



Diving into the Depths of Belladonna: Uncovering the Secrets of the Deadly Nightshade

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Abstract

Tropane alkaloids, such as hyoscyamine and scopolamine, are vital medicinal compounds found in various therapeutic formulations. These alkaloids are synthesized within the roots of specific genera of the Solanaceae family through a complex, partially understood multistep pathway. In efforts to deepen our comprehension of tropane alkaloid biosynthesis, a novel de novo transcriptome assembly was crafted for Deadly Nightshade (*Atropa belladonna*). A crucial intermediate in the biosynthesis of hyoscyamine and scopolamine is littorine, formed by the condensation of tropine and phenyllactic acid. Phenyllactic acid originates from phenylalanine through transamination to phenylpyruvate. Through transcriptome analysis, a distinct aromatic amino acid aminotransferase (ArAT), designated Ab-ArAT4, was identified. This enzyme coexists with known tropane alkaloid biosynthesis genes in the roots of *A. belladonna*. Silencing Ab-ArAT4 resulted in diminished synthesis of hyoscyamine and scopolamine due to reduced phenyllactic acid levels. In vitro studies revealed that recombinant Ab-ArAT4 primarily catalyzes the initial step of phenyllactic acid synthesis: the transamination of phenylalanine to phenylpyruvate.

Keywords: Tropane alkaloids, hyoscyamine, scopolamine, medicinal compounds, biosynthesis, Solanaceae family, Deadly Nightshade, *Atropa belladonna*, transcriptome assembly, littorine, phenyllactic acid,

phenylalanine, transamination, aromatic amino acid aminotransferase, Ab-ArAT4, gene silencing, in vitro studies

Introduction to Belladonna

Belladonna, also commonly referred to as deadly nightshade, is a perennial herbaceous plant of the Solanaceae family, which also includes tomatoes, potatoes, and eggplants¹. The plant's botanical name, *Atropa belladonna*, derives from the Greek word "atropos," named after one of the three Fates in Greek mythology and the Italian "bella donna," meaning "beautiful lady."² The combination of these words highlights the contrasting nature of the plant, foreshadowing its ability to both provide beauty and bring death. Belladonna is indigenous to regions of Europe, North Africa, and Western Asia and prefers calcareous soils and partial shading³. The plant grows up to five feet, has oval-shaped leaves, and features beautiful bell-shaped flowers of deep purple and ranges of greenish yellow (Bowerbank, Gallidabino, & Dean, 2022). Nevertheless, the most striking feature is a shiny black berry that is commonly confused with cherries. The unpleasant aroma released by belladonna further showcases its uniqueness and deters herbivores away from its geographical location. **Error! Bookmark not defined.** Nevertheless, the plant's intriguing appearance and properties have fascinated humans for centuries, driving its use and intense cultural symbolism (Bowerbank, Gallidabino, & Dean, 2022).

Methods:

This article compiles insights from a diverse range of sources, including scholarly literature, historical records, and cultural contexts, to offer a comprehensive exploration of belladonna. Given the nature of the topic, statistical methodologies are not employed.

Results:

The findings illuminate belladonna's rich historical legacy, its traditional and contemporary medicinal applications, toxicity profiles, regulatory landscapes, and its presence in various cultural narratives. Recent scientific investigations have shed light on its therapeutic potential while also prompting discussions about safety and regulatory considerations.

¹ Sadia Javed et al., "Belladonna," in Springer eBooks, 2023, 83–93.

² Imane Ouasti et al., "Atropa Belladonna L.Solanaceae," in Ethnobotany of Mountain Regions, 2023, 1–6.

³ Elmira Danaie, Shiva Masoudi, and Nasrin Masnabadi, "Chemical Composition Analysis of Atropa Belladonna Grown in Iran and Evaluation of Antibacterial Properties of Extract-Loaded Nanofibers," Iranian Journal of Pharmaceutical Research 22, no. 1 (August 2023).

Discussion:

The discourse navigates the intricate terrain of belladonna, weighing its therapeutic efficacy against potential risks and the evolving discourse surrounding its utilization in modern healthcare. The article delves into the complexities of belladonna's pharmacology and regulatory frameworks, advocating for informed decision-making and precautionary measures.

Historical Significance

Historically, Belladonna served as one of the most critical plants of mysticism, shamans, and severe rituals for many thousands of years. Nowadays, according to the myth, the ancient people considered the plant a mystically personification of the sorcery power of frightening and crystallizing the devil, and the shamans, witches, and healers used during the exorcism of the demoniacal spirit (Bowerbank, Gallidabino, & Dean, 2022). Another example one can cite is women of the high society of the Renaissance era who used the berry extracts to dilate their pupils and get a distinctive sight, which was seen by men as desirable. The belladonna received the name “bella donna,” translated as “beautiful lady” which emphasized its appeal for women for many more hundreds of years². Throughout history, the belladonna theatre attraction has been associated with numerous legends and superstitions. In some nations, it was believed that it could frighten away evil spirits and ensure one’s transparent visibility, while in others, it served as one of the components of love potions and aphrodisiacs.

Medicinal Uses

Moreover, despite the toxicity, belladonna is a highly appreciated substance in traditional medicine, indeed because of the tropane alkaloids it contains, including atropine, hyoscyamine, and scopolamine⁴. In addition to the general paralysis of major blood vessels and simultaneously stimulation of the heart and the central nervous system, belladonna and its extracts have been widely used to relax smooth muscles and dilate pupils. The most common modern application is in ophthalmology, where compounds like atropine are used to dilate the pupils during eye exams and to treat diseases like uveitis and lazy eye (Javed et al., 2023). Currently, belladonna and its extracts are used in medicine to manufacture drugs to treat irritable bowel syndrome, bladder problems and Parkinson’s, to alleviate nausea, motion sickness, and to relieve the pain of neuralgia and myofascial (Javed et al., 2023). Thus, the extract’s therapeutic nature is also appreciated.

⁴ Lingfeng Zeng et al., “Development of *Atropa Belladonna* L. Plants with High-Yield Hyoscyamine and without Its Derivatives Using the CRISPR/Cas9 System,” *International Journal of Molecular Sciences* 22, no. 4 (February 2021): 1731.

Toxicity and Dangers

The toxicity of belladonna results from tropane alkaloids that act as potent anticholinergic agents (Javed et al., 2023). Anticholinergic compounds lead to the blocking of acetylcholine action and disruption of the nervous system. Therefore, anticholinergic syndrome can follow ingestion of the drug and be manifested as dilated pupils, dry mouth, flushed skin, rapid heartbeat, urinary retention, hallucinations, delirium, and convulsions that may progress to coma and lethal consequences (Javed et al., 2023). It does not take large doses to cause toxicity, and the effects can be fast and severe. As belladonna has such an attractive appearance, mimicking cherry-like berries, poisoning by ingestion can be accidental and is most likely to occur in children who may assume it to be edible. Symptoms of belladonna poisoning also resemble other conditions, which make rapid diagnosis and treatment challenging. Untreated severe belladonna poisoning can lead to respiratory failure, cardiovascular shock collapse, and inevitably, death.

Legal Status and Regulation

Due to the high toxicity and dangerous potential for misuse, the cultivation, sale, and use of belladonna are subject to strict regulation and restrictive measures in many countries across the globe¹. In the United States, belladonna is classified as a plant species of poisonous nature; therefore, its possession, distribution, and usage fall under the jurisdiction of federal and multiple state laws (Javed et al., 2023). Special orders and permits are required to use belladonna or its components for scientific and research purposes, pharmacological production, and horticultural purposes. Tight regulations and safety standards apply to the handling of belladonna and its derivatives serve to prevent dramatic complications, with the Drug Enforcement Administration being responsible for the final supervision (Javed et al., 2023).

Cultural References

In the cultural domain, the entwining of belladonna's appeal and mystique with its toxicity has fascinated artists, writers, and storytellers enough to portray it in numerous art and literary forms or popular culture. Renaissance and Baroque paintings have depicted belladonna and its metaphors, and writers like William Shakespeare have heavily alluded to the atropa's toxicity. Recently, it has been incorporated in modern literature and popular culture as a narrative or horror device, which reinforces its existing sinister significance.

Current Research and Controversies

Despite the well-known toxicology and availability of alternative safe options, the belladonna plant still needs additional consideration by the scientific community (Bowerbank, Gallidabino, & Dean, 2022). One can target the ability to increase the therapeutic influence of the extremist compounds present in the plant, as well as consider the use of the substances for specific neurological disorders and pain management (Javed et al., 2023). Nevertheless, the scientific use of the species raises a lot of controversy and objections. For example, the dangers of using the notorious toxicology should outweigh the perceived benefits of the substance due to significantly safer similar formulations (Bowerbank, Gallidabino, & Dean, 2022). The standardization and safety of the belladonna plant drop use should be further debated, as well as the ability for abuse (Bowerbank, Gallidabino, & Dean, 2022). Additionally, some trials have dubious ethical implications, particularly those involving test volunteers. At the current level of scientific understanding of the extremist compounds in the belladonna plant, all parties should be involved. While controversial situations may occur, it is the duty of the scientific community to determine the delicate balance between the apparent benefit and actual harm (Javed et al., 2023).

Safety Precautions and Recommendations

The toxicity associated with statistics on belladonna should make its management infested with all measures of safety (Bowerbank, Gallidabino, & Dean, 2022). Ingesting any part of the belladonna plant, including its leaves, flowers, and berries, should be entirely prevented, as it is highly toxic and extensively absorbed in the gastrointestinal system, resulting in fatal poisoning (Maurya et al., 2020). Additionally, individuals, especially children and pets, should be restricted from contacting it because the berries are enticing and may be confused with other fruit for ingestion. It should be ensured that all persons who require contact with the belladonna plant have a legitimate reason, such as scientific research and pharmaceuticals, followed by several safety protocols. These include comprehensive safety guidance, gloves, and protective clothing must be worn and wear a respiratory gas mask to prevent absorption through the skin, inhalation, or in case of accidental consumption. Indicators should also be enforced, including storage and labelling, with the belladonna plant stored in only official government-regulated establishments, and labelling to prevent unauthorized contact. In addition, if the species is ingested, prompt medical attention is vital and can be life-threatening. Ecologically, measures should be taken to decrease environmental pollution and prevent animal life from becoming infected with the toxic substances produced by this plant.

Conclusion

In conclusion, it is ensured by the evidence above that Belladonna indeed has an extremely rich and interesting history, and while its deadly affairs entail cautious and rare studies of it. If conducted with serious security measures observed, with knowledgeable medical professionals in consultation and due caution concerning its special toxicity warning, the research of it can yield knowledge and minimize the risks of exposure. For the layman, enjoying its mystery and intrigue from afar is the way to go, for the cultivation and use of belladonna are best left to professionals and scholars well versed in the field, and in accordance with the rules.

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