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Review of *Drimia indica* in Terms of Geographical Distribution, Phytochemistry, Pharmacology and Toxicity

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ABSTRACT:

Plant-based medicines have been utilized for thousands of years1. These remedies were initially composed of raw herbal formulations such as powders, tinctures, teas, poultices, and other concoctions. The specific plants to be used and the application methods for different illnesses were passed down orally. Eventually, the knowledge of medicinal plants was gathered from herbalists. In more recent times, the use of plants as medicines has required the isolation of the active ingredient. The identification and isolation of pharmacologically active compounds from medicinal plants continues to this day. This review is critically based on the geographical distribution, phytochemistry, pharmacology, toxicity of plant *D. Indica* which has been proven to have great medicinal properties. From various studies it has been observed that the extract of this plant contains phytochemicals like glycosides, alkaloids, saponins, flavonoids, tannins etc. which is responsible for its pharmacological activities such as anthelmintic, anticancer, antibacterial, antioxidant, antidiabetic, gastro- intestinal, broncho dialatory activity.

Keywords: *Drimia Indica*, phytoconstituents, anthelmintic, anticancer, antibacterial, antioxidant, antidiabetic, gastro-intestinal, bronchodialatory activity.

INTRODUCTION

Nine of the 99 recognized species in the genus *Drimia*, which is a member of the Asparagaceae family, are found in India [1]. This genus's members have an underground bulb and are primarily deciduous, seldom evergreen. These plants can be found all throughout Asia and Africa. Southern Africa is home to the majority of this genus's species, primarily in semiarid areas that receive winter rains [2]. In traditional medicine around the world, several species of this genus, including *D. maritima* (L.) Stearn, *D. elata* Jacq., *D. secunda* (B. Nord.) J.C. Manning & Goldblatt, and *D. indica* (Roxb.) Jessop, are highly valued [2,3].

Roxb., or *Drimia indica* Indian squill, true squill, or sea onion are other names for jessop (syn. *Urginea indica L.*; *Scilla indica* Roxb.). The plant is also known as jungli piyaz or ban piaz in Asian nations [4]. Commonly referred to as Kolkanda or Ban Palandu, *D. indica*, primarily its bulb, is used as a biocide and in Ayurvedic medicine to prepare a variety of medicinal products with medical uses [5]. Alkaloids, flavonoids, phenols, and tannins are found in all parts of the plant, according to phytochemical studies, but steroids are found only in the bulbs [6]. Glycosides, quinones, resins, and saponins are also present in the bulbs [7]. Strong antidiabetic, anticancer, antimicrobial, and cardiac effects have been demonstrated by the plant.

Figure 1. Leaves of plant *Drimia Indica*

Figure 2. Flowers of plant *Drimia Indica*

Figure 3. Dried leaves of plant *Drimia Indica*

GEOGRAPHICAL DISTRIBUTION & EVOLUTIONARY STATUS

A family of geophytes known as *Drimia* (Urgineoideae: Hyacinthaceae) produces tunicated bulbs. More than 100 species, spread across Asia, Africa, and Southern Europe, represent it. *Drimia indica*, *D. coromandeliana*, *D. govind*appae, *D. nagarjunae, D. polyantha*, *D. polyphylla*, *D. raogibikei*, *D. razii*, and *D. wightii* are the nine species of *Drimia* found in India. The species, namely *Drimia coromandeliana, D. govindappae* and *D. nagarjunae* have been reduced to a cosmopolitan species *D. indica* [8]. Given their similar morphologies and complex genomes, the taxonomic status and genetic relationships among Indian *Drimia* species are debatable. The pollen morphology, karyotype, and hybridization behavior of the five species of Indian *Drimia* are used to classify them into two complexes: the indica complex and the wightii complex. It was discovered that these two groups were evolving independently. While the indica complex has adapted polyploidy and hybridization for evolution, the wightii complex is evolving through polyploidy and chromosome repatterning, according to cytomorphological studies. The indica complex and wightii complex are evolving in parallel, according to phylogeny derived from DNA sequences of molecular markers (ITS and matK), which grouped them into two clusters [9].

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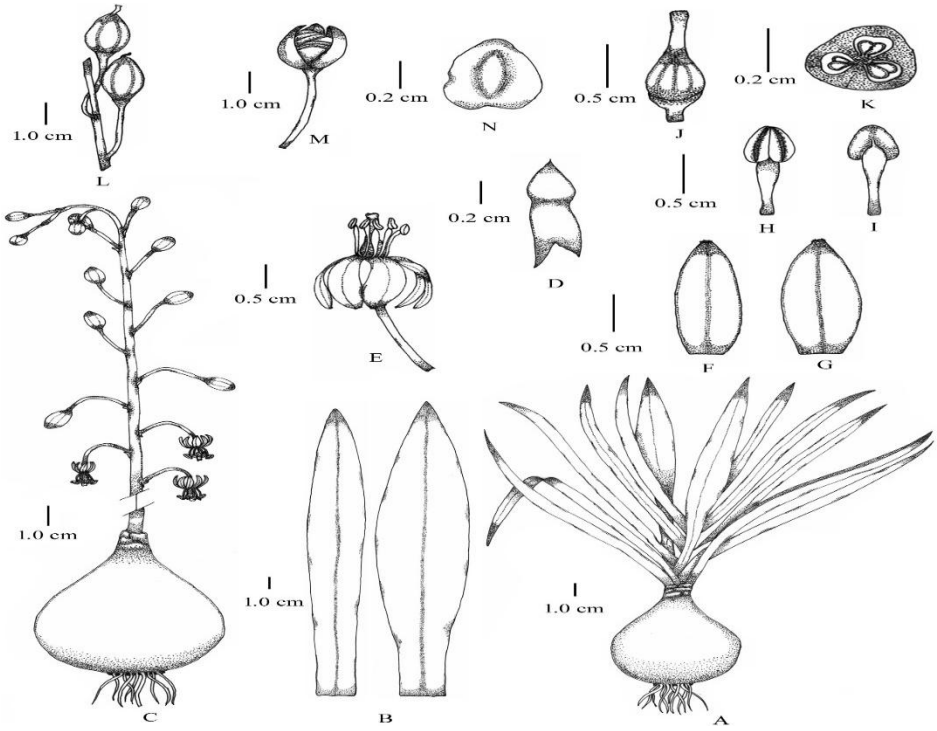

Figure 4. ***Drimia indica.*** **[A] vegetative phase; [B] single leaf; [C] bulb with inflorescence; [D] bract; [E] flower; [F] inner tepal; [G] outer tepal; [H] stamen (front view); [I] stamen (back view); [J] pistil; [K] T/S. of ovary; [L] infructescence; [M] dehisced capsule; [N] seed.**

PHYTOCHEMICAL CONSTITUENTS

More studies on the phytochemicals of *Drimia* species have concentrated on the bulb due to its therapeutic value, but they have also looked at the leaves and roots. The primary components identified in this genus are cardiac glycosides. Additionally, these plants were found to contain phytosterols, phenolic compounds, and other phytochemical constituents [10].

1. GLYCOSIDES

Scillaren A, which Stoll isolated from *D. maritima* in 1933, is the first cardiac glycoside to be isolated from this genus. 14 C-24 or C-23 steroidal substances with inotropic and chronotropic properties are known as cardiac glycosides. These substances are categorized as either cardenolides or bufadienolides based on whether the lactone ring has five or six carbon atoms. Numerous researchers isolated bufadienolide compounds from scillaren and *D. maritima* after Stoll separated them for the first time in 1933 [10].

2. PHENOLS

The primary phenolics found in *Drimia* species are flavonoides. From the red bulbs of Spanish *D. maritima*, cyanidin 3-monoglucoside and pelargonidin 3-monoglucoside were separated in both free form and acylated with caffeic and ρ-cumaric acid. Other significant phenolic compounds that were isolated included C-glycosyl flavones, quercetin-3-monoglucoside, and taxifolin 4′-glucoside. From *D. delagoensis*, a homoisoflavonoid compound was extracted. Phloroglucinol derivatives from *D. sanguinea*, 4-hydroxy-3-methoxybenzoic acid from *D. delagoensis*, and caffeic acid from *D. maritima* were also found to be additional phenolic constituents [10].

3. PHYTOSTEROLS

D. indica bulbs were used to isolate beta- and gamma-sitosterol. The primary sterol found in the bulbs, leaves, and roots of different *D. indica* cytotypes was stigmasterol, which was also examined for phytostrols. Only tryploides were used to isolate campesterol. Additionally, stigmasterol was extracted from *D. sanguinea* bulbs [10].

PHARMACOLOGICAL ACTIVITIES

D. indica has been researched for a number of human conditions, primarily to treat cancer and microbial infections. It has long been used in Ayurveda to treat a wide range of illnesses, and practitioners continue to prescribe it. It is a well-known Ayurvedic treatment for respiratory conditions, intestinal worms, and skin diseases.

1. ANTHELMINTIC ACTIVITY

In comparison to the control medication Albendazole at 5 mg/ml, the anthelmintic activity of *D. indica* bulb, leaf, and scape water extracts on Pheretima posthuma (earthworm) was very effective as measured by the time taken for paralysis and time taken for death (in minutes) at an effective concentration of 5 mg/ml. According to the results, the worms treated with hot water leaf extracts took 41.3 minutes to paralyze and 50 minutes to die, whereas the control group treated with albendazole took 92 minutes to paralyze and 110 minutes to die [11].

Table 1. In-Vitro Anthelmintic activity

S.No.	Treatment of extract	Conc. (mg/ml)	Time taken for paralysis (mins)	Time taken for death (mins)
1	Normal control	-	-	-
2	Albendazole	5 10 15	92±1.63 62±1.63 34.6±2.05	110.6± 0.94 71.3±0.94 40.6±0.47
3	Cold aqueous extract (Bulb)	5 10 15	120.3± 0.47 71.3± 0.47 62.3± 0.47	129± 0.57 83.3± 2.05 62.3± 1.69
4	Hot aqueous extract (Bulb)	5 10 15	123.3± 0.94 99.6± 0.47 80.3± 0.57	125.6± 0.47 111.6± 0.94 93.6± 0.47
5	Cold aqueous extract (Scape)	5 10 15	60.3± 0.47 48.3± 1.69 27.6± 0.94	68.3± 0.47 53.3± 1.24 34.3± 1.69
6	Hot aqueous extract (Scape)	5 10 15	68.6± 0.47 41.6± 0.47 26.6± 0.94	71± 0.81 50.6± 0.94 31± 0.81
7	Cold aqueous extract (Leaf)	5 10 15	49.6± 0.47 38.3± 0.47 25.6± 0.94	60.3± 0.94 39.6± 0.47 33.3± 1.69
8	Hot aqueous extract (Leaf)	5 10 15	41.3± 0.94 32.3± 1.24 28.3± 0.47	50± 0.81 36.6± 0.94 31.6± 1.24

2. ANTICANCER ACTIVITY

As an anticancer agents, selenium nanoparticles (SeNPs) have attracted a lot of attention. SeNPs (DI-SeNPs) were synthesized from the aqueous extract of the medicinal plant *Drimia indica* leaves (DI-LAE) and thoroughly characterized using FTIR, TEM, EDX, XRD, zeta potential measurements, and UV-visible absorbance. When tested against the human lung adenocarcinoma cell line (A549; IC50 of 43.21 µg/mL), DI-SeNPs demonstrated dose-dependent toxicity. In A549 cells, DI-SeNPs enhanced the production of reactive oxygen species (ROS). DI-SeNPs increased DNA damage in A549 cells and caused cell cycle arrest in the G2/M phase, which ultimately pushed the cells toward apoptosis. In A549 cells, DI-SeNPs markedly raised p53 levels while lowering Akt levels and raising cleaved caspase 3 levels**.** According to these results, DI-SeNPs have strong anticancer properties that are mediated by processes that include the production of ROS, cell cycle arrest, and the induction of apoptosis [12]**.**

3. ANTIBACTERIAL ACTIVITY

Silver nanoparticles made from *D. indica* leaf extract were tested for their antibacterial properties against pathogenic bacteria such as P. aeruginosa [ATCC2021], Klebsiella pneumonia [ATCC2075], and E. coli [ATCC2065]. The liquid nutrient broth was used to keep the bacterial cultures alive. Using varying concentrations of Ag NPs, the inhibitory activity of synthesized nanoparticles on specific pathogenic bacterial cultures was calculated. A 96-well microplate was used for the bacterial assay. With 260 µl of nutrient broth, 20 µl of bacterial culture, and 20 µl of Ag NPs, the assay volume was set at 300 µl. The concentrations of Ag NPs

used were 25 µl/ml, 50 µl/ml, and 100 µl/ml from mg/ml stock. As a negative control, 20 µl of discolored water was added to the assay mixture in place of 20 µl of Ag NPs.

MIC of the Ag NPs for the pathogenic bacteria is defined as the lowest concentration that prevents the growth of the bacterial strain. Using broad spectrum antibiotic streptomycin at varying concentrations (25 µg/ml, 50 c, and 100 µg/ml), the MIC values for bacterial strains against streptomycin were determined [13].

Table 2. MIC values of silver nanoparticles with streptomycin

S.No.	Bacteria	MIC values µg/ml Ag NP's	MIC values µg/ml Streptomycin
1	P.aeruginosa	25	100
2	K.pneumoniae	25	50
3	E.coli	50	100

4. ANTIOXIDANT ACTIVITY

Bulb extract of *Drimia indica* was used to determine antioxidant activities by evaluating its free radical scavenging potential, determining the total phenolics, proanthocyanidins and estimating its DPPH, superoxide anion-radical scavenging activity, ferrous ion chelating activity. Five replicates were used for all analyses, and the results were presented as mean ± SD. The relationship between ferrous ion chelating activities, DPPH, FRAP, and superoxide anion radical scavenging and total phenolic content in using SPSS, *Drimia Indica* was identified [14].

Table 3. Antioxidant activity profile of *Drimia indica*

DRIMIA INDICA	**Antioxidant activity profile**
Phenolic content (mg GAE g^{-1})	1.05 ± 0.12
Proanthocyanidins (mg CE g^{-1})	0.67 ± 0.32
% DPPH Free radical scavenging property	37.59 ± 4.5
% Superoxide anion-radical scavenging	7.76 ± 2.3
Ferric reducing / Antioxidant power	0.15 ± 0.5
% chelating ferrous ion	6.43 ±1.5

5. ANTIDIABETIC ACTIVITY

Rats with streptozotocin-induced diabetes were studied for antidiabetic effects using an ethanol extract of *Drimia indica* bulbs. Glibenclamide (10 mg/kg) and the extract (750 mg/kg and 1.5 g/kg of body weight) were taken orally for 14 days. Within 120 minutes, it was discovered that the extract (at 1.5 g/kg) significantly reduced the blood glucose levels of diabetic rats. The extract was found to lower triglyceride and total cholesterol levels in addition to lowering blood sugar levels. In addition, it was discovered that the high-density lipoprotein levels improved in comparison to the rats in the untreated group. The extract partially restored the damaged cellular population of the pancreatic islets in rats, according to the histopathological analysis.

The study's effective dose of 1.5 g/kg was too high to be used in a clinical setting: Purified plant bioactives or fractions guided by bioassay should be investigated in relation to diabetes. Furthermore, since the 10 mg/kg dose of glibenclamide was used against 1.5 g/kg of the crude extract, the activity should not be regarded as good in comparison to that drug. This is the only scientific report on the plant's antidiabetic properties that is currently available, and more research employing various methodologies ought to be done. For the activity, the extract or isolated compounds of D. indica that are guided by bioassay should be utilized [15].

6. GASTRO-INTESTINAL STIMULATORY ACTIVITY

Traditionally, *D. indica* has been used as a gastrointestinal stimulant to treat indigestion and constipation. Thus, both in vitro and in vivo models were used to investigate the gastrointestinal stimulatory activity of an aqueous methanol extract of *D. indica* bulbs. The findings demonstrated that, like a reference cholinergic medication, carbachol (10 mg/kg), the extract (6 and 12 mg/kg) accelerated the passage of charcoal meal through the small intestine. In the extract-treated mice, the distance covered by the charcoal meal was 80.2% and 87.9% with 6 and 12 mg/kg, respectively, whereas the distance covered by carbachol was 74.9%. In mice given atropine, the extract also demonstrated a laxative effect at 10 mg/kg, as evidenced by an increase in feces over a 6-hour period of 4.3 and 9.2 at 6 and 12 mg/kg, respectively. It was discovered that this effect was similar to that of carbachol (10 mg/kg), which produced 11 feces. It is evident from this study that, at a comparable or even lower dose, the crude extract's activity was nearly identical to that of the standard. Investigating the responsible chemical constituent or constituents of *D. indica* bulbs is

preferable. This research has the potential to be very beneficial for the treatment of gastrointestinal disorders, especially in the area of novel drug discovery.

Also, the extract demonstrated an in vitro contractile effect in rabbit jejuna at 0.01–0.3 mg/mL and guinea pig ilea at 0.01–1.0 mg/mL. Similar to the common medication verapamil, the extract inhibited K+-induced contractions in rabbit jejuna at concentrations ranging from 0.01 to 5.0 mg/mL and moved the Ca2+ concentration–response curves to the right. According to the study, *D. indica's* action may have been mediated by a cholinergic mechanism, which explains why it's used to treat constipation and indigestion [15].

7. BRONCHODIALATOR EFFECT

The bronchodilator (broncho-relaxant) effect of crude extract of Indian squill *(Drimia indica*) is comparable to that of dicyclomine and is most likely caused by anticholinergic and ca2+ antagonistic properties. Additionally, through muscarinic (m3 receptor) antagonist activity, Indian squirrel lowers the mucus secretion of the airway. Based on Squill's historical use for asthma and its previously mentioned pharmacologic effects on the respiratory system, a randomized clinical trial was created to assess the safety of Squill Oxymel and its effects on the symptoms, spirometry, and plethysmography parameters of patients with moderate to severe persistent asthma. The research was planned as a triple-blind, randomized, placebo-controlled clinical trial. The purpose of the study was to evaluate Squill Oxymel's effectiveness in treating 60 patients with moderate to severe persistent asthma.

According to the study's findings, the Squill Oxymel group outperformed the control group on lung function tests. Absolute FEV1 values were significantly higher in the Squill Oxymel group than in the control and simple honey oxymel groups. The Squill Oxymel group's mean FEV1 rose by more than 20%. The anti-inflammatory and anticholinergic properties of Squill may be responsible for the shown positive effects. The main ingredients are bufadienolides. According to the current study's findings, patients with moderate to severe persistent asthma may benefit from an additional Squill Oxymel treatment in terms of both safety and effectiveness [16].

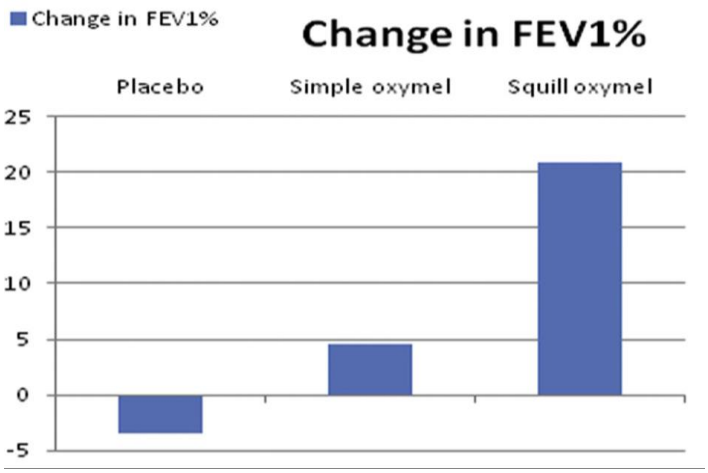

Figure 5. Change in FEV1%

TOXICITY STUDIES

A 55-year-old woman who consumed two bulbs orally due to arthritic pain died from *Drimia* species. She was diagnosed with hypothyroidism and Hashimoto's thyroiditis prior to consuming this herb, which may have been linked to significant toxicity. Vomiting, seizures, severe hyperkalemia, ventricular arrhythmias, and atrioventricular block were all symptoms of digitalis-like poisoning. Two patients experienced toxic effects after using squill opiate linctus as a cough remedy. Both patients experienced toxicity following an overdose of digitalis, as evidenced by bradycardia and other symptoms of intoxication. Fourteen poisoning patients have urinary tract, central nervous system, and gastrointestinal issues as their main symptoms.

When a person accidentally inhaled a substance containing scilliroside under the brand name "Silmurine," they experienced short-lived side effects like headache and nausea. Because of the calcium oxalate they contain, *Drimia* species' bulbs and leaves can itch and irritate skin. A 52-year-old woman developed nonallergic irritant contact dermatitis after using *D. maritima* bulbs topically to treat arthralgia. More thorough research utilizing in vitro and in vivo models in both animal and human clinical investigations is needed to ascertain the toxicology of poisonous plants, including *Drimia* species [17].

Table 4. Toxicological effect of *Drimia* species

Drimia species	Toxicity effects	Model used	Compounds
D. indica	Antidiabetic effects, acute toxicity	Rat model	Not specified
D. robusta	Hemolytic activity includes toxicity	In vitro	Saponins, Proscillaridin A
U. maritima	Mortality rate was 10mg/ml after 48 h	Mice	Quercitin, Kaempferol, Bufadienolides
D. altissima	Rodenticides 80-100% fatalities	Rat model	Not specified
D. pancration	Repellent activity and contact toxicity	Stegobium paniceum beetles	Steroidal saponins
C- glycosyl flavone of D. indica	No motality at 250 mg/kg, nonetheless,50 & 100% mortality was detected at 500-1000 mg/kg bw	Mice	C-glycosyl flavone
D. maritima	10% crude extract resulted in 100% mortality in larvae and 48% mortality in adult beetles. LC_{50} and LC_{90} values were 16.6 and 34.4 g/L, respectively.	Larvae and beetle	Not specified

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Conflict of Interest Statement:
The authors have no conflicts of interest to declare.