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# The Chemical Components and Pharmacological Functions of *Strobilanthes Cusia* (Nees) Kuntze

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## Abstract

Strobilanthes cusia (Nees) Kuntze is a member of the Acanthaceae family, and widely used as an antiinflammatory Traditional Chinese Medicine (TCM) in China since 1500's. As the development of the modern phytochemistry technologies, more and more compounds that have bioactivities were separated from the leaf, stem and root of *Strobilanthes cusia* (Nees) Kuntze. Through in vitro and in vivo experiments, people found many new functions of the extracts of this plant, such as antiviral, antibacterial and anticancer activities. Here we review the chemical components and pharmacological functions of *Strobilanthes cusia* (Nees) Kuntze, which may help people to understand this old TCM material and its new applications.

**Keywords:** Southern Ban-Lan-Gen; Traditional Chinese Medicine (TCM) application; Natural chemical components; Pharmacological activities; Anti-inflammatory; Antibacterial; Anticancer; Antiviral

### Introduction

Strobilanthes cusia (Nees) Kuntze, also known as Strobilanthes balansae Lindau or Baphicacanthus cusia (Nees) Bremek, is a member of the Acanthaceae family. It is mainly distributed in tropics and subtropics area of Asian including India, Thailand, Vietnam and Southern China. This herbaceous plant is listed in the Chinese Pharmacopoeia as the typical species for "Southern Ban-Lan-Gen". The root and stem of this plant has been widely used as herbal traditional Chinese medicines (TCM) to treat the diseases of fever, inflammatory and sore throat.

According to the "Compendium of Materia Medica", which was published in 1578, the source plants of medicinal materials "Ban-Lan" has two types of plants: "Songlan, leaves are like white woad; Malan, leaves are like bitter selling, that is, Guo Pu's

so-called big blue leaf, and the common so-called Ban-Lan". The Songlan is also known as "Northern Ban-Lan-Gen", which belongs to the Brassicaceae family, and its Latin name is Isatis indigotica Fort. The Malan is Strobilanthes cusia (Nees) Kuntze. These two types of herbs had both been used with the name of Ban-Lan-Gen for many years until 1995, when the Chinese Pharmacopoeia defined them separately as Northern and Southern Ban-Lan-Gen. Although share some common bioactive compounds such as indigo and indirubin, Northern and Southern Ban-Lan-Gen have very different profile of chemical components. Many papers had reviewed the chemical components and pharmacological functions of "Northern Ban-Lan-Gen": Isatis indigotica Fort [1-3]. In this review, we mainly focus on discussing the natural chemical components, pharmacological functions including anti-inflammatory, antibacterial, anticancer and antiviral, and applications of "Southern Ban-Lan-Gen", the plant species of Strobilanthes cusia (Nees) Kuntze.

#### **Chemical components**

Strobilanthes cusia (Nees) Kuntze has been used as an antiviral, antibacterial herb for many years, and the efforts to find out its active components had started as early as in 1970's. As more and more people devoted to the study, many chemicals were identified in *Strobilanthes cusia* (Nees) Kuntze, including alkaloids, glycosides, sterols, pentacyclic triterpenoids, flavonoids, organic acids, anthraguinones and polysaccharide.

**Alkaloids:** The alkaloids from *Strobilanthes cusia* (Nees) Kuntze include indoles, quinazolones and some other alkaloids. The most frequent reported indoles from *Strobilanthes cusia* (Nees) Kuntze are Indirubin and indigo, which were found in the root, stem and leaf of this plants [4,5]. Indigo is widely used in food, medicine and industrial dyeing, and indirubin has many pharmacological activities, for example, it can be used in the treatment of chronic myeloid leukemia (CML) and psoriasis [6,7]. The Quinazolone alkaloids from *Strobilanthes cusia* (Nees)

Kuntze include 4 (3H)-quinazolone and 2,4, (1H, 3H)quinazolone, etc. [8]. At present, there are 17 kinds of alkaloids had been identified in *Strobilanthes cusia* (Nees) Kuntze, and they were summarized in Table 1 [9-14].

**Table 1:** Alkaloids isolated from *Strobilanthes cusia* (Nees)Kuntze.

N o.	Compounds	Re f.
1	indirubin	5
2	indigotin	5
3	trptanthrin	8
4	4(3H)-quinazolinone	8
5	2 ,4,(1H,3H)-benzoyleneurea	8
6	2-methyl-4(H)-quinazolinone	8
7	indican	9
8	1H-indole-3-carboxylic acid	10
9	3-(2'-methyl-butyric acid methyl ester)-1H-indole	10
10	2-benzoxazolinone	11
11	2-hydroxy-1,4-benzoxazin-3-one	11
12	$(2R)$ -2-O- $\beta$ -D-glucopyranosyl-2H-1,4-benzoxazin-3(4H)-one	12
13	(2R)-2-O-β-D-glucopyranosyl-4-hydroxy-2H-1,4- benzoxazin-3(4H)-one	12
14	baphicacanthin A	13
15	baphicacanthin B	13
16	(2R) -2-O-β-D- glucopyranosyl-5-hydroxy-2-1,4- benzoxazin-3(4H)-one	14
17	7-chloro-(2R)-2-O- $\beta$ -D-glucopyranosyl-2H-1,4-benzoxazin-3(4H)-one	14

**Glycosides:** Many phenylpropanoid glycosides, lignans and their glycoside derivatives were found in *Strobilanthes cusia* (Nees) Kuntze. Xiao et.al had isolated a variety of glycosides from the root of *Strobilanthes cusia* (Nees) Kuntze with methanol extraction [14]. Many of those extracts, such as akoside, isoakoside, carrageenin, alloflavin and (+)-clove-o- $\beta$ -d-glucoside, had good antioxidant activities. The glycosides found in *Strobilanthes cusia* (Nees) Kuntze were summarized in Table 2 [12,14-16].

**Table 2:** Glycosides isolated from *Strobilanthes cusia* (Nees)Kuntze.

N o.	Compounds	Re f.
18	Uridine	12
19	pinoresinol-4-O- $\beta$ -D-apiosyl-(1 $\rightarrow$ 2)- $\beta$ -D-glucopyranoside	12
20	Isoacteoside	14
21	Martynoside	14
22	Isomartynoside	14

23	Verbasoside	14
24	β-phenylethoxy-β-D-glucopyranoside	14
25	1,2-O-[2S-(3,4-dihydroxyphenyl)-I,2-ethanediyl]-3-O-a-L- rhamnopyranosyl-6-O-caffeoyl-β-D-glucopyranoside	14
26	$\label{eq:2-(3,4-dihydroxyphenyl)ethyl-(6-O-ethyl)-\beta-D-glucopyranoside} 2-(3,4-dihydroxyphenyl)ethyl-(6-O-ethyl)-\beta-D-glucopyranoside$	14
27	(+)-syringaresinol	14
28	(-)-episyringaresinol	14
29	(+)-syringaresinol-O-β-D-gIncopyranoside	14
30	5',5"-dimethoxy-4"-hydroxy-2,4,6,8-diepoxylingan-4'-O-β-D- glucopyranoside	14
31	Eleutheroside E	14
32	(+)-lyoniresinol-3a-O- $\beta$ -apiofura-nosyl-(1 $\rightarrow$ 2)- $\beta$ -D-glucopyranoside	15
33	cusianoside A	15
34	cusianoside B	15
35	$(+)$ -5,5'-dimethoxy-9-O- $\beta$ -D-glucopyranosyl lariciresinol	15
36	(+)-9-O-β-D-glucopyra-nosyl lyoniresinol	15
37	(+)-5,5'-dimethoxy-9-O- $\beta$ -D-glu-copyranosyl secoisolariciresinol	15
38	Acteoside	15
39	[(2-(3,4-dihydroxyphenylethyl))-3-O-a-L-rhamnopyranosyl-(1 $\rightarrow$ 4)- (4-O-caffeoyl)- $\beta$ -D-glucopyranoside]	16
40	adenosine	16

**Sterols:** Several sterols were found in the roots, leaves and fruits of *Strobilanthes cusia* (Nees) Kuntze, and they were reported having many physiological effects, such as antioxidation, immune regulation, cholesterol reduction, on human. Wu et al. had extracted stigmasterol-5,22-diene-3  $\beta$ , 7  $\beta$ -diol and stigmasterol-5,22-diene-3  $\beta$ , 7  $\alpha$ -diol from *Strobilanthes cusia* (Nees) Kuntze with petroleum ether, and found that they have some antitumor activity [17]. The sterols isolated form *Strobilanthes cusia* (Nees) Kuntze were summarized in Table 3.

Table 3: Sterols isolated from Strobilanthes cusia (Nees) Kuntze.

No.	Compounds	Ref.
41	β-daucosterol	14
42	spinasterol-3-O-β-D-glucopyranoside	16
43	stigmasterol-3-O-β-D-glucopyranoside	16
44	stigmasta-5,22-diene-3β,7β-diol	17
45	stigmasta-5,22-diene-3β,7a-diol	17
46	β-sitosterol	18

**Pentacyclic triterpenoids:** Chen et.al had extracted lupanone, lupinol and betulin, all of which were soluble in organic matter and insoluble in water, and identified as pentacyclic triterpenoids, from *Strobilanthes cusia* (Nees) Kuntze in 1987 [18]. However, not too many pentacyclic triterpenoids are identified since then. At present, only four pentacyclic

triterpenoids were found from *Strobilanthes cusia* (Nees) Kuntze , and they were summarized in Table 4 [18,19].

**Table 4:** Pentacyclic triterpenoids isolated from *Strobilanthescusia* (Nees) Kuntze.

No.	Compounds	Ref.
47	lupenone	18
48	lupeol	18
49	betulin	18
50	2,3-dihydroxy-12-oleanen-28-oic acid	19

**Other compounds:** Many other compounds such as flavonoids, organic acids, anthrones, sugars and amides were found in *Strobilanthes cusia* (Nees) Kuntze. Wu et.al had isolated 5,7,4 '-trihydroxy-6-oxyflavone and 3', 4 ', 5,7-tetrahydroxydihydroflavonol from the root of *Strobilanthes cusia* (Nees) Kuntze in 2005, and these are the first reported flavonoids obtained from the plant of *Acanthaceae* family [10]. All other compounds isolated form *Strobilanthes cusia* (Nees) Kuntze were summarized in Table 5 [10,11,14,16,19-21].

**Table 5:** Other compounds isolated from *Strobilanthes cusia*(Nees) Kuntze.

No.	Compounds	Ref.
70	5,7,4'-trihydroxy-6-methoxyflavone	10
71	3',4',5,7-quadrihydroxy-flavanonols	10
72	4-hydroxy-3-methoxybenzoic acid	11
73	lauric acid	19
74	11,12-dihydroxy-7,9-octadecadienoic acid	19
75	sucrose	16
76	polysaccharide	20
77	Chrysophanol	21
78	monobutyl phthalate	14
79	dibutyl phthalate	14
80	Nicotinamide	14
81	Squalene	14

#### Pharmacological activities

Many ancient TCM books had recorded that "Ban-Lan-Gen" has the functions of "detoxification, cooling blood and eliminating swelling", and modern researches show that *Strobilanthes cusia* (Nees) Kuntze has many pharmacological functions with anti-inflammatory, anti-bacterial, anti-tumor and anti-virus activities.

Anti-inflammatory: People had found that *Strobilanthes cusia* (Nees) Kuntze has anti-inflammatory activities and can enhance the mouse immune system. Tao et al. reported that injection of the water extracts of *Strobilanthes cusia* (Nees) Kuntze into the mouse can inhibit auricle inflammation induced by xylene, and

increase the permeability of capillary [22]. Luo et al. found that *Strobilanthes cusia* (Nees) Kuntze can significantly alleviate the ear swelling induced by xylene injection in mice, reduce the weight of granuloma in rats, and improve the spleen and thymus index in mice [23].

Zhou et al. found that oleoresin acetate from *Strobilanthes cusia* (Nees) Kuntze can block NF- $\kappa$  B signal pathway, and down regulating the expression of inflammatory factors induced by influenza A virus (IAV). IL-17 is a cell factor that induces inflammation [24]. It was found that indirubin and tryptophan can significantly reduce the expression of IL-17, suggesting that indirubin and tryptophan have anti-inflammatory activities [25]. In addition, many benzodiazinone derivatives were found in *Strobilanthes cusia* (Nees) Kuntze, and those benzodiazinone derivatives were found to be able to inhibit the inflammatory response through reducing the release of histamine [12,13].

Anti-bacterial: Strobilanthes cusia (Nees) Kuntze extract has a broad-spectrum anti-bacterial effect, and its inhibitory effect on Staphylococcus aureus and Escherichia coli is stronger than that of Isatis indigotica Fort extract [10]. Wei et al. found that Strobilanthes cusia (Nees) Kuntze extract can enhance the inhibitory effect of lincomycin on Staphylococcus aureus, Escherichia coli and Bacillus subtilis [26]. Tryptamine and indole derivatives may be the main components of Strobilanthes cusia (Nees) Kuntze that responsible for its antibacterial function, for example, Kataoka et al. found that tryptamine can significantly inhibit the growth of Helicobacter pylori in a dose-dependent manner both in vitro and in vivo [27]. Wei et al. found that n '- $\beta$ -D-glucopyranosyl indirubin from Strobilanthes cusia (Nees) Kuntze had some antibacterial activity against Staphylococcus aureus [25]. In addition, indirubin was also reported to be able to inhibit the growth of Staphylococcus aureus and Staphylococcus epidermidis, with the minimum inhibitory concentrations of 12.5 mg/L and 25 mg/L respectively [28].

Sterols from Strobilanthes cusia (Nees) Kuntze, such as stigmasterol and  $\beta$  - sitosterol, also have good inhibitory effects on the inhibition of Agrobacterium, Escherichia coli, Staphylococcus and Bacillus subtilis [29]. Chrysophanol was found to have very strong anti-inflammatory effect, for example, the commonly used anti-bacterial and anti-inflammatory agents ferrofluid tincture and Mongolian prescription "TRSDL" all contain chrysophanol as the active component [30,31]. So, the chrysophanol from Strobilanthes cusia (Nees) Kuntze may also contribute to its anti-bacterial effect.

**Antitumor:** Many researchers had found that *Strobilanthes cusia* (Nees) Kuntze has the antitumor effect. Xiao et.al reported that akoside, a phenylethanolic glycoside isolated from *Strobilanthes cusia* (Nees) Kuntze, can significantly inhibit the growth of tumor cell line CB3 with IC50 at  $2.26 \pm 0.22 \mu$  mol/L [14]. Indirubin was found to inhibit the growth of a variety of human tumor cells form liver, lymphoid, cervical and leukemia [32]. Zhang et al. showed that indirubin can inhibit the growth of Bcl-2 gene [33]. Tryptophan is also an important active antitumor component from *Strobilanthes cusia* (Nees) Kuntze. It can inhibit the proliferation of hepatoma cell BEL-7402 and ovarian carcinoma cell A2780, induce tumor differentiation,

reduce telomerase activity and reverse the tumor transformation [34]. Ren had studied the effects of chrysophanol on the growth of breast cancer cells, and found that chrysophanol can affect the cell cycle and proliferation of breast cancer cells through inhibiting the phosphorylation of NF -  $\kappa$  B, reducing the downstream gene expressions regulated by NF- $\kappa$  B/Bcl-2 signal pathway, thus promote the apoptosis of breast cancer cells [35].

**Antiviral:** *Strobilanthes cusia* (Nees) Kuntze has been used to treat influenza, pneumonia and other viral diseases in China for many years, for examples, it has been used to treat viral pneumonia, cough and asthma, and it was also reported to be used in treating herpes simplex virus induced keratitis [36,37].

Many studies have shown that *Strobilanthes cusia* (Nees) Kuntze has antiviral effects. Qin et al. found that *Strobilanthes cusia* (Nees) Kuntze extracts can inactivate the influenza A virus through chicken embryo culture experiment [38]. Luo et al. studied the antiviral effects of *Strobilanthes cusia* (Nees) Kuntze using influenza virus FM1 mice model and herpes simplex virus rabbit model, and the results showed that *Strobilanthes cusia* (Nees) Kuntze could significantly prolong the average survival days and lower the death rate of influenza A virus infected mice, and reduce the degree of keratitis in herpes simplex virus infected rabbits [39]. In addition, it showed that extracts of *Strobilanthes cusia* (Nees) Kuntze extract significantly inhibits the expression of TMV coat protein [40,41].

Some compounds separated from *Strobilanthes cusia* (Nees) Kuntze were also proved to have antiviral activities. It is found that lectin from *Strobilanthes cusia* (Nees) Kuntze has the hemagglutination activity and can prevent influenza virus from infecting cells [42]. The *Strobilanthes* A and 2 (H)-benzoxazolone from *Strobilanthes cusia* (Nees) Kuntze can also inhibit the influenza A virus with IC50 of (29.2 ± 5.8)  $\mu$  mol/L and (46.0 ± 8.4)  $\mu$  mol/L, respectively. In addition, 4 (3H)-quinazolone from *Strobilanthes cusia* (Nees) Kuntze can also lower the infectivity of influenza virus and Coxsackie virus, while promote the proliferation rate of spleen cell and lymphocyte [43].

#### **Medicinal applications**

Strobilanthes cusia (Nees) Kuntze is widely used in many TCM products that were effectiveness at relieving pain, eliminating inflammation and detoxification. For example, " Southern banlangen preparation" is commonly used in treating mumps, pharyngitis, mastitis and furuncles diseases. " Children antipyretic suppository", a Strobilanthes cusia (Nees) Kuntze based prescription, can relieve children's fever, sore throat, phlegm and cough. In addition, Strobilanthes cusia (Nees) Kuntze has also been used in the breeding industry as antibiotic substitutes to improve animal immunity and prevent animal diseases. Lin et.al had invented an animal feed additive, which containing Strobilanthes cusia (Nees) Kuntze as the major ingredient, to improve the pig immunity and reduce the illness and mortality rate of pigs [44,45].

## Conclusion

As a traditional Chinese medicine ingredient, *Strobilanthes cusia* (Nees) Kuntze plays an important role in disease prevention. In many areas of South China and South Asia, *Strobilanthes cusia* (Nees) Kuntze is one of the most frequently used TCM in cold and fever treatment, and will have more prospect applications and a greater market potential in the near future. However, more comprehensive and in-depth exploration of *Strobilanthes cusia* (Nees) Kuntze is needed to identify more chemical components, dig out the mechanism under its pharmaceutical effects, especially the targets and pathway of the effective components. We believe these researches will give *Strobilanthes cusia* (Nees) Kuntze a greater opportunity for the drug development and market application.

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# **Conflict of Interest**

The authors declare no financial or commercial conflict of interest.

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