Supplemental data

Pharmacology, Research & Perspectives

Effect of Mitoquinone on Liver Metabolism and Steatosis in Obese and Diabetic Rats

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SYNTHESIS OF MITOQ MESYLATE AND PREPARTION OF THE β – CYCLODEXTRIN COMPLEX OF MITOQ MESYLATE

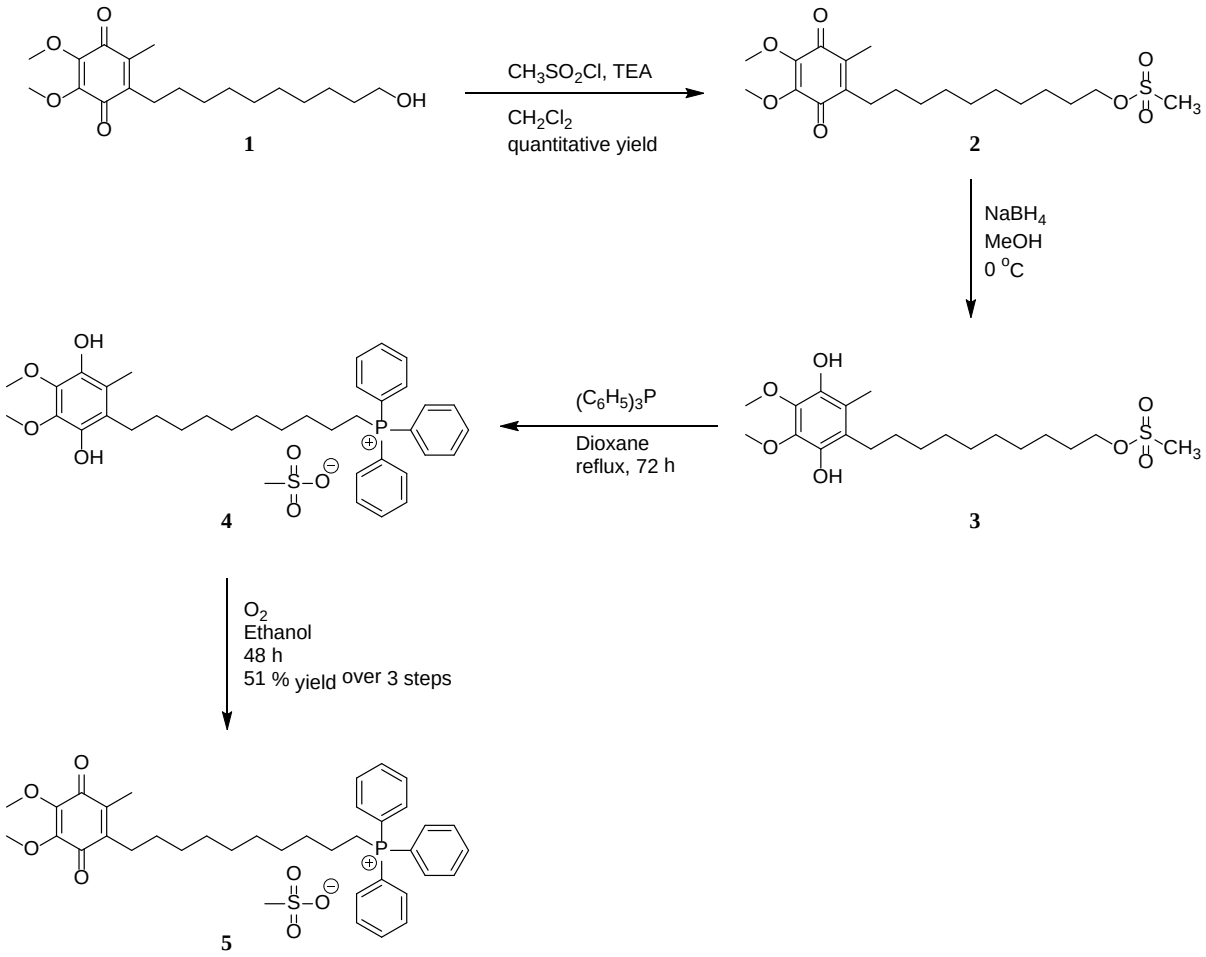
General Methods:

All reagents were purchased from commercial sources and used without further purification. Idebenone was from Brookview Scientific, LLC (Carmel, IN). NMR spectra were obtained using a Bruker Ultrashield 300 MHz instrument at ambient temperature. Chemical shifts are reported in parts per million from low to high field and referenced to residual solvent. Standard abbreviations indicating multiplicity are used as follows: m = multiplet, s = singlet. High resolution mass spectrometry (HRMS) was determined using a Waters Q-Tof Premier mass spectrometer with electrospray ionization (ESI). MitoQ mesylate was purified >95%, as determined by analytical high performance liquid chromatography (HPLC). The analytical HPLC analysis was determined using a Shimadzu system equipped with SPDM10A vp photodiode array detector. The system was connected to a Dell Optiplex GX400 PC and controlled by Shimadzu Client/Server Version 7.4 software. A Restek Allure PFP Propyl (150 mm x 4.6 mm) 5 μm column was used as stationary phase, while mobile phase consisted of solvent A (water, 0.1% TFA) and solvent B (acetonitrile, 0.1% TFA). Gradient elution used the following program: from t = 0 min [solvent A (0.95 mL/min), solvent B (0.05 mL/min)] to t = 40 min [solvent A (0.05 mL/min), solvent B (0.95 mL/min)].

Synthesis of MitoQ mesylate:

Methods adapted from previously reported synthesis of MitoQ bromide (S1). Idebenone (**1**) (Scheme S1) (3 g, 8.9 mmol) was dissolved in dichloromethane (50 mL). Triethylamine (2.5 mL, 17.9 mmol) was added to the solution and the resulting mixture stirred in an ice bath for 30 min. Methanesulfonyl chloride (1.4 mL, 18.1 mmol) in dichloromethane (20 mL) was added dropwise and the reaction stirred at room temperature overnight. TLC indicated reaction was complete as observed for disappearance of idebenone. The organic layer was washed with 1 N HCl four times. The organic layer was dried over sodium sulfate and concentrated *in vacuo* to give idebenone mesylate (**2**) in as an orange oil, which was used without further purification. Idebenone mesylate (8.9 mmol, assuming 100 % yield from the previous step) was dissolved in methanol (50 mL) and cooled in an ice-bath under Argon atmosphere. Sodium borohydride (0.84 g, 22.1 mmol) was added to the solution in small portions over 30 min. Effervescence and color change was observed. The reaction was stirred for another 30 min until the solution remains colorless. The reaction was acidified with 1 N HCl and the product extracted with 50 mL chloroform. The organic layer was dried *in vacuo*. The idebenol mesylate (**3**) obtained as a colorless oil was immediately dissolved in dioxane (25 mL). Triphenylphosphine (3.4 g, 13.3 mmol) was added to the solution and the reaction was refluxed under Ar atmosphere for 3 days. The solvent was partially removed under reduced pressure and mitoquinol (**4**) was precipitated by addition of 50 mL diethyl ether. The precipitated product was collected by decantation and further dried under vacuum. The dried precipitate was then dissolved in ethanol and bubbled with air for 48 h to oxidize mitoquinol to mitoquinone. The ethanol was removed *in vacuo* and the product was placed under vacuum overnight to obtain mitoquinone mesylate (**5**) as an orange foam (3.1 g, 51 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (m, 15H), 3.93 (s, 6H), 3.55 (m, 2H), 2.68 (s, 3H), 2.42 (m, 2H), 1.99 (s, 3H), 1.58 (m, 2H), 1.25 (m, 14H). HRMS (ESI) calculated for (M^+) 583.2972, found 583.2991

(S1) 11.Rao, V. A., Klein, S. R., Bonar, S. J., Zielonka, J., Mizuno, N., Dickey, J. S., Keller, P. W., Joseph, J., Kalyanaraman, B., and Shacter, E. (2010) *J Biol Chem* **285**, 34447-34459.

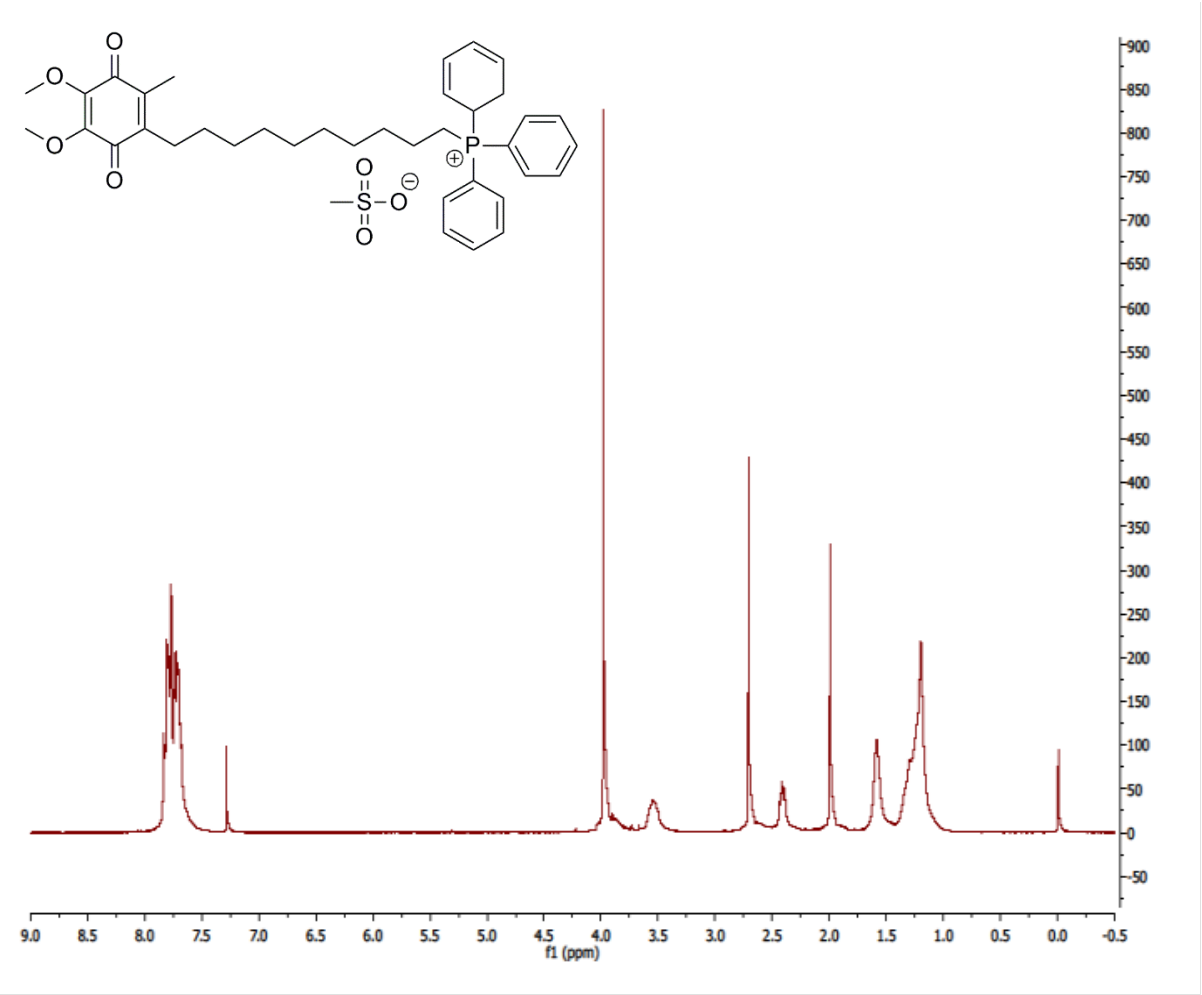


Scheme S1: Synthesis of MitoQ mesylate from commercially available Idebenone.

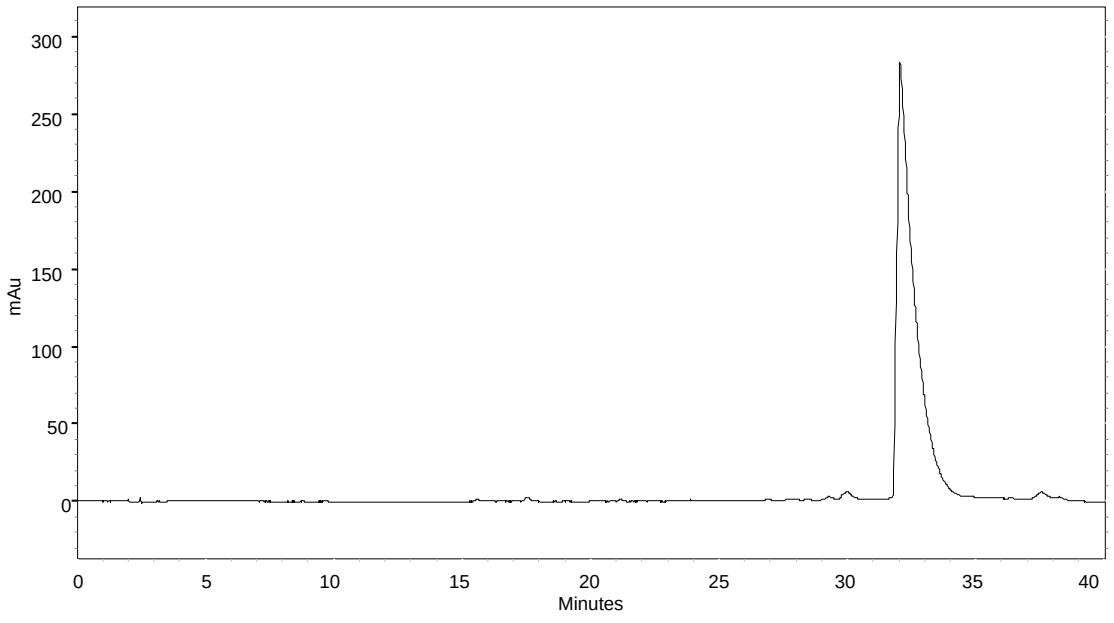
Preparation of β – cyclodextrin complex of MitoQ mesylate:

Mitoquinone mesylate (1.5 g) was dissolved in nanopure water (25 mL) with warming to 40 ^{o}C to give a clear orange solution. Beta-cyclodextrin (4.5 g) was separately dissolved in nanopure water (75 mL) with heating to 60 ^{o}C to obtain a clear colorless solution. The two solutions were allowed to cool to room temperature, combined and stirred for 1 hour at room temperature. The resulting orange solution was stored in a refrigerator at 5 ^{o}C for 12 hours. The solution was then frozen and lyophilized to a constant weight over 2 days to obtain a yellowish-orange free flowing powder. Based on the ratio of MitoQ mesylate and cyclodextrin used, MitoQ constituted 25 % w/w of the complex (250 mg per gm of the complex). The MitoQ ratio in final powder was further confirmed by establishing a standard curve on analytical HPLC using known concentrations of MitoQ mesylate, then determining the amount of MitoQ mesylate in different samples of the MitoQ mesylate-cyclodextrin complex. The experimentally determined level of MitoQ mesylate in the cyclodextrin complex product was found to be within error of the expected level based on ratio of MitoQ mesylate and β – cyclodextrin used.

^{1}H NMR of MitoQ mesylate (**5**).



Analytical reversed-phase HPLC of MitoQ mesylate (**5**). Retention time = 32.05 min. Purity >95%. Absorbance wavelength shown = 273 nm.



Metabolite data

SampleD	class	Weight	1-Octadecanol	2-Hydroxybutyrate	2-Hydroxyglutarate	3-Phosphoglycerate	6-Phosphogluconate	Adenine	Alanine
NC	Contr	38.5	30.15077195	39.13393114	16.20970682	15.3723465	24.80283371	29.51941	33.9345
NC	Contr	40	24.94522976	25.34817572	29.00535688	19.86225374	24.06318135	23.25569	27.5745
NC	Contr	34.4	34.83914958	29.16708664	30.7434206	22.91841202	32.20534563	25.3347	29.7785
NC	Contr	39.3	29.6480116	24.368988	29.57753577	13.91063361	30.13526406	21.59255	25.2692
		Mean	29.89579072	29.50454537	26.38400502	18.01591147	27.80165619	24.92559	29.1392
		SE	2.022194776	3.372539928	3.410656977	2.067309714	1.995982146	1.711925	1.84456
		CV	14%	23%	26%	23%	14%	14%	13%
DM	Diabe	38.3	19.6046319	35.32139637	24.14880195	36.46128178	23.57223609	26.44994	8.7774
DM	Diabe	38.1	23.91524059	27.59977797	22.01221557	40.11091371	20.93206138	25.79941	11.2503
DM	Diabe	38.5	27.19697069	30.64711924	27.63079049	42.97480846	24.7138106	28.85526	17.5721
DM	Diabe	38.3	26.1786451	31.38243906	25.10804913	40.71282954	21.92118371	26.23625	17.3784
		Mean	24.22387207	31.23768316	24.72496428	40.06495837	22.78482295	26.83521	13.7446
		SE	1.685553474	1.588521004	1.164815742	1.350171639	0.842595742	0.686819	2.21263
		CV	14%	10%	9%	7%	7%	5%	32%
DM-MQ	Diabe	37.2	27.13728944	26.5383413	24.13825636	41.74728926	27.81625367	30.93595	13.9821
DM-MQ	Diabe	36.4	27.13599248	31.1950647	16.29175658	50.11267902	30.64090601	32.63862	16.1894
DM-MQ	Diabe	38.7	25.63679667	25.74211906	25.84390655	32.72943323	24.59732457	29.34211	17.9632
		Mean	26.63669286	27.82517502	22.0913065	41.5298005	27.68482808	30.97223	16.0449
		SE	0.499948239	1.700549892	2.941280621	5.019288945	1.745868805	0.951793	1.15149
		CV	3%	11%	23%	21%	11%	5%	12%
HF	High F	37.5	25.14214864	28.58940337	24.18979703	13.44205064	23.37220763	19.49358	28.1002
HF	High F	34.8	24.1348977	27.97397064	18.32108156	18.26810869	29.35245596	26.99486	28.6481
HF	High F	31.8	28.78459871	35.27559305	39.0680915	15.74787697	33.7171602	24.92948	34.4874
HF	High F	33.7	31.22025041	29.25430722	18.95908174	19.96436796	26.76613788	22.98753	27.1779
		Mean	27.32047386	30.27331857	25.13451296	16.85560106	28.30199042	23.60136	29.6034
		SE	1.639230382	1.687792083	4.826971938	1.430005496	2.181153038	1.595055	1.65601
		CV	12%	11%	38%	17%	15%	14%	11%
HF-MQ	High F	37.1	30.52112136	29.86525809	32.53873418	15.38412879	30.77131561	28.0266	32.0814
HF-MQ	High F	39.8	34.32515589	33.42262742	27.82673264	20.79108109	35.27885418	21.34177	30.2241
HF-MQ	High F	39.8	24.21680249	29.08837231	39.55065649	17.32766707	31.47561665	21.03049	29.4021
HF-MQ	High F	35.8	28.66669917	38.14064601	24.48229982	16.8409303	24.46006687	24.62699	32.5502
		Mean	29.43244473	32.62922596	31.09960578	17.58595181	30.49646333	23.75646	31.0645
		SE	2.099863677	2.06523606	3.265881523	1.145376444	2.242461994	1.63945	0.74784
		CV	14%	13%	21%	13%	15%	14%	5%

t-test

	1-Octadecanol	2-Hydroxybutyrate	2-Hydroxyglutarate	3-Phosphoglycerate	6-Phosphogluconate	Adenine	Alanine
DM/NC	0.810277015	1.058741383	0.93711945	2.22386519	0.819549123	1.076613	0.47169
P-value	0.074638411	0.658391441	0.661494993	0.000110021	0.059808865	0.340452	0.00175
DM-MQ/	0.890984725	0.943080962	0.837299208	2.305173434	0.995797801	1.242588	0.55063
P-value	0.237384628	0.708158457	0.40542481	0.00472175	0.968070102	0.038987	0.00274
HF/NC	0.913856874	1.026056094	0.952642063	0.935595243	1.017996562	0.946873	1.01593
P-value	0.360713557	0.845210044	0.839567189	0.660633331	0.871179054	0.591952	0.85763
HF-MQ/N	0.984501297	1.105905058	1.178729528	0.976134449	1.096929734	0.953095	1.06607
P-value	0.878932253	0.45953182	0.356535698	0.861632807	0.403955288	0.639379	0.37076
DM- MQ/	1.099605083	0.890756682	0.893481837	1.036561679	1.21505566	1.154164	1.16737
P-value	0.289608381	0.207382832	0.393295397	0.757608818	0.039332171	0.014966	0.44713
HF-MQ/H	1.077303596	1.077821247	1.237326772	1.043329855	1.077537759	1.006572	1.04936
P-value	0.458085503	0.411067283	0.345543227	0.70396585	0.509272921	0.948142	0.45201

SampleD	class	Weight	alpha.Keto.beta.Methylvalerate..KMV.	Arachidic.acid..Eicosanoic.acid.	Arachidonate	Asparagine	Aspartate
NC	Contr	38.5	31.21038522	20.82047209	23.79551582	30.0079046	16.725594
NC	Contr	40	37.36971989	22.91812642	21.5535074	21.775129	17.362622
NC	Contr	34.4	25.86873064	25.15972142	29.94416833	26.3666127	19.2108
NC	Contr	39.3	22.71695437	21.59863598	26.07286949	23.4422493	11.234413
		Mean	29.29144753	22.62423898	25.34151526	25.3979739	16.133357
		SE	3.212991302	0.949582255	1.790214422	1.80599894	1.7159094
		CV	22%	8%	14%	14%	21%
DM	Diabe	38.3	27.21275436	21.94981482	20.03905756	29.5235228	47.251186
DM	Diabe	38.1	20.26797668	29.04969411	21.84795335	23.1329081	31.886777
DM	Diabe	38.5	23.01897549	26.45151176	22.87896783	27.1156781	41.071358
DM	Diabe	38.3	26.27765859	31.4597117	22.82017398	32.7820306	30.8214
		Mean	24.19434128	27.2276831	21.89653818	28.1385349	37.75768
		SE	1.587683119	2.034865387	0.662750948	2.03270713	3.9124439
		CV	13%	15%	6%	14%	21%
DM-MQ	Diabe	37.2	21.44932955	24.72742685	21.84496156	27.6846089	31.634343
DM-MQ	Diabe	36.4	26.0565713	26.04244753	24.34045943	33.268238	44.208532
DM-MQ	Diabe	38.7	19.42957268	23.52112205	23.30034208	35.1252603	39.287694
		Mean	22.31182451	24.76366548	23.16192102	32.0260357	38.376856
		SE	1.961054211	0.728069472	0.723705212	2.23592808	3.6583135
		CV	15%	5%	5%	12%	17%
HF	High F	37.5	22.82809642	20.01667993	26.65896376	18.8326934	16.887072
HF	High F	34.8	29.63173392	24.41140195	29.04587801	20.3552938	14.645616
HF	High F	31.8	33.54556632	27.78691727	31.47129703	25.438918	24.993595
HF	High F	33.7	22.88698955	25.8153022	26.39089751	30.9058471	22.42045
		Mean	27.22309655	24.50757534	28.39175908	23.8831881	19.736683
		SE	2.644065808	1.649283278	1.187344804	2.73391615	2.395777
		CV	19%	13%	8%	23%	24%
HF-MQ	High F	37.1	28.23928244	19.83782071	29.823279	28.286558	21.92723
HF-MQ	High F	39.8	24.39318128	25.13877673	30.99012023	22.8180098	23.918
HF-MQ	High F	39.8	27.38494958	24.37444657	29.58429115	25.5666205	22.641073
HF-MQ	High F	35.8	25.54920326	21.90803349	26.7354621	21.2775196	20.279941
		Mean	26.39165414	22.81476938	29.28328812	24.487177	22.191561
		SE	0.871013941	1.208235506	0.903091276	1.54619193	0.7586618
		CV	7%	11%	6%	13%	7%

t-test

	alpha.Keto.beta.Methylvalerate..KMV.	Arachidic.acid..Eicosanoic.acid.	Arachidonate	Asparagine	Aspartate
DM/NC	0.825986536	1.203473988	0.864057968	1.10790471	2.3403486
P-value	0.204797837	0.086235788	0.121171089	0.35240996	0.0023069
DM-MQ/	0.761718057	1.094563468	0.913991164	1.26096813	2.3787272
P-value	0.152675121	0.154994	0.367920687	0.06689507	0.0017708
HF/NC	0.929387205	1.083244186	1.120365487	0.940358	1.2233463
P-value	0.636823521	0.36057964	0.20544003	0.6601502	0.2672662
HF-MQ/N	0.901002045	1.008421516	1.15554606	0.96413899	1.3755079
P-value	0.417196538	0.905376994	0.09690345	0.71485406	0.0179314
DM- MQ	0.922191857	0.909503221	1.057789173	1.13815577	1.0163987
P-value	0.484406317	0.366686036	0.257619135	0.25806525	0.9155043
HF-MQ/H	0.969458198	0.930927236	1.031400979	1.02528929	1.1243815
P-value	0.775267444	0.439365469	0.571934466	0.85385033	0.3663644

SampleD	class	Weight	beta.Alanine	β-Hydroxy.beta.Methylbutyric.acid	β-Hydroxybutyrate..3.Hydroxybutyrate	Cholesterol	Citrate
NC	Contr	38.5	20.53511262	15.70080091	6.065619916	27.85244361	19.605
NC	Contr	40	15.7315078	16.55483699	3.905838737	26.40696457	24.055
NC	Contr	34.4	19.01045874	18.13729414	3.397125565	26.73831461	23.859
NC	Contr	39.3	16.57481269	15.22891845	3.935315317	22.60598183	20.308
		Mean	17.96297296	16.40546262	4.325974884	25.90092616	21.957
		SE	1.103764566	0.639163347	0.592892287	1.140992724	1.1643
		CV	12%	8%	27%	9%	11%
DM	Diabe	38.3	26.01141786	41.8229682	56.14868859	27.66583916	25.899
DM	Diabe	38.1	22.56429021	41.04927286	66.24694085	26.56405599	28.291
DM	Diabe	38.5	28.15181736	34.54459705	64.46368186	27.8375619	29.659
DM	Diabe	38.3	24.53604295	34.80945807	52.0891087	26.27756136	21.867
		Mean	25.31589209	38.05657405	59.737105	27.0862546	26.429
		SE	1.179890737	1.958309554	3.367579142	0.390198353	1.7076
		CV	9%	10%	11%	3%	13%
DM-MQ	Diabe	37.2	29.47866612	45.45777523	63.16880408	30.27746595	22.452
DM-MQ	Diabe	36.4	22.88291331	29.53389927	33.05670484	29.01235401	26.716
DM-MQ	Diabe	38.7	25.04559092	25.09387909	21.39563781	23.5566349	30.87
		Mean	25.80239012	33.3618512	39.20704891	27.61548496	26.68
		SE	1.941266556	6.182285945	12.44480352	2.062023671	2.4302
		CV	13%	32%	55%	13%	16%
HF	High F	37.5	17.68787839	15.29701479	3.089352648	24.70386186	26.391
HF	High F	34.8	18.1315053	18.23060361	3.135502263	26.6169556	24.988
HF	High F	31.8	18.74788317	20.94716451	2.838972192	27.73932287	36.888
HF	High F	33.7	18.84561776	17.34216982	3.628873717	21.3592535	28.722
		Mean	18.35322116	17.95423818	3.173175205	25.10484846	29.247
		SE	0.272343446	1.171517878	0.165277106	1.396936984	2.6608
		CV	3%	13%	10%	11%	18%
HF-MQ	High F	37.1	21.67314178	17.86116759	4.48711156	27.82101023	24.286
HF-MQ	High F	39.8	17.73462905	13.50815048	4.043237849	28.01708347	18.73
HF-MQ	High F	39.8	19.3440495	17.82727414	3.515525508	26.00916814	28.137
HF-MQ	High F	35.8	17.80067998	17.11211374	4.556198287	23.27290137	20.196
		Mean	19.13812508	16.57717649	4.150518301	26.2800408	22.837
		SE	0.923186285	1.037483164	0.240242276	1.099551559	2.122
		CV	10%	13%	12%	8%	19%

t-test

	beta.Alanine	beta.Hydroxy.beta.Methylbutyric.acid..	beta.Hydroxybutyrate..3.Hydroxybutyrate.	Cholesterol	Citrate
DM/NC	1.409337538	2.31975013	13.80893477	1.045763941	1.2037
P-value	0.003887885	4.35773E-05	3.51268E-06	0.363584324	0.0737
DM-MQ/	1.436420918	2.03358186	9.063170721	1.066196814	1.2151
P-value	0.013137349	0.022854867	0.020496694	0.469249067	0.1125
HF/NC	1.021725145	1.094406089	0.733516789	0.969264509	1.332
P-value	0.743106137	0.289915033	0.110226438	0.674412495	0.0459
HF-MQ/N	1.065420803	1.010466871	0.959441146	1.014637108	1.0401
P-value	0.445321152	0.892549201	0.793073802	0.818872412	0.7285
DM- MQ	1.0192171	0.876638322	0.656326565	1.019538706	1.0095
P-value	0.829300294	0.445213291	0.124903851	0.778888544	0.9337
HF-MQ/H	1.042766548	0.92330158	1.308001618	1.04681137	0.7808
P-value	0.445960296	0.412722614	0.015388628	0.533125936	0.1086

SampleD	class	Weight	Cysteine	Cytidine	Dihydroxyacetone.phosphate	Fructose	Fructose.6.phosphate	Fumarate
NC	Contr	38.5	29.34634	28.7455	48.72204124	25.61569	51.14836423	20.107868
NC	Contr	40	26.69439	36.51765	35.8741456	17.00889	35.76979103	21.258384
NC	Contr	34.4	21.15482	18.83508	38.19272329	22.00072	40.73768214	24.566052
NC	Contr	39.3	19.27526	34.42311	31.38234432	13.60269	20.78045415	18.767248
		Mean	24.1177	29.63034	38.54281361	19.557	37.10907289	21.174888
		SE	2.348863	3.955232	3.675746497	2.655594	6.31589247	1.2396986
		CV	19%	27%	19%	27%	34%	12%
DM	Diabe	38.3	25.70519	46.87687	13.68231277	23.34386	20.94632939	17.825311
DM	Diabe	38.1	23.54791	21.12682	18.93743138	30.24153	20.09154252	25.269447
DM	Diabe	38.5	23.89061	37.88843	18.12389447	26.85022	24.86535268	38.156798
DM	Diabe	38.3	25.94873	27.5974	23.03314014	35.4821	23.95490488	32.696845
		Mean	24.77311	33.37238	18.44419469	28.97943	22.46453237	28.4871
		SE	0.614462	5.672082	1.916590168	2.584743	1.151852475	4.4276787
		CV	5%	34%	21%	18%	10%	31%
DM-MQ	Diabe	37.2	24.13925	19.37546	13.03471864	24.18353	23.39985026	29.870395
DM-MQ	Diabe	36.4	25.34807	19.87556	19.81349675	29.59021	17.97980929	37.550591
DM-MQ	Diabe	38.7	24.37609	32.18684	16.15955349	34.22257	18.54747856	39.020763
		Mean	24.62114	23.81262	16.33592296	29.3321	19.9757127	35.480583
		SE	0.369841	4.189599	1.958850665	2.900895	1.719893467	2.8370177
		CV	3%	30%	21%	17%	15%	14%
HF	High F	37.5	21.2441	14.16453	21.53034589	14.64015	19.28296873	16.432363
HF	High F	34.8	19.42349	20.16747	37.00184303	17.45331	32.4224475	18.372042
HF	High F	31.8	22.92741	16.62057	33.11474925	14.61299	24.007253	26.711065
HF	High F	33.7	28.22397	14.99528	35.53456366	18.88164	24.36125323	21.312837
		Mean	22.95474	16.48696	31.79537546	16.39702	25.01848062	20.707077
		SE	1.896523	1.32862	3.514261567	1.062953	2.725945574	2.2386822
		CV	17%	16%	22%	13%	22%	22%
HF-MQ	High F	37.1	29.26792	19.80629	23.52991634	23.23303	27.48894143	21.415168
HF-MQ	High F	39.8	22.64259	36.98976	15.34485107	21.85125	28.95782803	24.954195
HF-MQ	High F	39.8	27.26808	46.69346	21.21460187	50.79956	18.59854134	22.18463
HF-MQ	High F	35.8	21.24192	14.96704	24.89003196	18.74689	24.53694005	22.232343
		Mean	25.10513	29.61414	21.24485031	28.65768	24.89556271	22.696584
		SE	1.892873	7.398393	2.107917259	7.439987	2.291446069	0.775481
		CV	15%	50%	20%	52%	18%	7%

t-test

	Cysteine	Cytidine	Dihydroxyacetone.phosphate..DHAP.	Fructose	Fructose.6.phosphate	Fumarate
DM/NC	1.027175	1.126291	0.478537838	1.481793	0.605364958	1.3453247
P-value	0.796245	0.607892	0.002856284	0.043926	0.062708694	0.1628663
DM-MQ/	1.020874	0.803657	0.423838361	1.499826	0.538297272	1.6755972
P-value	0.864197	0.365429	0.004979463	0.057086	0.074153561	0.0036854
HF/NC	0.95178	0.556422	0.824936544	0.838422	0.674187703	0.9779073
P-value	0.713359	0.019813	0.232824728	0.311601	0.129324393	0.8609684
HF-MQ/N	1.040942	0.999453	0.551201335	1.465342	0.670875362	1.0718632
P-value	0.75454	0.998522	0.006484964	0.293136	0.118977071	0.3381468
DM- MQ	0.993865	0.713543	0.885694563	1.01217	0.889211152	1.2454965
P-value	0.855048	0.262419	0.485096198	0.931533	0.264692403	0.2782799
HF-MQ/H	1.093679	1.796215	0.668174223	1.747737	0.995086916	1.0960786
P-value	0.452854	0.131345	0.042075309	0.153932	0.973584745	0.433233

SampleD	class	Weight	Gamma.aminobutyric.acid..GABA.	Glucose	Glucose.6.phosphate	Glutamate	Glutamine	Glycerate	Glycerol
NC	Contr	38.5	28.23449721	30.1403	54.36399639	19.8374469	26.9616318	20.808435	25.04596
NC	Contr	40	26.14082371	20.8332	40.2444372	17.0126263	30.4038682	19.507328	19.20149
NC	Contr	34.4	44.18788309	25.7816	50.52309514	25.6604244	30.9176218	19.080655	20.76896
NC	Contr	39.3	23.01092464	17.5452	22.80196543	13.0560681	25.6746541	16.500528	16.50395
		Mean	30.39353216	23.5751	41.98337354	18.8916414	28.489444	18.974237	20.38009
		SE	4.721704958	2.76659	7.054295287	2.65040225	1.28511736	0.9027287	1.787343
		CV	31%	23%	34%	28%	9%	10%	18%
DM	Diabe	38.3	34.56255181	27.5985	20.19945565	42.3907403	23.3370328	29.675456	23.45812
DM	Diabe	38.1	26.4741247	32.6763	16.60471449	26.1533193	19.9822086	36.571683	25.80609
DM	Diabe	38.5	34.41373752	31.5459	27.25322779	23.4636989	25.6109031	43.790913	23.66263
DM	Diabe	38.3	27.33505599	30.2862	23.14731801	28.07651	27.1776656	32.694782	23.53874
		Mean	30.6963675	30.5267	21.80117899	30.0210671	24.0269525	35.683208	24.11639
		SE	2.196435943	1.09131	2.256577189	4.23033359	1.56183212	3.0488803	0.564799
		CV	14%	7%	21%	28%	13%	17%	5%
DM-MQ	Diabe	37.2	48.08056719	31.1743	24.89842603	22.1864928	23.6331931	37.709614	25.66529
DM-MQ	Diabe	36.4	28.44676196	32.0546	17.18642555	39.7914689	31.0178439	34.848727	23.01581
DM-MQ	Diabe	38.7	40.43296319	29.0997	19.22957464	53.3230571	37.495826	27.863159	21.48915
		Mean	38.98676411	30.7762	20.43814207	38.4336729	30.715621	33.473833	23.39008
		SE	5.713731872	0.87591	2.306817018	9.01395432	4.00464945	2.9243755	1.219985
		CV	25%	5%	20%	41%	23%	15%	9%
HF	High F	37.5	15.1951229	21.4637	16.99517749	18.9398205	24.5837808	16.758241	18.31579
HF	High F	34.8	20.65124038	22.0451	35.56333766	17.0964191	23.8520391	17.881402	22.74881
HF	High F	31.8	32.18603746	17.8274	29.17899016	30.230725	23.6205956	16.448257	19.61512
HF	High F	33.7	35.18747535	21.2778	27.41216492	26.3369621	25.8482325	18.915992	20.27687
		Mean	25.80496902	20.6535	27.28741756	23.1509817	24.476162	17.500973	20.23915
		SE	4.724750549	0.95611	3.851565353	3.0911816	0.50130518	0.5632396	0.930436
		CV	37%	9%	28%	27%	4%	6%	9%
HF-MQ	High F	37.1	27.30670727	24.6888	32.54605693	25.3679089	32.6826441	20.711504	22.70858
HF-MQ	High F	39.8	26.24621809	19.7773	29.36634485	21.5360981	25.0175626	21.234711	20.83997
HF-MQ	High F	39.8	24.18181722	14.4043	17.73169644	24.1022684	24.7242903	18.108503	17.03005
HF-MQ	High F	35.8	14.19041219	20.5586	27.69304299	17.0328079	21.5849046	18.479583	20.02035
		Mean	22.98128869	19.8573	26.8342853	22.0097708	26.0023504	19.633575	20.14974
		SE	3.001246801	2.11299	3.196746385	1.84051992	2.3583786	0.7843846	1.182274
		CV	26%	21%	24%	17%	18%	8%	12%

t-test

	Gamma.aminobutyric.acid..GABA.	Glucose	Glucose.6.phosphate	Glutamate	Glutamine	Glycerate	Glycerol
DM/NC	1.009963809	1.29487	0.519281257	1.58911904	0.84336334	1.8806137	1.183331
P-value	0.955515236	0.05805	0.034415624	0.06731783	0.06949345	0.0019108	0.093292
DM-MQ/	1.282732257	1.30545	0.486815145	2.0344274	1.07814042	1.7641729	1.147693
P-value	0.295212999	0.0846	0.053505927	0.06218618	0.57156349	0.0028691	0.25613
HF/NC	0.849028303	0.87607	0.649957716	1.22546163	0.85913091	0.9223545	0.993084
P-value	0.517772281	0.35677	0.117235259	0.33584016	0.0270025	0.2154638	0.946511
HF-MQ/N	0.756124315	0.8423	0.63916458	1.16505339	0.91270122	1.0347492	0.988697
P-value	0.233443909	0.32661	0.098234597	0.3711993	0.39016318	0.6013182	0.917903
DM- MQ	1.270077448	1.00817	0.937478752	1.28022341	1.27838189	0.9380836	0.969883
P-value	0.188104428	0.87314	0.696222129	0.39533245	0.14087666	0.6338079	0.577544
HF-MQ/H	0.890576101	0.96145	0.983394095	0.95070573	1.06235407	1.1218562	0.995582
P-value	0.63192165	0.74307	0.930813246	0.76183063	0.55008733	0.0692918	0.954539

SampleD	class	Weight	Glycine	Guanine	Heptadecanoic.acid	Histidine	Hypotaurine	Inotisol	Isoleucine	Lactate	Lauric.acid	Leucine	Linoleate
NC	Contr	38.5	38.7222	27.29546	29.65572209	26.0802	25.94151676	38.3439	28.015114	37.4869	21.7357803	28.0483	23.28746
NC	Contr	40	28.0385	25.85695	25.6828716	29.2894	21.21068056	33.1811	23.374523	29.9529	19.4758576	21.4138	22.197865
NC	Contr	34.4	36.4111	25.13165	36.86252076	30.86703	28.82642668	35.1211	24.792176	28.3742	27.5361388	25.3893	30.952352
NC	Contr	39.3	33.7347	24.22769	30.63428302	25.66787	24.89878655	29.5009	21.938269	29.576	18.5394679	22.4773	26.202253
		Mean	34.2266	25.62794	30.70884937	27.97613	25.21935264	34.0368	24.530021	31.3475	21.8218112	24.3322	25.659982
		SE	2.30067	0.648077	2.313776879	1.258459	1.573338239	1.84919	1.2995816	2.07396	2.0194516	1.49678	1.9561517
		CV	13%	5%	15%	9%	12%	11%	11%	13%	19%	12%	15%
DM	Diabe	38.3	19.2681	24.22362	17.75799024	22.86852	19.0328184	18.6307	34.157857	3.92911	22.678437	31.9613	21.04484
DM	Diabe	38.1	10.313	19.702	23.08725482	18.89555	18.63557659	19.116	21.801243	7.34093	26.9055215	22.4353	28.670817
DM	Diabe	38.5	17.6136	22.54548	23.03448359	23.91518	15.50939818	20.0374	21.289888	11.7898	25.4866871	21.4986	22.551904
DM	Diabe	38.3	26.789	22.56114	23.27055859	20.52784	17.66162386	22.284	33.502438	13.9223	25.894034	32.327	26.184535
		Mean	18.4959	22.25806	21.78757181	21.55177	17.70985426	20.017	27.687857	9.24555	25.2411699	27.0555	24.613024
		SE	3.38021	0.938589	1.344146023	1.133706	0.788010633	0.81	3.5503108	2.2405	0.90481012	2.94507	1.7300164
		CV	37%	8%	12%	11%	9%	8%	26%	48%	7%	22%	14%
DM-MQ	Diabe	37.2	19.3746	25.22113	20.56460281	22.80385	22.6343892	20.271	30.966273	8.29821	23.3253067	30.002	25.422151
DM-MQ	Diabe	36.4	27.2003	22.86736	23.93837788	25.46069	18.34521908	21.7421	34.149014	11.3446	27.332806	32.5587	27.019324
DM-MQ	Diabe	38.7	30.1439	23.41103	21.76186617	32.20191	17.4992462	20.0982	34.963564	13.1972	21.780459	31.5679	22.644857
		Mean	25.5729	23.83317	22.08828229	26.82215	19.49295149	20.7038	33.359617	10.9466	24.1461906	31.3762	25.028777
		SE	3.21354	0.711506	0.987505301	2.797086	1.589590164	0.52154	1.2195552	1.42814	1.65454193	0.74427	1.2780257
		CV	22%	5%	8%	18%	14%	4%	6%	23%	12%	4%	9%
HF	High F	37.5	24.7386	26.76007	25.46165253	22.13591	23.193295	24.4775	17.85295	30.693	22.261515	18.8254	23.998292
HF	High F	34.8	18.0647	78.76161	28.93102432	25.72004	31.01174507	29.8037	19.227814	31.341	27.8396696	20.0979	25.143543
HF	High F	31.8	24.9153	28.82522	31.09426974	26.67228	32.89417993	24.9086	23.676914	30.17	28.2788718	23.2204	27.301027
HF	High F	33.7	25.3179	22.44807	26.63442798	24.59112	23.82287483	41.9277	21.632838	29.9052	25.1607423	21.0767	26.573026
		Mean	23.2591	39.19875	28.03034364	24.77983	27.73052371	30.2794	20.597629	30.5273	25.8851997	20.8051	25.753972
		SE	1.73572	13.25436	1.249854104	0.978575	2.471266936	4.0663	1.2898097	0.31679	1.39060981	0.92768	0.73707
		CV	15%	68%	9%	8%	18%	27%	13%	2%	11%	9%	6%
HF-MQ	High F	37.1	44.2967	30.07506	24.94856296	30.04889	29.69608482	29.9524	30.399396	32.235	24.8806348	30.4627	19.824436
HF-MQ	High F	39.8	35.3023	26.12458	28.47106998	29.76951	32.81537644	24.0874	19.729993	27.387	29.1883439	18.8673	24.988595
HF-MQ	High F	39.8	31.1165	23.76407	26.5935873	36.13795	45.49852238	20.7779	25.059404	25.686	24.3745415	25.4698	22.576589
HF-MQ	High F	35.8	28.6492	23.76324	25.11096034	27.85904	27.67136781	23.3826	21.918911	30.7715	21.839106	22.7626	25.640639
		Mean	34.8412	25.93174	26.28104515	30.95385	33.92033786	24.5501	24.276926	29.0199	25.0706566	24.3906	23.257565
		SE	3.43794	1.489	0.818458846	1.795234	4.001762496	1.93629	2.3153788	1.50517	1.52531286	2.43572	1.3205304
		CV	20%	11%	6%	12%	24%	16%	19%	10%	12%	20%	11%

t-test

	Glycine	Guanine	Heptadecanoic.acid	Histidine	Hypotaurine	Inotisol	Isoleucine	Lactate	Lauric.acid	Leucine	Linoleate
DM/NC	0.5404	0.868508	0.709488381	0.770363	0.702232706	0.5881	1.1287335	0.29494	1.15669454	1.11192	0.9591988
P-value	0.00849	0.025464	0.015728974	0.009043	0.005276859	0.00044	0.4355656	0.00035	0.17325149	0.44127	0.7023688
DM-MQ/	0.74716	0.929969	0.719280688	0.958751	0.772936236	0.60828	1.3599506	0.3492	1.10651634	1.28949	0.9754012
P-value	0.07319	0.123736	0.029600647	0.694641	0.054293882	0.00188	0.0049505	0.00068	0.43833834	0.01326	0.8143125
HF/NC	0.67956	1.529532	0.912777399	0.885749	1.099573177	0.88961	0.8396907	0.97384	1.18620767	0.85504	1.0036629
P-value	0.00891	0.345922	0.347723769	0.091787	0.424258337	0.43251	0.0753465	0.70935	0.14855142	0.09205	0.9655964
HF-MQ/N	1.01796	1.011854	0.855813412	1.106438	1.345012235	0.72128	0.9896822	0.92575	1.14888065	1.0024	0.9063749
P-value	0.88676	0.857765	0.121258021	0.223246	0.089464073	0.01217	0.9271631	0.39873	0.24657719	0.98436	0.3479976
DM- MQ	1.38262	1.070766	1.013801927	1.244545	1.100683902	1.03431	1.2048465	1.18399	0.95661931	1.1597	1.0168916
P-value	0.20191	0.266599	0.873326297	0.108133	0.32231769	0.54309	0.246518	0.58395	0.55895235	0.27666	0.8642025
HF-MQ/H	1.49796	0.661545	0.937592685	1.249155	1.223213028	0.81079	1.1786272	0.95062	0.96853248	1.17234	0.9030671
P-value	0.02378	0.35829	0.286036143	0.023408	0.236199165	0.25041	0.2144222	0.36493	0.70676158	0.21807	0.1498855

SampleD	class	Weight	Linolenic.acid	Lysine	Malate	Mannose	Methionine	Myristic.acid	N.Acetylaspartate	N.acetylglutamate	Oleic.acid
NC	Contr	38.5	23.12896995	28.704	20.2988	28.12502	26.82408553	30.68139828	29.0554831	29.97047537	21.062415
NC	Contr	40	21.87992656	30.818	21.8806	26.70452	22.20415587	28.09845955	18.47245188	28.48223489	21.374464
NC	Contr	34.4	22.29127741	29.246	24.6291	22.75879	24.26861987	33.46840652	32.31688318	32.16894307	27.437448
NC	Contr	39.3	21.91608273	23.891	16.8474	16.63192	26.71489542	31.76060915	17.78397848	28.37434265	25.656793
		Mean	22.30406416	28.164	20.914	23.55506	25.00293917	31.00221838	24.40719916	29.748999	23.88278
		SE	0.290266452	1.4935	1.62409	2.571763	1.103773114	1.125165966	3.688472158	0.885040134	1.5819
		CV	3%	11%	16%	22%	9%	7%	30%	6%	13%
DM	Diabe	38.3	29.17849827	22.304	18.9662	28.77987	29.43708621	19.95276489	17.09283276	25.42323936	23.097425
DM	Diabe	38.1	32.67793821	15.991	25.2582	35.72647	23.08015084	28.55549697	22.41133577	23.27065309	30.578674
DM	Diabe	38.5	22.11319979	23.141	37.2397	42.20834	25.28773594	26.66897281	15.24500852	19.8415366	27.017416
DM	Diabe	38.3	29.14983118	19.921	31.7646	28.54192	24.70350799	26.36707933	31.08261063	22.00289926	26.514373
		Mean	28.27986686	20.339	28.3072	33.81415	25.62712025	25.3860785	21.45794692	22.63458208	26.801972
		SE	2.216137607	1.6018	3.9612	3.256529	1.353117852	1.874706435	3.549623538	1.168379291	1.5306936
		CV	16%	16%	28%	19%	11%	15%	33%	10%	11%
DM-MQ	Diabe	37.2	23.21146276	19.804	28.8386	26.93253	26.19596158	15.93484664	24.74775357	22.45447963	26.785277
DM-MQ	Diabe	36.4	24.6286002	25.759	42.7783	29.29344	30.11130453	22.89099384	17.48292304	27.75388154	27.800892
DM-MQ	Diabe	38.7	24.05279558	27.631	36.8989	31.44629	28.57613233	20.79261233	13.88478501	25.37948503	23.017439
		Mean	23.96428618	24.398	36.1719	29.22409	28.29446615	19.8728176	18.70515387	25.19594874	25.867869
		SE	0.411479069	2.3598	4.04044	1.303472	1.139002412	2.060057664	3.194860855	1.532555528	1.4550582
		CV	3%	17%	19%	8%	7%	18%	30%	11%	10%
HF	High F	37.5	27.50300946	26.023	17.2984	20.05071	24.23498409	26.83399369	21.33883942	27.85165708	21.689292
HF	High F	34.8	24.57084905	31.43	20.2473	23.12977	19.16578793	30.2474019	29.09046357	38.95820375	21.683807
HF	High F	31.8	28.02063352	22.556	26.5144	18.06477	23.80547866	34.84424188	20.41803741	23.63302547	25.519468
HF	High F	33.7	24.10992347	26.993	20.5826	19.88566	24.78575858	33.72275593	69.68657582	25.7101817	25.664715
		Mean	26.05110387	26.751	21.1607	20.28272	22.99800231	31.41209835	35.13347905	29.038267	23.63932
		SE	0.997764693	1.8275	1.93105	1.050256	1.293061016	1.812785787	11.68072072	3.416942786	1.1278232
		CV	8%	14%	18%	10%	11%	12%	66%	24%	10%
HF-MQ	High F	37.1	19.21138307	28.203	21.9282	24.20897	24.59296741	27.42793876	25.25923804	23.07209233	20.063716
HF-MQ	High F	39.8	27.252138	27.913	25.6129	21.10299	20.32052735	34.83074095	20.08328732	23.23346628	22.852121
HF-MQ	High F	39.8	27.9927916	30.334	20.9765	18.28998	22.25368486	32.05938747	14.31879057	22.0640652	24.837806
HF-MQ	High F	35.8	27.99577277	23.171	22.3068	20.28685	20.68788532	30.19224	21.08410371	22.67688372	22.35143
		Mean	25.61302136	27.405	22.7061	20.9722	21.96376623	31.1275768	20.18635491	22.76162688	22.526268
		SE	2.141037266	1.5112	1.00853	1.230101	0.971461862	1.55841459	2.254237313	0.260255469	0.9808211
		CV	17%	11%	9%	12%	9%	10%	22%	2%	9%

t-test

	Linolenic.acid	Lysine	Malate	Mannose	Methionine	Myristic.acid	N.Acetylaspartate	N.acetylglutamate	Oleic.acid
DM/NC	1.267924386	0.7222	1.35351	1.435536	1.024964308	0.818847161	0.879164659	0.760851889	1.12223
P-value	0.036846364	0.0117	0.13493	0.048305	0.732992426	0.042413564	0.585471799	0.002840693	0.2330325
DM-MQ/	1.074435852	0.8663	1.72956	1.240671	1.131645602	0.641012761	0.766378549	0.846951144	1.083118
P-value	0.018959659	0.2144	0.01114	0.139841	0.097371894	0.003737732	0.315880837	0.040298954	0.4146932
HF/NC	1.167998069	0.9498	1.0118	0.861077	0.919811953	1.013220989	1.43947197	0.976109045	0.9898061
P-value	0.011285727	0.571	0.9253	0.283409	0.282914553	0.853994169	0.414886519	0.847071901	0.9043675
HF-MQ/N	1.148356693	0.973	1.08569	0.890348	0.878447373	1.004043531	0.827065604	0.765122446	0.9432013
P-value	0.176531935	0.7331	0.38473	0.39985	0.084246547	0.950119217	0.366565729	0.000275242	0.493577
DM- MQ	0.847397419	1.1996	1.27784	0.864256	1.104082935	0.782823452	0.871712189	1.11316165	0.965148
P-value	0.163649833	0.1982	0.23166	0.303582	0.211673946	0.106925291	0.604112391	0.232403383	0.6864306
HF-MQ/H	0.983183725	1.0245	1.07303	1.033993	0.955029308	0.990942294	0.574561798	0.783849356	0.9529152
P-value	0.858977281	0.7918	0.50471	0.684781	0.546140118	0.909145924	0.255653492	0.116727146	0.4845955

SampleD	class	Weight	O.Phosphoethanolamine	Ornithine	Palmitate	Phenylalanine	Phosphoenolpyruvate	Proline	Prostaglandin.E2	Pterin
NC	Contr	38.5	24.08211962	26.103233	25.975275	34.14939431	24.68008102	25.0482	28.54612278	27.084
NC	Contr	40	16.57495234	31.60314	23.811049	27.56997421	21.29933268	26.4921	31.0185495	16.88
NC	Contr	34.4	25.81942458	22.577801	30.515504	29.48334388	24.36463504	18.8978	20.01048733	22.257
NC	Contr	39.3	17.98661593	17.759715	26.609325	25.13507552	18.22507652	18.1834	16.58784116	19.675
		Mean	21.11577812	24.510972	26.727788	29.08444698	22.14228131	22.1554	24.04075019	21.474
		SE	2.260793126	2.9176298	1.3974521	1.908401879	1.512016844	2.11273	3.425114805	2.1684
		CV	21%	24%	10%	13%	14%	19%	28%	20%
DM	Diabe	38.3	29.73276283	29.598664	20.258498	27.06903202	28.0236724	22.1513	37.5441278	25.806
DM	Diabe	38.1	22.67672895	18.667619	23.895641	18.658407	26.83075435	16.6772	31.53940249	48.844
DM	Diabe	38.5	27.36031183	26.668266	23.995249	18.44426337	27.62516076	18.689	27.76314438	39.976
DM	Diabe	38.3	25.5735501	20.438106	23.440656	25.85520376	24.33073411	21.819	25.86926919	29.148
		Mean	26.33583843	23.843164	22.897511	22.50672654	26.70258041	19.8341	30.67898596	35.944
		SE	1.487694155	2.5737081	0.8879137	2.297464205	0.828579205	1.30978	2.574004608	5.257
		CV	11%	22%	8%	20%	6%	13%	17%	29%
DM-MQ	Diabe	37.2	31.39004261	29.820942	23.771674	22.98827027	30.38627218	19.4503	28.33042253	34.757
DM-MQ	Diabe	36.4	32.54400071	23.477003	25.496659	34.35057271	27.02327123	22.4197	28.85448589	21.585
DM-MQ	Diabe	38.7	28.68704355	30.172314	23.82401	31.36636073	23.41855332	25.3072	26.81219005	15.794
		Mean	30.87369562	27.82342	24.364114	29.56840123	26.94269891	22.3924	27.99903282	24.045
		SE	1.142947986	2.1755743	0.5664739	3.400978925	2.01181058	1.69079	0.612401675	5.6106
		CV	6%	14%	4%	20%	13%	13%	4%	40%
HF	High F	37.5	27.83240054	16.001821	23.960737	21.69147225	19.89452984	22.4298	20.39372428	29.79
HF	High F	34.8	29.75896082	15.157078	26.529698	23.57157279	27.76355988	31.7179	24.5451319	33.612
HF	High F	31.8	24.58627207	21.67291	27.648033	26.32810658	21.9834104	27.9195	21.10114025	10.712
HF	High F	33.7	44.6545675	17.611994	24.966161	27.3427935	20.74507778	23.3661	19.98216127	18.515
		Mean	31.70805024	17.610951	25.776157	24.73348628	22.59664447	26.3583	21.50553942	23.157
		SE	4.445518752	1.4465563	0.8176992	1.289547414	1.774889516	2.15152	1.039209436	5.242
		CV	28%	16%	6%	10%	16%	16%	10%	45%
HF-MQ	High F	37.1	32.17099782	25.626812	24.253852	34.71198684	24.84058745	23.8956	23.75522643	32.545
HF-MQ	High F	39.8	21.67109581	24.04882	25.779409	21.9036797	23.92139996	19.1278	20.95070205	22.681
HF-MQ	High F	39.8	21.11308411	31.894253	24.303777	29.62127922	20.75721021	25.5485	22.98391103	12.051
HF-MQ	High F	35.8	28.3232721	17.991974	22.99292	25.39086536	21.86944018	24.3055	20.73132983	30.06
		Mean	25.81961246	24.890464	24.332489	27.90695278	22.84715945	23.2194	22.10529234	24.334
		SE	2.676596207	2.8561745	0.5697244	2.763110976	0.933254639	1.4084	0.748058878	4.599
		CV	21%	23%	5%	20%	8%	12%	7%	38%

t-test

	O.Phosphoethanolamine	Ornithine	Palmitate	Phenylalanine	Phosphoenolpyruvate	Proline	Prostaglandin.E2	Pterin
DM/NC	1.247211364	0.9727547	0.8566931	0.773840622	1.205954347	0.89523	1.276124319	1.6738
P-value	0.102012717	0.8693571	0.059987	0.06987641	0.038286952	0.38644	0.172268562	0.0438
DM-MQ/	1.462114986	1.1351414	0.9115649	1.016639624	1.216798691	1.0107	1.164648881	1.1197
P-value	0.018536551	0.434754	0.2277882	0.899209856	0.10807923	0.93744	0.377049037	0.6511
HF/NC	1.501628311	0.7184925	0.9643955	0.850402495	1.02052016	1.1897	0.894545272	1.0784
P-value	0.077871262	0.0784116	0.5781337	0.107792779	0.851925381	0.21281	0.505332396	0.7767
HF-MQ/N	1.22276396	1.0154825	0.9103817	0.959514644	1.031834034	1.04802	0.919492618	1.1332
P-value	0.227976113	0.9289723	0.1635624	0.737838165	0.705311412	0.68978	0.600846714	0.5941
DM- MQ	1.172307299	1.1669349	1.0640508	1.313758409	1.008992333	1.12898	0.912645315	0.669
P-value	0.07286979	0.3128729	0.2591624	0.13270105	0.906694989	0.27714	0.425211958	0.1873
HF-MQ/H	0.814292026	1.4133516	0.9439921	1.128306477	1.011086379	0.88091	1.027888299	1.0508
P-value	0.299762457	0.0633443	0.1976201	0.338101226	0.90466193	0.268	0.656036041	0.8715

SampleD	class	Weight	Pyruvate	Ribose	Ribose.5.phosphate	Serine	Sphingosine	Stearate	Succinate	Threonine
NC	Contr	38.5	31.04066	31.985	30.4385041	35.108	26.08265498	20.14442	26.092308	34.357019
NC	Contr	40	35.9622	27.93	26.27542557	31.409	26.87424309	19.02224	17.55856	24.967812
NC	Contr	34.4	31.99871	29.02	30.16363208	30.345	19.64081454	27.44166	25.466371	23.157509
NC	Contr	39.3	36.06818	23.762	21.9484185	25.917	23.91896219	23.10395	21.176198	23.746326
		Mean	33.76744	28.174	27.20649506	30.695	24.1291687	22.42807	22.573359	26.557166
		SE	1.312572	1.7021	1.993840543	1.8914	1.621240571	1.879885	1.9969309	2.6271378
		CV	8%	12%	15%	12%	13%	17%	18%	20%
DM	Diabe	38.3	10.96628	28.313	23.84674138	17.492	23.40643844	19.84858	24.593651	22.55582
DM	Diabe	38.1	12.36346	32.396	26.48191494	12.016	29.81435848	22.82454	28.065404	15.038191
DM	Diabe	38.5	15.66481	25.86	22.64098192	15.623	20.96998576	22.11494	33.511597	8.3586597
DM	Diabe	38.3	16.19793	29.198	23.33029369	22.935	21.56007634	23.42302	31.715107	21.179967
		Mean	13.79812	28.942	24.07498298	17.016	23.93771476	22.05277	29.47144	16.783159
		SE	1.268897	1.3507	0.83946098	2.2767	2.026445489	0.781852	1.9817223	3.249008
		CV	18%	9%	7%	27%	17%	7%	13%	39%
DM-MQ	Diabe	37.2	10.98127	28.878	33.02618681	18.29	22.65704038	22.56156	30.779163	19.132061
DM-MQ	Diabe	36.4	14.36668	29.523	29.65020817	22.524	26.26839489	27.02167	28.806284	18.042452
DM-MQ	Diabe	38.7	16.59718	22.469	26.4235547	27.21	21.42409993	24.58033	30.718721	20.208856
		Mean	13.98171	26.956	29.69998322	22.675	23.44984506	24.72119	30.10139	19.127789
		SE	1.632558	2.2515	1.906178188	2.5762	1.453524781	1.289447	0.6477878	0.6253906
		CV	20%	14%	11%	20%	11%	9%	4%	6%
HF	High F	37.5	29.18089	19.234	19.58675165	22.081	22.89772805	25.66901	20.517623	25.44499
HF	High F	34.8	29.13605	21.023	29.93522476	21.027	23.1337564	26.75361	22.29322	27.868936
HF	High F	31.8	40.81846	24.782	26.76234926	28.756	23.03142889	29.22295	21.406111	37.168518
HF	High F	33.7	34.50395	20.428	23.03688008	30.495	19.56909401	25.03418	18.436596	36.375145
		Mean	33.40984	21.367	24.83030144	25.59	22.15800184	26.66994	20.663387	31.714397
		SE	2.772395	1.1976	2.245444008	2.3667	0.864321042	0.922065	0.8260267	2.9659604
		CV	17%	11%	18%	18%	8%	7%	8%	19%
HF-MQ	High F	37.1	29.09082	25.303	27.97363973	38.256	26.79238786	27.33706	27.285141	37.443161
HF-MQ	High F	39.8	26.48241	30.438	22.49585378	27.229	30.02159328	27.94726	20.303541	28.437315
HF-MQ	High F	39.8	31.86033	16.303	22.20782515	36.18	34.4375234	26.26372	21.184087	39.681513
HF-MQ	High F	35.8	34.10237	26.128	25.86327554	27.479	19.02328651	24.66603	20.993782	29.287962
		Mean	30.38398	24.543	24.63514855	32.286	27.56869776	26.55352	22.441637	33.712488
		SE	1.655811	2.9684	1.388113237	2.8794	3.250950792	0.718972	1.6255436	2.842403
		CV	11%	24%	11%	18%	24%	5%	14%	17%

t-test

	Pyruvate	Ribose	Ribose.5.phosphate	Serine	Sphingosine	Stearate	Succinate	Threonine
DM/NC	0.408622	1.0272	0.884898364	0.5544	0.992065456	0.983266	1.305585	0.6319635
P-value	3.47E-05	0.7361	0.197904667	0.0036	0.94358884	0.859824	0.049662	0.0579033
DM-MQ/	0.414059	0.9568	1.091650474	0.7387	0.971846372	1.102243	1.3334918	0.7202496
P-value	0.000211	0.6772	0.421294778	0.0494	0.776901771	0.396193	0.026689	0.0650019
HF/NC	0.98941	0.7584	0.912660796	0.8337	0.918307718	1.189132	0.9153882	1.1941936
P-value	0.910997	0.017	0.45889869	0.143	0.324563417	0.089171	0.4108034	0.2407859
HF-MQ/N	0.899801	0.8711	0.90548777	1.0518	1.142546521	1.183941	0.9941647	1.2694309
P-value	0.160431	0.3294	0.330609382	0.6605	0.380293006	0.086275	0.9608617	0.1140016
DM- MQ	1.013305	0.9314	1.233645035	1.3325	0.979619203	1.121001	1.0213749	1.1397013
P-value	0.931441	0.4581	0.030312044	0.1619	0.863128871	0.119238	0.8039503	0.5719962
HF-MQ/H	0.909432	1.1487	0.992140535	1.2617	1.244186997	0.995635	1.086058	1.0630026
P-value	0.384913	0.3593	0.943472724	0.1225	0.15885798	0.92393	0.3671004	0.64395

SampleD	class	Weight	Thymidine	Tryptophan	Tyrosine	Uracil	Urea	Valine
NC	Contr	38.5	25.8993193	32.1467588	28.1712	26.66	31.6	24.039
NC	Contr	40	27.1815049	26.4095437	22.8671	20.36	36.3	19.968
NC	Contr	34.4	33.1745464	28.087871	23.66903	25.42	27.7	22.739
NC	Contr	39.3	29.2389713	26.0765287	21.00217	21.18	23.6	21.113
		Mean	28.8735855	28.1801755	23.92738	23.41	29.8	21.965
		SE	1.59010397	1.39351982	1.520906	1.552	2.72	0.8951
		CV	11%	10%	13%	13%	18%	8%
DM	Diabe	38.3	22.5019083	23.4765463	24.27639	22.71	23.7	37.087
DM	Diabe	38.1	22.175109	20.7853255	22.07453	25.74	24.2	24.997
DM	Diabe	38.5	23.3999182	19.1380922	19.19965	26.36	24.9	22.976
DM	Diabe	38.3	22.4683863	25.6675389	24.86013	25.54	25.1	36.358
		Mean	22.6363304	22.2668757	22.60268	25.09	24.5	30.354
		SE	0.26490031	1.44372464	1.283127	0.813	0.33	3.7027
		CV	2%	13%	11%	6%	3%	24%
DM-MQ	Diabe	37.2	21.4774872	21.4962668	29.00184	23.34	23.4	32.801
DM-MQ	Diabe	36.4	24.1132278	30.3552671	36.19826	24.89	24.5	35.504
DM-MQ	Diabe	38.7	23.5302665	27.5938035	27.89066	22.04	27.1	32.606
		Mean	23.0403272	26.4817791	31.03025	23.42	25	33.637
		SE	0.79933566	2.61711803	2.603836	0.826	1.08	0.9353
		CV	6%	17%	15%	6%	7%	5%
HF	High F	37.5	27.38741	23.414038	21.10849	22.95	17.4	16.275
HF	High F	34.8	28.0573111	26.9674762	25.19691	22.08	25.3	18.622
HF	High F	31.8	31.2975409	29.9455459	26.45081	24.2	27.5	23.004
HF	High F	33.7	23.5952976	30.1194747	26.26128	23.63	22.7	20.925
		Mean	27.5843899	27.6116337	24.75437	23.21	23.3	19.707
		SE	1.58015831	1.57509684	1.246226	0.456	2.17	1.4524
		CV	11%	11%	10%	4%	19%	15%
HF-MQ	High F	37.1	29.6352112	29.7330142	24.99394	25.75	24.4	26.422
HF-MQ	High F	39.8	29.1834787	25.4663269	19.62195	21.28	27.3	16.704
HF-MQ	High F	39.8	29.2779102	30.2203555	25.18173	22.11	26.3	24.58
HF-MQ	High F	35.8	26.3919033	25.5027772	24.57706	20.99	23.2	21.12
		Mean	28.6221259	27.7306184	23.59367	22.53	25.3	22.206
		SE	0.74974465	1.30059833	1.329922	1.098	0.92	2.1382
		CV	5%	9%	11%	10%	7%	19%

t-test

	Thymidine	Tryptophan	Tyrosine	Uracil	Urea	Valine
DM/NC	0.78398058	0.790161	0.944637	1.072	0.82	1.3819
P-value	0.00827334	0.02571287	0.530334	0.374	0.1	0.0699
DM-MQ/	0.7979725	0.93973081	1.296852	1.001	0.84	1.5314
P-value	0.03296169	0.56264716	0.053585	0.993	0.21	0.0003
HF/NC	0.95535035	0.97982476	1.034563	0.992	0.78	0.8972
P-value	0.58613266	0.79595619	0.688702	0.91	0.11	0.2338
HF-MQ/N	0.99129101	0.98404704	0.986053	0.963	0.85	1.011
P-value	0.89094314	0.82139784	0.874233	0.662	0.17	0.9204
DM- MQ	1.01784727	1.18929029	1.372858	0.934	1.02	1.1081
P-value	0.60790083	0.18954262	0.02471	0.219	0.62	0.4939
HF-MQ/H	1.03762041	1.00430923	0.953111	0.971	1.09	1.1269
P-value	0.57462949	0.95544124	0.547736	0.587	0.42	0.3708