Table 1. List of TRPA1 channel modulators

Compound Name	Type of the Modulator	EC_{50}	Isoform and expression system	Modulation of other TRP's	References
1-hexanol **1-heptanol** **1-octanol**	Non-electrophilic activator	7.9 ± 0.9mM 2.7 ± 0.4 mM 0.81±0.02mM	hTRPA1, HEK293T	Unknown	(Komatsu, Uchida, Fujita, Zhou, & Tominaga, 2012)
2-chloro-N-(4-(4-methoxyphenyl)thiazol-2-yl)-N-(3-methoxypropyl)acetamide, (JT010)	Electrophilic agonist	0.65nM 47nM	mTRPA1, HEK293T hTRPA1, HEK293T	Unknown	(Takaya et al., 2015) (Heber et al., 2019)
4-hydroxynonenal (or Trans-4-hydroxy-2-nonenal or 4-HNE or HNE)	Electrophilic agonist	20 ± 3µM 13 µM 27 µM 9.9 ± 1.2 µM 6.6 ± 1.5 µM 6.0 ± 0.8 µM	mTRPA1, CHO mTRPA1, CHO mTRPA1, HEK293T hTRPA1, HEK293T mTRPA1, HEK293T rTRPA1, HEK293T	No effect on TRPV1	(Andersson, Gentry, Moss, & Bevan, 2008) (Macpherson et al., 2007) (Trevisani et al., 2007) (Bianchi et al., 2012) (Trevisani et al., 2007)
5-nitro-2-(3-phenylpropylamino)	Non-electrophilic	0.32 µM	hTRPA1, HEK293T	Unknown	(Liu, Samuel, Ho,

benzoic acid (NPPB)	activator				Harrison, & Paslay, 2010)
6-gingerol	Non-electrophilic agonist	10.4 ± 0.03 μM	rTRPA1, HEK293T	Unknown	(Morera et al., 2012)
Acrolein	Electrophilic agonist	5 ± 1 μM 85 ± 9 μM 0.8 μM	hTRPA1, oocytes hTRPA1, WI-38 fibroblasts rTRPA1, HEK293T	Unknown	(Bautista et al., 2006) (Hu et al., 2010) (Andrè et al., 2008)
Allicin	Electrophilic agonist	1.3 μM 51 μM 1.9 μM 7.5 ± 0.4 μM	mTRPA1, CHO rTRPA1, CHO hTRPA1, CHO hTRPA1, oocytes	TRPV1 (+)	(Macpherson et al., 2005) (Macpherson et al., 2005) (Macpherson et al., 2005) (Bautista et al., 2005b)
Allyl isothiocyanate (AITC)	Electrophilic agonist	64 ± 3 μM 11 ± 1 μM 22 ± 3 μM	hTRPA1, oocytes rTRPA1, oocytes mTRPA1, CHO	Unknown	(Hinman et al., 2006) (Jordt et al., 2004) (Bandell et al., 2004)
Apomorphine	Non-electrophilic	7.1 μM	hTRPA1, HEK293T	Unknown	(Schulze, Oehler, Urban,

	activator				Schaefer, & Hill, 2013)
Arachidonic acid	Activator	13 ± 4 μM	hTRPA1, HEK293T	TRPV4 (+)	(Redmond, Gu, Camo, McIntyre, & Connor, 2014) (H. Watanabe et al., 2003)
Artepillin C	Activator	1.8 μM	hTRPA1, HEK293T	Unknown	(Hata et al., 2012)
Caffeine	Bimodal action	96 ± 11 μM 62 ± 3 μM - 1-2.5mM	rTRPA1 mTRPA1 hTRPA1, HEK293T mTRPA1, HEK293T	Unknown	(Bianchi et al., 2012) (Nagatomo & Kubo, 2008)
Camphor	Bimodal action	≤ 300 μM	rTRPA1, HEK293 mTRPA1, CHO,	TRPV1 (+), TRPV3 (+), TRPM8 (+)	(Xu, Blair, & Clapham, 2005) (Alpizar et al., 2013) (Moqrich et al., 2016; Selescu, Ciobanu, Dobre, Reid, & Babes, 2013; Xu et al., 2005)

Capsiate **Dihydrocapsiate** **Nordihydrocapsiate**	Activators (unknown mechanism)	2.76 ± 0.08 µM 2.9 ± 0.2 µM 2.82 ± 0.16 µM	hTRPA1, HEK293T hTRPA1, HEK293T hTRPA1, HEK293T	TRPV1 (+)	(Shintaku et al., 2012) (Iida et al., 2003)
Carbon dioxide	Electrophilic agonist	-	hTRPA1, HEK293	Unknown	(Y. Y. Wang, Chang, & Liman, 2010)
Carvacrol	Non-electrophilic agonist	0.75 ± 0.11mM 7 µM	WC frog TRPA1, oocytes hTRPA1, HEK293T	Unknown	(Saito et al., 2012) (Lee et al., 2008)
Chlorobenzylidene malononitrile	Electrophilic agonist	0.9nM 0.214 µM 0.7nM	hTRPA1, HEK293-T-Rex hTRPA1, HEK293-T-Rex hTRPA1, HEK293-T-Rex	Unknown	(Brône et al., 2008) (Nyman et al., 2013)
Cinnamaldehyde	Electrophilic agonist	61 ± 9 µM 250 ± 150 µM 400 ± 40 µM	mTRPA1, CHO mTRPA1, CHO hTRPA1	Unknown	(Bandell et al., 2004) (Alpizar et al., 2013)

					(Hu et al., 2010)
Crotalphine	Electrophilic agonist	0.046 µM	hTRPA1, mTRPA1, rTRPA1	Unknown	(Bressan et al., 2016)
Curcumin	Electrophilic agonist	3.3 µM	rTRPA1, HEK293T	TRPV1 (-), No effect on TRPV1	(Nalli, Ortar, Schiano Moriello, Di Marzo, & De Petrocellis, 2017; Yeon et al., 2010)
Diallyl disulfides	Electrophilic agonist	192 ± 3 µM 7.6 µM	hTRPA1, oocytes hTRPA1, CHO T-Rex	TRPV1 (+)	(Bautista et al., 2005b) (Koizumi et al., 2009)
Diallyl sulfides **Diallyl trisulfide**	Electrophilic agonist	254 µM 0.49 µM	hTRPA1, CHO T-Rex hTRPA1, CHO T-Rex	TRPV1 (+)	(Koizumi et al., 2009)
Diclofenac	Non-electrophilic agonist	210 ± 20 µM	hTRPA1, WI-38 fibroblasts	TRPM3 (+)	(Hu et al., 2010) (Suzuki et al., 2016)
Eugenol	Agonist	260 µM	hTRPA1, HEK293T	Unknown	(Chung et al., 2014)
Formaldehyde	Electrophilic agonist	357 µM ~200 µM	mTRPA1, CHO hTRPA1, HEK293T	Unknown	(Macpherson et al., 2007) (McNamara et al., 2007)

			rTRPA1, HEK293T		
Hypochlorite	Electrophilic activator	11 ± 1 ppm 7 ± 1 ppm	hTRPA1 mTRPA1, HEK293T	Unknown	(Bessac & Jordt, 2008)
Icilin	Bimodal action	<25 μM	-	TRPM8 (+), TRPV3 (-)	(Ding, Gomez, Werkheiser, Cowan, & Rawls, 2008) (Story et al., 2003) (McKemy, Neuhausser, & Julius, 2002; Sherkheli, Gisselmann, & Hatt, 2012)
Iodoacetamide (IA)	Electrophilic agonist	357 μM	mTRPA1, CHO	Unknown	(Macpherson et al., 2007)
Lidocaine	Non-electrophilic activator	5.7 ± 0.2mM 24 ± 0.6mM	rTRPA1, HEK293T hTRPA1, HEK293T	Unknown	(Leffler et al., 2011)
Ligustilide	Bimodal activator	44 μM	mTRPA1, CHO	No effect on TRPM8	(Zhong et al., 2011)
Menthol	Bimodal action	95 ± 15 μM	mTRPA1, CHO	TRPM8 (+)	(Yuji Karashima et al.,

		- 278 ± 30 μM 5.2 ± 0.7 μM 7.1 ± 1.1 μM	mTRPA1, CHO hTRPA1, HEK293T mTRPA1, HEK293T rTRPA1, HEK293T		2007) (Macpherson et al., 2006) (Bianchi et al., 2012) (Peier et al., 2002)
Methyl Parabens	Non-electrophilic activator	4.4mM	hTRPA1, mTRPA1 HEK293	Unknown	(F. Fujita et al., 2007)
Methyl p-hydroxybenzoate	Non-electrophilic activator	4.4mM	mTRPA1, HEK293T	Unknown	(F. Fujita et al., 2007)
Methyl Salicylate	Electrophilic agonist	-	mTRPA1, CHO	TRPV1 (+)	(Bandell et al., 2004) (Ohta, Imagawa, & Ito, 2009)
Methyl syringate	Electrophilic agonist	510 μM	hTRPA1, Flp-In 293	Unknown	(Son et al., 2012)
Methylglyoxal	Electrophilic agonist	700 ± 0.1 μM	hTRPA1, HEK293	No effect on TRPV1	(Eberhardt et al., 2012)
Ozone	Electrophilic agonist	3 μM	hTRPA1, HEK293T	No effect on TRPV1	(Taylor-Clark & Undem, 2010)

para-benzoquinone (pBQN)	Electrophilic agonist	0.36 ± 0.02 µM 0.44 ± 0.02 µM 3.2 ± 0.6 µM	mTRPA1 mTRPA1, CHO mTRPA1, CHO	Unknown	(Andersson et al., 2011)
PF-4840154	Non-electrophilic agonist	97 ± 5nM 23± 0.06nM	rTRPA1 hTRPA1	Unknown	(Ryckmans et al., 2011)
Plumbagin **Boropinal A** **Uglone**	Electrophilic agonist	0.46 ± 0.05µM 10 ± 3µM 1.7 ± 0.5 µM	hTRPA1, HEK293 hTRPA1, HEK293 hTRPA1, HEK293	Unknown	(Hill et al., 2016)
Polyunsaturated fatty acids (PUFAs)	Non-electrophilic activator	41 µM	rTRPA1	TRPM8 (+)	(Motter & Ahern, 2012) (Andersson, Nash, & Bevan, 2007)
Propofol (2,6-diisopropylphenol)	Non-electrophilic activator	65.4 µM 2.4 µM 17 µM	hTRPA1, HEK293 mTRPA1, CHO mTRPA1	TRPC5 (+), TRPV1 (+)	(Nishimoto, Kashio, & Tominaga, 2015) (Y. Karashima & Hoka, 2011)

					(Woll et al., 2017) (Bahnasi et al., 2008; Fischer et al., 2010)
Prostaglandins (PG) 15-deoxy-delta(12,14)-prostaglandin J2	Electrophilic agonist	5.6 ± 1.1 µM 40 ± 16 µM 60 ± 20 µM 5.4 ± 1.1 µM	mTRPA1, CHO hTRPA1, HEK293T mTRPA1, HEK293T rTRPA1, HEK293T	TRPV1 (+), TRPV3 (+)	(Andersson et al., 2008) (Bianchi et al., 2012)
ROS (H_2O_2)	Electrophilic agonist	1200 ± 400 (at 90 s) µM 230 (at 600 s) µM 290 ± 90 µM 297 ± 9 µM	mTRPA1, CHO mTRPA1, CHO hTRPA1, HEK293T mTRPA1, HEK293T	Unknown	(Andersson et al., 2008) Same as above (Bessac & Jordt, 2008) (Sawada, Hosokawa, Matsumura, & Kobayashi, 2008)

Thymol	Non-electrophilic activator	64 μM 127 μM 20 μM < 100 μM	hTRPA1, HEK293T hTRPA1, HEK293T hTRPA1, HEK293T mTRPA1, CHO	Unknown	(Lee et al., 2008) (Yuji Karashima et al., 2007)
Toluene diisocyanate	Electrophilic agonist	10mM	hTRPA1, HEK293T	TRPM8 (+)	(Taylor-Clark, Kiros, Carr, & McAlexander, 2009) (J. H. Kim et al., 2017)
Δ9 tetra-hydro cannabinol	Electrophilic agonist	12 ± 2 μM 0.23 ± 0.03 μM	rTRPA1, oocytes rTRPA1, HEK293T	Unknown	(Jordt et al., 2004) (De Petrocellis et al., 2008)

mTRPA1- mouse TRPA1, hTRPA1- human TRPA1, rTRPA1-rat TRPA1

(+) represents activation of the respective channel
(-) represents inhibition of the respective channel

Table 2. List of TRPA1 agonists involved in management of obesity and related complications

Compound	Pathways targeted	Probable mechanism	TRPA1 contribution	References
4-HNE	Anti-diabetic	a. Enhanced insulin secretion	TRPA1 mediated	(Cao et al., 2012; Numazawa et al., 2012)
Acrolein	Gastric functions	a. Activation of serotonergic pathway	Unknown	(Doihara et al., 2009)
AITC	1.Gastric functions 2.Transepithelial ion transport 3.BAT thermogenesis 4.Anti-obesity	a. Activation of serotonergic pathway b. Increased short circuit current in the duodenum c. Upregulation of UCP1 d. Gut hormone secretion (CCK due to calcium ion influx) e. Stimulation of GLP-1 secretion f. Enhanced insulin secretion	Unknown TRPA1 mediated TRPA1 mediated TRPA1 mediated	(Doihara et al., 2009) (Fothergill et al., 2016b) (Iwasaki et al., 2008) (Purhonen et al., 2008)

	5.Anti-diabetic	g. Better glucose homeostasis and insulin sensitivity	TRPA1 mediated Unknown Unknown	(Emery et al., 2015) (Cao et al., 2012) (Ahn et al., 2014)
Carvacrol	Anti-diabetic	a. Enhanced GLP-1 secretion	TRPA1 mediated	(Emery et al., 2015)
Cinnamaldehyde	1.Gastric functions 2.Transepithelial Ion transport 3.BAT thermogenesis 4.Energy expenditure 5.Anti-obesity	a. Activation of serotonergic pathway b. Increased short circuit current in the duodenum c. Upregulation of UCP1 protein d. Post-prandial fat oxidation e. Ghrelin secretion modulation f. PYY secretion modulation g. Enhanced Insulin secretion	Unknown TRPA1 mediated TRPA1 mediated Unknown	(Doihara et al., 2009) (Fothergill et al., 2016b) (Tamura et al., 2012) (Iwasaki et al., 2008) (Michlig et al., 2016) (Camacho et al., 2015; M. J.

	6.Anti-diabetic	h. Low liver fat i. High expression of PEPCK, GLUT4 and PPAR-γ	Unknown TRPA1 mediated Unknown	Kim et al., 2013) (Anand et al., 2010; S. H. Kim & Choung, 2010; Sartorius et al., 2014)
Eugenol	Gastric functions	a. Activation of serotonergic pathway	Unknown	(Doihara et al., 2009)
Garlic	Anti-obesity	a. Increased UCP1 expression	Unknown	(Kagawa et al., 2019)
Gingerol	Anti-obesity	a. Stimulation of 5-HT and CCK	TRPA1 mediated	(YANG et al., 2016)
Kaempferia extract	Anti-obesity	a. Enhanced energy expenditure	Unknown	(Matsushita et al., 2015)
Methyl syringate	Anti-obesity	a. Less ghrelin secretion	Unknown	(M. J. Kim et al., 2013)
Oleuropein	BAT thermogenesis	a. Upregulation of UCP1 protein	TRPA1 mediated	(Oi-Kano et al., 2017)
Prostaglandins	Anti-diabetic	a. Enhanced insulin secretion	Unknown	(Cao et al., 2012)
PUFA	Anti-obesity	a. Stimulation of CCK	TRPA1 mediated	(Motter & Ahern, 2012)

	Anti-diabetic	b. Stimulation of GLP-1	TRPA1 mediated	(Emery et al., 2015)
Royal jelly	Anti-obesity	a. Reduction in body weight b. Upregulation of UCP1	Unknown Unknown	(Pourmoradian et al., 2012; Yoneshiro et al., 2018b)
Trans-pellitorine	Anti-obesity	a. Reduction of lipid accumulation	TRPA1 mediated	(Lieder et al., 2017b)
Unsaturated aldehyde	Anti-obesity	a. Stimulation of CCK	TRPA1 mediated	(Nakajima et al., 2014)
Vomitoxin	Anti-obesity	a. GLP-1, PYY and CCK secretion	TRPA1 mediated	(Tominaga et al., 2016b; Zhou & Pestka, 2015)
β-eudesmol	Appetite stimulant	a. Enhanced Ghrelin secretion	TRPA1 mediated	(Ohara et al., 2017)

4-HNE :- 4-hydroxynonenal; AITC :- Allyl isothiocyanate; UCP1 :- Uncoupling protein 1; CCK : Cholecystokinin; GLP-1 : Glucagon-like peptide-1; PYY :- Peptide YY; BAT :- Brown adipose tissue; PEPCK : phosphoenolpyruvate carboxykinase; GLUT4 :- Glucose transporter type 4; PPAR-γ :- peroxisome proliferator-activated receptor gamma; 5-HT:- 5-hydroxytryptamine (serotonin); PUFA :- Polyunsaturated fatty acids