



Fritillaria roylei (Liliaceae). Traditional Use, Phytochemistry and Pharmacology

¹Subreena Sidiq

¹Assistant Professor (Guest Faculty)

¹Department of Botany

¹ Govt. Degree College Women, Kupwara, India.

Abstract: *Fritillaria roylei* (Liliaceae) is an important medicinal herb of the *Astavarga* group, distributed in sub-alpine to alpine regions of the Himalayas. *Fritillaria* naturally grows in the temperate region of Northern Hemisphere and mainly distributes in Central Asia, Mediterranean region, and North America. Its bulbs are an important constituent of many medicines and health tonics. The species is important constituent of *Astavarga*, *Chyavanprash* and other *Ayurvedic* preparations. The dried bulbs from a dozen species of this genus have been usually used as herbal medicine, named Beimu in China. Beimu had rich sources of phytochemicals and have extensively applied to respiratory diseases including coronavirus disease (COVID-19). *Fritillaria* species have alkaloids that act as the main active components that contribute multiple biological activities, including anti-tussive, expectorant, and anti-asthmatic effects, especially against certain respiratory diseases. Other compounds (terpenoids, steroidal saponins, and phenylpropanoids) have also been identified in species of *Fritillaria*.

Index Terms- *Fritillaria roylei*, Tradational uses, Phytochemistry, Pharmacology, Etano-medico botany, Antitussive.

I . INTRODUCTION

The genus *Fritillaria* (Liliaceae) is represented by 100 species distributed in the northern temperate zone (Mabberley, 1987), six of which are distributed in India (Anon., 1956). *Fritillaria roylei* is among the 36 species of globally significant medicinal plants of western Himalayas. The bulbs of the herb are important constituents of *Astavarga*, *Chyavanprash*, *Ghritham*, *Mahatraiphala*, *Jeevanthyadi*, *Ghrutham* and *Danwantharam Thailam*. The bulbs are important constituent of the Indian System of Medicine (ISM), health tonic, *Astavarga* Group (a combination of eight rejuvenating drugs) and *ayurvedic* medicines (Anon., 1956). *Fritillaria roylei* Hook., commonly known as Kakoli (Anon., 1956), grows in sunny meadows of sub-alpine to alpine regions between 3000 to 4200 m as in Garhwal Himalaya (Chauhan et al., (2011).

Fritillaria roylei is perennial, glabrous and bulbous herb, 15-60 cm high and have mottled stem. The leaves are opposite or whorled, linear-lanceolate, flowers are solitary, yellowish green to brownish-purple with chequered pattern in yellowish green or dull-purple. Flowers are bell shaped, hanging looking down, borne singly on the stem but sometimes in a group of two or more. Petals are narrow ovate 4-5 cm long. Leaves are 5-10 cm long, linear lanceolate often long pointed, arranged oppositely or in whorls of 2-6. Flowering takes place during June-July and fruiting during July-August. Seeds are arranged in two rows in each value. Bulbs are globose, small and covered with membranous scales.

The International Union for Conservation of Nature (IUCN) categorized the species as critically endangered (CR) for Uttarakhand and endangered (EN) for Himachal Pradesh and Jammu and Kashmir (Anon., 2003). The market demand of this species is increasing while supply is gradually decreasing (Ved and Goraya, 2008). This calls for conservation as well as cultivation measures to be implemented. *Fritillaria* is regarded as an important

genus in Liliaceae family and a plant source of significant chemically components utilized in conventional prescriptions by folklore of Turkey (Farooq et al. 1994), South East Asia (Zhou et al. 2010) China, Pakistan and Japan (Kaneko et al. 1981). *Fritillaria* species are presently popular in therapeutic plants industry (Day et al. 2014) and floriculture (Turktas et al. 2012). *Fritillaria* is utilized worldwide as medication and food; typically roasted bulbs of certain species are utilized as food by Native Americans. *Fritillaria* species have attracted much attention because of their commercial value, partly as ornamental plants but principally as a source of material for use in traditional medicine (Day et al., 2014).



Fig 1: *Fritillaria roylei* in natural habitat

II . TRADITIONAL USES

Fritillaria have been utilized as main Chinese crude drugs and furthermore as an anti hypertensive and anti asthmatic drugs from years. *Fritillaria* are utilized worldwide as medication and food; normally roasted bulbs of some species are utilized as food by Native Americans (Orhan et al. 2009). The bulbs of *Fritillaria roylei* are used traditionally in the treatment of bronchitis, asthma, burns, stomach troubles and as a stimulant. The roots are used for healing wounds, corns in Ayurvedic and unani medicine. Prior it was exported from Nepal to India and China due to its high therapeutic values (Thomson 2007). Genus *Fritillaria* have been utilized for long due to their effects of moistening the lung, clearing heat, resolving phlegm, soothing cough, remedy for cough brought about by lung heat and dryness, a cough because of a yin weakness, sputum with blood and a

low sputum dry cough. In Jammu and Kashmir, India, *F. roylei* is used traditionally for rheumatism, asthma, tuberculosis and as a tonic. The bulb of the species is boiled with orange peel and given in the treatment of tuberculosis and asthma. The bulb part of *Fritillaria* species utilized as decoction or in dried form to cure bronchitis, cough, tumours, struma, asthma, haemoptysis and insufficiency of milk (Perry 1980; Kang et al. 2002). It is also believed that *F. roylei* is very strong cough suppressant and source of expectorant drug in traditional Chinese medicine. Moreover, it is used as a lymphatic decongestant to decrease glandular or nodular breast tissue, goitre, swellings and lymphadenopathy. It has been utilized for the treatment of prolonged hypotension, sensory system, defective breathing and incitement of the heart muscle (Erika and Rebecca 2005) as well as treating swelling underneath the skin, for example, scrofulous swellings and breast nodules (Da-Cheng et al. 2013). It is likewise detailed that blood platelet conglomeration is restrained by *Fritillaria* bulbs.

III. PHYTOCHEMICALS

Fritillaria is rich in multiple secondary metabolites, whereas the alkaloids are the main compounds isolated and identified from the crude extracts in the bulbs in addition to terpenoids, steroidal saponins, and phenylpropanoids. The bulbs contain three major alkaloids, peimine (C₂₇H₄₅O₃N), peiminine (C₂₇H₄₃O₃N) and peimisine (C₂₇H₄₁O₃N). Alkaloids are organic components characterized by the basic nitrogen atoms. Based on the carbon framework, possessing a C₂₇ cholestane carbon skeleton with carbocyclic and heterocyclic rings, the alkaloids extracted from *Fritillaria* species mainly consist of isosteroidal and steroidal types. The isosteroidal alkaloids (*Veratrum* steroids), are further divided into cevanine (A1), veratramine (A2), and jervine (A3) types. These alkaloids have a five-membered carbocycle. genus *Fritillaria* (Xiao et al. 2007). The significant phytochemicals in *Fritillaria* species are reported as isosteroidal alkaloids: ebeiedine, ebeienine, ebeiedinone, verticinone, imperialine, verticine, hupehenine and isovorticine. However, quantity and kind of isosteroidal alkaloids differ in numerous *Fritillaria* species, and clinical results can likewise be unique (Li et al. 2000).

In excess of 120 alkaloids have been isolated from the genus *Fritillaria* (Xiao et al. 2007). The significant phytochemicals in *Fritillaria* species are reported as isosteroidal alkaloids: ebeiedine, ebeienine, ebeiedinone, verticinone, imperialine, verticine, hupehenine and isovorticine. However, quantity and kind of isosteroidal alkaloids differ in numerous *Fritillaria* species, and clinical results can likewise be unique (Li et al. 2000).

IV. PHARMACOLOGICAL ACTIVITIES

The dried bulbs of *Fritillaria* species have been used as an anti-tussive drug and other respiratory diseases, such as expectoration and asthma, in traditional folk medicine since Han Dynasty of China (around AD 220). Thus, several studies focused on the respiratory diseases in vivo and in vitro. Aside from studies on the respiratory system, the increasing pharmacological research indicates that the chemical components or extracts from herbal medicines have potential antineoplastic, anti-inflammatory, antihypertensive, bacteriostasis, and anti-tumor effects.

Anti-tussive effect

The anti-tussive efficacy is consistent pharmacological activity between the traditional clinical usage and modern utilization in the daily life. Anti-tussive pharmacological comparison of 11 commercial *Fritillaria* species indicated that the total alkaloid of 11 *Fritillaria* species had significant or extremely significant effect on ammonia-induced cough in mice. The ethanol extracts of 9 *Fritillaria* species, except for *F. delavayi* and *F. pallidiflora*, also have significant anti-tussive effect.

Respiratory diseases

Respiratory diseases seriously affect the physical and mental well-being of patients with symptoms of sneezing, cough, and difficulty in breathing, which are leading causes of mortality and morbidity. The natural botanical materials from *Fritillaria* have significant pharmacological effects on the respiratory system, including the alleviation of cough, phlegm, asthma, COPD, and acute lung injury (ALI).

Expectorant effect

The expectorant effect can be observed in the mixed preparations of fresh pear and dried powders, which are normally cooked by the elderly for their therapeutic effects. The total alkaloids and saponins are the prominent compounds contributing to the expectorant effect. Expectorant effects are generally related to the relaxation of smooth muscles.

Anti asthmatic effect

Asthma is an allergic disease caused by broad bronchial obstruction and exhalation dyspnea is the main symptom. The main inducements of bronchial obstruction are interpreted by three aspects, including bronchial smooth muscle contraction, excessive mucus secretion, and adhesion to the bronchial wall. The main anti-asthmatic mechanisms comprise the relaxation of bronchial smooth muscles, relief of trachea and bronchus spasm, and improvement of ventilation status. Current scientific research shows that the anti-asthmatic effect of *Fritillaria* is related to the antagonism of the tracheal M receptor.

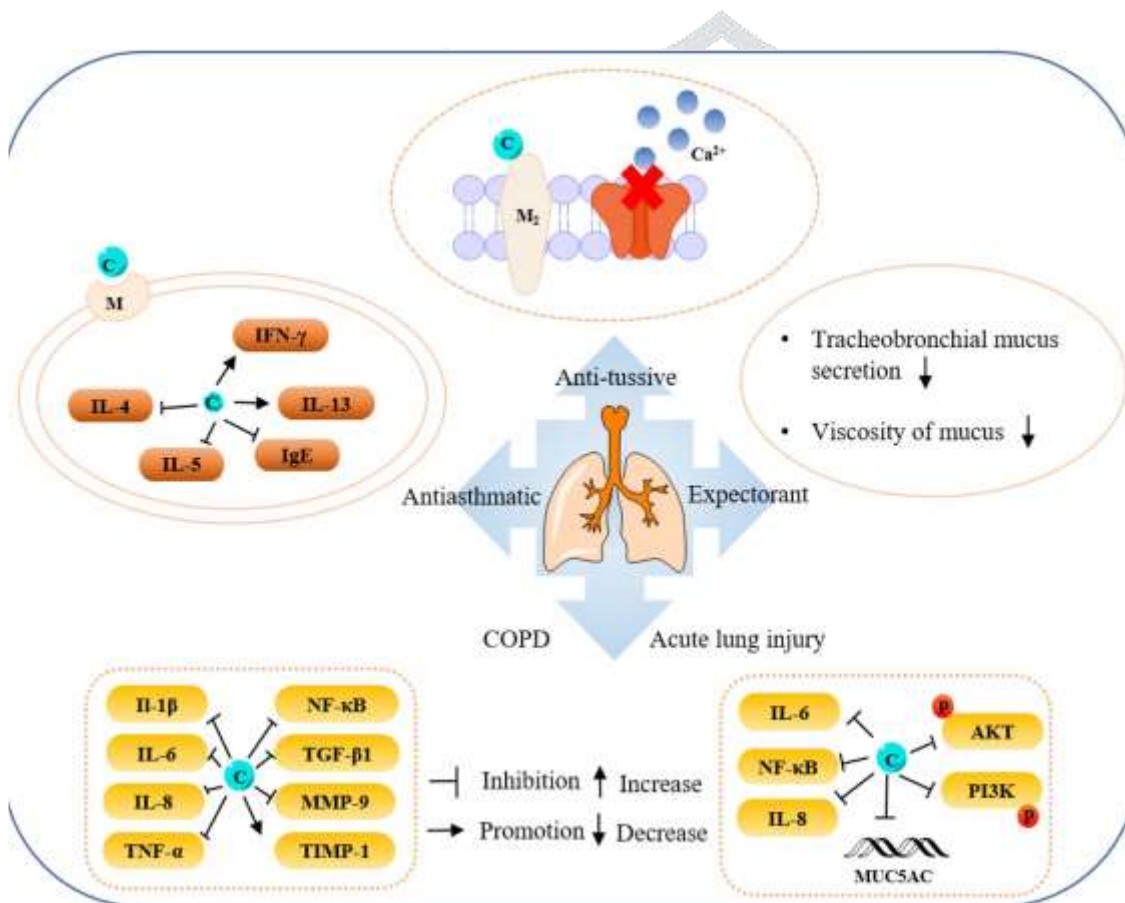


Fig 2: The action mechanism of respiratory diseases using chemical components from *Fritillaria* species

Anti-diabetic effect

The diabetes is a major concern worldwide caused by high-sugar intake or other induction factors. The relevant investigation of verticinone 13 demonstrated the component exhibited hypoglycemic effects by increasing insulin secretion and glucose uptake. What's more, the component can inhibit of carbohydrate-hydrolyzing enzymes on β-TC6 pancreatic and C2C12 skeletal muscle cells. In general, these summarized modern pharmacological activities are consistent with the traditional records of efficacy, which showed that the dried bulbs are mainly used for respiratory diseases including their anti-tussive, expectorant, and anti-asthmatic effects. It is necessary for researchers to conduct pharmacokinetics and pharmacodynamics, which will be beneficial for studying the action mechanism and developing the medicinal value of Bei Mu.

V. CONCLUSION

Fritillaria roylei have been utilized in traditional Chinese medication for more than 2000 years due to their activities of reducing heat, alleviating cough, moistening the lung etc., for the treatment of bronchitis, a low sputum dry cough, asthma, tumours, struma, hemoptysis and insufficiency of milk and so on. There is no doubt that alkaloids are the prominent constituents in the medicinal parts of *Fritillaria* species, and they have become the evaluation index for ensuring whether the target objective can be used as a substitution for the endangered medicinal Bei Mu. The extensive pharmacological activity and clinical application value show the development and utilization potential of the bulbs *Fritillaria*. However, their mechanisms of action are still unclear. Therefore, modern scientific methods should be used to further study the pharmacological actions to clarify the multi-target and multi-channel mechanism of Bei Mu materials. The pharmacological investigation should focus on the potential metabolism of the separated components in future, which have been conducted the detailed research in animals, and explore the relationship between their pharmacokinetics and pharmacodynamics, in addition, new dosage forms, administration methods, such as the research and development of nano-preparations and inhalation preparations, and *Fritillaria* materials should be developed and applied.

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