REVIEW

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Curcumin in age-related diseases

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The world's aging population continues to grow at an unprecedented rate. Consequently, age-related diseases including diabetes and diabetic complication, neurodegenerative disease, cardiovascular disease have become a health problem that cannot be ignored. The purpose of this review is to summarize the benefits of curcumin for age-related diseases, and present the molecular mechanisms for this effect. Curcumin—a natural plant extract, has received worldwide attention in recent years, due to its low toxicity, low cost and significant effects. It is derived from the spice turmeric and has been used in traditional medicine to improve diabetes. Many reports indicate that curcumin can regulate blood sugar levels, decrease blood pressure, protect nerve cells, and enhance immunity. In addition, there is evidence for its antioxidant, anti-infective, anti-inflammatory, as well as promoting wound recovery, which suggests that curcumin may be especially beneficial for the elderly.

1. Introduction

Population aging is anticipated to grow at unprecedented rates across the globe in the decades ahead (Banks 2017). Evidence suggests that by 2050, nearly 2 billion people will be aged 60 years or older (Johnson 2013). Consequently, determining how to treat and prevent aging and age-related diseases will grow in priority. Aging is generally characterized by the gradual decrease in physiological function and metabolism. The main traits of aging in mammals are telomere attrition, epigenetic alterations, loss of proteostasis, deregulated nutrient sensing, mitochondrial dysfunction, cellular senescence, stem cell exhaustion, and altered intercellular communication (Lopez-Otin et al. 2013). In addition, epigenetic modifications, such as DNA methylation and histone modification, and microRNAs (miRNAs) level, play a key role in the molecular mechanism of aging (Guillaumet-Adkins et al. 2017). Consequently, aging presents a major risk factor for age-related diseases like type 2 diabetes, neurodegenerative disease, cardiovascular disease (Santos and Lindner 2017). Safe and effective drugs against the diseases of the elderly are urgently needed.

It is well known that curcumin is a symmetrical compound with no chiral carbon atoms (Fig. 1) and has many beneficial pharmacological effects on the treatment of various diseases possessing anti-inflammatory, antioxidant, anti-arthritis, anti-cancer (Ramsewak et al. 2000; Panda et al. 2017). Curcumin has been studied widely and has achieved many results, especially in diabetes. In this review, we conclude that the natural compound curcumin may be a potential therapeutic agent for the treatment of age-related diseases through a variety of ways and signaling pathways (Fig. 2).

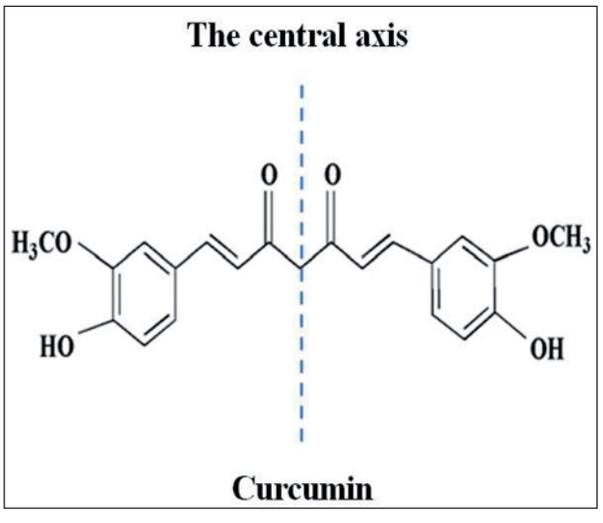

Fig. 1: Chemical structure of curcumin.

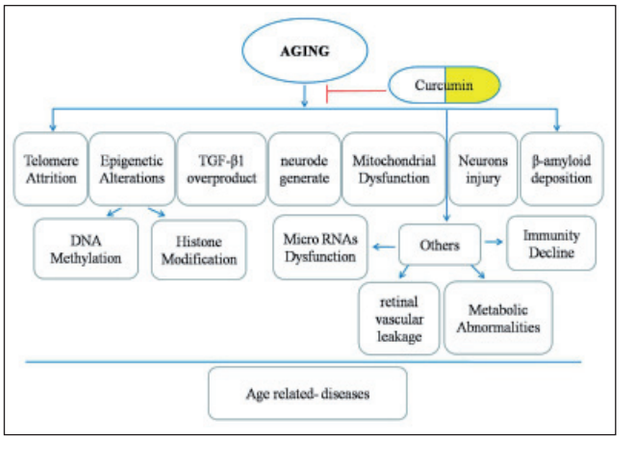

Fig. 2: Characteristics of aging.

2. Curcumin in diabetes and diabetic complications

2.1. Effect of curcumin on diabetes

Diabetes mellitus (DM) is a common chronic metabolic disease in which patients have persistently high blood sugar. Generally, hyperglycemia is caused by insulin deficiency or insulin resistance and produces four main clinical symptoms: polyphagia, polyuria, polydipsia and wasting. There are three main types defined according to these characteristics including type 1, type 2 and gestational diabetes. Type 1 is also called autoimmune diabetes. Although the etiology of type 1 is not completely understood, its pathogenesis is associated with T cell-mediated destruction of β-cells or pancreatic β-cells loss (Kaufman 2003). Type 2 is generally an age-related disease related to abdominal obesity and dyslipidemia, which fails to use insulin (Williams et al. 2015). Without appropriate control, some type 2 diabetic patients may suffer from life-threatening ketoacidosis or complications or both. The literature has revealed that there will be 366 million people worldwide with diabetes by 2030, and the most important demographic change in the global prevalence of diabetes seems to be an increase in the proportion of people over the age of 65 (Wild et al. 2004). Research shows that curcumin supplementation reduces blood sugar, TNF-α, IL-6, MCP-1 levels (Jain et al. 2009), has a beneficial effect on pancreatic β-cell function and enhances insulin sensitivity in diabetic rats (Weisberg et al. 2016). Curcumin has a potential value for the treatment of streptozocin-induced pancreatic cell destruction in T2D rats by blocking the phosphorylation of JNK and NF-κB signaling pathway, thereby inhibiting inflammation and apoptosis of β cells in pancreatic islets (Qihui et al. 2020). Besides, it can reduce NF-κB mediated inflammation and endoplasmic reticulum dependent apoptosis in spleen cells in type 2 diabetes (Rashid et al. 2017).

The damage development of peripheral arterial disease in DM is mainly attributed to the dysfunction of endothelial progenitor cells. However, curcumin promotes angiogenesis in type 2 diabetic wound healing (Kant et al. 2015). Zhao et al. (2017) revealed that curcumin exhibits anti-diabetes activity by inhibiting oxidative stress and modulating the Bax/Bcl-2-mediated cell death pathway. Previous research shows that 11β-hydroxysteroid dehydrogenase type 1 is a key enzyme to activate glucocorticoids. Excessive glucocorticoid may cause insulin sensitivity decline and finally type 2 diabetes, while curcumin can inhibit the activity of 11β-hydroxysteroid dehydrogenase type 1 (11βHSD1), reducing serum glucose, cholesterol, triglyceride, low density lipoprotein levels in high-fat-diet-treated rats (Hu et al. 2013). Curcumin can induce preadipocyte apoptosis caused by activation of caspases 8, 9, and 3and inhibit adipocyte differentiation via down-regulating the expression of PPARγ and C/EBPα, which is benefit for type 2 diabetes (Wu et al. 2019).

2.2. Effect of curcumin on diabetic cardiomyopathy (DCM)

The important characteristics of DCM are cardiac hypertrophy, early diastolic dysfunction, ventricular dilation and systolic dysfunction, which will develop into heart failure (Guo and Nair 2017). By analyzing left ventricular function, measuring myocardial cell size, $NADP^+$/NADPH ratio and detecting myocardial enzymes and inflammatory cytokines in serum, Yu et al. found that curcumin inhibits metabolic abnormalities and mitigates DM-induced left ventricular disfunction, oxidative stress, cardiac fibrosis, and apoptosis in heart of diabetic mice that were induced by low dose of streptozoticin (STZ) and high energy intake. They also found that curcumin treatment improves the inhibited phosphorylation of AKT and GSK-3β, which may be associated with mediating the positive effects curcumin exerts on diabetic cardiomyopathy in experimental diabetic rats (Yu et al. 2012). As reported, tetrahydrocurcumin (THC), which is a main bioactive metabolite of curcumin, has more effective antioxidative and antifibrotic properties as well as antidiabetic abilities by depressing the ROS-induced TGFβ1/Smad3 signaling pathway followed by reduced expression of cardiac fibrotic markers α-SMA, collagen I, and collagen III. Collectively, these findings demonstrated the tetrahydrocurcumin improves diabetic cardiomyopathy by reducing high glucose-induced oxidative stress and fibrosis via activating the sirt1 pathway (Li et al. 2019). Soetikno et al. (2012) found that curcumin prevents DCM by inhibiting the PKC and β(2)-MAPK pathways in STZ-induced diabetic rats, which may provide an adjuvant treatment (Soetikno et al. 2012). Curcumin has been reported to repair and prompt the efficient recovery of heart blood vessels in diabetic mice, especially improving arteriole, artery, and capillaries (Anupunpisit et al. 2015).

In short, the pathogenesis of DCM is complex and multifactorial and the molecular etiologies of DCM are not clearly understood. It is certain that curcumin is useful for the treatment of DCM, which may be inseparable from reversing insulin resistance, hyperglycemia, obesity, and antioxidant, anti-inflammatory activities (Karuppagounder et al. 2017).

2.3. Effect of curcumin on diabetic nephropathy (DN)

It is well known that the main structural features of DN are extracellular matrix accumulation, glomerular basement membrane thickening and podocyte foot processes destabilization (Zhao et al. 2016). It was reported that renal hypertrophy, mesangial matrix expansion and level of albuminuria are decreased in curcumin-treated mice. Furthermore, curcumin supplementation not only inhibits the increased mRNA and protein expressions of collagen IV as well as fibronectin in the renal cortices of the *db/db* rats, but also significantly reduces mature interleukin-1β. The renoprotective effects of curcumin may be involved with suppression of NLRP3 inflammasome activity (Lu et al. 2017). Because the sphingosine kinase 1-sphingosine 1-phosphate (SphK1-S1P) signaling pathway is crucial for the pathogenesis of DN, Huang et al. found that curcumin suppresses the SphK1-S1P signaling pathway and SphK1-S1P-mediated fibronectin and TGF-β1 overproduction in diabetic rats, and these effects may be closely associated with the inhibition of activator protein 1 activity (Huang et al. 2013). It is also found that curcumin protects renal tubular epithelial cells to reduce the incidence of renal fibrosis (Zhang et al. 2015).

Additionally, curcumin inhibits PKC-α and PKC-β1 activities in STZ-induced type 1 diabetic mice, attenuating the development of DN (Soetikno et al. 2011). Short-term curcumin activates anti-inflammatory efficacies and Nrf2 anti-oxidative system to ablate DN progress in patients with type 2 (Yang et al. 2015). Curcumin relieved DN *via* alleviating podocyte mesenchymal and inducing autophagy, curcumin administration is acting through the PI3k/Akt/mTOR pathway (Tu et al. 2019). A recent study also suggested that curcumin prevents diabetes mediated superoxide synthesis and resumes downregulation of the Wnt/β-catenin signaling, thus reducing the accumulation of extracellular matrix in DN (Ho et al. 2016). It is reported that curcumin significantly increased marker proteins (podocalyxin and nephrin) in podocytes and markedly decreased the progress of DN possibly *via* increasing autophagy-related proteins LC3, p62, Beclin1 in DN mice along with reducing expression of pro-apoptotic protein Bax and Caspase-3 and increasing anti-apoptotic protein Bcl-2 (Zhang et al. 2020).

2.4. Effect of curcumin on diabetic retinopathy (DR)

DR frequently causes vision loss, which correlates to the presence of inflammatory cytokines and vascular leakage in the retina (Vanlandingham et al. 2017). Curcumin showed the ability to reduce diabetes-induced retinal vascular leakage by suppressing the activation of CaMKII/NF-κB signaling and reducing the expression of VEGF, iNOS and ICAM-1. Given its activity of inhibiting CaMKII, the retina of diabetic rats is protected by curcumin that resists early retinal vascular injuries (Li et al. 2016). Recently, it was found that curcumin is beneficial to Müller cells and prevents the downregulation of GS in the diabetic retina by inhibiting diabetic retinal oxidative stress, which is a potentially therapeutic way for patients with DR (Zuo et al. 2013). Moreover, the structural degeneration and increase in capillary basement membrane thickness in the diabetic rat retinae were prevented with

curcumin treatment which was observed by using transmission electron microscopy. This indicates that curcumin may be useful to prevent retinopathy in diabetic patients (Gupta et al. 2011).

2.5. *Effect of curcumin on diabetic hepatopathy (DH)*

Individuals with diabetes are frequently showing symptoms of non-alcoholic steatohepatitis. Curcumin supplementation significantly reduces the levels of α-SMA and promotes insulin receptor binding to improve biochemical parameters and counteract oxidative stress-mediated hepatic damage. In addition, because of its anti-fibrotic properties, curcumin inhibits hepatic stellate cell activation and the transition to myofibroblast-like cells, which may be effective for hepatic dysfunction in diabetic patients (Mustafa 2016). Others have found that curcumin treatment can also improve and restore the levels of oxygen consumption, NO synthesis, thiobarbituric acid-reactive substances and ATPase activity and lipid oxidation in mitochondria from the livers and kidneys of diabetic mice, which way play protective effect on kidney and liver (Soto-Urquieta et al. 2014). A recent study also suggested that hepatic ERS marker protein and GRP78 were significantly decreased and liver function was improved by curcumin in diabetic rats. In addition, interleukin 1β, tumor necrosis factor α, MAPK and apoptosis signal-regulating kinase 1 are suppressed by curcumin supplementation in STZ-induced diabetic mice. Given these effects, curcumin may modulate hepatic ERS-mediated apoptosis to ameliorate the diabetic liver damage (Afrin et al. 2015). Other researchers have found that curcumin may have a beneficial role by regulating the expression of AMPK, PPARγ, and NF-κB in *db/db* mice liver. Moreover, the expression of AMPK and PPARγ are increased and NF-κB is diminished, it was mean that curcumin could improve hepatopathy in type 2 diabetes (Jimenez-Flores et al. 2014).

All in all, curcumin has a potential value for the treatment of diabetes and diabetic complications through various molecular mechanisms (Fig. 3).

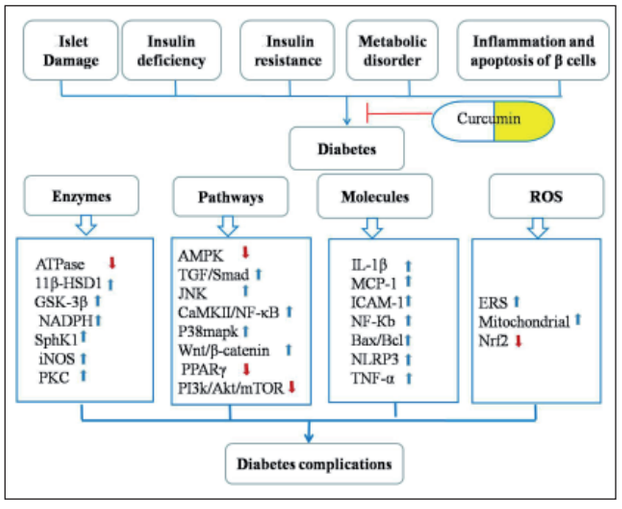

Fig. 3: Potential roles and molecular mechanisms of curcumin on diabetes and diabetic complications.

3. Curcumin and neurodegenerative diseases

Alzheimer's disease (AD), Parkinson's disease (PD) and stroke belong to the class of neurodegenerative diseases, which pose a serious threat to the health and life quality of the aging population. In traditional medicine, the symptoms of these neurodegenerative diseases can be mitigated by using medicinal plants (Manoharan et al. 2016).

3.1. *Effect of curcumin on Alzheimer´s disease (AD)*

Patients with AD frequently suffer from memory loss and cognitive disorders that may cause dramatic changes in their personalities (Mattson 2004). The two major pathological hallmarks of AD are senile plaques (SP) and neurofibrillary tangles (NFT). β-Amyloid and tau are major molecular constituents of these lesions and play a specific role in studies of pathogenesis (Armstrong 2009). Abundant data showed that curcumin plays a crucial role against β-amyloid. For instance, curcumin has been reported to have a protective effect against β-amyloid and to work better in prevention than treatment in AD by increasing biogenesis of neurons and synaptic proteins, enhancing activity of mitochondrial fusion and reducing fission machinery (Reddy et al. 2016). However, others found that curcumin can downregulate BACE1expression, prevent synaptic degradation and improve spatial learning and memory impairment of 5×FAD miceto dramatically reduce β-amyloid protein, which is a potential candidate for AD treatment (Zheng et al. 2017). Moreover, curcumin can also inhibit ROS-mediated oxidative damage and regulation of ERK pathway to effectively suppress β-amyloid-induced cytotoxicity and apoptosis (Fan et al. 2017). Curcumin can markedly improve Aβ25-35-induced neuroinflammation in microglia, partly by inhibiting the expression of High-mobility group box 1 protein (HMGB1), receptor for advanced glycation end products (RAGE) and toll-like receptor 4 (TLR4) (He et al. 2020).

Miyasaka et al. (2016) found that the tau-induced neuronal dysfunction of nematodes is improved by curcumin treatment. Das et al. (2019) found that curcumin reduced levels of GSK3, p35, p25, and Cdk5 in scopolamine-induced AD rats, decreasing Aβ40/42 and tau hyperphosphorylation. Therefore, curcumin, as a natural compound present in turmeric, may be a candidate drug in the treatment of ADa. Interestingly, others found that the development of AD can also be attenuated by anti-herpesviral activity of curcumin, as herpes simples virus type 1 (HSV-1) in the brain is a potent risk factor of AD (Mori 2015). Recent studies showed that curcumin derivatives have benefit for AD, and they are novel potent inhibitors against the tau protein or β-amyloid (Aathi and Piramanayagam 2019; Wan et al. 2019; Chainoglou and Hadjipavlou-Litina 2020; Sato et al. 2020).

3.2. *Effect of curcumin on Parkinson´s disease (PD)*

Parkinsonism is an age-associated disease that is incurable (Driver et al. 2009). PD can only be relieved by medication and surgical treatment by far. To find a kind of drug with low toxicity and high curative effects for treating PD is fairly important. However, curcumin has been reported to protect neurons, and is therefore promising for the management of PD (Phom et al. 2014; Khatri and Juvekar 2016; Song et al. 2016). Other research teams have reported that curcumin can inhibit oxidative stress and the mitochondrial cell death pathway in a PC12 inducible cell model for PD, aiming to protect against A53T mutant α-synuclein-induced cell death (Liu et al. 2011). In short, expression or function of heat shock proteins in the cell can be augmented by curcumin treatment, because modulation of heat shock proteins and the proteosomal pathway are crucial for the treatment of neurodegenerative diseases (Maiti et al. 2014; Sang et al. 2018). It also reported that a PD cell model was protected by curcumin with effect on dopamine neurons. It may be related to promoting autophagy and increasing the clearance of α-Syn (Wu et al. 2018). In a mice model of Parkinson's disease, animals' behavior was ameliorated after treatment with curcumin. This is associated with effects of antagonizing adenosine A_{2A} receptor (Motawi et al. 2020).

3.3. *Effect of curcumin on stroke*

Risk factors for stroke will increase with aging, and the health problems of the elderly may be worsen in the future with the growing influence of aging in our societies (Ly and Maquet 2014). Nevertheless, application of curcumin is beneficial to the elderly by activating the Notch signaling pathway to protect against stroke (Liu et al. 2016). Shah et al. (2016) found that curcumin has the ability to protect nerves and regulate expression of a variety of proteins in focal cerebral ischemia, which means that curcumin may have a preventive effect on cerebral ischemic stroke. Another

research team found that ischemic stroke-induced brain injury and inflammation can be decreased with curcumin pre-treatment (Miao et al. 2016). Therefore, curcumin is expected to be a candidate for treatment of stroke.

Some publications showed that curcumin treatment suppresses MAPK/RANK/c-Fos and nuclear factor of activated T cells signaling pathways to inhibit osteoclastogenic potential of PBMCs, which may be therapeutically useful for patients with rheumatoid arthritis (Shang et al. 2016), and supplementation of curcumin improves hind limb injury following ischemic surgery, which could be beneficial for patients with peripheral artery disease (Liu et al. 2016). It was reported that curcumin reduced heart failure by promoting the expression of sarcoplasmic reticulum Ca^{2+}-ATPase in rabbits (Zhang et al. 2010). In addition, curcumin has a stroke preventive effect in stroke-prone spontaneously hypertensive rats by reducing oxidative stress to promote vascular endothelial function, which might be related to UCP2 signaling (Lan et al. 2018). In a word, the symptoms of these neurodegenerative diseases can be improved by curcumin (Fig. 4).

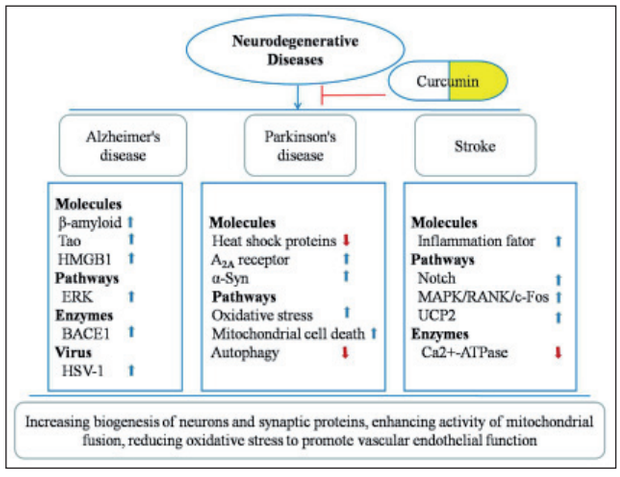

Fig. 4: Potential roles and molecular mechanisms of curcumin on neurodegenerative diseases

4. Curcumin and its experimental and clinical application

A large number of publications indicate that curcumin, a natural compound, has multiple therapeutic effects in age-related diseases, including anti-diabetes, anti-diabetic complications, anti-neurodegenerative disease. In experimental studies in rats (exposed to BSA) curcumin (100 mg/kg daily) inhibited SOD and CAT and histological alterations (Aslanturk and Uzunhisarcikli 2020). When preconditioned with 20 mg/kg curcumin, diabetic cardiomyopathy of diabetic rats was attenuated significantly (Tong et al. 2018). Curcumin administration (300 mg/kg•d) obviously decreased the expression of collagen I and collagen III in the heart tissues of diabetic rats (Guo et al. 2018). The same dose markedly alleviated renal histomorphological changes in DN rats (TuLi et al. 2019). In a TPA-induced inflammation mouse model, dermal inflammation could be decreased by oral combination treatment with curcumin (100 mg/kg) and tolfenamic acid (100 mg/kg) (Zhou et al. 2020). DN mouse model was ameliorated after administration with curcumin (1 g/kg•d) via oral gavage (Wu et al. 2020). In a randomized, double-blinded, placebo-controlled trial including T2DM patients receiving curcumin (250 mg /d) for 9 months, none was diagnosed with diabetes (Table). However, 16.4% of placebo group subjects were diagnosed. The curcumin group showed higher adiponectin levels and lower insulin resistance (Chuengsamarn et al. 2012). In addition, T2DM patients treated with curcumin capsules (300 mg) for 8 weeks have shown an improvement in the antioxidant status, like under atorvastatin (Usharani et al. 2008).

However, its use is limited for many reasons, such as solubility and low bioavailability. Fortunately, the solubility and stability of phytochemicals can be improved by chemical structural transformation and formulation (Peng and Qian 2014). This suggests that we should combine modern biological technology with natural medicines (such as nanocurcumin) or screen curcumin derivatives, to bring better, faster, safer and more effective treatment for human diseases, especially in age-related diseases. In diabetic polyneuropathy patients who were supplied with only 80 mg of nano-curcumin daily for 8 weeks, the painful symptoms of diabetic sensorimotor polyneuropathy (DSPN) could be relieved, and depression and anxiety scores were reduced (Asadi et al. 2019, 2020). Curcumin seems to be beneficial in non alcoholic fatty liver disease (NAFLD), because 42 patients who took 80 mg/day

Table: Curcumin for experimental and clinical application

Drug delivery	Source of curcumin	Species	Dose(/Kg)	Formulations	Duration	Disease	Mechanism of action	Reference
Experimental studies:								
Oral	Sigma (from Curcuma longa)	Rat	100 mg	In olive oil	28 days	Nephrotoxicity	Antioxidant roles	Aslanturk and Uzunhisarcikli 2020
Application	Sigma (from Curcuma longa)	Rat	400 mL	The pluronic F-127 gel (25%) and curcumin (0.3%)	19 days	Diabetic wounds	Increased expressions of various factors.	Kant et al. 2015
Oral	from Curcuma longa	Rat	100 mg	In 0.1 M sodium citrate buffer	8 weeks	Testicular dysfunction in DM	Release oxidative stress	Zhao et al. 2017
Oral	Xian, Chinafrom (from Curcuma longa)	Rat	20 mg	Curcumin/PBLG-PEG-PBLG nanoparticles	8 weeks	DM	Cross regulation effect of CaSR and endogenous CSE/H2S	Tong et al. 2018
Oral	Sigma (from Curcuma longa)	Rat	300 mg	In the drinking water	16 weeks	DCM	Iinhibition of TGF-β/p38 MAPK	Guo et al. 2018
Oral	From turmeric powder	Rat	200 mg	In vehicle	16 weeks	DCM	Ameliorating oxidative stress, AGEs-RAGE interaction pathways.	Yu et al. 2012
Oral	Sigma (from Curcuma longa)	Rat	100 mg	In 1% gum Arabic	8 weeks	DCM	inhibiting of PKC–MAPK	Soetikno et al. 2012
Oral	Sigma (from Curcuma longa)	Mice	200 mg	In 1% sodium carboxymethyl cellulose	16 weeks	DN	inhibition of NLRP3 inflammasome	Lu et al. 2017
Oral	Sigma (from Curcuma longa)	Rat	300 mg		8 weeks	DN	Inducing autophagy and inhibiting PI3K/Akt/mTOR pathway	TuLi et al. 2019
Oral	Sigma (from Curcuma longa)	Rat	150 mg'	In 1% sodium carboxymethyl cellulose	12 weeks	DN	inhibiting the activation of the SphK1-S1P signaling pathway	Lu et al. 2017
Oral	Henan Cancer Hospital. (from Curcuma longa)	Mice	100 mg	curcumin/PVP solid dispersion and tolfenamic acid (1:1)	6 hours	Anti-inflammatory activity	PKC/Akt/IKK/NF-κB signaling pathways	Zhou et al. 2020

Drug delivery	Source of curcumin	Species	Dose(/Kg)	Formulations	Duration	Disease	Mechanism of action	Reference
Experimental studies:								
Oral	MD Anderson Cancer Center	Mice	1 g	In sesame oil	2 months	Immune Nephritis	Reduced activation of the NFkB, MAPK, AKT and pBAD pathways	Wu et al. 2020
Clinical studies								
Oral	Kanchanaburi,Thailand	Human	250 mg	Each curcumin capsule has curcuminoid of 250 mg.	9 months	T2DM	Improve overall function of β-cells,	Chuengsamarn et al. 2012
Oral	NCB-02	Human	300 mg	C3 curcuminoids (curcumin, demethoxy curcumin and bisdemethoxy curcumin)	8 weeks	T2DM	Reductions in oxidative stress and inflammatory	Usharani et al. 2008
Oral	Nano-curcumin	Human	80 mg	curcumin 72%, desmethoxycurcumin 25%, and bisdemethoxycurcumin 3%.	8 weeks	DSPN	through the management of hyperglycemia in patients with T2DM	Asadi et al. 2019;
Oral	Nano-curcumin capsules	Human	80 mg	curcumin 72%, desmethoxycurcumin 25%, and bisdemethoxycurcumin 3%.	8 weeks	DPN	a beneficial effect on depression and anxiety	Asadi et al. 2020
Oral	Exir-Nano-Sina Company	Human	80 mg	nano-micelles containing curcumin	3 months	Obesity and NAFLD	increasing serum nesfatin and improving inflammatory, lipid and glucose profiles.	Jazayeri-Tehrani et al. 2019

DN: diabetic nephropathy; DCM: diabetic cardiomyopathy; T2DM: type 2 diebetes; DPN: diabetic peripheral neuropathy; DSPN: diabetic sensorimotor polyneuropathy;AD:Alzheimer's disease; PBLG , poly(gamma-benzyl l-glutamate)-poly(ethylene glycol)-poly(gamma-benzyl l-glutamate)

curcumin for 3 months showed improved inflammatory, lipid and glucose profiles (Jazayeri-Tehrani et al. 2019). Curcumin is used to treat age-related diseases, such as T2DM, DN, DSPN, DPN. Curcumin has the low oral bioavailability, so some pharmaceutical companies are developing curcumin nanoparticles. Most experimental curcumin came from Sigma Aldrich, however, clinical studies used curcumin came from pharmaceutical companies.

5. Conclusion

A great deal of information in animal and clinical studies has provided strong evidence that curcumin has efficacy against diabetes, diabetic complications, neurodegenerative diseases, and enhances the immune system. Data reported in this review indicate that curcumin has therapeutic potential to counteract age-related diseases. Given that curcumin can slow down the aging process through inhibiting the age-related changes in inflammatory, oxidative stress, epigenetic alterations, mitochondrial misfunction, neurons injury, could it then be used to treat senility as a clinical drug? Great progress has been made in research of curcumin and its experimental and clinical application, but before the compound or its derivatives will prove unique therapeutic success in age-related diseases, there is still a long way to go.

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