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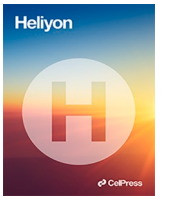

Review article

Modern pharmacological research and application of medicinal insect *Coridius chinensis*

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ABSTRACT

Coridius chinensis is a traditional insect medicine in China. It is the dried whole insect of *Coridius chinensis* (Dallas) form the Pentatomidae family. Modern medical and pharmaceutical studies have successfully isolated and identified over 100 natural small molecular compounds from *Coridius chinensis*. These studies have also confirmed its various pharmacological activities, including analgesic, antioxidant, anticancer, anticoagulant, and antibacterial properties. *Coridius chinensis* is commonly used in traditional Chinese medicine preparations to treat impotence, hemangioma, pain and other diseases. However, more research is needed to fully explore the pharmacological effects of this herbal medicine. This paper aims to summarize both domestic and international research literature on *Coridius chinensis*, focusing on its main components, pharmacological activity and clinical application. The findings will provide valuable references for further research and development of *Coridius chinensis* as a traditional Chinese medicine resource.

1. Introduction

Coridius chinensis, an insect form the genus Pentatomidae, is a medicinal insect that has a warm and salty taste. It is commonly used for both medicinal and culinary purposes, making it highly nutritious [1]. In southwest China, there is a traditional practice of consuming *Coridius chinensis* [2]. According to the Compendium of Materia Medica and the Pharmacopoeia of the People's Republic of China, *Coridius chinensis* is known for its ability to regulate qi, relieve pain, and warm the middle to aid Yang. It isprimarily used to treat conditions such as kidney deficiency, impotence, and waist and knee pain. Thus, it holds significant medicinal value in clinical practice [3–5]. Modern medical and pharmaceutical studies have validated the nutritional richness of *Coridius chinensis*, along with its pharmacological effects such as antibacterial properties, anticancer activity, reproductive protection, and promotion of angiogenesis [6–10]. As research on traditional Chinese medicine and insect medicine continue to advance, *Coridius chinensis* has emerged as an essential drug for treating various diseases [11]. This paper aims to review recent literature on the main components, pharmacological activity, and clinical applications of *Coridius chinensis*. The aim is to provide a scientific basis for its clinical usage, quality assessment, and potential development as a new drug in line with traditional Chinese medicine principles.

2. Main components

The separation and identification of the components of traditional Chinese medicine form the foundation of its component analysis

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Table 1
Main small molecular compounds in *Coridius chinensis*.

Serial number	Compound name	Molecular formula	Literature
Dopamine derivatives			
1	cotidione A	$C_{18}H_{17}NO_7$	[15]
2	*trans*-2-(3',4'-dihydroxyphenyl)-3-acetylamino-7-(*N*-acetyl-2"-aminoethylene)-1,4-benzodioxane	$C_{20}H_{20}N_2O_6$	[9]
3	*trans*-2-(3',4'-dihydroxyphenyl)-3-acetylamino-6-(*N*-acetyl-2"-aminoethylene)-1,4-benzodioxane	$C_{20}H_{20}N_2O_6$	[12]
4	*trans*-2-(3',4'-dihydroxyphenyl)-3-acetylamino-7-hydroxyphenyl-1,4-benzodioxane	$C_{20}H_{22}N_2O_6$	[9]
5	*trans*-2-(3',4'-dihydroxyphenyl)-3-acetylamino-6-hydroxyphenyl-1,4-benzodioxane	$C_{20}H_{22}N_2O_6$	[9]
6	*cis*-2-(3',4'-dihydroxyphenyl)-3-acetylamino-6-(*N*-acetyl-2"-aminoethyl-ene)-1,4-benzodioxane	$C_{20}H_{20}N_2O_6$	[12]
7	1,2-dehydro-N-acetyldopamine	$C_{10}H_{11}NO_3$	[8]
8	L-phenylalanine	$C_9H_{11}NO_2$	[16]
9	aspongamides D	$C_{11}H_{15}NO_5$	[17]
10	aspongamides E	$C_{12}H_{17}NO_5$	[17]
11	(±)-periplanamide B	$C_{11}H_{15}NO_5$	[17]
12	N-acetyldopamine-3-O-D-glucoside	$C_{16}H_{23}NO_8$	[17]
13	N-Acetyldopamine-4-O-β-D-glucoside	$C_{16}H_{23}NO_8$	[17]
14	N-acetyldopamine	$C_{10}H_{13}NO_3$	[9]
15	N-[2-(3,4-dihydroxyphenyl)-2-methoxyethyl]-acetamide	$C_{11}H_{15}NO_4$	[12]
16	N-acetylnoradrenaline	$C_{10}H_{13}NO_4$	[9]
17	aspongopusamide C	$C_{13}H_{19}NO_6$	[9]
18	aspongopusamide D	$C_{13}H_{19}NO_6$	[9]
19	aspongamides C	$C_{17}H_{18}N_2O_5$	[17]
20	(±)-aspongamide A	$C_{30}H_{31}N_3O_9$	[10]
21	aspongopusamide A	$C_{20}H_{20}N_2O_6$	[9]
22	aspongopusamide B	$C_{20}H_{20}N_2O_6$	[9]
23	Aspongamide B	$C_{21}H_{26}N_2O_7$	[12]
24	Aspongamide C	$C_{20}H_{24}N_2NaO_8$	[12]
25	Aspongamide D	$C_{17}H_{18}N_3NaO_5$	[12]
26	*Trans*-8-methoxy-3,4,7-trihydroxy-N-acetyldopamine	$C_{ll}H_{15}NNaO_5$	[12]
27	*Cis*-8-methoxy-3,4,7-trihydroxy-N-acetyldopamine	$C_{11}H_{l5}NNaO_5$	[12]
28	*Trans*-7,8-dimethoxy-3,4-dihydroxy-N-acetyl dopa	$C_{12}H_{17}NNaO_5$	[12]
Nucleosides			
29	thymine	$C_5H_6N_2O_2$	[16]
30	uracil	$C_4H_4N_2O_2$	[9]
31	adenine	$C_5H_5N_5$	[9,16,18]
32	hypoxanthine	$C_5H_4N_4O$	[18]
33	xanthine	$C_5H_4N_4O_2$	[18]
34	asponguanine A	$C_{11}H_{14}N_4O_3$	[12]
35	asponguanine B	$C_{11}H_{16}N_4O_2$	[16]
36	aspongadenine A	$C_{12}H_{17}N_5O_2$	[16]
37	aspongadenine B	$C_{11}H_{17}N_5O$	[16]
38	asponguanine C	$C_9H_{10}N_4O_3$	[16]
39	asponguanine D	$C_{10}H_{12}N_4O_2$	[16]
40	2'-O-methyluridine	$C_{10}H_{14}N_2O_6$	[16]
41	deoxyadenosine	$C_{10}H_{13}N_5O_3$	[16]
42	adenosine	$C_{10}H_{13}N_5O_4$	[16]
43	cordysinin B	$C_{11}H_{15}N_5O_4$	[16]
44	Uridine	$C_9H_{12}N_2O_6$	[18]
45	thymidine	$C_{10}H_{14}N_2O_5$	[9]
46	asponguanosine A	$C_{16}H_{23}N_5O_6$	[12]
47	asponguanosine B	$C_{16}H_{23}N_5O_6$	[12]
Alkaloids			
48	Aspongerine A	$C_{17}H_{28}NO_6P$	[12]
49	Aspongerine B	$C_{17}H_{28}NO_6P$	[12]
50	Aspongerine C	$C_{17}H_{30}NNaO_6P$	[12]
51	Aspongerine D	$C_{17}H_{30}NNaO_6P$	[12]
52	Aspongerine E	$C_{14}H_{2l}NO_3S$	[12]
53	Aspongerine F	$C_{14}H_{2l}NO_3S$	[12]
54	Aspongerine G	$C_{15}H_{22}NO_2$	[12]
55	Aspongerine H	$C_{15}H_{22}NO_2$	[12]
56	Aspongerine I	$C_{21}H_{26}NO_3$	[12]
57	Aspongerine K	$C_{14}H_{20}NO_2^+$	[12]
58	Aspongerine J	$C_{2l}H_{26}NO_3$	[12]
59	Aspongerine L	$C_{17}H_{25}NO_4S$	[12]
60	Transtorine	$C_{10}H_7NO_3$	[18]
61	choline	$C_5H_{14}NO^+$	[16]
62	2-pyridone	C_5H_5NO	[16]
63	2-pyrrolidinone	C_4H_7NO	[16]
64	valerolactam	C_5H_9NO	[16]
65	2-ethyl-3-hydroxy-6-methylpyridine	$C_8H_{11}NO$	[9]

(*continued on next page*)

Table 1 (*continued*)

Serial number	Compound name	Molecular formula	Literature
66	nicodine	$C_{10}H_{14}N_2$	[16]
67	2-quinolinol	C_9H_7NO	[16]
68	4-Quinolone	C_9H_7NO	[16]
69	aspongpyrazine B	$C_7H_{10}N_2O_2$	[16]
70	nicotinamide	$C_6H_6N_2O$	[9,16]
71	N-(2-hydroxyethyl) succinimide	$C_6H_9NO_3$	[16]
72	indole-β-carboxylic acid	$C_9H_7NO_2$	[16]
73	indole-3-aldehyde	C_9H_7NO	[16]
74	indole-3-carboxylic acid	$C_9H_7NO_2$	[16]
75	asponglactam A	$C_8H_{13}NO_3$	[9]
Glycerides			
76	Aspongester A	$C_9H_{16}O_4$	[18]
Acids			
77	Hex-2-enoic acid	$C_6H_{10}O_2$	[18]
78	Phenylacetic acid	$C_8H_8O_2$	[18]
79	Protocatechuic acid	$C_7H_6O_4$	[18]
Amino acids			
80	Tryptophan	$C_{11}H_{12}N_2O_2$	[18]
81	Phenylalanine	$C_9H_{11}NO_2$	[18]
Sesquiters			
82	aspongnoid A	$C_{21}H_{30}O_9$	[9]
83	aspongnoid B	$C_{21}H_{30}O_9$	[9]
84	aspongnoid C	$C_{15}H_{24}O_5$	[9]
85	aspongnoid D	$C_{21}H_{29}O_9$	[12]
86	3，4-dihydroxybenzalacetone	$C_{10}H_{10}O_3$	[9]
compounds containing benzene ring			
87	1，2-benzenediol	$C_6H_6O_2$	[9]
88	3，4-dihydroxybenzene ethanol	$C_8H_{10}O_3$	[9]
89	3，4-dihydroxyphenylacetic acid	$C_8H_8O_4$	[16]
90	vanillic acid	$C_8H_8O_4$	[16]
91	aspongopusin	$C_{10}H_9NO_3$	[8]
92	4-hydroxyisobenzofuran-1(3H)-one	$C_8H_6O_3$	[16]
93	4-(3，4-dihydroxy-phenyl)-but-3-en-2-one	$C_{10}H_{10}O_3$	[16]
94	2，4，5-trimethoxybenzaldehyde	$C_{10}H_{12}O_4$	[9]
Small molecule linear compounds			
95	2-hydroxy-3-methylbutanoic acid	$C_5H_{10}O_3$	[16]
96	2，3-butanediol	$C_4H_{10}O_2$	[9]
97	1，2-propanediol	$C_3H_8O_2$	[9]
Cyclic peptides			
98	cyclo-(L-Leu-L-Trp)	$C_{17}H_{21}N_3O_2$	[9]
99	cyclo(L-Val-L-Ala)	$C_8H_{14}N_2O_2$	[17]
Glycosides			
100	2-hydroxy-5-(2-hydroxyethyl)phenyl β-D-glucopyran-oside	$C_{14}H_{20}O_8$	[9]
101	3，4，5-trimethoxyphenol-β-D-glucopyranoside	$C_{15}H_{22}O_9$	[16]
Other compounds			
102	N-[2-(3, 4-Dihydroxyphenyl)-2-hydroxyethyl]acetamide	$C_{13}H_{16}NO_6$	[12]
103	Methyl 1-hydroxy-2-oxo-4, 5, 5-trimethoxycyclopent-3-ene-1-carboxylate	$C_{10}H_{14}O_7$	[12]
104	6-Hydroxymethyl-3-pyridinol	$C_6H_7NO_2$	[12]
105	3-Hydroxypyridine	C_5H_5NO	[12]
106	N-(2-Hydroxyethyl)succinimide	$C_{10}H_{14}O_7$	[12]
107	N–N'-(Oxydi-2, l-ethaneiyl)bis-N- methyl-acetamide	$C_{10}H_{20}N_2O_3$	[12]
108	4-Hydmxy-3-methoxybenzoic acid	$C_8H_8O_4$	[12]
109	3, 6, 9, 12, 15, 18, 2l, 24, 27-Nonaoxanonacosan-l,29-diol	$C_{20}H_{42}O_{11}$	[12]

and functional research. Early studies on the components of *Coridius chinensis* primarily focused on its nutritional components and content [7]. With advancements in component separation and purification technology, scholars have conducted recent research on the separation and purification of small molecular compounds of *Coridius chinensis*. In addition, they have investigated the biological activity of a very small number of these compounds [12,13]. It was discovered that both the water extract and alcohol extract of *Coridius chinensis* contain 124 types of fatty acids, nucleosides, amino acids, and peptides. Notably, 74 of these compounds were reported for the first time [14].

As a type of health food, *Coridius chinensis* possesses high nutritional value. The components of *Coridius chinensis* have been analyzed using modern detection technology, revealing that the main reported components are fatty acids, proteins, amino acids, nucleosides, and dopamines. *Coridius chinensis* is characterized by high levels of protein, unsaturated fatty acids, vitamins, and various trace elements. Furthermore, the composition of amino acids is well-balanced. These substances form the basis for the medicinal value of *Coridius chinensis*. Specifically, protein and unsaturated fatty acids can boost vitality and regulate human physiological functions.

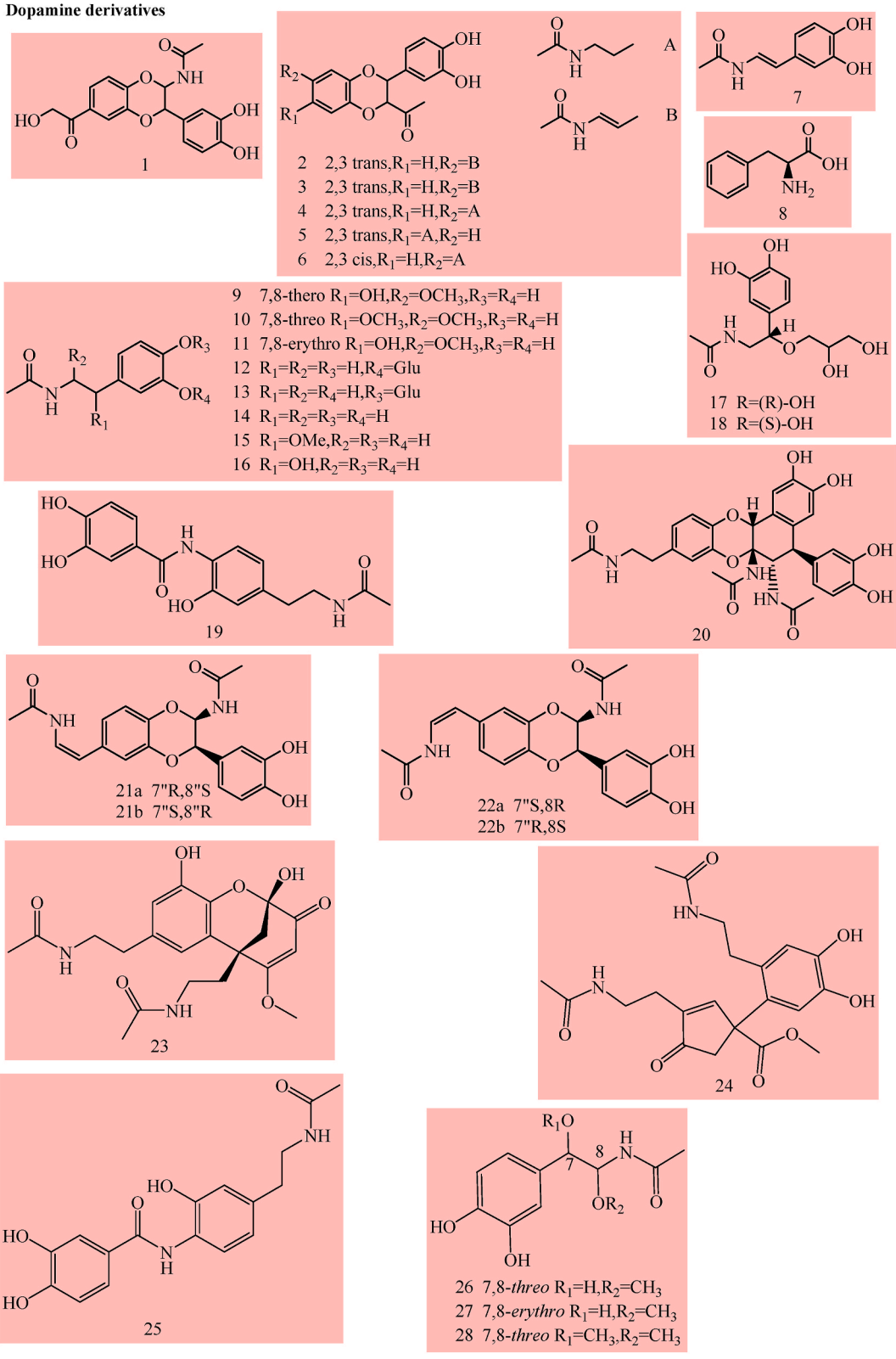


Fig. 1. Chemical structural formula of the main small molecule compounds in *Coridius chinensis* (1–109).

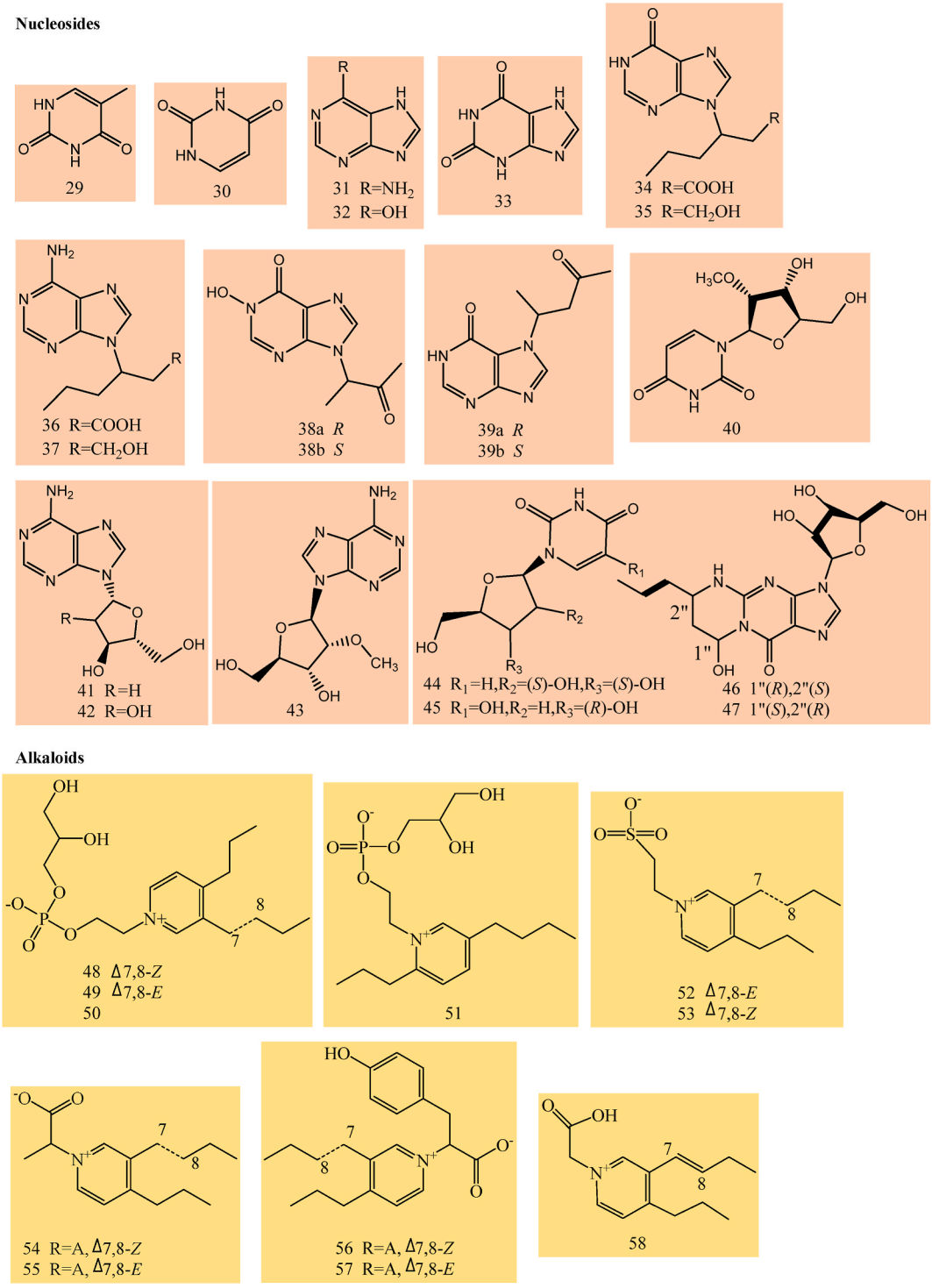
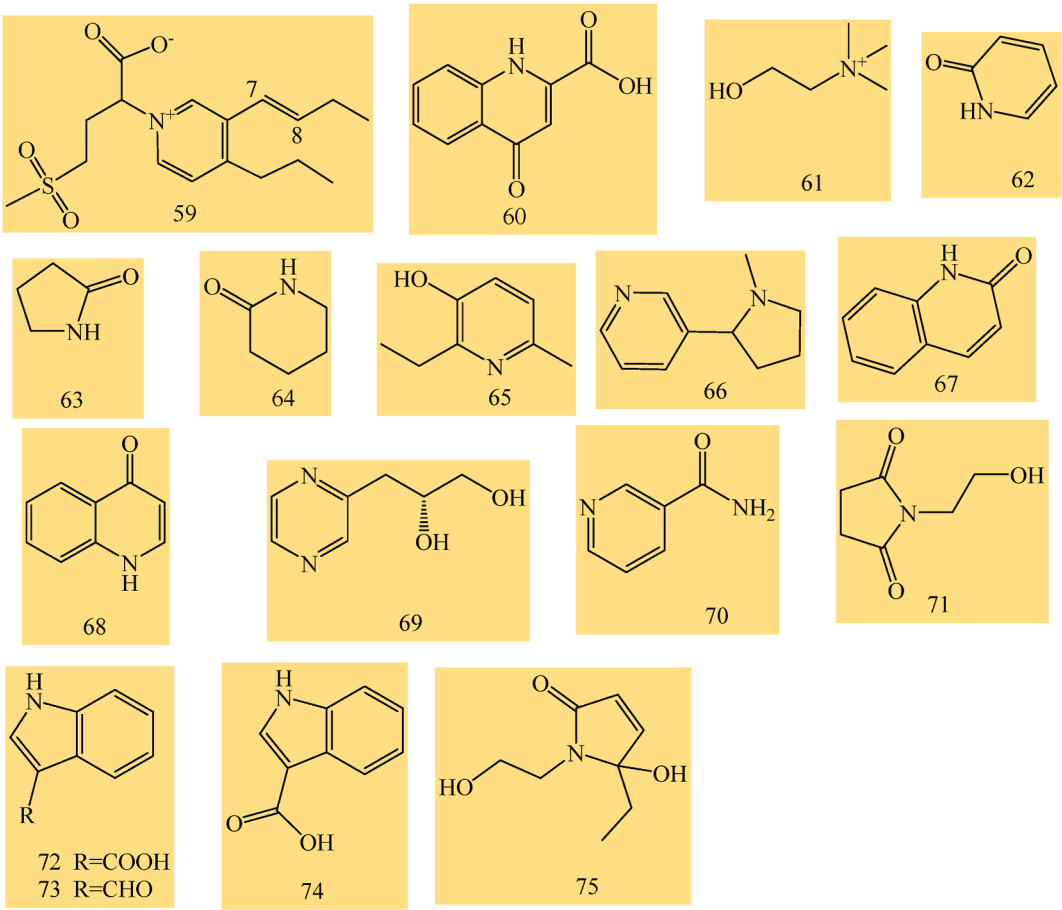


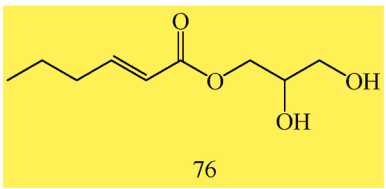
Fig. 1. (*continued*).

2.1. Non-peptide compounds

In the past, research on *Coridius chinensis* mainly focused on sugars, proteins and other macromolecular substances. However, the study of non-peptide small molecular compounds was lacking. Currently, more than one hundred compounds have been isolated and identified from *Coridius chinensis*. Most of these compounds have racemization, including nucleoside bases, benzene ring derivatives,



Glycerides



Acids

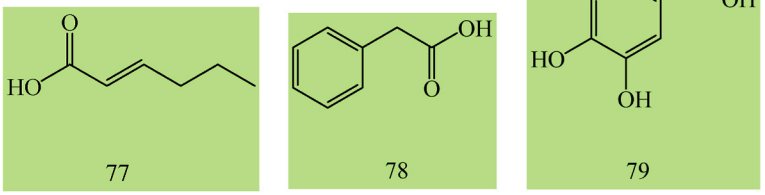
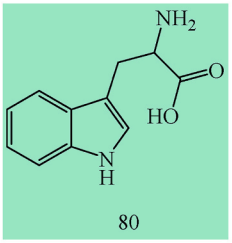


Fig. 1. (*continued*).

dopamine and its derivatives, base heteropolymers and sesquiterpenes [12,14]. Yongming Yan et al. have isolated and identified 59 compounds from *Coridius chinensis*, with 23 of them being new compounds. Among these new compounds, (±)-AspongamideA is a novel dopamine trimer that has been obtained for the first time. The other compounds are a novel dopamine dimer, pyridine salt, nucleoside or base derivatives, and new sesquiterpenes [12]. Tiantian Xu et al. have isolated a new dopamine derivative, CotidioneA,

Amino acids



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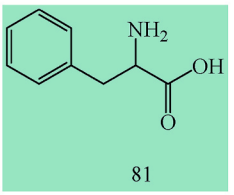

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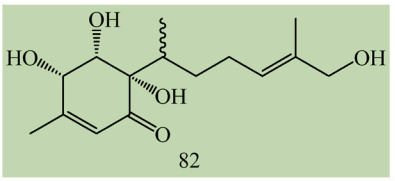
Sesquiters



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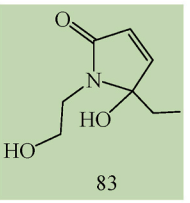

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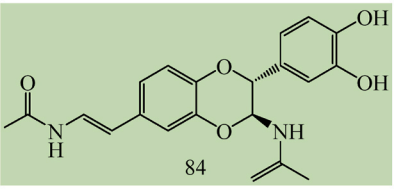

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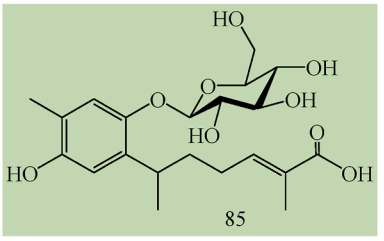

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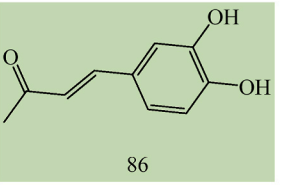

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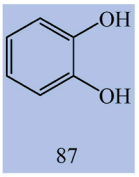
Compounds containing benzene ring



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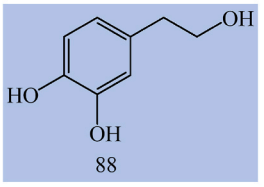

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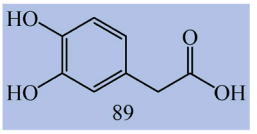

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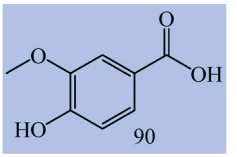

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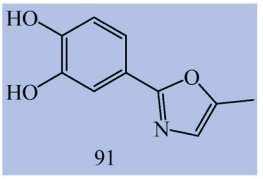

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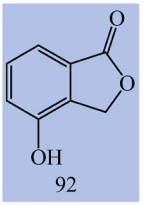

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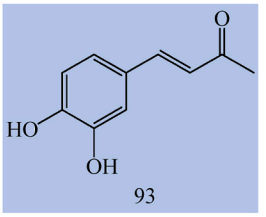

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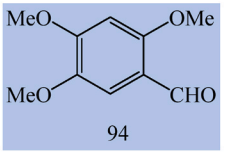

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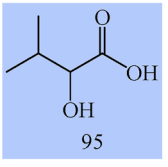
Small molecule linear compounds



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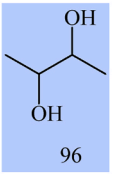

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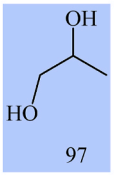

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Fig. 1. (*continued*).

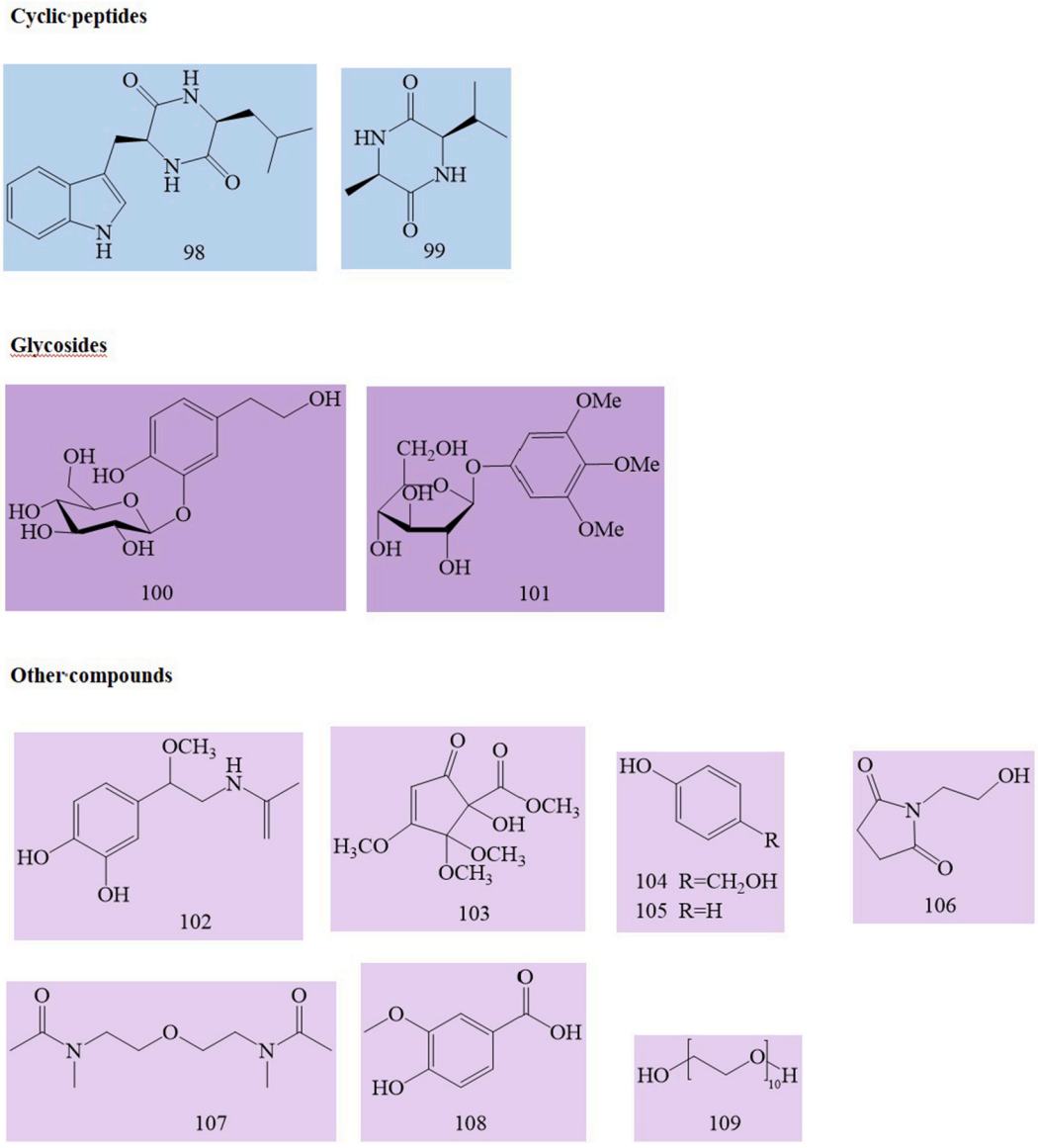

Fig. 1. (*continued*).

from *Coridius chinensis* and obtained three known analogues [15]. The structural classification and molecular formula of *Coridius chinensis* compounds are shown in Table 1 and Fig. 1.

2.2. Peptide compounds

In recent years, there have been many studies on antimicrobial peptides as metabolic compounds in insects. These peptides possess characteristics such as small molecular weight, stability, good water solubility, and a broad-spectrum antibacterial activity. They are considered to be promising new peptide drugs due to their high efficiency and low toxicity [19]. A study conducted by Songbai Zhao et al. determined the antibacterial spectrum of the hemolymph of *Coridius chinensis*. The results demonstrated which showed that it had the strongest antibacterial effect on Gram-positive bacteria [20]. Wu Mary and her colleagues isolated and purified a small molecular peptide from the hemolymph protein using gel filtration. The SDS-PAGE electrophoresis revealed a single zone, with a molecular weight of approximately 1–14.4ku. This small molecular protein exhibited a bacteriostatic effect [21]. Lastly, Li Shangwei et al. isolated an antimicrobial peptide called CcAMP1 from *Coridius chinensis*. This peptide is composed of 17 amino acid residues and has a relative molecular weight of 1997.37 [22].

2.3. Nutrition composition

Coridius chinensis is rich in fatty oil, protein, vitamins and other essential nutrients. Firstly, fatty oil is the earliest known nutrient component of *Coridius chinensis*, and its proportion is much higher compared to other insects. Lunpei Liu et al. detected the fatty oil components of *Coridius chinensis* and found 12 types of fatty acids, with palmitic acid, oleic acid and palmitic acid being the most abundant. These three fatty acids accounted for 68.58 % of the total oil [7]. Aiguo Tu et al. analyzed the composition of fatty oil in *Coridius chinensis* and found that it accounted for 45.87 % of the total content and identified 16 compounds, mainly consisting of oleic acid, linoleic acid, and palmitic acid [23]. Secondly, *Coridius chinensis* is a rich source of protein, with a high content that is easily absorbed. Lunpei Liu and Li Li et al. used the Kjeldahl nitrogen determination method to measure the crude protein content in *Coridius chinensis*. They found that it accounted for 44.3 % and 35.0 % of the dry weight, respectively, which was higher compared to other insects [7,24]. Ying Tian et al. discovered that the water extract of *Coridius chinensis* contained 0.843 mg/mL of protein, with the molecular weight primarily distributed in 12, 25, 30, 35, and 75 kDa [25]. Additionally, the amino acid composition of *Coridius chinensis* is well-balanced, consisting of 8 essential amino acids for the human body, as well as four delicious amino acids, such as glycine, alanine, glutamic acid and aspartic acid, which account for about 15 % of the total amino acids [7,26]. Finally, the study revealed that *Coridius chinensis* contains various vitamins, with high levels of vitamin A and vitamin C at 214.4 mg/kg [7] and 0.78 mg/g [23], respectively.

There are still numerous nutrients in *Coridius chinensis* that people should explore, including polysaccharides [27,28], and trace inorganic elements [7,24], among others. Although there have been some health food applications related to *Coridius chinensis*, its potential is still largely untapped. Therefore, it is crucial to enhance our understanding of the edible safety of *Coridius chinensis* and promote the use of *Coridius chinensis*-related products. This is not only a key issue, but also a prerequisite to enhance the competitiveness of *Coridius chinensis* products.

3. Pharmacological activity

In recent years, research on *Coridius chinensis* has primarily focused on various pharmacological activities, including anti-coagulation, analgesia, reproductive protection, antioxidation, anticancer, antibacterial, anti-ulcer, and anti-fatigue properties.

Table 2
Pharmacological active components of *Coridius chinensis*.

Pharmacological action	*Coridius chinensis* extract	Pharmacological mechanism	Literature
Anticoagulant	Water decoction	Promoting blood circulation and removing blood stasis	[29,30]
	Water extraction and alcohol precipitation extract	Inhibition of platelet aggregation	[31]
Reproductive protection	Water extract	Up-regulate the expression of steroid synthesis genes and increase testosterone content	[32]
	Petroleum ether extract	Down-regulation of FAK and c-Src expression inhibits the expression of BTB markers induced by Mn^{2+}	[33,34]
	Feed containing *Coridius chinensis*	Regulating the expression of apoptosis-related genes *Bcl-2* and *Bax* to inhibit apoptosis	[35]
	N-acetylnoradrenaline	Improvement of Manganese-induced TM4 Cell damage through PI3K/c-Src/FAK Pathway	[18]
	(±)Aspongamide A	Inhibit COX-2 activity and reduce the production of collagen IV, fibrin and IL-6	[10]
Antioxidation	Alcohol extract	Increase the expression level of antioxidant enzyme coding genes to increase the activity of antioxidant enzymes in skeletal muscle	[36]
Analgesia	Feed containing *Coridius chinensis*	Up-regulate the positive expression of P2X3, P2X4 and P2X7 receptors and enhance the effect of endogenous analgesia system	[37]
Anti-cancer	Water decoction	Regulate cell proliferation, autophagy and apoptosis, and inhibit the growth of HepG2 cells in vitro	[38]
	Oxazoles and N-acetyldopamine derivatives	It was resistant to Colon38, L210 and MDA cell lines	[8]
	Anticancer active components (CHP)	Inhibit cancer cell proliferation and promote apoptosis	[39]
Antibacterial	Hemolymph protein isolate	It is suggested that the bacteria are *Escherichia coli* and *Staphylococcus aureus*.	[21]
	Hemolymph	The antibacterial activity against Gram-positive bacteria was stronger than that against Gram-negative bacteria	[20]
	Antimicrobial peptide C CcAMP1	It has stronger antibacterial activity against gram-negative bacteria	[22]
	Lysozyme CcLys2	Have lysozyme activity	[40]
Promote the proliferation of adult neural stem cells	Nucleoside base derivative	Treatment of traumatic diseases of nervous system	[12]
Promote the transformation of effective components	Ether extract	Promote the growth of Ganoderma lucidum by increasing biomass and secretion of extracellular polysaccharides	[41]
	Ethanol extract	Increase the yield of extracellular triterpenes from Ganoderma lucidum	[41]
	Water extract	Promoting the synthesis of intracellular polysaccharides from Ganoderma lucidum	[41]

Table 2 displays the pharmacological activities of *Coridius chinensis* compounds.

3.1. Anticoagulant

Coridius chinensis has the ability to promote blood circulation and remove blood stasis, as well as promote qi and relieve pain. It is commonly used in traditional Chinese medicine for the treatment of vascular headaches. *Coridius chinensis* can also be used alone to treat hemangiomas and has a strong fibrinolytic effect on fibrin in laboratory tests. However, the active ingredient in *Coridius chinensis* that promote blood circulation and removes blood stasis may not be easily absorbed in high concentrations [29], so it is more appropriate to use a low dose of *Coridius chinensis* in clinical treatments targeting these effects. Additionally, the extract of *Coridius chinensis* has potential value for anticoagulation. The water decoction of *Coridius chinensis* significantly prolonged the clotting time in mice with cold coagulation models, and this effect was observed to be dose dependent [30]. Both the water extract and alcohol precipitation extract of *Coridius chinensis* can inhibit platelet aggregation through the endogenous coagulation pathway, resulting in an overall anticoagulant effect in animals [31]. The anticoagulant activity of *Coridius chinensis* may be due to the combined action of water-soluble and fat-soluble components rather than the efficacy of a single active component [31]. However, further studies are needed to fully understand this relationship.

3.2. Antioxidant reproductive protection

In recent years, there has been an increased focus on the reproductive damage caused by environmental pollution, as reproductive medicine has advanced and environmental pollution has worsened. The Great Dictionary of traditional Chinese Medicine states that *Coridius chinensis* has a notable effect on conditions such as sore and weak waist, impotence, and enuresis, which are caused by yang deficiency in the spleen and kidney [1]. Numerous studies have demonstrated that extracts and small molecular compounds derived from *Coridius chinensis* can enhance reproductive ability and safeguard against reproductive damage [18,33–35,42–44]. It has been reported that the alcohol extract of *Coridius chinensis* can enhance exercise ability and increase the activity of antioxidant enzymes in the skeletal muscle of trained rats [36,45]. Moreover, petroleum ether extract from *Coridius chinensis* is capable of significantly inhibiting Mn^{2+}-induced blood-testicular barrier (BTB) damage. Additionally, the water extract of *Coridius chinensis* can augment testosterone production in Leydig cells and regulate the hypothalamus-pituitary-testis axis to preserve the structure and function of the testis [32–34]. Furthermore, studies have shown that (±) AspongamideA isolated from *Coridius chinensis* possesses a certain protective effect against diabetic nephropathy and can inhibit the activity of COX-2 [10]. Xu et al. have demonstrated that N-acetylnor-epinephrine isolated from *Coridius chinensis*, can ameliorate manganese-induced damage to TM4 cells in mice [18](Fig. 2). In addition, Tianmu He et al. have identified potential components and targets involved in the renal protection provided by *Coridius chinensis*, thereby indicating the molecular mechanism of the "multi-component, multi-target, multi-pathway" approach to renal protection by *Coridius chinensis*, which necessitates further investigation [46].

3.3. Analgesia

Pain is one of the most common clinical symptoms and is an extremely complex physical and psychological activity. It is a defensive protective response of the body to various nociceptive stimuli. Severe pain not only brings emotional reactions like pain and

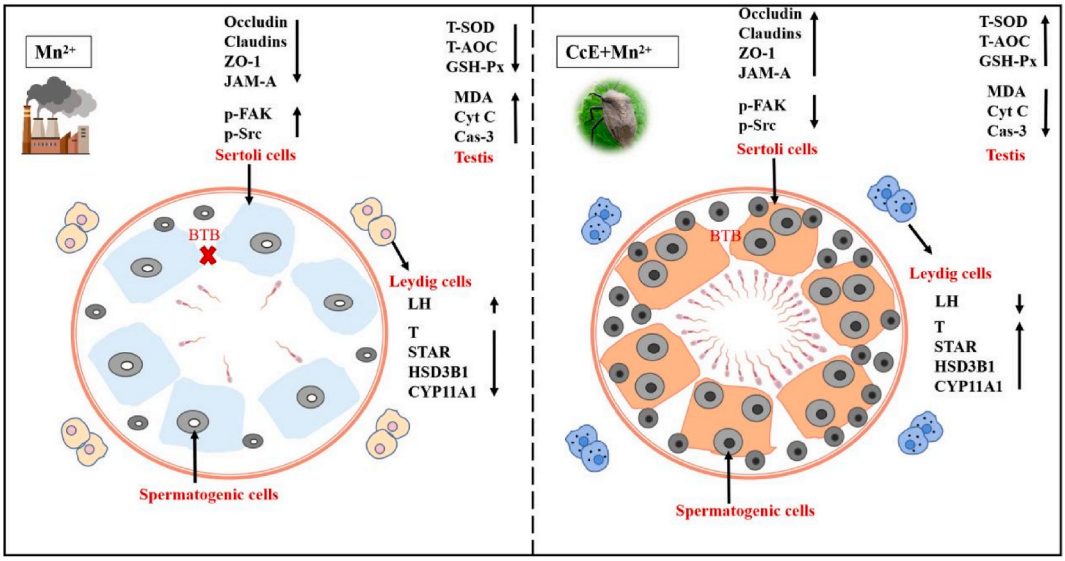

Fig. 2. Antioxidant reproductive protection mechanism of *Coridius chinensis*.

nervousness to patients, but can also cause physiological dysfunction such as shock [47]. Therefore, pain control is a major objective in clinical drug therapy. Traditional Chinese medicine has a long history and extensive experience in treating pain. When combined with other drugs, *Coridius chinensis* is widely used in traditional Chinese medicine for various types of pain and has a significant analgesic effect. Baixin Ji et al. developed a prescription mainly for the treatment of biliary colic and gastrointestinal pain in clinical practice, and it has the ability to relieve spasm and pain [48]. In a clinical observation of Jiuxiangyantongning for the treatment of cancer pain, it was found that Jiuxiangyantongning could improve the resistance of mice to heat-induced pain, increase the pain threshold, and have an analgesic effect [49]. Xiaolin Tong synthesized three small prescriptions that played an analgesic role in the treatment of stomachache caused by qi stagnation and blood stasis [50]. Additionally, *Coridius chinensis* can enhance the effect of the endogenous analgesia system and alleviate neuralgia symptoms in CCI rats, providing a new theoretical basis for the clinical use of *Coridius chinensis* in treating neuropathic pain [38]. However, further research is needed to understand the specific signaling mechanism that activates different receptors in the PAG (Table 3).

3.4. Anticancer

So far, millions of new cancer cases occur worldwide each year, posing a significant threat to human health. Currently, chemotherapy stands as one of the primary methods for cancer treatment, but it comes with substantial side effects and brings immense pain to patients. Traditional Chinese medicine has gained widespread recognition among Chinese scholars for its use in cancer treatment. The exploration of traditional Chinese medicine resources has become a critical aspect in China's search for new antineoplastic drugs [51]. Qinjian Yang et al. discovered that Xianglong San, a drug-containing serum, can induce apoptosis in human gastric cancer cells (HS-746T). Its main mechanism of action targets the DNA replication phase of cancer cells, and the induced apoptosis is not directly influenced by the drug concentration [52]. Bo Xu and his colleagues utilized a powder preparation made from *Coridius chinensis* to treat primary and metastatic middle and advanced tumors, achieving remarkable therapeutic effects [53]. Wentao Song et al. found that the combined components of *Coridius chinensis* effectively inhibit the rate of micronucleus increase in Vicia faba root tip cells and display a favorable inhibitory effect on cyclophosphamide-induced mutations [54] (Table 4). Moreover, the aqueous extract derived from *Coridius chinensis* can impede the proliferation, migration and invasion of non-small cell lung cancer cells [55]. Sha Yang and his team demonstrated that the decoction of *Coridius chinensis* hinders the growth of HepG2 cells in vitro by regulating cell proliferation, autophagy and apoptosis (Fig. 3A) [32]. Tan et al. purified an anticancer active component, named CHP, from *Coridius chinensis*, which has been proven to inhibit tumor cell proliferation (Fig. 3B) [39]. Luo et al. conducted antagonistic experiments on 10 tumor cell lines using an extract of *Coridius chinensis* and discovered that certain small molecule compounds in the extract displayed cytotoxic effects on specific tumor cells [8]. For instance, compound 1 and compound 4 inhibited colon 38 cells, compound 2 inhibited L1210 cells, and compound 3 and compound 4 inhibited U251 N cells. Additionally, compound 1 was found to inhibit MDA cells as well (Fig. 3C). *Coridius chinensis* is extensively used in anticancer treatments, but there are still many unexplored areas in understanding its mechanism of action. Therefore, further research into the medicinal components and mechanisms of *Coridius chinensis* holds significant importance.

3.5. Antibacterial

Antibacterial processes kill bacteria or inhibit their growth, reproduction and activity through physical or chemical methods. Antibiotics, as effective antibacterial substances, have successfully treated many previously incurable diseases, significantly protecting human health and increasing in demand. Studies have shown that antibiotics derived from insects, particularly antimicrobial peptides, have strong antibacterial activity, with many substances extracted from Pentatomidae insects showing this property [56]. In the case of *Coridius chinensis*, its hemolymph and hemolymph protein isolateare main sources of antibacterial substances [23]. Baisong Zhao et al. used various methods, including direct centrifugation, homogenization, and extraction, to extract the hemolymph of *Coridius chinensis*. Results demonstrated that the bacteriostatic zone diameter for ten tested bacteria species exceeded 0.7 cm, with stronger antibacterial activity against Gram-positive bacteria compared to Gram-negative bacteria [22]. Shangwei Li et al. synthesized the antimicrobial peptide CcAMP1 derived from *Coridius chinensis* and found that it exhibited excellent antibacterial activity against both Gram-positive bacteria such as *Staphylococcus aureus* and Gram-negative bacteria such as *Escherichia coli*. Furthermore, it showed stronger activity against Gram-negative bacteria [22]. This research laid the foundation for further exploration of the antimicrobial peptide resources of *Coridius chinensis* and its potential medicinal applications. Apart from antimicrobial peptides, Huang et al. identified a lysozyme called CcLys2 from *Coridius chinensis*, which is primarilly expressed in the fat body of adult *Coridius chinensis*. Bacteriostatic experiments recealed that CcLys2 exhibits lysozyme activity and plays a crucial role in the innate immunity and bacterial defense or digestive

Table 3
Analgesic effect of the compatibility of *Coridius chinensis*.

Compound preparation of *Coridius chinensis*	Formula	Clinical application	Literature
Zhitong Ling	*Coridius chinensis* and *Saussurea costus*	Treatment of biliary colic and gastrointestinal pain	[48]
Jiuxiangyan Tongning	*Coridius chinensis*、*Porcellio* and *Corydalis yanhusuo*	Treatment of cancer pain	[49]
Three small prescriptions	*Santali Albi Lignum*、*Coridius chinensis* and *Trogopterori Faeces*	Treatment of stomachache of qi stagnation and blood stasis	[50]

Table 4
Anticancer effect of the compatibility of *Coridius chinensis*.

Coridius chinensis compound preparation	Formula	Medicinal mechanism	Literature
Xianglong Powder	*Pinelliaternata*、*Scolopendra*、*Coridius chinensis*、*Atractylodes macrocephala Koidz* et al.	Induction of apoptosis of human gastric cancer cells (HS-746T)	[52]
Cancer pain	*Leiurus quinquestriatus*、*Phlyphaga plancyi*、*Coridius chinensis*、*Rheum tanguticum Maxim*、*Panax ginseng*、*Ganoderma*、*Scutellaria baicalensis Georgi* et al.	Inhibition of proliferation or induction of apoptosis of HepG2 cells	[53]
Mixed component	*Periplanetaamericana* and *Coridius chinensis*	Inhibition of cyclophosphamide-induced mutation	[54]

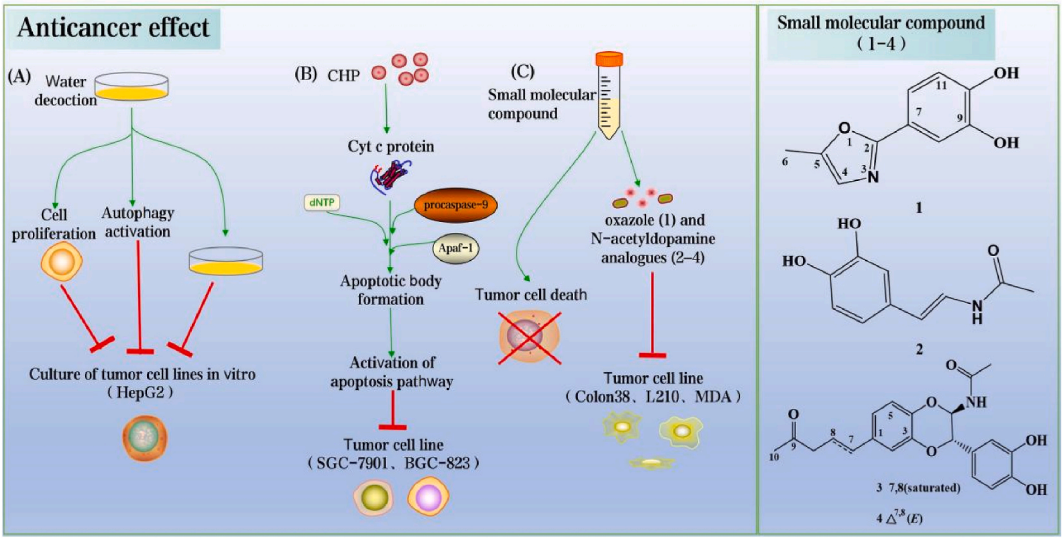

Fig. 3. Anticancer mechanism of *Coridius chinensis*.

function in the intestine of *Coridius chinensis* [41]. In conclusion, both the isolated and purified antimicrobial peptides from *Coridius chinensis*, as well as the entire organism, hemolymph or protein of *Coridius chinensis*, demonstrated significant antibacterial activity in vitro (Table 2).

3.6. Other functions

Coridius chinensis has the ability to promote metabolic processes and facilitate the metabolic transformation of receptor substances. For instance, it can enhance the production of anti-cancer active substances through the fermentation of Ganoderma lucidum [39]. Additionally, *Coridius chinensis* can promote the proliferation of receptor cells. The nucleoside base derivatives isolated from *Coridius chinensis* have been found to stimulate the proliferation of adult neural stem cells, indicating its potential therapeutic value for diseases related to nervous system damage [12] (Table 2).

4. Clinical application

Coridius chinensis has a variety of medicinal effects, with its main functions being the regulation of qi and relief of pain, as well as its ability to warm the middle and help restore yang energy. In modern Chinese medicine, *Coridius chinensis* is oftencombined with other traditional Chinese medicine to treat a range of conditions including stomachaches, cancer pain, and impotence. When it comes to andrological diseases, the use of *Coridius chinensis* decoction has shown positive therapeutic effects in cases of kidney qi loss and waist and knee pain [57–59]. Furthermore, *Coridius chinensis* has been used to effectively treat chest pain, epigastric pain, stomach cold pain, and biliary colic [46,60]. In the treatment of gynecological diseases, liver thinning pain relief soup and Warm menstrual pain capsules have been utilized to effectively treat adolescent dysmenorrhea, as well as cold coagulation and blood stasis dysmenorrhea [60,61,62]. *Coridius chinensis* can also be combined with other medications to treat a variety of diseases, including bronchitis, neurasthenia, viral hepatitis, coronary heart disease, chest pain caused by liver depression, dampness and heat, and conditions such as low menstruation and endometriosis (Table 5).

Table 5
Clinical application of *Coridius chinensis*.

Clinical application.	Compatibility of *Coridius chinensis*	Therapeutic effect	Literature
Internal medicine disease			
Chest pain and epigastric pain	*Coridius chinensis*, *Cyperi Rhizoma*, *Corydalis Rhizoma*, *Curcumae Radix*, etc.	Relieve pain and inflammation	[58]
Cold stomachache	*Coridius chinensis*, *Radix Aucklandiae*, *Corydalis Rhizoma*, *Magnoliae Officinalis Cortex*, etc.		[58]
Bile reflux gastritis	*Coridius chinensis*, *Rhei Radix et Rhizoma*, *Aurantii Immaturus Fructus*, *Arecae Semen*, etc.		[63]
Chronic wheezing bronchitis	*Coridius chinensis*, Egg, Oil of sesame or Cotton oil.	Treatment of 21 cases	[63]
Surgical disease			
Fracture of chest and ribs	*Coridius chinensis*, *BENINCASAE SEMEN*, *Dipsacus asperoides*, *Paeoniae Radix Alba*, etc.	17 cases were cured	[63]
Hemangioma	Contents of abdominal cavity of live *Coridius chinensis*	4 cases were cured	[63]
Lumbar muscle strain	*Coridius chinensis* and Chinese Baijiu.	Treatment of 7 cases	[63]
Lumbago	*Coridius chinensis* and *Citri Reticulatae Pericarpium*.	Relieve pain	[63]
Andrology disease			
Kidney qi loss, waist and knee pain	*Coridius chinensis* soup: *Coridius chinensis*、*Scolopendra*、*Cyperi Rhizoma*, etc.	It has a good effect on patients with ED	[57]
Sasuke warm tonic	*Coridius chinensis*, Hairy antler powder, *Hippocampus*, etc.	Treatment of kidney yang deficiency	[60]
Sasuke dispels evil	*Coridius chinensis*, *Scolopendra*, *Bombyx Batryticatus*, etc.	Treat those who have been ill for a long time.	[60]
Interdiaphragmatic qi stagnation and liver and kidney loss	Oolong pill: *Coridius chinensis*、*PLANTAGINIS SEMEN*, *Citri Reticulatae Pericarpium*, etc.	Treatment of 3 cases of qi stagnation, blood stasis and stomachache and hypochondriac pain	[59]
Impotence	Nine fragrant rose wine: *Coridius chinensis*、Dried rose flower and Rice wine.	Tonifying kidney and strengthening yang	[63]
Gynecological diseases			
Adolescent dysmenorrhea	Liver thinning pain relief soup: *Coridius chinensis*、*Paeoniae Radix Alba*, *Corydalis Rhizoma*, etc.	Treatment of 68 cases	[61]
Dysmenorrhea with cold coagulation and blood stasis	Warm menstrual pain capsules: *Coridius chinensis*, *Cinnamomi Cortex*, *Foeniculum vulgare*, etc.	Treatment of 60 cases	[62]
Uterine leiomyoma and ovarian cyst	*Coridius chinensis* and *Phlyphaga plancyi*	Promoting blood circulation and dispelling fatigue, regulating qi and eliminating syndrome	[63]

5. Discussion and prospect

Coridius chinensis, a type of artificially cultivable medicinal insect, has promising commercial prospects. In fact, the classification of *Coridius chinensis* has always been a subject of controversy in the market. Prior to Ji Wenxiang et al., there was a lack of thorough understanding regarding the morphology and biological characteristics of *Coridius chinensis*. To address this matter, Ji Wenxiang et al. conducted a systematic study on the morphology and biological characteristics of *Coridius chinensis* [64]. They also analyzed the detailed morphological characteristics, survival habits, and reproduction habits of *Coridius chinensis*. As a result, this study has filled the knowledge gap regarding the biology and physiological ecology of *Coridius chinensis*. Moreover, the scarcity of artificial culture and breeding technology has resulted in several technical bottlenecks in achieving large-scale artificial cultivation, leading to a noticeable conflict between the supply and demand of *Coridius chinensis* resources.

In modern pharmacological studies, there have been numerous reports on the anti-tumor, antibacterial, and reproductive damage-improving properties of *Coridius chinensis*. These findings are consistent with its clinical applications in andrology, gynecological diseases, and cancer. It is worth noting that *Coridius chinensis* is also effective in treating gastric diseases. Given the increasing incidence of gastric diseases, particularly among the younger population in China, the use of *Coridius chinensis* in the treatment of such conditions deserves attention. Analyzing and clarifying the pharmacological material basis and mechanism of *Coridius chinensis* is of particular importance. This medicinal plant has been utilized for thousands of years in China. However, due to the personalized nature of traditional Chinese medicine in diagnosis and treatment, its clinical efficacy cannot be comprehensively evaluated through evidence-based medicine. Consequently, this has hindered the development and application of *Coridius chinensis*. In fact, separating and identifying the components of traditional Chinese medicine is a crucial prerequisite for its production and application. In the case of *Coridius chinensis*, isolating and identifying its components is a vital aspect of studying its pharmacological activity. Previous research has repeatedly emphasized the wide range of biological and pharmacological activities exhibited by natural compounds found in *Coridius chinensis*. The effectiveness of these compounds depends on their specific biological activities and the relationship between these chemical compoments. Additionally, extensive biological tests have demonstrated that many isolated and identified chemicals from *Coridius chinensis* are effective in treating various diseases. However, in comparison to the vast pool of resources available, there is still a substantial gap in the research on individual compounds. This is currently the most challenging aspect. In many instances, the overall findings of the extract cannot be directly applied to clinical trials. Traditional Chinese medicine places emphasis on the balance among medicinal materials, while western medicine prioritizes pharmacological safety and a clear molecular mechanism. Therefore, further exploration of the pharmacological activity and action mechanism of single compounds derived from *Coridius chinensis* is of

utmost importance. Although current research has significantly enhanced our understanding of the value of *Coridius chinensis*, there are still unexplored areas, such as the identification of active components and elucidation of pharmacological mechanisms, that warrant investigation.

As a natural source of medicinal properties, *Coridius chinensis* holds immense potential for development. It occupies an unparalleled position, both as a health food and as a clinical drug used in the treatment of various diseases. Researchers have gathered substantial data on this valuable medicinal insect, analyzing its composition, exploring its pharmacological effects, and investigating its clinical applications. These studies have provided significant evidence regarding the efficacy and safety of *Coridius chinensis*. In fact, the role of the *Coridius chinensis* has been verified multiple times. However, the next step is to conduct a thorough exploration of its molecular mechanism as a single component. Before proceeding with this, it is crucial to first clarify the composition of the components present in the *Coridius chinensis*. Consequently, the identification of its components and the study of its pharmacological activities have become crucial areas of research, not only to better understand its potential as a new drug for treating clinical diseases but also as a necessary prerequisite for the advancement of this valuable medicinal insect.

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Consent to participate: not applicable

Consent for publication: All authors have read and agreed to the published version of the manuscript.

Availability of data and materials

Not applicable.

Code availability

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CRediT authorship contribution statement

Keyi Xiong: Writing – review & editing, Conceptualization. **Fengyin Zeng:** Writing – review & editing. **Xiqin Lei:** Writing – review & editing. **Yongqiu Wei:** Writing – review & editing, Supervision. **Xin Zhou:** Writing – review & editing, Supervision. **Xiaohui Hou:** Writing – review & editing, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Xiaohui Hou reports financial support was provided by Guizhou Provincial Health Commission. Xiaohui Hou reports financial support was provided by Zunyi Medical University. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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