Table S1. Preclinical trials of *Tinospora crispa* (L.) Hook. f. & Thomson on a diabetes mellitus model

Year	Reference	Model	Plant extract used	Administration	Results	Mechanisms
<2000	(Noor & Ashcroft, 1989)	Alloxan-induced diabetic rats (35–40 mg/kg BW, i.v.)	Water extracts of stems	4 g/L in the drinking water for 2 weeks	↑ plasma insulin ↓ plasma glucose	N/A
	(Noor et al., 1989)	Alloxan-induced diabetic rats (40 mg/kg BW, i.v.)	Water extracts of stems	4 g/L in the drinking water for 2 weeks	↑ plasma insulin ↓ plasma glucose	Stimulating insulin release
		Rat islets		0.01–1.0 mg/mL	↑ insulin release	
		HIT-T15 cells		0.01–4.0 mg/mL	↑ insulin release	
		Human islets		1.0 mg/mL	↑ insulin release	
	(Noor & Ashcroft, 1998a)	HIT-T15 cells	Water extracts of stems	0.10 mg/mL	↑ insulin release, intracellular Ca^{2+} accumulation, and Ca^{2+} uptake ↓ Ca^{2+} efflux	Promoting insulinotropic effects
	(Noor & Ashcroft, 1998b)	HIT-T15 cells	Water extracts of stems	0.10 mg/mL	↑ insulin release ↓ Rb-efflux	Stimulating insulin release through Ca^{2+} modulation
2005–2010	(M. Hamid et al., 2008)	BRIN-BD11 cells	Methanolic extracts of stems	0.1, 0.5, 1.0, and 5.0 mg/mL	↑ insulin secretory	Promoting insulinotropic effects
	(Noipha et al., 2008)	L6 myoblasts cells	Water extracts of stems	4 mg/mL	↑ glucose uptake	Enhancing glucose uptake
2011–2015	(Lam et al., 2012)	STZ-induced diabetic mice	Borapetoside C	5 mg/kg BW (i.p.), twice daily for 7 days	↑ plasma insulin ↓ plasma glucose and PEPCK	Reducing hepatic gluconeogenesis

	(Ruan et al., 2012)	STZ-induced diabetic mice (150 mg/kg BW)	Borapetoside C	5 mg/kg BW (i.p.), twice daily for 7 days	↑ IR, Akt, and GLUT-2	Enhancing insulin stimulation through the IR/Akt/GLUT-2 pathway
	(Saifudin et al., 2013)	PTP-1B assay	Water and methanolic extracts of stems	25 μg/mL	↓ PTP-1B activity	Inhibiting PTP-1B activity
	(Ruan et al., 2013)	STZ-induced diabetic mice (250 mg/kg BW, i.p.)	Borapetoside A	0.1, 0.3, 1, 3, and 10 mg/kg BW	↑ glycogen	Enhancing insulin signaling through the IR/Akt/AS-160/GLUT-2 pathway and suppressing hepatic gluconeogenesis through PEPCK
		High-fat and fructose-induced diabetic mice			↓ glucose	
		STZ-induced diabetic mice (250 mg/kg BW, i.p.)	Borapetoside A	10 mg/kg BW (i.p), twice daily for 7 days	↑ IR, Akt, AS-160, and GLUT-2	
					↓ PEPCK	
		C2C12 cells	Borapetoside A	10^{-8}, 10^{-7}, and 10^{-6} mol/L	↑ glycogen	
		Hep3B cells	Borapetoside A	10^{-7}, 10^{-6}, and 10^{-5} mol/L	↑ glycogen	
	(Lokman et al., 2013)	Wistar and Goto-Kakizaki rats	Borapetol B	100 μg/kg BW	↑ plasma insulin	Stimulating insulin release
					↓ plasma glucose	
		Rat pancreatic islets		0.1, 1, and 10 μg/mL	↑ insulin release	
	(Abu et al., 2014)	HepG2 cells	Methanolic extracts of stems	N/A	↑ IRS, Akt, GAPDH, and GLUT-4	Enhancing glucose uptake
	(Abu et al., 2015)	HFD-induced diabetic rats	Water extracts of stems	100 mg/kg BW (p.o.) for 8 weeks	↑ insulin and C-peptide	Ameliorating insulin resistance

					↓ adiposity index serum, AST, ALT, TC, TG, blood glucose, resistin, and leptin	
	(H. A. Hamid et al., 2015)	α-amylase and α-glucosidase assay	Borapetoside C	10 μL	↓ α-amylase and α-glucosidase	Inhibiting absorption of glucose at the intestine
2016–2020	(Hassani et al., 2016)	STZ-induced diabetic rats (55 mg/kg BW, i.p.)	Water, methanolic, chloroform, and petroleum ether extracts of stems	1 g/kg BW for 8 days	↑ HDL ↓ glucose, TC, LDL, and TG	N/A
	(Riyanti et al., 2016)	DPP-IV assay	Ethanolic extracts of stems	2.5 μg/mL	↓ DPP-IV activity	Inhibiting DPP-IV activity
	(Gao et al., 2016)	Alloxan-induced diabetic mice	Borapetoside E	20 mg/kg BW for 5 days	↓ blood glucose	N/A
	(Roestamadji et al., 2017)	Alloxan-induced diabetic rats (120 mg/kg BW, i.p.)	Ethanolic extracts of stems	250 mg/kg BW, p.o. for 14 days	↑ fibroblast ↓ blood glucose	Ameliorating traumatic ulcer healing
	(Arundina et al., 2017)	Alloxan-induced diabetic rats (120 mg/kg BW, i.p.)	Ethanolic extracts of stems	250 mg/kg BW, p.o. for 14 days	↑ lymphocyte ↓ blood glucose	Ameliorating traumatic ulcer healing
	(Chayarop et al., 2017)	Nicotinamide (80 mg/kg BW, i.p.) and STZ (65 mg/kg BW, i.v.) induced diabetic rats	Thai herbal formulation that consists of 26 plants extracts, including water extracts and	Water extracts (12.5, 25, and 50 mg/kg BW) and powdered suspensions (87.5, 175, and 350	↑ TG, TP, albumin, and globulin ↓ glucose, TC, ALP, ALT, AST, BUN, creatinine, and uric acid	N/A

			powdered suspensions of stems of *T. crispa*	mg/kg BW), p.o. for 2 weeks		
	(Xu et al., 2017)	HFD-induced mice	Borapetoside E	20 and 40 mg/kg BW, twice daily for 2.5 days	↑ Akt, GSK3β, GLUT-2, insulin sensitivity index, and AMPK ↓ glucose, TG, TC, LDL, FFA, AST, ALT, creatinine, creatinine kinase, and SREBP1	Enhancing glucose uptake and inhibiting SREBP pathway
	(Abu et al., 2017)	IR-HepG2 cells	Methanolic extracts of stems	12, 25, 50, and 100 μg/mL	↑ insulin receptor, Akt, GLUT-4, caspases 3, 8, 9, and Bad	Stimulating insulin sensitivity and enhancing glucose uptake through apoptotic
	(Adnan et al., 2018)	3T3-L1 cells	Tinocrisposide	50, 25, 12.5, and 6.25 μg/mL	↑ lipid droplets accumulation	Enhancing the adipocyte FFA and glucose uptake
	(Khanal et al., 2019)	Docking	Borapetoside C, cordifolioside A, and magnoflorine	N/A	Interacting with majority of protein-related DM pathogenesis	Interacting with majority of proteins related DM pathogenesis

ALP, alkaline phosphatase; ALT, alanine transaminase; AMPK, AMP-activated protein kinase; AST, aspartate transaminase; BUN, blood urea nitrogen; Ca, calcium; DPP-IV, dipeptidyl peptidase-IV; FFA, free fatty acid; GAPDH, glyceraldehyde 3-phosphate dehydrogenase; GLUT, glucose transporter; HDL, high-density lipoprotein; HFD, high-fat diet; IR, insulin receptor; LDL, low-density lipoprotein; N/A, not available; PEPCK, phosphoenolpyruvate carboxykinase; PTP-1B, protein tyrosine phosphatase-1B; SREBP, sterol regulatory-element binding protein; STZ, streptozotocin; TC, total cholesterol; TG, triglyceride; TP, total protein.

Table S2**.** Most impactful countries

No.	Country	Publication	Citation	Average citation per publication
1	Malaysia	6	60	10.00
2	United Kingdom	3	133	44.33
3	Taiwan	3	104	34.67
4	Indonesia	3	31	10.33
5	China	2	22	11.00
6	Thailand	2	12	6.00
7	Japan	1	23	23.00
8	India	1	16	16.00

Table S3. Most prominent institutions

No.	Institution	Country	Publication	Citation	Average citation per publication
1	John Radcliffe Hospital	United Kingdom	4	139	34.75
2	National Taiwan University	Taiwan	3	104	34.67
3	Universiti Putra Malaysia	Malaysia	3	32	10.67
4	Universiti Teknologi Mara	Malaysia	3	10	3.33
5	Biobiopha Co. Ltd.	China	2	22	11.00
6	Chinese Academy of Sciences	China	2	22	11.00
7	South-Central University for Nationalities	China	2	22	11.00
8	Yibin University	China	2	22	11.00
9	Universiti Malaysia Pahang	Malaysia	2	22	11.00
10	Airlangga University	Indonesia	2	16	8.00

Table S4. Most productive sources

No.	Source	Publication	Citation	Average citation per publication
1	Journal of Ethnopharmacology	2	95	47.50
2	Phytomedicine	2	64	32.00
3	Journal of Natural Products	2	55	27.50
4	Evidence-based Complementary and Alternative Medicine	2	30	15.00
5	Journal of International Dental and Medical Research	2	16	8.00
6	Asian Journal of Pharmaceutical and Clinical Research	2	15	7.50

Table S5. Most influential authors

No.	Authors	Publication	Citation	Average citation per publication	Institution/Country	Field	Experiments
1	Noor, H.	4	139	34.75	John Radcliffe Hospital, United Kingdom	Clinical Biochemistry	- Plant material test: water extracts of stems - Model test: HIT-T15 cells, rat islets, human islets, and alloxan - Mechanism: stimulating insulin release and promoting insulinotropic effects
2	Ashcroft, S.J.H.	4	139	34.75	John Radcliffe Hospital, United Kingdom	Clinical Biochemistry	- Plant material test: water extracts of stems - Model test: HIT-T15 cells, rat islets, human islets, and alloxan - Mechanism: stimulating insulin release and promoting insulinotropic effects
3	Lam, S.-H.	3	104	34.67	National Taiwan University, Taiwan	Pharmacy	- Plant material test: borapetoside A and borapetoside C

							- Model test: High-fat, fructose, and sterptozotocin - Mechanism: enhancing insulin stimulation, enhancing insulin signaling, and suppressing hepatic gluconeogenesis
4	Lee, S.-S.	3	104	34.67	National Taiwan University, Taiwan	Pharmacy	- Plant material test: borapetoside A and borapetoside C - Model test: High-fat, fructose, and streptozotocin - Mechanism: enhancing insulin stimulation, enhancing insulin signaling, and suppressing hepatic gluconeogenesis
5	Ruan, C.-T.	3	104	34.67	National Taiwan University, Taiwan	Pharmacology	- Plant material test: borapetoside A and borapetoside C - Model test: High-fat, fructose, and streptozotocin - Mechanism: enhancing insulin stimulation, enhancing insulin signaling, and suppressing hepatic gluconeogenesis
6	Su, M.-J.	3	104	34.67	National Taiwan University, Taiwan	Pharmacology	- Plant material test: borapetoside A and borapetoside C - Model test: High-fat, fructose, and streptozotocin - Mechanism: enhancing insulin stimulation, enhancing insulin signaling, and suppressing hepatic gluconeogenesis

7	Abu, M.N	3	10	3.33	Universiti Teknologi Mara, Malaysia	Health Sciences	- Plant material test: methanolic and water extracts of stems - Model test: HepG2 cells, HepG2 cells, and high-fat diet - Mechanism: stimulating insulin sensitivity, ameliorating insulin resistance, and enhancing glucose uptake

Table S6. Author-based bibliographic network coupling highlights

Cluster	Authors	Topics	Years
Cluster 1 (red nodes)	Fang, Y.-D., Gao, Y., Hai, P., Hu, J., Liu, J., Liu, J.-K., Lu, Y., Niu, Y., Niu, Y.-F., Peng, L., Qin, W., Wang, F., Xiong, W., Xiong, W.-Y., Xu, Y.	Exploring antidiabetic activity and mechanisms of action of borapetoside E through *in vivo* studies using streptozotocin and alloxan-induced mice	2016–2017
Cluster 2 (dark-green nodes)	Ali, A.M., Bastami, M.S., Bohari, S.P.M., Hamid, M., Herunsalee, A., Mustapha, N.M., Noipha, K., Purintrapiban, J., Ratanachaiyavong, S., Shari, K.	Exploring antidiabetic activity and mechanisms of actions of methanolic and water extracts through *in vitro* studies using BRIN-BD11 and L6 myoblasts cells	2008
Cluster 3 (dark-blue nodes)	Chia, K.L., Gu, H.F., Hamid, H.A., Karim, M.R., Liu, M., Lokman, F.E., Wan Mohamud, W.N., Yusoff, M.M., Östenson, C.-G.	Exploring borapetoside E and borapetol B on antidiabetic and its mechanisms through *in vitro* (α-glucosidase and α-amylase testing) and *in vivo* (spontaneous diabetic rats and rat pancreatic islets) studies	2013, 2015
Cluster 4 (yellow nodes)	Abu, M.N., Hassan, H.F., Ismail, W.I.W., Kamarapani, N., Nor Hussein, F., Samat, S., Wan Ismail, W.I., Yusoff, R.	Exploring antidiabetic activity and mechanisms of actions of water extracts through *in vivo* studies using high-fat diet	2015

Cluster 5 (purple nodes)	Arundina, I., Budhy, T.I., Diyatri, I., Irmalia, W.R., Jit, F.Y., Roestamadji, R.I., Sambodo, D.T.	Exploring antidiabetic activity and mechanisms of actions of ethanolic extracts through *in vivo* studies using alloxan	2017
Cluster 6 (Tosca nodes)	Adnan, A.Z., Afriani, T., Fauzana, A., Putra, A.E., Roesma, D.I., Taher, M.	Exploring tinoscrisposide on antidiabetic activity and mechanisms through *in vitro* test using 3T3-L1 cells	2018
Cluster 7 (orange nodes)	Chayarop, K., Chuakul, W., Peungvicha, P., Rojsanga, P., Temsiririrkkul, R., Wongkrajang, Y.	Exploring antidiabetic activity and mechanisms of actions of herbal formulation through *in vivo* studies using streptozotocin-nicotinamide	2017
Cluster 8 (dark-brown nodes)	Chi, T.-C., Hsieh, P.-H., Lam, S.-H., Lee, S.-S., Ruan, C.-T., Su, M.-J.	Exploring antidiabetic activity and mechanisms of actions of borapetoside C through *in vivo* studies using streptozotocin	2012
Cluster 9 (pink nodes)	Ashcroft, S.J.H., Hammonds, P., Noor, H., Sutton, R.	Exploring antidiabetic activity and mechanisms of actions of water extracts through *in vitro* and *in vivo* studies using alloxan, rat islets, HIT-T15 cells, and human islets	1989, 1998
Cluster 10 (light-brown nodes)	Hullatti, K.K., Khanal, P., Mandar, B.K., Patil, B.M.	Exploring antidiabetic activity and mechanisms of actions of cordifolioside A, borapetoside C, and magnoflorine through *in silico* studies using docking	2019
Cluster 11 (light-green nodes)	Ahmad, A., Asmawi, M.Z., Hassani, M.M.R.S., Mahmud, R.	Exploring antidiabetic activity of various extracts through *in vivo* studies using streptozotocin	2016
Cluster 12 (blue-gray nodes)	Riyanti, S., Suganda, A.G., Sukandar, E.Y.	Exploring antidiabetic activity of ethanolic extracts through *in vitro* studies using dipeptidyl peptidase-IV assay	2016

Table S7. Most impactful articles

No.	Authors	Title	Source	Citation
1	Noor and Ashcroft (1998)	Pharmacological characterization of the antihyperglycaemic properties of *Tinospora crispa* extract	Journal of Ethnopharmacology	58
2	Lam et al. (2012)	Hypoglycemic diterpenoids from *Tinospora crispa*	Journal of Natural Products	40
3	Noor et al. (1989)	The hypoglycemic and insulinotropic activity of *Tinospora crispa*: studies with human and rat islets and HIT-T15 B cells	Diabetologia	38
4	Noor and Ashcroft (1989)	Antidiabetic effects of *Tinospora crispa* in rats	Journal of Ethnopharmacology	37
5	Ruan et al. (2012)	Borapetoside C from *Tinospora crispa* improves insulin sensitivity in diabetic mice	Phytomedicine	35
6	Hamid et al. (2015)	α-Glucosidase and α-amylase inhibitory constituents of *Tinospora crispa*: Isolation and chemical profile confirmation by ultra-high performance liquid chromatography-quadrupole time-of-flight/mass spectrometry	Journal of Functional Foods	31
7	Ruan et al. (2013)	Hypoglycemic action of borapetoside A from the plant *Tinospora crispa* in mice	Phytomedicine	29
8	Saifudin et al. (2013)	Protein tyrosine phosphatase 1B inhibitory activity of Indonesian herbal medicines and constituents of *Cinnamomum burmannii* and *Zingiber aromaticum*	Journal of Natural Medicines	23
9	Lokman et al. (2013)	Antidiabetic effect of oral borapetol B compound, isolated from the plant *Tinospora crispa*, by stimulating insulin release	Evidence-based Complementary and Alternative Medicine	21

Table S8. Cited reference-based co-citation network highlights

Cluster	Authors	Title	Year	Cluster themes	Future directions
Cluster 1 (blue nodes)	Bays, H.E.	"Sick fat" metabolic disease, and atherosclerosis	2009	Underlying the mechanism of pathophysiological pathways of diabetes, isolation of phytochemical compounds, and exploration of antidiabetic effects	Extension research topic about mechanisms of actions of antidiabetic and active compounds
	Bays, H.E., Chapman, R.H., Grandy, S., the SHIELD Investigators' Group	The relationship of body mass index to diabetes mellitus, hypertension and dyslipidaemia: comparison of data from two national surveys	2007		
	Bessesen, D.H.	The role of carbohydrates in insulin resistance	2001		
	Cavin, A., Hostettmann, K., Dyatmyko, W., Potterat, O.	Antioxidant and lipophilic constituents of *Tinospora crispa*	1998		
	Chi, T.C., Chen, W.P., Chi, T.L., Kuo, T.F., Lee, S.S., Cheng, J.T., Su, M.J.	Phosphatidylinositol-3-kinase is involved in the antihyperglycemic effect induced by resveratrol in streptozotocin-induced diabetic rats	2007		
	Chou, C.H., Tsai, Y.L., Hou, C.W., Lee, H.H., Chang, W.H., Lin, T.W., Hsu, T.H., Kuo, C.H.,	Glycogen overload by postexercize insulin administration abolished the exercise-induced increase in GLUT-4 protein	2005		
	Choudhary, M.I., Ismail, M., Ali, Z., Shaari, K., Lajis, N.H., Atta-ur, R.	Alkaloidal constituents of *Tinospora crispa*	2010		
	Choudhary, M.I., Ismail, M., Shaari, K., Abbaskhan, A., Sattar, S.A., Lajis, N.H., Atta-ur, R.	Cis-clerodane-type furanoditerpenoids from *Tinospora crispa*	2010		

	Ginsberg, H.N.	Investigation of insulin sensitivity in treated subjects with ketosis-prone diabetes mellitus	1997		
	Granberry, M.C., Hawkins, J.B., Franks, A.M.	Thiazolidinediones in patients with type 2 diabetes mellitus and heart failure	2007		
	Hayashi, K., Kojima, R., Ito, M.	Strain differences in the diabetogenic activity of streptozotocin in mice	2006		
	Hosokawa, M., Dolci, W., Thorens, B.	Differential sensitivity of GLUT-1- and GLUT-2-expressing beta cells to streptozotocin	2001		
	Huang, B.W., Chiang, M.T., Yao, H.T., Chiang, W.	The effect of high-fat and high-fructose diets on glucose tolerance and plasma lipid and leptin levels in rats	2004		
	Jackson, C.	Diabetes: kicking off the insulin cascade	2006		
	Kahn, S.E., Hull, R.L., Utzschneider, K.M.	Mechanisms linking obesity to insulin resistance and type 2 diabetes	2006		
	Kuftinec, D.M., Mayer, J.	Extreme sensitivity of obese hyperglycemic mice to caffeine and coffee	1964		
	Lam, S.H., Ruan, C.T., Hsieh, P.H., Su, M.J., Lee, S.S.	Hypoglycemic diterpenoids from *Tinospora crispa*	2012		
	Lavoie, L., Band, C.J., Kong, M., Bergeron, J.J., Posner, B.I.	Regulation of glycogen synthase in rat hepatocytes. evidence for multiple signaling pathways	1999		
	Martin, T.S., Ohtani, K., Kasai, R., Yamasaki, K.	Furanoid diterpene glucosides from *Tinospora rumphii*	1996		
	Messmer, M.K.	*Tinospora tuberculata* (Lamk) Beumee, an indonesian antipyretic	1961		

	Pachaly, P., Adnan, A.Z., Will, G.	NMR-assignments of n-acylaporphine alkaloids from *Tinospora crispa*	1992		
	Pathak, A.K., Jain, D.C., Sharma, R.P.	Chemistry and biological activities of the genera *Tinospora*	1995		
	Ragasa, C.Y., Cruz, M.C., Gula, R., Rideout, J.A.	Clerodane diterpenes from *Tinospora rumphii*	2000		
	Sadasivam, S., Manickam, A.	Biochemical methods	1996		
	Shulman, G.I.	Cellular mechanisms of insulin resistance	2000		
	Taniguchi, C.M., Ueki, K., Kahn, R.	Complementary roles of IRS-1 and IRS-2 in the hepatic regulation of metabolism	2005		
	Thorens, B., Sarkar, H.K., Kaback, H.R., Lodish, H.F.	Cloning and functional expression in bacteria of a novel glucose transporter present in liver, intestine, kidney, and beta-pancreatic islet cells	1988		
	Vollenweider, P.	Insulin resistant states and insulin signaling	2003		
	Weng, Y.C., Chiu, H.L., Lin, Y.C., Chi, T.C., Kuo, Y.H., Su, M.J.	Antihyperglycemic effect of a caffeamide derivative, ks370g, in normal and diabetic mice	2010		
	Yonemitsu, M., Fukuda, N., Kimura, T.	Studies on the constituents of *Tinospora sinensis*: i. separation and structure of the new phenolic glycoside tinosinen	1993		
	Zafinindra, L.R., Diatta, W., Dieye, A.M., Nongonierma, R., Faye, B., Bassene, E.	Antipyretic effect of aqueous extract and alcaloid of *Tinospora bakis* (Miers) in rabbits	2003		

Cluster 2 (green nodes)	Ali, H., Houghton, P.J., Soumyanath, A.	α-amylase inhibitory activity of some Malaysian plants used to treat diabetes	2006	Revealing the mechanisms of the pathophysiology of diabetes, exploration of the antidiabetic and its mechanisms, isolation of phytochemical compounds, bioavailability of phytochemicals, and drug interaction issues	Extension research topic about isolation methods of *T. crispa* compounds, active compounds as antidiabetics, bioavailability, and drug interaction
	Borges de Melo, E., Gomes, A.S., Carvalho, I.	α-glucosidase and β-glucosidase inhibitors: chemical structure and biological activity	2006		
	Braithwaite, M.C., Tyagi, C., Tomar, L.K., Kumar, F., Choonara, Y.E., Pillay, V.	Nutraceutical-based therapeutics and formulation strategies augmenting their efficiency to complement modern medicine. an overview	2014		
	Cho, M., Han, J.H., You, S.	Inhibitory effects of fucan sulfates on enzymatic hydrolysis of starch	2011		
	Davis, S.N., Granner, D.K.	Oral hypoglycemic agents: Goodman and Gilman's the pharmacological basis of therapeutics	2001		
	Fan, P., Terrier, L., Hay, A.E., Marston, A., Hostettmann, K.	Antioxidant and enzyme inhibition activities and chemical profiles of *Polygonum sachalinensis* F.Schmidt ex Maxim (Polygonaceae)	2010		
	Fukuda, N., Yonemitsu, M., Kimura, T.	Isolation and structure elucidation of the five new furanoid diterpene glycoside borapetoside c-g	1993		
	Husain, K., Jamal, J.A., Jalil, J.	Phytochemical study of *Cananga odorata* (Lam) Hook. f. & Thomson & Thoms (Annonaceae)	2012		
	Husain, K., Jamal, J.A., Jalil, J.	Phytochemical study of *Cananga odorata* (Lam) Hook. f. & Thomson & Thoms (Annonaceae)	2012		
	Josse, R.G., Chiasson, J.-L., Ryan, E.D., Lau, D.C.W., Ross, S.A., Yale, J.F., Leiter, L.A., Meneilly, G.S.,	Acarbose in the treatment of elderly patients with type 2 diabetes	2003		

	Khaleque, A., Maith, M.A.W., Huq, M.S., Basar, K.A.	*Tinospora cordifolia*. isolation heptacosanol, β-sitosterol and three other compounds tinosporine, cordifol and cordifolone	1970		
	Kim, J.S., Kwon, C.S., Son, K.H.	Inhibition of α-glucosidase and amylase by luteolin, a flavonoid	2000		
	Kumar, S., Kumar, V., Prakash, O.	Enzymes inhibition and antidiabetic effect of isolated constituents from *Dillenia indica*	2013		
	Mitrakou, A., Kelley, D., Mokan, M., Veneman, T., Pangburn, T., Reilly, J., Gerich, J.	Role of reduced suppression of glucose production and diminished early insulin release in impaired glucose tolerance	1992		
	Noor, H., Ashcroft, S.J.	Antidiabetic effects of *Tinospora crispa* in rats	1989		
	Patel, M.B., Mishra, S.	Hypoglycemic activity of alkaloidal fraction of *Tinospora cordifolia*	2011		
	Porte, D., Kahn, S.E.	Beta cell dysfunction and failure in type 2 diabetes: potential mechanisms	2001		
	Ruan, C.T., Lam, S.H., Chi, T.C., Lee, S.S., Su, M.J.	Borapetoside c from Tinospora crispa improves insulin sensitivity in diabetic mice	2012		
	Ruan, C.T., Lam, S.H., Chi, T.C., Lee, S.S., Su, M.J.	Hypoglycemic action of borapetoside a from the plant *Tinospora crispa* in mice	2013		
	Sang, S.	Bioavailability and metabolism of bioactive components	2014		
	Shu, X.S., Lv, J.H., Tao, J., Li, G.M., Li, H.D., Ma, N.	Antihyperglycemic effects of total flavonoids from *Polygonatum odoratum* in STZ and alloxan-induced diabetic rats	2009		

	Sogaard-andersen, L., Valentin-hansen, P.	Protein-protein interactions in gene regulation: the camp-crp complex sets the specificity of a second DNA-binding protein, the cytr repressor	1993		
	Sri Fatmawati, S., Kondo, R.	Ganoderol b: a potent α-glucosidase inhibitor isolated from the fruiting body of *Ganoderma lucidu*	2011		
	Subramaniam, R., Asmawi, M.Z., Sadikun, A.	*In vitro* α-glucosidase and α-amylase enzyme inhibitory effects of *Andrographis paniculata* extract and andrographolide	2008		
	Svensson, E.I., Kristoffersen, L., Oskarsson, K., Bensch, S.	Molecular population divergence and sexual selection on morphology in the banded demoiselle (*Calopteryx splendens*)	2004		
	Teeri, T.T.	Engineering of enzymes of carbohydrate metabolism	1991		
	Thamilvaani, M., David, A., Hwee, M.C., Uma, D.P.	Flavonoids isolated from *Syzygium aqueum* leaf extract as potential antihyperglycaemic agents	2012		
	Wagner, H., Ulrich-Merzenich, G.	Synergy research: approaching a new generation of phytopharmaceuticals	2009		
	Wang, H., Du, Y.J., Song, H.C.	α-glucosidase and α-amylase inhibitory activities of guava leaves	2010		
	Yusoff, M., Hamid, H., Houghton, P.	Anticholinesterase inhibitory activity of quaternary alkaloids from *Tinospora crispa*	2014		
Cluster 3 (red nodes)	Bottini, N., Vang, T., Cucca, F., Mustelin, T.	Role of PTPN22 in type 1 diabetes and other autoimmune diseases	2006	Revealing the mechanisms of the pathophysiology of diabetes and	Extension research issue about the molecular mechanisms of the pathophysiology of
	Chen, A.C., Arany, P.R., Huang, Y.Y., Tomkinson, E.M.,	Low-level laser therapy activates NF-κB via generation of reactive oxygen	2011		

	Sharma, S.K., Kharkwal, G.B., Saleem, T., Hamblin, M.R.	species in mouse embryonic fibroblasts		antidiabetic activity experiments	diabetes and *T. crispa* against diabetes
	Chi, T.C., Lee, S.S., Su, M.J.	Antihyperglycemic effect of aporphines and their derivatives in normal and diabetic rats	2006		
	Davis, R.C., Castellani, L.W., Hosseini, M., Ben-zeev, O., Mao, H.Z., Weinstein, M.M., Jung, D.Y., Peterfy, M.	Early hepatic insulin resistance precedes the onset of diabetes in obese C57BLKS-db/db mice	2010		
	Eldar-finkelman, H., Schreyer, S.A., Shinohara, M.M., Leboeuf, R.C., Krebs, E.G.	Increased glycogen synthase kinase-3 activity in diabetes- and obesity-prone C57BL/6J mice	1999		
	Gould, G.W., Bell, G.I.	Facilitative glucose transporters: an expanding family	1990		
	Hollenbeck, C., Reaven, G.M.	Variations in insulin-stimulated glucose uptake in healthy individuals with normal glucose tolerance	1987		
	Jaiswal, D., Kumar Rai, P., Kumar, S., Mehta, S., Watal, G.	Effect of *Moringa oleifera* lam. leaves aqueous extract therapy on hyperglycemic rats	2009		
	Jong-yuh, C., Mei-fen, S.	Potential hypoglycemic effects of chlorella in streptozotocin-induced diabetic mice	2005		
	Kadir, F.A., Othman, F., Abdulla, M.A., Hussan, F., Hassandarvish, P.	Effect of *Tinospora crispa* on thioacetamide-induced liver cirrhosis in rats	2011		

	Kim, J.O., Kim, K.S., Lee, G.D., Kwon, J.H.	Antihyperglycemic and antioxidative effects of new herbal formula in streptozotocin-induced diabetic rats	2009		
	Kim, T., Davis, J., Zhang, A.J., He, X., Mathews, S.T.	Curcumin activates AMPK and suppresses gluconeogenic gene expression in hepatoma cells	2009		
	Kongkathip, N., Dhumma-upakorn, P., Kongkathip, B., Chawananoraset, K., sangchomkaeo, P., Hatthakitpanichakul, S.	Study on cardiac contractility of cycloeucalenol and cycloeucalenone isolated from *Tinospora crispa*	2002		
	Lam, S.H., Ruan, C.T., Hsieh, P.H., Su, M.J., Lee, S.S.	Hypoglycemic diterpenoids from *Tinospora crispa*	2012		
	Leahy, J.L.	Pathogenesis of type 2 diabetes mellitus	2005		
	Najib Nik, A.R.N., Furuta, T., Kojima, S., Takane, K., Ali Mohd, M.	Antimalarial activity of extracts of malaysian medicinal plants	1999		
	Noor, H., Ashcroft, S.J.H.	Antidiabetic effects of *Tinospora crispa* in rats	1989		
	Noor, H., Ashcroft, S.J.	Pharmacological characterization of the antihyperglycaemic properties of *Tinospora crisp*a extract	1998		
	Noor, H., Hammonds, P., Sutton, R., Ashcroft, S.J.	The hypoglycemic and insulinotropic activity of *Tinospora crispa*: studies with human and rat islets and HIT-T15 B cells	1989		

	Park, S.H., Ko, S.K., Chung, S.H.	*Euonymus alatus* prevents the hyperglycemia and hyperlipidemia induced by high-fat diet in ICR mice	2005		
	Patel, N., Huang, C., Klip, A.	Cellular location of insulin-triggered signals and implications for glucose uptake	2006		
	Pilkis, S.J., Granner, D.K.	Molecular physiology of the regulation of hepatic gluconeogenesis and glycolysis	1992		
	Rungruang, T., Boonmars, T.	*In vivo* antiparasitic activity of the Thai traditional medicine plant *Tinospora crispa* against *Plasmodium yoelii*	2009		
	Savage, D.B., Zhai, L., Ravikumar, B., Choi, C.S., Snaar, J.E., Mcguire, A.C., Wou, S.E., Depaoli-roach, A.A.	A prevalent variant in PPP1R3A impairs glycogen synthesis and reduces muscle glycogen content in humans and mice	2008		
	Sultan, K.R., Henkel, B., Terlou, M., Haagsman, H.P.	Quantification of hormone-induced atrophy of large myotubes from C2C12 and l6 cells: atrophy-inducible and atrophy-resistant C2C12 myotubes	2006		
	Tzeng, T.F., Liu, I.M., Cheng, J.T.	Activation of opioid mu-receptors by loperamide to improve interleukin-6-induced inhibition of insulin signals in myoblast C2C12 cells	2005		
	Warren, R.E.	The stepwise approach to the management of type 2 diabetes	2004		
	Weng, Y.C., Chiu, H.L., Lin, Y.C., Chi, T.C., Kuo, y.h., su, M.J.	Antihyperglycemic effect of a caffeamide derivative, ks370g, in normal and diabetic mice	2010		

	Yong, J., Rasooly, J., Dang, H., Lu, Y., Middleton, B., Zhang, Z., Hon, L., Kaufman, D.L.	Multimodality imaging of beta cells in mouse models of type 1 and 2 diabetes	2011		

Table S9. All keyword-based keyword co-occurrence network highlights

Clusters	Keywords	Themes
Cluster 1 (Red Nodes/ 31 items)	Animal tissue, borapetol B, borapetoside A, borapetoside B, borapetoside C, borapetoside E, diabetic mice, diterpenoid, drug isolation, drug mechanism, gluconeogenesis, GLUT-2, glycogen, hypoglycemia, in vivo study, insulin dependent diabetes mellitus, insulin receptor, insulin resistance, insulin sensitivity, liver, metformin, mice, non-insulin dependent diabetes mellitus, protein expression, protein kinase B, protein phosphorylation, signal transduction, skeletal muscle, structure activity relation, tinospora, type 2 diabetes mellitus	This cluster revealed about phytochemical compounds which tested, subjects related to pharmacological experiment of DM such as targets of action, and general fields of diabetes mellitus
Cluster 2 (Green Nodes/ 26 Items)	Acute toxicity, alanine aminotransferase, alcohol, animal model, antidiabetic activity, antidiabetic agent, body weight, chemistry, cholesterol, dose response, drug effect, drug efficacy, glibenclamide, glucose tolerance test, herbal formula, insulin blood level, isolation and purification, lipid diet, metabolism, obesity, phytotherapy, rats, Sprague Dawley rats, streptozotocin, traditional medicine, triacylglycerol	This cluster showed about pharmacological experiment of DM such as targets of action, general fields of diabetes mellitus
Cluster 3 (Dark Blue Nodes/ 20 Items)	*Andrographis paniculata*, bark, drug evaluation, drug screening, fruit, IC_{50}, *in vitro* study, insulin like activity, leaf, Malaysia, medicinal plant, methanol, molecular structure, *Momordica charantia*, nonhuman, plant extract, pomegranate extract, sitagliptin, stem, water	This cluster demonstrated extraction, other plants, and drug screening
Cluster 4 (Yellow Nodes/ 16 Items)	Animal cell, apoptosis, Ca^{2+}, calcium cell level, cell line, drug activity, glucose, glucose transport, human, human cell, insulin, insulin release, insulin secretion, insulinotropic, pancreas islet, pancreas islet beta cell	This cluster exhibited target of actions and pharmacological related diabetes mellitus
Cluster 5 (Purple Nodes/ 4 Items)	Diabetes mellitus, *Tinospora crispa*, traumatic ulcer, wound healing	This cluster described other disorders related to diabetes mellitus

References

Abu, M. N., Hassan, H. F., Yusoff, R., & Ismail, W. I. W. (2017). *Tinospora crispa* methanolic crude extract activates apoptotic pathway of insulin resistant-HepG2 cell lines by improving the insulin sensitivity. *Malaysian Applied Biology*, *46*(4), 145–152. https://doi.org/10.13140/RG.2.2.23644.28809

Abu, M. N., Ismail, W. I. W., Wan Yusoff, W. S. Y., Mustapha, M. H., Peter, R. P., Lokman, N., Yusoff, R., & Fansuri Hassan, H. (2014). Mechanism of apoptosis induced in hepatoma G2 (HepG2) cell lines by *Tinospora crispa*: Targeting signalling of the insulin-like growth factor (IGF) system and the insulin signalling (IS) pathway. *Asian Pacific Journal of Tropical Disease*, *4*(3), 237. https://doi.org/10.1016/S2222-1808(14)60539-9

Abu, M. N., Samat, S., Kamarapani, N., Nor Hussein, F., Wan Ismail, W. I., & Hassan, H. F. (2015). *Tinospora crispa* Ameliorates Insulin Resistance Induced by High Fat Diet in Wistar Rats. *Evidence-Based Complementary and Alternative Medicine*, *2015*, 1–6. https://doi.org/10.1155/2015/985042

Adnan, A. Z., Taher, M., Fauzana, A., Afriani, T., Imelda Roesma, D., & Putra, A. E. (2018). Antihyperglycemic activity of tinocrisposide by stimulating 3T3-L1 adipocyte cell differentiation. *Asian Journal of Pharmaceutical and Clinical Research*, *11*(11), 494–498. https://doi.org/10.22159/ajpcr.2018.v11i11.29304

Arundina, I., Diyatri, I., Budhy, T. I., & Jit, F. Y. (2017). The effect of Brotowali stem extract (*Tinospora crispa*) towards increasing number of lymphocytes in the healing process of traumatic ulcer on diabetic Wistar Rat. *Journal of International Dental and Medical Research*, *10*(3), 975–980.

Chayarop, K., Peungvicha, P., Temsiririrkkul, R., Wongkrajang, Y., Chuakul, W., & Rojsanga, P. (2017). Hypoglycaemic activity of Mathurameha, a Thai traditional herbal formula aqueous extract, and its effect on biochemical profiles of streptozotocin-nicotinamide-induced diabetic rats. *BMC Complementary and Alternative Medicine*, *17*(1). Scopus. https://doi.org/10.1186/s12906-017-1851-8

Gao, Y., Niu, Y.-F., Wang, F., Hai, P., Wang, F., Fang, Y.-D., Xiong, W.-Y., & Liu, J.-K. (2016). Clerodane Diterpenoids with Anti-hyperglycemic Activity from *Tinospora crispa*. *Natural Products and Bioprospecting*, *6*(5), 247–255. https://doi.org/10.1007/s13659-016-0109-3

Hamid, H. A., Yusoff, M. M., Liu, M., & Karim, M. R. (2015). α-Glucosidase and α-amylase inhibitory constituents of *Tinospora crispa*: Isolation and chemical profile confirmation by ultra-high performance liquid chromatography-quadrupole time-of-flight/mass spectrometry. *Journal of Functional Foods*, *16*, 74–80. https://doi.org/10.1016/j.jff.2015.04.011

Hamid, M., Bohari, S. P. M., Bastami, M. S., Ali, A. M., Mustapha, N. M., & Shari, K. (2008). Evaluation of the insulinotrophic activity of Malaysian traditional plants extract. *Journal of Biological Sciences*, *8*(1), 201–204. Scopus. https://doi.org/10.3923/jbs.2008.201.204

Hassani, M. M. R. S., Ahmad, A., Asmawi, Mohd. Z., & Mahmud, R. (2016). Preliminary invesigation of normoglycemic, anti-hyperglycemic, and dyslipidemic activities of different extracts of *Tinospora crispa* on diabetic rat. *Acta Poloniae Pharmaceutica ñ Drug Research*, *73*(1), 129–134.

Khanal, P., Mandar, B. K., Patil, B. M., & Hullatti, K. K. (2019). In silico Antidiabetic Screening of Borapetoside C, Cordifolioside A and Magnoflorine. *Indian Journal of Pharmaceutical Sciences*, *81*(3), 550–555. https://doi.org/10.36468/pharmaceutical-sciences.543

Lam, S.-H., Ruan, C.-T., Hsieh, P.-H., Su, M.-J., & Lee, S.-S. (2012). Hypoglycemic Diterpenoids from *Tinospora crispa*. *Journal of Natural Products*, *75*(2), 153–159. https://doi.org/10.1021/np200692v

Lokman, F. E., Gu, H. F., Wan Mohamud, W. N., Yusoff, M. M., Chia, K. L., & Östenson, C.-G. (2013). Antidiabetic effect of oral borapetol B compound, isolated from the plant *Tinospora crispa*, by stimulating insulin release. *Evidence-Based Complementary and Alternative Medicine*, *2013*, 1–7. https://doi.org/10.1155/2013/727602

Noipha, K., Purintrapiban, J., Herunsalee, A., & Ratanachaiyavong, S. (2008). In vitro glucose uptake activity of *Tinospora crispa* in skeletal muscle cells. *Asian Biomedicine*, *2*(5).

Noor, H., & Ashcroft, S. J. H. (1989). Antidiabetic effects of *Tinospora crispa* in rats. *Journal of Ethnopharmacology*, *27*, 149–161.

Noor, H., & Ashcroft, S. J. H. (1998a). Insulinotropic activity of *Tinospora crispa* extract: Effect on ß-cell Ca2+ handling. *Phytotherapy Research*, *12*, 98–102.

Noor, H., & Ashcroft, S. J. H. (1998b). Pharmacological characterisation of the antihyperglycaemic properties of *Tinospora crispa* extract. *Journal of Ethnopharmacology*, *62*(1), 7–13. https://doi.org/10.1016/S0378-8741(98)00008-7

Noor, H., Hammonds, P., Sutton, R., & Ashcroft, S. J. H. (1989). The hypoglycaemic and insulinotropic activity of *Tinospora crispa*: Studies with human and rat islets and HIT-T15 B cells. *Diabetologia*, *32*(6), 354–359. https://doi.org/10.1007/BF00277258

Riyanti, S., Suganda, A. G., & Sukandar, E. Y. (2016). Dipeptidyl peptidase-IV inhibitory activity of some Indonesian medicinal plants. *Asian Journal of Pharmaceutical and Clinical Research*, *9*(2), 375–377. Scopus.

Roestamadji, R. I., Arundina, I., Diyatri, I., Sambodo, D. T., & Irmalia, W. R. (2017). Brotowali extract (*Tinospora crispa*) for oral traumatic ulcer in diabetes mellitus Wistar Rat. *Journal of International Dental and Medical Research*, *10*(3), 991–996.

Ruan, C.-T., Lam, S.-H., Chi, T.-C., Lee, S.-S., & Su, M.-J. (2012). Borapetoside C from *Tinospora crispa* improves insulin sensitivity in diabetic mice. *Phytomedicine*, *19*(8–9), 719–724. https://doi.org/10.1016/j.phymed.2012.03.009

Ruan, C.-T., Lam, S.-H., Lee, S.-S., & Su, M.-J. (2013). Hypoglycemic action of borapetoside A from the plant *Tinospora crispa* in mice. *Phytomedicine*, *20*(8–9), 667–675. https://doi.org/10.1016/j.phymed.2013.02.009

Saifudin, A., Kadota, S., & Tezuka, Y. (2013). Protein tyrosine phosphatase 1B inhibitory activity of Indonesian herbal medicines and constituents of *Cinnamomum burmannii* and *Zingiber aromaticum*. *Journal of Natural Medicines*, *67*(2), 264–270. Scopus. https://doi.org/10.1007/s11418-012-0674-7

Xu, Y., Niu, Y., Gao, Y., Wang, F., Qin, W., Lu, Y., Hu, J., Peng, L., Liu, J., & Xiong, W. (2017). Borapetoside E, a clerodane diterpenoid extracted from *Tinospora crispa*, improves hyperglycemia and hyperlipidemia in high-fat-diet-induced type 2 diabetes mice. *Journal of Natural Products*, *80*(8), 2319–2327. https://doi.org/10.1021/acs.jnatprod.7b00365