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Mini Review

Evaluating the Therapeutic Potential of *Datura stramonium and Datura inoxia*: A Mini Review

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Abstract

Cancer remains a significant global health challenge, with increasing mortality rates. Despite advancements in conventional treatments, the exploration of alternative therapies remains vital. This study investigates the antioxidant properties of *Datura* in treatment of cancer disease. We searched three electronic databases: PubMed, Scopus, and Web of Science. *Datura* herb possesses antioxidant properties due to phytochemical compounds like phytol acetate, beta-damascenone, and beta-eudesmol, which scavenge free radicals and reduce nitric oxide production. Additionally, it exhibits anti-inflammatory effects by augmenting pro-inflammatory cytokine secretion and enhancing lymphocyte cytotoxic activity against cancer cells. Moreover, *Datura*'s anticancer potential lies in its ability to inhibit cellular signaling pathways involved in cancer development, particularly in breast and lung cancers by compounds like alkaloids, tannins, flavonoids, and cardiac glycoside. However, it is crucial to acknowledge the herb's toxicity, which can cause severe central nervous system damage, hallucinations, and even death at high doses, necessitating careful extraction and evaluation of its compounds for therapeutic use.

Keywords: *Datura stramonium*, *Datura inoxia*, cancer, free radicals, antioxidant

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1. Introduction

According to the World Health Organization (WHO), cancer is a leading cause of death globally, with an estimated 10 million deaths attributed to cancer each year [1]. Cancer was second only to cardiovascular diseases for the number of deaths, years of life lost, and disability-adjusted life years (DALYs) globally in 2019 [2]. The greatest increases are predicted in lower-resource settings, in countries currently assigned a low Human Development Index (HDI), whereas the predicted increases in national burden diminish with increasing levels of national HDI [3]. Cancer can result from abnormal proliferation of any of the different kinds of cells in the human body, so practically there are numerous types of cancer, which can vary substantially in their pathophysiology and also vary in the response towards the treatment [4]. At the genetic level, mutation in key oncogenesis, tumor suppressor genes, and deoxyribonucleic acid (DNA) repair mechanisms disrupt cellular homeostasis and unleash uncontrolled cell proliferation, leading to malignancies [5]. Beyond genetic factors, environmental exposures play a pivotal role in cancer etiology, such as tobacco smoke, ultraviolet rays, industrial pollutants, and dietary carcinogens can induce DNA damage, oxidative stress by free radicals, and inflammation, fueling the progression of cancerous growth [6].

Despite advancements in conventional cancer therapies, including surgery, chemotherapy, and radiation therapy, the quest for novel and efficacious treatment modalities continues unabated [7, 8]. In recent years, increasing attention for effective and better cancer treatment has been directed toward exploring the therapeutic potential of plant extract as an alternative treatment for various types of cancer [9]. Phytotherapy offers a diverse bioactive compound found in botanical sources. The aim of the current study is to investigate the antioxidative effect of plant *Datura* in the treatment of cancer disease.

2. Materials and Methods

We searched three electronic databases: PubMed, Scopus, and Web of Science. Utilizing Boolean operators (AND, OR), we employed the keywords "cancer," "free radicals," "antioxidant," "*Datura stramonium*", "*Datura inoxia*", individually and in various combinations. Only full-text articles written in English and published within the past decade were considered.

3. Results

Studies suggest that *Datura* possesses antioxidant properties, enabling it to scavenge free radicals the cause of cancer. Moreover, the unique chemical constituents found in *Datura* have been investigated for their potential therapeutic effects in various ailments. Here out of seven species, two species of *Datura* namely *Datura stramonium* and *Datura inoxia* come under our investigation (Figure **1**). *Datura*, a genus of flowering plants belonging to the Solanaceae family, consists of species like *Datura stramonium*, *Datura inoxia*, *Datura inoxia Mill*, *Datura metel*, *Datura alba*, *Datura xerox*, and *Datura wrightii* [10]. The morphological features of root, stem, leaves, number of leaves, and biomass depend upon the environmental conditions exhibited considerable variations [11].

Datura is native to North America but has spread to other continents, including Europe, Asia, India, Africa, and Australia [12]. *Datura* species can often

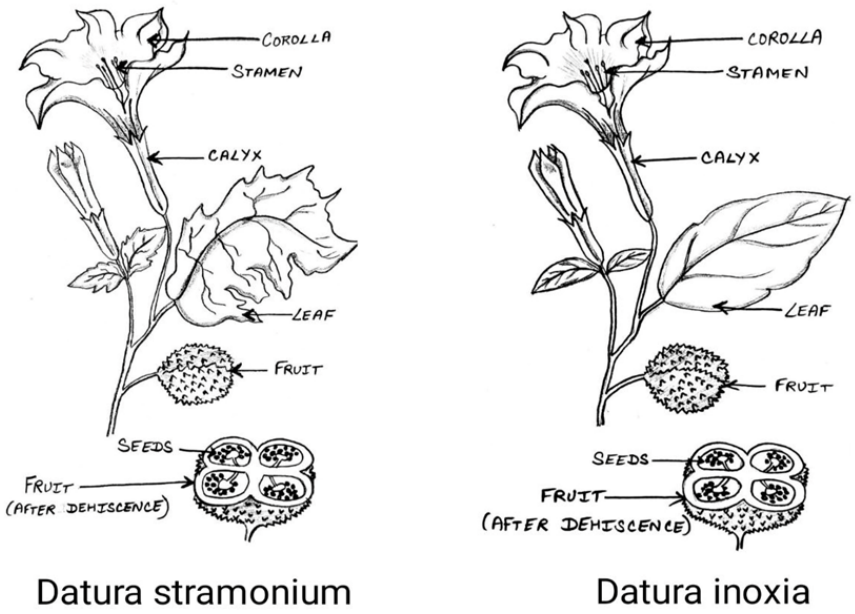

Figure 1: Botanical Illustration of *Datura stramonium* and *Datura inoxia*.

be found growing in average soils, but in nutrient-rich, moist, and alkaline soil as weeds along roadside, in disturbed areas, and in gardens [10].

3.1. Antioxidant property

Datura stramonium comprises phytochemical compounds: phytol acetate, beta-damascenone, and beta-eudesmol, which demonstrate *in vitro* scavenging of free radicals as assessed by DPPH (2,2-diphenyl-1-picrylhydrazl) and ABTS (2,2-azinobis [3-ethylbenzothiazoline-6-sulfonic acid]) assays. Furthermore, it leads to a reduction in nitric oxide (NO) production in Lipopolysaccharide (LPS) stimulated J774A.1 cells, while maintaining cell viability [13]. These compounds effectively mitigate reactive oxygen species (ROS) due to the presence of phenolic hydroxyl groups in their structure, thereby counteracting ROS-induced damage [14].

3.2. Anti-inflammatory property

The *Datura* extract augmented the secretion of pro-inflammatory cytokines, including Interleukin (IL)-2, Interferon (INF)-alpha, and Tumor necrosis factor (TNF)-alpha, along with the induced expression of Cluster of differentiation (CD) 3, CD8, and CD56, as well as intracellular granulysin levels in immune cells [13]. Ethanol extract derived from *Datura* roots exhibited anti-inflammatory properties when assessed for paw edema induced by carrageenan in albino Wistar rats [15]. Treatment of human lymphocytes with *Datura stramonium* enhanced their cytotoxic activity against colon cancer cells human colorectal carcinoma cell line (HCT)-116 and SW620 (derived from a later metastasis in the same donor, after further characterization). Additionally, these activated lymphocytes induced target cell death through the generation of reactive oxygen species and by disrupting the mitochondrial membrane potential of these cells [13].

Figure 2: Map showing the location of *Datura stramonium* and *Datura inoxia* in archaeological sites.

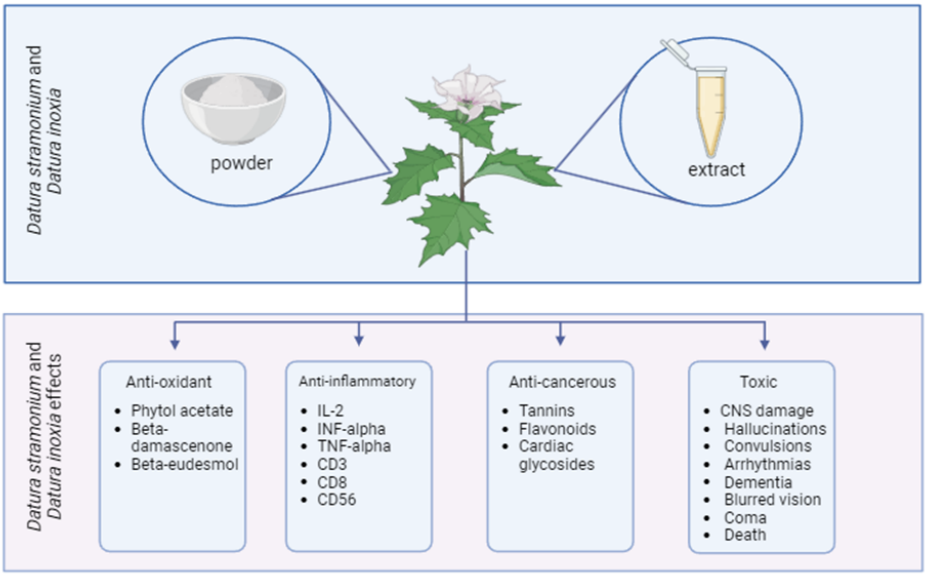

Figure 3: *Datura* stramonium and *Datura* inoxia have therapeutic effects on health conditions such as antioxidant, anti-inflammatory, anticancer, and toxicity.

3.3. Anticancer property

In addition to the major phytochemicals found in *Datura inoxia Mill.*, it also contains alkaloids, tannins, flavonoids, and cardiac glycosides [16]. Studies have suggested that pure tannins and their extracts can inhibit cellular signaling pathways and oncogenic proteins involved in the development of cancers such as lung cancer. Tannins can also target signaling pathways and genes associated with apoptosis, epithelial-mesenchymal transition (EMT), proliferation, migration, invasion, and unlimited replication potential [17].

In hormone-dependent breast cancers, Cytochrome P450 Family 19 Subfamily A Member 1 (CYP19A1) inhibitory potential of 14 flavonoids were found in in-vitro investigation and emerged as a promising alternative to existing chemotherapy which consist of unfavorable side effects [18]. These flavonoids exhibit high potency against

lung cancer through inhibition of receptor tyrosine kinase (RTK). RTKs are cell surface proteins commonly dysregulated in lung cancer. Flavonoids possess anti-inflammatory, antioxidative, and, most importantly, anticancer properties [19].

Another constituent of *Datura* is cardiac glycosides (e.g., neriifolin), which suppress the malignancy of cancerous cells by inducing increased deoxyribonucleic acid (DNA) damage and apoptosis through activation of endoplasmic reticulum stress (ERS) in cancers like prostate cancer. *In vivo* studies on nude mice have shown significant inhibition of tumor growth through the C/Enhancer Binding Protein homologous protein (CHOP-C/EBP-alpha) signaling axis of ERS [20].

3.4. Toxicity

In addition to its use for numerous human ailments, *Datura* herb is known for its toxicity also. Its toxic effects generally conceal the profit over different medical conditions. Intoxication due to high dose of *Datura* consisting atropine and scopolamine causes central nerve system damage, hallucinations, convulsions, arrhythmias, irregular pulse rate, dementia, blurred vision, dryness of mouth, coma, and leading to death [21]. Hence extensive research and clinical trials would be needed for extraction of potential compounds while separating the toxic contents for safety profile in treatment modalities.

4. Conclusion

The use of natural herb *Datura* in cancer therapy presents a promising yet complex avenue for research, necessitating robust strategies to evaluate safety profiles prior to clinical application. *Datura*, known for its potential alkaloids like scopolamine and atropine, possesses significant pharmacological effects but also carries a risk of toxicity. Prioritizing specific markers and endpoints is crucial for assessing the safety of *Datura* in preclinical and clinical studies.

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6. Author contribution

Conceptualization: Aditi Singh Chouhan (ACh) and Aliya Zhylkybekova (AZh); methodology: ACh, AZh; investigation: ACh, AZh, Rithish Bharadwaj (RBh), and Madhup Baxi (MBa); writing-original draft preparation: ACh, AZh; writing-review and editing: ACh, AZh, RBh, and MBa. All authors have read and agreed to the published version of the manuscript.

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