Phytochemical, ethanobotanical uses and pharmacological values of *Barleria cristata* Linn.

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 **ABSTACT**

In India, herbs have always been the main kind of medicine. Medicinal plants have therapeutic properties because they contain a variety of complex chemicals with varying chemical compositions. Globally, research on medicinal plants has recently attracted a lot of interest. The promising potential of medicinal plants utilized in many conventional, complementary and alternative ways of treating human ailments has been established by a substantial body of proof. Drugs derived from plants generally have lower adverse effects, are easier to obtain, and are well tolerated. The ability of medicinal plants to treat disease is caused by a number of secondary metabolites. Therefore, the initial screening tests are helpful in identifying bioactive principles and may facilitate the identification and creation of novel medications. One of the larger and most well-known genera of herbs and shrubs in the Acanthaceae family is *Barleria.* Fast-growing ornamental shrub *Barleria cristata*, a member of the Acanthaceae family, is frequently grown in gardening for its colorful flowers.*Barleria cristata* also known as Philippine violets is native to Southeast Asia and India, has a large presence in Central and South India. It is known as Kala Bansa and is an herbal remedy. It blooms as a shrub 60-100 cm tall. Leaf surfaces are dark green on the top and pastel green on the bottom. They are elliptic to narrowly ovate. The funnel-shaped, pink or violet flowers are around 5 cm long. The fruits are ellipsoid capsules that are roughly 1.5 cm tall. The phytochemical tests demonstrate the presence of sugars, proteins, amino acids, steroids, glycosides, alkaloids, tannins, phenolic compounds, and flavonoids. The plants contain highest amount of ascorbic acid than vitamins. The results of TLC analysis of methanolic extract point to the presence of a high level of phytoconstituents. This plant's leaf extract was analysed using GCMS. This study identified the 15 chemicals. The plant has been used ethnopharmacologically for illnesses such as tuberculosis, hepatic obstruction, diabetes, fever, toothache, anaemia, snake bite, and lungs ailments. The plant's anti-inflammatory, antibacterial, antidiabetic, antifungal, hepatoprotective antioxidant, anticancer, anti-herlipidemic, and thrombolytic properties were also studied. The purpose of this review was to present a scientific summary of *Barleria Cristata* in connection to its ethnobotanical characteristics, geographic distribution, medicinal applications, phytochemistry and pharmacological activity, and critical analyses research gaps and future research opportunities for investigations on this plant. This information may be useful for future studies aimed at enhancing human health care.

Key words: *Barleria cristata,* Phytoconstituents, Medicinal plants, Pharmacological activity, Philippine blue.

**I. INTRODUCTION**

Since ancient times, plants have been widely recognised as a tremendous source of therapeutic chemicals. Because of their affordable prices, fewer side effects, and growing trust in traditional medicine, the World Health Organisation estimates that up to 80% of people rely mostly on traditional plants for their medicine[1, 2].Natural biodiversity, in accordance with WHO, emphasises a critical role for their nutritional and therapeutic benefits to regulate and control diseases [3, 4]. According to evidence found in old books and other artefacts, ancient people employed plants in their healing rituals. India was renowned among the ancient civilizations as a rich source of medicinal plants. In India, the forest is the primary reservoir of a huge variety of plants with medicinal and aromatic properties that are gathered as raw materials for the production of pharmaceuticals and perfumery goods.In India's AYUSH system, almost 8000 herbal treatments have been codified. In India, Ayurveda, Unani, Siddha, homoeopathy, and folk (tribal) medicines are the primary indigenous medical systems. In India, medicinal plants have been utilised extensively to cure a wide range of ailments since the Rig Veda time, 5600 BC. Based on the accumulated knowledge of the herb, tribal peoples created a well-defined herbal pharmacopoeia [5]. Plants have various enriched nutrients having positive physiological effects to the human body. They are referred to as nutraceuticals, and they have significance for the development of new treatments [6].India is home to an estimated 8% of the world's biodiversity [7-13].

The Acanthaceae family, which includes the genus *Barleria,* has its highest species richness in open forest and is native to tropical Asia and Africa. With 300 species, *Barleria* stands third among genera in the Acanthaceae family. For India, Balkwill [14] listed 32 species; however, Karthikeyan and his colleagues [15] found one subspecies, six variants and 29 species. Philippine violet is a shrub that has no connection to the Philippine Islands or violets, despite the fact that its flowers are undoubtedly violet in colour. *Barleria cristata,* the ornamental  plant, is an evergreen sub shrub of the acanthus family that is dense, upright, hairy-stemmed, and normally grows to a height of 3 to 4 feet is now widely grown in South East Asia, South china, and tropical and subtropical India. This shrub may be grown in Florida, southern Texas, Louisiana, Arizona, and California in the US. It is also seen as a potential weed in waste areas and along the side of the road [16-18]. In India, this plant is found growing as a hedge surrounding fields, gardens, etc. The potential utilisation of *Barleria cristata* as a traditional medicine in order to treat of blood illnesses, inflammatory problems, diabetes, anaemia, snake bites, and toothaches has also been supported by ethnomedical accounts.

Triterpenes, flavonoids, phenolic compounds, iridoids, and phenylethanoid glycoside have all been identified in the phytochemical profile of *Barlerai cristata* [19, 20]. Biological activities  exhibited by *Barleria cristata* included anti-inflammatory, antibacterial, antidiabetic, antifungal, hepatoprotective, antiplasmodial, and antioxidant activity [21]. As a result, the purpose of this review was to emphasise the significance of *Barleria cristata* as a possible source of bioactive chemicals and to summarise the therapeutic applications as well as phytopharmacological investigations to highlight the future prospects of this plant. The significance of phytochemical ingredients and the activities of *Barleria cristata* are demonstrated in this, which may be helpful to scientists, research scholars, health professionals, and students working connected to phytochemical and pharmacological activities from medicinal plants. This review study outlined the scientifically supported facts concerning the pharmacological and phytochemical activities. The review also includes information on the plants' characteristics and ethanomedical applications.

**II.TAXONOMY OF *BARLERIA CRISTATA*** [22, 23]

Kingdom: Plantae

Subkingdom: Tracheobionta

Division: Magnoliophyta

Class: Magnoliopsida

Subclass: Asteridae

Order: Scrophulariales

Family: Acanthaceae

Genus: Barleria

Species: Cristata

**III. SYNONYMS**

Barleria ciliateRoxb.;

Barleria dichotomaRoxb.;

Barleria laciniateWall. and

Barleria napalensis Wall.

**IV. VERNACULAR NAME [24, 25, 26, 27]**

English: Blue bell barleria, bluebell, Philippine violet

Japan: Barureria

Philippines: Kolintang, violeta

Thailand: Kaanchang, luemthaoyai, thong ra‐aa

Tibet: Sa ha ra ca, sa ha ratsap, sa‐ha‐tsa

Vietnam: Hoach[oo]ng

India: Hindi – Raktajhinti; Oriya – Banpatoli; Tamil – Nilamulli, Semmuli; Telugu –December Puvvulu, Peddagorinta; Sanskrit – Artagala, Bana, Dasi; Bengali – Jati, Jhinti,Swetjhanti; Madhya Pradesh – Morani, mukaro; Arunachal Pradesh – Vahaka; Assam‐Sajhia

**V. GEOGRAPHICAL DISTRIBUTION AND HABBITAL**

 *Barleria Cristata* has been discovered all over the world in gardens and woodlands in Africa, the Pacific region, tropical Asia, and temperate Asia [28]. It can be found throughout the Asian tropical region, including Indochina (Cambodia, Laos, Myanmar, Thailand, and Vietnam) and the Indian subcontinent (Nepal, Pakistan, Bangladesh, India and Bhutan) [29, 30]. It can be found in India's subtropical north-eastern (Himalaya, Kashi Hills, Sikkim) and southern (typically at 1350 m) regions [31].


**Figure 1 : Geographical distribution of *Barleria cristata* indicating the native and naturalized ranges.**

 *Barleria cristata* can be grown by streams, on the sides of roads, and in xeric vegetation at elevations ranging from 100 metres to 2600 metres*.* It was also been grown as ornamental plants in garden and can be found naturalized in ruderal sides and semi- natural habitals in dry and wet regions [32]. *Barleria cristata i*s a fast growing perennial plant often cultivated in gardens for its showy flowers. The naturalisation of this species in disturbed areas, deserted gardens, riverbanks, and by the sides of roadways has occurred on several occasions [33].

 **VI. BOTANICAL DESCRIPTION**

A huge, branching, tall, and everlasting shrub called *Barleria cristata* L. thrives in a region of the landscape with good, well-drained soil that is not alkaline and receives either full sun or partial shade. The stem is made up of densely hairy nodes and appressed trichomes. The leaves are elliptic-lanceolate in shape, 2.5–10 cm long, ciliate at the margins and acute-acuminate at the apex, and are typically attenuate at the base. The top of the midrib is hair-covered and has 5-7 pairs of lateral veins. The petioles on the leaves, which are between 3 and 8 millimetres long, are green, typically the lower surface is pale green, funnel-shaped flowers at the tips of the stalks, about 2 cm long, and white pink. Auxiliary or terminal dense ovoid spikes make up the majority of inflorescence. The bracteoles are varied, linear, toothed at the margins, acute at the membranous pubescent and veined at the apex. Bracts are missing [34].Calyx is persistent, 2 cm long, green in hue, and laciniately serrated in shape. Corolla is 6-7 cm long, thin-tubed, winged above, and limb is violet or almost white. The corolla tube is rectangular, pink, exterior downy, and has a two-lipped border. It has glandular hairs. The lower lip is wider but shorter and whole, while the upper lip has four divisions. Flowers have four 2.5 cm long, hairy stamens, 3 mm long anthers, and 5 mm long staminodes with sterile anther cells [35]. Nectar is the lower half of the germ that is cupped on both lips [36].

The stigma has two pink lobes that are larger, pierced between two short and rounded lips, and the ovary bears two ovules in each locule. The style is terete, inflated at the apex, and hairy at the base [37].The seeds are compact, oval, and silky-hairy [38]. In the Indian subcontinent, flowering and fruiting season runs from September to February [39].

  

 **Figure 2: Flower Figure 3: Plant Figure 4: Leaves**

***BARLERIA CRISTATA*: CRESTED PHILIPPINE VIOLET.**

1. **Description**

Height: 4 to 6 feet

Spread: 3 to 4 feet

Plant habit: upright

Plant density: dense

Growth rate: fast

Texture: medium

1. **Foliage**

Leaf arrangement: alternate

Leaf type: simple

Leaf margin: entire

Leaf shape: ovate

Leaf venation: bowed; pinnate

Leaf type and persistence: evergreen

Leaf blade length: less than 2 inches

Leaf colour: green

Fall colour: no fall colour change

Fall characteristic: not showy

1. **Flower**

Flower colour: pink; white

Flower characteristic: summer flowering; fall flowering

1. **Fruit**

Fruit shape: no fruit

Fruit length: no fruit

Fruit cover: no fruit

Fruit colour: not applicable

Fruit characteristic: inconspicuous and not showy

1. **Trunk and Branches**

Trunk/bark/branches: not particularly showy; typically multi-trunked or clumping stems

Current year stem/twig colour: green

Current year stem/twig thickness: thin

**VII. MORPHOLOGICAL PARAMETERS**

The first layer of the epidermis is protected by a cuticle as a single layer, according to the transverse section of *Barleria cristata*. A single layer of the polygonal parenchymatous cell, which had covering trichomes on its surface, was visible in the upper and lower epidermis. A network of collenchymatous cells that was 5-7 layers thick followed the epidermal layer. The ground tissue layer was located next to this one and was made up of parenchymatous cells that were interspersed with intercellular gaps.The vascular bundle was located in the center, and the phloem was bordered by a radial row of xylem arteries. The sort of vascular bundle that was already there was open and bicollateral (a xylem layer was positioned between two phloem layers).



**Figure 5: The transverse section of *Barleria cristata* Linn. leaf at a magnification of 10x**

**Ep: Epidermis, Col: Collenchyma, Tr: Trichomes, Gt: Ground tissues, Xy: Xylem, Phl: Phloem.**

**VIII. ETHNOMEDICINAL USES**

 It fulfils a variety of conventional functions and qualities. *Barleria cristata* L. whole plant is traditionally used as medication for diabetes, insemination, wounds, burns, gingivitis, and nocturnal ejaculation. Additionally, it is advised in cases of cough, skin infections, anaemia, and tuberculosis. In addition to being chewed for toothache relief, leaves are frequently used to lessen irritations. The paste is applied to feet during the rainy season to prevent cracking, while the plant juice is used for fever and phlegm [40]. The root's decoction is used for anaemia and cough. However, root infusion is used to treat boils and ulcers to reduce swelling and toothache [41, 42].Wherever dry bark is administered to treat whooping cough, the acrid juice of the stem bark is used as an expectorant and diaphoretic [43]. It is regarded as a precious medicinal plant, particularly for the treatment of respiratory conditions like asthma, bronchitis, coughing, and Tuberculosis.

**IX. PHYTOCHEMISTRY**

 The phytochemical research with *Barleria cristata* resulted in the separation and identification of biologically active substances such glycosides, polysaccharides, triterpenes, notably oleanolic acid, and derivatives of the 4- hydroxy transcinnamate.The studies also revealed the presences of secondary metabolites like proteins, amino acids, steroids, triterpenes phenols, flavonoids, alkaloids, saponins, and tannins in the ethanolic extract of leaves of *Barleria cristata* [44].Phenolic compounds, flavonoids, phenylethanoid, and iridoidal glycosides are the main phytoconstituents among the huge variety of phytoconstituents present in plant. Phenylethanoid glycosides (desrhamnosyl acteoside, acteoside, and poliumoside) were consecutively isolated from the callus cultures of *Barleria cristata* L. and described using chromatography and spectroscopic techniques. The identification of additional chemicals from leaves includes two iridoidal glycosides (Barlerin and Schanshiside methyl ester), two flavonoids (luteolin and 7-methoxyluteolin), and two phenolic compounds (p-coumaric acid and tocopherol).Barlacristone and cristabarlone are two anthraquinones discovered in the roots. Additionally, it has been discovered that flowers contain sitosterol, quercetin, quercetin 3-β- D glucoside, apigene, naringenin, and apigenin -7- glucuronide [45, 46, 47]. Lead, zinc, iron, chromium, copper, nickel, and cadmium are just a few of the trace metals that have been found in the plant's leaf extract [46].

1. **Polyphenols**

 Polyphenols are naturally occurring substances that can be found in large quantities in vegetables, cereals, fruit, and drinks. In both health and disease, phytopolyphenolic substances serve as dietary antioxidants [48].These typically serve a role in defence against UV radiation or pathogen attack [49].

1. **Phenolic acids.**

α-Tocopherol and p-coumaric acid were extracted from *Barleria cristata* leaf petroleum ether extract. The most physiologically and chemically active form of Vitamin E, which is regarded as a leading antioxidant, is tocopherol [50,51]. A tiny monomeric phenolic acid called p-coumaric acid (4-hydroxycinnamic acid) inhibits the formation of free radical chains by acting as an oxygen radical scavenger in a number of biological systems [52-55]. It enhances probiotics' functional effectiveness by activating powerful antioxidant and detoxification processes [56-59]. Additionally, it effectively destroys microorganisms and reduces the peroxidation of low-density lipoprotein (LDL).Numerous pharmacological effects of p-coumaric acid have been discovered in vitro and in vivo, such as anxiolytic, antihyperglycemic, antiplatelet, and antimelanogenic effects [60]. The biological functions of p-coumaric acid are crucial for maintaining human health.

1. **Flavonoids**

 Flavonoids are the most common group of polyphenolic compounds which have versatile health benefits. Luteolin and 7‐methoxy luteolin compounds were reported from the ethylacetate extract of leaves of *Barleria cristata*.The most prevalent class of polyphenolic chemicals with a variety of health benefits are called flavonoids. It was discovered that *Barleria cristata* leaf ethyl acetate extract produced the compounds luteolin and 7-methoxy luteolin. A common dietary flavonoid called luteolin is essential for certain anti-inflammatory, antioxidant, and anticancer effects [61,62] .

1. **Glycosides**

 A novel chain of glycoside namely iridoidal glycosides which includes barlerin (or dimethyl 5‐hydroxy‐7‐methyl‐1‐((2R, 3S, 4S, 6S)‐3,4,5‐tridroxy‐6‐(hydroxymethyl) tetrahydro‐2H‐pyran‐2‐yloxy)‐1, 4a, 5,6,7,7a‐hexahydrocyclopetan pyran‐4,7‐dicaroxylate) and shanshiside methyl ester(5,7‐dihydroxy‐7‐methyl‐1‐(3,4,5‐trihydroxy‐6‐ydroxymethyl) tetrahydro‐2H‐pyran‐2‐yloxy)‐1,4a,5,6,7,7‐a(hexahydrocyclopentapyran‐4‐carboxylic acid) was found from ethanolicextraction of the leaves.Furthermore, ethanolic extraction of the callus culture of shoots of *Barleria cristata* revealed the presence of phenylethanoid glycosides which includes β‐[(3′,4′‐Dihydroxyphenyl)‐ethyl]‐(4″‐*O*‐cafeoyl)‐β‐D‐glucoside (desrhamnosylacteoside),β‐[(3′,4′dihydroxyphenyl)‐ethyl]‐(3″‐*O*‐L‐rhamnosyl)‐(4″‐*O*‐caffeoyl)‐β‐D‐glucoside (acteoside) and β‐[(3′,4′‐dihydroxyphenyl)‐ethyl]‐(3″,6″‐*O*‐L‐dirhamnosyl)‐(4″‐*O*‐caffeoyl)‐β‐D‐glucoside(poliumoside) phenylethanoid glycosides. These phenylethanoid glycosides play an important role in several pharmacological activity such as antibacterial, antifungal, antiviral, immunosuppressive, antiproliferative and analgesic and effect on cardiovascular system [63]. Acteoside has already been reported for having antioxidant, hepatoprotective and anti‐inflammatory effects [64].

1. **Triterpenes**

 Oleanolic acid was the name of the triterpene that was isolated from the entire plant. The anti-inflammatory, hepatoprotective, anticancer, antimicrobial, antiulcer, hypoglycaemic, anticariogenic, antifertility, and anti hyperlipidemic effects of this substance have been acknowledged [65, 66].

1. **Aromatic compounds**

 Protecting against insects and pathogens is the primary function of aromatic chemicals with plant origins [67]. From all parts of *Barleria cristata*, aromatic substances such derivatives of 4 hydroxy transcinnamate have been found. Nipa Chowdhury *et al* was isolated three aromatic compounds (4-hydroxy-trans-cinnamate derivatives) [68].



Chemical structure of 4-hydroxy-trans-cinnamate

derivatives (1-3)

 **X. PHARMACOLOGICAL ACTIVITY**

 Several extracts from the leaves, bark, seeds, and entire plant of *Barleria cristata* have demonstrated pharmacological action in both *in‐vitro* and *in‐vivo* models. The antibacterial, anti-inflammatory, anti-diabetic, antioxidant, hepatoprotective, and antifungal action has been the subject of several preclinical research.

1. **Antibacterial activity**

 The extracts of *Barleria cristata* bark shown antibacterial activity against four pathogenic bacterial strains at a concentration of 0.025-0.095 mg/ml when they were prepared using different solvents (chloroform, ethyl acetate, and ethanol by using diffusion method. With inhibition zone sizes ranging from 28 to 15 mm against *Staphylococcus aureus, Bacillus subtillis,* and *Streptococcus mutans*, with the exception of *Escherichia coli,* the ethanolic extract shown the best effectiveness. The ethanolic extract was shown to be the most effective extract, which was thought to be owing to its flavonoid concentration, after comparing the antibacterial activity of the three extracts of bark of *Barleria cristata* tested against the bacterial strains. The gossypetin 8-methylether had the best antibacterial activity among the discovered flavonoids, which promoted the usage of the ethanolic extract and/or active ingredient in modern medications [69].

K. Amutha and D. Victor Arokia Doss worked on *Barleria cristata* L. dry leaf extract's saponin profile was determined using a simple HPTLC procedure. *Barleria cristata* L. dried leaves from the saponin fraction were tested in vitro against four bacterial species using the agar disc diffusion method. The saponin fraction extract was found to be efficient against *Salmonella paratyphi* (8 mm*), E. coli* (9 mm), *S. aureus* (9 mm), and *Klebsiella pneumonia* (10 mm) among the four bacterial pathogens examined. Pure saponin has a zone of inhibition comparable to that of antibiotics such conventional Ciprofloxacin (5 g/disc). According to the current research, the saponin fraction has high antibacterial activity and might be exploited to create a new antimicrobial drug [70].

S. Baskar *et al* has discovered antipathogenic activity against gram positive, gram negative bacteria using the disk diffusion test.On Muller Hinton Agar (MHA) and Potato Dextrose Agar (PDA) plates for bacteria, the two tested concentrations of 0.60 and 1.20 mg/disc result in a zone of inhibition. In this investigation, higher (1.20 mg) concentrations were more sensitive to all strains than lower (0.60 mg) concentrations. This study has shown that *Barleria cristata* contains secondary metabolites that contribute to its exceptional antimicrobial properties. These compounds include steroids, triterpenes, alkaloids, phenols, flavonoids, and tannins. These compounds are potentially used as antimicrobial agents in new medications for the treatment of infectious diseases in humans [71].

In a recent study, gold nanoparticles of *Barleria cristata* leaf extract were found to have significant antibacterial activity has studied by S. Baskar and co-worker. To explore the production of gold nanoparticles, the leaves of *Barleria cristata*, which are regarded as one of the key therapeutic plants in indigenous systems of medicine and one of the dietary components used as a digestive in India, were employed. A significant amount of activity has been shown by the Au nanoparticles against various human diseases. According to research, gold has the best antibacterial properties of all the metals in the following order: Au>Zn>Fe>Mn>Mo>Sn.In the current investigation, all of the examined microorganisms responded more sensitively to higher (30 L/disc) Au sample concentrations compared to lower (15 L/disc) sample concentrations [72].

G. Madan Kumar *et al* has worked on synthesis of zinc oxide nanoparticles using leaf extract of *Barleria cristata* and its antimicrobial activity. He investigates a green method for producing biologically active zinc oxide (ZnO) nanoparticles using zinc nitrate (ZnNO3) and *Barleria cristata* leaf extract's bioactive components. The ZnO nanocrystallites, with an average size range of 30-35 nm, were created quickly, easily, and environmentally favourable. SEM scanning electron microscopy and X-ray diffraction (XRD) techniques were used to characterise zinc nanoparticles. The resulting particles are agglomerates of nanocrystallite and are spherical in shape. The hexagonal crystal form of ZnO is revealed by the X-ray patterns. Antimicrobial potential of ZnO on four pathogens (*Staphylococcus aureus* MTCC 3160*, Bacillus subtilis* MTCC 441, *Escherichia coli* MTCC 443 ) . Results showed that zinc oxide nanoparticles do indeed have powerful antibacterial properties. [73]

Based on the dimension of the inhibition zone against the ten bacteria tested, Darling Chellathai *et al* investigated the antimicrobial and antifungal properties of the ethanol extract of *Barleria cristata*. The plant extract demonstrated a strong antibacterial effect against *Vibrio spp.* with an inhibition zone diameter of 15 mm, followed by *Staphylococcus aureus* with a 14 mm diameter. *Salmonella, E. coli, Pseudomonas, Vibrio parahaemolyticus*, and *Aeromonas spp*. all exhibited moderate antibacterial activity at the same concentration, with inhibition zone sizes of 6 to 8 mm. In comparison to *Klebsiella* and *Proteus* species, the plant extract demonstrated the least antibacterial properties [74].

1. **Antifungal activity**

K. Amutha and D. Victor Arokia Doss [70] has reported antifungal activity of saponin fraction from leaves of *Barleria cristata in- vitro*  against four fungus species such as  *Aspergillus niger, Aspergillus fumigates, Aspergillus parasites* and *Candido albicans.*  by agar disc diffusion method by using Cotrimazole as a standard. The saponin fraction showed maximum activity against *Aspergillus parasites*(12 mm) followed by *Aspergillus parasites* (9mm),*Aspergillus fumigates* (9mm) *and Candido albicans* (9 mm).

S. Baskar *et al (*71) has investigated antifungal activity of ethanolic solvent extract of *Barleria cristata* leaves against *Candida albicans , Cryptococcus sp.Microsporum canis,Trichophyton rubrum* by usingItraconazole (10mcg/disc) as a standard.This was effective against *Trichophyton rubrum*. whereas smaller effect was observed in *Cryptococcus sp*.

 S. Baskar *et al* [72] has reported Antifungal activity of gold nanoparticles AuNps derived from *Barleria cristata* leaves against *Candida albicans , Cryptococcus sp. Microsporum canis, Trichophyton rubrum* by using Itraconazole (10mcg/disc) as a standard. Plant showed maximum activity against *Candida albicans (*10mm) followed by*, Cryptococcus sp.Microsporum canis* (9 mm), than , *Cryptococcus sp .Microsporum canis*(7mm).

G. Madan Kumar *et al* [73] has worked on antifungal potential of ZnO nanoparticles using leaf Extract of *Barleria cristata*

against *Aspergillus niger* at a concentration of12.5μg/ml and 6.25μg/ml, respectively. The Minimum fungal count for zinc oxide

nanoparticles was found to be same as minimum inhibitory concentration, i.e., 12.5μg/ml and6.25μg/ml, respectively.

 Darling Chellathai *et al* to evaluate the antifungal activity of the ethanolic leaf extracts of *Barleria cristata.* Among the five fungal spp. studied, the maximum zone of inhibition was shown by *Aspergillus niger* species which was only around 6 mm diameter at 1000μg/ml. All the other fungal species showed moderate susceptibility with inhibition zones ranging between 3 to 5 mm in diameter [74].

1. **Anti-inflammatory activity**

 Gambhire and his colleagues [75] investigated the anti inflammatory activity of fractions of the methanol extract of *Barleria Cristata* leaves in acute and chronic models of inflammation. Anti-inflammatory activity of pet ether, chloroform and methanol fractions of *Barleria Cristata* extract were studied by carrageenan induced rat paw edema and cotton pellet induced granuloma method at the dose levels of 50, 100 and 200 mg/kg. Indomethacin (10 mg/kg) was used as a positive control. Results of the study showed that chloroform fraction has moderate anti-inflammatory activity where as methanol fraction showed significant and dose dependent anti-inflammatory activity in both the models studied. Methanol fraction at dose of 200 mg/kg and indomethacin (10 mg/kg) significantly (P<0.05) inhibited (65.21% and 69.07 respectively) rat paw edema at the end of 4 h after carrageenan injection. In the cotton pellet induced granuloma method all the three fractions and Indomethacin showed significant (P<0.05) activity when compared with control group. Methanol fraction (200 mg/kg) showed maximum inhibition of 62.37 %(wet cotton) and 53.84 % (dry cotton) where as Indomethacin (10mg/kg) showed 68.04 % (wet cotton) and 59.61 % (dry cotton)inhibition of cotton pellet induced granuloma in rats. Results were analyzed by One-way ANOVA followed by Dunnett’s multiple comparison test P<0.05 and considered significant as compared to control. It is concluded that methanol fraction *of Barleria Cristata* Linn leaves exhibited significant anti-inflammatory activity.

Shahnaz banu was carried out the effect of methanolic extract of roots for its anti-inflammatory activity in rats. Oral administration of the extract at the doses 250 and 500 mg/kg b.w. exhibited dose dependent and significant anti-inflammatory activity in acute (carrageenan-induced hind paw edema) and chronic (cotton pellet granuloma models) inflammation. Animals receiving 500 mg/kg exhibited maximum inhibition (p<0.001) [76]. Apigenin, quercetin, naringenin, and luteolin, four therapeutically active flavonoids, may be responsible for the anti-inflammatory effect of BCW extract. Prostaglandin synthesis is known to be inhibited by flavonoids, and they can treat inflammation.

Gambhire MN [77] has investigated the anti inflammatory activity of the plant in different experimental screening methods. Anti inflammatory activity of aqueous extract of *Barleria cristata* leaves (BCW) at doses of 125, 250, and 500 mg/kg was evaluated in acute inflammatory models against carrageenan induced paw edema in rats, prostaglandins inhibitory activity, and acetic acid induced capillary permeability in mice. Results were analyzed by one-way ANOVA followed by Dunnettís test P < 0.05 and considered signifi cant compared to control. BCW significantly inhibited edema induced by carrageenan, inhibited significantly prostaglandin activity, and vascular permeability in mice dose dependently. Indomethacin (10 mg/kg) was used as a positive control. It is concluded that, aqueous extract of *Barleria cristata* Linn leaves exhibited significant anti inflammatory activity.

 M Gambhire [78] has worked on the methanol extract of *Barleria Cristata* leaves (BCM) was evaluated for anti-inflammatory activity using *in-vivo* and *in-vitro* methods. In the *in-vivo* inflammation tests, BCM significantly inhibited edema produced by histamine and serotonin in rats, also reduces significantly acetic acid-induced vascular permeability in mice dose dependently. In the *in-vitro* tests, the probable supporting mode by which BCM mediates its effects on inflammatory conditions was studied on red blood cells (RBC’s) exposed to hypotonic solution and thermally induced protein denaturation. BCM exhibited significant membrane-stabilizing property. Thermal induced protein denaturation was significantly inhibited by the extract. The effect was compared with the activity of Indomethacin and cyproheptadine as reference standard against different types of inflammation. Results of the study revealed that BCM possesses significant anti-inflammatory activity.

1. **Anti- hyperglycaemic activity**

 *Barleria cristata* leaf extracts have been studied for their *in- vitro* antidiabetic potential by Sakthivel Vasanth *et al* [79]. The anti-diabetic properties of *Barleria cristata's* leaf and root ethanol and petroleum ether extracts were investigated. The potential activity of the fractions was evaluated using the antidiabetic activity of α-amylase and α–glucosidase *in-vitro*. The results indicate that when compared to the control, ethanol and the petroleum ether leaf extract from *Barleria cristata* exhibit evidence of dose-dependent increases to inhibitory action on α-amylase and α-glucosidase enzymes. When when compared with petroleum ether extract, ethanolic leaf extract produced the highest levels of in vitro antidiabetic effect. According to the current identifying, *Barleria cristata* is capable of inhibiting alpha-glucosidase and alpha-amylase enzymes in vitro in a dose-dependent manner. In the rat model of alloxan-induced diabetes, the ethanol extracts from *Barleria cristata* seeds shown a dependent on the dose inhibitory effect on alpha-amylase activity and resulted in a significant decrease in blood glucose level.

 *Barleria cristata* (EtBc) ethanolic leaf extract was designed by Narmadha Rajasekaran *et al* to test the antihyperglycemic effects in diabetic rats induced by streptozotocin at dose level 400mg/kg body weight for the course of 45 days. Blood sugar levels in diabetic rats significantly decreased (P< 0.05) after EtBc administration. Alterations in body and organ weight were also noted, and the serum level of the glycemic profile, including insulin, C-peptide, total haemoglobin, and glycosylated haemoglobin levels, was normalised to be similar to that of control rats. So it was proposed that *Barleria cristata* could be effective by potentiating insulin release from the pancreas or by enhancing glucose absorption by muscle cells [80].

*Barleria cristata* Linn leaf extract was tested for its antidiabetic effects in rats by Mohd Nazam Ansari *et al* Alloxan (150 mg/kg) was administered intraperitoneally (IP) once to each of the seven groups of rats to cause diabetes. For a total of 21 days, ethyl acetate extract of leaves (EALE) and hydro-alcoholic leaves extract (HALE) were administered to animals at lower (250 mg/kg) as well as high (500 mg/kg) doses. Each week, blood sugar levels (BGL) and body weight were measured. On the 21st day, the rats were put to death under a light ether anaesthesia, and blood and vital organs were taken to calculate biochemical values and examine histological alterations. In all of the groups, only one dose of alloxan led to hyperglycemia. When compared to the normal control, the toxic control groups showed a consistent rise in BGL. Daily oral administration of the usual medication (Glimepiride, 5 mg/kg) along with the extracts (HALE and EALE) dramatically decreased high BGL (p< 0.001) and helped diabetic rats restore their body weight. The recovery of the biochemical profile showed that the extract treatment also enhanced the liver and kidneys' ability to operate normally. The research showed that *Barleria cristata* has potential anti-diabetic properties [81].

Ranjit Singh *et al* were screening for anti-diabetic activity of the ethanolic extract of *Barleria cristata* seeds. Alcoholic extracts of *Barleria cristata* dry seeds were tested for their ability to lower blood sugar levels in wistar rats (150–200 g). A digital glucometer was used to determine the blood sugar level. Taking seeds extracts orally at doses of 200 mg/kg resulted in a considerable drop in blood sugar levels. This provided the framework for investigating the substances in such anti-diabetic plants that are responsible for their hypoglycemic effects [82].

The objective of K. Amutha *et al* [83] was to assess the herb *Barleria cristata* L.'s hypoglycemic effects. *Barleria cristata* L. crude powdered leaf extract underwent phytochemical screening, which identified a number of bioactive phytoconstituents. In an acute toxicity investigation, *Barleria cristata* L. leaf extract in 50% hydroethanol was found to be safe for oral administration at all typical therapeutic levels. Alloxan was injected intraperitoneally into test subject rats to cause diabetes. In diabetic rats, the 50% hydroethanolic extract of *Barleria cristata* L. reduced blood glucose levels in a manner comparable to those of rats given Gibenclamid.

1. **Antiherlipidemic**

*Barleria cristata* Linn's hypolipidemic action in rats was examined by Mohd Nazam Ansari *et a*l [81]. In order to determine the normal functioning of essential organs including the liver and kidney, alloxan-treated groups had their blood lipid profile, creatine kinase, urea, serum glutamate oxaloacetate transaminase (SGOT), and serum glutamate pyruvate transaminase (SGPT) measured.

 The hypolipidemic potential of a 50% hydroethanolic extract of the leaves of *Barleria cristata* has been examined by K. Amutha et al. Rats with HLD treated with plant extract displayed dose-dependent hypolipidemic activity. All of the lipid components' levels—TC, TG, LDL, and VLDL cholesterol—were markedly decreased, while HDL, or beneficial cholesterol, was raised. The results of the current investigation made it abundantly evident that the leaf of *Barleria cristata* L., extracted with 50% hydroethanol, had created a hypolipidemic activity.

1. **Cardio protective activity**

Kowsalya J. *et al* [84] was intended to evaluate the *in vivo* cardio-protective activity of ethanolic extract of the leaves of Barleria cristata Linn. using Daphnia magna as the model. The ethanolic extract of *Barleria cristata* with a dose of 20, 40, 60, 80 and 100µg/ml were tested on lactose induced arrhythmia of Daphnia magna and compared with standard metoprolol. The cardio protective activity of ethanolic extracts of *Barleria cristata* Linn. were observed separately in the Daphnia magna of control, lactose induced, treated with metoprolol and ethanolic extract groups. The results showed that the ethanolic extract of the plant has dose dependent cardio-protective activity on Daphnia magna.

1. **Thrombolytic activity**

 Tasnuva Sharmin *et al* were performed with streptokinase as positive control and water as negative control. This assay reported that aqueous soluble fraction exhibited 0.22% of clot lysis. The extractives of *Barleria cristata* demonstrated mild tomoderate thrombolytic activity. The aqueous soluble fraction demonstrated 45.0±0.22% of clot lysis as compared to 65.66 % clot lysis by standard streptokinase [85].

1. **Hepatoprotective activity**

 *Barleria cristata* ethanolic leaf extracts have been shown to have in-vivo hepatoprotective efficacy against CCl4-induced liver damage in wistar rats at doses of 100 and 200 mg/kg bw, according to Balaji *et al* [86]. The serum levels of hepatospecific enzymes such SGPT, SGOT, ALP and total bilirubin levels, total protein levels, cholesterol and triglycerides levels are all significantly (P< 0.001) reduced by the ethanol-based extract of *Barleria.Cristata*. A well-known hepatoprotective medication utilised as a comparator, Silymarin (25 mg/kg), shown considerable efficacy (P< 0.001). Up to a dose of 2000 mg/kg body weight, the extract showed no signs of mortality. The biochemical analyses were supported by histopathological studies.

1. **Cytotoxic activity**

 Tasnuva Sharmin *et al* has worked on the methanol extract of leaves of *Barleria cristata* L. as well as its hexane, carbon tetrachloride, chloroform and aqueous soluble partitionates were subjected to screening for cytotoxic activities. In case of brine shrimp lethality bioassay, all the fractions demonstrated significant cytotoxic potential against A. salina with LC50 values ranging from 1.52 to 340.83 μg/ml. The hexane soluble fraction revealed the highest cytotoxic activity with LC50 value of 1.52±0.34 μg/ml as compared to 0.451 μg/ml for Vincristine sulphate [85].

 Mukul Pathy and its co-worker [87] has reported on cytotoxic activities of leaf and bark extracts. Hexane, Chloroform, Acetone and Methanol solvents were prepared using successive extraction method. All the extracts were tested for their cytotoxic activity using Brine shrimp lethality assay. Methanol extract of both leaf and bark showed highest activity to the tune of 94% and 83% respectively.

 Ali M. El-Halawany *et al* [88] has worked on Phenolics from *Barleria cristata* var. Alba as carcinogenesis blockers against menadione cytotoxicity through induction and protection of quinone reductase. The ethyl acetate fraction of B. cristata var. alba yielded five known compounds identified as verbascoside (1), isoverbascoside (2), dimethoxyverbascoside (3), p-hydroxy benzoic acid (4), and apigenin-7-O-glucoside (5). Among the tested compounds, isoverbascoside (2) was shown to potently induce the activity of the enzyme in a dose –dependent manner. As a functional assay for detoxification, compound 2 was the strongest toprotect Hepa-1c1c7 against the toxicity of menadione, a quinone substrate for NQO1.

 S. Baskar *et al* [72] has reported green synthesis of gold nanoparticles (AuNP) using leaves extract of *Barleria cristata* for some Pharmacological experiments. biological mechanism of gold nanoparticles (AuNPs) was studied with Hela cell line for the iranti cancer potentiality their anticancer activity confirmed by MTT assay on the cell lines of Hela carcinoma cells showed IC50 values of extract at 50 μg/mL.

1. **Antioxidant activity**

**In-vivo antioxidant activity**

Narmadha Rajase karan [88] has worked on antioxidants effect on ethanolic leaf extracts *Barleria cristata*(EtBc) in streptozotocin-induced diabetic rats at dose level 400mg/kg body weight for the treatment of 45 days. After the administration of EtBc and glibenclamide, the treated rats showed significant increase the activity of SOD, CAT, GPx and GR than diabetic rats. This result indicates the efficacy of the EtBc in preventing the oxidative stress a significant elevation of GSH level was observed in the extract treated diabetic control rats. This indicates that the extract can either increase the biosynthesis of GSH or reduce the oxidative stress leading to less degradation of GSH or have both effects.

 Mohd Nazam Ansari *In- vivo* evaluated the antioxidant activity of *Barleria cristata* extracts. Antioxidant marker such as TBARS, Protein carbonyl, SOD, catalyse, and GSH plays an important role by neutralizing free radical generated in the body (Table 6). A significant (*p* < 0.001) increase in TBARS and protein carbonyl level was observed in diabetic control when compared with the normal control. When therapy was started with lose dose of EALE, a significant ((*p* < 0.001)) decrease in TBARS and Protein carbonyl levels was observed while at high dose, a significant (*p* < 0.001) decrease in TBARS and moderate (*p* < 0.01) decrease in Protein carbonyl levels were observed [81].

 **In-vitro antioxidant activity**

 Sakthivel Vasanth and [79] his co-worker were to study the *in -vitro* antioxidant activity of *Barleria cristata* leaves extracts. Ethanol extract and petroleum ether extract of leaf and root of *Barleria cristata* were tested for their antioxidant activity.we evaluated the in vitro antioxidant activity of ethanol and petroleum ether extract of *Barleria cristata* by various assays such as DPPH and FRAP. For DPPH activity, it shows that the DPPH free radical scavenging capacity of ethanol extracts from *Barleria cristata* has proportionally increased from the increase in the concentration of *Barleria cristata* plant extract. Ferric reducing the ability of plasma assay shows that ethanol extracts from *Barleria cristata* inhibited more ferric reducing activity compared to petroleum ether extract.

 In the current study, the antioxidant profiles of the bark and leaves of the ornamental shrub *Barleria cristata* were investigated by Mukul Pathy *et al* both qualitative and quantitative assays were used to evaluate the extract's antioxidant properties. A DPPH assay based on thin layer chromatography was used for qualitative purposes, and ferric reducing antioxidant power (FRAP), nitric oxide radical scavenging, and DPPH radical scavenging were used for quantitative purposes. In comparison to bark extracts, leaf extracts displayed more anti-oxidant bands. This result was confirmed by the quantitative DPPH radical scavenging assay, in which acetone leaf extract demonstrated more than 80% radical scavenging while none of the bark extracts demonstrated more than 60% radical scavenging. Leaf and bark extracts in methanol and acetone demonstrated notable antioxidant properties [87].

Mohd Nazam Ansari *et al* [81] has evaluated *In-vitro* the antioxidant activity of *Barleria. Cristata* extracts. The antioxidant potential of three leaf extracts (HALE, EALE, and HLE) of *Barleria cristata* was as‐sessed by DPPH and H2O 2 radical-scavenging assay. Results show that all three extracts of B*arleria cristata* possess good antioxidant properties when compared to standard antioxidant (ascorbic acid). It would be pertinent to mention that HALE (DPPH-scavenging assay-IC50: 92 mg/mland H2O2-scavenging assay IC50: 464.83 mg/ml) and EALE (DPPH-scavenging assay. IC50:332 mg/ml and HO-scavenging assay IC50:544.19 mg/ml) showed the highest antioxidant activity, hence, used further for *in-vivo* animal studies. Whereas HLE extract showed mini‐mum antioxidant activity, hence not used for animal studies.

Tasnuva Sharmin has studied on methanol extract of leaves of *Barleria cristata* L. as well as its hexane, carbon tetrachloride, chloroform and aqueous soluble partitionates were subjected to screening for antioxidant,The antioxidant potential was evaluated by DPPH and Folin-Ciocalteau reagents using butylated hydroxytolune (BHT) and ascorbic acid as standards. In DPPH free radical scavenging assay, all the fractions demonstrated weak free radical scavenging activity. The carbon tetrachloride soluble fraction exhibited an IC50 value of 300.82±0.33 μg/ml that could be correlated to its phenolic content of 89.22±0.12 mg of GAE / g of extractives [85].

1. **Toxicity report**

Narmadha, R has worked on acute toxicity studies of ethanolic leaf extract of *Barleria cristata* were reported to be safe up tothe dose level of 2000 mg/kg p.o.in rats. The study was performed on wistar albino rats and observed periodically for any symptoms of toxicity and death within 24 h and then monitored daily for the next 14 days [88].

Administration of methanolic extract of root of *Barleria cristata* no side effects or mortality was detected in the mice up to 5 g/kg p.o., during 24‐h observation period. Based on the results, the dosages for the anti‐inflammatory activity were fixed at 250 mg/kgb.w.[76].

**XI. TLC and GC-MS Analysis Of**

***Barleria Cristata* Linn.**

Harini and his Co-worker [89] have investigated Thin-Layer Chromatography (TLC) analysis and Gas chromatography-mass spectroscopy (GCMS) analysis of the methanol extract of *Barleria cristata* Linn leaves. Thin-layer chromatography (TLC)of the methanolic extract was executed for five essential phytoconstituents Alkaloids, Flavonoids, Saponins, Glycosides, and Triterpenoids. The methanol extract of *Barleria cristata* Linn showed the presence of Alkaloid (Rf Value 0.42), Flavonoids (Rf Value 0.65), Saponin (Rf Value 0.33), Glycosides (Rf Value 0.54), and Terpenoids (Rf Value 0.17). TLC profiling of methanolic extract gives, the result which suggest towards the existence of high content of phytoconstituents.

The GC-MS examination of the methanolic extract of *Barleria cristata* leaves revealed a total of 15 compounds, each of which displayed distinct phytochemical properties. The major components present in leaves of *Barleria cristata* are Decanal, 4-Azido-Heptane, 2-Hydroxymethyl-9-[Beta-DRibofuranosyl]Hypoxanthine, 11-Tridecen-1-ol, Methyl Ester 13,16-Octadecadienoic Acid, N-[4-Bromo-N-Butyl]-2-Piperidinone, N-Methyl-N-Nitroso-1-Octanamine, 2-Methyl-6-Methylene-Octa-1,7-Dien-3-Ol, 4-Acetamido-1-Hexanol,1-(2-Propenyloxy)-Pentane, 4-Undecanone, (R, S)-2-Propyl-5-oxohexanal, 10-Methyl-4-undecanone, 1-Tetradecanamine, and N-Methyl-1-octadecanamine. The compounds N-[4-Bromo-N-Butyl]-2-Piperidinone was reported with high bactericidal inhibitor which can able totreat bladder spams, shrinkage, and ulcer inflammation, [90] Decanal were reported as it is used as a perfumes, [91]11-Tridecen-1-Ol were reported, it has antibacterial activity,[92] 4-undecanone were reported with antibacterial agent in pharmaceutical preparations [93]. GC-MS method is the direct analytical approach for identification of phytocompounds with only few grams of plant extract. The biological activity of several of these chemicals highlights the significance of our study. Therefore, from this study it can be concluded the methanolic extract of *Barleria cristata* Linn. has the ability to facilitate as a different source of therapeutic medications, because it contains phytoconstituents and other types of bioactive components which is described.

**XII. Synthesis of NanoPartical**

1. **Synthesis of zinc oxide nanoparticle**

 Madan Kumar *et al* synthesis of biologically active zincoxide (ZnO) nanoparticles by zinc nitrate (ZnNO3) and utilizin the biocomponents of leaves extract of *Barleria cristata*. The ZnO nanocrystallites of average size range of 30-35 nm have been synthesizedby rapid, simple and eco-friendly method. Zinc nanoparticles were characterized using scanning electron microscopy (SEM) and X-ray diffraction (XRD). The particles obtained are spherical in nature and are agglomerates of nanocrystallite. The X- ray patterns show hexagonal crystal type for ZnO. zinc oxide nanoparticles do have strong antibacterial and good antifungal activity against selected strains of bacteria and fungus as compared to that of conventional zinc oxide particles. In future, these nanoparticles might replace conventional preservatives in cosmetics. [73]

1. **Synthesis of Gold nanoparticle**

 S. Baskar *et al* has worked on the green synthesis of gold nanoparticles (AuNP) using leaves extract of *Barleria cristata* for some pharmacological experiments. Several human pathogens were used to screen the antimicrobial properties and biological mechanism of gold nanoparticles (AuNPs) was studied with Hela cell line for their anticancer potentiality. Aqueous extract (pH 7.4 - inherent pH of the extract) was reacted with 1mM Chloroauric acid (HAuCl4.3H2O) and kept at room temperature. The immediate change in colour from pale yellow to pink indicated the reduction of Au 3+ ions to Au 0. The synthesized AuNP’s were monitored using UV-Visible spectrophotometer. X-ray Diffraction (XRD), Fourier Transform Infrared Spectroscopy (FTIR), Scanning electron microscopy (SEM), and Dynamic Light Scattering (DLS). The *in-vitro* antimicrobial properties were confirmed by disc diffusion method on some human pathogens and their anticancer activity confirmed by MTT assay on the cell lines of Hela carcinoma cells showed IC50 values of extract at 50 μg/mL. AuNPs biosynthesized from *Barleria cristata* leaves also exhibits great antimicrobial and anticancer activities against some microbes and human cancer cell cultures. These biosynthesised gold nanoparticles can potentially be used for different medical applications [72].

**CONCLUSION**

The pharmacological and phytochemical studies have established that this is one of the most potential traditional medicinal plants which can be claimed for numerous medicinal application including tuberculosis, diabetes, skin infection, snakebite, bronchitis, toothache, inflammation and anaemia. It is pretty evident that *Barleria Cristata* acknowledged for numerous biological properties such as antibacterial, anti‐inflammatory, antidiabetic, antifungal, antioxidant, hepatoprotective and cytotoxic activity. Besides this, it is a good source of various compounds with diverse chemical structure such as triterpenes (oleanolic acid and β‐Sitosterol), Phenylethanoid glycosides (desrhamnosyl acteoside, acteoside and poliumoside), phenolic compounds (p‐Coumaric acid and α‐Tocopherol), flavonoidal compounds (luteolin, 7‐methoxyluteolin, apigene, narigenin) and iridoidal glycosides (Barlerin and Schanshiside methyl ester). Altogether, this data strongly support that this plant has potential therapeutic activity against certain disorders. In spite of scientific evidences regarding the medicinal properties of *Barleria cristata*, there are still several gaps in our understanding of the applications of this plant. The first gap is that it is worth the effort to do further pharmacological research on the crude extracts and active constituents from *Barleria cristata* which will standardize the medicinal use of this plant and would provide a scientific basis for the future development of new drugs from this plant.

 Although most of the data have been obtained on the pharmacological activity of plant extract through *in‐vitro* and animal‐based studies. Future research should be directed to bioassay‐guided isolation of individual compounds or chemical class of compounds responsible for the most promising pharmacological activity such as cytotoxic, antihyperglycaemic, antibacterial, anti‐ageing and antifungal in order to clarify their mechanism. Many of the isolated compounds should be tested for their pharmacological activity.

**CONFLIC OF INTEREST**

 We declare that we have no conflict of interest.

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