

Phytosome supplements for delivering *Gymnema inodorum* phytonutrients to prevent inflammation in macrophages and insulin resistance in adipocytes

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Table S1. Yield, total phenolic content (TPC) and total flavonoid content (TFC) in *G. inodorum* extracts prepared by organic solvents from low to high polarity index, such as hexane (HEX), dichloromethane (DCM), ethyl acetate (EtOAc) and methanol (MeOH).

Extracts	Yield (%w/w)	TPC (mg GAE/g extract)	TFC (mg QE/g extract)	GiA-1 (%w/w)
Hex	1.33	2.99 ± 0.60	n/d	n/d
DCM	1.10	15.35 ± 0.81	n/d	n/d
EtOAc	0.34	9.10 ± 0.86	2.83 ± 1.48	n/d
MeOH	13.87	27.72 ± 1.10	15.39 ± 2.63	14.95 ± 0.14

n/d = not detected

Table S2. GC/MS phytochemicals profile of the *G. inodorum* extract prepared by hexane.

Comp ound	RT (min)	Tentative compounds	Chemical formula	CAS no.	MW	Quality (%matching)	Anti-inflammation	Anti-insulin resistance
1	14.329	Dodecanoic acid (Lauric acid)	C ₁₂ H ₂₄ O ₂	000143-07-7	200.18	98	(Yeh et al., 2019), (Roshankhah et al., 2020)	(Tham et al., 2020)
2	17.247	Tetradecanoic acid (myristic acid)	C ₁₄ H ₂₈ O ₂	000544-63-8	228.21	98	(Alonso-Castro et al., 2022)	(Khalil et al., 2021), (Saraswathi et al., 2022)
3	17.68	Neophytadiene	C ₂₀ H ₃₈	-	278.3	99	(Arai et al., 2015), (Ratheesh et al., 2022), (Ferdous et al., 2020)	(Fazelipour et al., 2021), (Azemi et al., 2021)
4	17.876	6,10,14- trimethylpentadec an-2-one		000502-69-2	268.28	92	-	-
5	19.339	Palmitic acid	C ₁₆ H ₃₂ O ₂	000057-10-3	256.24	99	induced	induced
6	19.756	9-Octadecenoic acid (oleic acid)	C ₁₈ H ₃₄ O ₂	000112-80-1	282.26	91	(Tian et al., 2017)	(López-Gómez et al., 2020), (Tian et al., 2017)
7	20.148	9,12- Octadecadienoic acid, methyl ester	C ₁₉ H ₃₄ O ₂	000112-63-0	294.26	93	(Zhong et al., 2015), (Ezirim et al., 2019)	(Mahmood et al., 2020), (Nasution et al., 2018)
8	20.205	9,12,15- Octadecatrienoic acid, methyl ester	C ₁₉ H ₃₂ O ₂	007361-80-0	292.24	98	(Amor et al., 2009), (Ujita et al., 2009)	(Li et al., 2012)
9	20.373	Phytol isomer	C ₂₀ H ₄₀ O		296.31	95	(Islam et al., 2020)	(Elmazar et al., 2013), (Matsuda et al., 2017)
10	20.838	9,12- Octadecadienoic acid (linoleic acid)	C ₁₈ H ₃₂ O ₂	000060-33-3	280.24	99	(Djuricic and Calder, 2021)	(Zaky et al., 2022), (Yoon et al., 2021)
11	21.054	octadecanoic acid (Stearic acid)	C ₁₈ H ₃₆ O ₂	000057-11-4	284.27	99	induced	induced
12	25.871	Squalene	C ₃₀ H ₅₀	007683-64-9	410.39	97	(Ibrahim and Naina	(Ganbold et al., 2020)

							Mohamed, 2021)	
13	27.378	β -tocopherol	C ₂₈ H ₄₈ O ₂	000148-03-8	416.37	97	-	-
14	27.466	γ -tocopherol	C ₂₈ H ₄₈ O ₂	007616-22-0	416.37	93	(Reiter et al., 2007)	(Dey et al., 2018), (Zafar et al., 2021)
15	27.659	Octacosane	C ₂₈ H ₅₈	000630-02-4	394.45	98	(Okechukwu, 2020)	(Okokon et al., 2022), (Sulaimon et al., 2020)
16	27.955	α -tocopherol (DL)	C ₂₉ H ₅₀ O ₂	010191-41-0	430.38	99	(Reiter et al., 2007)	(Kim et al., 2013), (Pang and Chin, 2019)
17	28.757	Stigmasterol	C ₂₉ H ₄₈ O	000083-48-7	412.37	94	(Morgan et al., 2021)	(Wang et al., 2017), (Ward et al., 2017)
18	28.877	Octacosane	C ₂₈ H ₅₈	000630-02-4	394.45	98	(Okechukwu, 2020)	(Okokon et al., 2022), (Sulaimon et al., 2020)
19	29.094	γ -sitosterol	C ₂₉ H ₅₀ O	000083-47-6	414.39	98	-	-

Table S3 GC/MS phytochemicals profile of the *G. inodorum* extract prepared by dichloromethane.

Compound	RT (min)	Tentative compounds	Chemical formula	CAS no.	MW	Quality (%matching)	Anti-inflammation	Anti-insulin resistance
1	17.736	Neophytadiene	C ₂₀ H ₃₈	-	278.3	99	(Arai et al., 2015), (Ratheesh et al., 2022), (Ferdous et al., 2020)	(Fazelipour et al., 2021), (Azemi et al., 2021)
2	17.832	6,10,14-trimethylpentadecan-2-one	-	000502-69-2	268.28	86	-	-
3	18.176	Phytol	C ₂₀ H ₄₀ O	-	296.31	89	(Islam et al., 2020)	(Elmazar et al., 2013), (Matsuda et al., 2017)

4	18.633	Palmitic acid, methyl ester	C ₁₇ H ₃₄ O ₂	-	270.26	99	induced	induced
5	19.275	Palmitic acid	C ₁₆ H ₃₂ O ₂	000057-10-3	256.24	99	induced	induced
6	20.276	Linolenic acid, methyl ester	C ₁₉ H ₃₂ O ₂	-	292.24	98	(Pauls et al., 2018), (Kapoor and Huang, 2006)	(Wang et al., 2013), (Gonçalves et al., 2018)
7	20.437	Phytol	C ₂₀ H ₄₀ O	-	296.31	91	(Islam et al., 2020)	(Elmazar et al., 2013), (Matsuda et al., 2017)
8	20.886	9,12,15- Octadecatrien-1-ol	C ₁₈ H ₃₂ O	-	264.25	94	(Xia et al., 2018)	(Ali et al., 2020)

9	27.442	β-tocopherol	C ₂₈ H ₄₈ O ₂	000148-03-8	416.37	98	-	-
10	28.027	D, α-tocopherol	C ₂₉ H ₅₀ O ₂	010191-41-0	430.38	97	(Reiter et al., 2007)	(Kim et al., 2013), (Pang and Chin, 2019)
11	28.813	Stigmasterol	C ₂₉ H ₄₈ O	000083-48-7	412.37	99	(Morgan et al., 2021)	(Wang et al., 2017), (Ward et al., 2017)
12	29.173	γ-sitosterol	C ₂₉ H ₅₀ O	000083-47-6	414.39	93	-	-

Table S4. GC/MS phytochemicals profile of the *G. inodorum* extract prepared by ethyl acetate.

Comp ound	RT (min)	Tentative compounds	Chemical formula	CAS no.	MW	Quality (%matching)	Anti-inflammation	Anti-insulin resistance
1	14.329	Dodecanoic acid, methyl ester	C ₁₃ H ₂₆ O ₂	-	214.19	87	(Yeh et al., 2019), (Roshankhah et al., 2020)	(Tham et al., 2020)
2	14.433	Phenol-2,4-bis (1,1- dimethylethyl)	C ₁₄ H ₂₂ O	-	206.17	91	(George et al., 2018)	(George et al., 2018)
3	16.59	Tetradecanoic acid, methyl ester	C ₁₅ H ₃₀ O ₂	-	242.22	95	(Alonso-Castro et al., 2022)	(Khalil et al., 2021), (Saraswathi et al., 2022)
4	17.736	Neophytadiene	C ₂₀ H ₃₈	-	278.3	99	(Arai et al., 2015), (Ratheesh et al., 2022), (Ferdous et al., 2020)	(Fazelipour et al., 2021), (Azemi et al., 2021)
5	17.832	6,10,14- trimethylpentadecan -2-one	-	000502-69-2	268.28	98	-	-
6	17.99	Neophytadiene	C ₂₀ H ₃₈	-	278.3	89	(Arai et al., 2015), (Ratheesh et al., 2022), (Ferdous et al., 2020)	(Fazelipour et al., 2021), (Azemi et al., 2021)

7	18.169	Neophytadiene	$C_{20}H_{38}$	-	278.3	89	(Arai et al., 2015), (Ratheesh et al., 2022), (Ferdous et al., 2020)	(Fazelipour et al., 2021), (Azemi et al., 2021)
8	18.633	Pentadecanoic acid, 14-methyl-, methyl ester	$C_{17}H_{34}O_2$	-	270.26	99	-	-
9	19.259	Palmitic acid	$C_{16}H_{32}O_2$	000057-10-3	256.24	99	induced	induced
10	20.421	Phytol	$C_{20}H_{40}O$	-	296.31	87	(Islam et al., 2020)	(Elmazar et al., 2013), (Matsuda et al., 2017)
11	20.509	octadecanoic acid, methyl ester	$C_{19}H_{38}O_2$	-	298.29	95	induced	induced
12	24.717	Eicosane	$C_{20}H_{42}$	-	282.33	94	(Okechukwu, 2020)	-
13	27.442	β -tocopherol	$C_{28}H_{48}O_2$	000148-03-8	416.37	98	-	-
14	28.813	Stigmasterol	$C_{29}H_{48}O$	000083-48-7	412.37	99	(Morgan et al., 2021)	(Wang et al., 2017), (Ward et al., 2017)

Table S5 GC/MS phytochemicals profile of the *G. inodorum* extract prepared by methanol.

Compound	RT (min)	Tentative compounds	Chemical formula	CAS no.	MW	Quality (%matching)	Anti-inflammation	Anti-insulin resistance
1	17.744	Neophytadiene	$C_{20}H_{38}$	-	278.3	97	(Arai et al., 2015), (Ratheesh et al., 2022), (Ferdous et al., 2020)	(Fazelipour et al., 2021), (Azemi et al., 2021)
2	18.642	14-methyl-pentadecanoic acid, methyl ester	$C_{17}H_{34}O_2$	-	270.5	99	-	-
3	20.269	9-octadecanoic acid (E, Z)	$C_{19}H_{36}O_2$	-	296.27	99	-	-

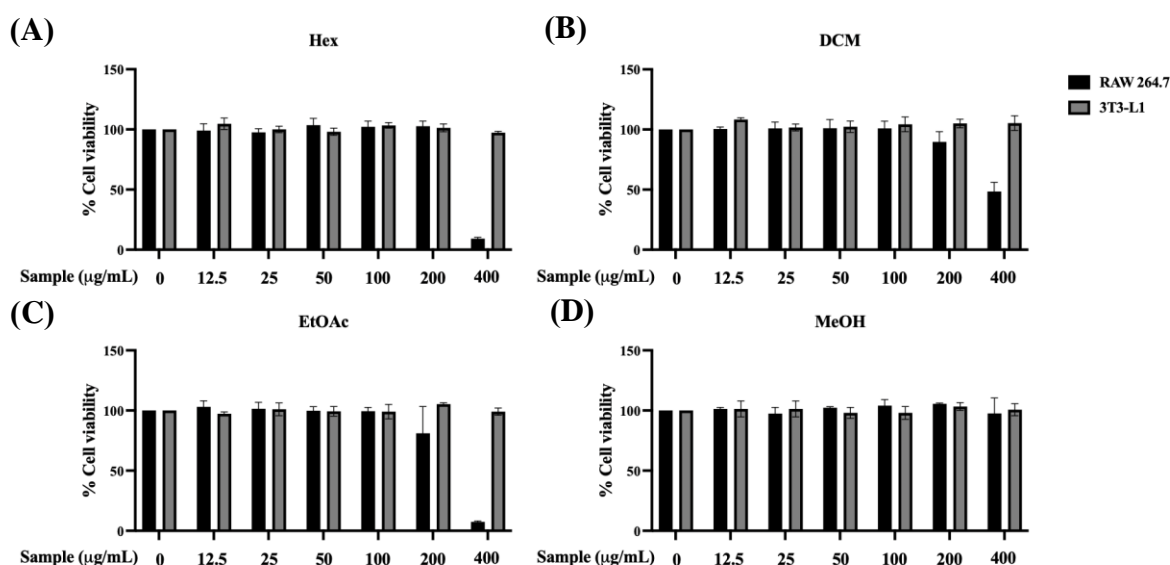


Figure S1 Effects of Hex (A), DCM (B), EtOAc (C) and MeOH (D) on cell viability of RAW 264.7 macrophages and 3T3-L1 mature adipocytes. The cells were treated with various concentrations of samples and each particle (0–800 µg/mL) for 24 hours.

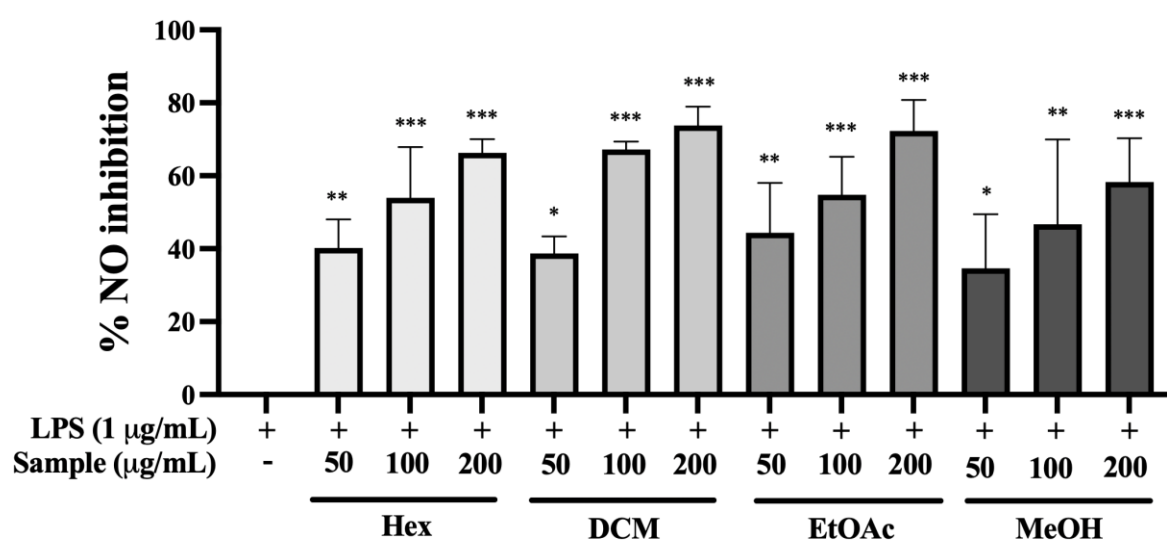


Figure S2 Inhibitory effects of the extracts prepared by hexane (Hex), dichloromethane (DCM), ethyl acetate (EtOAc) and methanol (MeOH) on nitric oxide (NO) production from inflamed RAW 264.7 macrophage cells induced by lipopolysaccharide (LPS). The percentages of NO inhibition are expressed relative to the control with LPS treatment. *, ** and *** represents the levels of *P*-values less than 0.05, 0.01 and 0.001, compared to the LPS-treated control.

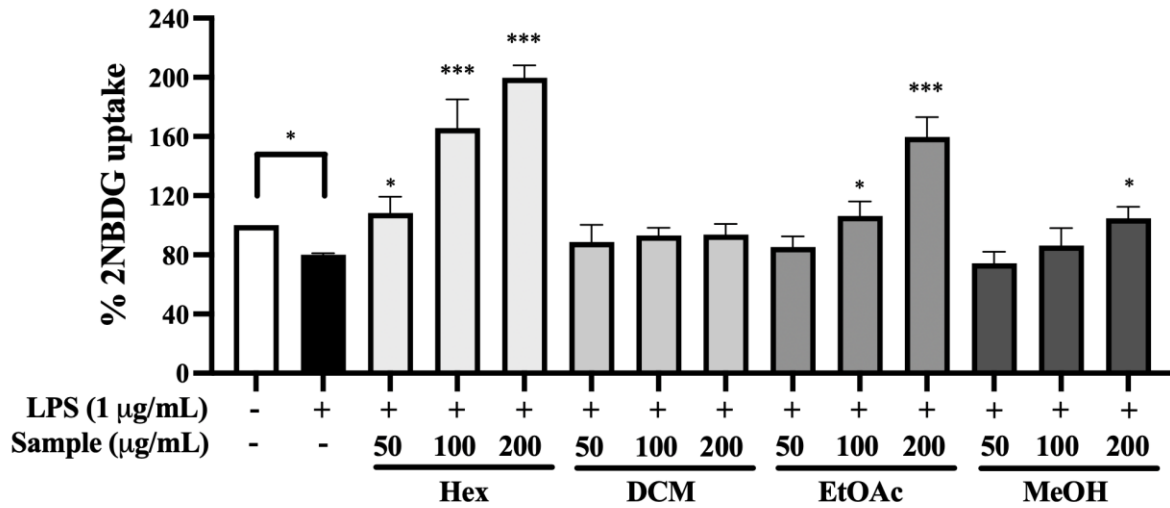


Figure S3 Effect of the extracts prepared by hexane (Hex), dichloromethane (DCM), ethyl acetate (EtOAc) and methanol (MeOH) on LPS- induced insulin resistance on 3T3-L1 adipocytes. The cells were co-treated with 1 µg/mL LPS and the samples at various concentrations for 24 h. The percentages of 2-NBDG uptake are expressed relative to the control without LPS treatment. * and *** represents the levels of *P*-values less than 0.05 and 0.001, compared to the LPS-untreated control.

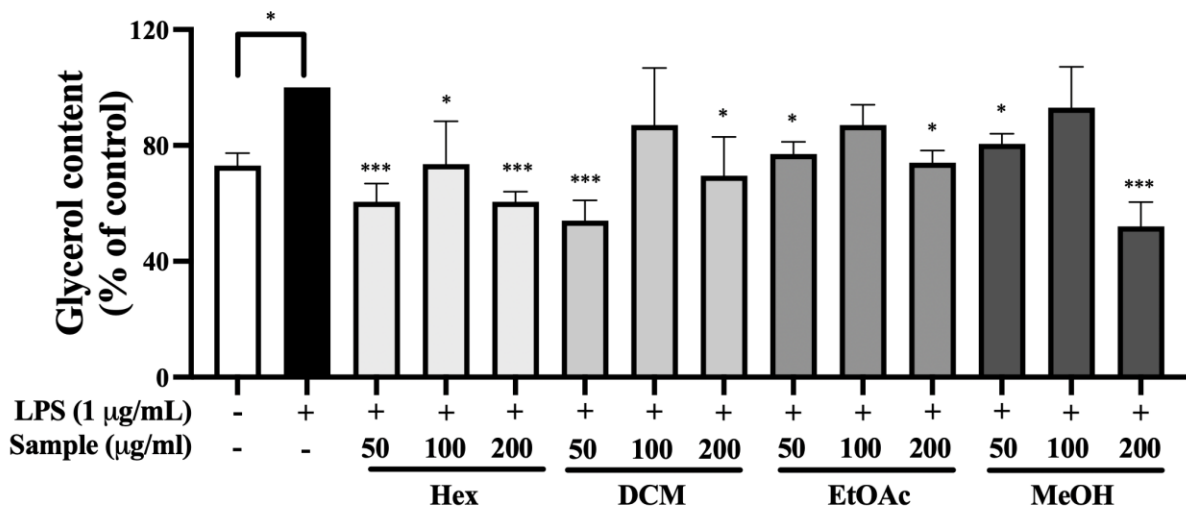


Figure S4 Effect of the extracts prepared by hexane (Hex), dichloromethane (DCM), ethyl acetate (EtOAc) and methanol (MeOH) on glycerol release from LPS- induced insulin resistance on 3T3-L1 adipocytes. The cells were co-treated with 1 µg/mL LPS and the samples at various concentrations for 24 h. The percentages of glycerol release are expressed relative to the control with LPS treatment. * and *** represents the levels of *P*-values less than 0.05 and 0.001, compared to the LPS-untreated control.

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