Table 1. Summary of Pharmacological Actions of Diminazene Aceturate (DIZE)

Effect	Reference	Potential benefit
↓AngII level, ↑Ang(1-7) level, ↑MasR expression in lung tissue	Li et al., 2018	Lung protection
↓ACE and ↓inflammatory markers in lung	Dhawale et al., 2016	Lung protection, ↓ inflammation
↑lung ACE2 expression/activity, ↓Ang II/Ang-(1-7) ratio, ↓NF-κB pathway in lung	Fang et al., 2019	
↑ACE2 activity, ↓inflammatory markers in lung, ↓pulmonary hypertension. Improved APCs and CD34+ cells function	Shenoy et al., 2013	Lung protection, ↓ inflammation, ↓ pulmonary hypertension. Vaso-reparative effect, cardiovascular protection
↓right ventricle systolic pressure, improved autonomic modulation	Rigatto et al., 2013	↓ pulmonary hypertension
↓lung profibrogenic cytokines and collagen (*DIZE combined with physical exercise*)	Prata et al., 2017	↓ pulmonary fibrosis
ASIC blocking?	Liao et al., 2020	↓ airway obstruction
↓ACE expression, ↑ACE2 expression and activity, ↓AT1R, ↑MasR, ↑CPCs, ↑circulating EPCs, ↓peri-infarct inflammatory cells	Qi et al., 2013	Cardiac protection
↓Fibrosis and improved cardiac function after MI	Castardeli et al., 2018	
↑Cardiac ACE2 activity, improved cardiac function after MI	Badae et al., 2019	
↓Inflammatory factors, ↑ACE2, ↑AT1R, ↑MasR, ↓infarct size	Chen et al., 2017	
↑expression of TGF-β, improved cardiac function; unchanged ACE2 and MasR expression	Macedo et al., 2016	
RAS-mediated inhibiting effect on KCa3.1 channels through ERK1/2 pathway, ↓fibrosis	Wang et al., 2016	
downregulation of ACE/Ang II/AT1R and upregulation of ACE2/Ang 1-7/ MasR	Awwad et al., 2020	
↑ACE2 activity, reversed cardiac electrical changes	Coutinho et al., 2014	
↓cardiac ACE activity and AngII levels, improved cardiac function, ↓fibrosis	Velkoska et al., 2016	
ACE2-mediated ↑human CD34+ proliferation and migration	Singh et al., 2015	Vaso-reparative effect, cardiovascular protection
Improved human CD34+ function	Jarajapu et al., 2013	
↑ACE2 activity mice aortas and plasma, improved endothelial function; unchanged ACE2 expression	Zhang et al., 2015	
↑ACE2 expression, ↓Ang II level,	Tao et al., 2016	↓ inflammation

↓AT1R expression, ↑Ang-(1-7). Inhibition of the MAPK and NF-kB pathways		
↓pro-inflammatory cytokines	Kuriakose et al., 2012	
↓pro-inflammatory cytokines, ↓phosphorylation of MAPKs , STATs and NF-kB , ↑SOCS1 and SOCS3 expression,	Kuriakose et al., 2014	
↓ inflammatory mediators (liver)	Ge et al., 2018	
↓histamine induced responses, ↓inflammation	Kuriakose & Uzonna., 2014	
↑ACE2 expression, ↓AngII expression, ↑Ang(1-7) expression, ↓NF-kB and other inflammatory mediators, ↓fibrogenic markers (kidney)	Hasan et al., 2020	↓ inflammation, ↓ fibrosis,
↓activation of fibroblastic stellate cells and Kupffer cells, , ↓cytokines, ↓fibrosis. ↓NF-kB activity? No effect on RAS components	Rajapaksha et al., 2018	
improved renal and liver function after renal ischemia/reperfusion injury	Malek & Nematbakhsh., 2014	↓ renal and liver damage
↑ ACE2 expression, ↑ AT2R expression, ↓ AngII levels, ↑ Ang(1-7) levels, ↓ diabetes-induced renal damage	Goru et al., 2017	↓ renal damage
↓ inflammatory mediators, improved renal function	Kangussu et al., 2019	

AngII = angiotensin II, **Ang(1-7)** = angiotensin (1-7), **MasR** = Mas receptor, **ACE** = angiotensin converting enzyme, **NF-kB** = nuclear factor-kB, **ACE2** = angiotensin converting enzyme 2, **APCs** = angiogenic progenitor cells, **ASIC** = acid-sensing ion channel, **AT1R** = angiotensin 1 receptor, **CPCs** = cardiac progenitor cells, **EPCs** = endothelial progenitor cells, **MI** = myocardial infarction, **TGF-β** = transforming growth factor beta, **ERK** = extracellular signal-regulated kinase, **MAPKs** = mitogen-activated protein kinase, **STATs** = signal transducer and activator of transcription, **SOCS** = suppressor of cytokine signaling, **AT2R** = angiotensin 2 receptor.