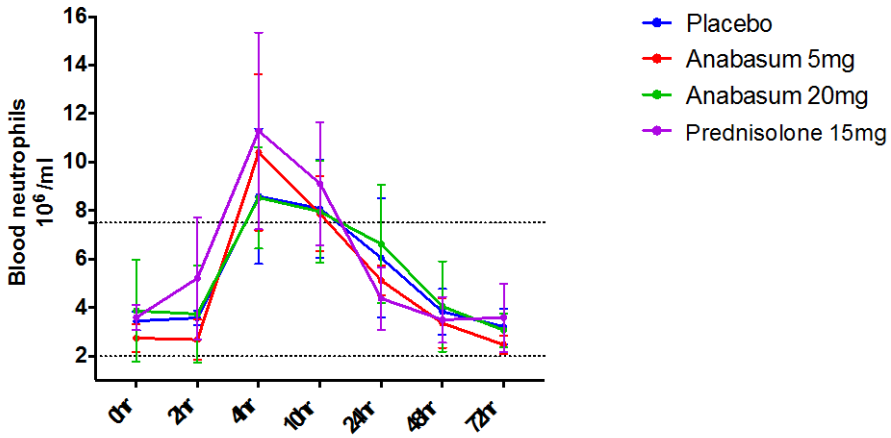
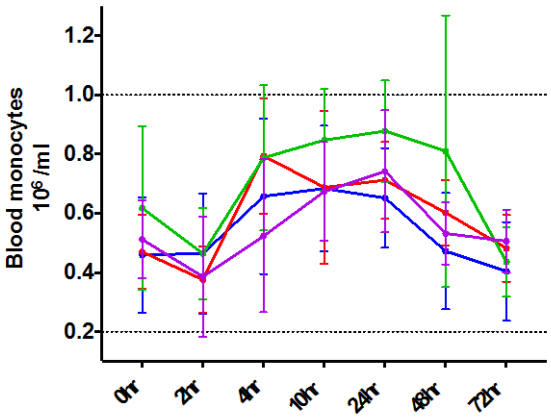
SUPPLEMENTARY INFORMATION

A



B



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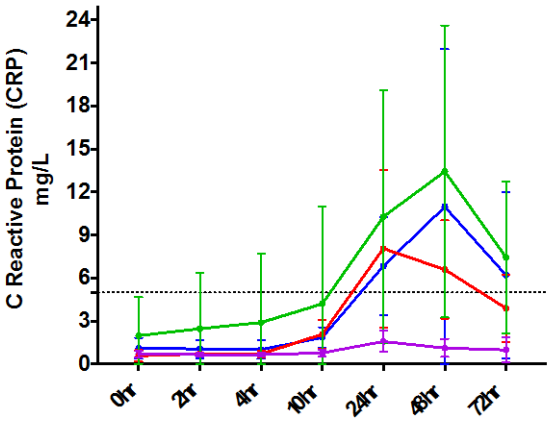
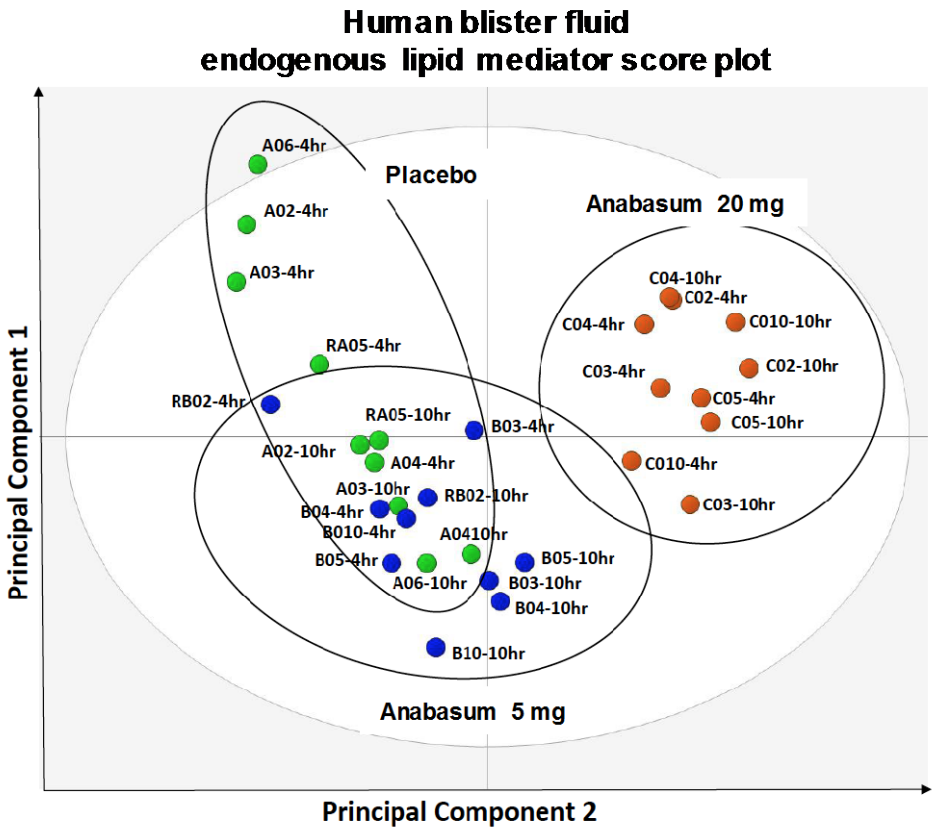


Figure S1: Effects of anabasum on peripheral blood neutrophils, monocytes and CRP

Healthy male volunteers were randomized to receive by oral route either placebo, 5 mg anabasum, 20 mg anabasum, twice daily or 15 mg prednisolone once daily for four days. On fourth day, acute inflammation was triggered by intradermal injection of 1.5 x 10^7UV killed *E. coli* (UVkEc) suspended in 100µl of saline in both the forearms. Peripheral blood was taken at specified intervals after inflammation and was processed by an external pathology lab (The Doctor's Laboratory, London, UK) for measurement of circulating neutrophil count **(A)**, circulating monocyte count **(B)** and CRP levels **(C)**. Data expressed as individual values with mean ± SD. n=5/group.

A


Human blister fluid
endogenous lipid mediator score plot
Placebo
Anabasum 20 mg
Anabasum 5 mg
A06-4hr
A02-4hr
A03-4hr
RA05-4hr
RB02-4hr
RA05-10hr
B03-4hr
A02-10hr
A04-4hr
A03-10hr
RB02-10hr
B04-4hr
B010-4hr
A0410hr
B05-4hr
B05-10hr
A06-10hr
B03-10hr
B04-10hr
B10-10hr
C04-10hr
C02-4hr
C04-4hr
C010-10hr
C03-4hr
C02-10hr
C05-4hr
C05-10hr
C010-4hr
C03-10hr
Principal Component 1
Principal Component 2

B

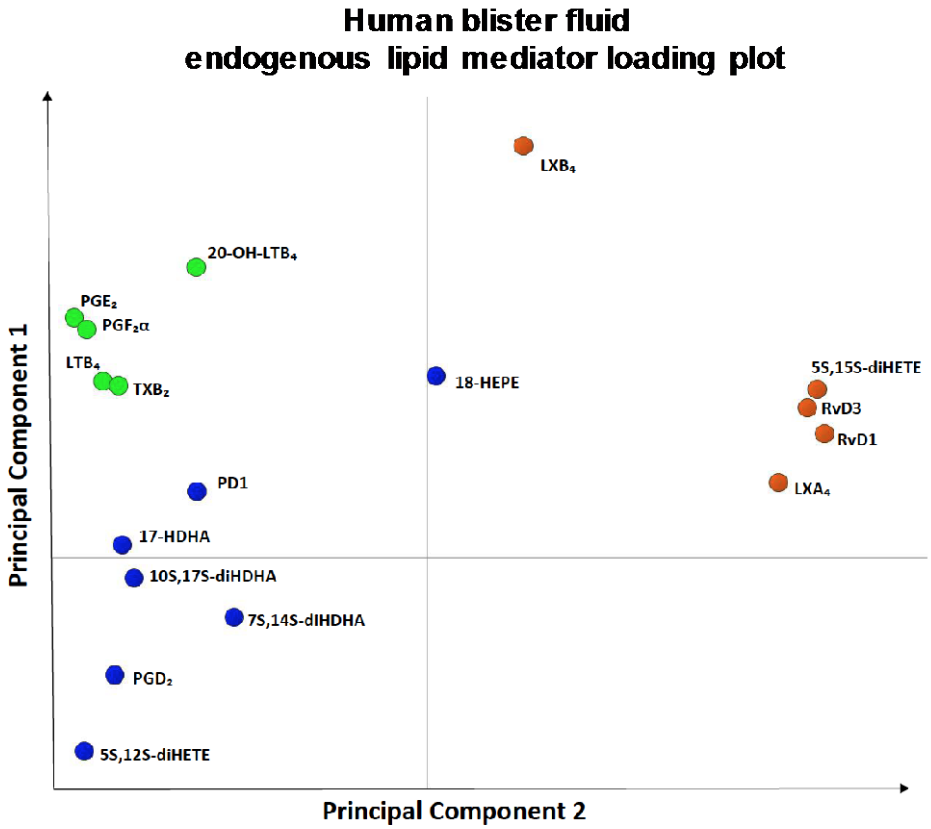

Human blister fluid
endogenous lipid mediator loading plot
LXB4
20-OH-LTB4
PGE2
PGF2α
LTB4
TXB2
18-HEPE
5S,15S-diHETE
RvD3
RvD1
PD1
LXA4
17-HDHA
10S,17S-diHDHA
7S,14S-diHDHA
PGD2
5S,12S-diHETE
Principal Component 1
Principal Component 2

Figure S2. Anabasum (20 mg) decreases pro-inflammatory prostanoids and increases specialized pro-resolving mediators

Principal component analysis (PCA) was carried out using SIMCA software version 13.03.3 from Umetrics (Umea,Sweden) following identification and quantitation of each mediator from LC-MS-MS according to reported criteria[35]. **Panel A** isthe 2-dimensional score plot of the values obtained from human blisters (green: placebo group, blue:anabasum 5 mg and orange:anabasum 20 mg). Gray shadow ellipse denotes 95% confidence interval. **Panel B** is the loading plot obtained for the endogenous lipid mediators identified using LC-MS-MS in human blister fluid. Green mediators identified in the placebo group; blue 5 mg and orange 20 mg anabasum group which included LXA_4, LXB_4, 5S,15S-DiHETE, RvD1 and RvD3.

S.no.	Neutrophil/ml	Placebo		Anabasum 5mg		Anabasum 20mg		Prednisolone 15mg	
		4hr		4hr		4hr		4hr	
		r	p	r	p	r	p	r	p
1	IFNγ	0.9	0.0833	-0.3	0.6833	-0.3	0.6833	-0.1	0.95
2	IL-1β	-0.3	0.6833	0.3	0.6833	0.8	0.1333	0.2	0.7833
3	IL-2	-0.5	0.45	-0.1	0.95	-0.8	0.1333	0.8	0.1333
4	IL-4	0.6	0.35	-0.7	0.2333	-0.5	0.45	-0.3	0.6833
5	IL-6	-0.6	0.35	0.2	0.7833	0.1	0.95	-0.3	0.6833
6	IL-8	-0.9	0.0833	0.1	0.95	0	>0.9999	0	>0.9999
7	IL-10	0.1	0.95	-0.4	0.5167	-0.2	0.7833	-0.1	0.95
8	IL-12p70	0.4	0.5167	-0.6	0.35	0	>0.9999	-0.4	0.5167
9	IL-13	-0.6	0.35	-0.1	0.95	0.1	0.95	0.4	0.5167
10	TNFα	0.5	0.45	0.3	0.6833	0.7	0.2333	0.6	0.35
11	LTB4	0.3	0.6833	0.5	0.45	1	0.0167	0	>0.9999
12	PGE2	0.6	0.35	0.1	0.95	0.2	0.7833	-0.8	0.1333
13	PGF2α	0.6	0.35	0.4	0.5167	-0.1	0.95	-0.4	0.5167
14	TXB2	0.1	0.95	0	>0.9999	0.1	0.95	-0.1	0.95
15	PGD2	0.1	0.95	0.6	0.35	0.6	0.35	-0.2	0.7833
16	LXA4	0	>0.9999	0.3	0.6833	-0.6	0.35	NA	NA
17	LXB4	0.4	0.5167	-0.8	0.1333	0.2	0.7833	-0.1	0.95
18	RvD1	NA	NA	-0.3536	0.8	0	>0.9999	-0.7	0.2333
19	RvD3	NA	NA	NA	NA	-0.2	0.7833	NA	NA
20	17-HDHA	-0.8	0.1333	0.2	0.7833	-0.1	0.95	0.4	0.5167
21	PD1	-0.2	0.7833	0.1	0.95	-0.1	0.95	-0.2	0.7833
22	14-HDHA	0.1	0.95	-0.4	0.5167	0.4	0.5167	0.2	0.7833
23	5,15-diHETE	NA	NA	NA	NA	-0.1	0.95	0.9	0.0833
24	Endotoxin	-0.3	0.6833	0	>0.9999	0.3	0.6833	-0.5	0.45
25	Blood flow	0.8	0.1333	0	>0.9999	-0.7	0.2333	-0.7	0.2333

S.no.	Neutrophil/ml	Placebo		Anabasum 5mg		Anabasum 20mg		Prednisolone 15mg	
		10hr		10hr		10hr		10hr	
		r	p	r	p	r	p	r	p
1	IFNγ	0.8	0.1333	-0.1	0.95	0.3	0.6833	0.9	0.0833
2	IL-1β	0.9	0.0833	-0.1	0.95	0.5	0.45	1	0.0167
3	IL-2	0.9	0.0833	-0.1	0.95	-0.9	0.0833	0.7	0.2333
4	IL-4	0.1	0.95	-0.3	0.6833	-0.8	0.1333	0.6	0.35
5	IL-6	0.7	0.2333	0.3	0.6833	-0.9	0.0833	0.9	0.0833
6	IL-8	0.8	0.1333	0.4	0.5167	0.8	0.1333	0.9	0.0833
7	IL-10	0.3	0.6833	0.5	0.45	-0.5	0.45	-0.1	0.95
8	IL-12p70	0.9	0.0833	-0.4	0.5167	-0.6	0.35	0.8	0.1333
9	IL-13	0.8	0.1333	-0.3	0.6833	-0.6	0.35	0.9	0.0833
10	TNFα	0.9	0.0833	-0.1	0.95	0.4	0.5167	0.6	0.35
11	LTB4	-0.1	0.95	-0.3	0.6833	-0.7	0.2333	0.6	0.35
12	PGE2	0.5	0.45	-0.4	0.5167	0.9	0.0833	0.6	0.35
13	PGF2α	0.9	0.0833	-0.2	0.7833	0.2	0.7833	1	0.0167
14	TXB2	0.6	0.35	0.8	0.1333	0.9	0.0833	-0.9	0.0833
15	PGD2	-0.3	0.6833	0.3	0.6833	-0.3	0.6833	-0.3	0.6833
16	LXA4	0.3	0.6833	0.9	0.0833	-0.7	0.2333	0	>0.9999
17	LXB4	0.6	0.35	0.3	0.6833	0.9	0.0833	0.9	0.0833
18	RvD1	-0.4472	0.5	0.0513	>0.9999	0.3	0.6833	0.3	0.6833
19	RvD3	NA	NA	NA	NA	0.8	0.1333	NA	NA
20	17-HDHA	0.8	0.1333	0.7	0.2333	-0.6	0.35	0.1	0.95
21	PD1	0.6	0.35	-0.7	0.2333	-0.7	0.2333	-0.6	0.35
22	14-HDHA	0.9	0.0833	0.6	0.35	0.2	0.7833	0.1	0.95
23	5,15-diHETE	NA	NA	NA	NA	0.1	0.95	0.9	0.0833
24	Endotoxin	0.6	0.35	-0.3	0.6833	-0.1	0.95	0.7	0.2333

Figure S3: Correlation between neutrophil count and soluble mediators of inflammation at 4hr and 10hr

S.no.	Endotoxin (Relative units)	Placebo		Anabasum 5mg		Anabasum 20mg		Prednisolone 15mg	
		4hr		4hr		4hr		4hr	
		r	p	r	p	r	p	r	p
1	Neutrophil/ml	-0.3	0.6833	0	>0.9999	0.3	0.6833	-0.5	0.45
2	IFNγ	-0.1	0.95	-0.2	0.7833	-0.3	0.6833	0.7	0.2333
3	IL-1β	-0.5	0.45	0.2	0.7833	0.3	0.6833	0.6	0.35
4	IL-2	-0.4	0.5167	-0.4	0.5167	-0.3	0.6833	-0.1	0.95
5	IL-4	0.1	0.95	-0.3	0.6833	-0.4	0.5167	0.6	0.35
6	IL-6	0.5	0.45	-0.2	0.7833	-0.6	0.35	0.6	0.35
7	IL-8	-0.1	0.95	0.9	0.0833	-0.8	0.1333	0.5	0.45
8	IL-10	-0.6	0.35	-0.6	0.35	0.3	0.6833	-0.3	0.6833
9	IL-12p70	-0.4	0.5167	0.1	0.95	-0.8	0.1333	0.3	0.6833
10	IL-13	0.1	0.95	0.6	0.35	-0.4	0.5167	-0.3	0.6833
11	TNFα	0.4	0.5167	0.7	0.2333	0.7	0.2333	0.3	0.6833
12	LTB4	0	>0.9999	-0.5	0.45	0.3	0.6833	0	>0.9999
13	PGE2	-0.1	0.95	1	0.0167	0.3	0.6833	0.6	0.35
14	PGF2α	-0.1	0.95	0.6	0.35	-0.6	0.35	0.8	0.1333
15	TXB2	0.4	0.5167	1	0.0167	0.5	0.45	0.2	0.7833
16	PGD2	0.4	0.5167	-0.1	0.95	-0.5	0.45	0.9	0.0833
17	LXA4	-0.2	0.7833	-0.3	0.6833	-0.5	0.45	NA	NA
18	LXB4	-0.4	0.5167	0.3	0.6833	0.3	0.6833	0.2	0.7833
19	RvD1	NA	NA	0	>0.9999	-0.1	0.95	-0.1	0.95
20	RvD3	NA	NA	NA	NA	-0.5	0.45	NA	NA
21	17-HDHA	0.8	0.1333	0.8	0.1333	-0.6	0.35	-0.8	0.1333
22	Blood flow	-0.8	0.1333	-1	0.0167	-0.8	0.1333	0.4	0.5167

Figure S4: Correlation between endotoxin and soluble mediators of inflammation at 4hr

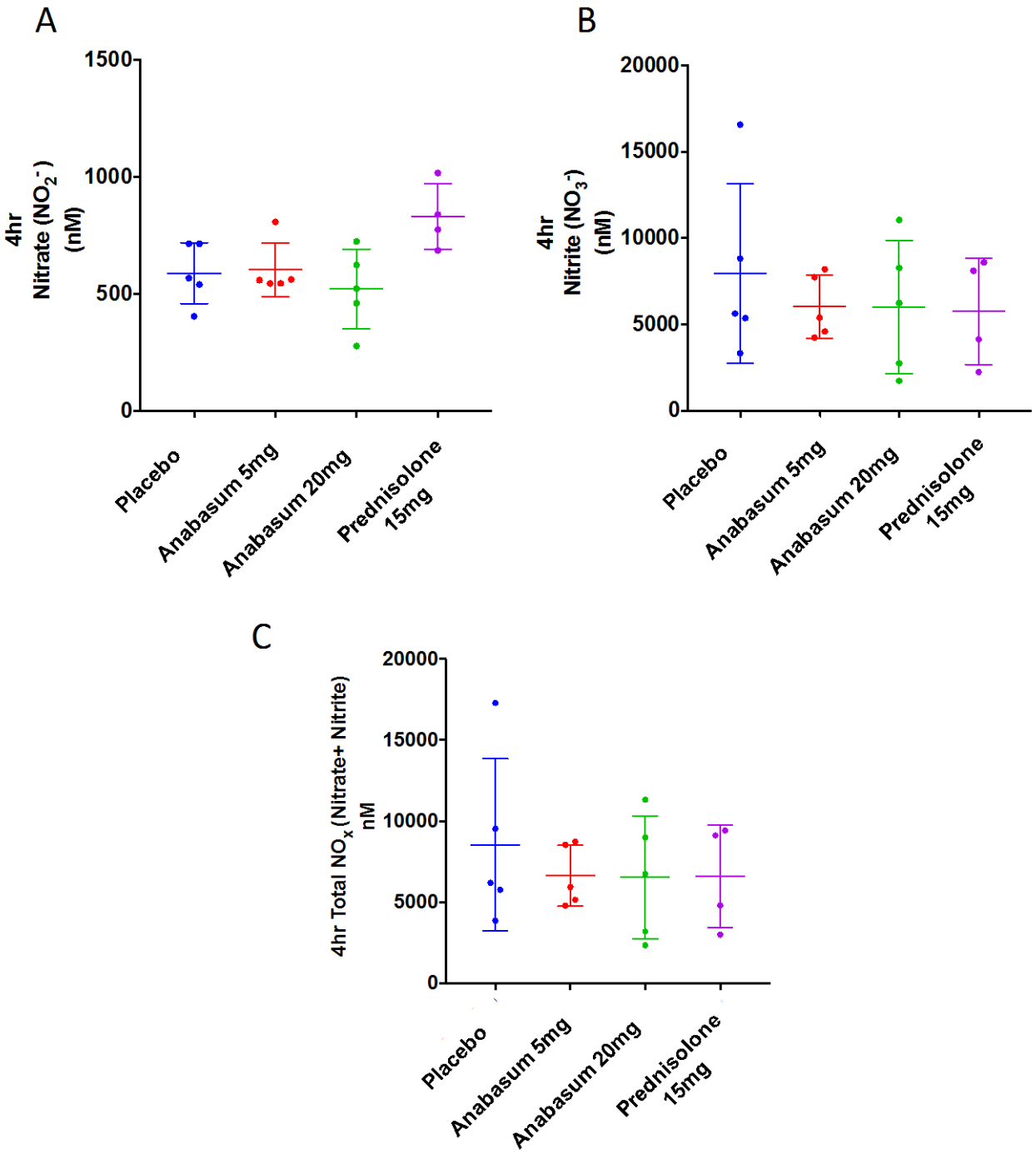


Figure S5: Effect of Anabasum on nitric oxide synthesis at the site of UVkEc triggered acute resolving inflammation

Healthy male volunteers were randomized to receive either placebo, 5 mg anabasum, 20 mg anabasum, twice daily or 15 mg prednisolone once daily for four days. On fourth day, acute inflammation was triggered by intradermal injection of 1.5 x 10^7UV killed *E. coli* (UVkEc) suspended in 100µl of saline in both the forearms. Total nitric oxide **(A)**, nitrate **(B)** and nitrite **(C)** in the cell free inflammatory exudate is shown here. Data expressed as individual values with mean ± SD. n=5/group.

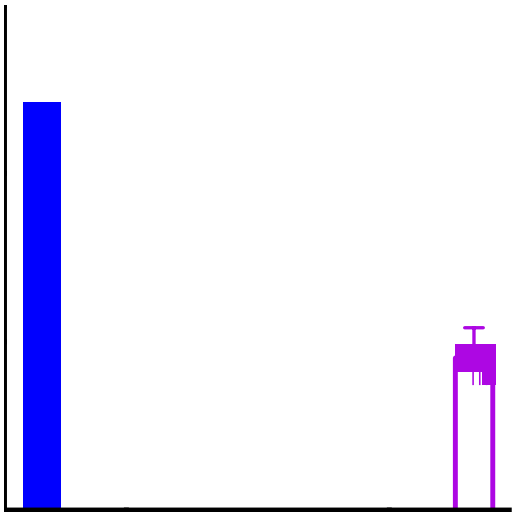


Figure S6: Effect of Anabasum on generation of 6-keto-PGF1α at the site of UVkEc triggered acute resolving inflammation

Healthy male volunteers were randomized to receive by oral route either placebo, 5 mg anabasum, 20 mg anabasum, twice daily or 15 mg prednisolone once daily for four days. On fourth day, acute inflammation was triggered by intradermal injection of 1.5 x 10^7UV killed *E. coli* (UVkEc) suspended in 100µl of saline in both the forearms. Inflammatory exudate at the injection site was acquired into a suction blister raised after 4hr (onset phase) on one forearm and after 10hr (resolution phase) on the contralateral forearm. The levels of 6-keto-$PGF_1\alpha$ in the inflammatory exudate at 4hr and 10hr are shown here. Data expressed as individual values with mean± SD. n=2/group.