Supplementary Material

Moringa oleifera in cardiometabolic disorders: A systematic review of recent studies and possible mechanism of actions

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Table S1. Search terms used in the study

Database	Search Term
PubMed	TITLE/ABS Moringa oleifera AND ((cardiovascular diseases [MeSH]) OR (Metabolic Diseases [MeSH]) OR (Blood Glucose [MeSH]) OR (Obesity [MeSH]) OR (hypertension [MeSH]) OR (Kidney Failure [MeSH]) OR (Molecular Mechanisms of Pharmacological Actions [MeSH]) OR (Pharmacological and Toxicological Phenomena [MeSH]) OR Oxidative Stress [MeSH]) OR (Inflammation [MeSH]) OR (Gastrointestinal Microbiome [MeSH]) OR (Immune System [MeSH])
Scopus	(TITLE-ABS-KEY (moringa AND oleifera) AND TITLE-ABS-KEY (((cardiovasc*) OR (cardiac) OR (cvd) OR (ischemi*) (metaboli*) OR (lipid) OR (cholesterol) OR (ldl) OR (hdl) OR (tg) OR (tryglyceride*) OR (diabetes) OR (dm) OR (dmt2) OR (insulin) OR (hyperglyc*) OR (hypoglyc*) OR (glucose) OR (kidney) OR (hypertens*) OR (blood AND pressure) OR (diuretic) OR (pharmacolog*) OR (toxic*) OR (oxidative AND stress) OR (antioxidant) OR (inflam*) OR (microbiome) OR (microbiota) OR (immune))))
CENTRAL	#1 Moringa oleifera #2 MeSH descriptor [cardiovascular diseases] explode all trees #4 MeSH descriptor [Metabolic Diseases] explode all trees #5 MeSH descriptor [Blood Glucose] explode all trees #6 MeSH descriptor [Obesity] explode all trees #7 MeSH descriptor [Hypertension] explode all trees #8 MeSH descriptor [Kidney Failure] explode all trees #9 MeSH descriptor [Oxidative stress] explode all trees #10 MeSH descriptor [Inflammation] explode all trees #11 MeSH descriptor [Gut microbiome] explode all trees #12 MeSH descriptor [Immune system] explode all tree #13 insulin #12 glucose #13 lipid #14 cholesterol #15 diuretic #1 AND {#2 - #15}

Table S2. Nonclinical studies of *Moringa oleifera*

Author, year	Type of extracts/ main bioactive compound used	Methods of extracts/ bioactive preparation	Yield of preparation from raw material (wt/wt)	*In vitro*/ *in vivo* models used	Treatment/ duration	Effects	Mechanism	Toxicity
Abarikwu, 2017 [1]	MO seed oil	Cold pressed from freshly shelled moringa seeds	Not reported	HgCl2-induced hepato- and nephrotoxicity in Male Wistar albino rats	1.798 mg/kg BW p.o. three times per week for 21 days.	- Amelioration of kidney and liver injury - ↓ MDA, SOD, CAT, GST, GSH. - normalization of creatinine, bilirubin GGT, LDH, ALP	Antioxidant	No toxicity was observed
Abd El Latif, 2014 [2]	MO leaves aqueous extracts	Dried water extract from fresh green leaves MO. Reconstitution were done in distilled water prior to administration	22%	Alloxan-induced diabetes in rats	250 mg/kg BW p.o for 18 days	- Improvement of blood glucose, TG, cholesterol, and MDA levels. - Normalization of hepatic pyruvate carboxylase mRNA expressions. - ↑ PC in hepatic tissues. - ↑ body weight - restoration of liver FAS mRNA expression - Improved histological structure of the liver and pancreas.	Glucose metabolism, lipid metabolism, hepatoprotective	Not reported
Abd Eldaim, 2017 [3]	MO leaves aqueous extract	Dried water extract from fresh green leaves MO	Not reported	Alloxan-induced diabetes in Wistar albino rats	250 mg/kg BW p.o for 18 days	- Protective effect on hepatic and pancreatic tissues - Normalized hepatic GSH, SOD, CAT, and glycogen synthase gene expression of glycogen synthase. - ↓ blood glucose - ↓ hepatic lipid peroxidation,	Antioxidant, glucose metabolism, antiapoptotic, hepatoprotective	Not reported

						- ↓ PC and caspase 3 gene expression.		
Abd Rani, 2019 [4]	MO ethanol extract and its isolates	Leaves, seeds, and pods were macerated separately. Fractionation were done sequentially using hexane, ethyl-acetate, and acetone.	Leaves: 5% Seed: 3.3% Pod: 3%	RBL-2H3 cells	7.81, 15.62 and 31.25 µg/mL	All extracts and isolated compounds significantly inhibited beta-hexosaminidase, histamine, and cytokine (IL-4 and TNF-α) release.	Anti-inflammation	Cytotoxicity test: at 7.81 - 31.25 µg/mL, extracts and isolates were found not cytotoxic.
Abd-Elhakim, 2021[5]	MO ethanol extract	Hydro distillation techniques with ethanol	Not reported	Melamine-induced hepatorenal impairment in male S.D. rats	- 800 mg/kg BW/day p.o for 2 weeks as prophylaxis. - 800 mg/kg BW/day p.o. for 2 weeks, co-treated with melamine	- ↑ CAT, GPx, and BCl-2 expression - ↓ p53 expression. - Suppressed expression of the proinflammatory cytokine, KIM-1 and TIMP-1. - Improved hepatorenal efficacy when given simultaneously with melamine.	Antioxidant, anti-inflammation.	Not reported
Abdel Fattah, 2020 [6]	MO leaves aquatic extract	Dried MO from fresh leaves macerated in cold water, boiled for 15 min, and then filtered.	Not reported	Lead acetate–induced liver injury in male Wistar rats	200 mg/kg BW p.o for 4 weeks	- Amelioration of weight gain reduction - ↓ TC, TGs, LDL-C AST, ALT, ALP, TNF-α. - ↑ in HDL-c, TP, albumin, GSH, and SOD. - ↓ DNA fragmentation - improved hepatic lesions and tissue score damage.	Antioxidant, lipid metabolism, hepatoprotective.	Not reported

Abdel-Daim, 2020 [7]	MO leaves methanol extract	Powdered leaves MO were extracted using methanol 70%.	Not reported	Lead acetate–induced liver injury in male Wistar rats	250 mg/kg BW i.p for 14 days	- ↓ in relative kidney weight, urea, and creatinine. - Attenuation of abnormal histopathological features - ↑ CAT, GPx1. - ↓ TNF-α, IL-1β, and NF-κB - Downregulation of iNOS. - Inhibiting the pro-apoptotic proteins and enhancing the antiapoptotic protein	Antioxidant, anti-inflammation, anti-apoptotic	Not reported
Abdel-Daim, 2020 [8]	MO leaves ethanol extract	Fine powdered leaves MO was extracted using ethanol absolute.	7.8%	Cobalt-induced renal oxidative damage and inflammatory injury in male S.D rats.	Prophylaxis: 400 mg/kgBW/ day for 2 weeks alone, 4 weeks with cobalt Treatment: 400 mg/kgBW/day for 4 weeks with cobalt, then for 2 weeks alone.	- Improved body weight gain. - ↓ urea, creatinine, MDA, and 8-OHdG. - ↑ globulin, SOD, CAT, GSH. - ↓ CRP, MPO, TNF-α, and NO. - Down-regulation of NF-kB and IL-6. - More effective when + CoCl2 as a prophylactic regimen.	Antioxidant, anti-inflammation	Not reported
Abdou, 2018 [9]	MO leaves ethanol extract	MO was macerated in ether for 72 h, and then evaporated. The residue was further macerated in ethanol and then freeze dried	Not reported	TiO_2 nanoparticles-induced nephrotoxicity in male albino rats.	400 mg/kgBW for 60 days	- ↓ creatinine, urea, uric acid, renin, MDA. - ↑ SOD, GST, GSH, GPx, total thiols. - ↓ TNF-α, NF-κB, HSP70. - Upregulation of Nrf2 and HO-1 mRNA. - Downregulation of KIM1 mRNA.	Antioxidant, anti-inflammation	Not reported

Abou-Zeid, 2021 [10]	MO leaves ethanol extract	Powdered leaves MO was extracted using ethanol absolute.	7.8%	Tilmicosin-induced renal damage in male S.D. rats.	400 and 800 mg/kg BW for 7 days	- ↓ creatinine, urea, sodium, potassium, and GGT activity - ↑ TP and albumin - ↓ renal tissue H2O2 and MDA - ↑ SOD, GPx - ↓ TNF-α, IL-1β - ↓ Desmin, nestin and vimentin mRNA expression - Histopathological alterations in renal glomeruli, tubules, and interstitial tissue. - ↓ in frequencies and severities of nephropathy.	Antioxidant, anti-inflammation, nephroprotective	Not reported
Abu-Zeid, 2021[11]	MO leaves ethanol extract, and MO leaves extract-Selenium nanoparticles	● Powdered leaves MO was extracted using ethanol absolute. ● Filtered suspension of dried leaves MO was mixed with deionized water, selenious acid, ascorbic acid subsequently. ● It forms a SeNPs nano-solution of MO leaves.	7.8%	Melamine induced nephrotoxicity in male S.D. rats	800 mg/kg BW extract and 200 µg mg/kg BW nanoparticle extract daily for 28 days.	- ↓ creatinine, urea, BUN. - ↑ TAC, GSH, SOD, CAT, GPx, MDA, PCO, TNF-α. - Down-regulation of Bax, Caspase-3, FasL mRNA expression. - Up-regulation of Bcl2, PCNA, and Ki-67. - ↓ in severity and frequency of nephrotoxic lesions but did not show the reestablishment of normal histology.	Anti-inflammation, antioxidant, Antiapoptotic, nephroprotective	No signs of toxicity.
Adedapo, 2015 [12]	MO food supplement extracted	Powdered leaves of MO was extracted using methanol.	9.6%	Carrageenan-induced paw edema, histamine-	50, 100 and 200 mg/kg BW	- ↓ size of edema, the number of writhes, licking time, and frequency.	Analgesic, anti-inflammation, antioxidant.	Acute toxicity test: - 200, 400, 800 mg/kg BW:

	with methanol			induced pedal edema, acetic acid-induced pain, formalin-induced pain, in female white Wistar strain albino rats		- Dose-related free radical-scavenging property		slightly dull and were fully recovered after 48h, no death - 1600 mg/kgBW: dull, severe lethargy. 2 out of 5 died. - 3200 mg/kg BW: Severe lethargy, rough hair coat. 4 out of 5 died.
Adepoju-Bello, 2017 [13]	MO leaves water or ethanol, or methanol extract	Cold-maceration using five different solvents: (1) 100% Methanol, (2) 100% Ethanol, (3) Water-Methanol (50/50), (40 Water- Ethanol (50/50) and (5) 100% Water	(1) 2.49 % (2) 3.17 %, (3) 9.42 %, (4) 8.52 % (5) 6.47 %.	Alloxan-induced diabetes in male and female Wistar rats	200 - 400 mg/kg BW once daily for 24 days.	- ↓ blood glucose levels. - 50% ethanolic extract at 300 mg/kg showed superior antioxidant properties, weight restorative, and pronounced hypoglycemic effects.	Glucose homeostasis, antioxidant	Not reported.
Aektham marat, 2019 [14]	MO leaves aqueous extract	Air-dried powdered leaves MO were extracted in distilled water.	4.975%	L-NAME-induced hypertension in Male Wistar rats	30 and 60 mg/kg BW once daily for 3 weeks.	- ↓ BP and tachycardia. - ↓ impairment of acetylcholine-induced relaxation - ↓ hyperreactivity of adrenergic-mediated contraction. - ↓ vascular O_2 production - ↓ MDA, SOD, CAT	Antihypertensive, vasculoprotective, antioxidant	Not reported.

Aektham marat, 2020 [15]	MO leaves aqueous extract.	Air-dried powdered leaves MO were extracted in distilled water.	4.975%	Mesenteric arterial beds isolated from L-NAME-induced hypertension in male Wistar rats	0.001–3 mg in 0.1 mL injection volume	- Relaxation in methoxamine pre-contracted arterial beds. - Inhibitory effect on $CaCl_2$ and phenylephrine-induced contractions.	Vasculoprotective	Not reported.
Aektham marat, 2020 [16]	MO leaves aqueous extract.	Air-dried powdered leaves MO were extracted in distilled water.	4.975%	L-NAME-induced hypertension in male Wistar rats Human pulmonary artery endothelial cells (HPAEC).	Rats: 1–30 mg/ kg BW HPAEC: 3–30 µg/mL.	- ↓ in MAP when administered alone. - Induced relaxation in methoxamine pre-contracted mesenteric arterial beds. - Induced NO production in HPAEC.	Vasculoprotective	Cytotoxicity test: At 0.1–300 µg/ mL did not significantly influence the cell viability. The viability was decreased at the concentrations of 1000 and 3000 µg/mL.
Aju, 2019 [17]	MO leaves methanol extract.	Dried leaf powder was serially extracted with petroleum ether, chloroform, and methanol.	Not reported	Streptozotocin- induced diabetes in male albino S.D. rats	300 mg/kg BW once daily for 60 days	- ↓ blood glucose and HbA1c, TBARS, HP, and conjugated dienes (CD). - ↑ plasma insulin, SOD, CAT, GPx, GR, GSH. - Improve the histopathology of the diabetic heart.	Glucose homeostasis, antioxidant	Not reported
Akinrinde, 2020 [18]	MO leaves methanol extract.	Air-dried powdered leaves MO were extracted sequentially in n-hexane and two	Not reported	Ischemia reperfusion-induced acute kidney injury in Wistar rats.	200 and 400 mg/kg BW for 7 days before IR induction	- ↓ BUN, creatinine, NO, MDA, AOPP, carbonyls. - Enhancement of thiols and GSH levels, GPx, and GST activities.	Antioxidant, Nephroprotective	Not reported

		times of methanol-water (80:20).				- Improvement in renal histology.		
Al-Malki, 2015 [19]	MO seed powder.	Not reported	Not reported	Streptozotocin-induced diabetes in male albino rats.	50 and 100 mg/kg BW in food for 4 weeks.	- ↓ water consumption, fasting blood sugar, MDA, IgG, IgA, IL-6, HbA1c, α-amylase, BUN, uric acid, creatinine, sodium, and potassium. - ↓ food intake, body weight gain, food efficiency ratio (FER). - ↑ CAT, SOD, GSH - Restored the kidney and pancreatic tissue of diabetic rats to normal.	Glucose metabolism, antioxidant, Nephroprotective	Not reported
Albasher, 2020 [20]	MO leaves methanol extract.	Fine powdered leaves MO was extracted using 70% of methanol.	14.3%	Lead-induced hepatotoxicity in male Wistar rats.	250 mg/kg BW p.o for 14 days	- ↓ Pb(II) concentration - ↓ ALT, AST, MDA, NO, TNFα, IL-1β levels, NF-κB p65 level, and iNOS mRNA expression. - ↓ Bax and caspase-3, and ↑ in Bcl-2 levels. - ↑ GSH, SOD, CAT, GPx, and GR. - Prevention of tissue injury.	Antioxidant, anti-inflammation, antiapoptotic, hepatoprotective	Not reported
Alhakmani, 2013 [21]	MO flowers ethanol extract.	Powder of MO flowered were macerated in 70% ethanol.	8.69%	Egg albumin	100-500 µg/mL	- Dose-dependent scavenging activity - inhibition of denaturation of egg albumin.	Anti-inflammation, antioxidant	Not reported

Anudeep, 2016 [22]	MO seeds	Kernels were obtained from matured and dried MO seeds.	6.5%	Splenocytes from male Swiss albino	0.01 to 10 µg	- ↑ proliferation of splenocytes at low concentration - ↑ NO production up to 6-fold.	Anti-inflammation	Not reported
Araújo, 2013 [23]	MO seeds aqueous extract, cMoL (coagulant MO lectin); WSMoL (water-soluble MO lectin)	Crushed MO seeds were extracted in distilled water.	Not reported	Carrageenan-induced pleurisy in male Balb/c mice Peritoneal macrophages isolated from LPS-stimulated male Balb/c mice.	Seed extract: 125, 250 or 500 mg/kg Seed extract (6.25–50 µg/mL), diluted seed extract (50–400 µg/mL) or cMoL or WSMoL (6.25–100 µg/mL)	- ↓ Leukocyte migration, myeloperoxidase activity, NO, TNF-α and IL-1β. - ↓ number of leukocytes in the lungs.	Anti-inflammation	Seed extract and cMoL are potentially cytotoxic for PBMCs, while the diluted seed extract and WSMoL are not cytotoxic to these cells. Acute toxicity test (2000 mg/kg) showed no signs of systemic toxicity
Arise, 2016 [24]	MO flowers ethanol extract	Air-dried MO from fresh flowers were pulverized and extracted in 95% ethanol.	Not reported	Streptozotocin-induced diabetes in male albino rats.	100, 200, 300 mg/kg BW once daily, 21 days.	- ↓ blood glucose, atherogenic index, TG, HDL-C, LDL-C, TC, MDA levels, AST, ALP. - ↑ body weight gain, SOD, CAT.	Glucose and lipid metabolism, antioxidant	Not reported
Atta, 2017 [25]	MO leaves methanol extract	Powders of MO leaves were extracted with 95% methanol.	Not reported	CCl4-induced hepatotoxicity in male and female S.D. rats	100, 200, 400 mg/kg BW p.o, 4 weeks.	- ↑ GPx, CAT, GSH, TP, and albumin. - ↓ TC, TG, ALT, AST, MCH, MHCH, RDW, WBC, urea, creatinine. - Improvement of the histopathological picture of the liver.	Antioxidant, lipid metabolism, hepatoprotective	Acute toxicity test: No symptoms of morbidity or mortality. LD50 > 4500 mg/kg BW p.o

Attakpa, 2017 [26]	MO leaves aqueous extract	MO leaves were suspended in distilled water and boiled for 30 min.	Not reported	Spontaneously hypertensive rats.	200, 400, 600 mg/kg BW in food, 8 weeks.	- ↓ blood glucose, TG, LDL, TC levels, BP, arachidonic acid - Inhibition of T cell proliferation, anti-CD3- stimulated T cell blastogenesis, IL-2 secretion - ↑ basal Ca2+, EPA, DHA	Anti-inflammation, Glucose & lipid metabolism, anti-hypertensive	Not reported
Azad, 2017 [27]	Leaves ethanol extract	Powdered leaves of MO were extracted in 80% ethanol.	Not reported	Streptozotocin (STZ) induced diabetes in Long Evan rats.	500 mg/kg BW p.o	- ↓ serum glucose but doesn't affect insulin secretion. - ↓ in the glucose absorption by inhibiting α-amylase - ↑ in gut motility and decrease in starch catabolism. - ↓ amount of glucose in the dialysate.	Glucose metabolism	Not reported
Azevedo, 2018 [28]	MO leaves aqueous extract	Powdered leaves of MO were macerated in distilled water.	Not reported	Streptozotocin- induced diabetes in Wistar rats.	100 mg/kg BW p.o + 200µL of 10% extract topically for 10 days.	- ↓ blood glucose, wound area, TNF-α, IL-1β, and IL-6. - ↑ collagen fibers, fibroblasts, vascular neoformation and macrophages	Anti-inflammation, wound healing	Not reported
Bao, 2020 [29]	Niazirin from MO seeds	MO seeds were boiled twice, followed with extraction using a macroporous resin column and silica gel chromatography. Niarizin was prepared by medium pressure	purity of niazirin: >95%	Saline-induced metabolic syndrome in male db/db mice.	10 and 20 mg/kg/BW p.o for 4 weeks.	- ↓ body weight, water, and food intake, - improved hyperglycemia, insulin resistance, inflammation, carbohydrate and lipid metabolism, non-alcoholic fatty liver.	Anti-inflammation, glucose & lipid metabolism	Not reported

		liquid chromatography from contracted fraction.				- Improved carbohydrate and lipid metabolisms via the AMPK signaling pathway.		
Bitrus, 2018 [30]	MO leaves methanol extract	Powdered MO leaves were extracted using absolute methanol.	10.6%	High cholesterol diet and Carbimazole induced hyperlipidemia and cardiac injury in male albino Wistar rats.	200 mg/kg BW p.o daily for six weeks.	- ↓ TC, LDL, TG, VLDL - ↓ CK-MB, LDH, and AST. - Improvement of histological findings of the heart.	Lipid metabolism, cardio-protective	Not reported
Chen, 2012 [31]	Moringa oleifera leaves hexane extract	Freeze-dried powder of MO leaves were extracted in hexane (1:2 w/v).	Not reported	Monocrotaline-induced pulmonary hypertension in rats	Acute: 1.5, 4.5 and 15.0 mg/kg i.v. Chronic: 4.5 mg/kg BW i.p for 7 days	- ↓ pulmonary arterial pressure. - ↑ heart rate - ↑ SOD - ↓ thickening of vessel walls of the histological sections.	Antioxidant, vasculoprotective	Not reported
Cheraghi, 2017 [32]	N,α-L-rhamnopyranosyl vincosamide isolated from MO leaves	Not reported	Not reported	Doxorubicin-induced cardiac toxicity in albino rats.	200, 400, 800, 1000, and 2000 µg/ml i.p every other day for 2 weeks.	- ↑ GSH, SOD. - ↓ MDA, and mRNA levels of β-MHC, ANP, BNP.	Antioxidant, cardioprotective	Not reported
Chin, 2018 [33]	MO leaves aqueous extract	MO leaves were extracted using cold-maceration in distilled water.	Not reported	Streptozotocin and high-fat-diet-induced diabetes in	0.1, 0.5, and 1% film dressing	- ↑ hydroxyproline and COL1α1 levels. - Downregulation of IL-6, TNF-α, and MCP-1 expression at 1%.	Anti-inflammation, wound healing	Acute dermal toxicity: no mortality, no abnormalities on the skin, fur, and

		The extract was formulated with sodium alginate-pectin in film dressing.		male S.D. rats.		- Enhancement of wound healing rate - Promote collagen deposition - Acceleration of wound contraction rate.		behavioral patterns up to 1% dose. No signs of edema, erythema, or any symptoms of toxicity on the skin.
Chumark, 2008 [34]	MO leaves extract	MO leaves were boiled in distilled water for 15 min.	10%	Human LDL; High cholesterol diet-induced hyperlipidemia in New Zealand white rabbits	1, 10, 30 and 50 µg/ml. 0.1 g/kg BW p.o. daily for 12 weeks.	- Delayed the lag-time of conjugated diene formation. - ↓ TBARS formation. - ↓ in TC, LDL, HDL, TG. - Reduced the formation of internal carotid atherosclerotic plaque.	Antioxidant, lipid metabolism, vasculoprotective,	Not reported
Cui, 2019 [35]	MRP-1 isolated from MO roots.	Dried MO roots were boiled in water to extract the polysaccharide MRP-1.	4.6%	RAW264.7 cells treated by LPS	12.5, 25, 50, and 100 µg/ml.	- Inhibition of NO, IL-6, IL-1β and TNF-α production. - Inhibit mRNA expression levels of iNOS and TNF-α.	Anti-inflammation	Lower concentrations (12.5, 25, 50, and 100 µg/ml) had no cytotoxicity while higher concentration (200 µg/ml) showed toxicity.
Das, 2012 [36]	MO leaves ethanol extract.	Powdered MO leaves were extracted using 80% ethanol.	10%	High-fat diet-induced hyperlipidemia in Swiss	150 mg/kg BW p.o for 15 days	- ↑ FRAP, GSH - ↓ MDS, AST, ALT, and ALP. - Prevention of liver damage Prevention of diet-induced	Antioxidant, hepatoprotective	Not reported

				strain male albino mice		obesity and early signs of fatty liver.		
de Yurre, 2020 [37]	Water-Soluble Lectin (WSMoL) isolated from MO seeds	Extraction was done with distilled water, followed with filtration and centrifugation. Afterward, lectin was further saturated, centrifugated, precipitated dialyzed with distilled water.	Not reported	Male C57BL/6 mice	5 mg/kg BW p.o for 21 days	- No change in blood glucose levels, body weight, glucose tolerance or insulin resistance. - No alterations in ECG parameters, cardiac action potential duration, left ventricular and mitochondrial function.	None	No toxicity was observed
Dou Z et al., 2019 [38]	MO leaves extract	a non-digestible fraction of MO leaves was suspended in sterilized basic nutrient growth medium.	Not clearly stated	In vitro gastrointestinal model	5 g/50 mL	- ↓ free radical scavenging activity after gastric and small intestine digestion. - ↓ pH in the colon. - ↑ SCFA and diversity of gut microbiota.	Antioxidant, gut microbiome modulation	Not reported
Edeogu et al., 2019 [39]	MO seed oil	MO seed oil was produced by cold press method with no additional chemicals.	Not reported	Gentamicin-induced nephrotoxicity in male Wistar rats	5 ml/kg BW p.o for 16 days	- ↓ kidney weight, urea, and creatinine. - ↓ MDA IL-6, IL-1b, TNF-α, NO, iNOS, NF-κB, caspase-3. - ↑ GSH, SOD, CAT, and GPx activities. - Histopathological alterations were ameliorated but still showed mild to moderate multifocal	Antioxidant, anti-inflammation, nephroprotective	Not reported

						degeneration and renal tubular epithelial cells necrosis.		
El Rabey, 2017 [40]	MO seed powder	Milled MO seeds were mixed to the 2% cholesterol diet powder.	Not reported	Basal fat-rich diet-induced hypercholesterolemia in male albino rats	50 mg/kg BW for 8 weeks	- ↓ TC, TG, LDL, VLDL, LDH, CK-MB, ALT, AST, ALP, GGT activities. - ↑ HDL, - ↑ water consumption. - Histopathological of the liver showed slight congestion of hepatic sinusoids and nearly restored normal appearance.	Lipid metabolism, hepatoprotective	Not reported
Ezzat SM et al., 2020 [41]	MO leaves ethanol extract	Powdered MO leaves were macerated using 70% ethanol and evaporated to yield dried ethanol extract.	10%	High-fat diet-induced obesity in rats	200 and 400 mg/kg BW p.o for 1 month	- ↓ body weight, adiposity index, glucose, insulin, HOMA-IR, TC, TG, and LDL. - ↑ Increased R-QUICKI, HD. - ↓ leptin and increased adiponectin, omentin, and GLUT-4 levels of the adipose tissue. - Suppressed FAS and HMG-CoA reductase - ↑ mRNA MC4R and PPAR-α.	Lipid metabolism, antiobesity	Not reported
Fahey JW et al., 2019 [42]	MO leaves aqueous tea	Powdered MO leaves were extracted in deionized water.	Not clearly stated	LPS-induced inflammation in RAW264.7 cells.		The doses required to produce a median effect of NO suppression were: moringin, 0.19 μM; cold moringa tea, 0.17 μM and hot moringa tea >100 μM	Anti-inflammation	Not reported
Gao X et al., 2017 [43]	MO leaves aqueous extract	Ultra-micro powder of MO leaves were boiled in ultrapure	31.5%	Healthy male	750 mg/kg BW p.o daily for 4 weeks	- ↓ liver TG content. - Higher levels of bacterial LPS were found in serum.	Anti-inflammation, lipid metabolism, gut microbiome	Not reported

		water, followed by centrifugation. The supernatant was dried in vacuum freeze-dryer.		C57Bl/6 J mice		- Enhanced mRNA expression levels of TNF-α, IL-1β, and IL-6, MCP-1 in the colon. - Upregulation of Reg3g, Pla2g2, Defa in the colon. - Downregulation of Lyz1, Muc2, and occludin. - ↓ ileum mRNA IL-1β, IL-6, increased MCP-1. - Moderate dosage of extract triggered an inflammatory response - Disruption of intestinal homeostasis. - Dominant gut microbial composition was changed.		
Ghasi S et al., 2000 [44]	MO leaves crude extract	Grounded MO leaves were decocted in distilled water for obtaining crude extract.	Not reported	High-fat diet in male Wistar rats	1 mg/g BW p.o once daily for 30 days	- ↓ cholesterol - ↑ albumin - No effect on total protein serum.	Lipid metabolism	Not reported
Gouda AS et al., 2018 [45]	MO extract	Purchased from Egyptian National Research Center (1 g/mL aqueous preparations).	Not reported	Aluminum phosphide-induced acute cardiac toxicity in rats	100 mg /kgBW p.o	- Cardiac muscle showed congestion of intermuscular capillaries with mild disruption and edema of muscular bundles. The extract showed a protective effect. - ↑CAT, GR - ↓ MDA, SOD.	Antioxidant, cardioprotective	Not reported
Gupta R et al., 2012 [46]	Methanol extracts of MO pods (MOMtE)	Dried powdered pods of MO were percolated with 100% methanol.	0.85%	Streptozotocin- induced diabetes in albino rats.	150, 300 mg/ kg BW for 21 days	- ↓ serum glucose, NO, TBARS, MDA.	Antioxidant, glucose metabolism.	Not reported

						- ↑ serum insulin, protein levels, SOD, GSH, CAT. - Reverse the damage of histoarchitectural to the islet cells.		
Huang L et al., 2020 [47]	Isothiocyanates isolated from MO seed	MO peeled seeds were extracted with 30% and 90% methanol for 3 times. It is followed by water-ethyl acetate extraction. The water extract was further fractionated using water and methanol in different concentrations (10%, 30%, 50%, 70%, 90%).	18.5%	3T3-L1 adipocytes	10, 20, 30, 60 µM	Inhibit intracellular lipid accumulation	Lipid metabolism	Not cytotoxic
Huang Q et al., 2020 [48]	MO seeds ethanol extract	MO seed was extracted with water then evaporated, lyophilized and further extraction using 90% ethanol.	4.13%	HepG2-insulin resistance model	10 ng/mL, 100 ng/mL, 1 µg/mL, 10 µg/mL	- ↑ glucose uptake by cells. - Suppressed SRC, PTPN1, caspase-3 expression.	Glucose metabolism, antiapoptotic	Not reported
Irfan HM et al., 2016 [49]	MO leaves ethanol extract	Powdered MO leaves were extracted with 95% ethanol by maceration.	Not reported	Streptozotocin- induced diabetes male S.D. rats	125, 250, 500, 1000 mg/kg BW p.o for 14 days	↓ fasting blood glucose concentration, body weight, cholesterol, TG.	Glucose and lipid homeostasis	Not reported

Jaiswal D et al., 2009 [50]	MO leaves aqueous extract	Crushed MO leaves were extracted hot distilled water.	11.7%	Streptozotocin- induced diabetes male albino Wistar rats	100, 200, 300 mg/kg BW p.o for 21 days	- ↓ fasting blood glucose, postprandial glucose, urine glucose, and protein. - ↑ Hb and total protein.	Glucose metabolism	Acute toxicity test: not toxic up to 15 x effective dose. Normal behavior and no death.
Jaiswal D et al., 2013 [51]	MO leaves aqueous extract	Fresh leaves macerated in distilled water.	10.5%	Streptozotocin- induced diabetes male albino Wistar rats	200 mg/kg BW p.o daily for 21 days	- ↑ SOD, CAT, GST. - ↓ MDA	Antioxidant	Not reported
Jaja-Chimedza A et al, 2017 [52]	Isothiocyanate-enriched MO seed extract	MO seed extract was prepared by incubating ground seeds in water, then ethanol, followed by filtration, drying and purification.	12.6 - 13.2%	RAW 264.7 cells Carrageenan-induced paw edema in male S.D. rats	0.05, 0.1, 0.5, 1, 5 and 10 μM 250 and 500 mg/kg BW	- ↓ NO production, iNOS, IL-1β and IL-6 expression. - Upregulation of all Nrf2 target genes (NQO1, HO1, GSTP1). - Inhibition of paw edema.	Anti-inflammation	No significant effect on cell viability.
Joung H et al, 2017 [53]	MO fermented extract	Powder of MO leaves was mixed in distilled water in three different mixtures. Those were inoculated with 2.5% culture media of each strain and incubated 37°C for 24 h. Samples were centrifuge at 4 °C, 12000 rpm, 15 min.	Not reported	High-fat diet-induced obesity in male C57BL/6J mice	250 mg/kg BW p.o daily for 10 weeks	- Improved glucose tolerance test. - ↓ liver weight, hepatic lipid accumulation. - Downregulation of lipogenic genes (ACC, FAS, C/ENPα, SREBP1c, LPL), lipid oxidative genes (CD36, ACOX1, CPT1 (NFM), HSL), and oxidative stress genes (UCP2 and UCP3). - Upregulation of lipolysis genes (ATGL, HSL). - Reduced expression of genes - related to ER stress (BiP, PDI, and CHOP).	Glucose metabolism, antioxidant, anti-inflammation	Not reported

						- ↓ mRNA proinflammatory cytokines (TNFα, IL-6, and IL-12). - Unchanged Akt phosphorylation level.		
Khalil SR et al., 2020 [54]	MO leaves ethanol extract	Powdered MO leaves was macerated in absolute ethanol	Not reported	Tilmicosin-induced cardiac injury in male S.D. rats	400 and 800 mg/kg BW p.o	- ↓ mortality rate. - ↓ CK-MB, CPK, troponin levels. - ↓ MDA, PC, and 8-OHdG levels. - ↑ CAT, SOD, GSH, TAC. - Up-regulation of Bcl-2 - Downregulation of Bax, caspase-3, Apaf-1, AIF, P53. - Heart sections revealed partial restoration.	Antioxidant, antiapoptotic, cardioprotective	Not reported
Kumar Gupta S et al., 2013 [55]	MO leaves aqueous extract	Dried leaves were extracted using water at 60-70°C.	Not reported	Streptozotocin- induced diabetes male albino Wistar rats	100 mg/kg BW p.o for 24 weeks	- ↓ blood glucose levels, HbA1c. - ↓ retinae dilated vessels and - Improvement of the thickened basement membrane. - ↓ clinical grading of fluorescein angiograms. - ↓ retinae TNF-α, IL-1β, VEGF, PKC-β. - ↑ retinae GSH, SOD, CAT	Antioxidant, anti-inflammation, Vasculoprotective	Not reported
Li C et al, 2020 [56]	Novel polysaccharides from MO leaves	(1) Hot water extraction followed by ethanol precipitation (crude MOPL)	Crude MOPL: 6.84%; further purification from	RAW 246.7 cells	31.3–500 μg/mL	- Stimulation of pinocytosis, ROS, NO, IL-6 and TNF-α - ↑ mRNA of NO, IL-6 and TNF-α.	Immunomodulation	Cytotoxicity test: Doses 31.3–500 μg/mL promoted cell proliferation.

		(2) Further purification using DEAE-Sepharose fast-flow ion-exchange	MOPL: 15.4%					Not toxic to cells.
Li YJ et al, 2020 [57]	MO seed	Not reported	Not reported	Myocardial infarction (MI) male C57/BL6 mice	600 mg or 900 mg in food, daily for 2 weeks pre- and post-MI surgery	- ↑ survival rate. - ↑ LVEF and LVFS) in ECG analysis. - ↓ heart volume, infarct areas, the volume of infarcted heart, and fibrotic scarring. - The thicker anterior wall of the left ventricle chamber. - Prevent cardiac remodeling. - ↓ TUNEL positive cells, Bax, cytochrome C - ↑ Bcl-2, which indicates reduced myocardial apoptosis. - ↓ gp91phox, and iNOS.	Antioxidant, antiapoptotic, cardio-protective	Not reported
Liao PC et al, 2018 [58]	β-Sitosterol isolated from MO woody stems	Woody stems of MO were extracted using ethanol followed with partitioned in *n*-hexane/water (1/1 v/v). The *n*-hexane fraction was applied to a silica gel column and then eluted with acetone/n-hexane (1:1 v/v), followed with purification in	5.9%	HaCaT and J774A.1 cells	7.5−60 μM	- ↓ IL-1β, IL-6, IL-8, TNF-α secretion. - Inhibition of NLRP3, expression, ROS production, caspase-1 activation. - Partially inhibited NF-κB in macrophages.	Anti-inflammation	Cytotoxicity test: no toxicity up to 60 μM

		HPLC to obtain stigmasterol and β-Sitosterol						
López M et al, 2018 [59]	MO leaf powder	Not reported	Not reported	High-fat and fructose diet-induced metabolic syndrome male Wistar rats	Preventive: 700 mg/kg BW p.o daily for 3 weeks before induction Treatment: 700 mg/kg BW p.o daily for 3 weeks after induction	- ↓ fasting glucose levels. - There are no significant differences in ITT, OGTT, TC, TG, SBP, DBP, or abdominal circumference. - ↓ glucose tolerance, TG, and abdominal circumference. - No significant differences in the ITT.	Glucose and lipid metabolism	Not reported
Luetragoon T et al., 2020 [60]	MO ethyl acetate extract and fractions	Dried MO powder was extracted by hexane and ethyl acetate (EtOAc) individually. Crude EtOAc were fractionated in column chromatography.	2.2% (hexane); 6.4% (ethanol)	Human MDM	Ethyl acetate extract: 56.98 µg/mL fraction 6: 144.66 µg/mL fraction 12: 162.08 µg/mL	- Downregulation of mRNA IL1, IL-6, TNF-α, PTGS2, NF-κB (P50), and RelA. - Inhibition of IL-6 and TNF-α production. - Inhibition of NF-κB (p65) translocation into the nucleus leads to the reduction of p65, phospho-IκB-α, and COX-2 proteins levels.	Anti-inflammation	Cytotoxicity test: LC50 of ethyl acetate extract, fraction 6, fraction 12 were 521.19, 693.42, 1119.43 µg/mL, respectively.
Mabrouki L et al., 2020 [61]	methanol extract of MO leaves	Fine powdered MO leaves were extracted with methanol.	Not clearly stated	in vivo: Rats ((high-fat diet-induced obesity)	200 mg/kg/bw and 400 mg/kg/bw for 12 weeks	- ↓ body weight gain - ↓TC, ↓ TG, ↓ HDL-C - ↑ CK-MB - ↑ CAT, GPx, SOD - ↓ MDA	Lipid metabolism, antioxidant	not reported

Madkhali HA et al., 2019 [62]	methanol extract of MO leaves (MEMO)	Powdered MO leaves was extracted with methanol using a Soxhlet apparatus	Not reported	in vivo: Rats (high-fat diet-induced dyslipidemia and vascular endothelium dysfunction)	200 and 400 mg/kg/day for 3 weeks	- ↓ liver weight - ↓ BMI, ↓ waist, ↓ Lee-index - ↓TC, ↓TG, ↓VLDL, ↓LDL, ↑HDL-C - reversing endothelial dysfunction (↓ endothelium relaxation) - improvement and photomicrographs architecture of aorta	Lipid metabolism, vasculoprotective	not reported
Mapfumo M et al., 2019 [63]	Crude hydroethanolic MO seed extract	Dried and dehulled MO seeds were grounded. It is extracted with 70% ethanol to obtain seed extract.	Not reported	in vivo: Rats (high fructose diet for induced metabolic syndrome)	50 and 500 mg/kg body mass for 12 weeks	- ↓ glucose tolerance (more pronounced in male than female rats) - ↓ fasting glucose, insulin, and HOMA-IR (more favorable in female than male rats) - ↓ TG - no change in total cholesterol	Glucose and lipid metabolism	not reported
Mehta K et al, 2003 [64]	MO fruit powder	The outer skin, pulp, and seed of MO fruits were collected and dried at 60 °C separately and then sifted.	3 - 7%	in vivo: Rabbits (hypercholesterolemia diet)	200 mg/kg p.o for 120 days in banana pulp	- ↓ TC, ↓ phospholipid, ↓ TG, ↓ VLDL, ↓LDL-C, and ↑ HDL ratio (HDL/HDL-TC) - ↓HDL-C - ↓ lipid profile in liver, heart, and aorta, but not in heart	Lipid metabolism	not reported
Muhammad AA et al., 2016 [65]	MO aqueous fraction	The dried and powdered leaves were macerated with 80% methanol, then was separated in hexane and dichloromethane, as well as butanol and ethyl-acetate. and water:methanol (1:3 v/v).	Not reported	*in vitro*: Pathogenic bacteria consisting of *P. aeruginosa* strain PAO1, methicillin-resistant *S.*	0.5%, 1%, and 2% w/w in ointment formulation	*in vitro* - inhibited growth *S. aureus*: 3.125 µg/mL and P. *aeruginosa*: 6.25 µg/mL against *E. coli* - The MIC for tetracycline standard antibiotic: 3.125 µg/mL against *E. coli* and 6.25 µg/mL against *S. aureus* and *P. aeruginosa*. *in vivo*: ↓ wound size	Antiinflammation, wound healing, antibacterial	not reported

				aureus, and *E. coli* *in vivo*: Rats (streptozotocin and nicotinamide-induced diabetic, followed by wound excision)		↑ wound contraction ↑ tissue regeneration ↓ inflammatory mediators: TNF-α, IL-1β, IL-6,iNOS, and COX-2 ↑ VEGF		
Murillo G et al., 2017 [66]	MO leaves powder	Not reported	Not reported	In vivo: guinea pigs (hypercholesterolemic diet with 0.25% cholesterol)	3 or 4.5 g/day a daily intake for 6 weeks	- no changes in plasma lipids, glucose, or insulin - ↑ the activity of lecithin cholesterol acyltransferase	Lipid metabolism	not reported
Nafiu AO, 2019 [67]	Ethanolic extract of MO seeds	MO seeds were extracted in ethanol for 24 h.	Not reported	in vivo: Rats (gentamicin-induced nephrotoxicity)	100, 200 and 400 mg/kg/day p.o for 28 days	- ↓ urine volume - ↑ body weight - ↓ urea in urine - ↓ creatinine plasma and ↑ creatinine urine - ↑ creatinine clearance - restoration electrolytes - ↑ SOD and ↓ MDA - improvement in the histoarchitecture of the kidney with mild distortion, few abortive glomeruli, and mild vascular congestion (400 mg/kg treatment seems to have fared better than others)	Antioxidant, nephroprotective	not reported

Nandave et al, 2007 [68]	Lyophilized hydroalcoholic extract of *Moringa oleifera*	MO leaves were macerated with (methanol: water, 50:50 v/v) and evaporated to yield the extract.	34.2%	in vivo: Rats (isoproterenol-induced) cardiotoxicity model	200 mg/kgBW for 1 months	- improvement hemodynamic parameters - ↑ SOD, CAT, GSH-Px, LDH, and CK-MB - prevention of the deleterious histopathological and ultrastructural perturbations	Antioxidant, cardioprotective	not reported
Ndong et al, 2007 [69]	MO leaves powder	Not reported	Not reported	in vivo: Rats (iron-deficient diet)	0,5-1% MO in a diet for 4 weeks	- ↓ Hb - ↑ liver weight - ↓ liver iron - ↓ liver copper - ↓ TC, TG, and phospholipids	Lipid metabolism	not reported
Ofem, O.E et al., 2015 [70]	Aqueous leaves of MO	Grounded MO leaves were extracted with distilled water at 100 °C for 9 hr using Soxhlet apparatus.	31%	in vivo: Rats (high salt diet)	600 mg /kgBW for 6 weeks	Resolved hematology parameter: ↑WBC, RBC, platelet counts, PCV, lymphocytes, P-LCR, MPV, and PDW	Hematology	not reported
Olayaki et al, 2015 [71]	Methanolic extracts of MO (MOLE)	Powdered MO leaves were soaked with methanol using a cold-extraction method.	Not reported	in vivo: Rats (alloxan-induced diabetes)	300 and 600 mg/kg body weight p.o for 6 weeks	- ↓ blood glucose - ↑ glucose tolerance - ↑ serum insulin - ↓ serum cholesterol, TG, LDL-C, ↑ HDL - ↑ glycogen synthase activities and glycogen contents.	Glucose and lipid metabolism	not reported
Oldoni TLC et al., 2021 [72]	Hydroalcoholic subfraction extract leaves of MO	Grounded MO leaves were extracted with ethanol water (80:20) for 48 hr at room temperature (HE). The HE was fractioned by solid-	Not reported	*in vitro*: ● Folin-Ciocalteu assay ● Ferric reducing antioxidant	in vitro: 25 - 1000 µg/mL hydroalcoholic extract in vivo: 500 mg/kg	Fr-EtOAc : - ↓ FRAP, DPPH and ABTS, and ORAC assay - isoquercitrin, astragalin and 3-O-caffeoylquinic acid were obtained. In vivo: - ↓ blood glucose	Antioxidant	no observed cytotoxicity effect (concentration up to 1000 mg/mL)

		liquid extraction using hexane, dichloromethane , ethyl acetate , acetone, ethanol and ethanol:water (50:50, v/v). The active Fr-EtOAc was purified in an open Column Chromatography and followed by TLC to obtain subfractions.		power (FRAP) assay ● DPPH assay ● ABTS assay ● cell viability using PBMCs *in vivo*: Rats (streptozotocin-induced)	hydroalcoholic extract	- ↑ CAT activity in liver and kidney - ↓ GST in liver and kidney - ↓ non-protein thiol groups and thiobarbituric acid reactive substances in liver and kidney		
Omodanisi EI et al., 2017 [73]	Methanolic extract of MO leaves	Not clearly stated	Not reported	in vivo: Rats (streptozotocin-induced)	250 mg/kg BW p.o for 6 weeks	- ↑ renal weight - ↓ plasma glucose - ↓ MDA, ↑ SOD, ↑CAT, and ↑ GSH in renal - ↓ TNF-α and ↓ IL-6 - protective effect on histological examination	Antioxidant	not reported
Ouédraogo M et al., 2011 [74]	Aqueous-ethanolic extract of MO leaves	The powdered MO leaves were extracted with ethanol/water (80/20) for 48 h at room temperature.	4.8%	in vivo: Rabbit (nephrotoxicity induced by gentamicin)	150 and 300 mg/kgBW	- ↓ serum urea and creatinine - ↓ lipid peroxidation - reparative tendencies from histological examination	Antioxidant, lipid metabolism, nephroprotective	no toxicity signs were observed
Panda S, 2013 [75]	N,a-L-rhamnopyranosyl vincosamid	70% ethanol of powdered leaves extract	Not reported	in vivo: Rats (isoproterenol-induced	40 mg/kgBW for 7 days	- ↓ serum LDH, CK-MB, troponin T, and glutamate pyruvate transaminase - ↓ cardiac Troponin T and MDA	Antioxidant, cardioprotective	not reported

	e (VR) isolated from MO leaves			cardiotoxicity model)		- ↓ myocardial necrosis		
Panda, 2015 [76]	MO poly-phenolic fraction (MOPF)	Powdered MO leaves was extracted with 70% ethanol. The crude extract was fractionated using n-hexane, dichloromethane, and n-butanol.	Crude extract: 20.1%; n-hexane: 1.1%, dichloromethane 0.9%; n- buta-nol: 1.9%	in vivo: Rats (isoproterenol-induced cardiotoxicity model)	50, 100 and 150 mg/kg/day for 28 days	- ↑ SOD, ↑ Catalase, ↑ GSH-Px, ↑ GSH (MOPF100) - ↓ cardiac infarcted area (MOPF100) - ↓LDH, CK-MB, and cardiac Troponin T (MOPF100)	Antioxidant, cardioprotetive	not reported
Paula PC et al., 2017 [77]	Isolated protein from MO leaves: Mo-LPI	Powdered MO leaves was extracted in Tris-HCl buffer containing NaCl, polyvinylpolypyrrolidone (PVPP), phenyl-methyl-sulfonyl fluoride (PMSF) and ethylenediaminetetraacetic acid (EDTA), (1:5, w/v), under agitation at 4 ◦C for 30 min. The crude extract was precipitated at	5%	in vivo: Mice (alloxan-induced diabetes)	500 mg/kgBW, single-dose intraperitoneal (i.p.)	- ↓ blood glucose - ↓ MDA and ↑ catalase activity	Antioxidant glucose metabolism	Mo-LPI (2500 mg/kgBW) did not cause acute toxicity to mice.

		90% saturation with ammonium sulphate.						
Rajanandh, M.G, et al., 2012 [78]	Hydroalcoholic extract of Moringa oleifera (HEMO)	Powdered MO leaves were extracted with ethanol using cold maceration methods.	0.09% of Beta-sitosterol	in vivo: Rats (atherogenic diet for inducing hyperlipidemia)	200 mg/kg p.o. for 28 days	- ↓ body weight - ↓ TC, TG, LDL-C, VLDL, and ↑ HDL-C - ↑ SOD, ↑ CAT, and ↓MDA - ↓ TNF-α and ↓ IL-1α	Antioxidant anti-inflammatory, lipid metabolism	Not reported
Randriamboavonjy JI et al, 2016 [79]	MO seed powder	Not reported	Not reported	*in vivo*: Wistar Rats induced by spontaneous hypertensive	750 mg/d each rat in their food for 8 weeks	- did not modify BP - ↓ nocturnal heart rate - ↓ isovolumetric relaxation time and deceleration time of the E wave - ↑ ejection volume and cardiac output - ↓Left ventricular anterior wall thickness, interseptal thickness on diastole, and relative wall thickness - ↓fibrosis in the left ventricle - ↑ PPAR-α and δ - ↑ plasmatic prostacyclins	Cardio-protective	Not reported
Randriamboavonjy JI et al, 2017 [80]	MO seed powder	Not reported	Not reported	in vivo: Wistar Rats induced by spontaneous hypertensive	750 mg/day/rat in food for 20 weeks	- ↓ free 8-isoprostane circulating level, vascular p22phox and p47phox expressions - ↑ SOD2 - ↓ circulating nitrites and CRP - ↓ iNOS and NF-κB - ↑ endothelium-dependent carbachol-induced relaxation	Antioxidant, anti-inflammatory	Not reported

Reddy VP et al., 2017 [81]	MO leaves polyphenols (MOP)	Dried MO leaves were extracted with 80% methanol.	Not reported	in vivo: Wistar Rats (high fat-cholesterol diet for 45 days)	100 and 200mg/kg p.o for 8 weeks	- ↓ TC, LDL-C - ↓ HMG-CoA - ↑ fecal bile acid	Lipid metabolism	not reported
Saka WA et al, 2020 [82]	MO seed oil	Pounded MO seeds were extracted with 97% ethanol using Soxhlet apparatus at 78 °C.	Not reported	in vivo: rats induced by DDVP via inhalation for 15 min daily for 28 days	300 mg/kg p.o for 28 days.	- ↓ lactate dehydrogenase, creatinine kinase, and troponin - ↓ MDA - ↑ SOD and GSH-Px	Antioxidant	Not reported
Sangkitikomol W et al, 2014 [83]	Methanol MO extract (MOE)	Powdered MO leaves were extracted with 80% methanol in an ultrasonic bath for 60 min at 40 °C and stored in the dark followed by centrifugation.	20%	in vitro: HepG2 cell line	Cell viability MOE (0-3000 mg/L) Treatment: 0,200,400, and 600 mg/L	- ↓ oxidative stress in a dose-dependent manner (MOE >100 mg/L, 24 h) - ↓ HMG-CoA-Reductase, PPARα1, and PPARγ genes expression	Antioxidant	MOE induced cytotoxicity in high dose (2000-3000 mg/L)
Shaikh S et al., 2020 [84]	MO root extract	Dried powder of roots MO was extracted serially in methanol followed by boiled in a water bath to evaporate methanol.	Not reported	in vitro - DPPH assay - Pancreatic amylase assay	100 to 1000 µg/mL with an interval of 100µg/mL	- MO IC50 DPPH assay: 480.64 µg/mL - MO IC50 pancreatic amylase assay: 728.97µg/mL	Antioxidant, glucose metabolism	not reported
Sholapur HN et al., 2013 [85]	Alcoholic and petroleum ether	Powdered bark was macerated in 80% ethanol and petroleum ether.	Not reported	in vivo: Rats were induced by dexamethas	Acute and chronic toxicity studies:	Alcoholic Extract 125 and 250 mg/kg: - ↓ TG and oral glucose intolerance but not fasting hyperglycemia	Lipid metabolism	no toxicity was observed

	extracts of MO bark			one for 11 days	- 2 doses of alc. extract (125 and 250 mg/kg) - 2 doses petroleum ether extracts (30 and 60 mg/kg) - single dose each of alc. extract (250 mg/kg) - single dose of petroleum ether extract (60 mg/kg)	Petroleum ether extract 30 and 60 mg/kg: - PEE30 had no effects - PEE 60 ↓TG		
Sinha et al, 2011 [86]	Aqueous ethanolic MO leaves extract (MOLE)	Powdered MO leaves were extracted with 50% methanol	Not reported	in vivo: Swiss albino mice using single dose of 5 Gy of 60Co c-irradiation	MOLE p.o 300 mg/kg of body weight for 15 days	- ↓ translocation of NF-kB from the cytoplasm to the nucleus - ↓ lipid peroxidation - ↑SOD, CAT, GSH, and FRAP	Antioxidant	not reported
Soliman MM et al., 2020 [87]	MO leaf extract (MOLE)	MO leaves soaked in a hydro-alcoholic solution and shaken at room temperature for 48 h.	Not reported	In vivo: mice induced by Methotrexate on day 7	MOLE p.o 300 mg/kgBW, 12 days.	- ↓ ALT, ALP, urea, and creatinine in serum - ↑ albumin and total protein - ↓ MDA, ↑ SOD and ↑catalase in serum - ↓ MDA, ↑ SOD, and ↑GSH in liver and kidney - Liver: ↓ BAX, ↓ TIMP, ↑XIAP mRNA expression level	Antioxidant, antiapoptotic	not reported

						- Renal: Nrf2 unchanged, ↑HO-1, ↓ NF-kB mRNA expression level - Restored liver histopathology architecture - Restored renal histological architecture - ↓ caspase-9 in liver and renal - ↑ Bcl2 in liver and renal		
Sun C et al, 2019 [88]	1-O-(4-hydroxymethylphenyl)-α-L-rhamnopyranoside (MPG) from MO seeds	Seed powder were de-oiled with petroleum ether and ddH2O at 95°C. n-Butanol was used for further fractionation, followed with sub-fractionation with MOE-BuOH and chromatography.	18.1%	*in vitro*: LO2 cells induced by CCl4 *In vivo*: ICR mice induced by single dose CCl4 on 8th days treatment	50, 100, 150 mg/kg BW p.o for 7 days	*in vitro*: - ↑ cell viability - ↑ intracellular SOD activities - ↓ LDH - leakage in CCl4-treated cells. *in vivo*: - ↓ abnormal enlargement liver weight - ↓ ALT, ALP, AKP in serum - improve histopathological analysis - enzymatic antioxidant activities (↑SOD, ↑CAT, and ↑GSH-Px) - non-enzymatic antioxidant activities (↑T-AOC and ↑GSH) - ↓ hepatic MDA level - ↓ hepatic ROS production - ↓ TNF-α, IL-1β, and MCP-1 levels in liver - ↑ IL-10 in the systemic circulation - ↓ apoptotic hepatic cells	Antioxidant, anti-inflammatory, antiapoptotic, hepatoprotective	- no notable cytotoxic effects at 24 h, 48 h, and 72 h (5–100 μg/mL) - first phase acute oral toxicity in mice: up to 1000 mg/kg→ no adverse effects and death - second phase oral toxicity in mice: up to 2000 mg/kg single administration → no adverse effects and death

Tan WS et al, 2015 [89]	80% hydroethanolic extract of MO flower	MO flower powder was macerated in hydroethanolic solvent under a rotary shaker at room temperature.	Not reported	*in vitro*: The murine macrophage cell line, RAW 264.7,	MTT assay: 15.625 - 1000 µg/mL *in vitro*: 100 µg/mL and 200 µg/mL	● ↓ secretion and expression of NO,PGE2, IL-6, IL-1β, TNF-α, NF-κB, iNOS, and COX-2. ● ↑ IL-10 and IκB-α ● dose-dependent manner (100 µg/mL and 200 µg/mL).	Antioxidant, anti-inflammatory	Not exhibited any toxicity to macrophages at concentrations ranging from 15.625 to under 250 µg/mL.
Tang Y et al, 2017 [90]	Aqueous and ethanolic extract MO leaves, stems, and seeds	Leaves, stems, and seeds of MO were boiled separately distilled water and with 70% ethanol.	Not reported	*in vivo*: db/db mice	MO leaves ethanolic extract 150 mg/kg/day for 5 weeks (gastric intubation)	DPPH activity: ethanolic leaf extract the strongest hydroxyl radical scavenging activity *In vivo*: - ↓ fasting plasma glucose, triglyceride, and LDL cholesterol - ↑ insulin levels - ↓ histopathological damage, TNF-α, IL-1β, IL-6, cyclooxygenase-2, and iNOS in renal tissue	Glucose metabolism, anti-inflammatory, nephroprotective	not reported
Tian et al, 2021 [91]	MO polysaccharides (MOP)	MO powder was macerated in boiled distilled water and centrifuged. Afterwards, the supernatant was collected and concentrated. The Sevag method was used to remove the protein impurities.	Purity of MOP: 83.42%	in vivo: male SPF C57BL/6 mice	MOP p.o: 0, 20, 40 and 60 mg/kg bw for 30 days	Serum: - ↓ glucose, total cholesterol, & MDA - Improved SOD and catalase in serum Small intestine - Improved the villi length and crypt depth in both ileum and jejunum - ↑ the ratio of villi length to crypt depth in jejunum - ↑ beneficial bacteria - ↓ harmful bacteria in the caecum - MOP regulated 114 metabolites enriched in the pathway related to the synthesis and metabolism of micromolecules.	Glucose metabolism, antioxidant, gut microbiome	not reported

Umar et al, 2018 [92]	Hexane, ethyl acetate, and methanol extracts of MO root	MO roots were extracted with hexane, ethyl acetate, and methanol separately in Soxhlet apparatus at 50°C.	Not reported	in vivo: male *Rattus norvegicus*, albino variety induced by alloxan	Powder root extract: 15g/kg BW/day p.o for 4 weeks. methanolic extract of MO roots (1 g/kg BW/day, i.p. injection for 4 weeks.	- ↓ fasting blood glucose levels - ↓ insulin resistance - ↑ SOD, CAT, GPx	Glucose metabolism, antioxidant	- LD50 was above 5000 mg/kg - no death observed
Vargas-Tineo et al., 2020 [93]	Aqueous extract of MO leaves	Water extraction at 90 C	Not reported	in vivo: male *Rattus norvegicus*, albino variety induced by alloxan	200 mg/kg po	↓ glycemia	Glucose metabolism	Not reported
Velaga MK et al., 2014 [94]	M. oleifera seed powder	Powder MO seeds were suspended in distilled water.	Not reported	in vivo: Male Wistar rats induced by 2000 ppm of lead acetate for 2 weeks	500 mg/kg p.o on 7 days after lead acetate for 1 week	Brain, liver, and kidney - ↓ reactive oxygen species (ROS) - ↓ lipid peroxidation products (LPP) - ↓ total protein carbonyl content (TPCC) - ↓ metal content Blood - ↑ delta-aminolevulinic acid dehydratase (ALAD) activity - ↑ RBC, WBC, hemoglobin, and hematocrit	Antioxidant	Not reported
Vera-Nuñez N et al., 2021 [95]	Lectin on MO seeds: WSMoL	Distilled water and ammonium sulfate were used to extract MO seeds, followed with centrifugation. The precipitate was	Not reported	in vivo: adult C57BL/6 mice by combining a high-fat diet	WSMoL: 5 mg/kg bodyweight for 21 days	- ↓ fasting blood glucose levels - ↓ insulin resistance - improve cardiac LV ejection fraction	Glucose metabolism, cardio-protective	no adverse effects on body weights were observed

		resuspended and dialyzed. Using a chitin column, the dialyzed fraction is loaded and the WSMoL is eluted with an acid solution of sodium acetate. Dialyzed against distilled water, the isolated lectin is characterized.		and low doses of STZ (6 wk)				
Villarruel-López A et al, 2018 [96]	Powdered leaves extract MO	Dried leaves from 40°C (24h) were pounded.	Not reported	in vivo-toxicity: Balb-C56 male mice in vivo-diabetic rats: Alloxan on S.D. rats	Acute toxicity: 100, 200, 500 mg/kg of Moringa oleifera for 7 days observed Diabetic-rats: Moringa oleifera was 50 mg/day, and the glibenclamide dose was 600 µg/kg/day for 8 weeks	- hypoglycemic effect - no change in enumeration of lactic acid bacteria	Glucose metabolism, gut Microbiome	- no lethal dose was determined - no adverse effects were observed - no genotoxicity was observed
Wang F et al, 2019 [97]	Niazirin from aqueous MO seed	Not reported	Not reported	in vitro: VSMCs (vascular	in vitro: 5 and 25 uM	- DPPH - ↓ radical scavenging activity - in vitro and in vivo - ↓ the proliferation of high glucose-induced VSMCs	Antioxidant	not observed

				smooth muscle cells) in vivo: ICR mice (high-fat diet for 8 wks+ inject STZ 40 mg/kg)	in vivo: 10 and 40 mg/kg/day for 2 weks	- ↓ ROS and MDA - ↑T-AOC, SOD, GPx levels - eliminate the high glucose-induced PKCζ activation, indicated by Thr410 phosphorylation and inhibition of the Nox4 protein expression		
Wang F et al, 2019 [98]	Polysaccharide from MO leaf: MOs-2-a	Chopped MO leaves were extracted using by deionized water and loaded into a macro-porous resin column. Ethanol was added, centrifuged and dried to obtain crude polysaccharide.	Not reported	in vivo: ICR mice	(50 mg/kg for MOs-2-a-H group and 10 mg/kg for MOs-2-a-L group)	- ↓ TNF-α, diamine oxidase (DAO), and d-lac levels in the intestine - improve the integrity of intestinal tissue in MOs-2-a group (villus height & mucosal thickness) - ↑ the activity of amylase; Lipase; Alkaline phosphatase; Trypsin. - ↓ the nitrogen content of feces - keep the pH at a faintly acidic level - restored gut microbiota composition - ↑ the bacteria for anti-obesity effects, SCFA, and lactic acid production.	Antioxidant, gut microbiome	28 days observation: - BW higher than in mice fed standard - increase the viscera index of the spleen and thymus
Wang F et al, 2017 [99]	The macroporous resin adsorption extract of MO seeds:	MO seeds were extracted two times with boiling water and passed over a macro-porous resin column to gain a crude extract. It was loaded into Medium Pressure	Not reported	in vitro: HepG2 cell in vivo: STZ-induced mice.	in vitro: 10, 20, 40, 80, 160, dan 320 ug/mL in vivo: dose of 20 mg/kg/day,	Compound 1, 4, and 5: - promote the glucose consumption of insulin resistance cells - reduce blood glucose levels of STZ-induced mice.	Glucose metabolism	

		Preparative Liquid Chromatography with an ODS column to obtained niazirin.						
Waterman C et al., 2015 [100]	Moringa isothiocyanates (MICs)	Fresh moringa leaves were blended in 25°C water at 25°C for 30 min, centrifuged, filtered, and lyophilized.	3	in vivo: C57BL/6L mice fed a very high-fat diet (VHFD) in vitro: H4IIE rat hepatoma cells	66 mg/kg/d of MICs for 12 weeks	in vivo: - ↑ glucose tolerance and insulin signaling (IRS-1, p-IRS-1 in the liver) - ↑ p-IRS1, IRS1, IRS2, IR β, and GLUT4 in the muscle - did not develop fatty liver disease - ↓ plasma insulin, leptin, resistin, cholesterol, IL-1β, TNFα, - ↓ hepatic G6P expression. in vitro: Inhibition of gluconeogenesis and G6P expression.	Glucose metabolism, anti-inflammatory	without any other observable side effect (12 weeks)
Yang Y et al, 2020 [101]	Bioactive compound :O-Ethyl-4-[(α-l-rhamnosyloxy) benzyl] carbamate	Not clearly stated	Not reported	DPP-IV assay		IC_{50} = 798 nM to inhibit DPP-IV	Glucose metabolism	not reported
Yassa HD et al., 2014 [102]	Aqueous extract of MO leaves	Dried and powdered leaves were boiled in water for 15 min.	Not reported	in vivo: 40 S.D male albino rats STZ-induced 60 mg/kg BW in 0.1 mol/L citrate buffer (pH 4.5) i.p	200 mg/kg aqueous extract of MO leaves (8 wk)	- ↓ glutathione and lipid peroxidation product and MDA, in pancreatic tissue. - Amelioration of the altered FPG (from 380% to 145%), reduced glutathione (from 22% to 73%) and MDA (from 385% to 186%) vs control.	Antioxidant	not reported

				after overnight fasting		- Marked reversed histopathological damage of islet cells. - ↑ areas of positive purple modified Gomori stained-cells (from 60% to 91%) morphometrically - ↓ percentage of collagen fibers (from 199% to 120%) vs. control.		

ALP: alkaline phosphatase, ALT: alanine aminotransferase, ANP: atrial natriuretic peptide, AST: aspartate aminotransferase, AOPP: advanced oxidation protein products, BiP: Binding immunoglobulin protein, BUN: Blood urea nitrogen, BNP: B type natriuretic peptide, BP: blood pressure, BW: body weight, CAT: catalase, CD: conjugated dienes, CHOP: CCAAT-enhancer binding protein homologous protein, CK-MB: Creatine kinase-MB, COL1α1: collagen type I alpha I, COX-2: cyclooxygenase-2, Cr: Creatinine, CRP: C-reactive protein, DDVP: dichlorvos, DPPH: 2,2-diphenyl-1-picrylhydrazyl, ECG: electrocardiogram, FAS: fatty acid synthase, FPG: fasting plasma glucose, FRAP: Ferric Reducing Antioxidant Power, G6P: glucose-6-phosphatase, G6PD: glucose-6-phosphate dehydrogenase, GGT: γ-glutamyl transferase, GPx: Glutathione peroxidase, GR: glutathione-reductase, GSH: Glutathione, GST: Glutathione S-transferase, Hb: hemoglobin, HDL: high-density lipoprotein, HK: hexokinase, HP: hydroperoxides, HOMA-IR: Homeostasis Model Assessment-Insulin Resistance, iNOS: inducible NO synthase, IκB-α: inhibitor of κB, IL-1β: interleukin-1β, IL-6: interleukin-6, IL-10: interleukin-10, iNOS: inducible nitric oxide synthase, i.p.: intraperitoneal, p-IRS-1: phospho-IRS-1, IRS-1: insulin receptor substrate-1; IRS-2: insulin receptor substrate-2; IRβ: insulin receptor beta ITT: insulin tolerance test, LDH: lactate dehydrogenase, LDL: low density lipoprotein, LPL: lipoprotein lipase, LPP: lipid peroxidation products, LPS: lipopolysaccharides, MCV: mean corpuscular volume, MCH: Mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentration., MCP-1: monocyte chemoattractant protein-1, MDA: malondialdehyde, MDM: monocyte-derived macrophages, β-MHC: beta major histocompatibility complex, MO: Moringa oleifera, MPV: Mean Platelet Volume, NF-κB: nuclear factor-kappa B (NF-κB), NO: nitric oxide, PC: pyruvate carboxylase, PCV: Pack cell volume, PDI: protein disulfide isomerase, P-LCR: Platelet Large Cell Ratio, PDW: Platelet Distribution Width, PGE2: prostaglandin E2
RBC: Red blood cell, RDWa: red blood cell distribution width absolute, ROS: reactive oxygen species, R-QUICKI: revised quantitative insulin sensitivity check index, SCFA: short-chain fatty acid, S.D.: Sprague Dawley, SOD: superoxide dismutase, STZ: streptozotocin, TAC: total antioxidant capacity, TBARS: Thiobarbituric acid-reactive substances, TC: total cholesterol, TG: triglyceride, TNF-α: Tumor Necrosis Factor-Alfa, TP: total protein, TPCC: total protein carbonyl content, WBC: White blood cells

Table S2. Clinical trials of *Moringa oleifera*

Author, year	Type of extracts / main bioactive compounds used	Methods of extracts / bioactive compounds preparation	Yield of preparation per raw material (wt/wt)	Sample size / subjects	Treatments and control	Duration	Effects	Adverse events (AE)
Anthanont, 2016 [103]	Leaf powder capsules	Dried MO leaves were powdered and filled into a gelatin capsule.	Not reported	10 / healthy subjects	Baseline: 0 g, Week 2: 1 g Week 4: 2 g Week 6: 4 g.	8 weeks	- No change in BUN, Cr, AST, and ALT, plasma glucose - ↑ plasma insulin - ↑ insulin secretion.	No AE up to high dose (4 g) administration.
Dominguez-Rodriguez M et al, 2016 [104]	MO. leaves extract	Not reported	Not reported	Crossover study Placebo: 24 Treatment: 24 / Obese type 2 diabetics treated with metformin subjects	NA	Period 1: 10 weeks Washout: 2 weeks Period 2: 10 weeks	- ↓ BMI, insulin - Trends to LDL and HbA1c reduction. - ↓ BP. - ↑ HDL	Not reported
Ezzat SM et al., 2020 [41]	MO leaves hard gelatin capsules	Powdered MO leaves were macerated using 70% ethanol and evaporated to yield dried ethanol extract.	10%	15 subjects / who were overweight or obese	400 mg/capsule	8 weeks	- ↓ significantly in BMI, TC, and LDL vs. baseline. - Normalization of AST, ALT, and alanine.	Not reported
Ifeoma, 2020 [105]	Steamed MO	Not reported	Not reported	Control placebo: 6 subjects	Group 1: control Group 2: 20 g	14 days	- No difference in the waist	Not reported

	leaves			Treatment: 3 groups, with each group, consists of 6 subjects / T2DM	Group 3: 40 g Group 4: 60 g		circumference, waist-hip ratio, and FBG in all groups. - ↓ SBP, no difference in DBP and TC in Groups 3 and 4. - ↓ LDL in Group 2. - ↑ TG and LDL in Group 3. - ↑ HDL in groups 1, 2, and 4. - ↓ Hb, packed cell volume, WBC, in Group 4. Significant changes observed in the parameters assessed were not dose-dependent.	
Leone A et al., 2018 [106]	Moringa oleifera leaf powder	The leaves were dried through a shade-dried and ground to a fine powder with an electric grinder.	Not reported	10 nondiabetic and 17 diabetic subjects, each received both control and Moringa oleifera leaf powder	20 g added to a meal	Single administration	Lower increment of postprandial blood glucose in diabetic subjects	Not reported

Sandoval & Jimeno, 2013 [107]	MO powdered leaf capsules	Leaves were dried and capsuled	Not reported	Placebo: 35 subjects Treatment group: 33 subjects / High baseline LDL-c patients	Placebo: 2 capsules 3x a day placebo capsule Treatment group: 2 capsules 3x a day (350 mg/capsule or 2100 mg/day)	30 days	A similar reduction of LDL-c vs. placebo	No serious adverse effects
Taweerutchana R et al., 2017 [108]	MO powdered leaf capsules	Dried leaves of MO, were ground, sifted to be powder. The powder was filled into capsule shells.	Not reported	Placebo: 16 subjects Treatment group: 16 subjects / Therapy naïve T2DM patients	Placebo: 8 placebo capsules Treatment group: 4 grams/day (8 capsules) 4 capsules each before breakfast and dinner time (500 mg MO powdered leaf/capsules)	4 weeks	no effect on glycemic control	No adverse effects

AE: adverse events, ALT: alanine aminotransferase, AST: aspartate aminotransferase, BUN: Blood urea nitrogen, BP: blood pressure, BMI: body mass index, BW: body weight, Cr: Creatinine, DBP: Diastolic blood pressure, FBG: fasting blood glucose, HDL: high-density lipoprotein, LDL: low-density lipoprotein, TC: total cholesterol, MO: Moringa oleifera, SBP systolic blood pressure, T2DM: type 2 diabetes mellitus TG: triglyceride, WBC: white blood cells.

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