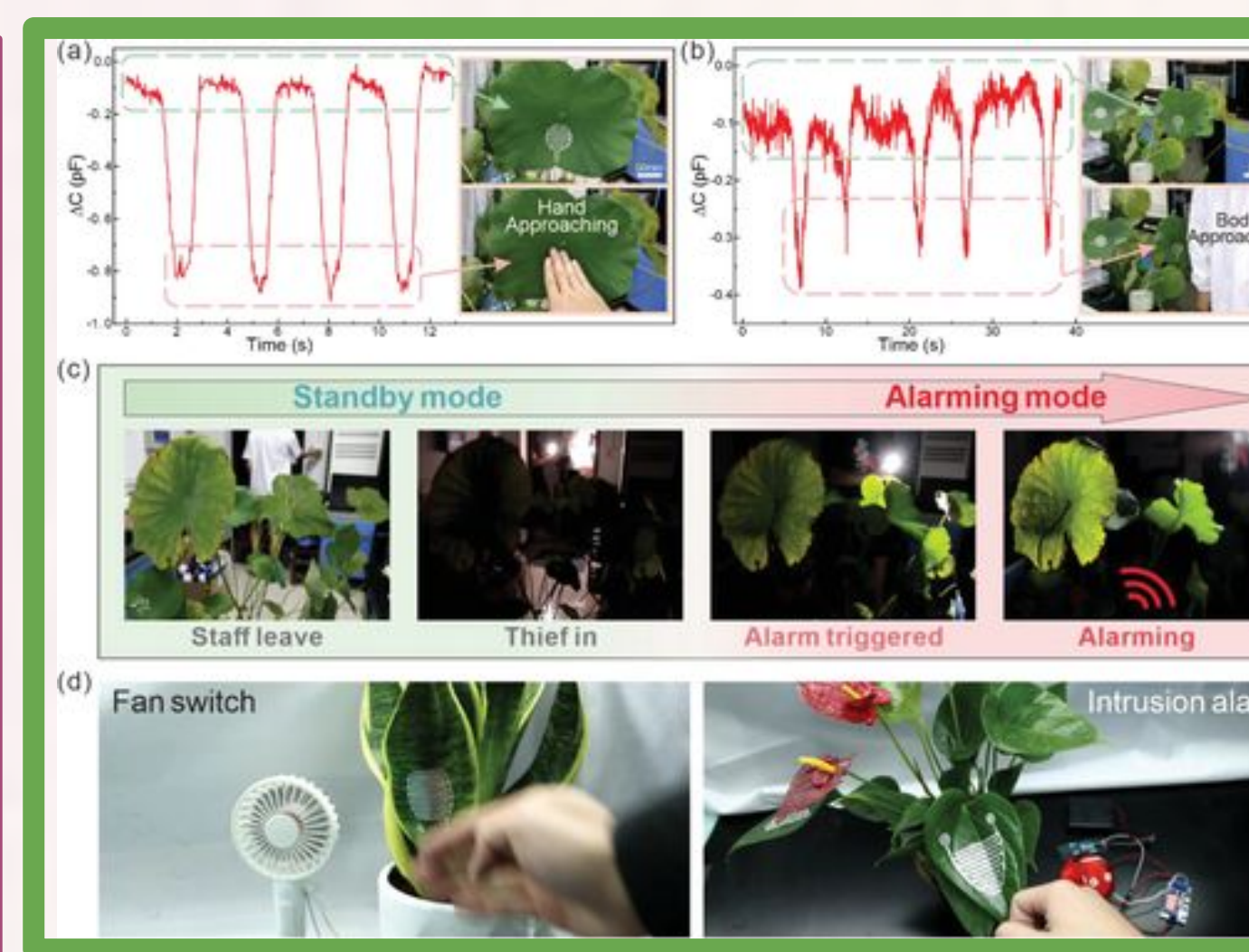
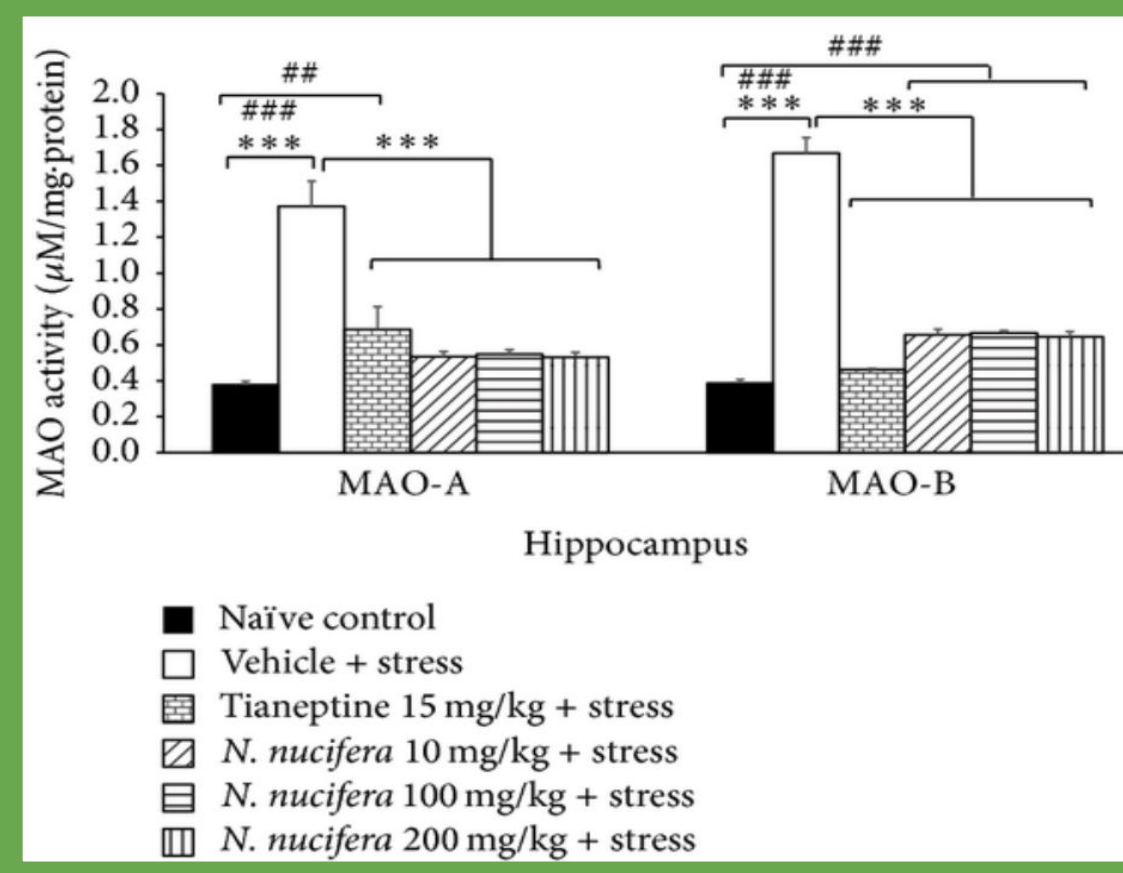
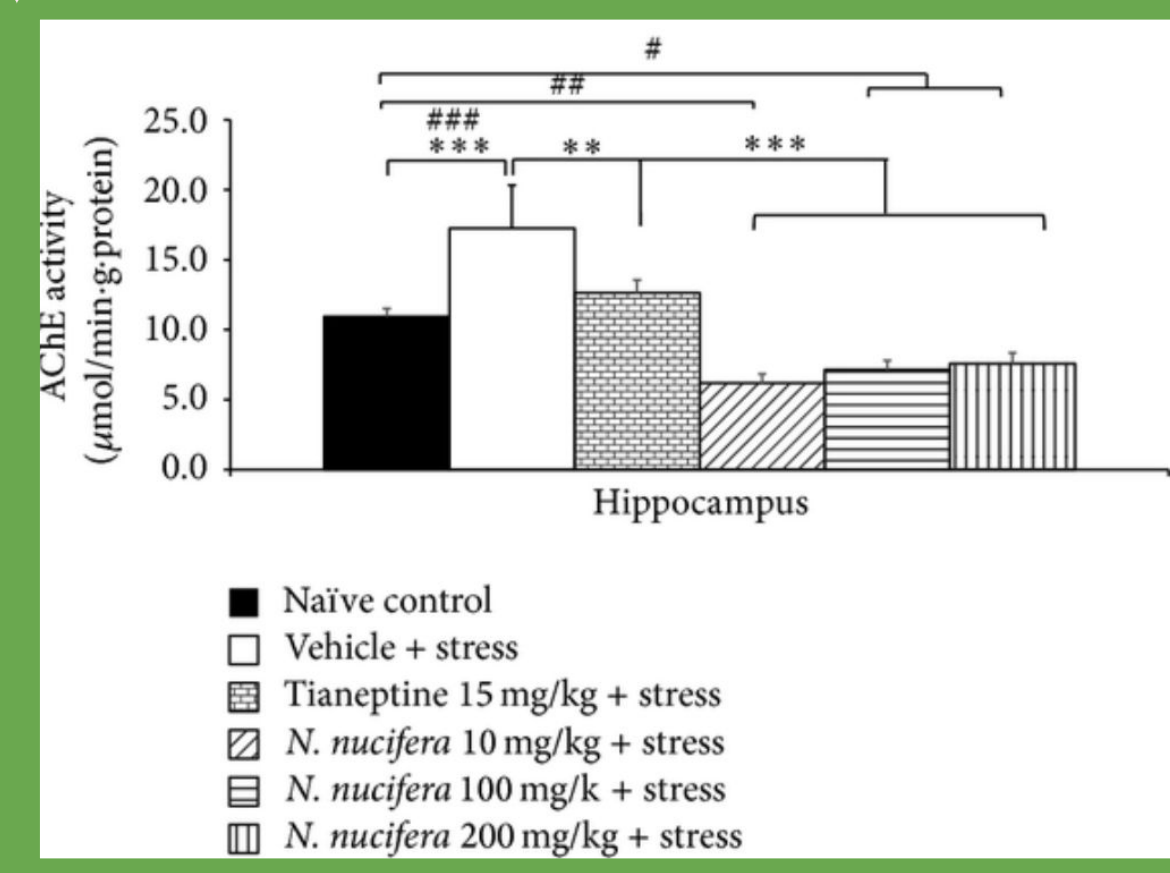
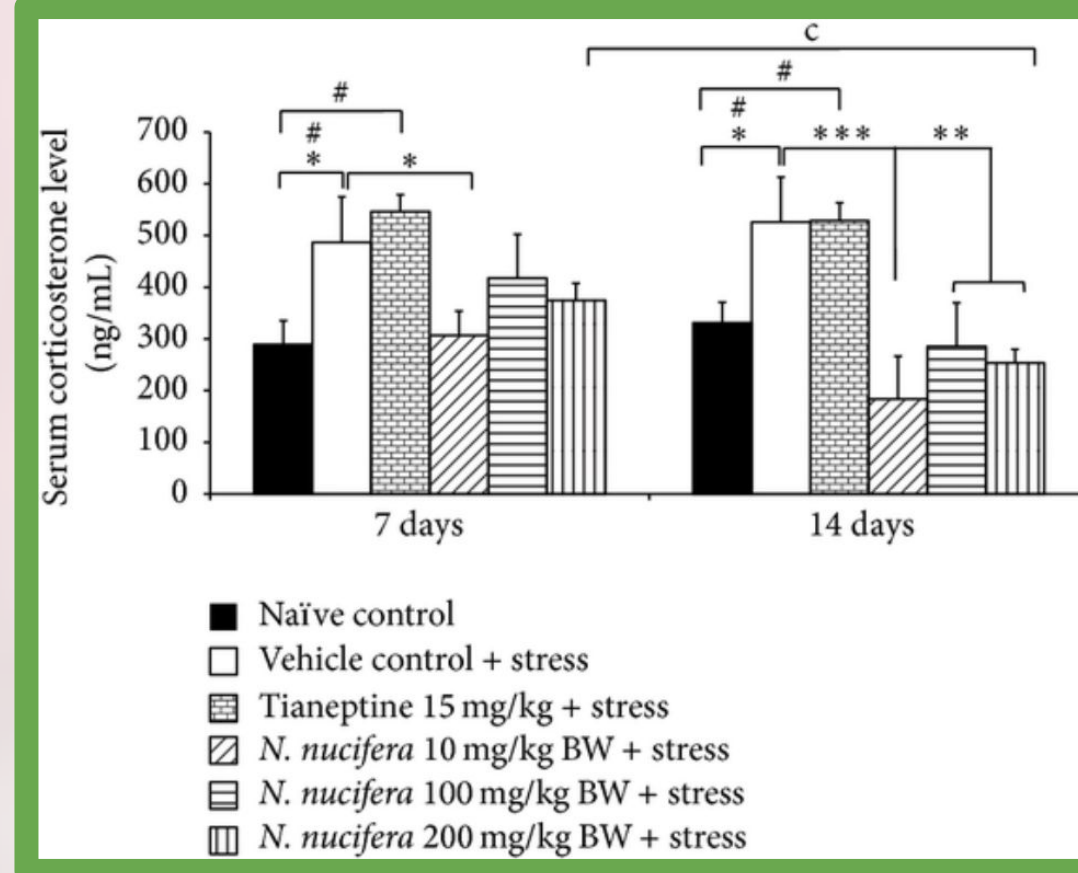
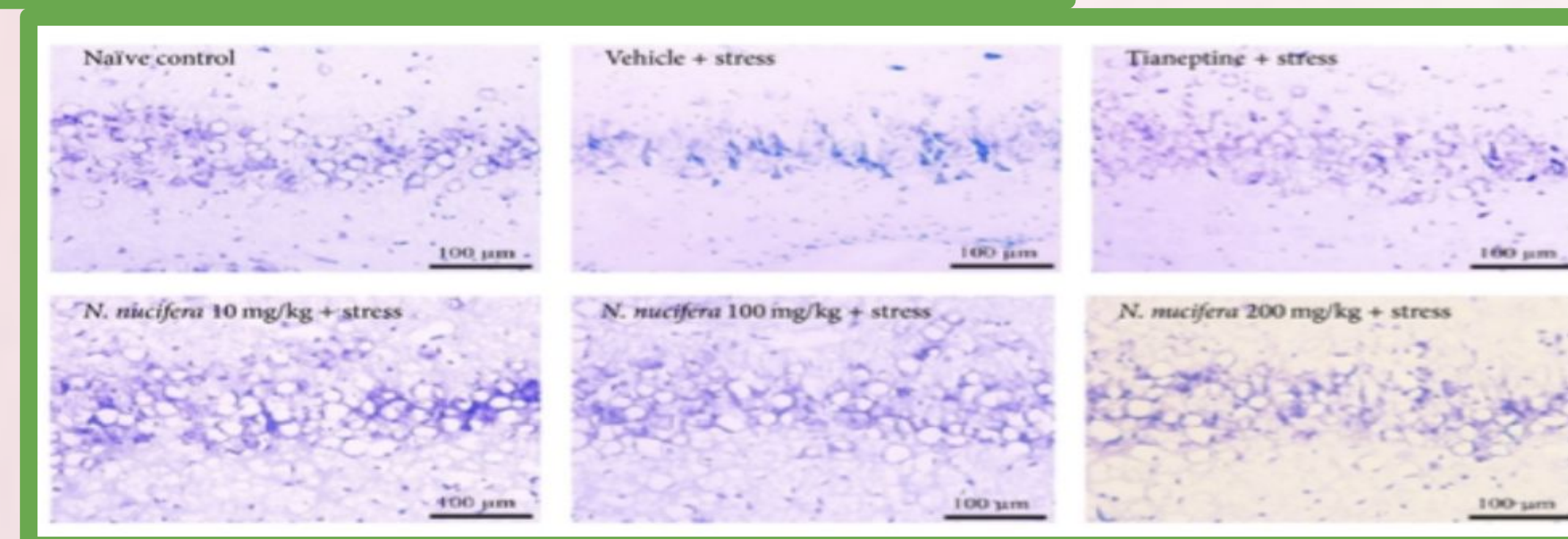
ABSTRACT

From medicine to technology, the discoveries and studies regarding the lotus plant are expansive, historical, and significant. There have been multiple new facts revealed by the many studies conducted by scientists all around the world. Our group has been able to find studies and peer-reviewed articles from multiple sources that have discussed new discoveries regarding the lotus plant (*Nelumbo nucifera*) and its expansive benefits. Only the surface of the true advantage of the lotus plant has been revealed. History, culture, and science all together have been immensely influenced by this plant, and will continue to be so. In this review, we aim to reveal the plethora of advantages that are stored in virtually every part of the lotus plant as well as the underappreciated, transformative effects the plant can have in nature, technology, and our daily lives. The lotus plant has a rich history of cultural applications in various remedies and food, including its sleep promotion properties due to the extract of the rhizome and stress relieving properties by combatting the harmful effects of memory and brain damage. The extracts from commonly discarded parts of the lotus, including the seedpod and epicarp, have antioxidative properties that prevent oxidative stress and are cytoprotective. Thus, they protect against free radicals, which contribute to chronic diseases such as heart disease, diabetes, and cancer. Simultaneously, recent research underscores the lotus plant's pivotal role in advancing material science and technology, particularly through plant-hybrid systems and biomimicry applications. The superhydrophobicity of lotus leaves serves as inspiration for plant-hybrid systems, contributing to applications like digital switches and sensors. Furthermore, the robustness of lotus fibers inspires the development of Biomimetic Hydrogel Fibers (BHF) with applications in the biomedical field, exemplifying the plant's impact in crafting innovative solutions. Lastly, the lotus root emerges as a promising element in bone tissue engineering, leveraging its natural porous structure and antioxidant properties.

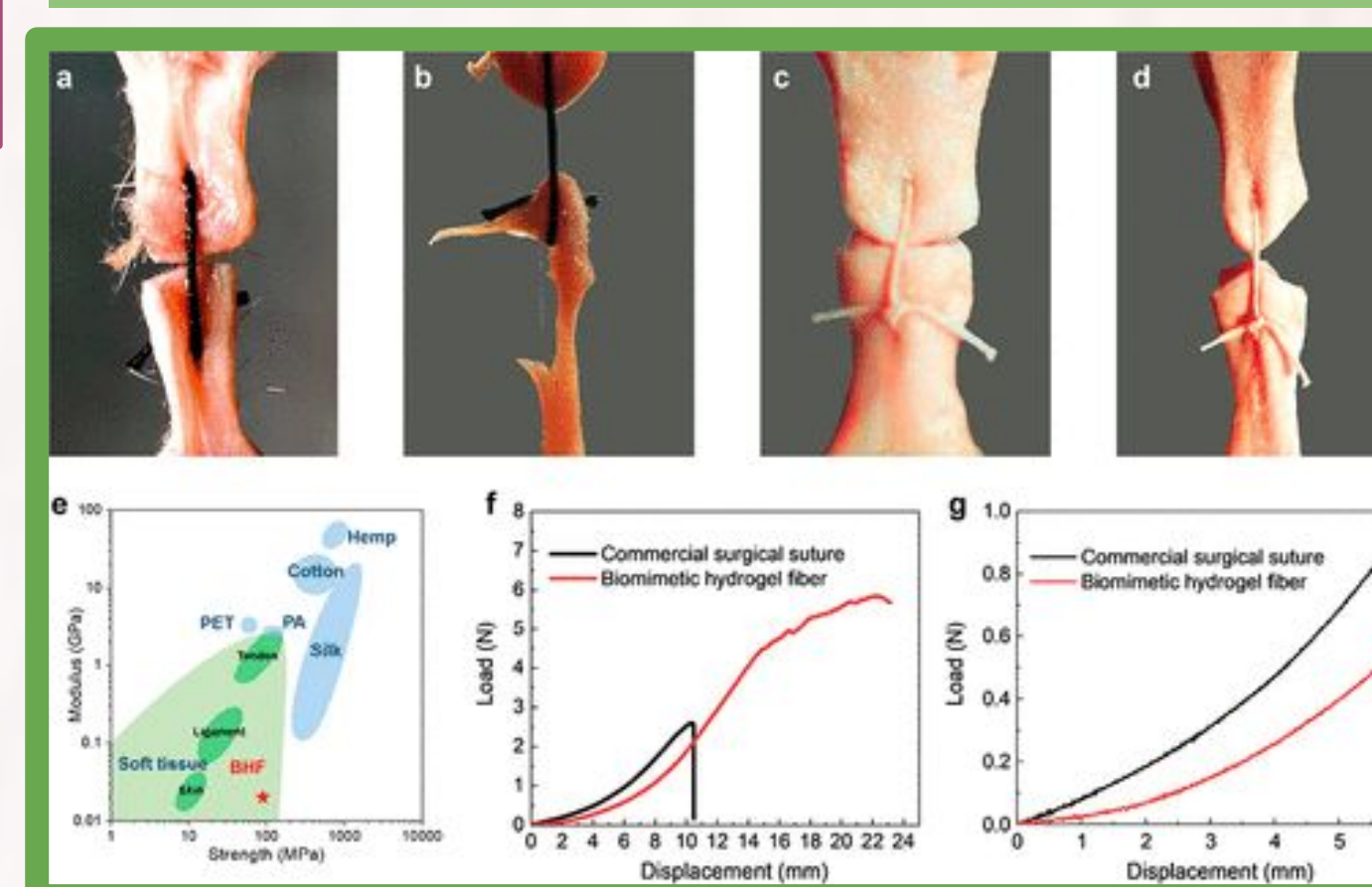


ANTIOXIDANTS

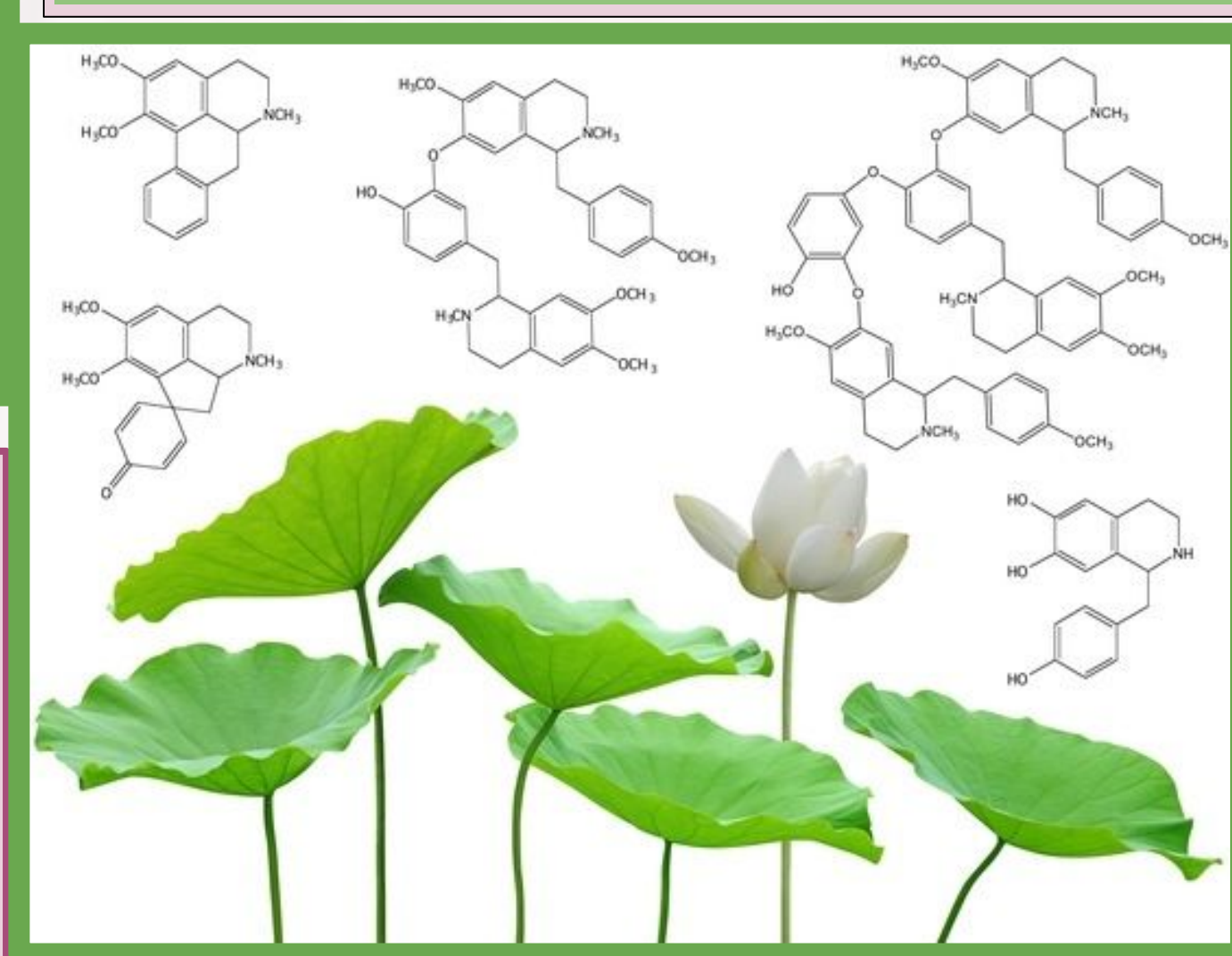
- Nelumbo nucifera is known to be able to work as an antioxidant, meaning that it can neutralize free radicals which can either prevent or lessen damage caused by oxidation in the body.
- A study showed lotus being used as an antioxidant to treat Wistar rats facing oxidative stress, which plays a role in stressed-induced memory deficit and brain damage. Orally-given extract of the Nelumbo nucifera showed to have decreased memory deficit and brain damages as well as corticosterone, oxidative stress, acetylcholinesterase(AChE), and monoamine oxidase type A and B(MAO-A and MAO-B).
- Recent studies have further solidified the notion that the lotus will continue to be a source of immense benefit for humanity in the years to come by arguing that even the seed pod and see epicarp have antioxidant and cytoprotective properties. Seed epicarp extract from the lotus was also found to have the most significant protection effect on oxidative DNA damage (as proven by its effective H₂O₂ scavenging activity).



Intrusion alarm sensor on various hydrophobic plants testing the proximity of hand/body and the capacitance variation curve[2]



(a,b) commercial suture and (c,d) BHF on in vitro skin of rat, showing that BHF will not cut through the skin like commercial suture under high tensile strain. Graphs highlight how BHF has similar modulus and strength to soft tissue, like skin.[14]



Technology

section 1: Lotus Leaves & Plant-Hybrid Systems:-

- Lotus Leaf Structure[3][4]:**
 - Superhydrophobicity from hierarchical micro- and nanostructures with an epicuticular wax coating.
 - Microscale "bumps" or "papillae" with nanostructures create a rough, textured surface.
 - Hydrophobic wax coating enhances water-repellent capabilities.
 - Lotus leaves' hydrophobicity enables self-cleansing and anti-icing effects.
 - Low adhesion extends beyond water, reducing stickiness to various substances.
 - "The Lotus Effect" has inspired synthetic water-repellent materials for applications in high-sanitation environments.
- Living Plant-Hybrid Systems[11]:**
 - Technique utilizing living plants in high-tech devices.
 - Exploits plants' physiology, water content, turgor pressure, biochemical reactions, and so on for energy harvesting, sensing, and robotics applications.
 - This process attempts to accommodate the plant's health and development, while exploiting their natural processes for a high-tech purpose.

- Recent Research Lotus-based Plant-Hybrid Systems[2]:**
 - Plants constitute 80% of Earth's biomass, playing vital roles in agriculture, ecology, and energy supply.
 - Integration of plants with epidermal electronics for addressing challenges like climate change.
 - Liquid alloy and soap solution overcome challenges in electronic integration on plants.
 - Successful demonstrations include intrusion alarm sensors, showcasing potential in home security and IoT.

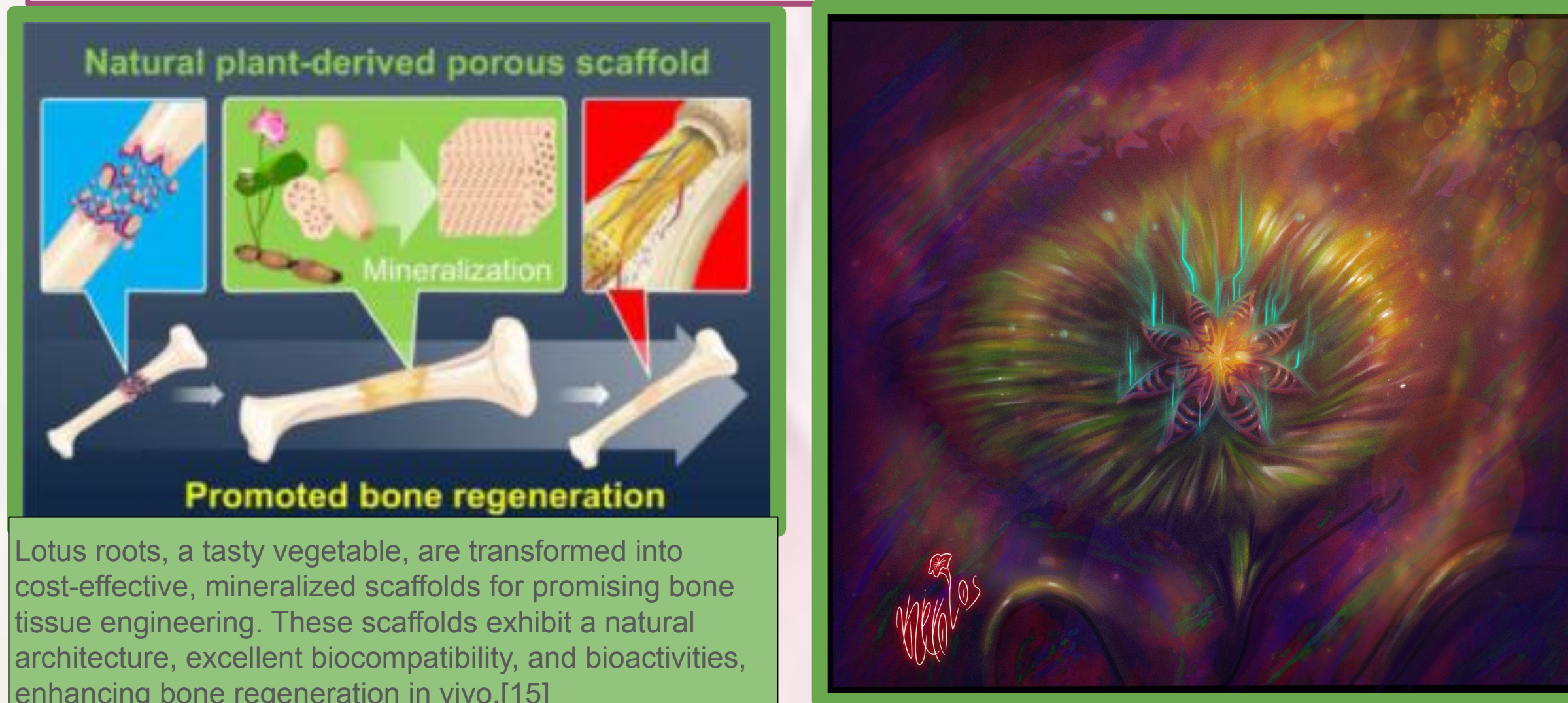
Section 2: Lotus Fibers & Hydrogel:-

- Lotus Fiber Properties[12]:**
 - Strong, resilient fibers with a unique (spiral) structural composition.
 - Natural porosity facilitates gas and moisture exchange.
- Biomimicry Developments in Lotus Fiber Research[13][14]:**
 - Introduction to Biomimicry: Learning from and emulating natural forms, processes, and ecosystems.
 - Biomimetic Hydrogel Fiber (BHF) mimics lotus fibers' spiral structure.
 - BHF exhibits high strength, hydrophilicity, and excellent biocompatibility.
 - Proposed applications in surgical sutures and biomedical materials.

Section 3: Lotus Roots & Root-based Scaffolds:-

- Lotus Root Characteristics[15]:**
 - Derived from the rhizome of the lotus plant, consumed as a vegetable in Asia.
 - Nutrient-rich structure with porous microstructure and traditional medicinal use.
- Recent Research in Lotus Root-Based Scaffolds (Biomimicry)[15]:**
 - Focus on lotus root in bone regeneration for cost-effective and biocompatible solutions.
 - Unique porous structure enhances cellular adhesion and stimulates bone growth.
 - Noteworthy attributes include antioxidative properties, angiogenic stimulation, and osteogenic promotion.

Conclusion: Unlocking Innovation Through the Lotus Plant:-
The exploration of various facets of this one case study, the lotus plant, unveils a treasure trove of possibilities that can resonate across diverse fields of research and innovation. Highlighting the varistile and expansiveness of research inspired by and incorporating nature processes and designs.



Lotus roots, a tasty vegetable, are transformed into cost-effective, mineralized scaffolds for promising bone tissue engineering. These scaffolds exhibit a natural architecture, excellent biocompatibility, and bioactivities, enhancing bone regeneration in vivo.[15]

REFERENCES

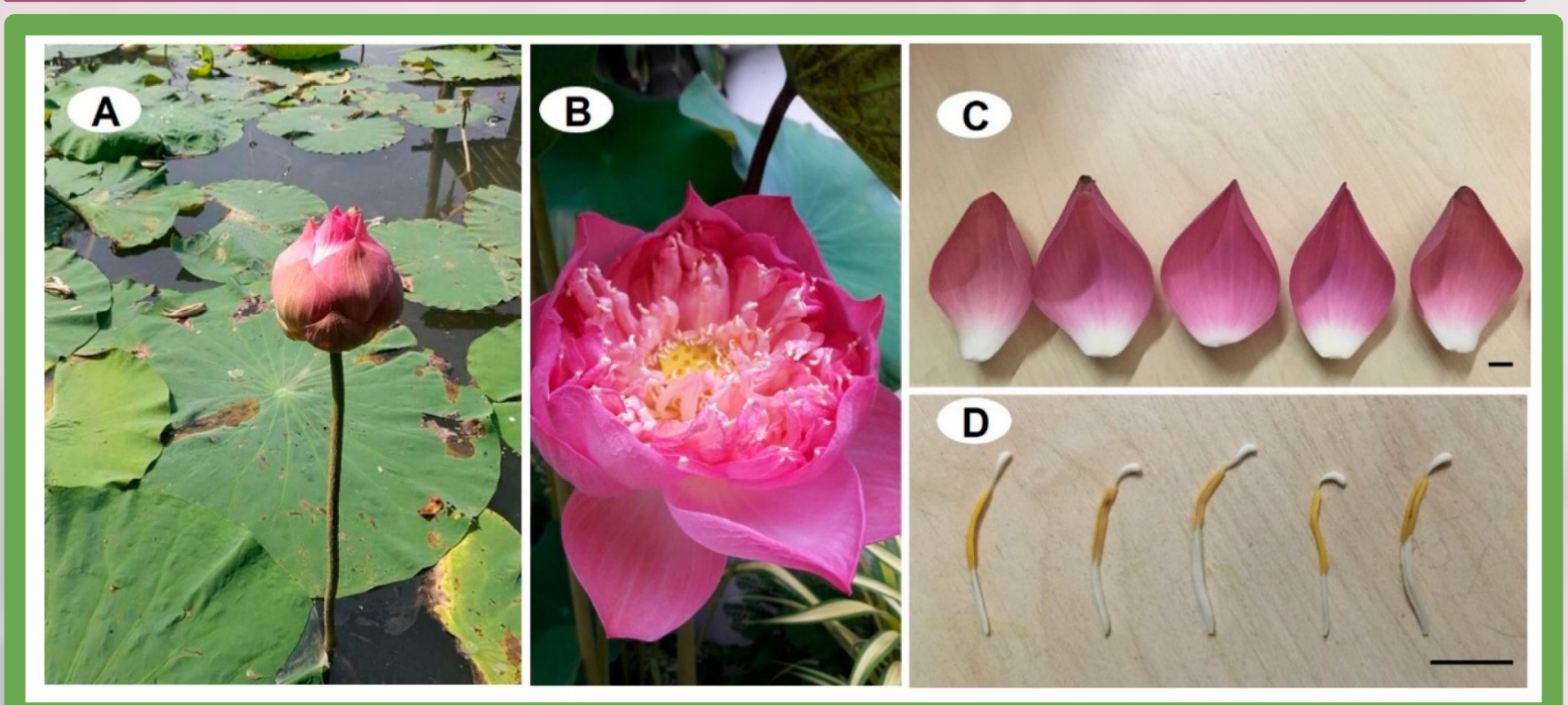
[1]Ahn, Y., Kim, S.; Park, C.; Kim, J. E.; Suh, H. J.; Jo, K. Sleep-Promoting Activity of Lotus (*Nelumbo Nucifera*) Rhizome Water Extract via GABA_A Receptors. *Pharmacological Biology* 2022, 60 (1), 1341–1348. <https://doi.org/10.1080/1388209.2022.2096076>. [2] Jiang, J.; Fei, W.; Pu, M.; Chai, Z.; Wu, Z. A Facile Liquid Alloy Wetting Enhancing Strategy on Super-Hydrophobic Lotus Leaves for Plant-Hybrid System Implementation. *Advanced Materials Interfaces* 2022, 9 (17), 2200516. <https://doi.org/10.1002/admi.202200516>. [3]Lotus Effect – an overview | ScienceDirect Topics. <https://www.sciencedirect.com/topics/engineering/lotus-effect>. [4]Lotus Effect in Nanotechnology. *Nanografi Nano Technology*. [https://nanografi.com/blog/lotus-effect-in-nanotechnology/#:~:text=This%20particular%20phenomenon%2C%20studied%20\(accessed%2023-11-04\)](https://nanografi.com/blog/lotus-effect-in-nanotechnology/#:~:text=This%20particular%20phenomenon%2C%20studied%20(accessed%2023-11-04)). [5]JU, C.-P., LIN, K.-H., WU, C.-C., SHH, M.-C., CHANG, W.-T., and YU, Y.-P. (2022) Antioxidant and cytoprotective properties of seeds and seed-by-products from Lotus (*Nelumbo nucifera*). *Notulae Botanicae Horti Agroboticae Cluj-Napoca* 50, 12711.[6]Mukherjee, P. K.; Mukherjee, D.; Maji, A. K.; Rai, S.; Heinrich, M. The Sacred Lotus (*Nelumbo Nucifera*) - Phytochemical and Therapeutic Profile. *Journal of Pharmacy and Pharmacology* 2009, 61 (4), 407–422. <https://doi.org/10.1211/jpp.61.04.0001>. [7]NELSON, C. A.; CARVER, L. J. The Effects of Stress and Trauma on Brain and Memory: A View from Developmental Cognitive Neuroscience. *Development and Psychopathology* 1998, 10 (4), 793–809. <https://doi.org/10.1017/s0954579498001874>. [8]Pizzino, G.; Irrera, N.; Cucinotta, M.; Pallio, G.; Mannino, F.; Arcoraci, V.; Squadrito, F.; Altavilla, D.; Bitto, A. Oxidative Stress: Harms and Benefits for Human Health. *Oxidative Medicine and Cellular Longevity* 2017, 2017 (8416763), 1–13. <https://doi.org/10.1155/2017/8416763>. [9]Prabstrot, T.; Wattanathorn, T.; Wattanathorn, J.; Somsat, P.; Sritragool, O. Positive Modulation of PinkNelumbo NuciferaFlowers on Memory Impairment, Brain Damage, and Biochemical Profiles in Restraint Rats. *Oxidative Medicine and Cellular Longevity* 2016, 2016, 1–11. <https://doi.org/10.1155/2016/5780857>. [10]Pandel, K. R.; Panth, N. Phytochemical Profile and Biological Activity of *Nelumbo Nucifera*. *Evidence-Based Complementary and Alternative Medicine* 2015, 2015, 1–16. <https://doi.org/10.1155/2015/789124>. [11]Meder, F.; Baytekin, B.; Del Dottore, E.; Meroz, Y.; Tauber, F.; Walker, L. D.; Mazzolai, B. A Perspective on Plant Robotics: From Bioinspiration to Hybrid Systems. *Bioinspiration & Biomimetics* 2022, 18 (1), 015006. <https://doi.org/10.1088/1748-3190/ac1988>. [12]Pan, Y.; Han, G.; Mao, Z.; Zhang, Y.; Hongtao, D.; Huang, J.; Qu, L. Structural Characteristics and Physical Properties of Lotus Fibers Obtained from *Nelumbo Nucifera* Petioles. *Carbohydrate Polymers* 2011, 85 (1), 188–195. <https://doi.org/10.1016/j.carbpol.2011.02.013>. [13]Benyus, J. An Introduction to biomimicry. *Next Nature Network*. <https://nextnature.net/story/2019/biomimicry-primer-#:~:text=Biominicry%20is%20learning%20from%20and%20make%20a%20more%20resilient%20company>. [14]Guan, Q.; Han, Z.; Zhu, Y.; Xu, W.; Yang, H.; Ling, Z.; Yan, B.; Yang, K.; Yin, C.; Wu, H.; Yu, S. Bio-Inspired Lotus-Fiber-like Spiral Hydrogel Bacterial Cellulose Fibers. *Nano Letters* 2021, 21 (2), 952–958. <https://doi.org/10.1021/acs.nanolett.0c02702>. [15]Huang, K.; Huang, J.; Zhao, J.; Gu, Z.; Wu, J. Natural Lotus Root-Based Scaffolds for Bone Regeneration. *Chinese Chemical Letters* 2021. <https://doi.org/10.1016/j.ccl.2021.10.073>.

PHARMACEUTICALS

- There are many pharmaceutical uses for the lotus plant. From the stem to the seeds to the petals, virtually every part of the lotus plant is somehow useful for pharmaceutical benefits.
- The article "Phytochemical Profile and Biological Activity of *Nelumbo nucifera*" talks about the studies conducting surrounding nelumbo nucifera and the aforementioned benefits it has. The studies concluded that the lotus plant is able to act as antioxidants, anti-steroids, and it can act against diabetes. Furthermore, it is very useful for antiviral activities and immunology.
- When it comes to antiviral activity, the lotus plant has leaves that have "isolated quercetin 3-O-β-D-glucuronide, (+)-1(R)-coclaurine, and (-)-1(S)-noroclaurine". These chemicals, specifically the latter two, were found to help patients with HIV. The embryo of the lotus also had much antiviral activity against HIV.
- A study was conducted in 2004 to test "the effect of ethyl alcohol extracts of lotus in primary human peripheral blood mononuclear cells (PBMC) stimulated by phytohemagglutinin". They wanted to inhibit cell proliferation and cytokines production. Basically, this study wanted to see if the lotus plant could truly help with immunity. A study created in 2006 was very similar to this, as it tested the effect that s-ampervine (a chemical from nelumbo nucifera) on mice. This s-ampervine was given orally to mice for 6 weeks, what was concluded was fascinating. "(S)-lirapervine was successful to prevent lymphadenopathy as well as extend the lifespan of mice". It also concluded that this chemical could be used to change one's immune system for the management of SLE (lupus).
- Overall, it is obvious that nelumbo nucifera is overly underappreciated and has the power to transform the pharmaceutical community if taken seriously and used to its full potential.
- Nelumbo nucifera is the "spinal cord" of some communities, it is sacred in others, and it is often utilized for medicinal purposes in many more communities. Thus, we must learn how to integrate this lucrative plant into our society and use it as true medicinal remedies in the healing of ailments faced by many people.

HERBAL REMEDIES

- Sleep is very important to allow the brain to rest and function, and sleep disorders affect 30-35% of the world population.
- Unfortunately, many of the drugs used for sleep disorders cause serious negative effects, so many resort to herbal remedies instead.
- The article "Sleep-promoting activity of lotus (*Nelumbo nucifera*) rhizome water extract via GABA_A receptors" by Yejin Ahn focuses on the rhizome of the lotus plant, and tested a rhizome extract on mice to see how it affected their sleep. The rhizome extract works by interacting with GABA_A receptors. GABA_A receptors are proteins in the brain that respond to the neurotransmitter GABA, also known as the primary inhibitor of the brain. GABA helps you fall asleep by lowering the activity in your brain.
- The extract was compared to a common drug used for anxiety and sleep disorders, Alprazolam, shown in Figure A below. The data found that the extract activated the GABA_A receptors faster and in a greater volume than.
- The rhizome was proven to be effective in sleep promotion in mice by promoting a longer duration of sleep than the drugs Flumazenil and Picrotoxin, shown in Figure B to the right..



DISCUSSION:

The lotus plant or *Nelumbo nucifera* has been a source of food, medicine and culture for humanity for centuries. In our research, we have explored its pharmaceutical uses, herbal uses, antioxidant properties, and its promising use in plant-hybrid systems. The discovery found in our research that commonly-discarded parts of the lotus plant (seed pod, seed epicarp, etc.) has antioxidant properties has substantial implications for the future of medicine. Also covered in our research, sleep disorders are a current, prevalent issue. Common drugs that are used for sleep disorders, including Alprazolam, have serious adverse effects, and many of those that suffer from sleep disorders resort to medicinal herbs. The rhizome extract was proven to be effective in sleep promotion in mice by activating the brain's primary inhibitor receptors (GABA_A receptors). The rhizome of *Nelumbo nucifera* is a promising herbal alternative to pharmaceutical remedies. Additionally, recent advancements in lotus plant-inspired technologies have demonstrated significant potential across diverse fields. In the domain of lotus leaves and plant-hybrid systems, the successful integration of living plants into high-tech devices has been achieved through innovative techniques involving liquid alloy and soap solutions. Furthermore, lotus fibers, with their distinctive structure, have inspired the development of the Biomimetic Hydrogel Fiber (BHF) in biomimicry research. Additionally, lotus roots have emerged as crucial contributors to innovation, particularly in the realm of bone regeneration, where their porous structures form the basis for advanced root-based bone scaffolds. This comprehensive exploration underscores the lotus plant's substantial impact on cutting-edge innovations and the development of sustainable solutions across various disciplines.

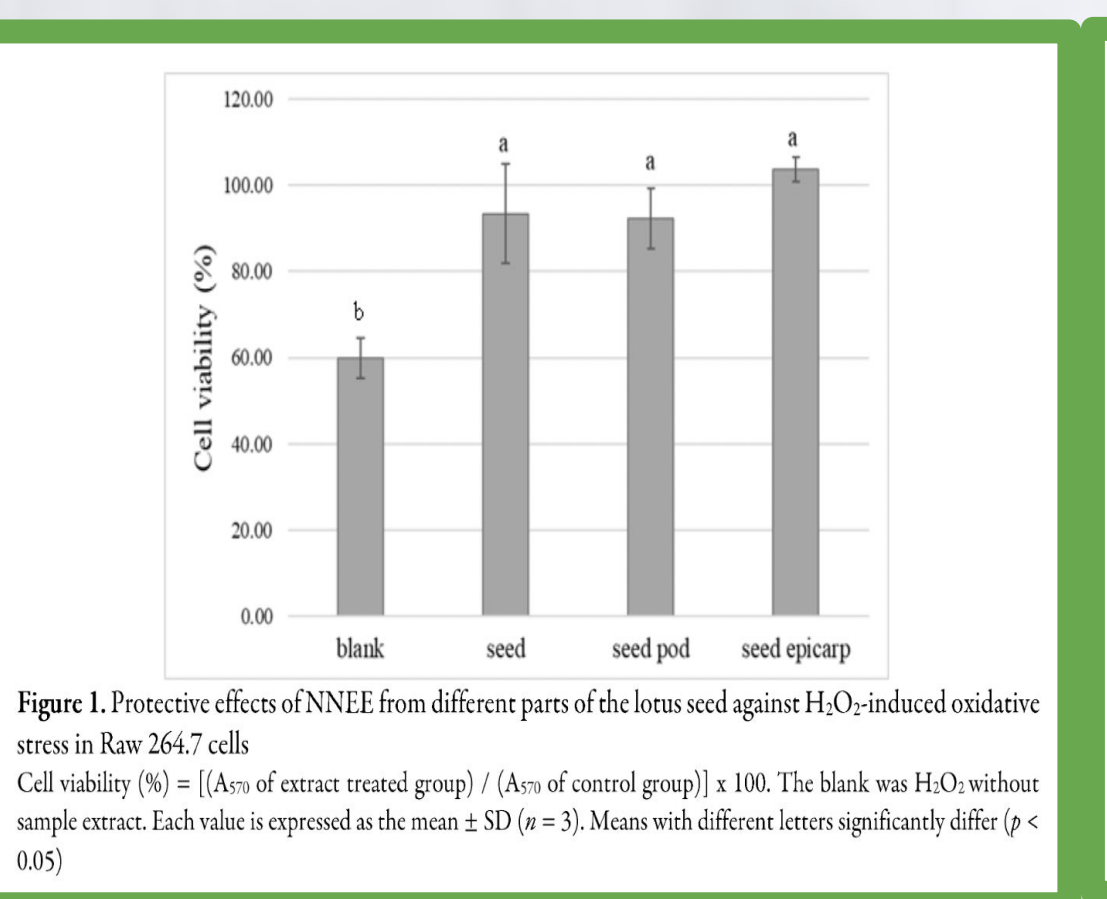
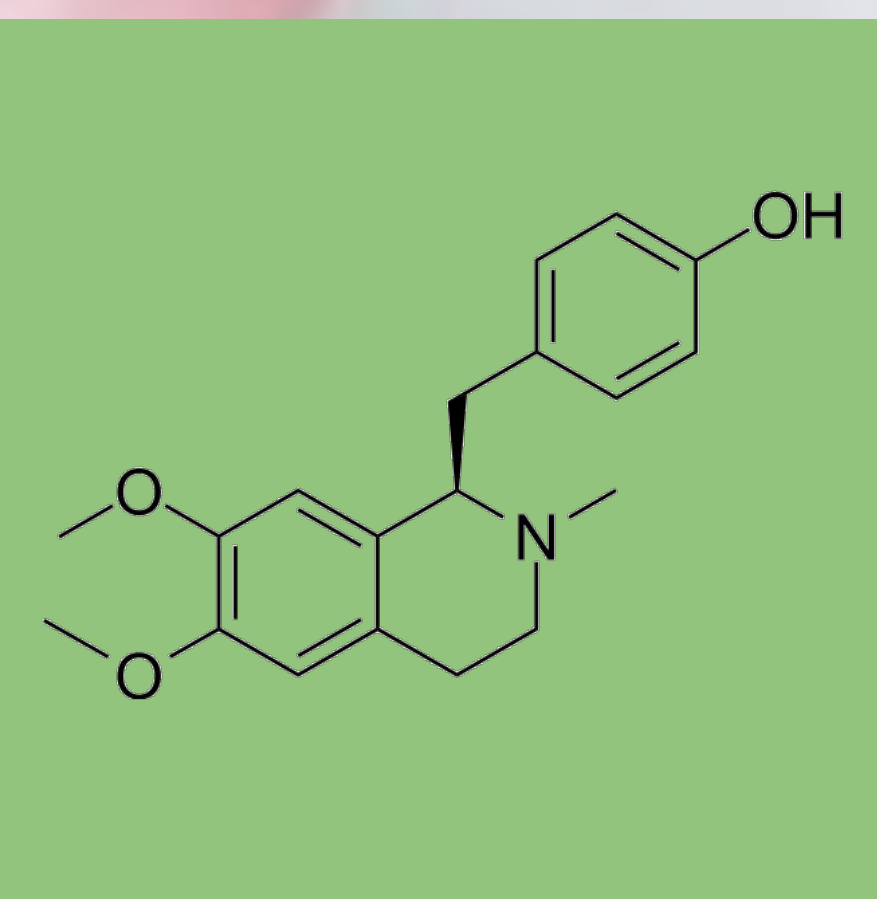
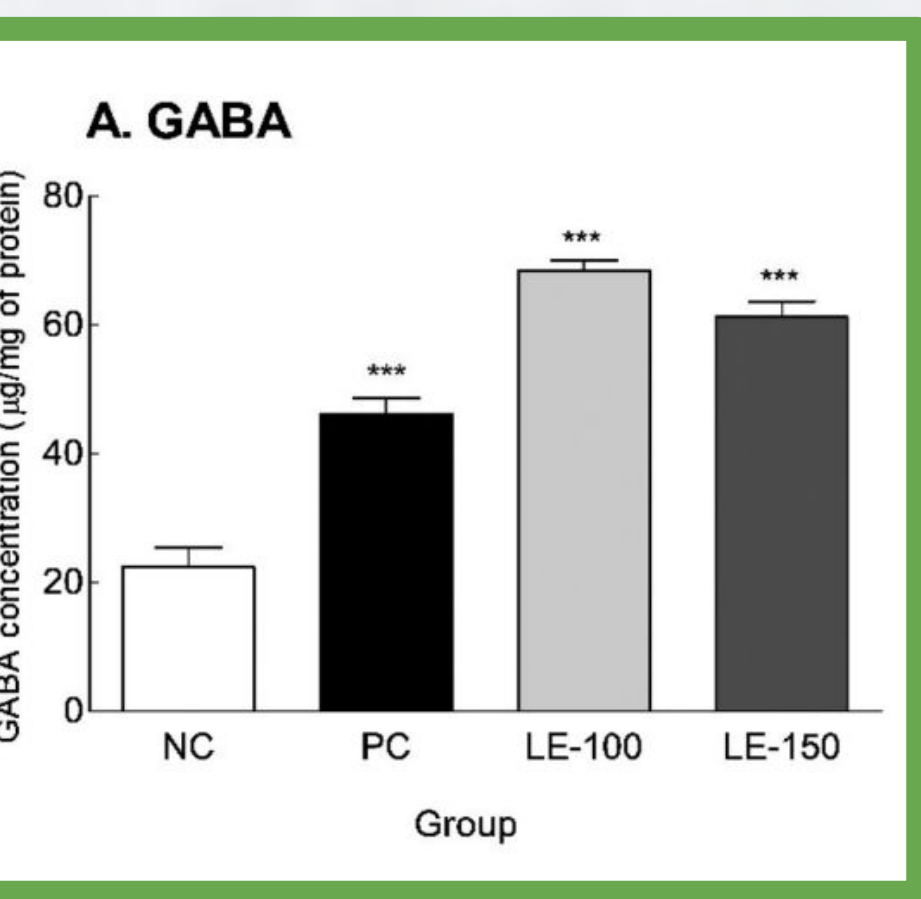
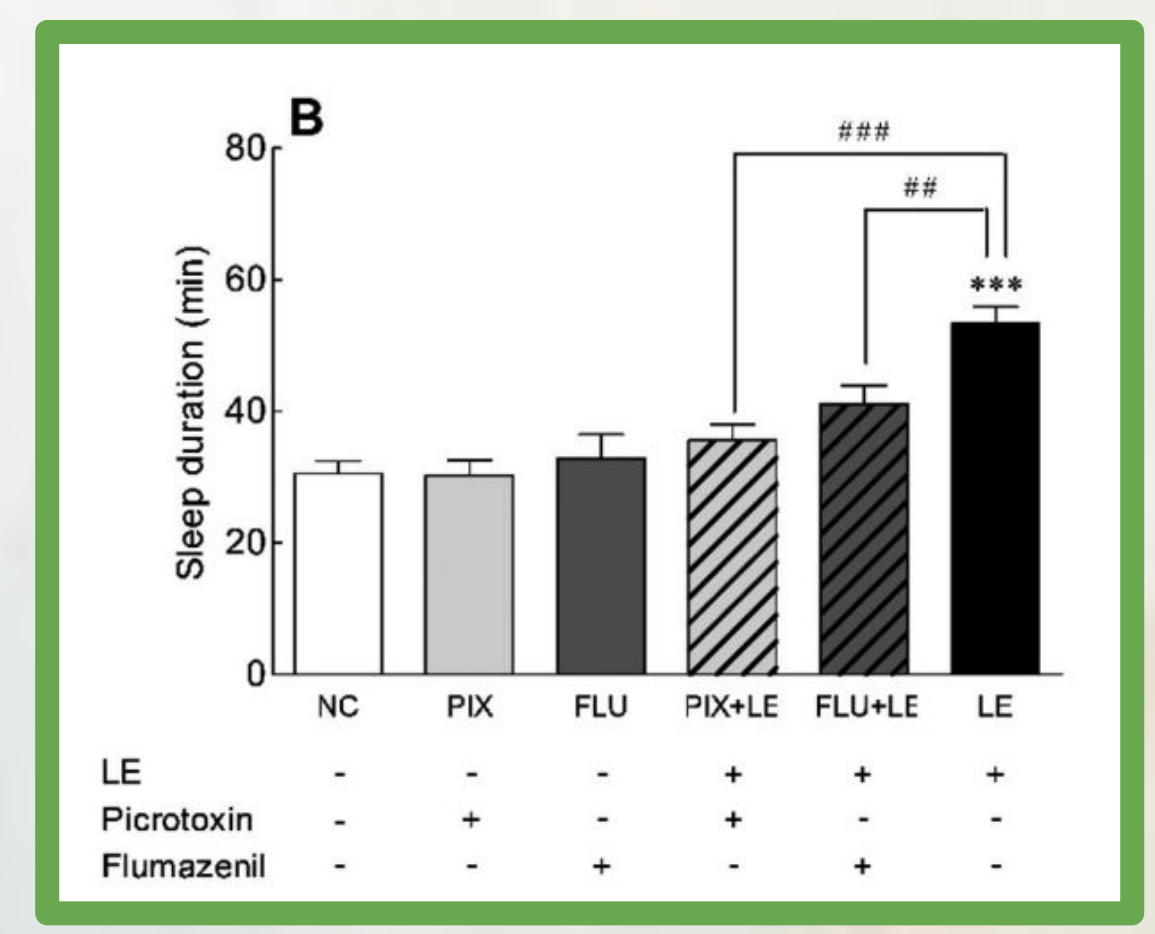


Figure 1. Protective effects of NNE from different parts of the lotus seed against H₂O₂-induced oxidative stress in HeLa cells. Cell viability (%) = [Abs of extract treated group] / [Abs of control group] × 100. The blank was H₂O₂ without sample extract. Each value is expressed as the mean ± SD (n = 3). Means with different letters signify differ (p < 0.05)



A. GABA concentration (µg/mg of protein) for various groups: NC (Naive control), PC (Vehicle + stress), LE-100 (Tianeptine 15 mg/kg + stress), and LE-150 (N. nucifera 150 mg/kg + stress).

NC- negative control group (Alprazolam)
PC- positive control group (Alprazolam)
LE-100- 100 mg/kg of rhizome extract
LE-150- 150 mg/kg of rhizome extract



NC- negative control group
PIX- 4 mg/kg of Picrotoxin
FLU- 10 mg/kg of Flumazenil
PIX+LE- Combination of 4 mg/kg of Picrotoxin and 150 mg/kg of rhizome extract
FLU+LE- Combination of 10 mg/kg of Flumazenil and 150 mg/kg of rhizome extract
LE- 150 mg/kg of rhizome extract