



## "Exploring the Phytochemistry and Pharmacological Effects of *Cynoglossum*: A Comprehensive Review"

Namita Joshi<sup>1\*</sup>, Dr Himanshu Joshi<sup>1</sup>, Karuna Dhaundhiyal<sup>2</sup>, Sarita Rawat<sup>2</sup>, Arpita Upreti<sup>2</sup>, Shivali Sagar<sup>1</sup>

<sup>1</sup>Graphic Era Hill University, Bhimtal-263136, Nainital, Uttarakhand

<sup>2</sup>Amrapali Group of Institute, Haldwani-263139, Nainital, Uttarakhand

(Received: 07 January 2024

Revised: 12 February 2024

Accepted: 06 March 2024)

### KEYWORDS

*Cynoglossum*,  
Pyrrolizidine,  
Antioxidant, Anti-  
inflammatory,  
Antidiabetic,  
Antifertility,  
Antitumor,  
Hepatoprotective

### ABSTRACT:

*Cynoglossum* belongs to the family Boraginaceae having around 75 species that are located in warm and temperate regions of Africa, Asia and Europe. It contains four pyrrolizidine alkaloids which are used traditionally as medicines by tribals for the treatment of wounds, burns, cuts chest pain, skin diseases, etc. It is a perennial or biennial herb with similar morphology externally. They produce pyrroles (powerful alkylating agents) when they are metabolized and these pyrroles further react with DNA and proteins causing cellular dysfunction, abnormal mitosis and necrosis of tissue. Few plants belonging to this genus have antioxidant, anti-tuberculosis, diuretic, analgesic, antidiabetic, anti-inflammatory, antitumor, antifertility and hepatoprotective property.

### INTRODUCTION :

*Cynoglossum* contains 75 species that are widely found in Africa, Europe and Asia, 12 species are found in China, 3 species are found in Taiwan<sup>1</sup> and in Turkey, there are eight species<sup>2</sup>. Plants from the Boraginaceae family have been used in many parts of the country because of their medicinal value like they are used for the treatment of wounds, fever, chest pain, skin diseases, etc<sup>3,4</sup>. According to the royal botanical garden, Global Compositae Checklist and Missouri Botanical Garden, only 83 specific names are accepted out of 266 plants of this species and 306 species includes infra specific names for *Cynoglossum*<sup>5</sup>. The species of *Cynoglossum* grow in road side, sand dunes and open woodlands. The external morphology of *Cynoglossum* have many similarities and due to this taxonomically it is identified as a difficult genus<sup>6</sup>.

### Morphology

*Cynoglossum* is perennial or biennial, rarely annually occurring herb. Leaves are normally basal, in the lower part of the stem lower petiolate leaves are present l. Cymes are terminal or axillary with crowded having bracteate, ebracteae or panicles. Flowers are usually pedicellate and calyx are 5, separated to base and are enlarging in fruit with reflexed and spreading lobes. It has campanulate, tubular or funnel form corolla which is blue, purplish red, white, blackish purple, or yellowish green in colour. Tubes are generally shorter than calyx

with 5 throat appendages. Lobes are ovate to orbicular. Stamens are inserted in corolla tube at middle or above. Anthers are usually ovoid or oblong. Ovary is 4 parted and ovule is anatropous<sup>7</sup>.

According to Flora Zambesiaca, it is perennial or biennial herb with height of 0.3-1.2 m. Its leaves are inferior with petiole 2.5 to 8 cm long, lamina of inferior leaves 8 to 15 cm x 2 to 6 cm and lamina of inferior leaves are 2 to 6 cm x 0.4 to 1.8 cm. Cymes are above the first flower without bracts. Flowers with pedicels 0.5 to 2.5 mm long. Calyx is 1.0 to 1.5 mm long. Stamens are inserted from the corolla base at 0.6 to 0.9 mm. Lobes are ovate to oblong-ovate and rounded at apex. Anthers and filaments are long from 0.4 to 0.6 mm and 0.2 to 0.3 mm. Style is thick up to 1.5 mm long in fruit. Nutlets are 1.5 to 2.5 mm x 1.2 to 1.8 mm usually ovate which is joined to the style and after the complete maturity it detaches<sup>8</sup>.

### General Distribution

*Cynoglossum L* has its enormous species widely distributed in Asia, Mediterranean regions and in many parts of Europe mainly in Turkey, Pakistan, Bhutan India, China, Malaysia and Kenya. *Cynoglossum Germanicum* is protected legally by the Act on Biological Diversity Annex 3 (2007) and has been described as an endemic species<sup>9</sup>. *Cynoglossum Montanum* is widely distributed in the western parts of Mediterranean areas ranging from Centre of Spain to the Black sea region's eastern part and it is located in France, Spain and Italy<sup>10</sup>.



*Cynoglossum L* is viewed as in the mountains of Eastern Europe and Western Asia and it is also said to be found in Great Britain. Its northern limit is 60° N and is extensively dispersed across Europe. Its isolated occurrence in Sweden extends up to 68° N. Its occurrence is rare in Mediterranean region. It does not grow in Europe's southernmost region<sup>11</sup>.

According to Tisner Heidy R, Upadhyaya Mahesh K, Pitt Michael D-*Cynoglossum* was introduced as a crop seed contaminant in North America from Europe<sup>12</sup>. In 1859, its herbarium species was collected in Ontario. It was described as 'common' in the Montreal area and as 'pest' at Ontario in 1884. As of 1988, *Cynoglossum* was reported to be widespread across across Ontario and Southern British Columbia, with the exception of Newfoundland and Prince Edward Island.

While *Cynoglossum* is found in the United States, reports of its presence in Hawaii or Alaska are lacking<sup>13</sup>. It is said to be a problematic plant in parks and natural areas in the number of states like Michigan, Missouri and Indiana<sup>14</sup>. The checklist of flowering plant in Afganistan states that *C. zeylanicum*, *C. nervosum* and *C. lanceolatum* were found in the Kabul, *C. stylosum* was found in

Badakhshang and Takhar, *C. intermedium* was found in Bamian, Ghazni, Kunar, Logar and Paktia, *C. anchusoides* was found in the province of Badakhshan, *C. golchidiatum* was found in province of Kabul, Badakhshan, Parwan, Baghlan, Maidan, Takhar, *C. stamineum* was found in the province of Badghis, Orozgan Herat, Parwan<sup>15</sup>.

The checklist of flowering plants in Afghanistan states that *C. intermedium* was found in Bamian, Ghazni, Kunar, Logar, and Paktia; *C. anchusoides* was found in the province of Badakhshan; *C. stamineum* was found in the province of Badghis, Orozgan Herat, and Takhar; *C. zeylanicum*, *C. nervosum*, and *C. lanceolatum* were found in Kabul; *C. golchidiatum* was found in the province of Badakhshan, Baghlan, Kabul, Maidan, Parwan, and Takhar; *C. stylosum* was found in Badakhshang and Takhar; *C. intermedium* was found in Bamian, Ghazni, Kunar, Logar, and Paktia; *C. intermedium* was found in Bamian, Ghazni, Kunar, and Takhar; and *C. intermedium* was found in Bamian, Ghazni, Kunar, Logar, and Takhar.

Table 1: Scientific classification of genus *Cynoglossum*

| Scientific name       | Habitat                | Altitude (metres) | Duration           | Habit | Plant height (centimetres) |
|-----------------------|------------------------|-------------------|--------------------|-------|----------------------------|
| <i>C. alpestre</i>    | Taiwan                 | 1200-1500         | Perennial          | Herb  | 50                         |
| <i>C. aequinocle</i>  | Kenya, Zambia          | 1760-2300         | Perennial          | Herb  | 20                         |
| <i>C. castaneum</i>   | Malaysia               | Plains            | Perennial/Biennial | Herb  | 75                         |
| <i>C. alpinum</i>     | Ehiopia                | 1400-2200         | Perennial          | Herb  | 20-50                      |
| <i>C. amplifolium</i> | Africa                 | 1980-2440         | Perennial          | Herb  | 100                        |
| <i>C. amabile</i>     | Central America, China | 3325              | Annual             | Herb  | 45-60                      |
| <i>C. baeticum</i>    | Africa                 | 1000-1800         | Biennial           | Herb  | 40-50                      |
| <i>C. bottae</i>      | Arabia                 | 2500              | Perennial          | Herb  | 50                         |
| <i>C. columnae</i>    | Turkey                 | Upto 1800         | Annual             | Herb  | 120                        |
| <i>C. coeruleum</i>   | Africa                 | 3150              | Perennial          | Herb  | 120                        |



|                         |                                      |           |                     |      |        |
|-------------------------|--------------------------------------|-----------|---------------------|------|--------|
| <i>C. birkinshawii</i>  | Africa, Asia, Europe                 | 2050      | Perennial           | Herb | 12-30  |
| <i>C. creticum</i>      | Mediterranean                        | 1000      | Biennial            | Herb | 30-60  |
| <i>C. bottae</i>        | Arabia                               | 2500      | Biennial            | Herb | 50     |
| <i>C. divaricatum</i>   | China                                | 500-2500  | Perennial           | Herb | 25-100 |
| <i>C. dioscorides</i>   | Europe                               | 500-2300  | Biennial            | Herb | 75     |
| <i>C. grande</i>        | Washington, California               | -         | Perennial           | Herb | 60-90  |
| <i>C. germanicum</i>    | Asia                                 | 1300-1400 | Biennial            | Herb | 30-60  |
| <i>C. hispidum</i>      | Switzerland, Africa                  | 2200      | Perennial/ Biennial | Herb | 30-60  |
| <i>C. lanceolatum</i>   | Pakistan, China, Asia, India, Africa | 300-2800  | Perennial           | Herb | 20-90  |
| <i>C. microglochin</i>  | Bhutan, Pakistan, Nepal              | 3000      | Perennial           | Herb | 12     |
| <i>C. macrocalycinm</i> | China                                | 1500-1800 | Biennial            | Herb | 50-60  |
| <i>C. monophlebium</i>  | Africa                               | 100-2500  | Perennial           | Herb | -      |
| <i>C. hellwigii</i>     | Malaysia                             | 1200-1300 | Annual              | Herb | 100    |
| <i>C. celebicum</i>     | England                              | 1800      | Perennial/ Biennial | Herb | -      |
| <i>C. gansusense</i>    | China                                | 1600-2900 | Perennial           | Herb | 30-60  |
| <i>C. glabellum</i>     | Malaysia                             | 1750      | Perennial           | Herb | -      |
| <i>C. macrolimbe</i>    | Malaysia                             | 2050      | Biennial            | Herb | 30     |
| <i>C. novaguineense</i> | Malaysia                             | 2014      | Perennial/ Biennial | Herb | 50-75  |
| <i>C. javanicum</i>     | Malaysia                             | 7620      | Biennial            | Herb | 30-100 |
| <i>C. nebrodense</i>    | France, India                        | 4000-6000 | Biennial            | Herb | 30-70  |
| <i>C. papuanum</i>      | Malaysia                             | Plains    | Annual              | Herb | 15     |



|                        |                                       |             |                     |      |         |
|------------------------|---------------------------------------|-------------|---------------------|------|---------|
| <i>C. obtusicalyx</i>  | South Africa                          | 975-1676    | Perennial/ Biennial | Herb | 30-40   |
| <i>C. suaveolens</i>   | Australia                             | Dam Places  | Perennial           | Herb | 10-60   |
| <i>C. officinale</i>   | Europe                                | 2100        | Biennial            | Herb | 30-120  |
| <i>C. wallichii</i>    | Kashmir,<br>Pakistan,<br>China, Nepal | 1300-3600   | Biennial            | Herb | 20-60   |
| <i>C. virginianum</i>  | North America                         | Forest gaps | Perennial           | Herb | 75      |
| <i>C. zeylanicum</i>   | Tamil Nadu                            | 1200-4100   | Biennial            | Herb | 2       |
| <i>C. viridiflorum</i> | China                                 | 700-1700    | Perennial           | Herb | 500-100 |
| <i>C. triste</i>       | China                                 | 2500-3100   | Perennial           | Herb | 15-50   |

## DISCUSSION:

### Phytochemistry

On the basis of spectroscopic analysis and other methods, few compounds like hexadecenoic acid, methyl ester, beta-sitosterol, 5-alpha-stigmastane-3,6-dione, 6-beta-hydroxy-stigmasta-4-en-3-one and daucosterol were isolated from the petroleum ether extraction of *Cynoglossum Lanceolatum Forsk*<sup>16</sup>. Shikonin was extracted from the herbal extract of *Cynoglossum Lanceolatum* using a method guided by bioassay. Based on the Shikonin scaffold, (E)-1-(6-bromo-2,3-dihydrochromen-4-ylidene) thiosemicarbazide was synthesized<sup>17</sup>.

*Cynoglossum Cheirifolium* provided crude methanol and tannin extract as well as their phenolic contents (flavonoids, phenolics and tannins). The leaves crude methanolic extract revealed significant levels of phenolic, flavonoid and tannin contents. Phenolic acids and flavonoids such as rutin, naringenin, sinapic acid, rosmarinic acid, caffeic acid, ferulic acid, syringic acid, and p-coumaric acid were identified using RP-HPLC-PDA<sup>18</sup>.

Pyrrolizidine alkaloids like trachelanthamine, viridiflorine, echinatine, 7-angeloylheliotridine, rinderine, heliosupine were obtained from *Cynoglossum Officinale*. The PA<sub>s</sub> level in new leaves are higher as

compared to older leaves. From 14C labelled putrescine, Isolated rosette plants roots and shoots produced PA<sub>s</sub><sup>19</sup>.

Solvent partition, column chromatography and prep. TLC were applied to the methanolic extract of *Cynoglossum Columnae Ten.* roots and aerial parts which yields in the isolation of seven secondary metabolites. Three pyrrolizidine alkaloids (2'-epi-heliosupine N-oxide, rinderine N-oxide, and 3'-O-acetyl-rinderine N-oxide) were found and isolated from the aerial section of the plant, together with beta arbutin. Echinatine N-oxide, rosmarinic acid, and 9" methyl lithospermate were identified and isolated<sup>20</sup>.

An investigation is conducted for naphthoquinone red pigments in the underground portions of *Cynoglossum Columnae Ten.* In order to test for naphthoquinone growth and production, the roots were cultivated in several liquid medium (MS, B5, LS, and DCR). The DCR medium produced the best outcomes. In the phytochemical screening, six naphthoquinone derivatives were found in roots and their post-culture medium using the RP-HPLC DAD technique and none were found in the transformed root culture.

The pyrrolizidine alkaloid which is found in the perennial plant *Cynoglossum Golchidiatum*, is used in the treatment of burns, wounds and infections. In the phytochemical study, the extract of roots has resulted in



the presence of flavonoids, coumarins, alkaloids, glycosides phenols, xanthoproteins and tannins<sup>27</sup>.

The whole plant of *Cynoglossum Zeylanicum* was dried and powdered in a wiley mill. The soxhlet apparatus was used to extract the dried powder using ethanol. Rotary evaporator was used to concentrate the extract. For the investigation, Adult Wistar Albino rats were employed<sup>28</sup>.

### Pharmacological effects

#### Anti-tuberculosis

The herbal extract of *Cynoglossum Lanceolatum* exhibiting anti-TB properties yielded Shikonin, the active component with anti-mycobacterium capabilities. Using MABA, it was discovered that the MIC of Shikonin against Mtb was 128 µg/ml. The scaffold of shikonin yields (E)-1-(6-bromo-2,3-dihydrochromen-4-ylidene, which has strong anti-Mtb action (MIC=4µg/ml)<sup>17</sup>.

#### Antioxidant

The extract of *Cynoglossum Cheirifolium* was assessed in the solvents like methanol using different methods for its antioxidant activity. Results from the activity revealed that the tannin extract of stem showed the highest ability to scavenge DPPH radical which indicated the inhibitory concentration of 50% (IC<sub>50</sub>) value of 70± 1µg/ml<sup>18</sup>.

The hydroalcoholic extract obtained from the roots and aerial parts of *Cynoglossum Creticum Mill* was assessed for its antioxidant and  $\alpha$ -amylase, lipase, cholinesterases, tyrosinase and  $\alpha$ -glucosidase inhibitory properties. The aerial part of the plant contains the highest number of phenolic compounds. With hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>), the extracts showed protective effects on intestinal HCT116 cell lines and cardiomyocyte C2C12. The best inhibitory effect of lipase enzyme was showed by leaves, which is followed by flowers and then roots. The scalar concentration of flower and root extract could be used for the treatment of both cell lines. The protective effect of *Cynoglossum* extracts can lead to the production of pharmaceuticals and nutraceuticals which are derived from *Cynoglossum*<sup>21</sup>.

#### Diuretic, analgesic and anti-inflammatory

The anti-inflammatory evaluation was done by the following methods- By inducing inflammation in rat's paw using fresh egg white and the substance being tested was administered to observe its effect on reducing the edema, by inducing carrageenam to elicit paw edema in

adrenalectomized rats and dimethyl benzene to induce inflammation in mice. The hot plate and the acetic acid-induced writhing test were used to measure the analgesic activity in mice. Rats and rabbits were used to estimate the diuretic effect of *Cynoglossum Lanceolatum* extract. When CLE was orally administered upto 12g/kg, there was no sign of mice death<sup>22</sup>.

#### Antidiabetic

Anitha M. (2012) evaluated the ethanolic extract of *Cynoglossum Zeylanicum* whole plant for its antidiabetic activity. The phytochemical analysis revealed the presence of potent phytochemicals like xanthoproteins, coumarins, saponins, alkaloids, tannins, catechin, phenols, flavonoids, steroids and glycosides. They are beneficial for the protection of alleviated complications of diabetics. A total 45 rats were collected and were assigned to 9 groups. For the oral glucose tolerance test, 4 groups of normal rats were used, and 5 rats were chosen from each group. For the oral glucose tolerance test, 5 groups of diabetic-induced rats were used, and 5 rats were picked from each group. Rats treated with drug 100mg/kg and 150mg/kg suppressed the increase in blood glucose level when compared to vehicle control<sup>23</sup>.

Plants provide a variety of novel bioactive phytoconstituents with hypoglycemic and anti-hyperglycemic properties that show some anti-diabetic potential.<sup>24</sup> Alkaloids, phenolics, flavonoids, and triterpenoids make up this phytoconstituents.<sup>25</sup>

#### Hepatoprotective and Antioxidant

In phytochemical analysis, the ethanolic extract of *Cynoglossum Zeylanicum* showed the existence of potent phytochemicals like xanthoproteins, catechin, alkaloids, phenols, glycosides, steroids, coumarin, tannin, saponins and flavonoid. The antioxidant and hepatoprotective effect of an ethanolic extract of the whole plant of *Cynoglossum Zeylanicum* (50mg/kg, 100mg/kg and 150mg/kg) on CCl<sub>4</sub> induced hepatotoxicity in rats is studied. For the antioxidant activity, the ethanolic extract of *Cynoglossum Zeylanicum* showed the rise in levels of GSH, CAT, SOD, GRD and GPx by decreasing levels of MDA.<sup>26</sup>

#### Toxic Evaluation of *Cynoglossum Golchidiatum*

Although, *Cynoglossum Golchidiatum* has numerous benefits like antidiabetic, antioxidant and antidiabetic but it also has few toxic effects like in phase 1 trial, there are mild and moderate degenerative changes in liver, spermatogenesis is decreased in testis, vacuolization in



uterus sub-mucosal layer. In phase 2 trial, it showed stimulation of gland with hypertrophy of capsule and epithelial layer of seminal vesicle, increased spermatogenesis and mild fatty degenerative changes in kidney of one rat. Phototoxic reaction, urticaria, allergic dermatitis, asthma exacerbations and anaphylaxis has rarely been reported<sup>27</sup>.

### Anti-inflammatory

Using an approach that involved inducing paw edema in rats with carrageenan, the entire plant *Cynoglossum zeylanicum* was extracted with ethanol and tested for anti-inflammatory efficacy.

One may compute the percentage inhibition of paw edema generated by carrageenan by utilizing the following formula:

% inhibition is equal to  $1 - dt \times 100 / dc$ .

Where:

dt is the treated paw diameter;

dc is the control's paw diameter<sup>28-37</sup>

The ethanolic extract of *Cynoglossum Zeylanicum* is evaluated for its anti-inflammatory activity in rats. The ethanolic extract of whole plant *Cynoglossum Zeylanicum* showed the decrement in edema at the doses of 50, 100, 150 mg/kg by 66.81%, 74.72% and 80.53% respectively after the administration of extract when compared to controlled group. The result shown here is same to that observed at 10 mg/kg which inhibited 79.57% in Indomethacin<sup>38</sup>.

### Ethno-pharmacology

*Cynoglossum* mainly contain pyrrolizidine alkaloids. It is traditionally used for curing numerous diseases described in the table given below.

Table 2: Traditional uses of genus *Cynoglossum*

| S.No | Plant Name             | Region                                                                              | Traditional Uses                                                                                                                                                                                                              |
|------|------------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1    | <i>C. amplifolium</i>  | Ethiopia                                                                            | Arthritis and Ear Infection <sup>39</sup> .                                                                                                                                                                                   |
| 2    | <i>C. lanceolatum</i>  | India, Japan, Tibet, China, England, Rwanda, Congo, South Africa, Mongolia, Burundi | Heal sores, used to join fractured and cracked bones, diarrhoea, relieve swollen limbs, regulates the menstrual cycle. It also function as sedative and aphrodisiac. It is also helpful in mental problems <sup>39,40</sup> . |
| 3    | <i>C. denticulatum</i> | India, Nepal, China                                                                 | It's root part enhances potency and stops vomiting.<br><br>It is used in the wound healing and also controls vomiting in infants <sup>39</sup> .                                                                              |
| 4    | <i>C. javanicum</i>    | Papua New Guinea                                                                    | Its leaves are used in the treatment of topical ulcers <sup>39</sup> .                                                                                                                                                        |
| 5    | <i>C. officinale</i>   | China and Tibet                                                                     | Antiseptic, Antihemorrhagic, Diuretic, venereal diseases <sup>39</sup> .                                                                                                                                                      |



|   |                        |                                     |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|---|------------------------|-------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 6 | <i>C. monophlebium</i> | Madagascar                          | Antirheumatic <sup>39</sup> .                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| 7 | <i>C. meeboldii</i>    | India                               | Roots juice are applied on ripe boils <sup>39</sup> .                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| 8 | <i>C. zeylanicum</i>   | England, India, China, Nepal, Tibet | <p>Roots and leaves- Antiseptic for cuts and wounds and powder in ring worms<sup>40</sup>.</p> <p>Diluted juice of leaves is used for fractured bone, conjunctivitis of cornea and to terminate tumors in uterus<sup>41</sup>.</p> <p>Poultice of whole plant is used for healing wounds and cuts<sup>42</sup>.</p> <p>Decoction of whole plant or paste of leaves are used for Inflammation, vomiting, Dyspepsis and digestive disorders.</p> <p>Leaf paste or juice for Ulcer and Earache<sup>43</sup>.</p> |

## REFERENCES:

- Hsiao Ju-Ying, Liu Ho-Yih. 126. Boraginaceae, Flora of Taiwan, Second edition, 1998, 4-390.
- Oznur Ergen Akcin, Kamil Coskunceleb and Gulcan Senel, Foliar Anatomy of *Cynoglossum L.* (Boraginaceae) from north Anatolia, Turkey, Bangladesh J Plant Taxon, 19, (2012), 101-108.
- Neuwinger H.D. African traditional medicine: a dictionary of plant use and applications. With supplement: search system for diseases, (Eng.). Medpharm GmbH Scientific Publishers, Stuttgart Germany, (2000), 589 ISBN 10: 3887630866, ISBN 13: 9783887630867.
- Bensaid I., Bekkara F.A., El Haci I.A., Belarbi K., Beddou F., Bekhechi C. *Orient. Pharm. Exp.Med.*, 17 (2017), 381–387.
- Joshi K, Mehra D, Kumar N, Bisht M, Sharma KD. *Journal of Pharmacognosy and Phtochemistry*. 5(2016), 32.
- Oznur Ergen Akcin, Kamil Coskunceleb, Gulcan Senel. Foliar anatomy of *Cynoglossum L* from north Anatolia, Turkey, Bangladesh. 19(2012), 101-108.
- Shu LL, *Cynoglossum Linnaeus* Sp, Flora of China, 1995; 16: 420-424.
- E.S Martin. *Cynoglossum Lanceolatum*, Flora Zambesiaca. 1990; 7(4).
- Marinov Y. *Cynoglossum Germanicum* (Boraginaceae), A new endemic species from SE Spain, Willdenowia, 2006; 26: 137-144.
- Sutory K. *Cynoglossum Montanum* L in the western part of Mediterranean area, Bocconeia, 2007; 21: 93-199.
- De Jong, Tom J.; Klinkhamer, Peter G.L; Journal of Ecology. 78(4). 1123-1144.
- Upadhyaya KM, Tisner R H, Pitt DM. *Canadian Journal of Plant Science*. 1988; 68(3): 763-774.
- U.S Department of Agriculture, National Resource Conservation Service. 2002. Plants Database (2002).
- Pestana EK. Research/Resource management report MWR-6. Omaha, NE: US. Department of the Interior, National Park Service, Midwest regional office.1873; 75.
- Podlech D, Munchen. Checklist of flowering plant of Afganistan. 2012; 215-216
- Zhang Yuanhu, Xiang Guiqiong, Lu Fusun. Europe PMC. 1996; 8(2): 46-48.



17. Zhao X, Wang L, Xia YM, Yang CZ. *Biochemistry & Biodiversity*. 2022; 20(2). DOI: 10.1002/cbdv.202200965
18. Bensaid I, Bekkara AF, El Hacı LA, Belarbi K, Beddou F, Bekhechi C. *Oriental Pharmacy and Experimental Medicine*. 2017; 17: 381-387. <https://doi.org/10.1007/s13596-017-0291-9>
19. Dam NM, Witte L, Theuring C, Hartmann T. *Phytochemistry* 1995; 39(2): 287-292. [https://doi.org/10.1016/0031-9422\(94\)00944-O](https://doi.org/10.1016/0031-9422(94)00944-O)
20. Damianakos H, Jeziorek M, Baranek KS, Buchwald W, Pietrosiuk A, Chinou I. *Phytochemistry Letters*. 2016; 15: 234-237. DOI: 10.1016/j.phytol.2016.02.005
21. Menghini L, Ferrante C, Zengin G. *Lant Biosystems-An International Journal Dealing with All Aspecets of Plant Biology*. 2018; 153(5): 633-639. <http://dx.doi.org/10.1080/11263504.2018.1527790>
22. Cheng-Hao Yu, Wei-Zhong Tang, Cheng Peng, Tao Sun, Bin Liu, Min Li, Xiao-Fang Xie, Hong Zhang. *Journal of Ethnopharmacology*. 2011; 139(1): 149-154. DOI:10.1016/j.jep.2011.10.031
23. Anitha M, Sakthidevi G, Muthukumarasamy S, Mohan V.R. *Journal of Applied Pharmaceutical Science*. 2012; 2(11): 75-78. DOI: 10.7324/JAPS.2012.21113
24. Shukla A. Kaur A. Shukla RK. *Res J Pharm Technol*. 2019; 12(4): 1811-6. DOI:10.5958/0974-360X.2019.00302.0
25. Saffiya BA. Sheila J. Sarah JM. Saraswathi K. *Res J Pharm Technol*. 2021; 14(12): 6289-6294. DOI: 10.52711/0974-360X.2021.01088.
26. Anitha M, Daffodil ED, Muthukumarasamy S, Mohan VR. *Journal of Applied Pharmaceutical Science*. 2012; 2(12): 99-103. DOI: 10.7324/JAPS.2012.21219
27. Acharya RN, Shukla VJ, Skandhan KP, Sharma PP, Ravishankar B. *AYU*. 2009; 30(2): 175-180.
28. Goli V, Bhaskar KV, Macharla SP, Bhaskar J, Devi PS, Ramchander T. *Asian Journal of Pharmaceutical Research*. 2011; 1(3): 69-71.
29. Manvar MN, Desai TR. *Asian Journal of Pharmaceutical Research*. 2014; 4(4): 186-8.
30. Anbarasi A, Vidhya R. *Asian Journal of Pharmaceutical Research*. 2015; 5(2): 83-9. DOI: 10.5958/2231-5691.2015.00012.X
31. Shakkeel MK, Kumar A, Babu D, Swamy VB. *Asian Journal of Pharmaceutical Research*. 2015; 5(3): 138-44. DOI: 10.5958/2231-5691.2015.00021.0
32. Jaseela KP, Kumar A, Babu D, Swamy VB. *Asian Journal of Pharmaceutical Research*. 2016; 6(2): 79-86. DOI: 10.5958/2231-5691.2016.00014.9
33. Narapusetty N, Sivaiah O, Balanasaraiah B, Haranadhababu M, Prasad B, Crown BH, Rao CM. *Asian Journal of Pharmaceutical Research*. 2017; 7(2): 88-93. DOI: 10.5958/2231-5691.2017.00015.6
34. Karthik KN, Kumar KR. *Asian Journal of Pharmaceutical Research*. 2017; 7(2): 94-97. DOI: 10.5958/2231-5691.2017.00016.8
35. Gorla SN, Savithri M, Koteswara Rao GSN, Niharika Y, Devi Sree Sathya P, Harika V. *Asian Journal of Pharmaceutical Research*. 2018; 8(1): 33-35. DOI: 10.5958/2231-5691.2018.00006.0
36. Shinde PP, Khule SD, Sonawane S, Shelke S. *Asian Journal of Pharmaceutical Research*. 2021; 11(3). DOI: 10.52711/2231-5691.2021.00027
37. Kumari A, Lalitha KG, Venkatachalam T, Kalaiselvi P, Sethuraman MG. *Asian Journal of Pharmaceutical Research Sci*. 2011; 1(4): 113-116.
38. Anitha M, Daffodil E.D, Muthukumarasamy S, Mohan V.R. *J. Adv. Pharm. Edu. & Res*. 2013; 3(1): 25-27.
39. Gidaya M, Asfawb Z, Woldub Z. *Ethnopharmacology*. 2010; 132(1): 75-78. DOI: 10.1016/j.jep.2010.07.046
40. Roeder E, Wiedenfeld H. *Die Pharmazie-An International Journal of Pharmaceutical Sciences*. 2009; 64(11): 699-716. DOI:10.1691/ph.2009.9653
41. Manikandan Arul PN. *Ancient Science of Life*. 2008; 27(3): 50-59.
42. Sharmila S, Kalaichelvi K, Rajeswari M, Anjanadevi N, *International Journal of Plant, Animal and Environmental Sciences*, 4 (2014) 14-21.
43. Bhagwati U, Vandana S, *Indian Journal of Traditional Knowledge*, 4 (2005) 259-256.