REVIEW
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Botanical, quality control, phytochemistry, pharmacology and toxicity characteristics of *Corydalis bungeana* Turcz.: a review

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Author contributions

HY wrote the first draft, AB and MF made critical revision and all authors approved the final version of the manuscript.

Competing interests

The authors declare no conflicts of interest.

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Abbreviations

CB, *Corydalis bungeana* Turcz.; HPLC, high-performance liquid chromatography; NMR, nuclear magnetic resonance; TLC, thin layer chromatography; HPLC-Q-TOF-MS, high-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry; HPLC-Triple-TOF-MS/MS, high performance liquid chromatography tandem triple time-of-flight mass spectrometry; NO, nitric oxide; iNOS, Inducible Nitric Oxide Synthase; HO-1, Heme oxygenase-1; Nrf2, Nuclear factor-E2-related factor 2; MPO, Myeloperoxidase; MDA, Malonaldehyde; NQO1, Quinone oxidoreductase 1; NLRP3, NOD-like receptor protein 3; ROS, Reactive oxygen species; mTOR, Mammalian target of rapamycin; LPS, lipopolysaccharide; GSK3, glycogen synthase kinase 3 beta; UC, Ulcerative colitis; LSD1, Lysine-specific demethylase1.

Citation

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Abstract

Corydalis bungeana Turcz. (CB) is a medicinal herb with significant medicinal value in traditional Chinese medicine. This paper reviews the progress of research on CB's botany, quality control, phytochemistry, pharmacology and toxicity. The plant's information was gathered from scientific databases such as PubMed, GeenMedical, Springer Link (https://link.springer.com), Chinese National Knowledge Infrastructure, Pharmacopoeia and Flora. Currently, 137 phytochemicals have been identified and isolated from CB, including alkaloids, flavonoids, amino acids, terpenoids, coumarins and organic acids. In addition, many phytochemicals reported various antiinflammatory, antibacterial, antiviral, antitumor, analgesic, hepatoprotective, immunomodulatory, neuromodulatory, and lipid reduction activities. However, the study of its toxicity is still at the preliminary exploration stage and needs further intensive exploration. Herein, we provide an in-depth investigation of the progress of CB to elucidate the underlying mechanisms of activity of CB extracts and its major components, deliver valuable resources and information for further research and rational drug use, and explore the potential research directions and prospects of CB.

Keywords: *Corydalis bungeana* Turcz.; botany; quality control; phytochemistry; pharmacology; toxicity

Introduction

Dried whole herb *Corydalis bungeana* Turcz. (CB, named Kudiding in Chinese) is among the most conventionally applied medications in China. It is a perennial plant in the *Papaveraceae* family. It is widely spread in northern and eastern China, southeastern Mongolia, northern Korea, and the Razdolnoye River Valley in Russia [1]. It was first included in the Chinese Pharmacopoeia in 1977 for its bitter and cold properties [2]. CB has been used since the Tang Dynasty and was first described in the journal of traditional Chinese medicine. Traditionally, it has been used to clear heat and detoxify toxins, disperse nodules and eliminate swelling, and is widely used to treat various inflammatory diseases such as colds and coughs, particularly rheumatism and myocarditis [3, 4].

Scholars have conducted comprehensive investigations on CB in recent years. Phytochemical studies on the dried whole herb of CB showed a variety of phytochemicals that have been structurally sequestered and recognized. Among them were alkaloids [5–8], flavonoids [9, 10], amino acids [11], triterpenes [12], and other components. Particularly alkaloids considered the primary active ingredients in CB, have a range of biological activities [13]. In addition, pharmacological investigations proved that CB possesses a variety of pharmacological activities such as antiinflammatory [4, 14], analgesic [15, 16], antitumor [17], antiviral bacteriostatic [18], immunomodulatory [19], neuromodulatory [20] and lipid reduction effects [21]. Furthermore, some studies and reports have shown that CB causes malformation in fetal rats at a specific dose. Other authors proved no effect on pregnant rats, thus highlighting the need for further investigation of its teratogenicity mechanism [22, 23]. The chemical composition of CB and the pharmacological effects of its extracts and isolated components have been studied to date, but the safety aspects remained elusive.

We have systematically collected and compiled the CB-related literature from 1973 to 2023. We have further summarized the recent advances in its botany, quality control, phytochemistry, pharmacology and toxicity. This allowed us to elucidate the underlying mechanisms of activity of CB extracts and its major components, deliver valuable resources and information for further research and rational drug use, and explore the potential research directions and prospects of CB.

Materials and methods

Searches in multiple literature databases were used to find the material for this study, including GeenMedical (https://www.geenmedical.com/), PubMed (https://pubmed.ncbi.nlm.nih.gov/), Springer Link (https: // link. springer.com/), the Chinese National Knowledge Infrastructure (https: //kns.cnki.net/), by searching with the keywords "*Corydalis bungeana* Turcz." and its isolate components, "pharmacological activities", "chemical composition", etc. Among them, the earliest literature was published in 1973, and the latest paper was published in 2023. Different online websites like https://image.cubg.cn/ and http://www.iplant.cn/ were used to find botany information. Pub Chem (https://pubchem.ncbi.nlm.nih.gov/) and Chem Spider (http://www.chemspider.com/) were used to proofread CB chemical structure. Finally, the Chem Draw 14.0 software was used to sketch the chemical structure of the compounds isolated and identified from CB.

Results

Botany

CB has been found to grow in large numbers in the northern and eastern parts of China, as well as in the southeastern parts of Mongolia, the northern parts of Korea, and the Razdolnaya River Valley in Russia [1]. CB is a perennial herb with a height of 10–50 cm. The stems are tender and grow erect or obliquely, branched from the base to the periphery, with longitudinal ridges, grey-green, and smooth and glabrous. The inflorescences are racemose, first dense, then sparse, with flowers pink to lavender and spreading. The sepals are broadly oval to triangular, about 0.7–1.5 mm long and with toothed margins. These sepals are often caduceus. Apices of outer petals are depressed, with shallow corolla-like projections and toothed margins. The spur obliquely extends upward, with terminal saccate expansion. The nectaries occupy about 2/3 of the spur length, with thickened ends. The lower petals project slightly forward, while the apices of the inner petals are dark purple. The leaves are primarily crinkled and broken, the sides of the leaves are dark green or grey-green, the entire leaf blade is 2-3-pinnately divided, one pinnule is in 3–5 pairs, with a short stalk, the second pinnule is in 2–3 pairs, apically split into short lobes, and the lobes are apically rounded. The capsules are oval, grey-green, usually pendulous, 1.2–2 cm long, 3–5 cm wide, and contain 2 rows of seeds. When the fruit is ripe, it splits into 2 valves, containing about 5–12 seeds. The seeds are tiny, heart-shaped, black, shiny, and with a white membrane next to the seed navel. The roots are slender, less branched, conical and yellowish brown. It is found on rocky slopes or river floodplains near the sea to 1500 m. According to the Chinese Pharmacopoeia (Edition 2020), CB is harvested, washed, cut and dried in summer [3, 24]. CB images and their slices are shown in Figure 1.

Quality control

In this paper, we have compiled literature on the quality control of CB from a wide range of scholars in recent years. CB contains alkaloids, flavonoids, amino acids and other chemical components. However, the quality of CB is affected by geographical location, climatic environment, harvest time, cultivation techniques, processing method and other aspects [25]. According to the 2020 edition of the Chinese Pharmacopoeia, CB content and quality control were identified using thin-layer chromatography. There is a requirement for the impurities and moisture content not to exceed 2% and 13%, respectively. Moreover, there is another requirement in the hot leaching method to determine quality control: the leachate should not drop below 18%. Notably, when high-performance liquid chromatography (HPLC) is used to determine content, corynoline concentration must exceed 0.14%, and its peak value must be above 6000. The ratio of methanol to 0.015 mol/L phosphate buffer (pH 6.7) must be 70:30 to create the mobile phase, and the detection wavelength must be 289 nm. Nevertheless, according to the theory of traditional Chinese medicine, it is difficult to reflect the overall quality of medicinal materials only by measuring the content of index components [26]. Employing more advanced detection techniques is required to examine as many physiologically active substances as qualitatively and quantitatively as feasible. Columbamine, coptisine, berberrubine, sanguinarine, worenine, berberine, jateorhizine, protopine, tetrahydropalmatine,

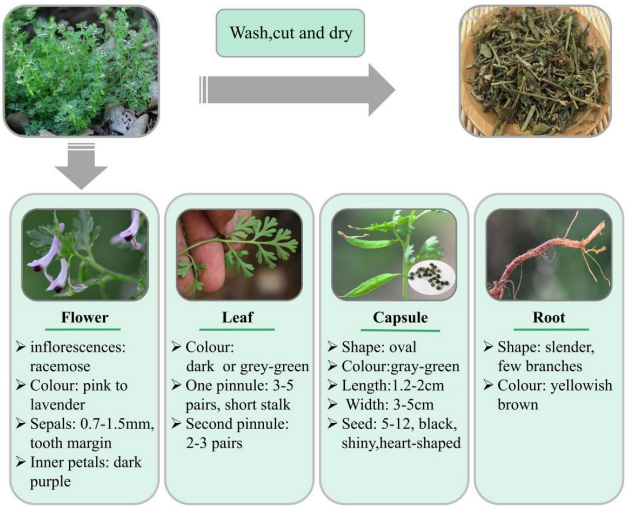

Figure 1 Botanical description of *Corydalis bungeana* Turcz.

corynoline, 8-oxocorynoline, and acetylcorynoline were all detected by Dong et al. by UHPLC-MS/MS (ultra HPLC method) that helped him to create the fingerprint profile of CB [6]. Tian et al., on the other hand, used UHPLC-ESI-MS/MS and detected 44 compounds, among which quantified 14 alkaloids, in the range of 9.74–13 ng/mL, whereas the linearity of the standard curves was between 0.9991–0.9995 [12]. Han et al. used HPLC to perform a comprehensive spectroscopic data analysis, including high-resolution electrospray ionization mass spectroscopy, nuclear magnetic resonance, electronic circular dichroism, and electronic circular dichroism computation, was used to explain the structures and absolute configurations of 17 alkaloids [8]. Additionally, an HPLC-Q-TOF/MS method was developed to identify 31 compounds in CB, including corynoline, 8-oxocorynoline, sanguinarine, and kaempferol. Meanwhile, measurements of the plasma, bile, urine, and faeces of rats given oral CB extracts at various times revealed the entry of 21 compounds, including corynoline, into the body [7]. One recent study compared the chemical composition and relative contents of CB treated by different drying methods, using HPLC-Triple-TOF-MS/MS. The findings demonstrated that the various drying techniques significantly impacted the quality of CB, and a total of 37 distinct chemical components were found [11].

Study on phytochemistry

CB contains various chemical components, including alkaloids, flavonoids, coumarins, and triterpenes. In addition, CB is also rich in amino acids required by the human body [11]. In this section, we summarize the main chemical constituents of CB, and the structures are shown in Figure 2.

Alkaloids compounds. Alkaloids are an important class of natural organic compounds, cyclic compounds containing negative oxidation state nitrogen ions and present in biological organisms, including isoquinolines, pyrroles, piperidines, indoles, tropanes, etc. Recent studies mainly focused on alkaloid compounds, and at least 104 components have been isolated and identified from the extracts of CB. The components of alkaloids isolated from CB are summarized in Table 1.

Flavonoids compounds. Flavonoids are derived from the parent nucleus 2-phenyl chromogenic ketone-compounds composed of C_6-C_3-C_6 units and have various physiological properties like antioxidant, antiviral, hepatoprotective, antiinflammatory, anticancer, and others. Flavonoid components isolated from CB were summarized in Table 2. They were mainly kaempferol and quercetin. Due to the paucity of research on flavonoid components in CB, researchers should pay close attention to this pharmacologically active component.

Amino acid compounds. Amino acids are the basic units that build proteins. They also contain carbon and nitrogen, making them safe and effective plant nutrients. Currently, there are exceptionally few studies of amino acid components in CB, and 11 components have been isolated, namely aspartic acid, leucine, L-tyrosine, L-proline, L-glutamic acid, L-threonine, phenylalanine, Trans-4-hydroxy-L-proline, γ-glutamyl valine and γ-aminobutyric acidas (Table 3).

Table1 Chemical composition of alkaloids in *Corydalis bungeana* Turcz.

No.	Chemical compounds	Method	Molecular weight	Ref.
1	Corybungine A	HPLC, NMR	464	[5]
2	Corybungine B	HPLC, NMR	366	[5]
3	Corybungine C	HPLC, NMR	402	[5]
4	Corybungine D	HPLC, NMR	462	[5]
5	Corybungine E	HPLC, NMR	554	[5]
6	Corybungine F	HPLC, NMR	418	[5]
7	Corybungine G	HPLC, NMR	418	[5]
8	Corybungine H	HPLC, NMR	458	[5]
9	Corybungine I	HPLC, NMR	446	[5]
10	Corybungine J	HPLC, NMR	376	[5]
11	Corybungine K	HPLC, NMR	328	[5]
12	7'-(3',4'-dihydroxy phenyl)-N-[(4-meThoxyphenyl)-ethyl]propena-mide	UHPLC-MS/MS	314	[6]
13	Coptisine	UHPLC-MS/MS	320	[6]
14	Sanguinarine	UHPLC-MS/MS	332	[6]
15	Columbamine	UHPLC-MS/MS	338	[6]
16	Palmatine	UHPLC-MS/MS	352	[6]
17	Tetrahydropalmatine	UHPLC-MS/MS	355	[6]
18	Scoulerine	HPLC-Q-TOF-MS	328	[7]
19	Cheilanthifoline	HPLC-Q-TOF-MS	326	[7]
20	Isopordine	HPLC-Q-TOF-MS	328	[7]
21	Tetrahydroberberine	HPLC-Q-TOF-MS	340	[7]
22	Tetrahydroepiberberine/sinactine	HPLC-Q-TOF-MS	340	[7]
23	N-trans-feruloyl tyramine	HPLC-Q-TOF-MS	314	[7]
24	Spallidamine	HPLC-Q-TOF-MS	392	[7]
25	Hengzhou aconitine	HPLC-Q-TOF-MS	300	[7]
26	Corytuberine	HPLC-Q-TOF-MS	328	[7]
27	Bicullinine	HPLC-Q-TOF-MS	368	[7]
28	Oxysanguinarine	HPLC-Q-TOF-MS	348	[7]
29	13,14- dihydrosanguinarine	HPLC-Q-TOF-MS	334	[7]
30	Norsanguinarine	HPLC-Q-TOF-MS	318	[7]
31	Protopine	HPLC-Q-TOF-MS	355	[7]
32	Corynoloxine	HPLC-Q-TOF-MS	366	[7]
33	Corycavine	HPLC-Q-TOF-MS	368	[7]
34	Acetylisocorynoline	HPLC-Q-TOF-MS	410	[7]
35	11-epicorynoline	HPLC-Q-TOF-MS	369	[7]
36	13-epicorynoline	HPLC-Q-TOF-MS	368	[7]

HPLC, high-performance liquid chromatography; NMR, nuclear magnetic resonance; HPLC-Q-TOF-MS, high-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry.

Table1 Chemical composition of alkaloids in *Corydalis bungeana* Turcz. (*Continued*)

No.	Chemical compounds	Method	Molecular weight	Ref.
37	8-oxycorynoline	HPLC-Q-TOF-MS	382	[7]
38	12-hydroxycorynoline	HPLC-Q-TOF-MS	384	[7]
39	Diding-corydaline	HPLC-Q-TOF-MS	394	[7]
40	Tetrahydrocoptisine	HPLC-Q-TOF-MS	325	[7]
41	D-isocorydine	HPLC-Q-TOF-MS	354	[7]
42	Corysamine	HPLC-Q-TOF-MS	338	[7]
43	Bungeanoline A	HPLC, NMR, UV	398	[8]
44	Bungeanoline B	HPLC, NMR, UV	388	[8]
45	Bungeanoline C	HPLC, NMR, UV	438	[8]
46	Bungeanoline D	HPLC, NMR, UV	286	[8]
47	Corynoline	HPLC, NMR, UV	367	[8]
48	Adlumidiceine	HPLC, NMR, UV	399	[8]
49	6,7-Methylenedioxy-1(2H)-isoquinolinone	HPLC, UV, NMR	189	[9]
50	6,7-Methylenedioxy-2-(6-acetyl-2,3-methylenedioxybenzyl)-1(2H)-isoquinolinone	HPLC, UV, NMR	366	[9]
51	1, 2, 3, 4, 4α, 9β-hexahydro-5- (4- methoxy - 1, 4- dioxobutyl) - 2, 2, 8 - trimethyl - , (4αS, 9βR) - 5H - pyrido[4, 3 - b]indo-lium	TLC, NMR	318	[10]
52	Boldine	HPLC-Triple-TOF-MS/MS	328	[11]
53	Papaverine	HPLC-Triple-TOF-MS/MS	340	[11]
54	Noscapine	HPLC-Triple-TOF-MS/MS	414	[11]
55	Rhoeadine	HPLC-Triple-TOF-MS/MS	384	[11]
56	Oxoglaucine	HPLC-Triple-TOF-MS/MS	352	[11]
57	Berberine	UHPLC-ESI-MS/MS, UV, NMR	336	[12]
58	Berberrubine	UHPLC-ESI-MS/MS, UV, NMR	322	[12]
59	Salutaridine	UHPLC-ESI-MS/MS, UV, NMR	327	[12]
60	Isobokline	UHPLC-ESI-MS/MS, UV, NMR	311	[12]
61	Jateorhizine	UHPLC-ESI-MS/MS, UV, NMR	338	[12]
62	Protopine	UHPLC-ESI-MS/MS, UV, NMR	353	[12]
63	8-oxocorynoline	UHPLC-ESI-MS/MS, UV, NMR	381	[12]
64	Corydaline	UHPLC-ESI-MS/MS, UV, NMR	369	[12]
65	Corynoxeine	UHPLC-ESI-MS/MS, UV, NMR	382	[12]
66	Hydrastine	UHPLC-ESI-MS/MS, UV, NMR	383	[12]
67	N-Methylcoclaurine	UHPLC-ESI-MS/MS, UV, NMR	299	[12]
68	Isocorynoline	UHPLC-ESI-MS/MS, UV, NMR	354	[12]
69	Lythranidine	UHPLC-ESI-MS/MS, UV, NMR	426	[12]
70	N-methyl canadine	UHPLC-ESI-MS/MS, UV, NMR	354	[12]
71	Worenine	UHPLC-ESI-MS/MS, UV, NMR	334	[12]
72	Erysothiopine	UHPLC-ESI-MS/MS, UV, NMR	408	[12]
73	Coryptopine	UHPLC-ESI-MS/MS, UV, NMR	336	[12]
74	Bassianin	UHPLC-ESI-MS/MS, UV, NMR	396	[12]
75	Isomer-dehydrocorydaline	UHPLC-ESI-MS/MS, UV, NMR	366	[12]
76	Acetylcorynoline	HPLC	410	[27]
77	Protostephanone	TLC	286	[28]
78	Salutaridine NO oxide	HPLC, TLC, NMR, UV	344	[29]
79	Norjuziphine	HPLC, NMR, UV	285	[30]
80	Laudanidine	HPLC, NMR, UV	343	[31]
81	Reticuline	HPLC, NMR, UV	329	[32]
82	Armepavine	HPLC, NMR, UV	313	[33]

HPLC-Q-TOF-MS, high-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry; HPLC, high-performance liquid chromatography; NMR, nuclear magnetic resonance; TLC, thin layer chromatography; HPLC-Triple-TOF-MS/MS, high performance liquid chromatography tandem triple time-of-flight mass spectrometry; NO, nitric oxide.

Table1 Chemical composition of alkaloids in *Corydalis bungeana* Turcz. (*Continued*)

No.	Chemical compounds	Method	Molecular weight	Ref.
83	Corycaline A	HR-ESIMS, NMR, UV	425	[34]
84	Corycaline B	HR-ESIMS, NMR, UV	425	[34]
85	Corycaline C	HR-ESIMS, NMR, UV	383	[34]
86	Corycaline D	HR-ESIMS, NMR, UV	461	[34]
87	Corycaline E	HR-ESIMS, NMR, UV	461	[34]
88	14-epiacetylcorynoline	HR-ESIMS, NMR, UV	409	[34]
89	Yuziphine	CC, TLC, MS	299	[35]
90	Bungeanine	CC, TLC, MS	393	[35]
91	Bicuculine	CC, TLC, MS	367	[35]
92	6-acetonylcorynoline	GC-MS, NMR, UV	423	[36]
93	Corygaline A	HPLC, UV, TLC	382	[37]
94	Dehydrocheilanthifoline	HPLC, UV	327	[38]
95	Izoteolin	-	327	[39]
96	Neoechinulin A	HPLC	323	[40]
97	N-trans-p-coumaroyltyramine	CC, TLC	283	[41]
98	(-)-dicentrine	UV, NMR	339	[42]
99	(-)-asimilobine-2-O-*β*-D-gluco side	UV, NMR	430	[42]
100	(-)-crebanine	TLC, NMR	339	[43]
101	(-)-stephanine	TLC, NMR	338	[43]
102	(*R*)-roemerine	HPLC, UV	279	[44]
103	(*R*)-vireakine	HPLC, UV	339	[44]
104	(*R*)-tuduranine	CC, NMR, UV	297	[45]

HPLC, high-performance liquid chromatography; NMR, nuclear magnetic resonance; TLC, thin layer chromatography.

Table2 Chemical composition of flavonoids in *Corydalis bungeana* Turcz.

No.	Name	Method	Molecular weight	Ref.
105	Kaempferol	HPLC-Q-TOF-MS	286	[7]
106	Kaempferol 3-O-α-arabinopyranosyl(1‴→6‴)-β-glucopyranoside	HPLC, UV, NMR	581	[9]
107	Kaempferol 3-O-α-arabinopyranosyl(1‴→6‴)-β- glucopyranoside 7-O-β-glucopyranoside	HPLC, UV, NMR	743	[9]
108	Quercetin 3-O-α-arabinopyranosyl (1‴→6‴)- β-glucopyranoside	HPLC, UV, NMR	581	[9]
109	Quercetin 3-O-α-arabinopyranosyl(1‴→6‴)-β- glucopyranoside 7-O-β-glucopyranoside	HPLC, UV, NMR	758	[9]
110	Rutin	HPLC-Triple-TOF-MS/MS	610	[11]
111	Isopongaflavone	HPLC-Triple-TOF-MS/MS	352	[11]
112	Daidzein	UHPLC-ESI-MS/MS, UV, NMR	254	[12]
113	Quercetin	LC-MS	302	[46]

HPLC-Q-TOF-MS, high-performance liquid chromatography coupled with quadrupole time-of-flight mass spectrometry; HPLC, high-performance liquid chromatography; NMR, nuclear magnetic resonance; HPLC-Triple-TOF-MS/MS, high performance liquid chromatography tandem triple time-of-flight mass spectrometry.

Table3 Chemical composition of amino acid in *Corydalis bungeana* Turcz.

No.	Name	Method	Molecular weight	Ref.
114	aspartic acid	HPLC-Triple-TOF-MS/MS	134	[11]
115	Leucine	HPLC-Triple-TOF-MS/MS	132	[11]
116	L-tyrosine	HPLC-Triple-TOF-MS/MS	182	[11]
117	L-proline	HPLC-Triple-TOF-MS/MS	116	[11]
118	L-glutamic acid	HPLC-Triple-TOF-MS/MS	148	[11]
119	L-threonine	HPLC-Triple-TOF-MS/MS	120	[11]
120	Phenylalanine	HPLC-Triple-TOF-MS/MS	166	[11]
121	Trans-4-hydroxy-L-proline	HPLC-Triple-TOF-MS/MS	132	[11]
122	γ-glutamyl valine	HPLC-Triple-TOF-MS/MS	247	[11]
123	γ-aminobutyric acid	HPLC-Triple-TOF-MS/MS	105	[11]

HPLC-Triple-TOF-MS/MS, high performance liquid chromatography tandem triple time-of-flight mass spectrometry.

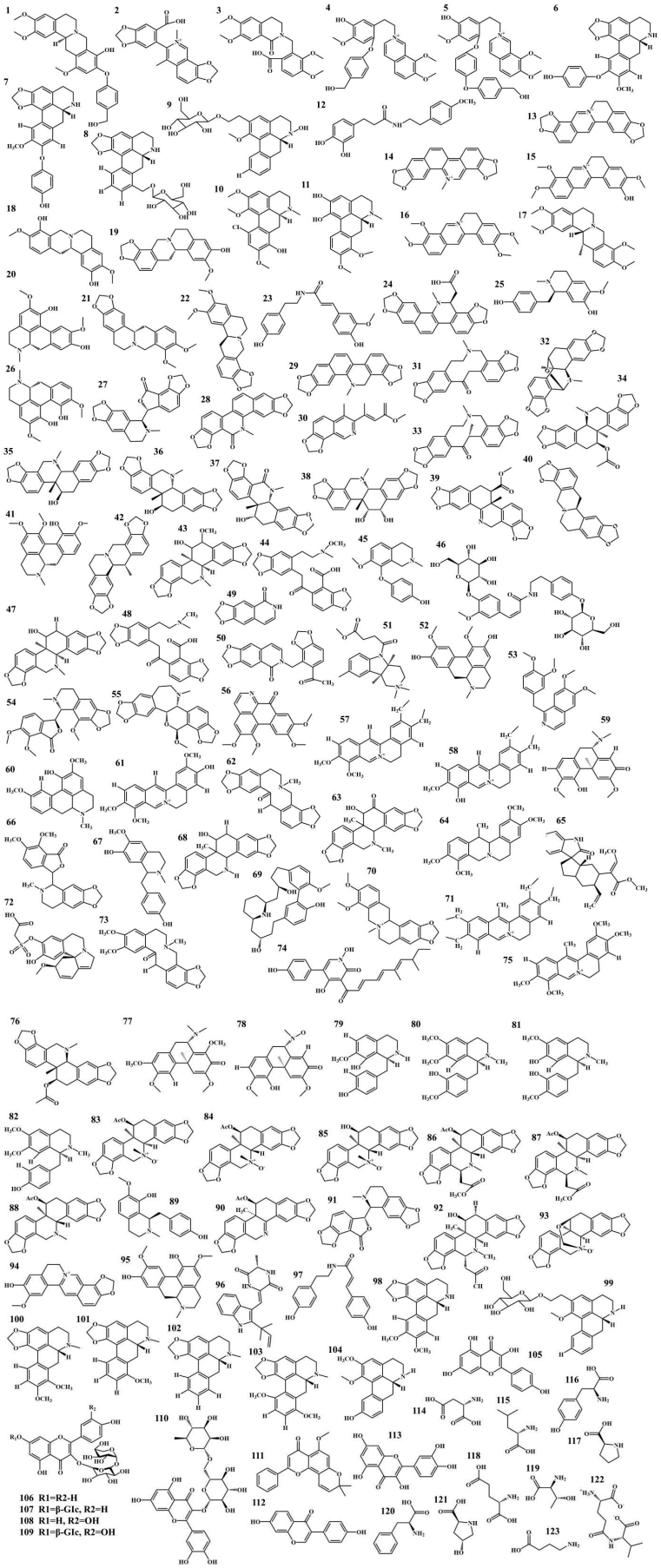

Figure 2 Structures of *Corydalis bungeana* Turcz.

Other compounds. Besides the above chemical constituents, CB also contains coumarins, triterpenoids and organic acids, including aesculin, soysaponin 1, acacia-7-o-β-d-apiose-(1→2)-β-d-glucose, bilatriene, bupleurynol, dipsacussaponin L, gloeosteretriol, tanshinone II A, caftaric acid, isolinolic acid, tianshic acid [12], and trihydroxy-octadecenoic acid [47]. In addition, a morphine derivative (bungeanoline B) and a new phthalic acid derivative (bungeanoline F) [8] have been isolated from CB.

Study on pharmacological effects

CB contains many vital pharmacological effects because of the valuable phytoconstituents in it. Alkaloids, however, are responsible for most pharmacological effects, including antiinflammatory, antitumour, antiviral, antibacterial, analgesic, immunomodulatory, and lipid-lowering [48, 49]. The following paragraphs will review each of these biological effects and health advantages of CB, and Table 4 provides a recapitulative overview.

Table 4 Summary of biological activities of *Corydalis bungeana* Turcz.

Biological activities	Active ingredients	Types	Experimental subjects	Doses	Effects/Mechanisms	Ref.
Antiinflammatory						
	Total alkaloids	In vivo/In vitro	Mouse CIA model; Mouse macrophages induced by LPS	200 mg/kg; 30, 100 ug/mL	Disease time, swelling and erythema, anti-CII antibody level in serum↓; TNF-α, IL-1↓	[50]
	Corydalis bungeana Turcz.	In vitro	Macrophages induced by LPS	0.1, 1, 10, 100 ug/mL	IL-6, TNF-α, IL-10, NO↓	[51]
	Corydalis bungeana Turcz.	In vitro	RAW264.7 cells induced by LPS	10, 20, 50, 100 μg/mL	NO↓; mRNA expressions of iNOS, TNF-α, IL-1β and IL-6↓; TNF-α, IL-1β and IL-6↓; NF-κB↓	[52]
		In vivo	Female BALB/c mice	1, 2, 4 g/kg	NO, IL-1β↓; mRNA expressions of iNOS, IL-1β↓	[52]
	Corynoline	In vitro	HepG2 cells; RAW264.7 cells induced by LPS	1, 2, 4 μM	ARE↑, NO↓; COX-2, iNOS↓, NQO1, HO-1 and Nrf2↑; mRNA expressions of IL-β, TNF-α↓ and NQO1, HO-1 and Nrf2↑; Protein expressions of P38, JNK↓	[53]
	Corynoline	In vitro	HUVEC cells	1, 2, and 4 μM	IL-8, TNF-α↓; Protein expressions of VCAM-1, ICAM, and HO-1, Nrf2↑; NF-κB↓	[54]
	Corynoline	In vitro	C57BL/6 mice chondrocytes	2, 4 μM	mRNA expressions of TNF-α, IL-6, iNOS and COX-2↓; Protein expressions of iNOS, COX-2↓; NO, PGE2, IL-6, TNF-α↓; Protein expressions of HO-1, Nrf2↑, NF-κB↓	[55]
		In vivo	Male C57BL/6 mice	15, 30 mg/kg	Reduced cartilage destruction, loss of proteoglycan, and cartilage erosion	[55]
	Corynoline	In vivo	Female BALB/c mice	15, 30, and 60 mg/kg	Improved the inflammatory cell infiltrations and thickening of the alveolar wall; MPO activity, MDA, IL-1β and TNF-α↓; NF-κB↓, protein expressions of and HO-1, Nrf2, p-AKT and p-GSK3↑	[56]
	Corynoline	In vivo	BALB/c mice	5, 10 mg/kg	Nose-rub score, IgE, IgG1↓ and IgG2a↑; TSLP, TNF-α, IL-1β and MIP-2↓; Protein expressions of caspase-1↓	[57]
	Sanguinarine	In vivo	C57BL/6 mice	5, 10 mg/kg	Improved body weight loss and colonic injury; TNF-α, IFN-γ, IL-1β, IL-6, IL-13 and IL-18↓, IL-4 and IL-10↑	[58]
		In vitro	THP-1 cells	0.25, 0.5, 1.0 μM	Protein expressions of NLRP3, caspase-1 and IL-1β↓	
	Dihydrosanguinarine	In vivo	Male BALB/c mice	10, 20 mg/kg	Decreased inflammatory cell infiltration, relieved oedema and haemorrhage, and subdued necrosis; IL-17A, TNF-α and IL-6T↓, GF-β↑, MPO activity↓; mRNA expressions of Fos, VCAMI, Creb5, ICAM-1, CCI2, IL-17A, IL-17RA, IL-17RE, TRAF3IP2, IL-23, IL-1β, IL-6, TNF-α, AKT3, CXCL1, CXCL2, CXCL3↓ and PI3KCA↑	[59]
Analgesic						
	Corydalis bungeana Turcz.	In vivo	KM mice	0.2, 0.4 mL/10 g	Squirming in the abdominal region↓, the pain threshold↑	[16]
	Corydalis bungeana Turcz.	In vivo	Male swiss mice	5, 10, and 20 mg/kg	Squirming in the abdominal region, paw licking↓	[60]
Antitumor						
	Corynoline	In vitro	Melanoma cells (B16F10, A375)	5, 10, 20, 40 μM	Melanoma cells growth and G2 arrest↓; apoptosis↑; protein expressions of Bcl-2↓ and Bax, cleaved caspase-3 and γ-H2AX↑; ROS generation↑	[17]
	Sanguinarine	In vitro	Nasopharyngeal carcinoma cell lines CNE2, 5-8F	1, 2, 3, 4, 5 μmol/L	Nasopharyngeal carcinoma cells proliferation, cloning formation ability, migration and invasion↓; the expression level of mTOR and p-mTOR↓; apoptosis↑	[61]

↓, decrease or inhibit; ↑, increase or promote; CIA, collagen-induced arthritis; LPS, lipopolysaccharide; NO, nitric oxide; iNOS, Inducible Nitric Oxide Synthase; CXO-2, Cyclooxygenase-2; ICAM-1, Intercellular adhesion molecule-1; HO-1, Heme oxygenase-1; Nrf2, Nuclear factor-E2-related factor 2; MPO, Myeloperoxidase; MDA, Malonaldehyde; NQO1, Quinone oxidoreductase 1; NLRP3, NOD-like receptor protein 3; ROS, Reactive oxygen species; mTOR, Mammalian target of rapamycin.

Table 4 Summary of biological activities of *Corydalis bungeana* Turcz. (*Continued*)

Biological activities	Active ingredients	Types	Experimental subjects	Doses	Effects/Mechanisms	Ref.
	Sanguinarine	In vitro	Human normal liver L02 cells and HepG2 HCC cells	0.5, 1, 2 μM	HCC cells proliferation and invasion↓; apoptosis↑; protein expressions of CDK4↓, mRNA expressions of CDK4↓, miR-487-5p↑	[62]
	Sanguinarine	In vitro	Human lung cancer cell lines H1975 and A549	0.5, 0.7, 0.8, 0.9, 1.1, 1.3, 1.4, 1.7 μM	Cells proliferation, migration, invasion↓; EMT process, apoptosis↑; protein expressions of Bcl-2↓ and Bax↑; LSD1↓	[63]
	Sanguinarine	In vitro	Human cervical cancer cell line HeLa	0.5, 1, 2.5, 5, 10, and 20 μM	HeLa cells proliferation↓, apoptosis↑; ROS generation↑, protein expressions of Bcl-2, p-STAT3, STAT3↓ and Bax↑	[64]
		In vivo	Athymic nude mice	5 mg/kg	Tumours' volume and weight↓, MDA level↑, protein expressions of p-STAT3, STAT3↓	
	Sanguinarine	In vitro	Gastric cancer cell	1.25, 2.5, and 5 μM	protein expressions of TOX↓, DNA-PKcs and KU70/80↓	[65]
	Sanguinarine	In vitro	Human papillary thyroid cancer cell lines BCPAP and TPC-1	0.5 μM, 1 μM, 2 μM 4 μM and 8 μM	Papillary thyroid cancer cells proliferation and growth↓, apoptosis↑, protein expressions of p-STAT3, ALDH2 and SOX2↓	[66]
Anti-viral bacteriostasis						
	Corynoline	In vivo	Institute of Cancer Research mice	40 mg/kg	TNF-α, IL-6↓, survival rate↑	[18]
		In vitro	RAW264.7 cells	10, 20, 40, 80, 160, 320 μg/mL	TNF-α, IL-6↓	
Immunomodulatory						
	Corydalis bungeana Turcz.	In vivo	KM mice	0.5 mL/d	Spleen and thymus atrophy, lymphocyte proliferation, phagocytic function of macrophages and IL-2↓	[19]
	Acetylcorynoline	In vivo	C57BL/6 mice	10 or 20 μM	Allostimulatory capacity and hypersensitivity responses↓	[67]
		In vitro	Dendritic cells (mBM-DC)		TNF-α, IL-6, and IL-12p70↓, endocytic capacity, migration and NF-κB p65 translocation↓, IKK and p38 MAPK activity↓	
Neuromodulation						
	Corydalis bungeana Turcz.	In vivo	Swiss or LACA mice	50 mg/kg	Behavioural activity, spontaneous activity↓, excitatory nerve action↓, nerve depressant effect↑	[20]
	Acetylcorynoline	In vitro	C. elegans of wild-type Bristol N2, transgenic BZ555 and transgenic OW13	5, 10, 20, 40 mM	Selective degeneration of DA neurons↓, aggregation of the a-synuclein protein↓, recovered of the lipid content and dopamine levels; increased the life	[13]
Lipid reduction						
	Corydalis bungeana Turcz.	In vivo	Wistar rats	0.18, 0.9, 1.8 g/kg	Body weight, feed intake, Lee's index, TC, TG, perirenal, epididymal, mesenteric fat↓	[21]
		In vivo	Wistar rats	0.18, 0.9, 1.8 g/kg	Body weight, feed intake, CKK, TC, TG, gastric emptying, perirenal fat, Prevotellaceae↓; Shannon index, Lachnospiraceae, Sutterellaceae, Porphyromonadaceae↑	[49]
Others						
	Corynoline	In vivo	Female BALB/c mice	15, 30, and 60 mg/kg	MDA, MPO, TNF-α, IL-1β, IL-6, NF-κB↓; HO-1, Nrf2↑	[68]
	Corynoline	In vivo	Male BALB/c mice	15, 30, and 60 mg/kg	AST, ALT, MDA, MPO, TNF-α, IL-1β↓; NF-κB↓, HO-1, Nrf2 and SIRT1↑	[69]
	Corynoline	In vivo	Male C57BL/6 mice	20 mg/kg	CK-MB, ANP↓; mRNA/protein expressions of β-MyHC, COL-1, TGF-β1, Myh7, Col1a1, Tgfb1, IL-1β, IL-6, TNF-α↓; PPARa↑, NF-κB↓	[70]
	Corynoline	In vitro	H9c2 cells	5, 10 μM	mRNA/protein expressions of β-MyHC, COL-1, TGF-β1, Myh7, Col1a1, Tgfb1, IL-1β, IL-6, TNF-α↓; PPARa↑, NF-κB↓	
	Sanguinarine	In vitro	Airway smooth muscle cells	0.005, 0.05 and 0.5 μM	Cell stiffness, traction force↓, $[Ca^{2+}]i$↑, mRNA of calponin, α-SMA, and histamine receptors 1 and 2↓	[71]

↓, decrease or inhibit; ↑, increase or promote; HCC, hepatocellular carcinoma cells; CDK4, Cyclin-dependent kinase 4; LSD1, Lysine specific demethylase1; ROS, Reactive oxygen species; HO-1, Heme oxygenase-1; Nrf2, Nuclear factor-E2-related factor 2; MPO, Myeloperoxidase; MDA, Malonaldehyde; TG, Triglycerides; TC, Total cholesterol; NQO1, Quinone oxidoreductase 1.

Antiinflammatory properties. Several authors have confirmed that CB has an antiinflammatory effect. The mice type II collagen arthritis model was established by intradermal injection of chicken type II collagen and administered intragastrically with CB total alkaloids at a 200 mg/kg dosage, after which the disease was delayed, the swelling and erythema of joints were diminished, the TNF-α and interleukin-1 (IL-1) levels in macrophages considerably decreased, and anti-chicken type II collagen antibody levels in serum were also reduced [50]. Dong et al. used macrophage binding with HPLC analysis and HPLC-MS to identify compounds with potential antiinflammatory activity. They discovered that 12-hydroxycorynoline and corynoline significantly reduced IL-6, IL-10, TNF-α, and nitric oxide (NO) levels induced by lipopolysaccharide (LPS) [51]. Additionally, CB decreased the secretion of NO, TNF-α, IL-6, and IL-1 by blocking protein expression of inducible nitric oxide synthase, TNF-α, IL-6, and IL-1 in RAW 264.7 macrophages and murine of LPS-induced sepsis. Some scholars argue that this action inhibits the phosphorylation of IBa and p65 and the subsequent activation [52].

While significantly upregulating the ARE and the expression of nuclear factor-E2-related factor 2 (Nrf2), quinone oxidoreductase 1, and hemeoxygenase-1 (HO-1) at the protein and mRNA levels by LPS-induced RAW 264.7 cells, the antiinflammatory agent corynoline, an essential active ingredient extracted from CB, reduced NO production and downregulated the expression of inducible nitric oxide synthase and cyclooxygenase-2 [53]. According to Liu et al. corynoline had antiinflammatory effects on HUVEC cells (LPS-induced human umbilical vein endothelial cells), decreased cellular infection (IL-6, IL-8, and TNF-α), and decreased the expression of vascular cell adhesion molecule-1 and intercellular adhesion molecule-1 while activating NF-κB and expressing Nrf2, which were found to be present. The authors further discovered that corynoline raised the expression of Nrf2 and HO-1, reduced NF-κB activation, and prevented the generation of inflammatory factors. These findings revealed that corynoline activated the Nrf2 signalling pathway and blocked NF-κB activation [54]. Corynoline inhibited extracellular matrix degeneration and pro-inflammatory factor levels, modulated the NF-κB pathway in IL-1-treated chondrocytes, and decreased the level of Nrf2 in osteoarthritis mice as discussed by Li et al. thus highlighting the importance and mechanisms of action of corynoline in osteoarthritis progression. They concluded that corynoline reduced osteoarthritis by inhibiting inflammation and extracellular matrix degradation through the Nrf2/NF-κB [55]. Wu et al. established a mastitis model with LPS. They found that applying corynoline at 15, 30 and 60 mg/kg reduced mammary tissue history damage and decreased myeloperoxidase (MPO), malonaldehyde, and secretion of TNF-α and IL-1β in mammary tissue. It also inhibited NF-κB activation. Moreover, there was a considerable rise in the expression of Nrf2 and the phosphorylation of AKT and glycogen synthase kinase 3 beta (GSK3). According to these findings, corynoline cured LPS-induced mastitis by controlling the AKT/GSK3/Nrf2 signalling pathway and reducing the inflammatory response [56]. In addition, Wei et al. reported the effect of corynoline against allergic rhinitis (AR). They established an AR model using ovalbumin. Then they found that treatment with 5 mg/kg and 10 mg/kg corynoline considerably diminished the nose-rub score and serum protein levels of immunoglobulin E and immunoglobulin G1 in mice while concentration-dependently increasing the levels of immunoglobulin G2a. The authors also examined the effect of corynoline on cytokines in the nasal mucosa of mice and found that IL-1β, TNF-α and macrophage inflammatory protein 2 levels were significantly reduced. Finally, western blot and molecular docking analyses showed that corynoline significantly decreased caspase-1 expression and inhibited NF-κB activity, acting as a therapeutic agent for AR [57].

One of the primary chemical components of CB is sanguinarine. Using in vivo and in vitro investigations, Li et al. looked into the mechanism of sanguinarine's improvement of ulcerative colitis (UC). In the in vivo experiments, a UC model was prepared using dextran sulfate sodium. Treatment with 5 and 10 mg/kg sanguinarine revealed that weight loss and colonic injury were improved. In contrast, the levels of colonic pro-inflammatory cytokines TNF-α, interferon-γ, IL-1β, IL-6, IL-13 and IL-18 were decreased, and the levels of IL-4 and IL-10 were increased. In in vitro tests, sanguinarine reduced NOD-like receptor protein 3 (NLRP3) expression and stimulated caspase-1 and IL-1 in LPS-induced human monocytic leukaemia cells. Intestinal flora examination of *Helicobacter*, *Escherichia-Shigella*, *Lachnospiraceae NK4A136* group, and *Muribaculaceae* unclassified revealed strong correlations with sanguinarine's ability to reduce intestinal inflammation. This shows that by inhibiting the NLRP3-(caspase-1)/IL-1 pathway and enhancing intestinal microbial dysbiosis, sanguinarine has a therapeutic impact on dextran sulfate sodium-induced UC [58]. Using RNA-seq in conjunction with network pharmacology, molecular docking, and HPLC-Q-TOF/MS techniques, Xiang et al. investigated the protective properties of dihydrosanguinarine on LPS-triggered hepatitis in mouse models for the first time. They discovered that dihydrosanguinarine prevented LPS-induced macrophage hyperinfiltration and downregulated the activation of TNF/IL-17/PI3K [59].

In conclusion, the literature confirmed that CB and its chemical constituents have antiinflammatory properties. Moreover, in recent years, more studies have reported the therapeutic effects of CB extracts and individual components such as corynoline on colitis, arthritis, hepatitis, etc. However, the current studies still have some questions that need to be explored in more depth. For example, current studies have mainly focused on individual components, and the pharmacological activities of other components have not been investigated in depth. On the other hand, CB has a diverse and complicated chemical makeup, and there might be interactions between the constituent parts. As a result, in the subsequent investigation, we should examine the active components of CB in greater detail while tracking their interactions.

Analgesic properties. Pain is one of the vital human signs, both as a self-protection of the organism and as an early warning of the organism to injurious stimuli [15]. The antinociceptive properties of plant extracts with analgesic action, which can be related to abdominal torsion, are frequently studied using acetic acid. Hot plate analysis is an established technique for evaluating analgesia sensitive to central pain. Before this study, Wang et al. used acetic acid and hot plate induction of nociception to examine the analgesic impact of CB. They discovered that CB significantly decreased the number of abdominal writhing and raised the pain threshold in mice, demonstrating considerable analgesic benefits [16]. Additionally, Lei et al. studied the analgesic effect of corynoline by inducing nociception using various techniques, including acetic acid, formalin, glutamate, capsaicin, a hot plate, and tail dipping. They found that corynoline dose-dependently reduced the amount of writhing and paw licking in mice and exhibited a high nociceptive inhibitory response [60].

Antitumor. It has been found that the three alkaloids of CB, corynoline, corynoloxine and 6-oxocorynoline have toxic effects on A549, SK-OV-3, SK-MEL-2 and Hematopoietic Cell Transplantation human cancer cell lines [72]. In addition, corynoline can concentration-dependently inhibit the propagation of melanoma B16F10 and A375, arrest G2 cells and reduce the activation of conventional type 2 dendritic cells. Meanwhile, data proved that corynoline could lead to apoptosis of melanoma cells by regulating Bcl-2, Bax and cleaved caspase-3. Additionally, it promoted the production of reactive oxygen species, which caused the cells to arrest in the G2 cell cycle phase. Pretreatment with a reactive oxygen species inhibitor reversed the corynoline-induced G2 arrest and cell apoptosis, indicating that corynoline significantly caused oxidative stress in melanoma cells, which in turn caused G2 cell cycle arrest and cell apoptosis [17]. In addition, other active components, like sanguinarine, also exhibited cytotoxic activity that hindered tumour metastasis and development [73]. Yang et al. further showed that sanguinarine inhibited the growth, cloning ability, invasion and migration of nasopharyngeal carcinoma cells (hypodifferentiated CNE2 cells and highly metastatic 5-8F cells). The mammalian target of rapamycin signalling pathway was the target of the suggested

mechanism of action, which promoted apoptosis [61]. Ding et al. used the Swiss Target Prediction method to predict the targets of sanguinarine. They verified the target by Western blot and qRT-PCR and detected cell proliferation, invasion and apoptosis, further proved by transwell and flow cytometry. This allowed them to detect that sanguinarine inhibited the propagation and metastasis of hepatocellular carcinoma cells and induced programmed cell death by regulating the expression of miR-497-5p/CDK4 [62]. Lysine-specific demethylase1 (LSD1) is associated with the development and carcinogenesis of many cancers, and inhibition of LSD1 production offers a strategy for tumour treatment. The sanguinarine had a potent inhibitory effect on LSD1 and inhibited the formation, migration and invasion of human tumour lung cells H1975 and A549. It further promoted apoptosis in these cells [63]. In addition, sanguinarine inhibited the proliferation of cervical [64], gastric [65] and papillary thyroid cancer [66] cells and promoted apoptosis, showing antitumor effects in these cancer cells.

Antiviral and bacteriostatic properties. Ma et al. determined the antifungal activity of corynoline and actylcorynoline using a thin-layer chromatography plate bioassay technique and found that they have anti-Dendrobacterial effects [74]. He et al. investigated the effect of corynoline on septic mice. They found that the mortality rate of septic mice was reduced by a mechanism possibly related to TNF-α and IL-6, suggesting that corynoline has therapeutic anti-septic potential [18]. Studies conducted in vivo and in vitro have revealed that sanguinarine works in concert with aminoglycosides to greatly increase the death of many harmful bacteria, including Escherichia coli, Acinetobacter baumannii, Klebsiella pneumoniae, and Pseudomonas aeruginosa [75]. Zhang et al. studied sanguinarine in vitro antibacterial and antimicrobial membrane activity against *Plasmodium reuteri*. They found that sanguinarine inhibited cell growth, disrupted cell membrane integrity and strongly inhibited the formation of *Pseudomonas leprae biofilm* [76]. In addition, sanguinarine has a potent inhibitory effect on the biofilm formation of Escherichia coli and *Salmonella* [77].

Immunomodulatory properties. Some data show that CB aqueous decoction has a significant inhibitory effect on immune function in mice, causes the atrophy of the spleen and thymus, reduces the phagocytosis of macrophages, and inhibits the proliferation of lymphocyte by promoting antiinflammatory activity [19]. Fu et al. found that actylcorynoline may be a potent immunosuppressive agent. The authors showed that it blocked the secretion of TNF-α, IL-6, and IL-12p70 by dendritic cells and blocked dendritic cells maturation and function by modulating the initiation of ikappaB kinase and mitogen-activated protein kinase [67].

Neuromodulatory properties. Specific literature show that CB has noticeable central pharmacological effects. CB improved the central nervous system inhibitory effects of sodium pentobarbital and chloral hydrate, and it was found to decrease behavioural and spontaneous activity in mice considerably. It is thought that CB possesses sedative and hypnotic properties [20]. Acetylcorynoline has the potential to treat Parkinson's disease. Acetylcorynoline reduced dopaminergic neuron degeneration, stopped a-synuclein aggregation, restored lipid content, food-sensing behaviour, and dopamine levels in the OW13 strain, and extended the strain's lifespan, according to research by Fu et al. using a transgenic strain of a-synuclein (OW13). Moreover, dopamine D2 receptors were intensely antagonistic to (S)-reticuline [8] and (R)-stephanine [5] isolated from CB extracts, giving potential target substances for the creation of D2 receptor-targeting medications.

Lipid reduction. Obesity is a metabolic disease induced by several factors affecting people's average quality of life. Recent studies have shown that CB could target obesity. Fu et al. established an obesity model in rats fed a high-fat and sugar diet for 10 weeks, treated with 0.12, 0.18, and 0.9 g/kg CB for 6 weeks and found that CB significantly reduced body mass, food intake, Lee's index, and serum triglycerides and total cholesterol levels, and reduced perirenal, mesenteric, and epididymal fat accumulation in rats. Moreover, nine distinct metabolites were discovered using metabolomic analysis, including pyruvic acid, D-glucuronic acid, malic acid, dimethylglycine, oxoglutaric acid, pantothenic acid, sorbitol acid, fumaric acid, glucose 6-phosphate [21]. In another study, the effect of CB on the intestinal flora of obese rats was analyzed, proving that CB could positively regulate intestinal flora's structure. In the meantime, the findings demonstrated a strong correlation between the differentially expressed metabolites and the differential bacteria, suggesting the regulatory role of CB on intestinal microflora and their associated metabolites, which in turn modulated lipid metabolism [49].

Others. In addition to the actions mentioned above, CB also reportedly engages in additional pharmacological actions. Clinical studies have shown its significant efficacy in damp-heat-quiescent haemorrhoids [78]. Otherwise, corynoline has potential protective effects against acute liver and lung injury. Some authors used LPS to create a lung injury model and discovered that corynoline inhibited NF-κB, increased Nrf2 and HO-1 expression, suppressed MPO activity, the release of inflammatory factors like IL-1, TNF-α, and IL-6, and improved lung histopathological changes, treating LPS-induced acute lung injury [68]. Additional research showed that corynoline inhibited the phosphorylation of I-B and p65 NF-κB and increased the expression of Sirtuin1, Nrf2, and HO-1 while inhibiting pro-inflammatory factors, MPO activity, and malonaldehyde content. Sirtuin1 inhibitors also reversed corynoline's protective effect against liver injury. According to theory, corynoline prevents liver damage by turning on the SIRT1/Nrf2 signalling pathway [69]. In addition, corynoline reduced angiotensin II-induced hypertensive heart failure by increasing the interaction between PPAR and P65 and inhibiting NF-κB pathways [70]. Interestingly, sanguinarine was reported as a bronchodilator for asthma. It is supposed that its mechanism of action may be through activation of the bitter taste receptor, which increases intracellular calcium ion concentration and rapidly relaxes airway smooth muscle to treatment in asthma [71].

In conclusion, studies on the pharmacological activity of CB have mainly concentrated on typical chemical components like corynoline, sanguinarine, and acetylcorynoline. The lack of studies on other chemical components may be due to their low content or negligible efficacy in CB. Therefore, the knowledge of the active ingredients of CB is relatively limited. In subsequent studies, researchers can use more advanced methods and instruments to enrich the studies related to CB and its active ingredients.

Toxicity

So far, research has clarified the chemical makeup and various physiological functions of CB. However, there are fewer studies on the safety and side effects of CB. In addition, natural botanicals contain multiple chemical components with relatively complex active ingredients, which may have different degrees of toxic side effects. Therefore, studies on the toxicity of CB are critical. Some authors observed the teratogenic effects of CB alkaloids on mice and found that CB alkaloids had no significant effects on the reproductive function of pregnant mice and fetal mice's growth and visceral development. However, the dose of 60–120 mg/kg could cause significant malformation of fetal appearance (cerebral exposure, microcephaly) and skeletal effects (incomplete ossification of the parietal bone, parietal bone, occipital bone, sternal bone and sternal misalignment). The 10–30 mg/kg dose was safe for fetal mice and did not cause malformation [22]. According to recent research, sanguinarine is hazardous to zebrafish larvae's development, decreasing hatching rates and leading to morphological defects like pericardial oedema, shortening of the body's length, and bent body form. Also, it hinders the zebrafish embryos' average ability to grow their nervous system, heart, and liver [23]. In addition, Liu et al. evaluated the hepatotoxicity of corynoline in mice and found no significant hepatotoxicity or acute liver injury at doses of 125–500 mg/kg [14]. However, abnormal behaviour and hypothermia were observed after administration, and three of them died. According to research on the tissue distribution in mice, the liver was corynoline's primary target organ, followed by the kidney, heart, and brain.

Corynoline had harmful effects on mice and could cross the blood-brain barrier. However, there was no hepatotoxicity at the experimental dose, suggesting that corynoline may also have had toxic effects on other organs [14].

Generally, CB has a certain degree of toxicity to the organism. However, the study of its toxicity is still at the preliminary exploration stage, and the research is not deep enough. Therefore, in future research, the study of chronic or acute toxicity of CB and its mechanism should be strengthened to provide a scientific explanation for safe clinical use.

Conclusions and prospect

This paper summarizes the recent research developments in botany, phytochemistry, pharmacology, toxicology, and quality control and made some suggestions to provide new ideas for further research. CB is frequently used as an adjuvant in compound formulations and has a long history of use. It is also broadly dispersed, abundant, and well-resourced. The phytochemistry of CB has been thoroughly investigated recently. So far, 137 compounds have been identified and isolated by different methods, including alkaloids, flavonoids, amino acids, terpenoids, coumarins and organic acids, among which 104 alkaloids have been identified. Several pharmacological actions, including antiinflammatory, antibacterial, antiviral, anticancer, analgesic, hepatoprotective, immunomodulatory, neuromodulatory, and fat-reduction activities, are demonstrated by the literature for some of this plant's constituents. These findings lay the groundwork for contemporary research as well as the scientific underpinning for the conventional pharmacological efficacy of CB.

However, the current research on CB mainly focuses on corynoline, acetylcorynoline and sanguinarine. There are fewer reports on other components, and the pharmacological activities are mainly focused on antiinflammatory effects. The research on other pharmacological activities is still not deep enough. Therefore, advanced techniques are needed to elucidate the chemical composition identification and structural analysis aspects of CB. In addition, to further understand its molecular mechanisms and in vivo metabolic regulation, it is necessary to utilize current pharmacological approaches such as metabolomics, transcriptomics and network pharmacology.

In terms of safety and toxicity evaluation, high doses of CB alkaloids can alter bone growth and result in abnormalities in the appearance of embryonic rats, according to safety and toxicity evaluation tests. In addition, it can pass the blood-brain barrier to cause abnormal behaviour, decreased body temperature and even death in experimental animals. Thus, it is clear that CB has some toxicity, but there are few safety evaluation studies. Therefore, the potential toxicity study of CB must be thoroughly studied to identify its hazardous components, target organs, and mode of action and establish the foundation for future clinical safety usage.

Overall, although CB research has achieved important challenges, there are still many opportunities and challenges. There are a wide range of research prospects in the extraction and purification of CB, pharmacodynamic studies, and safety.

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