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Comprehensive overview of different medicinal parts from *Morus alba* L.: chemical compositions and pharmacological activities

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Morus alba L., a common traditional Chinese medicine (TCM) with a centuries-old medicinal history, owned various medicinal parts like Mori folium, Mori ramulus, Mori cortex and Mori fructus. Different medical parts exhibit distinct modern pharmacological effects. Mori folium exhibited analgesic, anti-inflammatory, hypoglycemic action and lipid-regulation effects. Mori ramulus owned anti-bacterial, anti-asthmatic and diuretic activities. Mori cortex showed counteraction action of pain, inflammatory, bacterial, and platelet aggregation. Mori fructus could decompose fat, lower blood lipids and prevent vascular sclerosis. The main chemical components in *Morus alba* L. covered flavonoids, phenolic compounds, alkaloids, and amino acids. This article comprehensively analyzed the recent literature related to chemical components and pharmacological actions of *M. alba* L., summarizing 198 of ingredients and described the modern activities of different extracts and the bioactive constituents in the four parts from *M. alba* L. These results fully demonstrated the medicinal value of *M. alba* L., provided valuable references for further comprehensive development, and layed the foundation for the utilization of *M. alba* L.

KEYWORDS

***Mori folium*, *Mori ramulus*, *Mori cortex*, *Mori fructus*, chemical constituents, pharmacological activities**

1 Introduction

Morus alba L., a deciduous tree species, belonging to the Moraceae family and *Morus* genus. China is the relatively early known country raising silkworms and growing *M. alba* L. The presence of *M. alba* L. could be traced back to thousands of years ago (Zeng et al., 2022). Besides, many medical classics such as *Shennong Ben Cao*, *Tang Ben Cao* and *Ben Cao Gang Mu also* recorded it (Wenmin Du, 2022). For the past few years, dozens of varieties of *M. alba* L. were widely planted in China, including cultivated and wild species (Ai et al., 2021). In TCM, *M. alba* L. is regarded as a treasure due to the rich active ingredients and modern activities of its different parts.

TABLE 1 Alkaloid in *Morus alba* L.

No.	Sequential number	Name	Source	Pharmacological properties	Reference
1	141	fagomine	B	anti-obesity; anti-inflammatory	D'Urso et al. (2019)
					Ramos-Romero et al. (2022)
2	142	morusimic acid B	B	—	D'Urso et al. (2019)
3	143	morusimic acid C	B	—	D'Urso et al. (2019)
4	144	morusimic acid E	B	—	D'Urso et al. (2019)
5	145	1-deoxynojirimycin	A; B	antidiabetic	D'Urso et al. (2019)
					Asai et al. (2011)
6	146	1,4-dideoxy-1,4-imino-D-arabinitol	D	hyperamnesia	Lei et al. (2022)
					Gibbs (2016)
7	147	2-formyl-1H-pyrrole-1-butanoic acid	B	—	D'Urso et al. (2019)
8	148	3-epi-fagomine	A	anticancer; neuroprotection	Amezqueta et al. (2012)
					Zabady et al. (2022)
					Bhuiyan et al. (2011)

Note: A, Mori folium; B, Mori fructus; C, Mori cortex; D, Mori ramulus.

TABLE 2 Coumarins in *Morus alba* L.

No.	Sequential number	Name	Source	Pharmacological property	Reference
1	149	aesculetin	A	anti-inflammatory	Li et al. (2020)
2	150	coumarin	C	anticancer; anti-inflammatory	Kavitha and Geetha (2018)
					Bhattarai et al. (2021)
3	151	mulberroside B	C	anti-obesity	Yang et al. (2011)
4	152	scopoletin	A	anti-inflammatory	Li et al. (2020)
5	153	scopolin	D	anti-inflammatory; anti-hyperuricemic	Yao et al. (2019)
					Li et al. (2020)
6	154	skimmin	A	cardioprotection	Doi et al. (2001)
					Su et al. (2023)
7	155	umbelliferone	C	antidiabetic nephropathy	Hyun et al. (2021)
					Jin and Chen (2022)
8	156	5,7-dihydroxycoumarin 7-O-β-d-apiofuranosyl-(1→6)-O-β-d-glucopyranoside	C	anti-obesity	Yang et al. (2011)
9	157	5,7-dihydroxycoumarin 7-O-β-D-glucopyranoside	C	anti-obesity	Yang et al. (2011)

Note: A, Mori folium; B, Mori fructus; C, Mori cortex; D, Mori ramulus.

Mori cortex and Mori fructus taste slight cool and sweet. Mori cortex could purge and promoting water, relieve cough and asthma, reduce blood pressure, and against inflammatory (Batiha et al., 2023). Mori fructus could nourish blood and enhance immune function. Mori ramulus, which is mild and taste a litter bitter, owned functions of dispelling wind dampness and promoting blood circulation. Mori folium is a slight muted and possessed effects of dispelling wind, clearing heat, cooling blood, and improving eyesight. Mori fructus and Mori folium exhibit both medicinal and edible properties, making them widely used in medicine and food fields (Maqsood et al., 2022). In some Asian countries, Mori folium is used as a nutritional supplement (Liu et al., 2024). In South Korea, it is widely used as one ingredient of ice cream (Polumackanycz et al., 2021). In Japan, it is used as an anti-hyperglycemic supplement for the treatment of diabetes (Suthamwong et al., 2020). Recently, with the deepening awareness of *M. alba* L., its role in lowering blood sugar, alleviating depression, antioxidant and liver protection have been widely concerned.

TABLE 3 Carbohydrates in *Morus alba* L.

No.	Sequential number	Name	Source	Pharmacological property	Reference
1	158	adenosine	C	anti-obesity	Yang et al. (2011)
2	159	arabinose	A	anti-obesity	Zhao et al. (2022)
3	160	D-galactose	A	anti-obesity	Zhao et al. (2022)
4	161	D-galacturonic acid	A	anti-obesity	Zhao et al. (2022)
5	162	D-glucose	A	anti-obesity	Zhao et al. (2022)
6	163	D-glucuronic acid	A	anti-obesity	Zhao et al. (2022)
7	164	D-mannose	A	anti-obesity	Zhao et al. (2022)
8	165	fucose	A	anti-obesity	Zhao et al. (2022)
9	166	L-rhamnose	A	anti-obesity	Zhao et al. (2022)

Note: A, Mori folium; B, Mori fructus; C, Mori cortex; D, Mori ramulus.

TABLE 4 Terpenoids in *Morus alba* L.

No.	Sequential number	Name	Source	Pharmacological property	Reference
1	167	betulinic acid	C	anticancer; anti-obesity	Yang et al. (2011)
					Aswathy et al. (2022)
2	168	grasshopper ketone	B	anti-inflammatory	Lee et al. (2021b)
3	169	lanosterol acetate	A	antigout	Oh et al. (2021)
4	170	loliolide	A	antidiabetic; anti-inflammatory; anti-aging	Hunyadi et al. (2013)
					Park et al. (2019)
5	171	roseoside	B	anti-inflammatory	D'Urso et al. (2019)
					Wang et al. (2023b)
6	172	ursolic acid	C; D	anti-inflammatory; antioxidant; antiviral	Yang et al. (2011)
					Liu Ying (2023)
					Al-Kuraishy et al. (2022)
					Kornel et al. (2023)
7	173	uvaol	C	anti-obesity	Yang et al. (2011)
				anticancer	Bonel-Perez et al. (2020)
8	174	7-ketositosterol	B	kidney protection	Lee et al. (2021b)
9	175	β-sitosterol	C	anti-obesity; anticancer	Yang et al. (2011)
					Khan et al. (2022)

Note: A, Mori folium; B, Mori fructus; C, Mori cortex; D, Mori ramulus.

The current pharmacological researches on *M. alba* L. mainly focus on Mori folium, Mori ramulus, Mori cortex and Mori fructus. With the rapid advance of science and technology, more bioactive substances covered flavonoids, alkaloids and phenols from *M. alba* L. were identified. In addition, there were several same biological active ingredients and some unique chemical components from different parts of *M. alba* L., the compositions were closely relevant to the pharmacological activities of each part. For example, 1-deoxynojirimycin, an alkaloid component only found in *M. alba* L., was the characteristic component with high-content from Mori folium, owns the intense inhibitory effect on α-glucosidase and exhibit obvious action in lowering blood glucose (Wang Shirui, 2023). Besides, on account of other affluent ingredients like proteins, carbohydrates, vitamins, trace elements and dietary fibre, Mori folium was also recognized as a high-quality food or mulberry tea (Polumackanycz et al., 2021). Thus it could be seen that due to the multifarious functional materials and particular pharmacological characteristics, different parts of *M. alba* L. maybe owned broad research prospects and were widely used in various scopes like medicine, food, and other fields (Maqsood et al., 2022).

On account of the favourable value of *M. alba* L., this review aimed to summarize the chemical components and the

TABLE 5 Organic acids in *Morus alba* L.

No.	Sequential number	Name	Source	Pharmacological property	Reference
1	176	Acetic acid	A	skin protectant	Chen et al. (2021)
2	177	citric acid	A	immuno-enhancement	Chen et al. (2021)
					Hu et al. (2024)
3	178	fumaric acid	A	anticancer	Chen et al. (2021)
					Das et al. (2016)
4	179	lactic acid	A	anti-inflammatory; anticancer	Chen et al. (2021)
					Zhou et al. (2022a)
5	180	malic acid	A	antioxidant; liver protection	Chen et al. (2021)
					Koriem and Tharwat (2023)
6	181	succinic acid	A	anticancer	Chen et al. (2021)
					Kasarci et al. (2021)

Note: A, Mori folium; B, Mori fructus; C, Mori cortex; D, Mori ramulus.

TABLE 6 Anthocyanins in *Morus alba* L.

No.	Sequential number	Name	Source	Pharmacological property	Reference
1	182	anthocyanins	B	antioxidant; antibacterial	D'Urso et al. (2019)
					Suriyaprom et al. (2021)
2	183	cyanidin-3-glucoside	B	anticancer	Zabady et al. (2022)
3	184	cyanidin-3-O-glucoside	B	anticancer	Chen et al. (2022c)
					Wei et al. (2021)
4	185	cyanidin-3-O-rutinoside	B	antioxidant	Chen et al. (2022d)
					Delazar et al. (2010)

Note: A, Mori folium; B, Mori fructus; C, Mori cortex; D, Mori ramulus.

pharmacologic bioactivities of *M. alba* L., including Mori folium, Mori ramulus, Mori cortex and Mori fructus. The overall data in this present paper, could provide a helpful reference for further development and comprehensive utilization of *M. alba* L.

2 Chemical profiles of *Morus alba* L

Up to 198 active compounds have been identified in the different parts of *M. alba* L. (Supplementary Table S1; Tables 1–7). Their structures are summarized in Figures 1–8.

3 The pharmacological activities of components in *Morus alba* L

3.1 Hypoglycemic activity

1-deoxynojirimycin was the important active ingredient in *M. alba* L. Researchers have confirmed that 1-deoxynojirimycin exhibit an inhibitory effect on α-glucosidase, further reduced the postprandial blood glucose in pre-diabetic and mildly diabetic individuals (Asai et al., 2011). Current evidence showed that the same dose of Mori folium has similar biological activities like lowering blood sugar and protecting kidney in diabetic patient as the purified 1-deoxynojirimycin (Huang et al., 2014). In addition, Mori ramulus extract was reported effective hypoglycemic action and well inhibition of PTP1B and α-glucosidase, the main components were oxyresveratrol and kuwanon G (Kwon et al., 2022). Compared with Mori folium and Mori fructus, the hypoglycemic effects of Mori ramulus and Mori cortex were much more significant (Zhou Q. Y. et al., 2022). The various bioactive components of medicinal parts from *M. alba* L. expressed multiple antidiabetic targets and less adverse reactions. Thanks to the favourable hypoglycemic effect and the accessibility of *M. alba* L. resources, *M. alba* L. may exhibit a promising prospect in the preventing and treating of diabetes. The main hypoglycemic compounds in *M. alba* L. and their mechanisms are shown in Table 8.

3.2 Antioxidant activity

Studies found that isoquercetin and 4-O-caffeoylquinic acid in Mori folium showed strong antioxidant activity, and the 50%

TABLE 7 Other constituents in *Morus alba* L.

No.	Sequential number	Name	Category	Source	Pharmacological property	Reference
1	186	butyl pyroglutamate	amino acid derivatives	B	kidney protection	Lee et al. (2018)
2	187	γ-aminobutyric acid	amino acids	A	antifatigue	Chen et al. (2016)
3	188	L-proline	amino acids	B	anti-inflammatory; kidney protection	Lee et al. (2021b)
						Li et al. (2019)
4	189	L-tryptophan	amino acids	A	antipyretic; mood improvement; sleep improvement	Qu et al. (2019)
						Sutanto et al. (2022)
						Kikuchi et al. (2021)
5	190	chalcomoracin	Diels–Alder adducts	A	anti-bacteria	Jeon and Choi (2019)
						Kim et al. (2012)
6	191	guangsangon E	Diels–Alder adducts	A	anticancer	Shu et al. (2021)
7	192	isobavachalcone	chalcones	B	antidiabetic; antioxidant; anti-inflammatory; neuroprotection; antimicrobial	Wang et al. (2013)
						Wang et al. (2021)
8	193	morachalcone A	chalcones	D	anti-melanogenesis	Zhang et al. (2016)
9	194	2,4,2′,4′-tetrahydroxychalcone	chalcones	D	anti-melanogenesis	Zhang et al. (2016)
10	195	lignin	phenylpropanoids	A	anti-microbial	Chao et al. (2021)
						Das et al. (2024)
11	196	melatonin	amines	A	antioxidant; anticancer; anti-aging	Panyatip et al. (2022)
						Bhattacharya et al. (2019)
12	197	vitamin E	vitamins	C	antioxidant; anti-inflammatory	Kavitha and Geetha (2018)
13	198	cyclo (L-Pro-L-Val)	peptides	B	anti-inflammatory	Lee et al. (2021b)

Note: A, Mori folium; B, Mori fructus; C, Mori cortex; D, Mori ramulus.

radical-scavenging concentrations were 10.63 ± 0.96 μg/mL and 10.63 ± 0.96 μg/mL, respectively (Ganzon et al., 2018). The researchers comprehensively evaluated the antioxidant activities of bioactive components from *M. alba* L. in DPPH and ABTS radical scavenging assays, found that the acetone extract showed potential antioxidant activities with SC_{50} values of 242.33 ± 15.78 and 129.28 ± 10.53 μg/mL, respectively (Hsu et al., 2022). The antioxidant mechanisms of components from *M. alba* L. are summarized in Table 9.

3.3 Anti-inflammatory activity

Studies have demonstrated that *M. alba* L. and its active compounds could inhibit the inflammation by suppressing leukocyte chemotaxis, further data about the mechanism showed that oxyresveratrol in *M. alba* L. could inhibit the CXCR4-mediated leukocyte migration of the CXCR4 receptor by inactivating the MEK/ERK pathway (Chen et al., 2013). In addition, oxyresveratrol was alos reported favourable anti-inflammatory effect through the inhibitions of iNOS/NO production, synthesis of PGE2 and activation of NF-κB(Chung et al., 2003). The methanol extraction of mulberry bark showed that components named kuwanon T and sanggenon A in mulberry bark contribute to the anti-inflammatory activities on microglia (BV2) and macrophages (RAW264.7) by the inhibitions of productions of prostaglandin E2, interleukin-6 and tumour necrosis factor-α, and the stimulation of expression of cyclooxygenase-2 (Ko et al., 2021). The anti-inflammatory active ingredients in mulbery are displayed in Table 10.

3.4 Anti-cancer activity

Moracin D was demonstrated that it could decrease cell proliferation and induce apoptosis in breast cancer cells by inhibiting the transduction pathway of Wnt3a/FOXM1/β-catenin signal and the activation of caspase and GSK3β(Hwang et al., 2018). Sanggenol L, another natural flavonoid compound in Mori cortex, could induce the apoptosis through inhibiting the PI3K/Akt/mTOR signaling pathway, and accelerate the cycle arrest of prostate cancer cells by activating the p53 protein (Won and Seo, 2020). In addition, sanggenol L could also reduce cytotoxicity and apoptosis in ovarian

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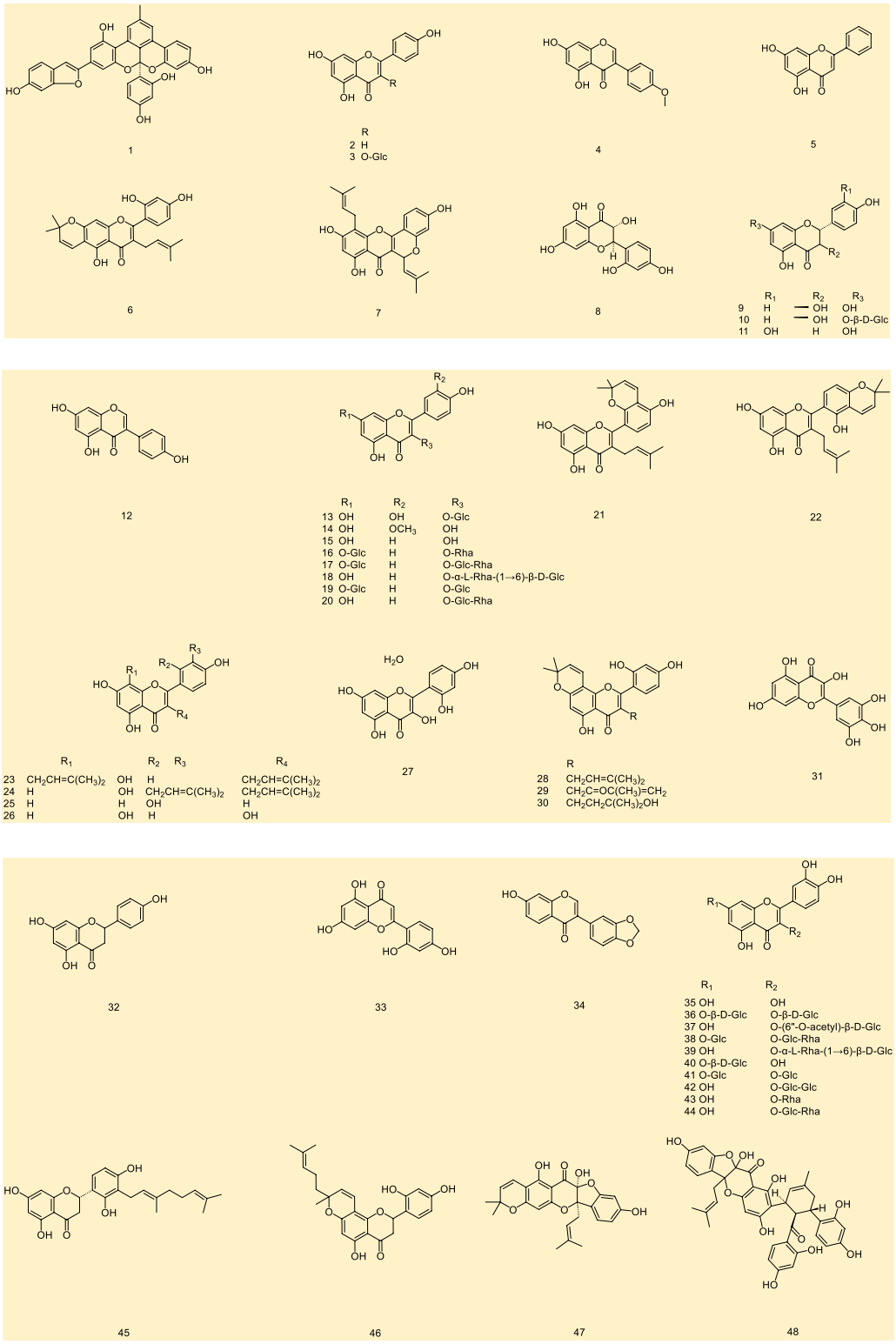

FIGURE 1
(Continued).

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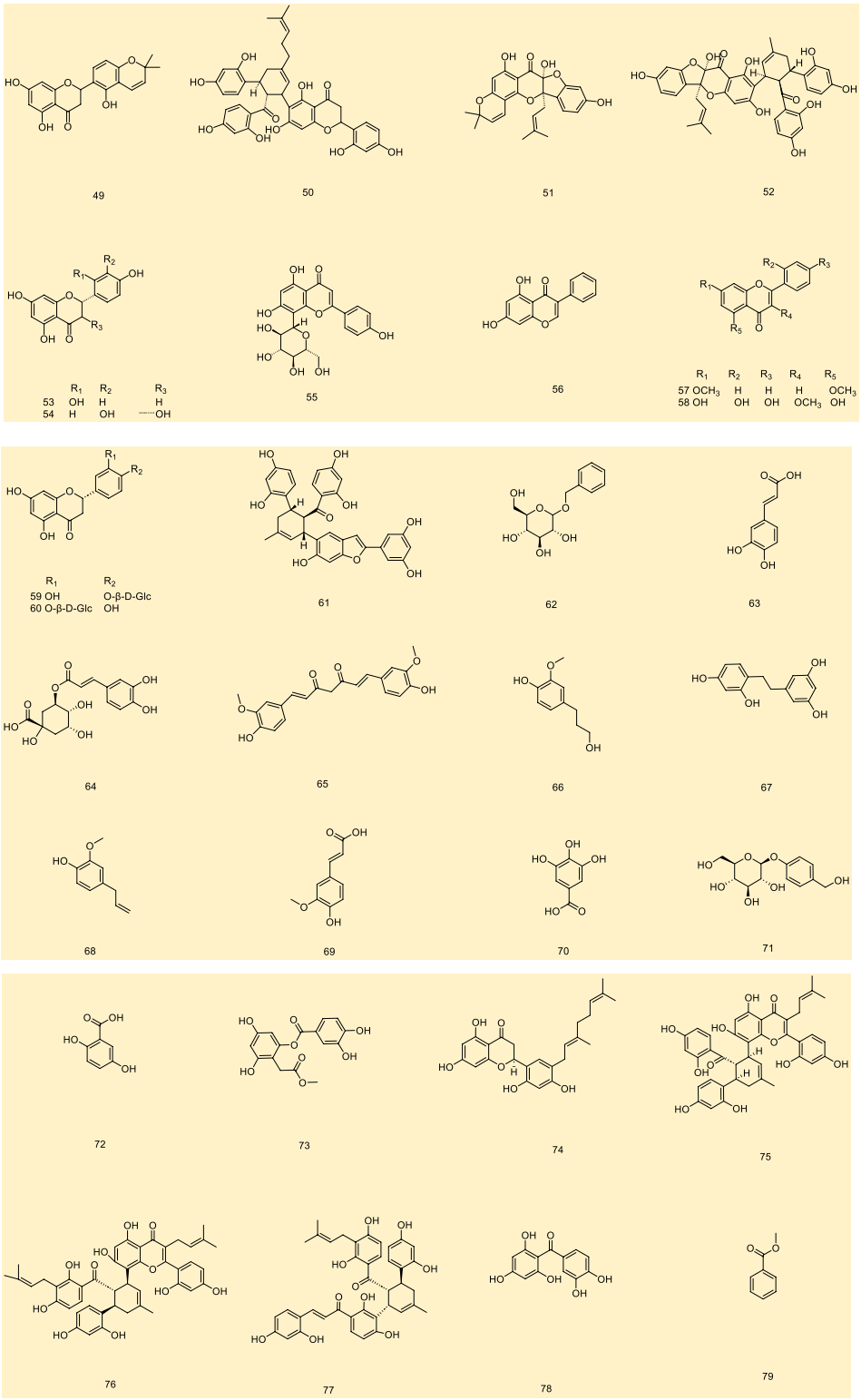

FIGURE 1
(Continued).

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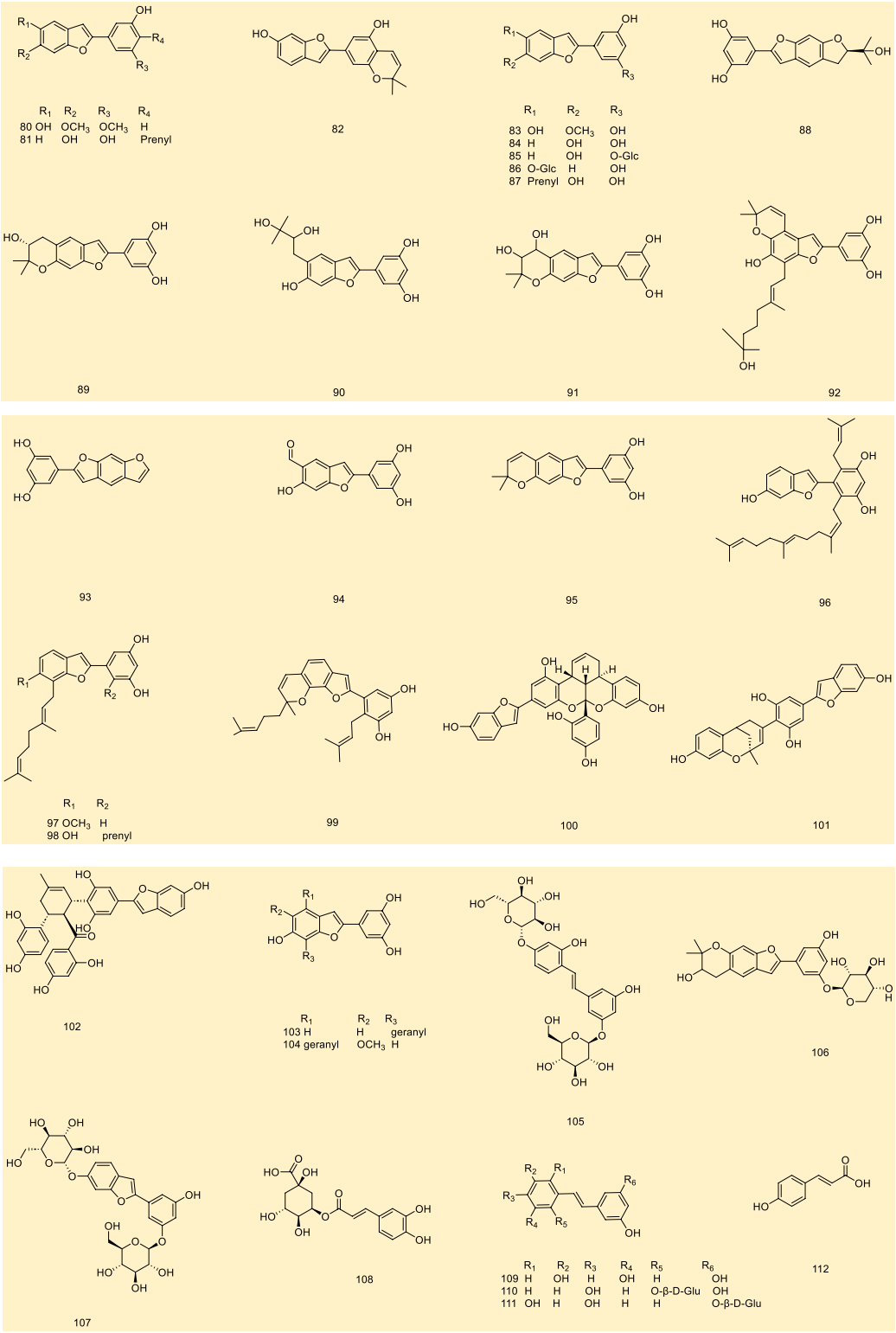

FIGURE 1
(Continued).

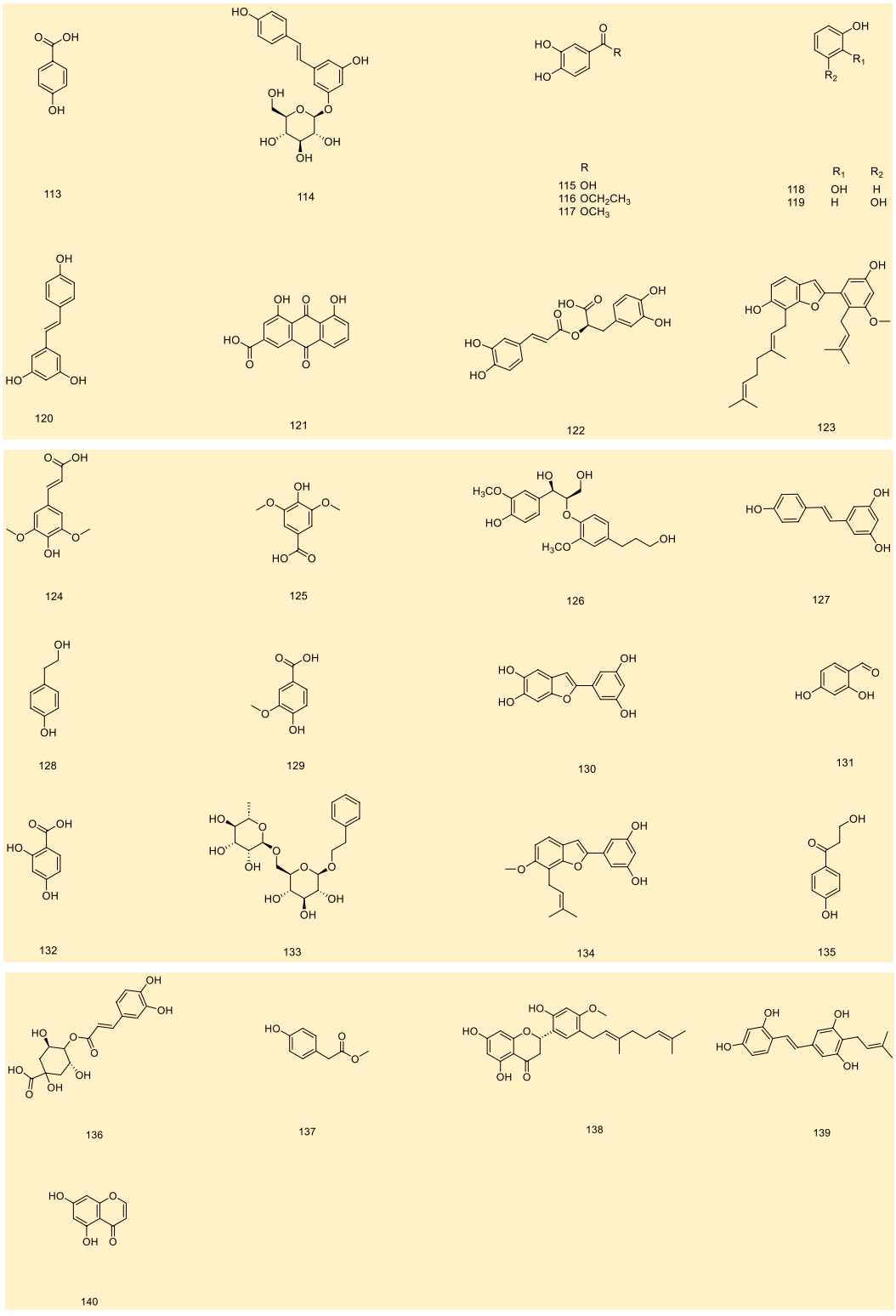

FIGURE 1
(Continued). Phenols.

cancer cells through activating cysteine aspartase and inhibiting NF-κB (Ko et al., 2021). Moracin N was an active ingredient in Mori folium, which exhibit anti-lung cancer properties through apoptosis and autophagy (Gao C. et al., 2020). Morusin, which separate from Mori cortex, was demonstrated effective anticancer activity by inhibiting the vitality of prostate cancer cells with minimal

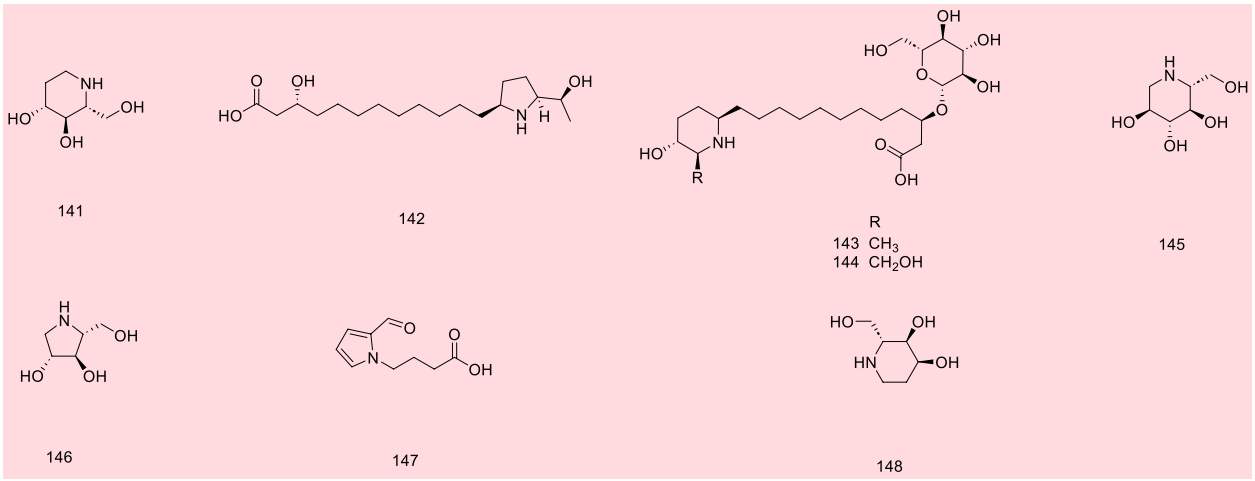

FIGURE 2
Alkaloids.

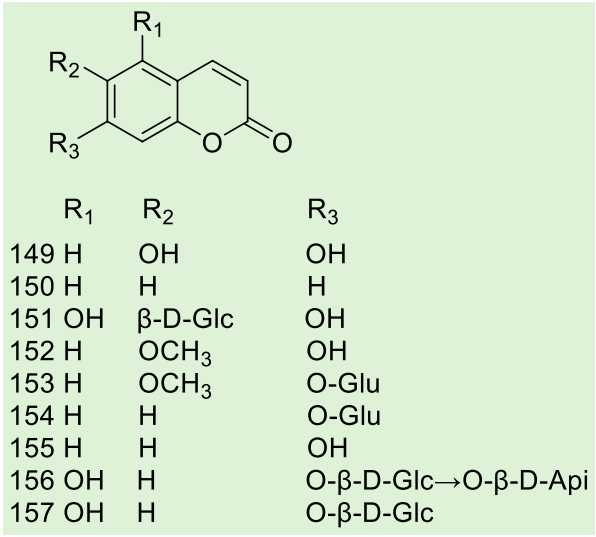

FIGURE 3
Coumarins.

impact on normal prostate epithelial cells, reducing STAT3 activity via the inhibition of phosphorylation, nuclear accumulation and DNA-binding activity. Moreover, morusin showed well downregulation effect on the expression of STAT1 target genes of Cyclin D2. Furthermore, morusin could also decrease the activity of STAT3 in inducing the apoptosis in prostate cancer cells (Lim et al., 2015). The anti-cancer components in *M. alba* L. and their mechanisms are summarized in Table 11.

3.5 Other activities

Beside the aforementioned activities, the ingredients in the different parts from *M. alba* L. also exhibit other activities such as melanin inhibition effect, hair growth, *etc.* Up to now, multiple constituents including norluciferin, moracin B, moracin J, moracin M-3′-O-β-glucopyranoside and moracin M-6-O-β-D-glucopyranoside againsting melanin were separated from the ethanol extracts of *M. alba* L. These components have a significant dose-dependent inhibition of melanin production, effectively suppressed the activity of tyrosinase in B10-F1 cells induced by α-melanocyte stimulating hormone and exhibited inhibitory effects on the expression of associated proteins, such as microphthalmia-associated transcription factor, tyrosinase, and tyrosinase-associated protein-1 (Li Y. et al., 2018). Mulberroside F in Mori folium exhibit inhibitory effect on melanin and through the inhibition of tyrosinase and the formation of melanin in melanin-A cells (Lee et al., 2002). Moreover, little Mori cortex extract showed the stimulating on hair growth, enhance the secretion of growth factors, facilitating the transition of hair follicles from the resting phase to the growth phase, activating β-linker proteins, which is essential for inducing the growth phase (Hyun et al., 2021). Other pharmacological activities and the related mechanisms are summarized in Table 12.

4 Future perspective

In recent years, with the continuous advancement of modern science and technology, researchers conducted in-depth investigations of multifarious constituents and pharmacological activities of *M. alba* L., including Mori folium, Mori ramulus, Mori cortex and Mori fructus, making its high medicinal potential valuable in contemporary society. Until now, there were some reviews about the pharmacologic activities of *M. alba* L. (Hao et al., 2022), however, in view of the crucial connection between pharmacological actions and ingredients, the revelation of the overall constituents of *M. alba* L. was extremely important. When referred to constituents of *M. alba* L. concluded in this paper, the primary constituents were phenols, flavonoids, alkaloids, *etc.*. Summing up the pharmaceutical actions of *M. alba* L., hypoglycemic, antioxidant and anti-inflammatory were the

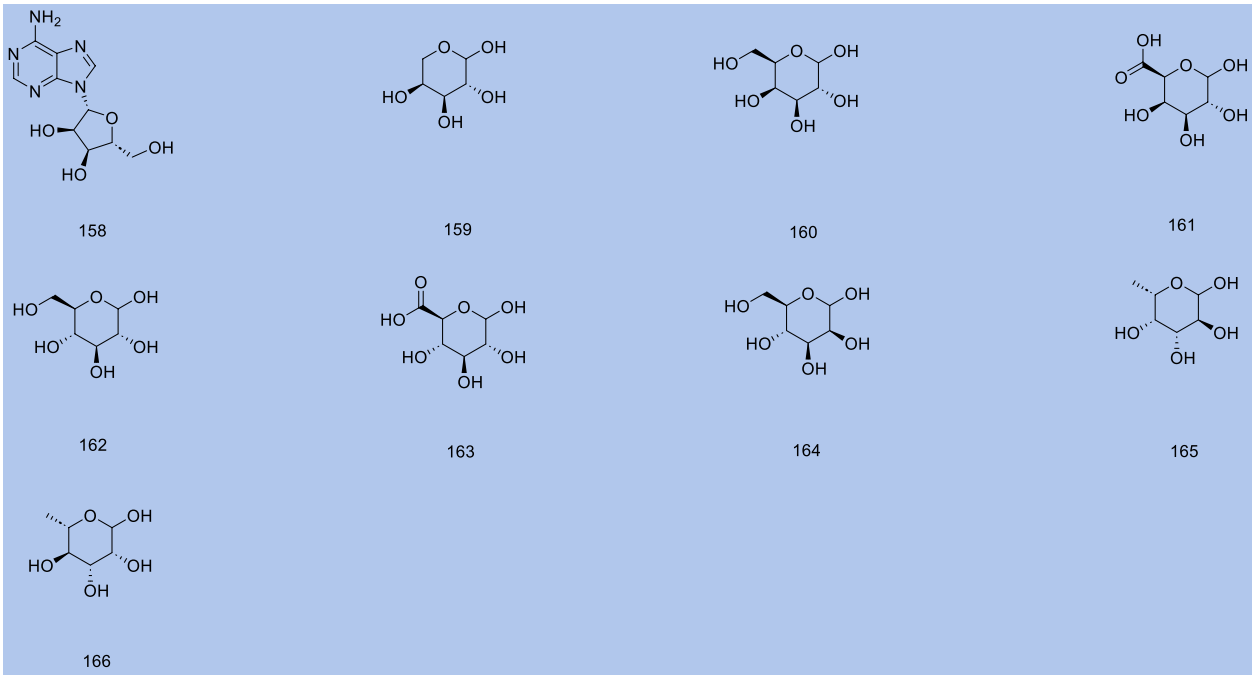

FIGURE 4
Carbohydrates.

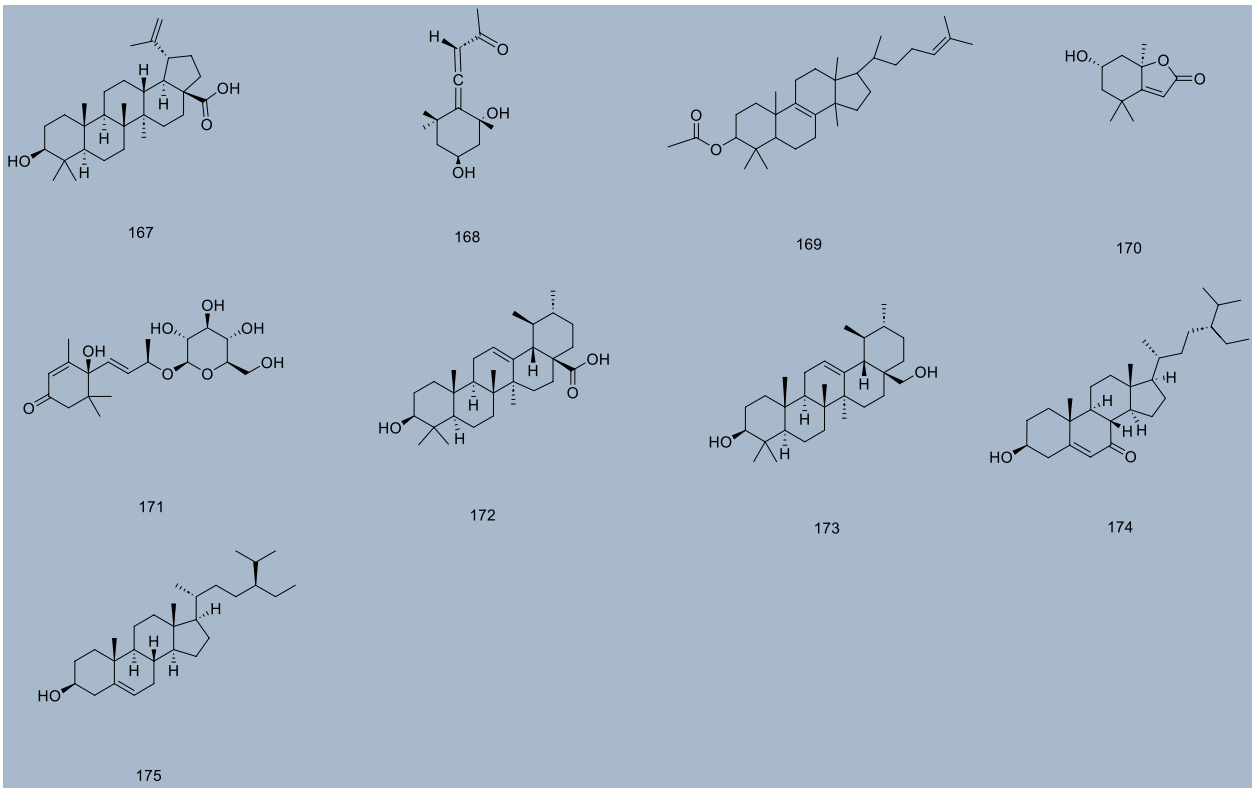

FIGURE 5
Terpenoids.

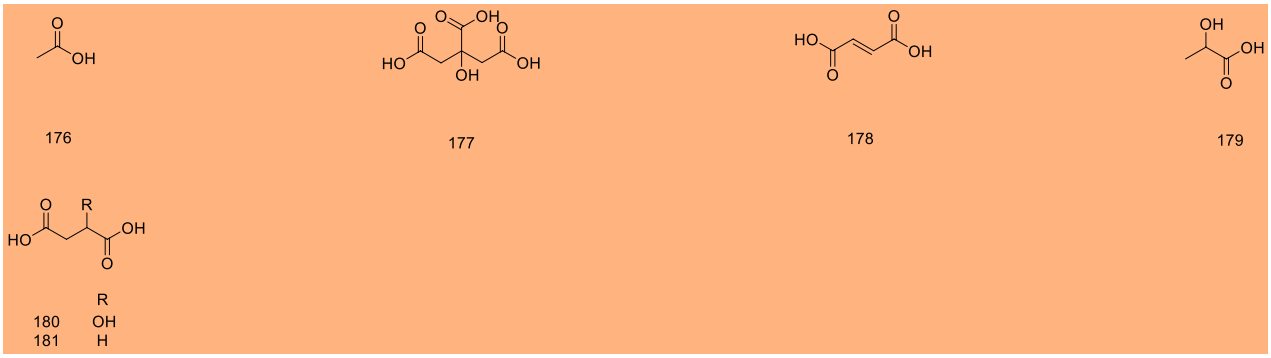

FIGURE 6
Organic acids.

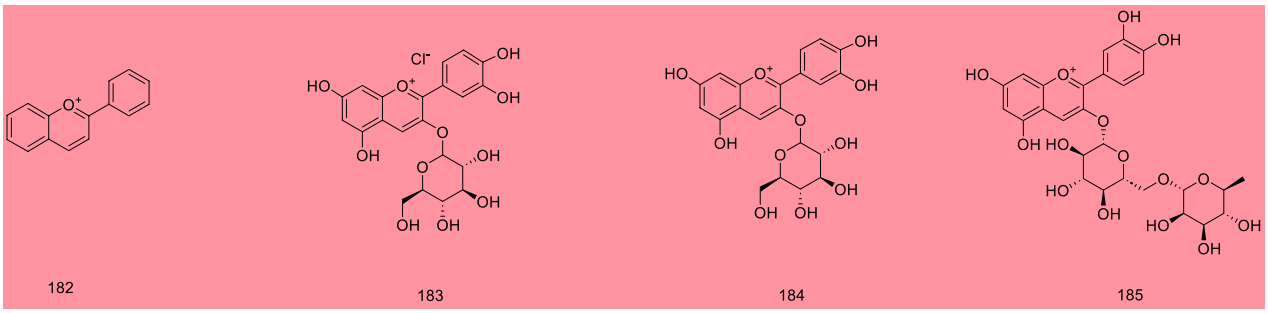

FIGURE 7
Anthocyanin.

TABLE 8 Hypoglycemic mechanisms of components from *Morus alba* L.

Mechanism	Component	Reference
inhibition of α-glucosidase	chalcomoracin	Liu et al. (2022)
	chlorogenic acid; rutin	Hunyadi et al. (2012)
	dihydromorin; kuwanon C; kuwanon G; moracin M; norartocarpetin	Kwon et al. (2022)
	kuwanon H	Zhou et al. (2022b)
	morin	Przeor (2022)
	morusin; morusinol	Zhou et al. (2022b)
	oxyresveratrol	Kwon et al. (2022)
	1-deoxynojirimycin	Jan et al. (2022)
Enhancement of glucose uptake via in-sulin signaling pathway/AMP-activated protein kinase	isoquercetin	Lim et al. (2021)
Increase insulin secretion of pancreatic β-cells	syringic acid	Jan et al. (2022)

common activities, and different constituents may owned similar effects. As is well konwn that, the connection between ingredients's structure and pharmaceutical effects was extremely important. Take flavonoids ingredients, for example, the diversiform flavonoids in *M. alba* L. exhibited anti-inflammatory action. Popularly, the modifications could affect the mechanisms of inflammation, including glycosylation, hydroxylation, *etc.* (Chen et al., 2018). For example, both quercetin and its glycoside derivative quercetine-3-glucoside exhibit same anti-inflammatory activity with distinctive mechanisms of action. Quercetin downregulated the INOS

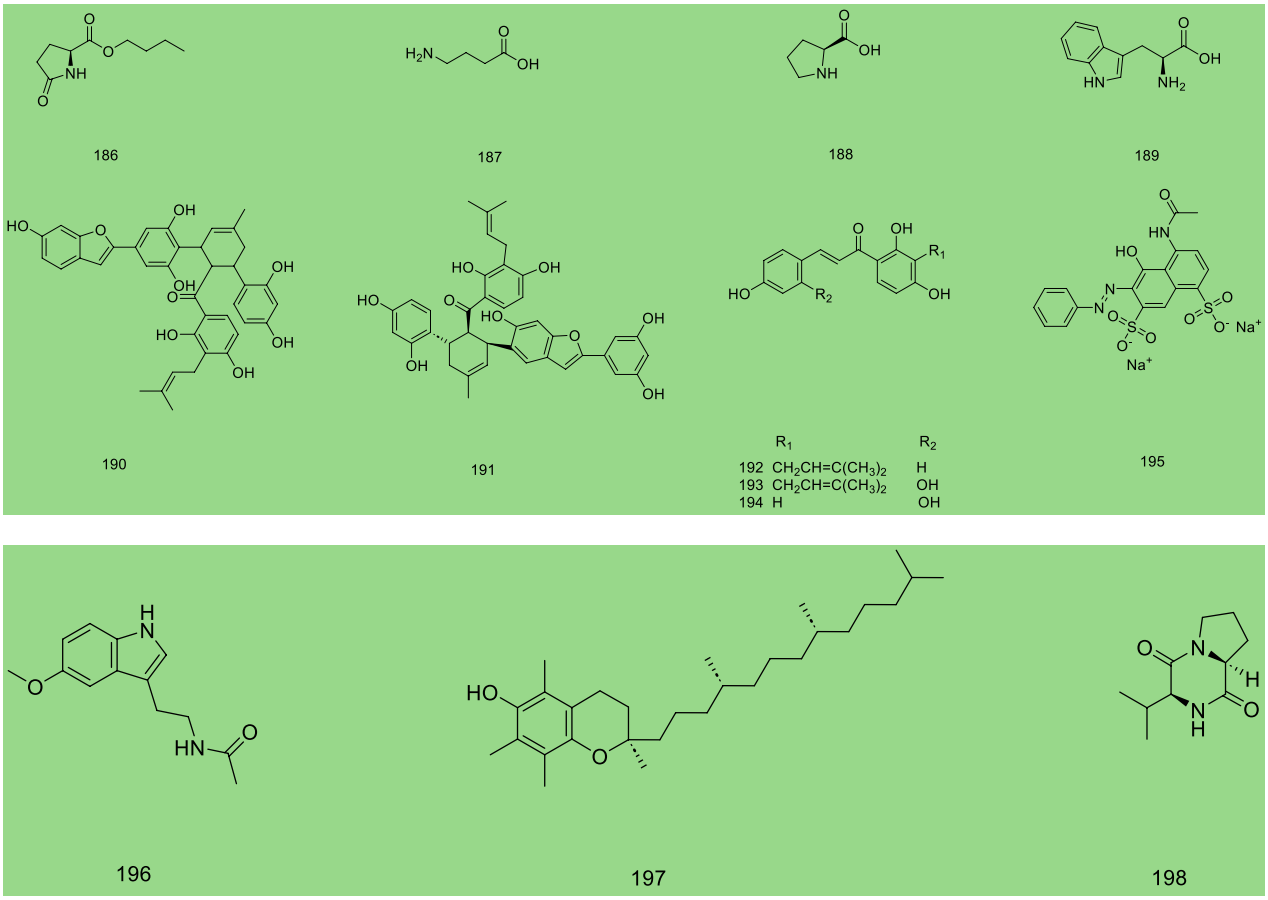

FIGURE 8
Other categories.

TABLE 9 Antioxidant mechanisms of components from *Morus alba* L.

Mechanism	Component	Reference
inhibition of ROS production	astragalin; kaempferol; luteolin; quercetin; taxifolin	Yu et al. (2021)
inhibition of soluble epoxide hydrolase	aesculetin; moracin B; moracin J; moracin M; moracin M 3′-O-β-glucopyranoside; mulberroside F; scopoletin; scopoline	Li et al. (2020)
scavenging or inhibiting the production of free radicals	anthocyanins	Suriyaprom et al. (2021)
	caffeic acid; chlorogenic acid; ferulic acid; gallic acid; myricetin; naringenin; p-coumaric acid; rosmarinic acid; rutin; sinapinic acid	Polumackanycz et al. (2021)
	mulberroside A; oxyresveratrol	Thomas et al. (2022)
	protocatechuic acid; isoquercetin	Leyva-Jimenez et al. (2020)
	4-O-caffeoylquinic acid	Ganzon et al. (2018)

expression (Leyva-Jimenez et al., 2020), however, isoquercetin inhibited the release of pro-inflammatory cytokines (Yu et al., 2021). Besides, different activities of constituents may owned the similar mechanisms. For example, AMP-activated protein kinase was related to both the anti-hpyerglycemic effect and anti-cancer action of *M. alba* L. Besides, when referred to the anti-oxidant and anti-inflammatory activities of *M. alba* L., the inhibition of soluble epoxide hydrolase was the same mechanism. These information indicated that one mechanism maybe related to diversified activities of *M. alba* L. based on the similar compounds. To sum up, the ingredients of *M. alba* L. were diverse, and the effect owned the characteristics of multiple approaches and multiple targets.

Nowadays, in order to extend the application of *M. alba L.* in TCM and food, the toxicity assessments of *M. alba* L. were evaluated

TABLE 10 Anti-inflammatory mechanisms of components from *Morus alba* L.

Mechanism	Name	Reference
inhibition the release of pro-inflammatory cytokines	mulberroside A	Shi et al. (2023)
	protocatechuic acid; isoquercetin	Leyva-Jimenez et al. (2020)
inhibiting MEK/ERK signaling in leukocyte migration	oxyresveratrol	Chen et al. (2013)
inhibition of NF-κB pathway activity	morusin	Jia et al. (2020)
	moracin O; moracin P	Hardianti et al. (2020)
	neochlorogenic acid	Gao et al. (2020a)
	kuwanon T	Ko et al. (2021)
	sanggenon A	
downregulating INOS expression	astragalin; kaempferol; luteolin; quercetin; taxifolin	Yu et al. (2021)
regulating Nrf2 signaling pathways	neochlorogenic acid	Gao et al. (2020b)
	kuwanon T	Ko et al. (2021)
	sanggenon A	
removal of excess reactive oxygen/nitrogen species or interaction with their interacting enzymes	cudraflavone B; kuwanon E; 4′-O-methylkuwanon E	Kollar et al. (2013)
selective inhibition of COX-2 activity	kuwanon A	Baek et al. (2021)

TABLE 11 Anticancer mechanisms of components from *Morus alba* L.

Mechanism	Component	Reference
inhibition of the Akt/mTOR signalling pathway	morusin	Wu et al. (2023)
activating AMP-activated protein kinase	morusin	Park and Park (2020)
reducing STAT3 activity	morusin	Cho et al. (2017)
regulating bax and survivin expression	morusin	Kang et al. (2017)
induces autophagy	guangsangon E	Shu et al. (2021)
	moracin N	Gao et al. (2020b)
regulation of autophagy protein ATG3L16-related RNA molecule expression	cyanidin-3-glucoside	Zabady et al. (2022)
activating protein and inhibiting of signaling	sanggenol L	Won and Seo (2020)
	moracin D	Hwang et al. (2018)
inhibition of HIF-1α in tumours and DLL4 activity in the endothelium	steppogenin	Cha et al. (2023)
targeting the KDM4B-MYC axis	sanggenon C	Tang et al. (2023)
induces CHK1 degradation through the ubiquitin-proteasome pathway	morusinol	Guo et al. (2023)

by various experiments. When referred to Mori folium, the LD_{50} was higher than 15.0 g/kg bw in the acute toxicity test, indicating that Mori folium was deemed as safe and it may own a wide application as food or nutritional supplements (Li Y. et al., 2018). Besides, Mori fructus was a familiar edible food in daily life, and it was widely made into diverse foods such as fresh/dried fruit, fruit wine/juice, and other healthcare foods. From the sub-chronic oral toxicity test, the safe dose without observed adverse was up to 4200 mg/kg, meaning that Mori fructus was nontoxic under conventional edible dosage. Until now, there were none reports about the acute or chronic toxicity of the extracts of Mori cortex. However, the maximum tolerated dose of oral administration of the active ingredient named sanggenon C, an active ingredient derived from Mori cortex as well as identificated in Mori ramulus, was up to 100 mg/g (Langeder et al., 2023b). However, resveratrol, another active constituent in Mori cortex and Mori ramulus, was reported controversial toxicity, the metabolites of resveratrol may exhibit cytotoxic effects (Shaito et al., 2020), meaning that Mori cortex and Mori ramulus may owned a ralative reasonable safe space when applied. Hence, in order to improve the expansive value of *M. alba* L., the detailed illustrations of acute and long-term toxicity of Mori cortex and Mori ramulus were particularly vital in further studies for researchers.

TABLE 12 Other pharmacological effects and their mechanisms of components from *Morus alba* L.

Activity	Mechanism	Component	Reference
antigout	blocking the RAS signaling pathway	lanosterol acetate	Oh et al. (2021)
antiviral	interference with cell damage caused by influenza virus infection	gallic acid	Kim and Chung (2018)
	direct inhibition of influenza virus entry	morin hydrate	Hong et al. (2020)
	inhibition of viral neuraminidase	sanggenon C	Langeder et al. (2023a)
	inhibition of SARS-CoV-2 proteases	sanggenon C; sanggenon G; sanggenon O	Wasilewicz et al. (2023)
antiulcer	inhibition the releasion of histamine	quercetin	Garg et al. (2022)
	inhibition the formation of platelet-activating factor	rutin	Garg et al. (2022)
antidepressant	interacts with the 5-hydroxytryptaminergic	sanggenon G	Lim et al. (2015)
antiplatelet	inhibition of thromboxane release	mulberroside C	Kwon et al. (2021)
	inhibition of platelet aggregation	morusinol	Lee et al. (2012)
anti-fatigue	increased glucose phosphatase activity	γ-aminobutyric	Chen et al. (2016)
anti-melanogenic	inhibition of tyrosinase activity	kuwanon G; mulberrofuran G	Koirala et al. (2018)
	inhibition of S1P lyase activity	mulberroside A; oxyresveratrol	Zheng et al. (2023)
anti-obesity	regulation of gut microbial communities and lipid indices	arabinose; D-galactose; D-galacturonic acid; D-glucose; D-glucuronic acid; D-mannose	Yang et al. (2022a)
		fucose	
		L-rhamnose	
anti-bacteria	blocking the binding of [1–^{14}C]acetate to *Staphylococcus aureus* membrane lipids	chalcomoracin; moracin C	Kim et al. (2012)
neuroprotection	maintenance of mitochondrial membrane potential and mitochondrial function	cyanidin-3-glucoside	Bhuiyan et al. (2011)
	promoted nuclear translocation of the mitophagy regulator TFEB and activated the AMPK-ULK1 pathway	morin	Wang et al. (2023c)
cardioprotection	enhancement autophagy of hypoxia-induced	sanggenon C	Gu et al. (2017)
prevent hair loss	increased secretion of angiogenic paracrine factors	chlorogenic acid; umbelliferone	Hyun et al. (2021)
anti-alzheimer's disease	reduction of intracellular amyloid-β oligomer-induced cytotoxicity	anthocyanins	Ochiishi et al. (2021)
against Benzo [a]pyrene in epidermal keratinocytes	activation of Nrf2-mediated signaling/inhibition of aryl hydrocarbon receptor signaling	maclurin	Kim et al. (2021)
relieve fever	inhibition of arachidonic acid metabolic pathway	tryptophan	Qu et al. (2019)
anti-hyperuricemia	inhibition of xanthine oxidase activity, and downregulation expression of mURAT1, mGLUT9, and mABCG2	polydatin	Ge et al. (2023)

5 Conclusion

This review summarized the chemical profiles and the pharmacological activities of *M. alba* L., as well as the safety and the structure-activity relationship. Totally 198 of constituents including phenols, alkaloids, coumarins, carbohydrates, terpenoids, organic acids, anthocyanins, and other constituents were concluded. Among the chemical ingredients, 140 of them were phenols, indicating that phenols may played a critical role in this plant. Modern pharmacological research showed that *M. alba* L. exhibited hypoglycemic, antioxidant, anti-inflammatory, anti-cancer and other activities, illustrating that *M. alba* L. has showed favourable applications in pharmaceutical and food fields. Furhter biological activities and the related mechanisms of the ingredients in *M. alba* L. were needed in order to promote the development of pharmaceutical industry. In addition, more nutritional valve analysis and toxicity research data were particularly important for the development of *M. alba* L. in food scope.

Author contributions

YW: Conceptualization, Data curation, Formal Analysis, Investigation, Methodology, Resources, Supervision, Writing–original draft, Writing–review and editing. QA: Conceptualization, Data curation, Formal Analysis, Methodology, Resources, Supervision, Writing–original draft, Writing–review and editing. MG: Data curation, Formal Analysis, Investigation, Methodology, Resources, Supervision, Writing–review and editing. HG: Investigation, Resources, Supervision, Writing–review and editing. WY: Investigation, Resources, Supervision, Writing–review and editing. MZ: Data curation, Investigation, Supervision, Writing–review and editing. JM: Investigation, Methodology, Supervision, Writing–review and editing. ZL: Investigation, Resources, Writing–review and editing. QL: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Writing–review and editing. JL: Conceptualization, Data curation, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Writing–review and editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

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