TABLE 1 Traditional Chinese Medicine for treating inflammation-related diseases through cholinergic anti-inflammatory pathway

Disease	Traditional Chinese Medicine	Composition (Herb)	The species investigated	Dosage	Control drug	Efficacy	Refs.
Acute lung injury	Liang-Ge-San	*Forsythiae fructus, Rhei radix et rhizoma, Scutellaria baicalensis, Gardeniae radix et rhizoma, Glycyrrhiza uralensis, Menthae haplocalycis herba and Natrii Sulfas*	RAW264.7, Male Wistar rats	Cell: 25-400μg/mL. Rats: 30g/kg, 5d, i.g.	MLA, PNU282987	↓IL-6, TNF-α, IκBα, and nuclear translocation of NF-κB p65, activating α7nAChR.	Liu *et al*., 2016
	Scutellaria baicalensis	NA	Male Sprague Dawley rats	3, 1.5g/kg, 7d, i.g.	Galanthamine	↓TNF-α, NO, ↑ACh, improve lung tissue inflammatory lesions.	Cui *et al*., 2012
	Coptidis Rhizoma	NA	Male Sprague Dawley rats	1.67, 0.83g/kg,7d, i.g.	Galanthamine	↓TNF-α, NO, ↑ChAT, ACh, improve inflammatory lesions.	Cui, 2012
	Total flavonoids of litchi	NA	Male Sprague Dawley rats	25, 50, 100mg/kg, 7d, i.g.	Dexamethasone	↓wet-dry weight of lung tissues, IL-1β, NO, TNF-α, NF-κB, ↑ACh, ChAT, AChE.	Chen *et al*., 2016
	3-dehydroandrographolide	NA	RAW264.7, Male Wistar rats	Cell: 2.5-10μM. Rats: 5,10g/kg, 3d,	MLA, PNU282987	↑α7nAchR, ↓NF-κB/Akt signaling pathway.	Lu *et al*., 2018

				i.g.			
Sepsis	Huanglian Jiedu Decoction	*Coptidis Rhizoma, Scutellaria baicalensis, Phellodendri Chinensis Cortex, Gardeniae radix et rhizoma*	Male Sprague Dawley rats	390mg/kg, i.g.	NA	↑CAP, ↓HMGB-1/TLR4/ NF-κB signaling pathway.	Xu *et al*., 2017
	Shenfu Injection	*Ginseng Radix Et Rhizoma Rubra, Aconiti Lateralis Radix Praeparata*	Sprague Dawley rats	10mL/kg, i.p.	NA	↑ChAT, ACh, ↓TNF-α.	Hong, 2016
	Rhei radix et rhizoma-Scutellariae Radix	*Rheum palmatum, Scutellariae Radix*	Male Sprague Dawley rats	*Rheum palmatum*: 0.0154g/kg, *Scutellariae Radix*: 0.0077g/kg, *Rheum palmatum-Scutellariae Radix*: 0.0231g/kg, i.g.	NA	↑ChAT, AChE.	Li, 2013
	Astragalus polysaccharide combined with ibuprofen	NA	Sprague Dawley rats	IBU 20 mg/kg, APS 25 mg/kg, i.p.	NA	↓TNF-α, IL-6, ↑α7nAChR mRNA, ACh.	Liu *et al*., 2017
	Emodin	NA	Male BALB/c mice	20mg/kg, i.p.	NA	↓brain damage, S100β, IL-6, TNF-α, nerve-specific enolase, lactic acid, AChE.	Dong *et al*., 2019
Alzheimer's	Mailuoning	*Achyranthes Bidentatae*	Male Sprague	1.8mL/kg/d, 4w, i.g.	Vitamin C,	↑α7nAChR mRNA,	Tian,

disease		*Radix, Scrophulariae Radix, Dendrobii Caulis, Lonicerae Japonicae Flos*	Dawley rats		Vitamin E	M3mAChR mRNA, ERα mRNA, NMDAR1 mRNA, protect nerves.	2009
	Naoling decoction	*Epimedii Folium, Polygoni Multiflori Radix, Testudinis Carapax Et Plastrum, Os Draconis, Polygalae Radix, Acori Tatarinowii Rhizome*	Male Sprague Dawley rats	9.6g/kg/d, 4w, i.g.	Donepezil	↑α7nAChR, α4nAChR, ↓Aβ deposition, improve learning, memory and cognitive ability, pyramidal cell nuclear shrinkage.	Jin, 2010
	Tianshen Yizhi recipe	*Gastrodiae Rhizoma, Ginseng radix, Epimedii Folium, Acori Tatarinowii Rhizome*	SH-SY5Y cells	0.25mg/mL, 2d	Vitamin E	↑α3, α7nAChR, ↓cell damage, ↑ lipid peroxidation.	Gu *et al*., 2007
	Liuwei Dihuang Decoction	*Rehmanniae Radix Praeparata, Corni Fructus, Moutan Cortex, Alismatis Rhizoma, Dioscoreae Rhizoma, Poria*	PC12 cells	3g/mL,1d,10d, i.g. Preparation of drug-containing cerebrospinal fluid	NA	↑α7nAChR, ↓neurotoxic effect of $A\beta_{1\text{-}40}$.	Ma *et al*., 2008
	Daicong solution	*Ginseng radix et rhizoma, Rehmanniae Radix, Anemarrhenae Rhizoma, Astmgali Radix*	Sprague Dawley rats	5, 10, 20 g/kg, 4w, i.g.	NA	↑M1, M3 mRNA.	Wang *et al*., 2007
	Naosuikang	*Astmgali Radix, Chuanxiong Rhizoma, Puerariae Lobatae Racix,*	Sprague Dawley rats	100, 200, 400mg/kg, 4w, i.g.	Nimodipine	↑ACh, ChAT, ↓AChE, ↑NGF, BDNF, ↑spatial memory	Cai *et al*., 2019

	Salviae Miltiorrhizae Radix Et Rhizoma, Scorpio, Ligustri Lucidi Fructus, Polygalae Radix, Corni Fructus, Gastrodiae Rhizoma				ability.	
Nao Yikang	*Polygoni Multiflori Radix Praeparata, Anemarrhenae Rhizoma, Acori Tatarinowii Rhizome*	Male Sprague Dawley rats	1.73, 3.45, 6.90 g/kg, 4w, i.g.	Naofukang	↑ChAT, ACh, ↓AChE, BuChE.	Geng *et al*., 2008
Dangshen Yuanzhi powder	*Polygalae Radix, Codonopsis Radix, Poria, Acori Tatarinowii Rhizome, Coptidis Rhizoma*	ICR mice	8.58 g/kg, 6w, i.g.	Naofukang	↑ChAT, ↓AChE.	Yang *et al*., 2020
Polygonati Rhizoma and *Pheretima mixtures*	*Polygonati Rhizoma, Pheretima*	Sprague Dawley rats	2, 4, 8g/kg,4w, i.g.	Naofukang	↑ACh, ChAT, SOD, GSH-Px, ↓MDA, AChE.	Xiao *et al*.,2013
Polygalae Radix	NA	Male Sprague Dawley rats	10g/kg/d, 4w, i.g.	NA	↓AChE.	Mu *et al*., 2007
Tenuigenin	NA	Male Wistar rats	125, 375mg/kg/d, 6w, i.p.	NA	↑α7nAChR, ACh, ↓AChE.	Zhao *et al*., 2012; Zeng *et al*., 2009; Chen *et*

							al., 2002
	Lycium barbarum polysaccharides	NA	Male Sprague Dawley rats	100mg/kg, b.i.d, 7d. Preparation of medicated serum with 10% concentration	MLA, Nicotine	↓TNF-α, IL-6, high expression of α7nAChR in hippocampal astrocytes.	Ren *et al*., 2016
	Triptolide	NA	Male Sprague Dawley rats	0.4mg/kg, 15d, i.p.	NA	↓Aβ-induced activation of astrocytes, ↓inflammatory mediators, cholinergic fibers damage.	Huang *et al*., 2010
	Bilobalide	NA	Sprague Dawley rats	2, 4mg/kg, 22d, i.p.	Donepezil	↓AChE, MDA, TNF-α, IL-1β, ↑ChAT, SOD, CAT.	Jin *et al*., 2019
Vascular dementia	Bushen Xingnao decoction	*Rehmanniae Radix Praeparata, Ligustri Lucidi Fructus, Polygoni Multiflori Radix Praeparata, Ginseng radix, Salviae Miltiorrhizae Radix Et Rhizoma, Paeoniae Radix Rubra, Chuanxiong Rhizoma, Polygalae Radix, Acori Tatarinowii Rhizome, Gastrodiae Rhizoma, Borneolum Syntheticum*	Male Wistar rats	5.73g/kg, 7d, 15d, 30d, i.g.	Co-dergocrine Mesylate	↑ChAT, ACh; ↓TNF-α, IL-1β, IL-10, TGF-β, NF-κB, AChE.	Hu *et al*., 2011; Hu, 2011

Bushen Jiannao recipe	*Cuscutae Semen, Lycii Fructus, Salviae Miltiorrhizae Radix Et Rhizoma, Ginkgo Folium, Chuanxiong Rhizoma, Schisandrae Chinensis Fructus*	Male Sprague Dawley rats	14, 28, 56g/kg, 30d, i.g.	Donepezil	↑ACh, ERK1, ERK2.	Liu *et al*., 2012
Dihuangyinzi	*Rehmanniae Radix Praeparata, Crotonis Semen Pulveratum, Corni Fructus, Caulis Dendrobii, Cistanches Herba, Aconiti Lateralis Radix Praeparata, Schisandrae Chinensis Fructus,Cinnamomi Cortex, Poria, Ophiopogonis Radix, Acori Tatarinowii Rhizome, Polygalae Radix, Menthae haplocalycis herba , Zingiberis Rhizoma Recens, Jujubae Fructus*	Male Sprague Dawley rats	10, 20g/kg, 8w, i.g.	Yangxue Qingnao granule	↑total antioxidant capacity (T-AOC), ChAT; ↓apoptosis rate.	Bai *et al*., 2011
Modified Yiqi Congming decoction	*Astmgali Radix, Ginseng radix et rhizoma,*	Male Sprague Dawley rats	14.58g/kg, 30d, i.g.	Nimodipine	↑ACh; ↓AChE.	Bai *et al*., 2016

		Puerariae Lobatae Racix, Acori Tatarinowii Rhizome, Polygalae Radix, Hirudo, Pheretima, Cuscutae Semen, Ligustri Lucidi Fructus, Eucommiae Cortex					
	total flavone of Hawthorn leaf	NA	Male Sprague Dawley rats	70, 140g/kg, 36d, i.g.	Ginkgobiloba tablet	↑ChAT;↓AChE.	Mao *et al*., 2014
	Puerarin	NA		18mg/kg, 5d, i.v.	Nicotine	↑infiltration of inflammatory cells in hippocampus, IL-10.; ↓nerve function damage, IL-1β, IL-6, TNF-α; α-bungarotoxin blocks the above anti-inflammatory effects.	Wang *et al*., 2012
Traumatic brain injury	Arctiin	NA	BALB/c mice	0.1-10 μmol/L, 7d	NA	↑miRNA-16, miRNA-199a; ↓NF-κB pathway.	Swarup *et al*., 2008
Atrial fibrillation	Shensongyangxin capsule	*Ginseng radix, Ophiopogonis, Cornus officinalis, Salvia miltiorrhiza, Ziziphi spinosae Semen, Taxilli herba, Paeoniae Radix Rubra, Eupolyphaga*	Mongrel dogs	0.2g/kg, 8w, i.g.	NA	↑ACh, α7nAChR; ↓increase of sympathetic nerves, TNF-α, IL-6.	Zhao *et al*., 2017

		steleophaga, Nardostachy0s Radix Et Rhizoma, Coptis chinensis, Schisandrae sphenantherae fructus, and Os draconis					
Myocardial ischemia reperfusion injury	Breviscapine	NA	Sprague Dawley rats	25, 50 mg/kg,7d, i.p.	NA	↑NF-κB p65, α7nAChR; ↓IκB-α.	Ding *et al*., 2018
Obesity-related hypertension	Astragaloside IV	NA	Male Wistar rats	20 mg/kg, 6w, i.g.	NA	↑p-STAT3, LepRb mRNA, POMC mRNA, α7nAchR; ↓p-PI3K, SOCS3 mRNA, PTP1B mRNA, IKKβ/NF-KB pathway, proinflammatory cytokines.	Jiang *et al*., 2018
Shock	Anisodamine	NA	Sprague Dawley rats	10mg/kg, i.v.	MLA	↑ACh, α7nAChR; ↓mAChR.	Zhao *et al*., 2011
Arthritis	Hebi Recipe	*Angelicae Sinensis Radix, Paeoniae Radix Alba, Atractylodis Macrocephalae Rhizoma, Atractlodis Rhizoma, Chuanxiong Rhizoma, Saposhnikoviae Radix,Sinomenii Caulis,*	Male Wistar rats	3g/kg, 60d, i.g.	PNU-282987, MTX	↑α7nACh, CAP, JAK2/STAT3 pathway; ↓TNF-α, IL-6, IL-17, joint swelling.	Xing *et al*., 2018

		Sarcandrae Herba,Glycyrrhiza uralensis					
	Tripterygium wilfordii polyglucoside	NA	Human Fibroblast-Like Synoviocyte	Cell: 10mg/L,200μL	MTX	↓IL-17, HMGB1;↑CAP;↓NF-κB pathway, JAK2/STAT3 pathway.	Liu *et al*., 2019
	Sinomenine	NA	RAW264.7	①300μM	Nicotine	↑α7nAChR; ↓NF-κB pathway.	Yi *et al*., 2015
			RAW264.7	②300μM	Nicotine	↓CD14/TLR4, intracellular free calcium; ↑α7nAChR, JAK2/STAT3 pathway.	Zhu *et al*., 2019
			Female Wistar rats, PC12 cells	③Rats: 120 mg/kg, i.g. Cell: 0.03, 0.1, or 0.3 mM	Nicotine, Pilocarpine	↑α7nAChR-PI3K/AKT/ MTOR pathway; ↓production of vasoactive intestinal polypeptide.	Yue *et al*., 2018
			Fibroblast-Like Synoviocyte from Male Sprague Dawley rats	④50,100, 200, 400μM	NA	regulating α7nAChR expression through ERK/Egr-1 pathway.	Yi *et al*., 2018
Diabetes	Berberine	NA	HepG2 Cells	187.5 mg/kg, 6w, i.g.	Nicotine, Metformin	↑α7nAChR, glucose uptake; ↓TNF-α, IL-1β, IL-6, AChE, pIKKβ Ser181/IKKβ, NF-κB p65.	Li *et al*., 2016; Zhou *et al*., 2015

Postoperative ileus	Fuan granule	*Artemisiae Scopariae Herba, Rheum palmatum, Gardeniae fructus, Magnoliae Officmalis Cortex, Aurantii Fructus Immaturus*	Male Sprague Dawley rats	3mL, i.g.	NA	↑small intestine propulsion rate; ↓gastric residual rate, TNF-α, MCP-1, it may compete with ACh for receptors on CAP.	Chen, 2013
	Dajianzhong decoction	*Ginseng radix, Zingiberis Rhizoma, Zanthoxylum fructus*	Male C57BL/6J mice	95 mg/kg, i.g.	Ginseng radix, Zingiberis processsum rhizoma, Zanthoxylum fructus, 6-shogaol, 6-gingerol	↑TRPA1 channel, 5-HT, 5-HT4R, ACh; ↑α7nAChR, mAChR.	Endo *et al*., 2017; Endo *et al*., 2018
Acute pancreatitis	Chaiqin Chengqi Decoction	*Bupleuri Radix, Scutellaria baicalensis, Magnoliae Officmalis Cortex, Aurantii Fructus Immaturus, Rhei radix et rhizoma, and Natrii Sulfas*	Human	4 g/kg, i.g.	NA	↓IL-6, TNF-α, AChE; ↑ChAT, CAP.	Xue *et al*., 2006
Stress gastric ulcer	Banxiaxiexin Decoction	*Pinelliae Rhizoma, Scutellaria baicalensis, Zingiberis Rhizoma, Ginseng radix, Glycyrrhiza uralensis,*	Male Wistar rats	7.5ml/kg, b.i.d, 3d, i.g.	NA	↓gastric mucosal bleeding; ↓ChAT.	Zhang *et al*., 2005

	Coptidis Rhizoma, *Jujubae Fructus*	

Abbreviations: NA, not applicable; d, day; w, week; i.p., intraperitoneal; i.g., intragastric; i.v., intravenous injection.

TABLE 2 Anti-AChE activity effects of Chinese herbal medicines and ingredients

No.	Traditional Chinese Medicine	Classification	IC_{50}	Refs.
1	Huanglianjiedu decoction	Prescriptions	84.67μg/mL	Song *et al*., 2010
2	Aqueous Extract of *Cortex Phellodendri*	Extracts	20.03 μg/mL	Shi *et al*., 2011
3	Aqueous Extract of *Magnoliae Officmalis Cortex*	Extracts	127.17 μg/mL	Shi *et al*., 2011
4	Volatile Oil of Radix Peucedani	Extracts	0.5656 μL/mL	Liu *et al*., 2012
5	Polycyclic-meroterpenoid of Ganoderma	Extracts	0.05 μmol/ mL	Peng *et al*., 2014
6	Lanostane-type triterpene of Ganoderma	Extracts	0.01835 μmol/ mL	Lee *et al*., 2011
7	Galanthamine	Alkaloids	0.0008 μmol/mL	Anand *et al*., 2011; Samochocki *et al*., 2013
8	Huperzine A	Alkaloids	0.000065 μmol/ mL	Zhang *et al*., 2002
9	Berberine	Alkaloids	0.000067 μmol/mL	Xiang *et al*., 2009
10	Columbamine	Alkaloids	0.00024 μmol/mL	Li *et al*., 2019
11	Dauricine	Alkaloids	0.00141 μmol/mL	Li *et al*., 2019
12	Jatrorrhizine	Alkaloids	0.00293 μmol/mL	Li *et al*., 2019
13	Palmatine	Alkaloids	0.0366 μmol/mL	Zhao *et al*., 2016
14	Carinatumin A	Alkaloids	0.0046 μmol/mL	Choo *et al*., 2007
15	Carinatumin B	Alkaloids	0.007 μmol/mL	Choo *et al*., 2007
16	Geissoschizine methyl ether	Alkaloids	0.0037 μmol/mL	Yang *et al*., 2012
17	Stenine A	Alkaloids	0.0021 μmol/mL	Lai *et al*., 2013
18	Stenine B	Alkaloids	0.0198 μmol/mL	Lai *et al*., 2013
19	Volvalerenal acid K	Terpenoid	0.000161 μmol/mL	Chen *et al*., 2016
20	Epigallocatechin Gallate	Terpenoid	0.0148 μmol/ mL	Okello *et al*., 2020
21	Epigallocatechin	Terpenoid	0.0341μmol/ mL	Okello *et al*., 2020
22	Leoheteronin A	Terpenoid	0.0116 μmol/ mL	Hung *et al*., 2011
23	Leopersin G	Terpenoid	0.0129 μmol/ mL	Hung *et al*., 2011
24	Icariin	Flavonoids	0.000035 μmol/mL	Xin *et al*., 2001
25	tOMe-byakangelicin	Coumarins	0.0369 μmol/mL	Seo *et al*., 2013
26	Byakangelicol	Coumarins	0.0463 μmol/mL	Seo *et al*., 2013
27	Demethoxycurcumin	Ketones	0.03314 μmol/mL	Ahmed *et al*., 2009
28	Bisdemethoxycurcumin	Ketones	0.01684 μmol/mL	Ahmed *et al*., 2009
29	Ginsenoside Rg3	Saponins	0.04199 μmol/ mL	Choi *et al*., 2016
30	Ginsenoside Rg1	Saponins	0.04369 μmol/ mL	Choi *et al*., 2016
31	Ginsenoside Re	Saponins	0.03153 μmol/ mL	Choi *et al*., 2016
32	Ginsenoside Rb1	Saponins	0.03698 μmol/ mL	Choi *et al*., 2016
33	Ginsenoside Rb2	Saponins	0.03980 μmol/ mL	Choi *et al*., 2016