

## **Impact of reperfusion on plasma oxylipins in ST-segment Elevation Myocardial Infarction**

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**Table S1: List of oxylipin compounds that were quantified in plasma of by reversed-phase HPLC-MS/MS**

Analyte	Pathway	Fatty Acid	Q1 Mass (Da)	Q3 Mass (da)	Internal standard name	Retention time (min)	Response factor	LLOD in 100ul (ng/ul)	ULOD in 100ul (ng/ul)
PGD2	COX	AA	351	271	(d4) PGD2.IS	7.91	2.28045	0.003	22.22
PGE2	COX	AA	351	271	(d4) PGE2.IS	7.59	8.68273	0.003	22.22
5-HETE	LOX	AA	319	115	(d8) 5-HETE.IS	17.13	0.90038	0.0002	22.22
5-oxoETE	LOX	AA	317	203	(d7) 5-oxoETE.IS	17.5	1.04473	0.0002	22.22
8-HETE	LOX	AA	319	155	(d8) 5-HETE.IS	16.66	1.24638	0.0009	22.22
9-HETE	LOX	AA	319	123	(d8) 5-HETE.IS	16.8	0.29958	0.003	22.22
11-HETE	LOX	AA	319	167	(d8) 12-HETE.IS	16.39	7.67408	0.0009	22.22
12-HETE	LOX	AA	319	135	(d8) 12-HETE.IS	16.56	0.15621	0.003	22.22
12-oxoETE	LOX	AA	317	153	(d7) 5-oxoETE.IS	16.54	0.12689	0.04	22.22
tetranor-12-HETE	LOX	AA	265	109	(d8) 12-HETE.IS	13.29	2.40204	0.0002	22.22
15-HETE	LOX	AA	319	175	(d8) 15-HETE.IS	16.05	0.85626	0.003	22.22
15-oxoETE	LOX	AA	317	113	(d7) 5-oxoETE.IS	16.11	3.26434	0.0002	22.22
9-HOTrE	LOX	ALA	293	171	(d4) 9-HODE.IS	14.46	1.50163	0.003	22.22
9-oxoOTrE	LOX	ALA	291	185	(d7) 5-oxoETE.IS	14.96	2.2951	0.0002	22.22
13-HOTrE	LOX	ALA	293	195	(d4) 13-HODE.IS	14.6	1.15092	0.003	22.22
5-HEPE	LOX	EPA	317	115	(d8) 5-HETE.IS	15.79	0.68513	0.003	22.22
12-HEPE	LOX	EPA	317	179	(d8) 12-HETE.IS	15.32	1.73582	0.003	22.22
15-HEPE	LOX	EPA	317	219	(d8) 15-HETE.IS	14.98	1.56695	0.148	22.22
4-HDoHE	LOX	DHA	343	101	(d8) 5-HETE.IS	17.32	0.39766	0.003	22.22
7-HDoHE	LOX	DHA	343	141	(d8) 5-HETE.IS	16.66	0.51513	0.0009	22.22
8-HDoHE	LOX	DHA	343	109	(d8) 5-HETE.IS	16.73	0.25003	0.003	22.22
10-HDoHE	LOX	DHA	343	153	(d8) 12-HETE.IS	16.35	1.68431	0.0002	22.22
14-HDoHE	LOX	DHA	343	205	(d8) 15-HETE.IS	16.29	0.78401	0.003	22.22
16-HDoHE	LOX	DHA	343	233	(d8) 15-HETE.IS	15.97	3.11823	0.0009	22.22
17-HDoHE	LOX	DHA	343	245	(d8) 15-HETE.IS	16.03	0.2437	0.042	22.22
17keto-DHA	LOX	DHA	341	297	(d7) 5-oxoETE.IS	16.28	0.11372	0.042	22.22
11-HDoHE	LOX/non-enz	DHA	343	149	(d8) 12-HETE.IS	16.48	0.88676	0.003	22.22
13-HDoHE	LOX/non-enz	DHA	343	221	(d8) 12-HETE.IS	16.17	0.50603	0.003	22.22
17-Keto DPA	LOX	DPA	343	247	(d7) 5-oxoETE.IS	16.86	0.1154	0.012	22.22
9-HODE	LOX	LA	295	171	(d4) 9-HODE.IS	15.93	1.33961	0.0002	22.22
9-oxoODE	LOX	LA	293	185	(d7) 5-oxoETE.IS	16.26	0.95769	0.012	22.22
13-HODE	LOX	LA	295	195	(d4) 13-HODE.IS	15.78	3.34877	0.0002	22.22
13-oxoODE	LOX	LA	293	167	(d7) 5-oxoETE.IS	15.95	0.65942	0.012	22.22

9,10,13-triHOME	LOX/CYP-e	LA	329	171	(d4) 9,10 diHOME.IS	7.44	39.48725	0.0002	22.22
9,12,13-triHOME	LOX/CYP-e	LA	329	211	(d4) 12,13 diHOME.IS	7.38	61.41712	0.0002	22.22
13-HOTrE- $\gamma$	LOX	GLA	293	193	(d4) 13-HODE.IS	14.88	3.26494	0.0034	22.22
8-HETrE	LOX	DGLA	321	157	(d8) 5-HETE.IS	17.07	1.87458	0.0009	22.22
15-HETrE	LOX	DGLA	321	221	(d8) 15-HETE.IS	16.7	3.79631	0.0009	22.22
5,6-DiHETrE	CYP-e	AA	337	145	(d11) 8,9 DiHETrE.IS	15.55	1.78532	0.0034	22.22
8,9-DiHETrE	CYP-e	AA	337	127	(d11) 8,9 DiHETrE.IS	14.85	1.77545	0.0034	22.22
11,12-DiHETrE	CYP-e	AA	337	167	(d11) 11,12 DiHETrE.IS	14.27	9.12136	0.0034	22.22
14,15-DiHETrE	CYP-e	AA	337	207	(d11) 14,15 DiHETrE.IS	13.56	8.93326	0.00028	22.22
12,13-EpODE	CYP-e	ALA	293	183	(d4) 12,13 diHOME.IS	16.17	21.70636	0.0009	22.22
12,13-diHODE	CYP-e	ALA	311	183	(d4) 12,13 diHOME.IS	11.24	34.86462	0.00028	22.22
16,17-DiHDoPE	CYP-e	DHA	361	233	(d11) 14,15 DiHETrE.IS	13.93	6.23301	0.00098	22.22
19,20-EpDoPE	CYP-e	DHA	343	241	(d11) 14,15 DiHETrE.IS	16.87	1.10022	0.012	22.22
19,20-DiHDoPE	CYP-e	DHA	361	229	(d11) 14,15 DiHETrE.IS	13.35	0.91613	0.012	22.22
9,10-EpOME	CYP-e	LA	295	171	(d4) 9,10 diHOME.IS	17.35	37.33091	0.0009	22.22
9,10-diHOME	CYP-e	LA	313	201	(d4) 9,10 diHOME.IS	13.24	79.72576	0.0009	22.22
12,13-EpOME	CYP-e	LA	295	195	(d4) 12,13 diHOME.IS	17.17	22.85861	0.0034	22.22
12,13-diHOME	CYP-e	LA	313	183	(d4) 12,13 diHOME.IS	12.71	34.6768	0.00028	22.22
16-HETE	CYP-h	AA	319	189	(d8) 15-HETE.IS	15.5	0.72228	0.0009	22.22
17-HETE	CYP-h	AA	319	247	(d8) 15-HETE.IS	15.4	2.73902	0.0034	22.22
18-HETE	CYP-h	AA	319	261	(d6) 20-HETE.IS	15.26	2.58404	0.0034	22.22
19-HETE	CYP-h	AA	319	231	(d6) 20-HETE.IS	14.88	0.17759	0.148	22.22
20-HETE	CYP-h	AA	319	245	(d6) 20-HETE.IS	15.01	0.32666	0.0034	22.22
20-COOH-AA	CYP-h	AA	333	271	(d5) EPA.IS	14.41	0.64699	0.012	22.22
18-HEPE	CYP-h	EPA	317	215	(d8) 15-HETE.IS	14.49	1.1901	0.003	22.22
20-HDoHE	CYP-h	DHA	343	241	(d6) 20-HETE.IS	15.7	0.8816	0.012	22.22

**Abbreviations:** AA: Arachidonic acid, ALA: Alpha linoleic acid, COX: Cyclooxygenase, CYP-e: Cytochrome P450 epoxygenase, CYP-h: Cytochrome P450 hydroxylase, DGLA: Dihomo gamma-linoleic acid, DHA: Docosahexaenoic acid, DiHDPE: Dihydroxydocosapentaenoic acid, DiHETE: Dihydroxyeicosatetraenoic acid, DiHETrE: Dihydroxy-eicosatrienoic acid, DPA: Docosapentaenoic acid, EPA: Eicosapentaenoic acid, EpDPE: Epoxydocosapentaenoic acid, EpODE: Epoxy-octadecadienoic acid, EpOME: Epoxy-octadecenoic acid, GLA: Gamma-linolenic acid, HDoHE: Hydroxy-docosahexaenoic acid, HEPE: Hydroxyeicosapentaenoic acid, HETE: Hydroxyeicosatetraenoic acid, HETrE: Hydroxyeicosatrienoic acid, HODE: Hydroxyoctadecadienoic acid, HOTrE: Hydroxy-octadecatrienoic acid, LA: Linoleic acid, LLOD: Lower limit of detection, LOX: Lipoxygenase, MPO: Myeloperoxidase, non-enz: Non-enzymatic oxidation, Oxo-ETE: Oxo-eicosatetraenoic acid, OxoODE: Oxo-octadecadienoic acid, OxoOTrE: Oxo-octadecatrienoic acid, PG: Prostaglandin, TriHOME: Trihydroxy-octadecenoic acid, ULOD: Upper limit of detection.

**Table S2. All quantified oxylipins in STEMI groups during I/R.**

Compounds	FA	Pathway	Isch (nM)	R-2h(nM)	R-24h(nM)	R-48h(nM)	R-30d(nM)
11,12 DiHETrE	AA	CYP-e	0.32±0.04	0.35±0.05	0.23±0.03	0.25±0.03	0.33±0.02
14,15 DiHETrE	AA	CYP-e	0.39±0.05	0.40±0.05	0.24±0.03	0.23±0.02 b	0.33±0.02
5,6 DiHETrE	AA	CYP-e	0.20±0.03	0.19±0.03	0.08±0.01 a,b	0.08±0.01 a,b	0.11±0.01
8,9 DiHETrE	AA	CYP-e	0.19±0.03	0.20±0.04	0.10±0.01	0.09±0.01 b	0.13±0.01
16-HETE	AA	CYP-h	0.29±0.03	0.27±0.03	0.20±0.02	0.20±0.02	0.33±0.03
18-HETE	AA	CYP-h	0.11±0.02	0.15±0.03	0.04±0.01 b	0.03±0.01 b	0.05±0.01 b
20-COOH-AA	AA	CYP-h	60.69±7.59	73.59±11.27	46.92±6.28	50.57±5.86	65.58±11.03
20-HETE	AA	CYP-h	0.87±0.14	0.69±0.09	0.39±0.05 a	0.38±0.05 a	0.54±0.13
12-HETE	AA	LOX	0.75±0.30	0.52±0.16	0.46±0.14	0.53±0.16	0.12±0.07 a
5-HETE	AA	LOX	3.95±0.92	2.51±0.25	1.33±0.19 a	1.44±0.18 a	1.21±0.21 a
5-oxoETE	AA	LOX	0.10±0.01	0.07±0.01	0.03±0.007 a	0.03±0.01 a	0.05±0.01
8-HETE	AA	LOX	1.00±0.15	0.70±0.07	0.57±0.06 a	0.54±0.06 a	0.62±0.14
tetranor 12-HETE	AA	LOX	0.47±0.07	0.65±0.10	0.38±0.05 b	0.29±0.04 b	0.38±0.04
15-HETE	AA	LOX/COX	1.61±0.32	1.15±0.14	0.8±0.11 a	0.8±0.09 a	0.58±0.07 a
11-HETE	AA	LOX/COX/non-enzyme	0.44±0.12	0.25±0.05	0.16±0.04 a	0.15±0.04 a	0.13±0.02 a
9-HETE	AA	LOX/non-enz	0.30±0.20	0.10±0.06	0.10±0.05	0.12±0.06	0.27±0.13
15-oxoETE	AA	LOX	0.06±0.01	0.05±0.01	0.02±0.00 a	0.03±0.00 a	0.02±0.01 a
12,13 diHODE	ALA	CYP-e	0.16±0.05	0.1±0.01	0.09±0.01	0.13±0.03	0.17±0.02
12,13 EpODE	ALA	CYP-e	0.07±0.01	0.09±0.01	0.06±0.01	0.08±0.03	0.07±0.01
9 oxoOTrE	ALA	LOX	0.28±0.03	0.28±0.04	0.10±0.02 a,b	0.10±0.03 a,b	0.09±0.02 a,b
9-HOTrE	ALA	LOX	5.29±0.71	4.59±0.71	1.84±0.22 a,b	1.84±0.29 a,b	2.32±0.34 a,b
15-HETrE	DGLA	LOX	0.31±0.06	0.21±0.03	0.09±0.01 a	0.12±0.02 a	0.10±0.01 a
8-HETrE	DGLA	LOX	0.26±0.06	0.17±0.02	0.07±0.01 a	0.08±0.01 a	0.09±0.01 a
16,17 DiHDPE	DHA	CYP-e	0.04±0.01	0.04±0.01	0.03±0.00	0.03±0.00	0.04±0.01
16,17 EpDPE	DHA	CYP-e	0.03±0.02	0.03±0.02	0.01±0.01	0.01±0.01	0.06±0.06
19,20 DiHDPE	DHA	CYP-e	1.59±0.17	1.72±0.26	0.93±0.12 a,b	0.89±0.11 a,b	0.83±0.07 a,b
19,20 EpDPE	DHA	CYP-e	0.02±0.01	0.01±0.01	0.001±0.00 a	0.002±0.00 a	0.008±0.01
20-HDoHE	DHA	CYP-h	0.52±0.11	0.35±0.06	0.21±0.05 a	0.17±0.05 a	0.14±0.05 a
10-HDoHE	DHA	LOX	0.18±0.04	0.08±0.01	0.08±0.03	0.05±0.01 a	0.08±0.02
14-HDoHE	DHA	LOX	0.63±0.12	0.35±0.05	0.28±0.05 a	0.26±0.05 a	0.22±0.04 a
16-HDoHE	DHA	LOX	0.27±0.06	0.16±0.03	0.12±0.03	0.09±0.02 a	0.09±0.02 a
17-HDoHE	DHA	LOX	1.17±0.23	0.84±0.14	0.58±0.10 a	0.53±0.09 a	0.27±0.15 a
17-keto DHA	DHA	LOX	5.30±0.92	4.27±0.63	6.74±1.25	6.36±1.09	3.87±0.70
4-HDoHE	DHA	LOX	2.67±0.45	1.68±0.23	0.82±0.09 a	0.96±0.09 a	0.80±0.16 a
7-HDoHE	DHA	LOX	0.57±0.07	0.37±0.06	0.25±0.04 a	0.26±0.05 a	0.20±0.08 a
8-HDoHE	DHA	LOX	0.86±0.16	0.69±0.11	0.30±0.09 a	0.28±0.07 a	0.26±0.11 a
11-HDoHE	DHA	LOX/non-enz	0.06±0.04	0±0.00	0.03±0.03	0.00±0.00	0.00±0.00
13-HDoHE	DHA	LOX/non-enz	0.24±0.10	0.06±0.03	0.08±0.04	0.02±0.02	0.00±0.00
17-keto DPA	DPA	LOX	4.55±0.82	4.08±0.49	4.08±0.99	3.97±0.77	2.89±0.85
14,15 diHETE	EPA	CYP-e	1.12±0.12	1.12±0.21	0.77±0.09	0.63±0.05	0.65±0.04
17,18 diHETE	EPA	CYP-e	2.67±0.26	2.63±0.39	1.6±0.19 a,b	1.57±0.18 a,b	1.18±0.10 a,b
18-HEPE	EPA	CYP-h	0.56±0.08	0.41±0.06	0.15±0.03 a,b	0.09±0.01 a,b	0.14±0.02 a,b

12-HEPE	EPA	LOX	0.80±0.23	0.47±0.07	0.15±0.03 a	0.10±0.03 a	0.08±0.02 a
5-HEPE	EPA	LOX	1.18±0.17	0.94±0.14	0.38±0.07 a,b	0.18±0.05 a,b	0.29±0.08 a,b
15-HEPE	EPA	LOX/COX	0.25±0.04	0.19±0.04	0.07±0.01 a	0.07±0.01a	0.08±0.01 a
13-HOTrE	GLA	LOX	3.02±0.39	2.35±0.28	1.84±0.32 a	1.50±0.18 a	2.07±0.24
13-HOTrE-y	GLA	LOX	0.47±0.06	0.34±0.05	0.11±0.02 a,b	0.10±0.01 a,b	0.19±0.03 a
9,10 diHOME	LA	CYP-e	3.59±0.84	3.05±0.49	2.86±0.91	3.93±1.86	3.21±0.40
12,13 EpOME	LA	CYP-e	1.84±0.16	2.16±0.20	1.32±0.16 b	1.38±0.25 b	1.12±0.13 b
12,13 diHOME	LA	CYP-e	5.99±2.38	3.96±0.42	3.78±0.55	4.25±1.24	4.97±0.60
9,10 EpOME	LA	CYP-e	0.78±0.10	0.83±0.10	0.39±0.07	0.51±0.16	0.34±0.08 b
13-HODE	LA	LOX	27.48±3.60	23.23±2.84	14.82±2.03 a	14.19±1.98 a	13.63±1.19 a
13-oxoODE	LA	LOX	3.58±0.27	3.09±0.27	2.06±0.18 a,b	2.15±0.25 a,b	1.77±0.16 a,b
9-HODE	LA	LOX	31.68±3.61	28.23±3.75	13.18±1.62 a,b	13.41±1.97 a,b	12.59±1.4 a,b
9-oxoODE	LA	LOX	4.05±0.32	4.12±0.42	1.87±0.24 a,b	2.05±0.27 a,b	1.5±0.20 a,b
9,10,13 triHOME	LA	LOX/CYP-e	11.83±0.98	9.01±0.85	6.83±0.67 a	7.00±0.61 a	5.87±0.70 a
9,12,13 triHOME	LA	LOX/CYP-e	3.58±0.37	2.74±0.24	2.43±0.27	2.31±0.22 a	2.59±0.31

Values are means ± SEM. a Significant difference from Isch, b Significant difference from R-2h (One way analysis of variance (ANOVA) with a post-hoc Tukey test for multiple comparisons was used to determine statistical significance between study groups, (p<0.05). (Isch, n=45), (R-2h, n=42), (R-24h, n=442), (R-48h, n=43), (R-30d, n=29), Control n=44). Abbreviations: AA: Arachidonic acid, ALA: Alpha-linoleic acid, COX: Cyclooxygenase, CYP-e: Cytochrome P450 epoxygenase, CYP-h: Cytochrome P450 hydroxylase, DGLA: Dihomo gamma-linoleic acid, DHA: Docosahexaenoic acid, DiHDPE: Dihydroxy-docosapentaenoic acid, DiHETE: Dihydroxy-eicosatetraenoic acid, DiHETrE: Dihydroxy-eicosatrienoic acid, DPA: Docosapentaenoic acid, EPA: Eicosapentaenoic acid, EpDPE: Epoxy-docosapentaenoic acid, EpODE: Epoxy-octadecadienoic acid, EpOME: Epoxy-octadecenoic acid, GLA: Gamma-linoleic acid, HDoHE: Hydroxy-docosahexaenoic acid, HEPE: Hydroxy-eicosapentaenoic acid, HETE: Hydroxy-eicosatetraenoic acid, HETrE: Hydroxy-eicosatrienoic acid, HODE: Hydroxy-octadecadienoic acid, HOTrE: Hydroxy-octadecatrienoic acid, LA: Linoleic acid, LOX: Lipoxigenase, non-enz: Non-enzymatic oxidation, Oxo-ETE: Oxo-eicosatetraenoic acid, OxoODE: Oxo-octadecadienoic acid, OxoOTrE: Oxo-octadecatrienoic acid, PG: Prostaglandin, TriHOME: Trihydroxy-octadecenoic acid.

## Overall study design

Title of the study	Impact of reperfusion on plasma oxylipins in ST-segment Elevation Myocardial Infarction		
Document creation date	11/20/2023	Corresponding Email	amir.ravandi@umanitoba.ca
Principle investigator	Amir Ravandi	Is the workflow targeted or untargeted?	Targeted
Institution	Precision Cardiovascular Medicine Group; St. Boniface Hospital, Albrechtsen Research Centre, 2Department of Physiology and Pathophysiology, Rady Faculty of Health Sciences, University of Manitoba	Clinical	Yes

## Lipid extraction

Extraction method	Solid-Phase Extraction	Solid-Phase Extraction	Reverse-Phase
pH adjustment	Hydrochloric acid	Were internal standards added prior extraction?	Yes

## Analytical platform

Which solvents were used	water/acetonitrile/acetic acid	Ion source	ESI
Number of separation dimensions	One dimension	MS Level	MS2
Separation type 1	LC	Mass window for precursor ion isolation (in Da total isolation window)	1
Separation mode 1 (liquid)	RP	Mass resolution for detected ion at MS2	Low resolution
Detector	Mass spectrometer	Resolution at MS2	Low
MS type	QQQ	Was/Were additional dimension/techniques used	No
MS vendor	SCIEX		

## Quality control

Blanks	Yes	Quality control	Yes
Type of Blanks	Extraction blank, Injection blank	Type of QC sample	Sample pool

## Method qualification and validation

Method validation	Yes	Precision	No
Lipid recovery	No	Accuracy	Yes
Dynamic quantification range	Yes	Guidelines followed	None
Limit of quantitation (LOQ)/Limit of detection (LOD)	Yes		

## Reporting

Are reported raw data uploaded into repository?	Available on request	Raw data upload	Available on request
Are metadata available?	No	Additional comments	-

## Sample Descriptions

### Plasma Oxylipins / Human / Plasma

Provided information	-	Additives	EDTA
Temperature handling original sample	4-8 °C	Were samples stored under inert gas?	No
Instant sample preparation	Yes	Additional preservation methods	No
Storage temperature	-80 °C	Biobank samples	No