Drug Design, Development and Therapy

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REVIEW

Dauricine: Review of Pharmacological Activity

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Background: Dauricine is an important natural organic compound in *Menispermum dauricum*, which often has significant biological activity.

Purpose: The purpose of this review is to systemically summarize and discuss the pharmacological activity and underlying mechanisms of dauricine in recent years.

Methods: Web of Science (121 articles) and PubMed databases (97 articles) were used to search for articles related to "dauricine" published from 2000 to 2024. Meanwhile, we classified the pharmacological activity of dauricine by screening these articles.

Results: Emerging evidence suggests that dauricine possesses numerous pharmacological activities, including neuroprotection, anti-cancer, anti-arrhythmia, anti-inflammatory and anti-diabetes.

Conclusion: Dauricine has a potential value in the treatment of many diseases. We hope that this review will contribute to therapeutic development and future studies of dauricine.

Keywords: menispermum dauricum, dauricine, toxicity, pharmacology, pharmacokinetics

Introduction

Since the 21st century, researchers have increasingly turned their attention to traditional Chinese herbs. Traditional Chinese herbs have the advantage of fewer side effects. *Menispermum dauricum*, a traditional Chinese medical plant, has been widely used to treat various diseases. A series of phytochemical investigations revealed that *Menispermum dauricum* contains many alkaloids, such as benzylisoquinoline, bisbenzylisoquinoline, oxoisoaporphine, aporphine, protoberberine and morphinane.[1–3] Bisbenzylisoquinoline alkaloids are naturally occurring phytochemicals that are common constituents of hundreds of plant species around the world. More than 400 bisbenzylisoquinoline alkaloids have been identified mainly among the following four families: Menispermaceae, Berberidaceae, Ranunculaceae, and Annonaceae. Dauricine is a bisbenzylisoquinoline alkaloid isolated from the roots of *Menispermum dauricum*. Over the past few years, dauricine has been widely investigated in both animal and human models. Both in vivo and in vitro studies have revealed that dauricine has many positive effects, such as neuroprotection, anti-cancer, anti-arrhythmia, anti-inflammatory and anti-diabetes (Figure 1). Regrettably, there is still a lack of comprehensive and critical review of dauricine pharmacological activity. Therefor, we systemically summarize and discuss the pharmacological activity and underlying mechanisms of dauricine in recent years. We hope that this review will contribute to therapeutic development and future studies of dauricine.

Chemical Properties and Plant Sources of Dauricine

Menispermum dauricum, a herbaceous deciduous vine, is widely distributed in China, Japan, South of Korea and Russia (Figure 2). The rhizome of *Menispermum dauricum* was known as "Bei Dou Gen". Its roots are vertical and brown. New stems from subapical buds are usually glabrous, striate and slender. Its petiole is 3–10 cm long or slightly longer. The leaf is blade usually cordate-oblate in outline. The peduncle is 3–10 cm long and very slender. In addition, inflorescences are paniculate, solitary or paired. The flowering period is from June to July and the fruiting period is from August to September[4] (Figure 3).

Received: 29 March 2024
Accepted: 23 August 2024
Published: 27 September 2024

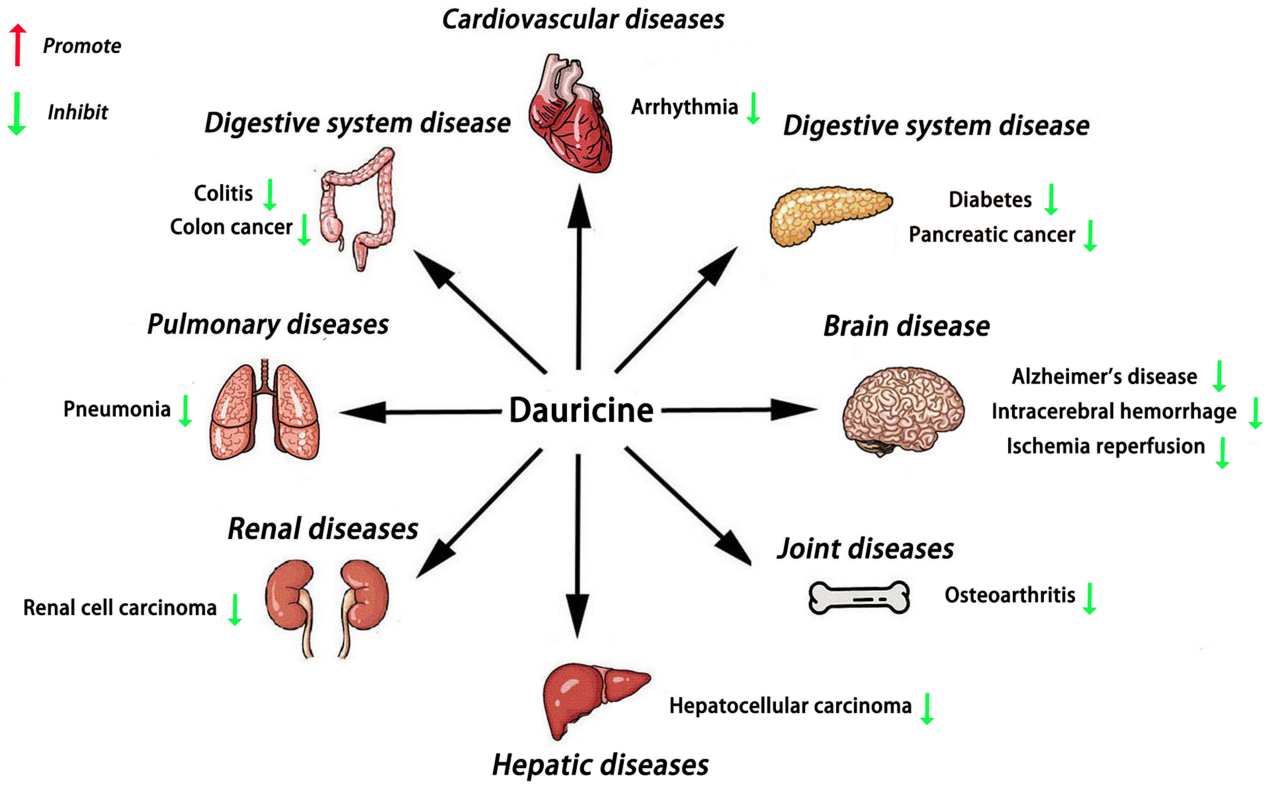

Figure 1 Main roles of dauricine in various tissues. Dauricine plays an important role in various organs, such as the bone, brain, heart, pancreas, kidney, liver, lungs, colon and so on.

Dauricine is an isoquinoline alkaloid with a molecular formula of $C_{38}H_{44}N_2O_6$, a molecular weight of 624.766, and soluble in ethanol, acetone and benzene. Dauricine has one OH group and two CH3 groups. It is also known as 4-{[(1R)-6,7-Dimethoxy-2-methyl-1,2,3,4-tetrahydro-1-isoquinolinyl]methyl}-2-(4-{[(1R)-6,7-dimethoxy-2-methyl-1,2,3,4-tetrahydro-1-isoquinolinyl]methyl}phenoxy)phenol[2] (Figure 3). Interestingly, Mikulak-Klucznik et al successfully validated computer-designed syntheses of natural products (dauricine) in the laboratory. 4-hydroxyethylphenol is used as a substrate to produce dauricine through the sequence of iodization, benzylation, coupling, bisoxidation, coupling, reduction, and debenzylation.

Pharmacokinetics

The liver is the main organ of dauricine metabolism. Early studies pointed out that the main metabolite of dauricine was N-desmethyl dauricine (N-ddau).[5] In later years, Han et al discovered seven other metabolites of dauricine[6] (Figure 4). Due to the low concentration of dauricine in human plasma, it is very important to investigate the pharmacokinetics of dauricine in humans by using a high sensitivity analysis method.[7] Liquid chromatography–mass spectrometry (LC–MS/MS) and reverse-phase high-performance liquid chromatography (RP-HPLC) are two highly sensitive and selective methods.[8,9] The pharmacokinetics of dauricine can be measured via LC–MS/MS and RP-HPLC. Shi et al examined the pharmacokinetics of dauricine (6 mg/kg, iv) in beagle dogs via RP-HPLC.[7] They found that the $T_{1/2\alpha}$ and $T_{1/2\beta}$ were (0.049±0.016) h and (2.7±0.6) h. The V_d and AUC were (16 ±3) L/kg and (1.48±0.17) mg·h/L.[7] The two-compartment pharmacokinetic model describes the evolution of drug levels in the organism by depicting the body as two pharmacokinetic compartments (the central and the peripheral compartments, also commonly referred to as compartment 1 and compartment 2, in that order). The pharmacokinetics of dauricine was fitted to a two-compartment open model.[7] Liu et al examined the pharmacokinetics of dauricine (60mg, 120mg and 180mg PO) in twelve healthy male volunteers via LC–MS/MS.[10] The corresponding pharmacokinetic parameters are presented in Table 1.[10]

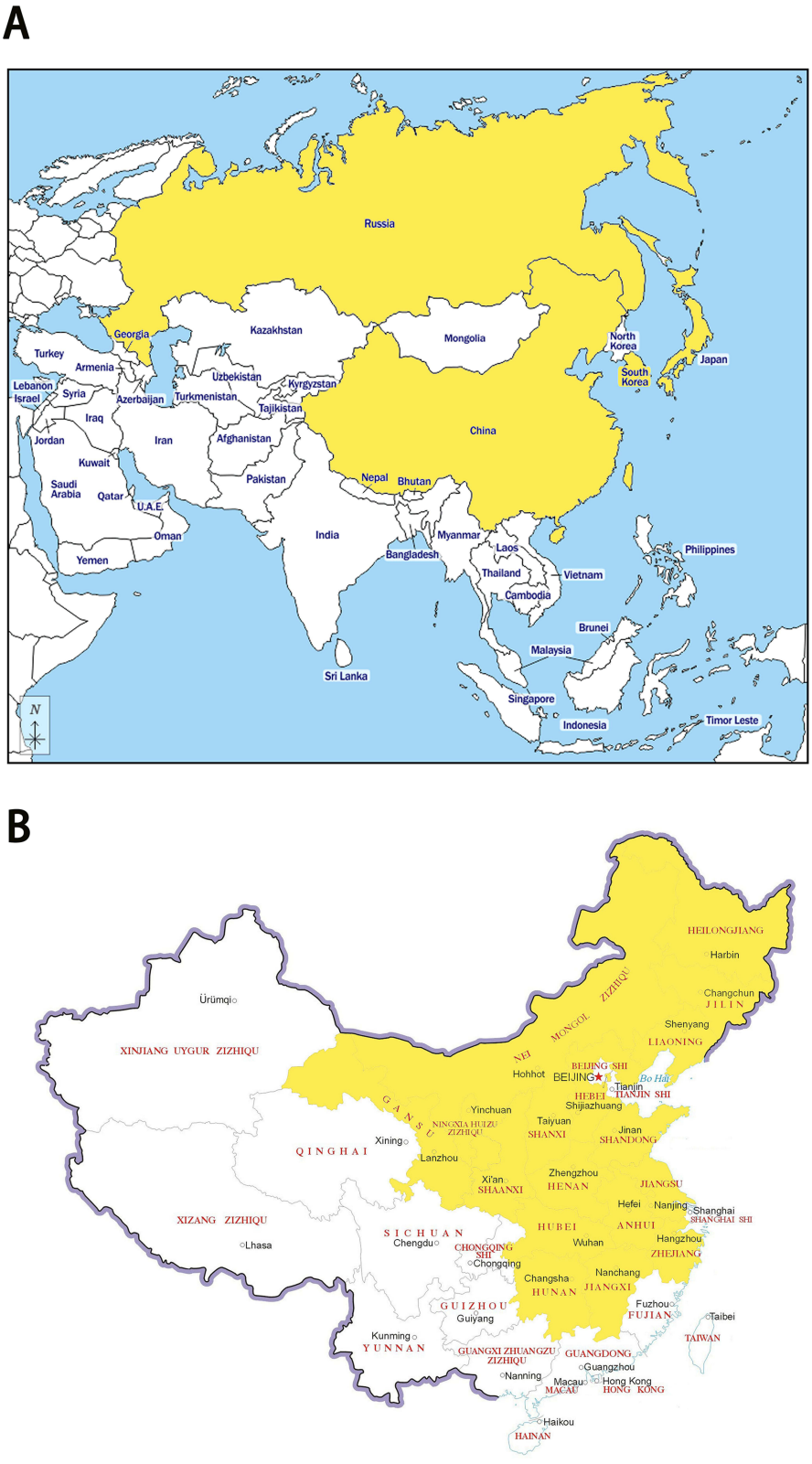

Figure 2 Distribution of *Menispermum dauricum* in World (**A**) and China (**B**). (**A**) *Menispermum dauricum* is widely distributed in China, Japan, South of Korea and Russia. (**B**) *Menispermum dauricum* is widely distributed in An hui province, Gan su province, Gui zhou province, He bei province, Hei long jiang province, Hu bei province, Hu nan province, Jiang su province, Jiang xi province, Ji lin province, Liao ning province, Nei Mon gol autonomous region, Ning xia autonomous region, Shan xi province, He nan province, Shan dong province, Shan xi province and Zhe jiang province.

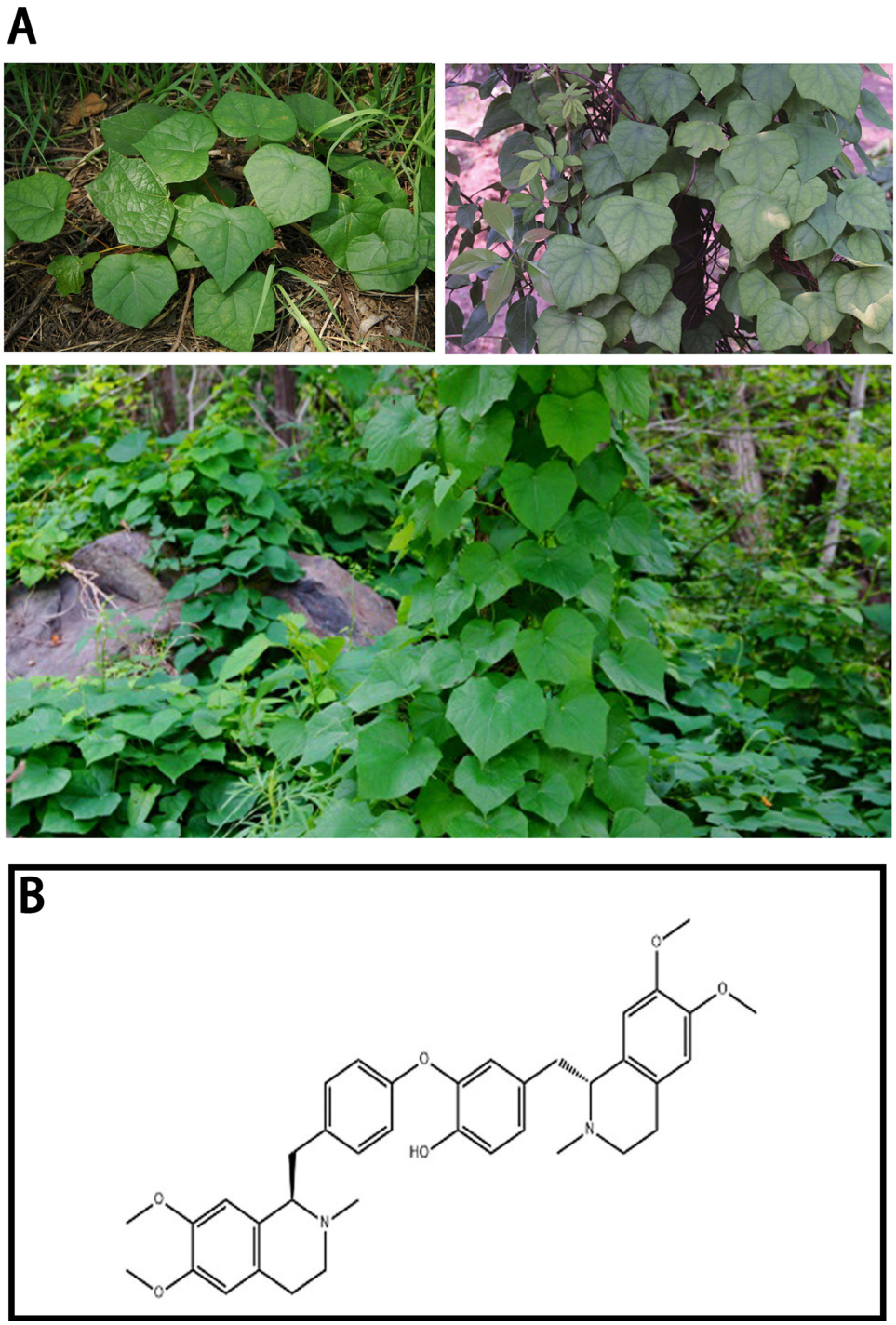

Figure 3 The whole plant of *Menispermum dauricum* (**A**) and structures (**B**) of dauricine.

Toxicity

Although dauricine has good pharmacological activity, an increasing number of studies have reported its toxicity. In male CD-1 mice, dauricine (150mg/kg) caused significant alveolar edema and hemorrhage. In human lung cell lines BEAS-2B, WI-38 and A549, dauricine (40uM, 24h) resulted in up to 60% cell death.[11] Mechanistically, CYP3A mediates the metabolism of dauricine. Dauricine is metabolized to an electrophilic quinone methide metabolite. This metabolite may exacerbate cytotoxicity and apoptosis by depleting cellular glutathione (GSH).[12] Ketoconazole is a known CYP3A inhibitor. Pretreatment with ketoconazole protected mice from dauricine-induced pulmonary injury. Protein adduction derived from the electrophilic quinone methide

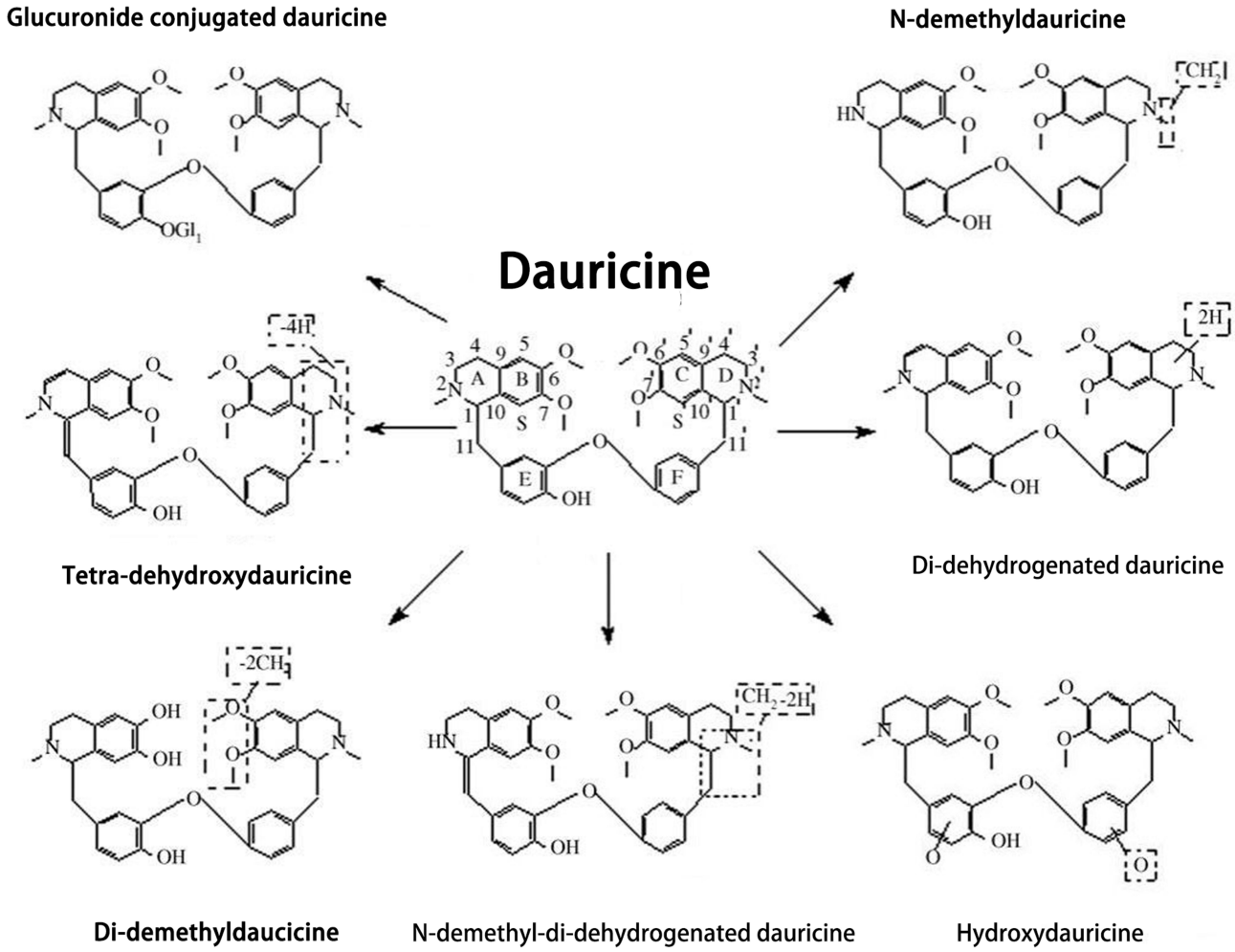

Figure 4 The metabolic pathways of dauricine in rat.

metabolite is considered to initiate the process of toxicity.[13] Another study found that dauricine had severe liver toxicity.[14] This toxic effect is also associated with the metabolism of CYP3A4-mediated dauricine.[14] These quinone methide metabolites could cause acute cytotoxicity and carcinogenesis by reacting with proteins and/or DNA in vivo. As a known CYP3A inhibitor, Ketoconazole can reduce liver toxicity and increase therapeutic effects.

Anti-Inflammatory Activities

Lipopolysaccharide (LPS) can cause inflammatory bone loss.[15] Dauricine ameliorated the LPS-induced bone loss in female C57BL/6J mice. In vivo, dauricine decreases the number of osteoclasts (OCs). In vitro, dauricine reduces the differentiation and activity of OCs. In terms of mechanism, dauricine ameliorated the LPS-induced bone loss by decreasing the production of ROS

Table 1 The Pharmacokinetics Parameters of Dauricine

Parameters	100 mg (n = 12)	300 mg (n = 12)	600 mg (n = 12)
$T_{1/2}$ (h)	3.57 ± 1.28	2.87 ± 0.86	3.07 ± 0.85
AUC (0–12 h) (ng h/mL)	44.4 ± 9.39	121 ± 28.1	243 ± 76.7
AUC (0–∞) (ng h/mL)	53.0 ± 10.2	132 ± 29.9	267 ± 85.9
MRT (h)	4.01 ± 0.33	4.28 ± 0.41	4.34 ± 0.30
CL/F (L/h)	1168 ± 210	1428 ± 316	1474 ± 440
V/F (L)	5922 ± 2198	5891 ± 1946	6592 ± 2871

via the ROS/PP2A/NF-κB axis.[16] Osteoarthritis (OA) is a non-inflammatory degenerative disease characterized by pain and stiffness in the joints.[17] Dauricine also has the therapeutic potential for OA. In LPS-stimulated macrophages, dauricine inhibited the expressions of proinflammatory cytokines, such as NO, iNOS and COX2[18]. In IL-1β-treated mouse chondrocytes, dauricine can reverse the IL-1β-induced inflammatory response and promote factors associated with cartilage regeneration. In terms of mechanism, dauricine regulates the NF-κB signaling pathway and Ca^{2+} signaling pathway.[18] Ulcerative colitis (UC) is a non-specific inflammatory disease. In dextran sulfate sodium mice, dauricine attenuated the levels of inflammatory cytokines. In HT-29 cells, dauricine also reduced LPS-induced inflammation. Mechanically, dauricine suppresses the NF-κB signaling pathway.[19] Endothelial dysfunction is associated with the development of various diseases such as pneumonia. The study points out that endothelial inflammation is an important component of endothelial dysfunction. In IL-1β-induced human umbilical vein endothelial cells (HUVECs) and lung tissues, dauricine can alleviate endothelial inflammation by inhibiting the NF-κB pathway.[20] In H5N1-induced BEAS-2B cells and Streptococcus pneumoniae (D39)-induced mice, Dauricine significantly decreased the expressions of TNF-α, IL-6 and IL-1β and reversed the lung histological alterations.[21] To summarize, these results indicate that dauricine could be a promising drug for the treatment of inflammation. However, whether dauricine can prevent endothelial inflammation in other organs (kidney) or other inflammatory diseases (atherosclerosis) remains to be explored. (The anti-inflammatory mechanisms of dauricine are shown in Figure 5).

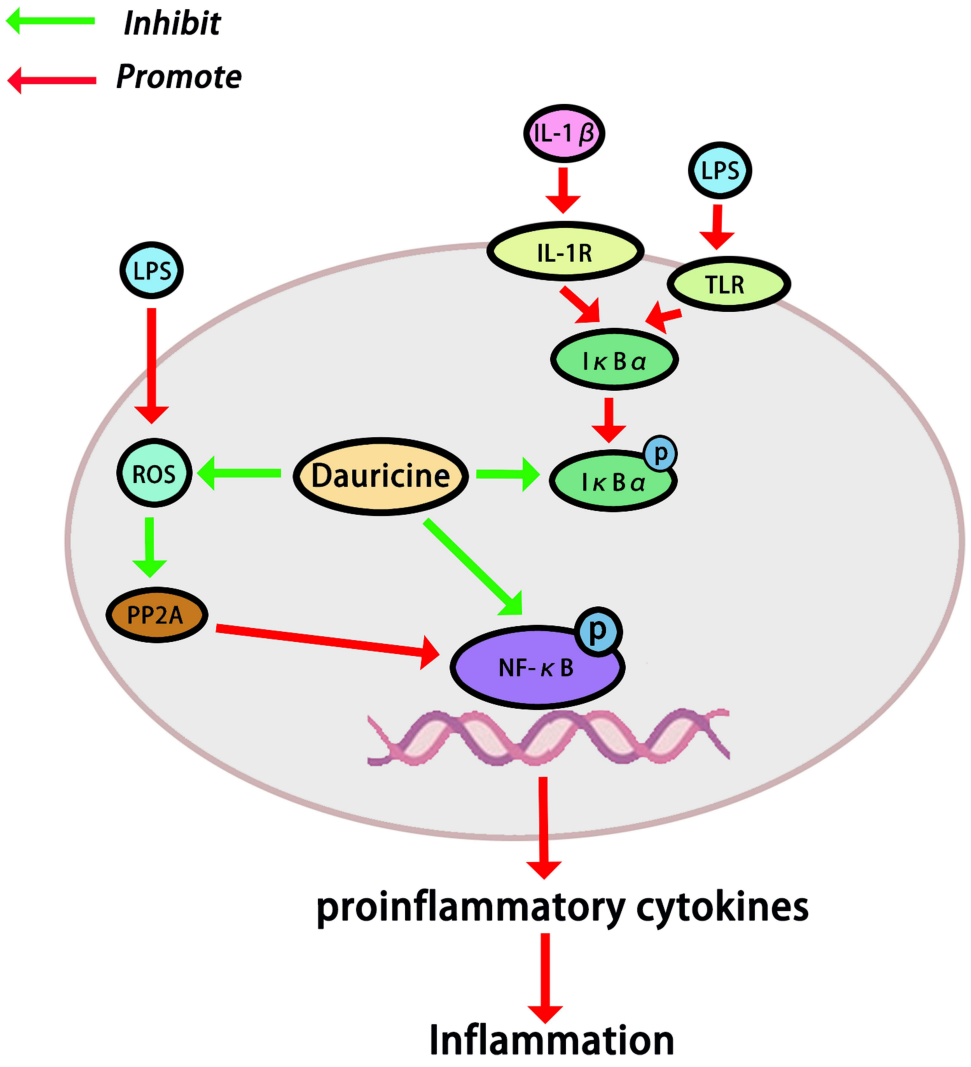

Figure 5 The anti-inflammatory mechanisms of dauricine.

Anti-Arrhythmia Activities

At the end of the 20th century, a large number of studies began to investigate the anti-arrhythmic effects of dauricine. The experimental animals involved mice, dogs, rabbits and so on. In the isolated canine heart and rabbit heart, dauricine decreased the monophasic action potentials (MAP) and prolonged the effective refractory period (ERP).[22,23] At the same time, dauricine has an antagonistic effect on early afterdepolarizations (EAD). This effect may be related to the blockade of calcium current.[24,25] In guinea pig ventricular myocytes, dauricine inhibited the IKs, IKr and IKl. Interestingly, dauricine not inhibit the deactivation of IKs and IKr.[26] Zhao et al also found that dauricine can prolong APD by inhibiting the human aether associated gene (HERG) channels.[27] Zhu et al suggest that dauricine inhibits arrhythmias by inhibiting the conduction of ischemic zone.[28] Taken together, dauricine is likely a promising anti-arrhythmia drug. However, there are only a few reports on exploring the anti-arrhythmia mechanisms of dauricine, which maybe requires further elaboration in the future. (The anti-arrhythmia mechanisms of dauricine are shown in Figure 6).

Anti-Cancer Activities

In the field of cancer, pancreatic cancer is known as the "king of cancer". According to the Lancet, pancreatic cancer kills about 200,000 people per year worldwide.[29] A large number of studies indicate that miRNA play a crucial role in tumorigenesis. Jiang et al found that 79 known miRNA was affected by dauricine in pancreatic cancer.[30] The hedgehog (Hh) signaling pathway is a potential therapeutic target of pancreatic cancer. Studies have shown that dauricine can significantly inhibit tumor growth in pancreatic cancer BxPC-3 cells. This inhibitory effect may be mediated by the inhibition of the Hh signaling pathway.[31]

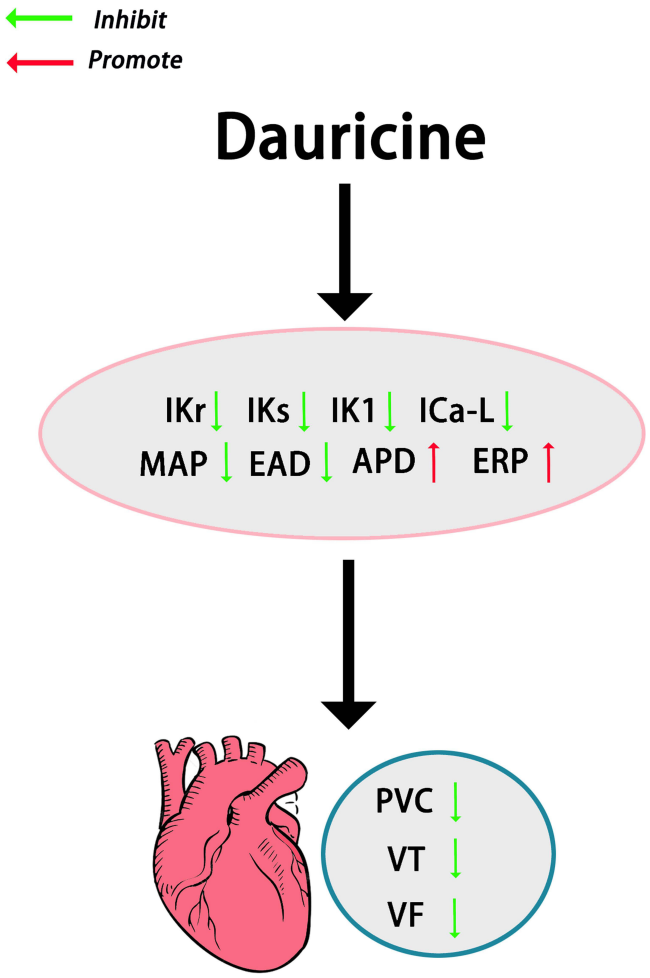

Figure 6 The anti-arrhythmia mechanisms of dauricine.

Colon cancer is a common malignancy of the digestive tract. Dauricine significantly inhibited the growth of colonic tumor by suppressing NF-κB-regulated genes.[32] Autophagy is a kind of programmed death that maintains cell homeostasis. As an autophagy inhibitor, dauricine induced massive formation of autophagic vacuoles and impaired lysosomal function in HeLa cells.[33] Zhou et al synthesized the eleven dauricine derivatives. They found that carbamates 2a, carbamates 2b, carbonyl ester 3a and sulfonyl ester 4a induced autophagy-dependent cell death in HeLa cells.[34] Dauricine can also significantly inhibit the proliferation of major urinary tumor cells, such as bladder cancer EJ cells and prostate cancer PC-3M cells.[35] M2 type tumor-associated macrophages (TAMs) have been proved to contribute to tumor metastasis. Dauricine prevented the proliferation, epithelial-mesenchymal transition, migration, and invasion of prostate cancer (PCa) cells by inhibiting the M2 polarization of macrophages via downregulation of the PI3K/AKT signaling pathway.[36]

In addition, dauricine also plays a crucial role in some other tumors. Renal cell carcinoma (RCC) is a prevalent solid tumor. As a result of its intrinsic resistance to chemotherapy and radiotherapy, surgery is still the only effective treatment for RCC. Zhang et al found that dauricine effectively suppresses viability and induces apoptosis by inhibiting the PI3K/AKT pathway in four RCC cell lines.[37] In neuroblastoma and glioblastoma, dauricine induced cell apoptosis by attenuating Octamer binding transcription factor 4 (OCT4)/Sonic hedgehog (SHH) co-activated stemness.[38] In MCF-7 cells, dauricine inhibited human breast cancer angiogenesis by inhibiting Hypoxia inducible factor 1 alpha (HIF-1α) protein accumulation and Vascular endothelial growth factor (VEGF) expression.[39] In A375 and A2058 melanoma cells, dauricine significantly promoted cell death by suppressing the Signal transducer and activator of transcription 3 (STAT3) signaling pathways.[40]

Interestingly, dauricine plays a crucial role in drug resistance of tumor cells. Li et al found that dauricine increased the sensitivities of HCC cells to chemotherapy agents, including cisplatin, sorafenib, and isoliensinine.[41] Dauricine can be used as an adjuvant reagent for HCC treatment. Dauricine also significantly enhanced the vincristine-induced apoptosis in MCF-7 drug-resistant cells.[42] In addition, Dauricine reduced doxorubicin resistance in HL60 cells.[43] The mechanism is involved in the accumulation of intracellular dox.[43]

Up to date, the incidence and mortality of malignant tumors are still high. Many anti-cancer drugs have the disadvantages of high price and great adverse reactions. Therefore, dauricine has great prospect in the treatment of cancer as a bisbenzylisoquinoline alkaloid. (The anti-cancer mechanisms of dauricine are shown in Figure 7).

Neuroprotection

Alzheimer's disease (AD) is the most common degenerative disease in the elderly. Due to the complex pathogenesis of the disease, there is no effective treatment at present. Dysregulation of intracellular Ca^{2+} homeostasis, amyloid-beta (Aβ) toxicity, hyperphosphorylated tau and mitochondrial dysfunction play a critical role in the pathological development of AD. In D-galactose and AlCl3 combined-induced AD mice, dauricine (1–10mg/kg) improved the neuronal damage, learning and memory deficits.[44] Mechanically, dauricine has a high affinity with Calmodulin. Dauricine can reduce the levels of Ca^{2+} and suppress the expression of Calmodulin in the hippocampus and cortex of AD mice.[44] In addition, dauricine reduced the formation of NFTs by decreasing the phosphorylation of Tau in the hippocampus and cortex.[44] X-box binding protein 1 (XBP-1) is an ER stress response factor. It can show the neuroprotective activity by accelerating Aβ clearance. In the Aβ1-42-transgenic Caenorhabditis elegans CL2120, dauricine delays the progression of AD by activating the XBP-1[46]. Conversely, the effects of dauricine on Aβ-associated toxicity are offset by XBP-1 depletion.[45] In 3xTg-AD mice, dauricine significantly alleviated cognitive impairments by raising the hippocampal ATP levels, reducing Aβ plaques and hyperphosphorylated Tau.[46] According to the proteomic and Western blot, the expression of synapse-related proteins (Synapsin 1 and Synapsin 2) and mitochondrial energy metabolism proteins (Aconitase 2, Ndufs1, Cytochrome c oxidase subunit 5a, and Succinate dehydrogenase B) were modified by dauricine.[46] N2a cells transfected with Swedish mutant amyloid precursor protein (N2a/APP) are a common AD-like cell model. Liu et al found that dauricine decreased the accumulation of Aβ and inhibited the processing of APP in N2a/APP cells.[47] Furthermore, dauricine reduced tau hyperphosphorylation through the protein phosphatase 2A (PP2A), p35/25, and cyclin-dependent kinase 5 (CDK5) pathways.[47] The SH-SY5Y cells that overexpress the Swedish mutant APP are another AD-like cell model. Wang et al found that dauricine decreased the level of Aβ1-42 and reactive oxygen species (ROS) and restored the activity of mitochondrial membrane potential (MMP) and superoxide dismutase (SOD) on SH-SY5Y cells.[48] At the same time, dauricine also regulated the levels of nuclear factor erythroid 2-related factor 2, and Kelch-like ECH-associated protein 1 (KEAP1).[48] Graphene oxide (GO) is a new carbon material with excellent properties and has a wide range of

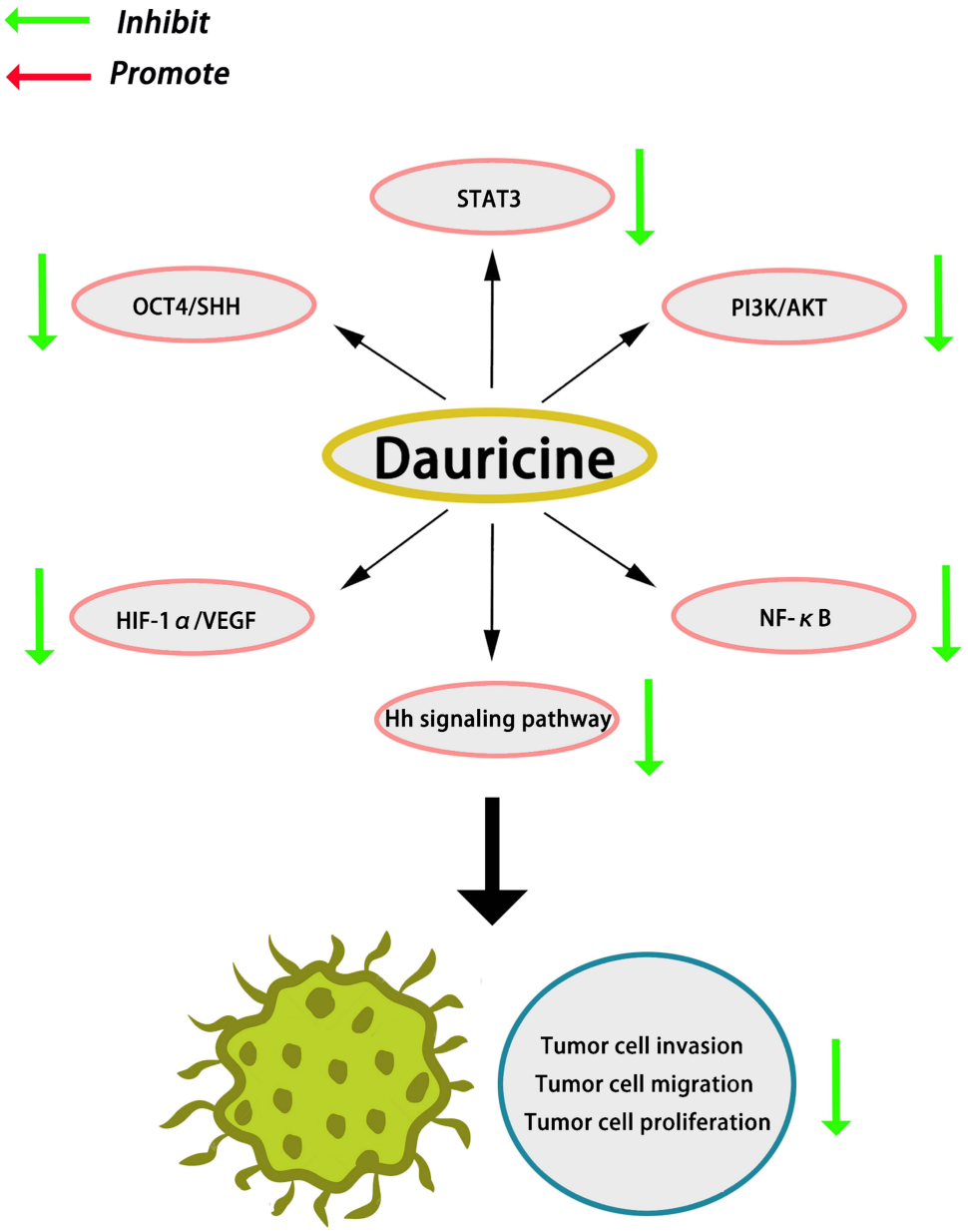

Figure 7 The anti-cancer mechanisms of dauricine.

application prospects. Interestingly, GO loaded with dauricine significantly reduced the cognitive memory deficits in Aβ1-42-induced AD mice.[49]

Intracerebral hemorrhage (ICH) is a common cerebrovascular disease in clinic. In the past, anti-ICH drugs mainly targeted at cell apoptosis, inflammation and oxidative stress. Unfortunately, there are no good effects. In recent years, ferroptosis has emerged as a hot topic in the study of nervous system diseases. Glutathione peroxidase 4(GPX4) is a key protein that affects ferroptosis. Dauricine has the potential to prevent the ferroptosis of nerve cells and ICH by increasing the expression of glutathione reductase (GSR) and GPX4[51]. Drug delivery vectors to treat ICH cannot achieve satisfactory results due to their short lives, lack of specific targets and effective control of drugs. Li et al developed a metal ion-responsive nanocarrier.[50] Dauricine-loaded nanocarriers can restore ICH by inhibiting ferroptosis and decreasing inflammatory injury.[50]

Yang et al investigated the effect of dauricine on ischemia/reperfusion (I/R).[51] After treatment with dauricine, the expression of MPO, ICAM-1, IL-1β, TNF-α were significantly reduced.[51] These findings suggest that dauricine reduces the I/R-induced inflammatory process. The neuroprotective effect of dauricine may be related to the inhibition of I/R-induced inflammation.

Yang et al also found that the neuroprotective effect of dauricine may be related to the inhibition of neuronal cell apoptosis in the brain penumbra.[52] Dauricine (42 mg/kg and 84 mg/kg) treatment improved histopathological recovery and decreased DNA fragmentation in the penumbra.[53] Another study pointed out that dauricine (5 mg/kg and 10 mg/kg) increased Bcl-2 expression and decreased DNA fragmentation in the penumbra.[54] Li et al then evaluated the effect of dauricine on neurotoxicity. They found that dauricine suppressed the decrease of mitochondrial membrane potential induced by 30 min of hypoxia and hypoglycemia.[55] This effect may be the basis of the dauricine treatment on cerebral ischemia.

To summarize, dauricine has considerable neuroprotective effects. However, whether dauricine can prevent other neurodegenerative disease (Parkinson's disease) remains to be explored. (The Neuroprotective mechanisms of dauricine are shown in Figure 8).

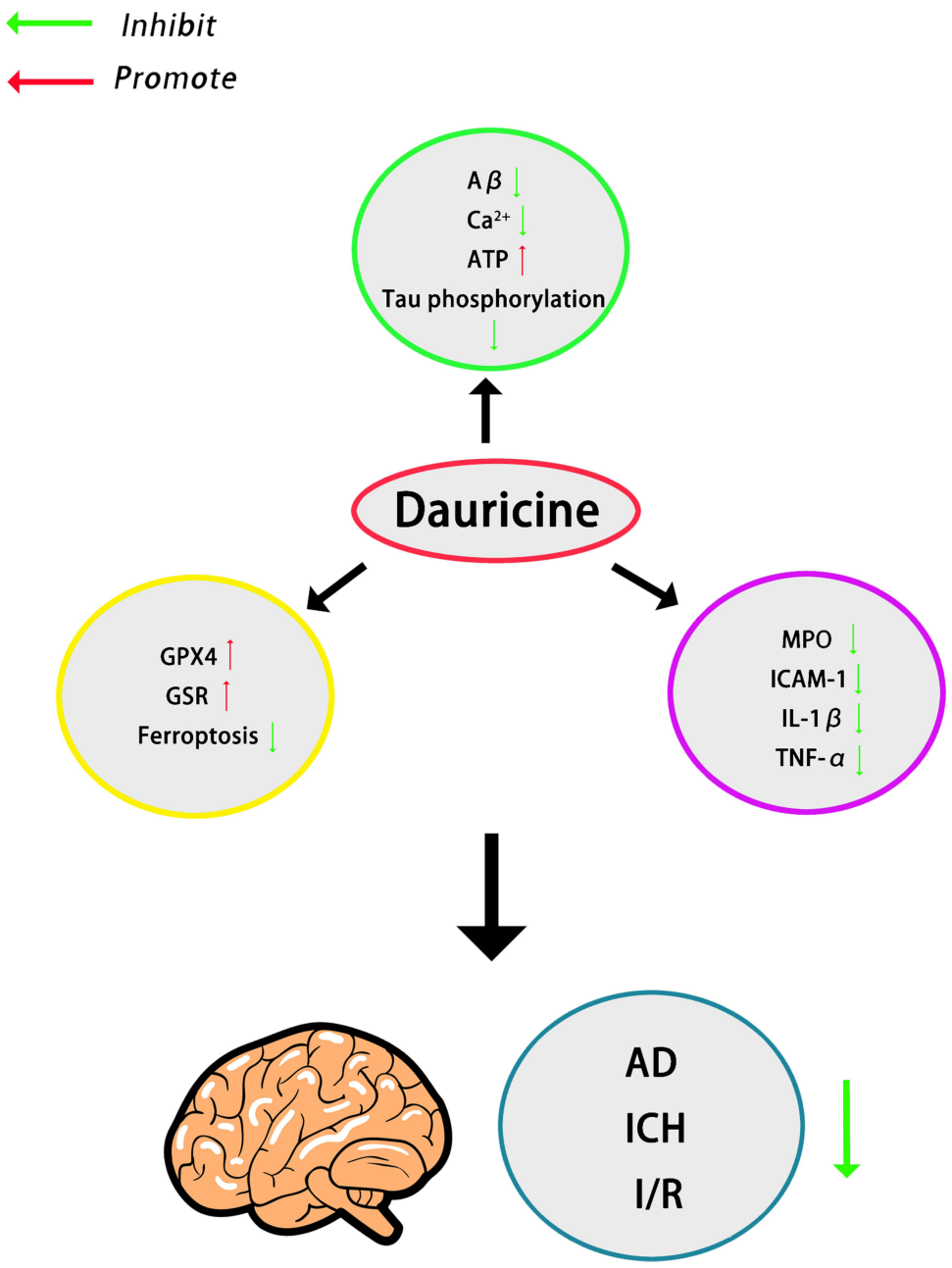

Figure 8 The Neuroprotective mechanisms of dauricine.

Other Activities

As the virus continues to evolve, several SARS-CoV-2 variants start to appear.[56] Regrettably, these variants are partially resistant to current vaccinations and antiviral medications.[56] Dong et al found that dauricine can pass the blood-brain barrier.[57] Dabrell et al found that dauricine can effectively block the Spike-ACE2 interaction.[58] Dauricine may be an effective agent for targeting the entry of the SARS-CoV-2 virus. Previous studies have shown that dauricine is a potent inhibitor of platelet activating factor.[59] In rats and humans, dauricine can inhibit the platelet aggregation induced by arachidonic acid (AA).[60] The main metabolic pathway of AA is inhibited by dauricine.[61] Diabetes is one of the major diseases that seriously harm the health of people in the world. Li et al found that dauricine can inhibit the increase of blood glucose by interfering with the binding of glucagon (GCG) and glucagon receptor (GCGR).[62] Taken together, dauricine has a variety of activities. In the future, it is significant to explore more activities of dauricine.

Conclusion and Prospect of the Future

Numerous studies have shown that dauricine possesses numerous pharmacological activities, including neuroprotection, anti-cancer, anti-arrhythmia, anti-inflammatory, and anti-diabetes (Table 2). In addition, dauricine also plays an important role in other aspects. In global public health, such as the SARS-CoV-2 variants, dauricine may be an

Table 2 Pharmacological Activities of Dauricine

Subjects	Pharmacologic Action	Function	Ref.
Female C57BL/6 J mice Whole bone marrow cells	Anti-LPS-induced bone loss Anti-osteoarthritis	TRAP↓ calcitonin↓ cathepsin K↓ ROS↓ MCP-1↓	[16]
RAW264.7 cells C57BL/6 J mice	Anti-lung injury	NO↓ IL-1β↓ IL-6↓ TNF-α↓ iNOS↓ COX2↓	[63]
Mouse chondrocytes	Anti-osteoarthritis	ADAMTS5↓ MMP3↓ MMP13↓ iNOS↓ COX2↓	[18]
Male C57BL/6 J mice HT-29 cells	Anti-colitis	IFN - γ↓ TNF-α↓ IL-1β↓ IL-6↓	[19]
Male C57BL/6 J mice Human umbilical vein endothelial cells	Anti-endothelial inflammation	E-selectin↓ VCAM-1↓ ICAM-1↓	[20]
Female BALB/c mice BEAS-2B cells	Anti- pneumonia	TNF-α↓ IL-1β↓ IL-6↓	[21]
Canine	Anti-arrhythmia	APA↓ MDP↓ ERP↑	[22]
Rabbit	Anti-arrhythmia	EAD↓ MAP↓ APD50↑ APD90↑ ERP↑	[23–25]
Guinea pig ventricular myocytes	Anti-arrhythmia	IKs↓ IKr↓ IKl↓	[26]
HEK293 cells	Anti-arrhythmia	HERG ↓	[27]
BALB/c nude mice BxPC-3 cells	Anti-pancreatic cancer	Cells proliferation↓ apoptosis↑	[31]
HCT116 and HCT8 cells SW480 and SW620 cells	Anti-colon cancer	Cells proliferation↓ invasion↓ apoptosis↑	[32]
EJ cells PC-3M cells	Anti-prostate cancer	Cells proliferation↓	[35]

(*Continued*)

Table 2 (Continued).

Subjects	Pharmacologic Action	Function	Ref.
Male BALB/c nude mice DU145 and PC3 cells	Anti-prostate cancer	Cells proliferation↓ invasion↓ migration↓ EMT↓	[36]
786-O, Caki-1, A-498 and ACHN cells	Anti-renal cell carcinoma	Cells viability↓ apoptosis↑	[37]
SH-SY5Y cells and T98-G cells	Anti-neuroblastoma and Anti-glioblastoma	Cells proliferation↓	[38]
A375 cells and A2058 melanoma cells	Anti-melanoma	Cells viability↓ Cells proliferation↓ invasion↓ apoptosis↑	[40]
Male KM mice	Anti-alzheimer's disease	Learning deficits↓ Memory deficits↓ Neuronal damage↓	[44]
Caenorhabditis elegans CL2120	Anti-alzheimer's disease	Aβ-associated toxicity↓ Aβ-associated expression↓	[45]
3xTg-AD mice and wild type mice	Anti-alzheimer's disease	Cognitive impairment↓ Tau hyperphosphorylation↓ Aβ accumulation↓	[46]
Neuroblastoma neuro2a cells	Anti-alzheimer's disease	APP↓ Tau hyperphosphorylation↓ Aβ accumulation↓	[47]
SH -SY5Y cells	Anti-alzheimer's disease	Aβ secretion↓ ROS↓ MMP↑ SOD↑	[48]
Male C57BL/6 mice SH-SY5Y neuroblastoma cells	Anti-intracerebral hemorrhage	ROS↓ Fe^{2+}↓ neurological deficits↓ ferroptosis damage↓ GPX4↑	[64]
Male C57BL/6 mice SH-SY5Y neuroblastoma cells	Anti-intracerebral hemorrhage	ROS↓ neurological deficits↓ brain edema↓ blood-brain barrier permeabilization↓	[50]
Male SD rats	Anti-ischemia/reperfusion	MPO↓ ICAM-1↓ TNF-α↓ IL-1β↓	[51]
Rat cortical neurons	Anti-ischemia/reperfusion	Neuronal loss↓ neuronal survival↑	[55]
HEK293 cells	Anti-diabetes	GCGR ↓	[62]

Notes: (↓: Inhibit ↑: Promote).

effective agent for targeting the entry of the SARS-CoV-2 virus. In drug resistance, dauricine reduced the drug resistance of tumor cells. Nevertheless, there are still many questions of dauricine that need to be discussed. Firstly, some of dauricine's biological activities are only reflected in its effects on cells, and whether these effects can be achieved in vivo requires further investigation. Secondly, the protein modification triggers the cytotoxicity of dauricine. Development of an analytical approach to assess protein modification derived from the reactive metabolite of dauricine is an essential step to gain the insight into the role of protein modification in dauricine-induced toxicity. Thirdly, many studies have shown that *Menispermum dauricum* is effective in treating respiratory tract inflammation, asthma and gastric cancer.[65,66] We speculate that dauricine, a main active component of *Menispermum dauricum*, also plays an important role in these diseases. At the same time, the underlying mechanisms of dauricine in various diseases remain to be further studied. In the future, we believe that the development of nutritional agents containing dauricine has good prospects. Meanwhile, it is very meaningful to explore the therapeutic role of dauricine in more diseases. In summary, we expect more research on dauricine to safeguard people's health.

Consent to Participate

All the authors give their consent for participation.

Consent for Publication

All the authors give their consent for publication.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

There is no funding to report.

Disclosure

The authors declare no competing interests.

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