

**Suppl. Materials:**

**Metabolomic profiling to reveal the therapeutic potency of *posidonia oceanica*  
nano-particles in diabetic rats**

Naglaa M. Ammar<sup>a\*</sup>, Heba A. Hassan<sup>a</sup>, Mona A. Mohammed<sup>b</sup>, Ahmed Serag<sup>c\*</sup>, Sameh Hosam Abd El-Alim<sup>d</sup>, Heba Elmotasem<sup>d</sup>, Mohamed El Raey<sup>e</sup>, Abdel Nasser El Gendy<sup>b</sup>, Mansour Sobeh<sup>f</sup>, Abdel-Hamid Z. Abdel-Hamid<sup>a</sup>

<sup>a</sup>Therapeutic Chemistry Department, National Research Centre, 12622, Dokki, Giza, Egypt

<sup>b</sup>Department of Medicinal and Aromatic Plants Research, National Research Centre, Cairo, Egypt

<sup>c</sup>Pharmaceutical Analytical Chemistry Department, Faculty of Pharmacy, Al-Azhar University, 11751 Nasr City, Cairo, Egypt

<sup>d</sup>Pharmaceutical Technology Department, National Research centre, El-Buhouth St., Dokki, Cairo 1262, Egypt

<sup>e</sup>Department of Phytochemistry and Plant Systematics, National Research Center, Dokki, Cairo 12622, Egypt

<sup>f</sup>AgroBioSciences, Mohammed VI Polytechnic University, Lot 660–Hay MoulayRachid, Ben-Guerir 43150, Morocco

\*Corresponding authors:

E-mails: [ahmedserag777@azhar.edu.eg](mailto:ahmedserag777@azhar.edu.eg), [ahmedserag777@hotmail.com](mailto:ahmedserag777@hotmail.com) (Ahmed Serag)

[naglaaammar@yahoo.com](mailto:naglaaammar@yahoo.com) (Naglaa M. Ammar)

**Table S1.** GC-MS assignments of differential metabolites identified in the studied sera along with their calculated retention indices (RI).

<b>Peak number</b>	<b>Name</b>	<b>Ontology</b>	<b>RI</b>	<b>m/z</b>
<b>S1</b>	Propane 1,2-diol (2 TMS)	1,2-diols	988	117
<b>S2</b>	Butane-2,3-diol (2 TMS)	1,2-diols	1017	117
<b>S3</b>	Lactic acid (2 TMS)	Alpha hydroxy acids and derivatives	1050	147
<b>S4</b>	Alanine (2 TMS)	Amino acids and derivatives	1093	116
<b>S5</b>	Beta-Hydroxybutyric acid (2 TMS)	Beta hydroxy acids and derivatives	1151	147
<b>S6</b>	Aminobutyric acid (2 TMS)	Alpha-amino acids	1162	130
<b>S7</b>	Valine (2 TMS)	Amino acids and derivatives	1204	144
<b>S8</b>	2-hydroxyhexanoic acid (2 TMS)	Medium-chain fatty acids	1223	103
<b>S9</b>	Leucine (2TMS)	Amino acids and derivatives	1260	158
<b>S10</b>	Isoleucine (2TMS)	Amino acids and derivatives	1281	158
<b>S11</b>	Proline (2TMS)	Amino acids and derivatives	1288	142
<b>S12</b>	Uracil	Pyrimidones	1336	99
<b>S13</b>	Serine (3TMS)	Amino acids and derivatives	1347	204
<b>S14</b>	Threitol (3TMS)	Sugar alcohols	1485	147
<b>S15</b>	Methionine (2TMS)	Amino acids and derivatives	1513	176
<b>S16</b>	GABA (3 TMS)	Gamma amino acids and derivatives	1516	174
<b>S17</b>	Phenylalanine (2TMS)	Amino acids and derivatives	1618	218

<b>S18</b>	1,5-Anhydro-D-glucitol (5TMS; 1 MEOX)	Monosaccharides	1824	147
<b>S19</b>	Glucose isomer (5 TMS; 1 MEOX)	Hexoses	1857	319
<b>S20</b>	Beta-Glucose (5 TMS; 1 MEOX)	Hexoses	1868	73
<b>S21</b>	Myo-inositol (6 TMS)	Cyclitols and derivatives	1909	217
<b>S22</b>	Tyrosine (3 TMS)	Amino acids and derivatives	1925	218
<b>S23</b>	Glucosamine (5 TMS)	Amino saccharides	2119	203
<b>S24</b>	Linoleic acid (1 TMS)	Long-chain fatty acids	2165	73
<b>S25</b>	Oleic acid (1 TMS)	Long-chain fatty acids	2169	117

**Table S2.** Metabolites contributing for groups segregation were revealed from calculating the variable influence of projection (VIPs) along with their coefficients.

Name	vip	PLS-DA Coefficients				
		Butanol-extract treated group	Control	Diabetic group	Drug treated group	Nano-extract treated group
Beta-hydroxybutyric acid	1.849	0.001	0.075	-0.049	0.052	-0.079
Glucosamine	1.829	0.027	0.066	-0.022	-0.007	-0.064
Butane-2,3-diol	1.668	0.026	-0.076	0.043	-0.028	0.035
Beta-Glucose	1.665	0.005	0.042	0.010	-0.072	0.015
1,5-Anhydro-D-glucitol	1.629	-0.020	0.089	-0.020	-0.047	-0.001
Aminobutyric acid	1.450	0.011	0.059	-0.034	0.032	-0.067
Glucose isomer	1.377	-0.036	0.043	-0.008	-0.036	0.037
Myo-inositol	1.344	0.007	-0.037	0.034	-0.050	0.046
GABA	1.339	-0.002	0.076	-0.026	-0.012	-0.036

**Table S3.** Differential metabolites as revealed from combined univariate and multivariate analysis of *P. oceanica* butanol and nano-extracts therapeutic potentials on streptozotocin-induced type 2 diabetes mellitus (T2DM) rats.

Metabolites	T2DM vs control			T2DM vs butanol treated group			T2DM vs nano-extract treated group		
	VIP	Fold change	qvalue	VIP	Fold change	qvalue	VIP	Fold change	qvalue
Propane 1,2-diol	1.355	2.924	0.004	0.686	1.434	0.110	0.403	1.255	0.065
Butane-2,3-diol	2.747	58.689	0.000	0.518	1.467	0.241	1.872	11.159	0.003
Lactic acid	0.261	0.900	0.505	3.122	5.351	0.018	0.425	0.805	0.032
Alanine	1.590	3.143	0.036	0.555	0.720	0.163	1.333	3.107	0.001
Valine	0.969	2.000	0.054	0.679	0.744	0.138	1.347	3.557	0.001
2-hydroxy-hexanoic acid	1.461	4.090	0.036	0.056	1.096	0.474	1.079	3.091	0.012
Leucine	1.296	2.591	0.004	0.722	0.717	0.122	1.608	5.346	0.001
Isoleucine	0.865	1.711	0.071	1.047	0.581	0.020	1.491	4.369	0.001
Proline	1.897	4.767	0.023	1.082	0.568	0.024	1.747	6.955	0.001
Uracil	0.055	0.972	0.875	1.562	0.311	0.004	0.632	1.665	0.029
Serine	0.626	1.508	0.513	0.137	0.993	0.440	1.320	3.385	0.005
Threitol	1.371	3.598	0.007	0.017	1.097	0.457	1.296	3.840	0.002
Methionine	0.926	2.320	0.189	0.654	0.725	0.167	1.493	5.584	0.001
GABA	1.293	0.448	0.185	0.639	1.050	0.250	0.485	3.007	0.076
Phenylalanine	0.852	2.264	0.311	0.150	1.021	0.413	1.504	5.956	0.002
beta-Glucose	0.678	1.449	0.533	1.035	0.577	0.032	1.669	2.148	0.045
Myo-inositol	1.510	6.143	0.021	0.186	1.167	0.421	0.684	2.111	0.055
Tyrosine	0.789	2.751	0.495	0.441	0.831	0.298	1.646	8.639	0.003
Glucosamine	0.801	2.343	0.723	2.256	0.211	0.039	1.913	5.344	0.011
Linoleic acid	1.235	4.626	0.326	1.405	0.404	0.073	1.302	7.207	0.014
oleic acid	0.029	1.719	0.860	1.080	0.612	0.150	1.432	12.113	0.012