Acupuncture and Herbal Medicine

Rhizoma Atractylodis: a review on processing, chemical composition, pharmacological effects, and product development

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Abstract

Rhizoma Atractylodis has a long history of medicinal use, a broad spectrum of applications, and diverse clinical utility. This review provides a comprehensive overview of Rhizoma Atractylodis, focusing on its processing, chemical composition, pharmacological effects, and product development. Processing methods include stir-frying with bran, stir-frying until cooked, and rinsing with rice-washed water. The chemical composition includes terpenes, alkynes, sugars and their glycosides, organic acids and their esters, coumarins, and other compounds. Its pharmacological effects include the treatment of gastrointestinal diseases, arthritis, liver diseases, lung diseases, cancer, cardiovascular conditions, etc. Finally, product development prospects include decoction-ready products, Chinese patent medicines, health products and daily necessities, epidemic prevention, and veterinary medicine. Notably, this review simultaneously discusses, analyzes, and explores the quality control and industrial development of Rhizoma Atractylodis, offering guidance for advancing related industries, enhancing production quality control, and exploring innovative strategies for the clinical application and development of new Rhizoma Atractylodis-based products.

Keywords: Active ingredient, Chinese patent drug, Pharmacological activity, Processing, Rhizoma Atractylodis

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Introduction

Rhizoma Atractylodis, the dried rhizome of *Atractylodes lancea (Thunb.) DC.* or *Atractylodes chinensis (DC.) Koidz.*, belongs to the Asteraceae family and was first listed as a top-grade herb in the Shen Nong Ben Cao Jing. According to the Chinese Pharmacopoeia, Rhizoma Atractylodis is known for its ability to dry dampness, tonify the spleen, expel wind, dispel cold, and improve eyesight[1].

Maoshan, located in Jurong City, Jiangsu Province, is the geo-authentic area of *Atractylodes lancea* (*A. lancea*). Due to its depletion in the wild, cultivating *A. lancea* has been introduced to various areas to meet growing market demand. Following cultivation, notable morphological changes in medicinal components have been observed in *A. lancea*, resulting in a distinction between *A. lancea (Thunb.) DC.*, and *A. chinensis (DC.) Koidz*, both of which are included in the Chinese Pharmacopoeia. Many researchers believe that the division between these two species is based on the Qinling Mountains and the Huai River as geographic boundaries[2]. *A. lancea (Thunb.) DC* is primarily cultivated in Jiangsu, Hubei, Henan, Anhui, and other provinces, while *A. chinensis (DC.) Koidz* is mainly produced in Hebei, Shanxi, and Inner Mongolia[3]. *A. lancea (Thunb.) DC.* prefers cool, dry climates, and cannot tolerate high temperatures or humidity. Hilly areas are suitable for its cultivation, growing best on semi-shaded, semi-sunny barren slopes with sandy soils, deep soil layers, and good drainage[4]. Conversely, *A. chinensis (DC.) Koidz* prefers a cool climate with sufficient sunlight and a significant day-night temperature variation. This species is resistant to extreme cold but not too intense light or high temperatures. *A. chinensis (DC.) Koidz* thrives in sandy loam soils with good drainage, loose texture, low groundwater levels, and high humus content[2].

A. lancea has attracted significant attention from several researchers as a bulk medicinal material. Recent reviews of *A. lancea* have mainly focused on its chemical composition and pharmacological effects. This review aims to provide a comprehensive summary of *A. lancea* from four key perspectives: processing methods, chemical composition, pharmacological effects, and product development, highlighting recent research advancements. Furthermore,

Chang Ke and Linghang Qu contributed equally to this work.

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this study aims to provide guidance for developing related industries, offer quality control references, and propose innovative strategies for the clinical application and development of new *A. lancea*-based products.

Processing of Rhizoma Atractylodis

Ancient processing methods

Using classical medical and herbal literature written since the Tang Dynasty, this section provides a comprehensive and systematic review of the ancient historical evolution of Rhizoma Atractylodis processing as a reference for studying its processing.

Processing without excipients

Cleansing

The practice of "cleansing" was first proposed in the Song Dynasty's "Chuan Xin Shi Yong Fang," laying the foundation for subsequent processing. This practice involves removing impurities, non-medicinal components, and insect infestations from medicinal herbs.

Cutting

After cleansing, Rhizoma Atractylodis is cut into slices, segments, and other shapes to facilitate the extraction of active ingredients. During the Song and Yuan Dynasties, processes such as "thin cutting" and "filing and crushing" were recorded. These processes are extremely common before further processing.

Stir-frying

Stir-frying was first recorded during the Song Dynasty and involved methods such as stir-frying to yellowness, stir-frying to coking, and stir-frying to carbonization. The different degrees of stir-frying are associated with different clinical needs. Rhizoma Atractylodis stir-frying to yellowness can alleviate dryness, while stir-frying to coking can enhance intestine-protective and antidiarrheal effects. Stir-frying to carbonization produces a hemostatic effect.

Steaming

Steaming of Rhizoma Atractylodis was first recorded during the Song Dynasty. By the Ming Dynasty, auxiliary materials were incorporated during steaming to adjust drug performance.

Processing with excipients

Processing with rice-washed water

This method, first mentioned during the Tang Dynasty, was believed to remove the dryness effect of Rhizoma Atractylodis, while enhancing its spleen-tonifying effects. This method gained popularity during the Song Dynasty and saw improvements during the Ming and Qing Dynasties.

Stir-frying with bran

In this common processing technique, Rhizoma Atractylodis is stir-fried with bran to reduce its gastrointestinal irritation effects. The Song Dynasty medical book "Taiping Huimin Heji Ju Fang" has records of this method.

Stir-frying with soil

This method, reported in the literature from the Ming and Qing Dynasties, enhances the spleen-tonifying and antidiarrheal effects of Rhizoma Atractylodis.

Processing with salt water

This method alleviates the dryness effect of Rhizoma Atractylodis. During the Qing Dynasty, medical experts believed that Rhizoma Atractylodis processed with salt water exhibited diuretic effects.

Processing with yellow wine

Introduced during the Yuan Dynasty, soaking or stir-frying Rhizoma Atractylodis in yellow wine was used to enhance its blood-circulating effect.

Processing with vinegar or sesame

These excipients were commonly used to nourish yin, reduce fires, and regulate the herb's medicinal properties.

Modern processing methods

Rhizoma Atractylodis has been recorded in the Chinese Pharmacopoeia from 1963 to 2020. The 1963 edition listed both raw Rhizoma Atractylodis and Rhizoma Atractylodis processed with rice-washed water. The 1977 edition included both raw and stir-fried Rhizoma Atractylodis, while the 1985–2020 editions included both raw and stir-fried Rhizoma Atractylodis processed with bran.

Local Chinese medicine processing standards primarily recorded methods such as stir-frying until yellow, stir-frying until coking, stir-frying with bran, and processing with rice-washed water. Among these, stir-frying with bran and processing with rice-washed water are the most commonly employed. Additionally, local standards in the Fujian and Henan provinces contain records of stir-frying with soil. Modern processing techniques for Rhizoma Atractylodis tend to be more standardized and typically involve stir-frying with bran, stir-frying to coking, processing with rice-washed water, stir-frying with soil, and steaming. These methods are designed to "reduce dryness and increase efficiency," thereby reducing the irritability of volatile oils and enhancing the spleen-tonifying effect[5].

Processing techniques

The processing techniques for decoction-ready products generally include various methods such as the single-factor test, orthogonal design, and response surface method.

Cleansing and cutting

Scientists have examined the water-washing process of Rhizoma Atractylodis using the weight-grade method, focusing on indicators such as volatile oil and ash content. In a study, to determine the optimal water-washing process, 10 times the amount of water was added twice and washed for 2 minutes each time for a thorough cleaning while ensuring that the main components remained unaffected[6]. Another study used an orthogonal experimental design to investigate the preparation of Rhizoma Atractylodis. The optimal process involved cutting the plant into 2-mm-thick pieces, washing once with 10 times the amount of water in a rotary machine at 45 rpm for 60 seconds, and drying at 50°C for 4 h[7]. Researchers recommend a cutting thickness of 2 to 4 mm and a drying temperature of 70°C for *A. chinensis (DC.) Koidz*[8]. However, some studies have indicated that a drying temperature above 60°C is inappropriate and may affect the stability of the components of *A. chinensis (DC.) Koidz*. Thus, it has been suggested that the temperature should not exceed 60°C.

Stir-frying with bran

Stir-frying Rhizoma Atractylodis with bran can reduce its dryness and associated side effects while enhancing its spleen-tonifying effect. Several studies have optimized the processing technology for stir-frying Rhizoma Atractylodis with bran. A study conducted an L_9 (3^4) orthogonal experiment using indicators such as atractylodin and β-eudesmol to optimize the stir-frying process with 100 g of bran per kilogram of decoction pieces at 200°C for 80 seconds[9]. Another study performed uniform design experiments and found that the optimal conditions were 15 kg/100 kg of bran, a stir-frying temperature of 195°C, stir-frying time of 5 minutes, and flipping frequency of 65 times/min[10]. Additionally, some studies have employed the Box–Behnken response surface method to optimize the process, identifying an optimal formulation of 10% excipient, 140°C stir-frying temperature, and 3 minutes stir-frying time[11]. The process parameters, such as the amount of excipient, stir-frying temperature, and time, significantly impact the final quality of the stir-fried Rhizoma Atractylodis with bran.

Stir-frying to coking

Coking Rhizoma Atractylodis has been recorded in the processing standards of several regions. However, the Chinese Pharmacopoeia has not yet included coking Rhizoma Atractylodis, and research on the stir-frying and coking processing technology remains limited. A study employed the L_9 (3^4) orthogonal experimental method to examine the quality fraction of tannins in Rhizoma Atractylodis and the antidiarrheal effects in mice. The study investigated the impact of temperature, time, and flipping frequency on the stir-frying to cooking process. The optimal conditions were determined to be 220 to 230°C for 6 minutes, with a flipping frequency of 50 times/min[12]. Currently, the clinical use of coked Rhizoma Atractylodis is limited, and research on its processing technology is sparse, necessitating additional studies.

Rice-washed water processing

The practice of processing Rhizoma Atractylodis using rice-washed water originated during the Song Dynasty and is still being employed in the Fujian, Gansu, Jiangxi, and Henan provinces to date. One study applied the central composite design–response surface methodology to investigate the effects of rice-washed water dosage, bleaching time, and temperature on the composition of Rhizoma Atractylodis. The predicted optimal processing conditions were a rice-washed water volume of 7.28 times the weight of the material, a rinsing duration of 72 h, and a temperature of 20°C[13]. Another study adopted the L_9 (3^4) orthogonal design to optimize the rice-washed water bleaching technique of Jianchang Bang. The optimal processing conditions involved using 10 times the rice-washed water to allow the Rhizoma Atractylodis to float for 12 h, rinsing with clean water for 2 h, and drying[14]. Due to variations in processing techniques, the quality and efficacy of Rhizoma Atractylodis produced from rice-washed water differ. Therefore, comparative studies on the active components and efficacy of Rhizoma Atractylodis processed using different rice-washed water techniques are essential. Figure 1 illustrates the common processing steps for Rhizoma Atractylodis.

Chemical components of Rhizoma Atractylodis

The chemical components of Rhizoma Atractylodis are diverse and generally classified into volatile and non-volatile components. Currently, various compounds have been isolated from Rhizoma Atractylodis, including terpenes, alkynes, carbohydrates and their glycosides, organic acids and their esters, coumarins, and other components (Table 1).

Chemical components

Terpenoids

Volatile oils, which constitute 2% to 9% of Rhizoma Atractylodis, are the main active ingredients. Terpenoids are the primary components of these volatile oils and can be divided into monoterpenes, sesquiterpenes, and triterpenes. Approximately 100 terpenoids have been isolated and identified from Rhizoma Atractylodis[15–21].

Processing significantly reduces the volatile oil content of Rhizoma Atractylodis, leading to notable changes in the composition of its constituent compounds[22]. In a study, after stir-frying Rhizoma Atractylodis with bran, the levels of α-pinene, β-terpinene, atractylon, hinesol, β-eudesmol, α-bisabolol, and 4-styrylpyridazine decreased[23–24], while those of atractylenolide I and II increased[25]. In Rhizoma Atractylodis processed with rice-washed water, the content of α-pinene, zingiberene, and atractylon increased, while those of phellodendron and limonene decreased[26].

Alkynes

Alkynes, which are unsaturated compounds containing carbon-carbon triple bonds, are important active ingredients in Rhizoma Atractylodis. According to the 2020 edition of the Chinese Pharmacopoeia, the acetylene compound, atractylodin, is a quality control indicator for Rhizoma Atractylodis. Several studies have demonstrated that atractylodin content decreases after processing Rhizoma Atractylodis[24–25]. To date, 15

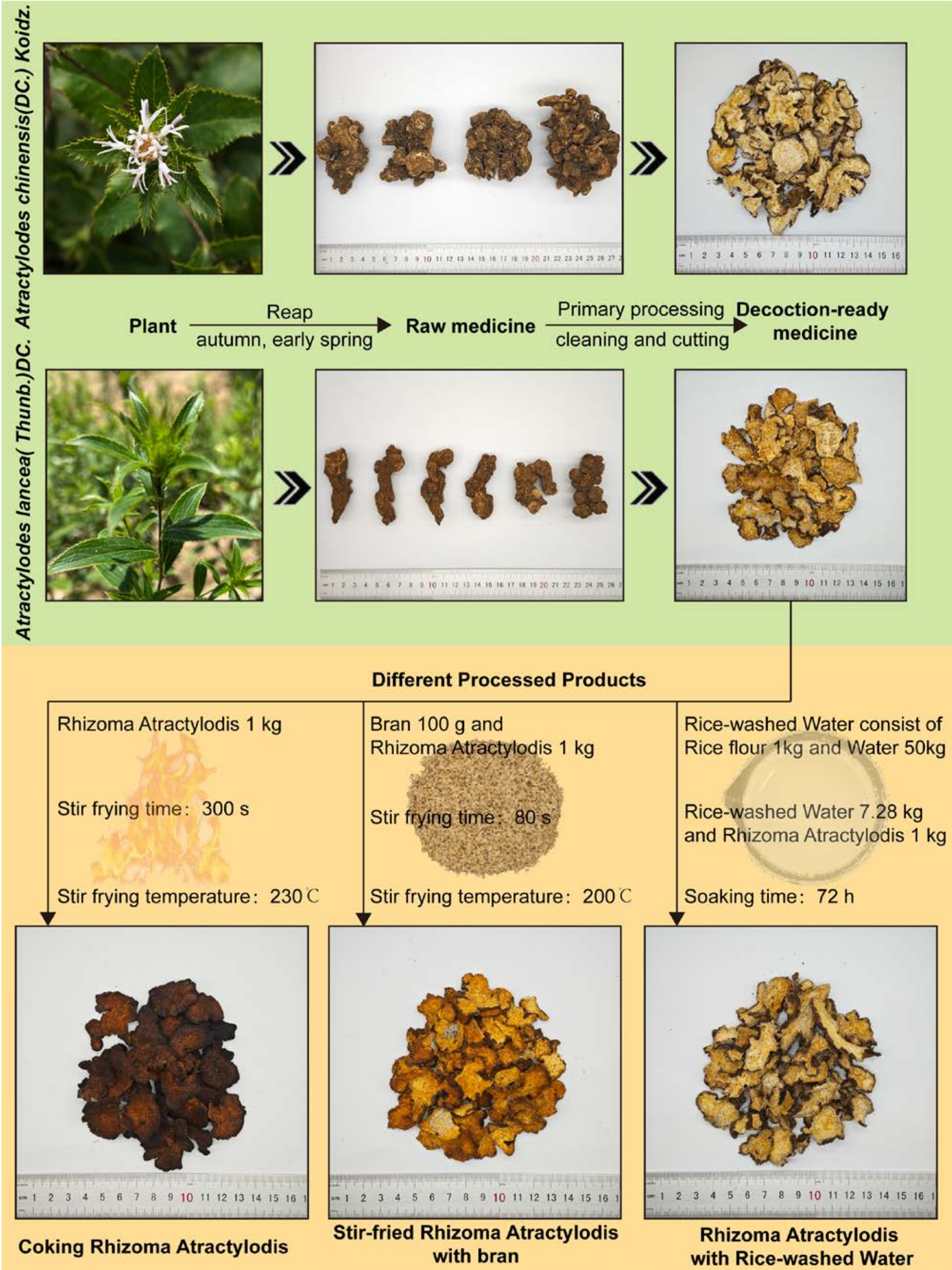

Figure 1. The processing of Rhizoma Atractylodis.

alkyne compounds have been isolated from Rhizoma Atractylodis[15,27].

Carbohydrates and their glycosides

Rhizoma Atractylodis contains various carbohydrates, including xylose, glucose, galactose, etc, which exhibit certain pharmacological activities. Polysaccharides derived from Rhizoma Atractylodis can regulate the intestinal immune system. After processing, the total polysaccharide content of *A. lancea (Thunb.) DC* increases significantly. Scanning electron microscopy has revealed that both raw and bran-stir-fried Rhizoma Atractylodis polysaccharides exhibit coral-like structures, with the latter having a denser structure[28]. Glycosides are key active substances in Rhizoma Atractylodis, with glycoside A and β-daucosterol being the compounds that increase in concentration following processing[28]. To date, 38 carbohydrates and glycosides have been isolated from Rhizoma Atractylodis[15,29–30].

Organic acids and their esters

Rhizoma Atractylodis contains several organic acids and their esters. Specifically, researchers have identified 40 organic acids and their esters in *A. lancea (Thunb.) DC.* and *A. chinensis (DC.) Koidz*[15,31–32].

Other components

Rhizoma Atractylodis also contains several coumarins such as 7-hydroxycoumarin, scopoletin, and hydroxymethylcellulose[15]. Additional components include 5-hydroxymethylfurfural, 5,5′-oxybis (5-methylene-2-furaldehyde)[33], and two flavonoids—baicalin methyl ester and baicalein[34–35].

Table 1

Chemical components of Atractylodis Rhizoma

Class	Name	Molecular formula	MW (g/mol)	PubChem CID
Monoterpene	3-Carene	$C_{10}H_{16}$	136.23	26049
	Thymol	$C_{10}H_{14}O$	150.22	6989
	α-Pinene	$C_{10}H_{16}$	136.23	2723720
	α-Phellandrene	$C_{10}H_{16}$	136.23	7460
	β-Terpinene	$C_{10}H_{16}$	136.23	7461
	2-Cycloheptylidenepropanedinitrile	$C_{10}H_{12}N_2$	160.22	534961
	3,4,5-Trimethoxybenzyl alcohol	$C_{10}H_{14}O_4$	198.22	77449
Sesquiterpenes	Atractylenolide I	$C_{15}H_{18}O_2$	230.30	5321018
	Atractylenolide II	$C_{15}H_{20}O_2$	232.32	14448070
	Atractylenolide III	$C_{15}H_{20}O_3$	248.32	155948
	Hinesol	$C_{15}H_{26}O$	222.37	10878761
	Atractylon	$C_{15}H_{20}O$	216.32	3080635
	Cadinene	$C_{15}H_{24}$	204.35	3032853
	Cyperene	$C_{15}H_{24}$	204.35	12308843
	α-Guaiene	$C_{15}H_{24}$	204.35	5317844
	α-Humulene	$C_{15}H_{24}$	204.35	5281520
	Germacrene D	$C_{15}H_{24}$	204.35	5317570
	Selinene	$C_{15}H_{24}$	204.35	520383
	Valencene	$C_{15}H_{24}$	204.35	9855795
	Aromadendrene dehydro	$C_{15}H_{22}$	202.33	589433
	Spathulenol	$C_{15}H_{24}O$	220.35	92231
	Cineole	$C_{10}H_{18}O$	154.25	2758
	Curzerene	$C_{15}H_{20}O$	216.32	12305301
	Dihydrokaranone	$C_{15}H_{22}O$	218.34	10353347
	Caryophyllene	$C_{15}H_{24}$	204.35	5281515
	Elixene	$C_{15}H_{24}$	204.35	94254
	Eremophilene	$C_{15}H_{24}$	204.35	12309744
	Longifolene-V4	$C_{15}H_{24}$	204.35	570529
	Germacrene B	$C_{15}H_{24}$	204.35	5281519
	Patchoulene	$C_{15}H_{24}$	204.35	101731
	Caryophylleneoxide	$C_{15}H_{24}O$	220.35	1742210
	Carotol	$C_{15}H_{26}O$	222.37	442347
	Juniper camphor	$C_{15}H_{26}O$	222.37	521214
	Selina-4(15),7(11)-dien-8-one	$C_{15}H_{22}O$	218.33	13986100
	Caryophyllene	$C_{15}H_{26}O$	204.35	5281515
	Guaiol	$C_{15}H_{26}O$	222.37	227829
	Agarospirol	$C_{15}H_{26}O$	222.37	21675005
	Elemol	$C_{15}H_{26}O$	219.28	92138
	Alloaromadendrene	$C_{15}H_{24}$	204.35	10899740
	Aristolene	$C_{15}H_{24}$	204.35	530421
	d-δ-Cadinene	$C_{15}H_{24}$	204.35	441005
	Aromadendrene	$C_{15}H_{24}$	204.35	11095734
	Calarene	$C_{15}H_{24}$	204.35	28481
	Aristolone	$C_{15}H_{22}O$	218.34	165536

(*Continued*)

Table 1
(Continued)

Class	Name	Molecular formula	MW (g/mol)	PubChem CID
	Geranyl acetate	$C_{12}H_{20}O_2$	196.29	1549026
	Furanodienone	$C_{15}H_{18}O$	230.30	6442374
	Ostunolide	$C_{15}H_{20}O_2$	232.32	5367559
	α-Bisabolol	$C_{15}H_{26}O$	222.37	442343
	α-Caryophyllene	$C_{15}H_{24}$	204.35	5281520
	α-Eudesmol	$C_{15}H_{26}O$	222.37	92762
	α-Bisabolol	$C_{15}H_{26}O$	222.37	442343
	a-Guaiene	$C_{15}H_{24}$	204.35	107152
	α-Zingiberene	$C_{15}H_{24}$	204.35	92776
	α-Acorenol	$C_{15}H_{24}$	204.35	11972555
	β-Eudesmol	$C_{15}H_{26}O$	224.38	12309818
	β-Selinene	$C_{15}H_{24}$	204.35	28237
	β-Cedrene	$C_{15}H_{24}$	204.35	11106485
	β-Patchoulene	$C_{15}H_{24}$	204.35	101731
	β-Caryophyllene	$C_{15}H_{24}$	204.35	5281515
	β-Himachalene	$C_{15}H_{24}$	204.35	11586487
	β-Sesquiphellandrene	$C_{15}H_{24}$	204.35	12315492
	β-Maaliene	$C_{15}H_{24}$	204.35	101596917
	β-Caryophyllene	$C_{15}H_{24}$	204.35	5281515
	β-Elemene	$C_{15}H_{24}$	204.35	6918391
	β-Caryophyllene	$C_{15}H_{24}$	204.35	5281515
	γ-Elemene	$C_{15}H_{24}$	204.35	12309452
	γ-Caryophyllene	$C_{15}H_{24}$	204.35	5281522
	γ-Muurolene	$C_{15}H_{24}$	204.35	12313020
	γ-Selinene	$C_{15}H_{24}$	204.35	10655819
	γ-Eudesmol	$C_{15}H_{26}O$	222.37	6432005
	γ-Himachalene	$C_{15}H_{24}$	204.35	577062
	γ-Gurjunene	$C_{15}H_{24}$	204.35	90805
	γ-Eudesmol	$C_{15}H_{26}O$	222.37	6432005
	δ-Guaiene	$C_{15}H_{24}$	204.35	94275
	3β-Hydroxyatractylon	$C_{15}H_{20}O_2$	232.32	71448961
	7-Methoxy-2-methyl-2-(4-methylpent-3-enyl)-2H-chromene	$C_{17}H_{22}O_2$	258.35	501675
	Guaia-3,9-diene	$C_{15}H_{24}$	204.35	585005
Triterpenoids	Limonin	$C_{26}H_{30}O_8$	470.50	179651
	β-Amyrin	$C_{30}H_{50}O$	426.72	92156
Alkynes	Atractylodin	$C_{13}H_{10}O$	182.22	5321047
	Atractylodinol	$C_{13}H_{10}O_2$	198.22	10012964
	Acetylatractylodinol	$C_{15}H_{12}O_3$	240.25	5315531
	Diacetyl-atractylodiol	$C_{17}H_{20}O_4$	288.34	6443553
	Tetradeca-1,3,5-trien-8,10-diyne-1,3-diyl diacetate	$C_{18}H_{20}O_4$	300.35	155905902
	7-Phenyl-2-heptene-4,6-diyn-1-Ol	$C_{13}H_{10}O$	182.22	6437824
	(6E,12E)-Tetradecadiene-8,10-diyne-1,3-diol-diacetate	$C_{18}H_{22}O_4$	338.40	71326873

(*Continued*)

Table 1
(Continued)

Class	Name	Molecular formula	MW (g/mol)	PubChem CID
	2-[(2E)-3,7-dimethylocta-2,6-dienyl]-4-methoxy-6-methylphenol	$C_{18}H_{26}O_2$	274.40	10061923
Sugar and glycosides	Rhamnose	$C_6H_{12}O_5$	164.16	25310
	Ribose	$C_5H_{10}O_5$	150.13	10975657
	Arabinose	$C_5H_{10}O_5$	150.13	439195
	Xylose	$C_5H_{10}O_5$	150.13	135191
	Fucose	$C_6H_{12}O_5$	164.16	17106
	Glucose	$C_6H_{12}O_6$	180.16	5793
	Mannose	$C_6H_{12}O_6$	180.16	18950
	Mannitol	$C_6H_{14}O_6$	182.17	6251
	Galactose	$C_6H_{12}O_6$	180.16	6036
	Fructose	$C_6H_{12}O_6$	180.16	2723872
	Atractan A	-	-	381122996
	Atractan B	-	-	381122997
	Atractan C	-	-	381122998
	Atractyloside A	$C_{21}H_{36}O_{10}$	448.50	71307451
	Atractyloside B	$C_{21}H_{38}O_{10}$	450.50	71448952
	Atractyloside C	$C_{21}H_{36}O_7$	400.50	71448953
	Atractyloside D	$C_{27}H_{46}O_{12}$	562.60	71448954
	Atractyloside E	$C_{32}H_{54}O_{16}$	694.80	71448955
	Atractyloside F	$C_{37}H_{62}O_{20}$	826.90	71448956
	Atractyloside G	$C_{21}H_{36}O_8$	416.50	71448957
	Atractyloside H	$C_{32}H_{54}O_{17}$	710.80	71448958
	Atractyloside I	$C_{27}H_{44}O_{13}$	576.60	71448959
	Daucosterol	$C_{35}H_{60}O_6$	576.80	5742590
	Syringing	$C_{17}H_{24}O_9$	372.40	5316860
	Dihydrosyringin	$C_{17}H_{26}O_9$	374.38	500777372
	Icariside F2	$C_{18}H_{26}O_{10}$	402.40	14079045
	Icariside D1	$C_{19}H_{28}O_{10}$	416.42	13893575
Organic acids and their esters	Palmitic acid	$C_{16}H_{32}O_2$	256.42	985
	Oleic acid	$C_{18}H_{34}O_2$	282.50	445639
	Stearic acid	$C_{18}H_{36}O_2$	284.50	5281
	Vanillic acid	$C_8H_8O_4$	168.15	8468
	Quinic acid	$C_7H_{12}O_6$	192.17	6508
	Malic acid	$C_4H_6O_5$	134.09	525
	Nonanedioic acid	$C_9H_{16}O_4$	188.22	2266
	Sanleng acid	$C_{18}H_{34}O_5$	205.25	5321100
	Oleanolic acid	$C_{30}H_{48}O_3$	456.70	10494
	Myristic acid	$C_{14}H_{28}O_2$	228.37	11005
	Neochlorogenic acid	$C_{16}H_{18}O_9$	354.31	5280633
	Chlorogenic acid	$C_{16}H_{18}O_9$	354.31	1794427
	Cryptochlorogenic acid	$C_{16}H_{18}O_9$	354.31	9798666
	Isochlorogenic acid A	$C_{25}H_{24}O_{12}$	516.40	6474310
	Isochlorogenic acid B	$C_{25}H_{24}O_{12}$	516.40	5281780
	Isochlorogenic acid C	$C_{25}H_{24}O_{12}$	516.40	6474309

(*Continued*)

Table 1
(Continued)

Class	Name	Molecular formula	MW (g/mol)	PubChem CID
	Syringic acid	$C_9H_{10}O_5$	198.17	10742
	Palmitic acid	$C_{16}H_{32}O_2$	256.42	985
	Linoleic acid	$C_{18}H_{32}O_2$	280.40	5280450
	Caffeic acid	$C_9H_8O_4$	180.16	689043
	Ferulic acid	$C_{10}H_{10}O_4$	194.18	445858
	p-Methoxycinnamic acid	$C_{10}H_{10}O_3$	178.18	699414
	Palmitoleic acid	$C_{17}H_{32}O_2$	254.41	445638
	9-Octadecenoic acid	$C_{18}H_{34}O_2$	282.50	637517
	6-Nonynoic acid	$C_9H_{14}O_2$	154.21	534311
	Heptadecanoic acid	$C_{17}H_{34}O_2$	270.50	10465
	Octacosanoic acid	$C_{28}H_{56}O_2$	424.70	10470
	Protocatechuic acid	$C_7H_6O_4$	154.12	72
	2-Furoic acid	$C_5H_4O_3$	112.08	6919
	3,4-Dihydroxybenzaldehyde	$C_7H_6O_3$	138.12	8768
	5-O-Feruloylquinic acid	$C_{17}H_{20}O_9$	368.30	10133609
	3-O-Feruloylquinic acid	$C_{17}H_{20}O_9$	368.30	6451331
	4-O-Feruloylquinic acid	$C_{17}H_{20}O_9$	368.30	10177048
	4-Hydroxy-1,2-benzenedicarboxylic acid	$C_8H_6O_5$	182.13	11881
	9,10-Epoxy-12(Z)-octadecenoic acid	$C_{18}H_{32}O_3$	296.40	5283018
	(9Z,11E,15Z)-13-Hydroxy-9,11,15-octadecatrienoic acid	$C_{18}H_{30}O_3$	294.43	22041877
	9,12-Octadecadienoic acid	$C_{18}H_{32}O_2$	280.40	5280450
	Geranyl acetate	$C_{12}H_{20}O_2$	196.29	1549026
	Neryl acetate	$C_{12}H_{20}O_2$	196.29	1549025
	Citronellyl acetate	$C_{12}H_{22}O_2$	198.30	9017

Pharmacological effects of Rhizoma Atractylodis

Rhizoma Atractylodis is widely used in clinical practice. The Chinese Pharmacopoeia recommends a daily dosage of 3 to 9 g; however, based on ancient Chinese medical records and modern clinical experience, the clinical dosage often exceeds the Pharmacopoeia's recommendation, ranging from 9 to 50 g. For instance, Zhiyuan Zhang used Rhizoma Atractylodis at a dose of 9 g to treat diarrhea caused by cold dampness by strengthening the spleen and transforming dampness. In Guicheng Xia's formula for treating Yang deficiency of the spleen and kidney, the dosage was 10 g. Xiaolin Tong combined Rhizoma Atractylodis with Phellodendri Chinensis Cortex to treat gout, using a dose of 15 to 30 g to strengthen the spleen and dry dampness. A combination of Rhizoma Atractylodis, Chinese Angelica, and Cinnamomi Ramulus is used to treat damp-heat-type vessel impediments, with Rhizoma Atractylodis clearing heat and drying dampness at a dosage of 30 g. Zhang's diabetes treatment with Liuliang Decoction and Rhizoma Atractylodis, at a 30 to 50 g dosage, can remove dampness and improve dryness[36]. The raw and processed products of Rhizoma Atractylodis have different uses. Raw Rhizoma Atractylodis has a strong drying effect and is commonly used to treat wind-cold-dampness impediments and anemofrigid colds. Processing reduces its drying effect and may alter or enhance its efficacy (Table 2).

Modern pharmacological research has demonstrated that Rhizoma Atractylodis has broad clinical applications, due to its therapeutic effects against gastrointestinal diseases, arthritis, liver and lung diseases, cancer, cardiovascular diseases, and other disorders (Figure 2).

Gastrointestinal effects

Spleen deficiency syndrome

Spleen deficiency syndrome refers to the functional damage of multiple systems and organs caused by digestive disorders, including immune system-induced intestinal mucosal barrier damage and gastrointestinal motility dysfunction[37]. Numerous studies have shown that raw, bran stir-fried, and coked Rhizoma Atractylodis exhibit significant therapeutic effects on spleen deficiency[29]. Rhizoma Atractylodis and its processed products can effectively regulate the release of gastrointestinal hormones, such as vasoactive intestinal peptide, somatostatin, substance P, and gastrin, in animals with spleen deficiency, thereby enhancing gastrointestinal motility. These treatments can also inhibit inflammation and

Table 2

Traditional therapeutic effects, pharmacological effects, and main indications of different processed products of Rhizoma Atractylodis

Type of decoction pieces	Traditional therapeutic effects	Modern pharmacological effects	Main indications
Raw Rhizoma Atractylodis	Warm-dryness and pungency. Drying dampness, removing wind, dissipating cold, and brightening the eyes	Anti-inflammatory, antioxidant, anti-cancer, regulating water metabolism, protecting vision	Wind-cold-dampness impediment, anemofrigid cold, fever, night blindness, dry eyes
Stir-fried Rhizoma Atractylodis with bran	Relenting dryness and pungency. Enhancing the effects of strengthening the spleen and harmonizing the stomach	Anti-inflammatory and promotes gastrointestinal function	Disharmony between the spleen and stomach pattern, dampness obstructing the middle-jiao pattern, abdominal distension
Coking Rhizoma Atractylodis	Significantly relenting dryness and pungency. Astringing the intestine, eliminating dampness, and arresting leucorrhea	Anti-inflammatory, protects the intestinal barrier, and anti-diarrhea	Spleen-deficient diarrhea, chronic dysentery, abnormal leucorrhea
Rhizoma Atractylodis with rice-washed water	Relenting dryness and pungency. Preserve spleen and stomach function	Anti-inflammatory and promotes gastrointestinal function	Disharmony between the spleen and stomach pattern, limb pain, anemofrigid cold, nausea, and vomiting

intestinal microbiota disorders, improve energy metabolism abnormalities, and help maintain intestinal barrier integrity[38–43].

These findings suggest that processing enhances the spleen-tonifying effect of Rhizoma Atractylodis. Atractyloside A, an incremental component in processed Rhizoma Atractylodis, has been shown to inhibit colon inflammation in mice with spleen deficiency by suppressing the toll-like receptor 4 (TLR4) / nuclear factor Kappa B (NF-κB) pathway, regulating gut microbiota, and addressing metabolic disorders to maintain intestinal barrier integrity[37,44–45].

In addition to atractyloside A, β-eudesmol may contribute to the spleen-tonifying effect by stimulating gastric emptying and small intestinal peristalsis by inhibiting the dopamine receptor D2 and 5-HT receptor 3[46] and activating the transient receptor potential ankyrin 1 (TRPA1) to regulate gastric vagus nerve activity and promote appetite[47].

Gastric ulcer

A study revealed that Rhizoma Atractylodis exhibits significant anti-inflammatory activity. Its ethanol extract can inhibit protein kinase B (Akt) / inhibitor of κB alpha (IκBα)/NF-κB signaling transduction, thereby suppressing the production of nitric oxide (NO), prostaglandin E2 (PGE2), and other inflammatory factors in rats with gastritis[48]. Another study showed that stir-frying Rhizoma Atractylodis with bran offers better therapeutic effects on gastric ulcers than raw Rhizoma Atractylodis, due to its enhanced ability to regulate inflammatory cytokines such as interleukin 6 (IL-6), IL-8, tumour necrosis factor-α (TNF-α), and PGE2, while protecting the stomach by upregulating epidermal growth factor (EGF) and trefoil factor 2 (TFF2)[49–50].

Irritable bowel syndrome

Irritable bowel syndrome (IBS) is commonly accompanied by abdominal distension and pain. Studies have demonstrated that the volatile oils of Rhizoma Atractylodis exhibit significant therapeutic effects on diarrhea-predominant irritable bowel syndrome (IBS-D). These oils regulate gastrointestinal motility through the stem cell factor (SCF)/c-kit pathway and mediate myosin light chain kinase (MLCK) signal transduction to maintain tight intestinal connections and preserve intestinal barrier integrity[51]. Atractylenolide-I, an active ingredient in the volatile oils of Rhizoma Atractylodis, regulates glucose metabolism by modulating lactate dehydrogenase (LDH) activity *via* miR-34a-5p and alleviates colonic epithelial cell dysfunction in IBS-D[52].

Ulcerative colitis and other intestinal diseases

Ulcerative colitis is a chronic, nonspecific inflammatory bowel disease characterized by clinical symptoms such as diarrhea, abdominal pain, and purulent or bloody stools. Existing research has widely reported the pharmacological effects of Rhizoma Atractylodis and its active components on ulcerative colitis. Both raw and bran stir-fried Rhizoma Atractylodis have exhibited therapeutic effects in mice with dextran sulfate sodium (DSS)-induced ulcerative colitis. They have been shown to help maintain intestinal microbiota homeostasis, mediate mitogen-activated protein kinase (MAPK) and NF-κB signal transduction to inhibit inflammatory responses, protect colonic epithelial cells, and alleviate colonic damage[53–54]. Atractylodin and atractylenolide-I are likely responsible for these effects on ulcerative colitis. Atractylenolide-I targets the enzymes—sphingosine kinase 1 (SPHK1) and β-1,4-galactosyltransferase 2 (B4GALT2), regulates intestinal metabolism and microbiota composition, and ameliorates inflammation in mice with colitis[55]. Similarly, atractylodin mediates MAPK signaling transduction and activates the peroxisome proliferator activated receptor (PPAR)α signaling pathway to inhibit inflammatory responses, resolve intestinal microbiota imbalances, and alleviate ulcerative colitis in mice[56–57].

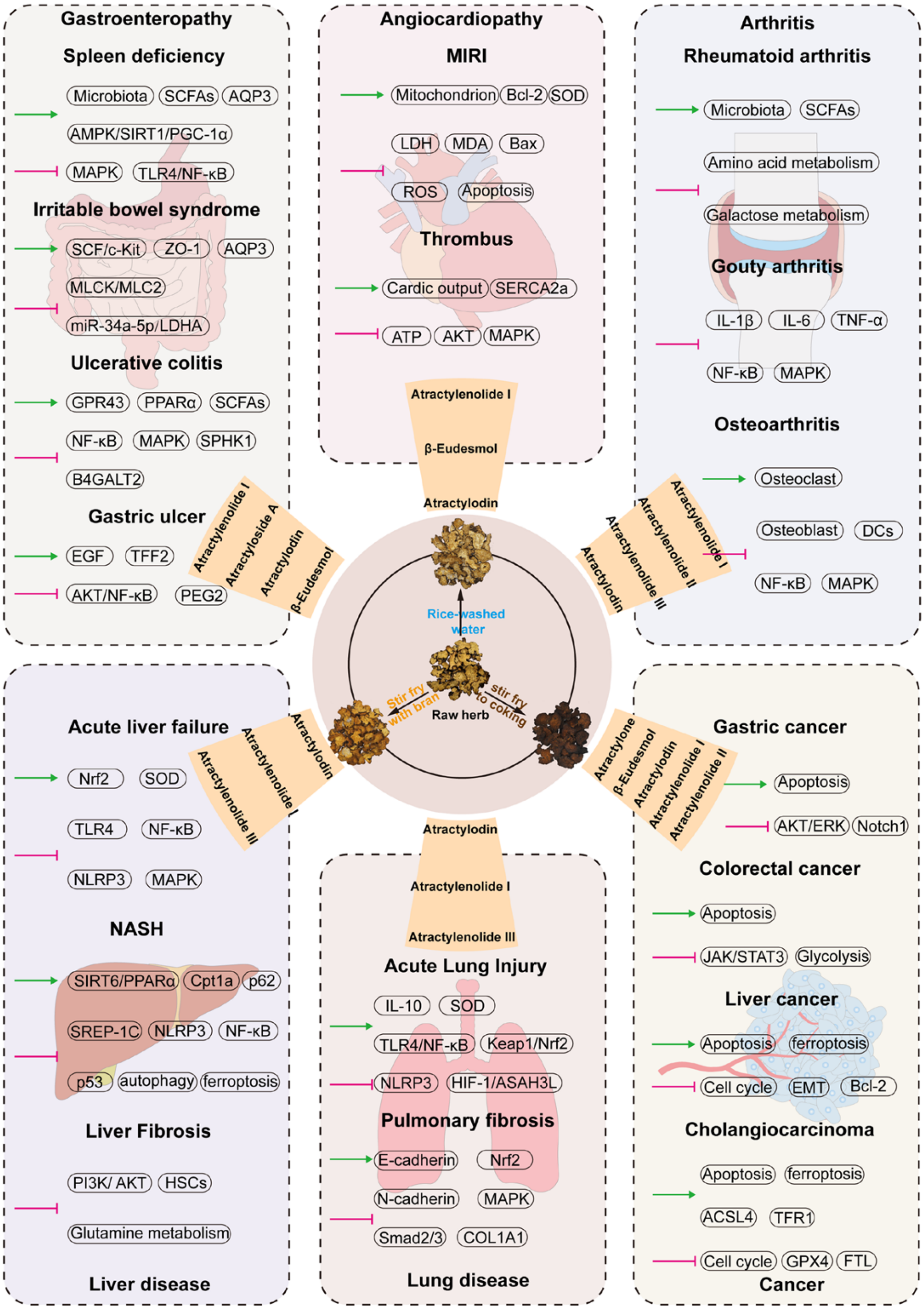

Figure 2. The main pharmacological effects and mechanisms of Rhizoma Atractylodis. ACSL4: Acyl-CoA synthetase long chain family member 4; AKT: Protein kinase B; AMPK: AMP-activated protein kinase; AQP3: Aquaporin 3; ASAH3L: Acid ceramidase-like protein; ATP: Adenosine triphosphate; B4GALT2: Beta-1,4-galactosyltransferase 2; Bax: Bcl-2-associated x protein; Bcl-2: B-cell lymphoma 2; CPT1A: Carnitine palmitoyltransferase 1A; DCs: Dendritic cells; EGF: Epidermal growth factor; EMT: Epithelial-mesenchymal transition; ERK: Extracellular signal-regulated kinase; FTL: Ferritin light chain; GPR43: G protein-coupled receptor; GPX4: Glutathione peroxidase 4; HIF-1α: Hypoxia-inducible factor 1-alpha; HSCs: Hepatic stellate cells; IL-10: Interleukin-10; JAK/STAT3: Janus kinase/signal transducer and activator of transcription 3; Keap1: Kelch-like ECH-associated protein 1; LDH: Lactate dehydrogenase; LDHA: Lactate dehydrogenase A; MAPK: Mitogen-activated protein kinase; MDA: Malondialdehyde; miR-34a-5p: MicroRNA-34a-5p; MIRI: Myocardial ischemia-reperfusion injury; MLC2: Myosin light chain 2; MLCK: Myosin light chain kinase; NF-κB: Nuclear factor kappa B; NLRP3: NOD-like receptor thermal protein domain associated protein 3; Nrf2: Nuclear factor erythroid 2-related factor 2; p62: Sequestosome-1 (SQSTM1/p62); PEG2: Prostaglandin E2; PGC-1α: Peroxisome proliferator-activated receptor gamma coactivator 1-alpha; PI3K: Phosphatidylinositol 3-kinase; PPARα: Peroxisome proliferator-activated receptor alpha; ROS: Reactive oxygen species; SCF: Stem cell factor; SCFAs: Short-chain fatty acids; SERCA2a: Sarco/endoplasmic reticulum calcium ATPase 2a; SIRT1: Sirtuin 1; SIRT6: Sirtuin 6; SOD: Superoxide dismutase; SPHK1: Sphingosine kinase 1; SREBP-1C: Sterol regulatory element-binding protein 1C; TFF2: Trefoil factor 2; TFR1: Transferrin receptor 1; TLR4: Toll-like receptor 4; ZO-1: Zonula occludens-1.

Polysaccharides derived from Rhizoma Atractylodis have been shown to promote the expression of G protein-coupled receptor 43, increase the production of short-chain fatty acids, and stimulate the growth of beneficial intestinal bacteria, thereby promoting intestinal health, reducing alcohol-induced intestinal damage, and alleviating cyclophosphamide-induced intestinal immune deficiency[58–59].

Arthritis

Rheumatoid arthritis and osteoarthritis are categorized under "Bi syndrome" in traditional Chinese medicine, and their etiology and pathogenesis are often similar. Numerous studies have confirmed that the active components of Rhizoma Atractylodis exhibit therapeutic potential for treating arthritis and are expected to become effective drugs.

The volatile oils of Rhizoma Atractylodis have strong dampness-drying properties. Studies have shown that these oils exhibit significant therapeutic effects in rats with rheumatoid arthritis. By inhibiting inflammatory factor release and synovial vascular proliferation, cartilage damage can be avoided[60]. Other studies have shown that Rhizoma Atractylodis extract exerts its therapeutic effect on rheumatoid arthritis by regulating the gut microbiota to alleviate short-chain fatty acid disorders[61]. Furthermore, reports indicate that Rhizoma Atractylodis simultaneously regulates MAPK and NF-κB pathways to suppress inflammatory responses and improve the balance between proinflammatory and anti-inflammatory mediators in treating gouty arthritis[62].

Rhizoma Atractylodis and its active ingredients can induce osteoclast apoptosis, protect chondrocytes, and exert anti-osteoarthritic effects. Multiple polyacetylene components in Rhizoma Atractylodis inhibit RANKL-induced osteoclastogenesis[63]. In osteoarthritis, atractylodin can reduce NF-κB activation in chondrocytes to alleviate inflammatory responses and oxidative stress, while protecting chondrocytes. Additionally, the activation of inflammation-related pathways in bone marrow-derived dendritic cells is inhibited, leading to the alleviation of arthritis in mice with collagen-induced arthritis (CIA)[64]. Finally, atractylenolide promotes the differentiation of bone marrow stem cells into chondrocytes while inhibiting inflammation, protecting chondrocytes, and preventing arthritis progression[65–66].

Liver disease

Poor dietary habits, irregular lifestyle, and emotional disorders due to modern life can damage the spleen, affect stomach function and blood circulation, and subsequently stagnate the liver qi, resulting in poor qi circulation. Atractylodin has been shown to significantly protect against lipopolysaccharide (LPS) / galactosamine (GalN)-induced acute liver failure, reduce mortality, and improve pathological liver injury in mice by downregulating NOD-like receptor thermal protein domain associated protein 3 (NLRP3) and TLR4/NF-κB signaling, upregulating Nrf2 signaling, and modulating inflammatory factors and reactive oxygen species levels[67].

Atractylenolide-I and III exhibit therapeutic effects against acute liver injury, non-alcoholic fatty liver disease, liver fibrosis, and other liver diseases. Atractylenolide-I regulates the TLR4/MAPK/NF-κB pathway to inhibit inflammation and oxidative stress, thereby alleviating acute liver injury induced by acetaminophen[68]. Additionally, in the treatment of non-alcoholic fatty liver disease, atractylenolide-I intervenes in hepatic gluconeogenesis and adipogenesis by modulating sirtuin-6[69]. Atractylenolide-III significantly impacts liver metabolic pathways by affecting glutamine metabolism, inhibiting hepatic stellate cell proliferation, and alleviating liver fibrosis caused by bile duct ligation[70].

Rhizoma Atractylodis has also demonstrated hepatoprotective effects by reducing lipid accumulation and inflammation in the liver, while decreasing autophagy and ferroptosis in liver cells, thereby preventing non-alcoholic steatohepatitis (NASH)[71].

Lung diseases

According to traditional Chinese medicine, the spleen and lungs are physiologically interdependent, with the lungs regulating qi and the spleen being the source of qi and blood.

Rhizoma Atractylodis and its active ingredients exert protective effects in acute lung injury. Its extract has been shown to alleviate inflammation and oxidative stress by inhibiting the TLR4/NF-κB and Keap1/Nrf2 signaling pathways, preventing LPS-induced acute lung injury in rats. Atractylodin also demonstrates significant therapeutic effects in lung diseases alleviating acute inflammation and preventing acute lung injury by modulating NLRP3 and hypoxia-inducible factor 1/N-acylsphingosine amidohydrolase 3-like (HIF-1/ASAH3L) signaling transduction[72–73]. Furthermore, atractylodin can alleviate idiopathic pulmonary fibrosis by reversing Smad2/3 and MAPK pathway overactivation, reducing collagen deposition, and decreasing E-cadherin expression[74]. In addition to atractylodin, atractylenolide-I can prevent LPS-induced acute lung injury, effectively inhibit TLR4 expression and NF-κB activation, and reduce LPS-induced inflammatory responses[75]. Moreover, atractylenolide-III can inhibit oxidative stress and alleviate pulmonary fibrosis by upregulating Nrf2 signaling transduction[76].

Cancer

Modern research has confirmed that the active ingredients in Rhizoma Atractylodis inhibit various digestive tract cancers, including cholangiocarcinoma, gastric, colorectal, and liver cancers.

Gastric cancer

Gastric cancer is a malignant tumor originating from the gastric mucosal epithelium, with an extremely high incidence in China. Studies have demonstrated that extracts and polysaccharides from Rhizoma Atractylodis exhibit inhibitory effects on various gastric cancer cell lines[77–78]. Additionally, atractylenolide-I has been shown to inhibit the spheroidization and viability of gastric cancer stem cells by suppressing the activation of the Notch1 signaling pathway[79]. Atractylenolide-II affects tumor cell proliferation, apoptosis, and migration by regulating the protein Kinase B (Akt) / extracellular signal-regulated kinase (ERK) signaling pathway[80].

Colorectal cancer

Colorectal cancer is the third most common cancer worldwide. *A. lancea (Thunb.) DC.* exhibits notable anti-colorectal cancer effects[81] along with atractylenolide-I, which induces cancer cell apoptosis and inhibits cancer cell glycolysis by targeting the Janus kinase 2 (JAK2) / Signal transducer and activator of transcription 3 (STAT3) signaling pathway.

Hepatoma

Hepatoma, a malignant liver tumor, poses a significant threat to human health. Multiple components of Rhizoma Atractylodis have been reported to mediate anti-hepatoma activity. Atractylone inhibits epithelial-to-mesenchymal transition (EMT) and reduces matrix metalloproteinase (MMP) levels to decrease cancer cell migration and invasion, thereby inhibiting tumor progression in tumor-bearing mice[82]. Additionally, atractylone inhibits the proliferation, migration, and invasion of Huh7 and hepatocellular carcinoma-M (HCCM) cells by inducing ferroptosis and regulating the cell cycle[83]. β-Eudesmol-treated HepG2 cells exhibited typical apoptotic characteristics, accompanied by mitochondrial membrane potential loss and caspase-3 activation[84]. In other studies, inulin-type fructans derived from Rhizoma Atractylodis have exhibited inhibitory activity against various liver cancer cells such as HepG2 and 7721[85].

Cholangiocarcinoma

Cholangiocarcinoma is a tumor caused by malignant transformation of the biliary epithelium, and Rhizoma Atractylodis is considered a potential chemotherapeutic drug for treating cholangiocarcinoma[86]. A study suggested that Rhizoma Atractylodis can induce autophagy and inhibit the growth, migration, and invasion of cholangiocarcinoma cells by regulating the PI3K/AKT and p38 MAPK signaling pathways[87]. Furthermore, β-eudesmol can promote cell cycle arrest in cholangiocarcinoma cells and activate caspase-3/7 to induce apoptosis, ultimately enhancing the inhibitory effects of 5-fluorouracil and doxorubicin[88].

Cardiovascular disease

Hypoxia/reoxygenation (H/R) injury in myocardial cells is the primary pathological basis for myocardial infarction. Research has shown that both water extracts and volatile oils of raw and bran stir-fried Rhizoma Atractylodis can improve the survival rate of H/R-injured myocardial cells and alleviate oxidative stress, with the effect of bran stir-fried Rhizoma Atractylodis being stronger[89–90]. Similarly, atractylenolide-I protects mitochondrial function, inhibits apoptosis-related protein activation, and alleviates myocardial ischemia–reperfusion injury[91]. Additionally, atractylenolide has been shown to exert inhibitory effects on thrombosis[92]. Atractylodin also significantly increases cardiac output in rats, demonstrating a strengthening effect on positive inotropic function[93]. Finally, β-eudesmol has been shown to exhibit significant anti-angiogenic activity by inhibiting STAT3 phosphorylation *via* high mobility group box 1 (HMGB1) downregulation and suppressing proliferation, migration, and lumen formation in endothelial cell angiogenesis[94].

Product development of Rhizoma Atractylodis

Decoction-ready medicine

Chinese medicinal granules, as supplements to traditional Chinese medicine decoction products, effectively address the limitations of conventional decoctions, including the temporary decoction and inconvenient storage of traditional Chinese medicines. The formula granules of *A. chinensis (DC.) Koidz* and its bran stir-fried products have been nationally standardized. However, the process for *A. lancea (Thunb.) DC.* and its bran stir-fried products have not yet been standardized, although relevant research has provided important experimental evidence supporting their potential.

Chinese medicine ultrafine powder decoction products are processed using ultrafine grinding technology to produce powders with granule sizes <45 μm. Compared with traditional decoctions, the cell walls of ultrafine powder decoctions are disrupted, enhancing the bioavailability and absorption efficiency of the drugs[95]. A previous study demonstrated that ultrafine grinding does not significantly affect the main active ingredients of Rhizoma Atractylodis[96].

Chinese patent medicines

Rhizoma Atractylodis is often combined with other traditional Chinese medicines to treat disorders such as spleen–stomach disharmony, muscle and bone pain, and wind-dampness conditions. The 2020 edition of the Chinese Pharmacopoeia lists 68 Chinese patent medicines containing Rhizoma Atractylodis[1], including Yueju Wan, Wushicha Jiaonang, Huoxiang Zhengqi Koufuye, Xiangsha Pingwei Wan, and others [Supplementary Table S1, http://links.lww.com/AHM/A165]. Functions and indications for their use include strengthening the spleen and stomach, clearing heat and drying dampness, dispelling wind and cold, resolving swelling, and alleviating pain. According to a report from China Report Hall (https://m.chinabgao.com/info/1246672.html), the cumulative sales of various dosage forms of Huoxiang Zhengqi reached 3.47 billion Yuan in 2022, making it the top-selling traditional Chinese patent medicine for digestive tract diseases. Other Chinese patent medicines containing Rhizoma Atractylodis, such as Xiangsha Pingwei Keli and Xiangsha Yangwei Wan, also ranked highly in sales, reflecting the promising market prospects and good curative effects of Rhizoma Atractylodis-based Chinese patent medicines.

The market usage of Rhizoma Atractylodis has been increasing annually and is gradually expanding into multiple fields. In medicine, Rhizoma Atractylodis, as one of the main ingredients of Huashi Baidu Keli, played an important role in treating the coronavirus disease 2019 (COVID-19). Additionally, Rhizoma Atractylodis can also be used to strengthen the spleen and transform dampness for daily prevention. In the treatment of chronic diseases, a study has shown that combining Rhizoma Atractylodis-Root Figwort and metformin is more effective than metformin alone in treating type 2 diabetes mellitus[97].

Health products and daily necessities

Health products containing Rhizoma Atractylodis are already on the market, including Pneumonia No.1 Formula Tea Drink, Xiangsha Weiling Tea, Paederia Scandens Rhizoma Atractylodis Tea, Gentiana Rhizoma Atractylodis Tea, and Ermiao San Tea. Due to its strong effects in dispelling wind and drying dampness, Rhizoma Atractylodis has broad prospects for the development of essential oil-based health products.

Rhizoma Atractylodis exhibits anti-aging and moisturizing effects, indicating its suitability for treating conditions like eczema. Commonly used as a fragrance in modern cosmetics, it also offers preservative benefits. Furthermore, as a dual-purpose medicinal and edible product, Rhizoma Atractylodis finds applications across the food, pharmaceutical, and health product industries. Although the patent application scope related to Rhizoma Atractylodis is broad in terms of treating obesity, skin diseases, sterilization, and dandruff, few formal health products containing Rhizoma Atractylodis exist. Therefore, expanding Rhizoma Atractylodis-based patents and developing associated health products hold significant potential.

Epidemic prevention and control

Rhizoma Atractylodis has been effective in preventing epidemics since ancient times[98], with its efficacy primarily attributed to its volatile components, which have significant inhibitory effects on bacteria, fungi, and viruses[99]. During outbreaks such as SARS (2003), H7N9 avian influenza (2013), and COVID-19 (2020), Rhizoma Atractylodis played a significant role. Notably, 36 external-use prescriptions for COVID-19 prevention included 51 traditional Chinese medicines, with Rhizoma Atractylodis being the most frequently used, followed by *Artemisia argyi*[100].

Animal feed and veterinary medicine

Due to its significant efficacy, Rhizoma Atractylodis has been widely applied in animal feed and veterinary medicine. Its extracts exhibit antiviral effects. Viruses such as swine and avian influenza pose great harm to animal husbandry. Rhizoma Atractylodis extracts significantly inhibit the proliferation of swine influenza virus in cells and directly inactivate viruses[101]. Its key active ingredient, atractylon, effectively blocks the adsorption and replication of avian influenza virus[102]. Furthermore, Rhizoma Atractylodis enhances piglet immunity, strengthens disease resistance[103], regulates gut microbiota in livestock such as pigs and cows, promotes the colonization of beneficial bacteria, and reduces the abundance of harmful bacteria[104–105].

Discussion

As a commonly used traditional Chinese medicine in clinical practice, Rhizoma Atractylodis is recorded in various versions of the Chinese Pharmacopoeia, with each version listing different types of processed products. Since the early use of raw, stir-fried, and rice-washed water Rhizoma Atractylodis, Rhizoma Atractylodis has gradually evolved into two main types: raw Rhizoma Atractylodis and bran stir-fried Rhizoma Atractylodis. The “National Chinese Medicine Processing Standards” (1988) and processing standards formulated by various provinces and cities still record different processed forms, including coked Rhizoma Atractylodis and Rhizoma Atractylodis processed with rice-washed water. Records of processing standards from different regions show inconsistencies, such as variations in processing techniques and significant differences in process details, even for the same processed products. Although reflecting the characteristics of local processing, this hinders the effective control of the quality of processed Rhizoma Atractylodis products. Currently, most standardized research on the processing technology of Rhizoma Atractylodis is based on traditional methods, with the key process parameters digitized to form a standardized workflow. In the actual production process of Chinese herbal processing enterprises, although standard operating procedures (SOPs) have been established, the degree of processing is still mainly determined manually, with parameters serving only as references. This highlights the low level of automation in the processing technology, underscoring the need for related industries to develop intelligent equipment with advanced process control capabilities. By adjusting heating time and controlling processing temperature based on the characteristics of the decoction pieces, more consistent and stable quality can be achieved in Rhizoma Atractylodis decoction pieces.

The significant changes in the chemical composition of Rhizoma Atractylodis before and after processing are the primary factors contributing to the variations in the efficacy and properties of its processed forms. Rhizoma Atractylodis has a warm-dry medicinal peculiarity, making it suitable for tonifying the spleen and eliminating dampness. However, improper use can lead to the loss of body fluids and side effects such as dryness. Therefore, processing Rhizoma Atractylodis is necessary to reduce dryness, alter its medicinal peculiarity, and enhance its curative effects. The chemical components of Rhizoma Atractylodis are mainly divided into volatile and non-volatile constituents. Processing typically reduces the content of most volatile components, such as β-eudesmol and atractylodin. Previous studies have shown that the volatile oils in Rhizoma Atractylodis are primarily responsible for its drying effect, with excessive volatile oils stimulating the digestive tract. By reducing the volatile oil content during processing, the dryness effect can be minimized, and gastrointestinal irritation can be alleviated.

Rhizoma Atractylodis traverses the spleen, stomach, and liver channels, with its spleen-strengthening effects enhanced through processing. This enhancement may result from an increase in certain non-volatile components after processing, including β-daucosterol and atractyloside A. Some researchers suggest that the increase in these components may be due to reduced glycosidase activity in Rhizoma Atractylodis caused by heating. Atractyloside A has been proven to possess significant anti-inflammatory, spleen-strengthening, and antidiarrheal effects. Additionally, atractylodes polysaccharides have been found to regulate immunity and protect the intestinal barrier, with their content increasing after stir-frying with bran. However, the mechanisms behind this increase require further investigation.

Given the precise efficacy and broad applications of Rhizoma Atractylodis, products derived from it have continuously emerged in the market in recent years. Numerous traditional Chinese patent medicines, with Rhizoma Atractylodis as the primary ingredient, have been developed by pharmaceutical enterprises in China. A total of 1,484 clinical Chinese medicine prescriptions and 325 traditional Chinese patent medicines require Rhizoma Atractylodis to be compatible. Simultaneously, the export volume of Atractylodes macrocephala has grown at an average annual rate of 10%, reaching over 120 countries and regions worldwide, indicating promising prospects of Rhizoma Atractylodis-related industries.

In conclusion, this article provides a comprehensive review of the recent advancements in the processing, chemical composition, pharmacological effects, and product development of Rhizoma Atractylodis. Compared to previous reviews, this study not only focuses on the chemical composition and pharmacological effects of Rhizoma Atractylodis, but also emphasizes its practical production applications, thus filling a gap in literature related to Rhizoma Atractylodis product development. However, this review has limitations. Due to the different sources and decoction pieces of Rhizoma Atractylodis, quality control remains a significant challenge in its production and application processes. Further sorting of relevant materials is needed to provide a reference for the improvement of quality control standards for Rhizoma Atractylodis.

Overall, this review offers a detailed overview of the basic characteristics of Rhizoma Atractylodis varieties, providing valuable insights for pharmacological research, product development, and clinical application, while guiding the advancement of the Rhizoma Atractylodis industry.

Conflict of interest statement

The authors declare no conflict of interest.

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Author contributions

Chang Ke and Linghang Qu wrote the manuscript. Yi Xia, Chunli Wang, Kang Xu, and Yanju Liu revised the manuscript. All the authors have read and approved the final version of the manuscript.

Ethical approval of studies and informed consent

Not applicable.

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None.

Data availability

All data generated or analyzed during this study are included in this published article.

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