

Table S1 Results of mouse kidney histopathology

No.	GROUP	SAMPLE	GENERAL	RESULTS	
1.	Physiological group	SL-1	- The sample is 2 kidney tissues d# 0.9 - 1cm.	Kidney – The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
2.		SL-3	- The sample is 2 kidney tissues d# 1 – 1.1cm.	Kidney – The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
3.		SL-4	- The sample is 2 kidney tissues d# 1 – 1.1cm.	Kidney – The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
4.		SL-5	- The sample is 2 kidney tissues d# 1 – 1.1cm.	Kidney – The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
5.		SL-6	- The specimen is 2 kidney tissue d# 1.1cm.	Kidney – The specimen is renal tissue with multiple lymphocyte permeability, plasma cells in the interstitial and peritubular tissue, and the renal pyelonephritis is scattered with destroyed renal tubules. There was no detection of gravel on this specimen.	– Kidney: Chronic pyelonephritis, mild.
6.	Physiological group treatment with EGE 200 mg/kg	SLC-2	- The specimen is 2 kidney tissue d# 1.1cm.	Kidney – The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
7.		SLC-5	- The specimen is 2 kidney tissue d# 1.1cm.	Kidney – The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
8.	Physiological group treatment with EGE 400 mg/kg	SLC-1	- The sample is 2 kidney tissues d# 0.9 - 1cm.	Kidney The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
9.		SLC-2	- The sample is 2 kidney tissues d# 1 – 1.1cm.	Kidney The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
10.		SLC-3	- The sample is 2 kidney tissues d# 0.9 – 1.0cm.	Kidney The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
11.		SLC-4	- The sample is 2 kidney tissues d# 1 – 1.1cm.	Kidney The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
12.		SLC-5	- The specimen is 2 kidney tissue d# 1.1cm.	Kidney The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
13.		SLC-6	- The specimen is 2 kidney tissue d# 1cm.	Kidney The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
14.	Pathological group	BL-1	- The specimen is 2 kidney tissue d# 1.1cm.	Kidney – The specimen is kidney tissue with mild inflammation of the renal slit, scattered with very few inflammatory cells. Suspected stone presence in the tubules of the kidney.	– Kidney: Very mild nephritis, with microstones.
15.		BL-2	- The sample is 2 kidney tissues d# 1.2 – 1.3cm.	Kidney – The test sample is kidney tissue with the phenomenon of penetration of many lymphocytes and plasma cells in the interstitial tissue and around the renal tubules, renal pelvis. Scattered accompaniment has destroyed renal tubules and small calcifications (microstones) in the renal tubules in the renal tower region (renal medulla).	– Kidney: Chronic pyelonephritis, mild, with microstones.
16.		BL-3	- The sample is 2 kidney tissues d# 0.9 – 1.1cm.	Kidney – The test sample is kidney tissue with the phenomenon of penetration of many lymphocytes and plasma cells in the interstitial tissue and around the renal tubules, renal pelvis. Scattered accompaniment has destroyed renal tubules and small calcifications (microstones) in the renal tubules in the renal tower region (renal medulla).	– Kidney: Chronic pyelonephritis, mild, with microstones.

No.	GROUP	SAMPLE	GENERAL	RESULTS	
17.		BL-4	- The sample is 2 kidney tissues d# 0.9cm.	Kidney – The specimen is renal tissue with multiple lymphocyte permeability, plasma cells in the interstitial and peritubular tissue, and the renal pyelonephritis is scattered with destroyed renal tubules. Suspected stone presence in the tubules of the kidney.	– Kidney: Chronic pyelonephritis, mild, with microstones.
18.		BL-5	- The specimen is 2 kidney tissue d# 1cm.	Kidney – The specimen is kidney tissue with mild inflammation of the renal slit, scattered with very few inflammatory cells. Suspected stone presence in the tubules of the kidney.	– Kidney: Very mild nephritis, with microstones.
19.		BL-6	- The sample is 2 kidney tissues d# 0.9 - 1cm.	Kidney – The specimen was kidney tissue with no stone detection, mild inflammation of the renal slit, scattered with very few inflammatory cells.	– Kidneys: Almost normal.
20.	Pathological group treatment with Cystone 750 mg/kg	CY-3	- The sample is 2 kidney tissues d# 1 – 1.1cm.	Kidney – The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
21.		CY-4	- The sample is 2 kidney tissues d# 1.2 – 1.3cm.	Kidney – The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
22.		CY-6	- The sample is 2 kidney tissues d# 0.9 - 1cm.	Kidney – The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
23.	Pathological group treatment with EGE 200 mg/kg	BLC-1	- The sample is 2 kidney tissues d# 0.9 - 1cm.	Kidney – The specimen is kidney tissue with mild inflammation of the kidney slit, scattered with few inflammatory cells. There was no detection of gravel on this specimen.	– Nephrology: Very mild nephritis.
24.		BLC-2	- The sample is 2 kidney tissues d# 1.2 – 1.3cm.	Kidney – The specimen is renal tissue with the phenomenon of permeability of many lymph cells, plasma cells in the interstitial tissue and around the renal tubules, the renal pelvis has the renal tubules destroyed. There was no detection of gravel on this specimen.	– Kidney: Chronic pyelonephritis, moderate.
25.		BLC-3	- The sample is 2 kidney tissues d# 1 – 1.2cm.	Kidney – The test sample is kidney tissue with the phenomenon of penetration of many lymphocytes and plasma cells in the interstitial tissue and around the renal tubules, renal pelvis. There was no detection of gravel on this specimen.	– Kidney: Chronic pyelonephritis, mild.
26.		BLC-4	- The specimen is 2 kidney tissue d# 1.1cm.	Kidney – The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
27.		BLC-5	- The sample is 2 kidney tissues d# 0.8 – 0.9cm.	Kidney – The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
28.		BLC-6	- The sample is 2 kidney tissues d# 1 – 1.1cm.	Kidney – The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
29.	Pathological group treatment with EGE 400 mg/kg	BLC-1	- The sample is 2 kidney tissues d# 1 – 1.1cm.	Kidney The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
30.		BLC-2	- The sample is 2 kidney tissues d# 1.2 – 1.3cm.	Kidney The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
31.		BLC-3	- The sample is 2 kidney tissues d# 1.1 – 1.2cm.	Kidney The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.
32.		BLC-4	- The sample is 2 kidney tissues d# 1.2cm.	Kidney – The specimen is kidney tissue with no stone detection, no inflammation on this specimen.	– Kidneys: Normal.

Table S2 The phytochemical analysis of *E. glaucum* seeds

Metabolites	Diethyl ether extract	Ethanol extract	Aqueous extract	Presence
Lipids	+	-	-	+
Carotenoids	-	-	-	-
Volatile oils	-	-	-	-
Triterpenoids	+	-	-	+
Alkaloids	+	+	+	+
Coumarins	+	-	-	+
Anthraquinone	-	-	-	-
Flavonoids	-	+	+	+
Anthocyanosides	-	+	+	+
Proanthocyanidins	-	+	+	+
Tannins	-	+	+	+
Saponins	-	+	+	+
Organic acid	-	-	-	-
Reductant	-	-	-	-

Note: (-) absent, (+) present

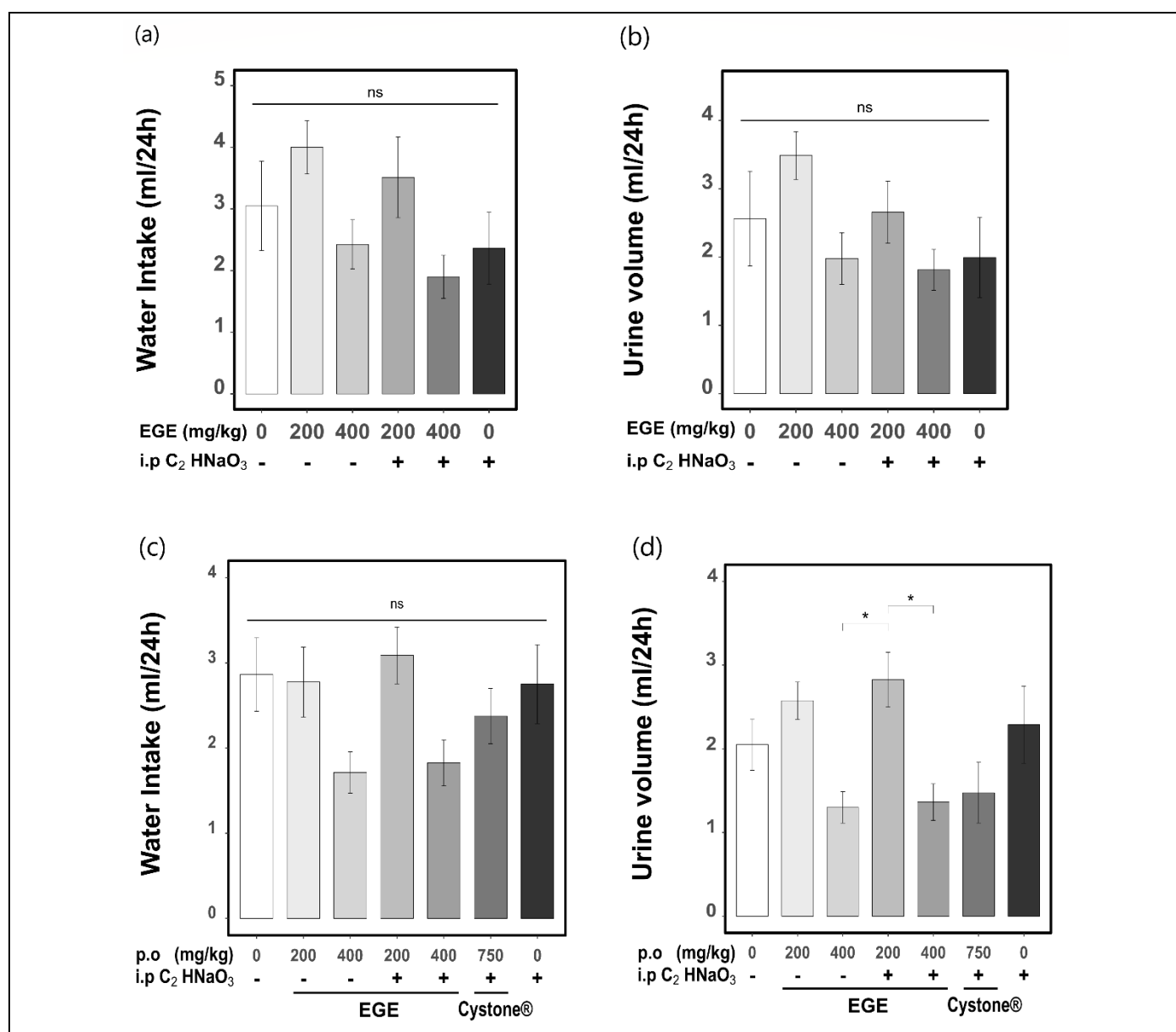


Figure S1 Effect of EGE on water intake and urine volume in sodium glyoxylate induced urolithiasis in mice after 7 (a-b) and 14 (c-d) days of treatment. EGE: *E. glaucum* aqueous seed extract, data was expressed as mean \pm SEM ($n = 8$), ^{ns} $p > 0.05$: not significantly different and ^{*} $p < 0.05$: significant difference (Kruskal–Wallis test and Dunn's multiple comparison test)

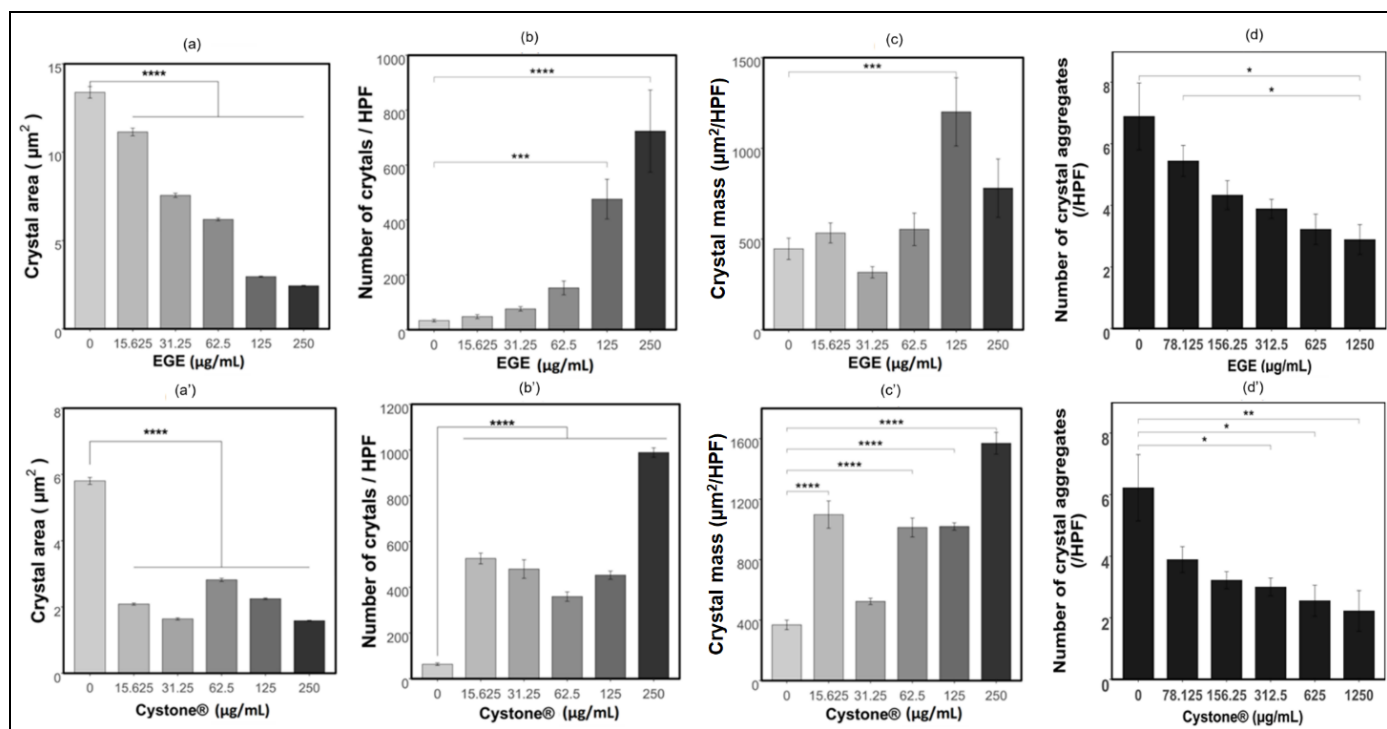


Figure S2 EGE inhibited the formation and aggregation of calcium oxalate crystals. EGE: *E. glaucum* aqueous seed extract, data was expressed as mean \pm SEM ($n = 8$), $^{ns}p > 0.05$: not significantly different, $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$, and $^{****}p < 0.0001$: significant difference (One-Way Anova and Tukey test). (a-c) Effect of EGE in nucleation assay, (a'-c') Effect of cystone in nucleation assay, (d) Effect of EGE in aggregation assay, and (d') Effect of cystone in aggregation assay

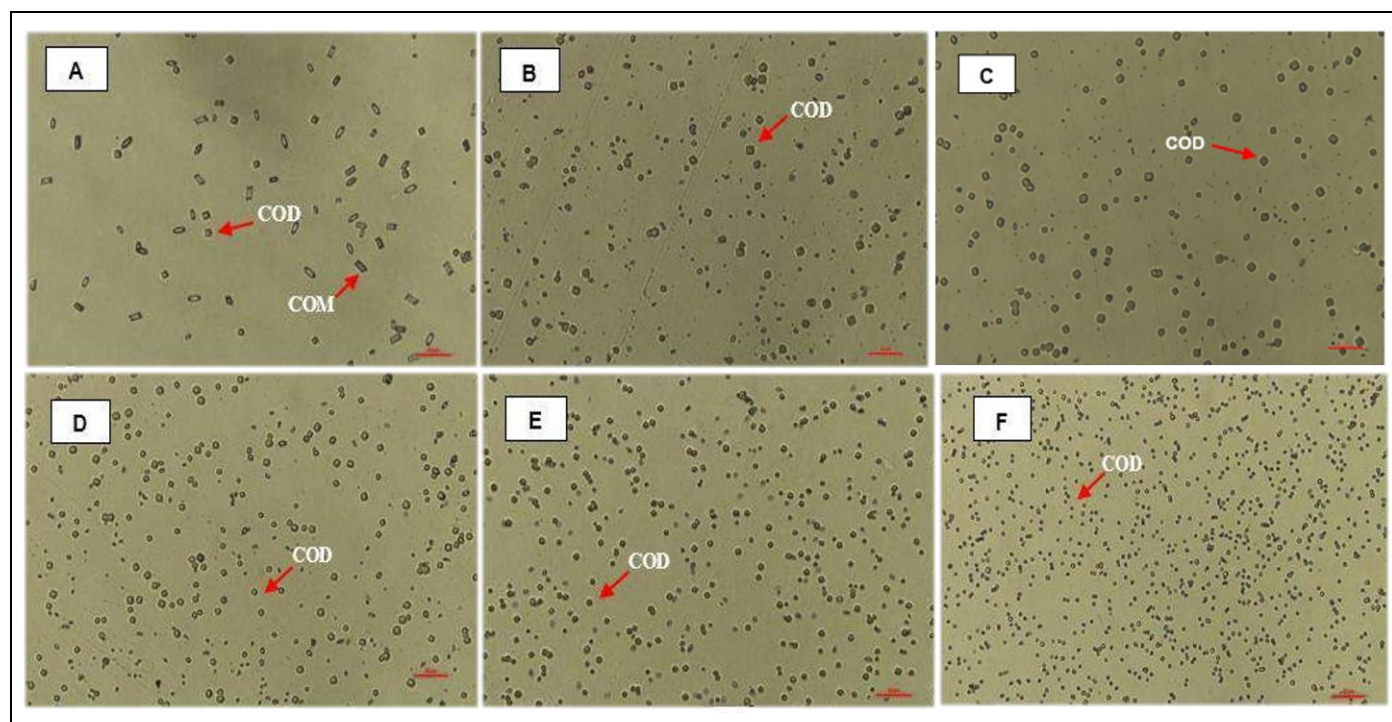


Figure S3 Effect of cystone on CaO_x crystallization. a (Negative control, 0 $\mu\text{g/mL}$); b (15.625 $\mu\text{g/mL}$); c (31.25 $\mu\text{g/mL}$); d (62.5 $\mu\text{g/mL}$); e (125 $\mu\text{g/mL}$); f (250 $\mu\text{g/mL}$). COM (Calciumoxalate monohydrate) and COD (Calcium oxalate dihydrate) crystals were indicated by a red arrow. COM crystal had a hexagonal lozenge elongated shape, while the COD crystal got a square envelope shape. The scale bar was 10 μm for all captured images

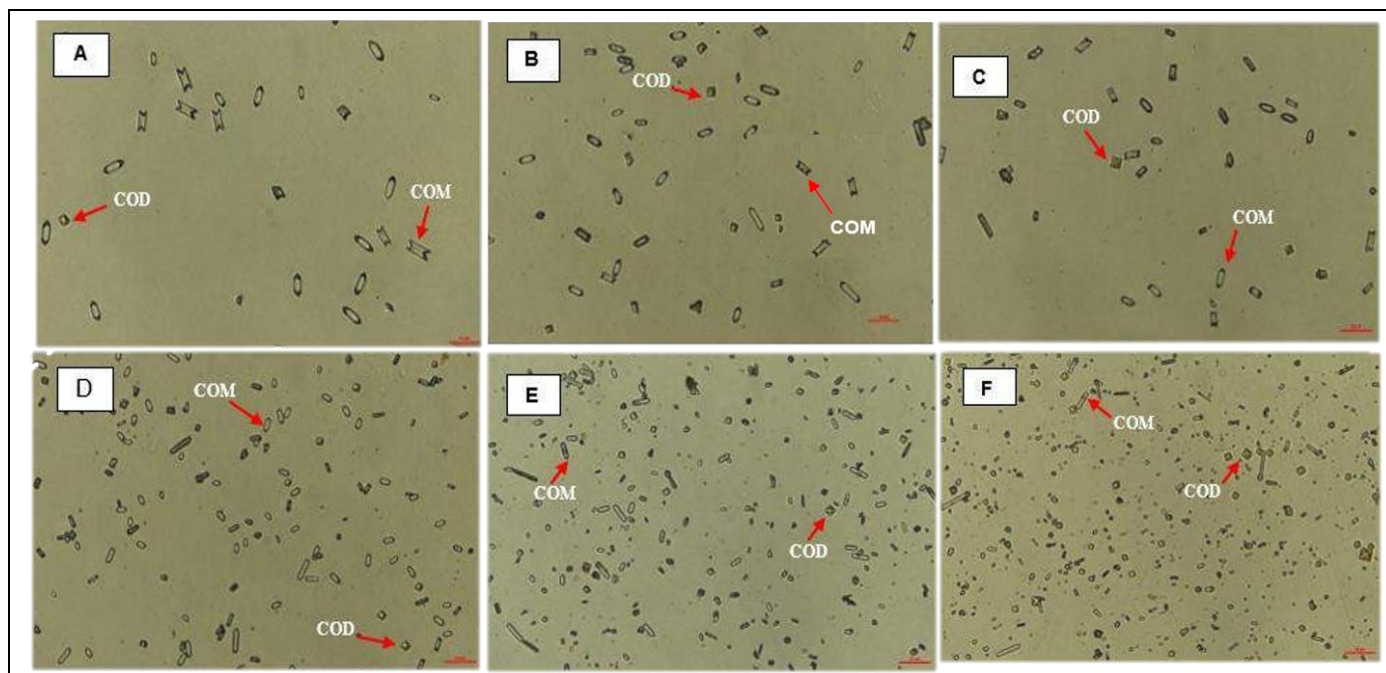


Figure S4 Effect of EGE on CaO_x crystallization. a (Negative control, 0 $\mu\text{g/mL}$); b (15.625 $\mu\text{g/mL}$); c (31.25 $\mu\text{g/mL}$); d (62.5 $\mu\text{g/mL}$); e (125 $\mu\text{g/mL}$); f (250 $\mu\text{g/mL}$). COM (Calciumoxalate monohydrate) and COD (Calcium oxalate dihydrate) crystals were indicated by a red arrow. COM crystal had a hexagonal lozenge elongated shape, while the COD crystal got a square envelopeshape. The scale bar was 10 μm for all captured images

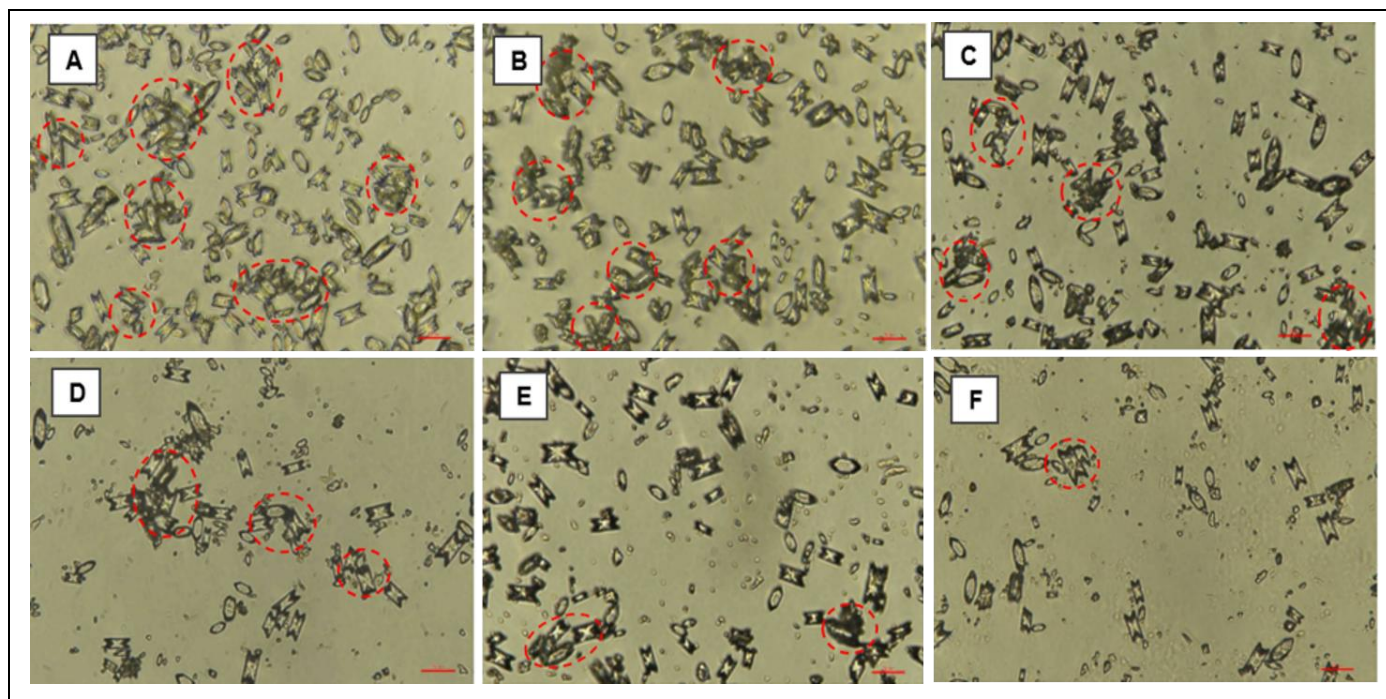


Figure S5 Effect of EGE on crystal aggregation. a (Negative control, 0 $\mu\text{g/mL}$); b (78.125 $\mu\text{g/mL}$); c (156.25 $\mu\text{g/mL}$); d (312.5 $\mu\text{g/mL}$); e (625 $\mu\text{g/mL}$); f (1250 $\mu\text{g/mL}$). Aggregated COM crystals, which were derived from three or more individual crystals, tightly joined together and it was indicated by the dashed circle. The scale bar was 100 μm for all captured images

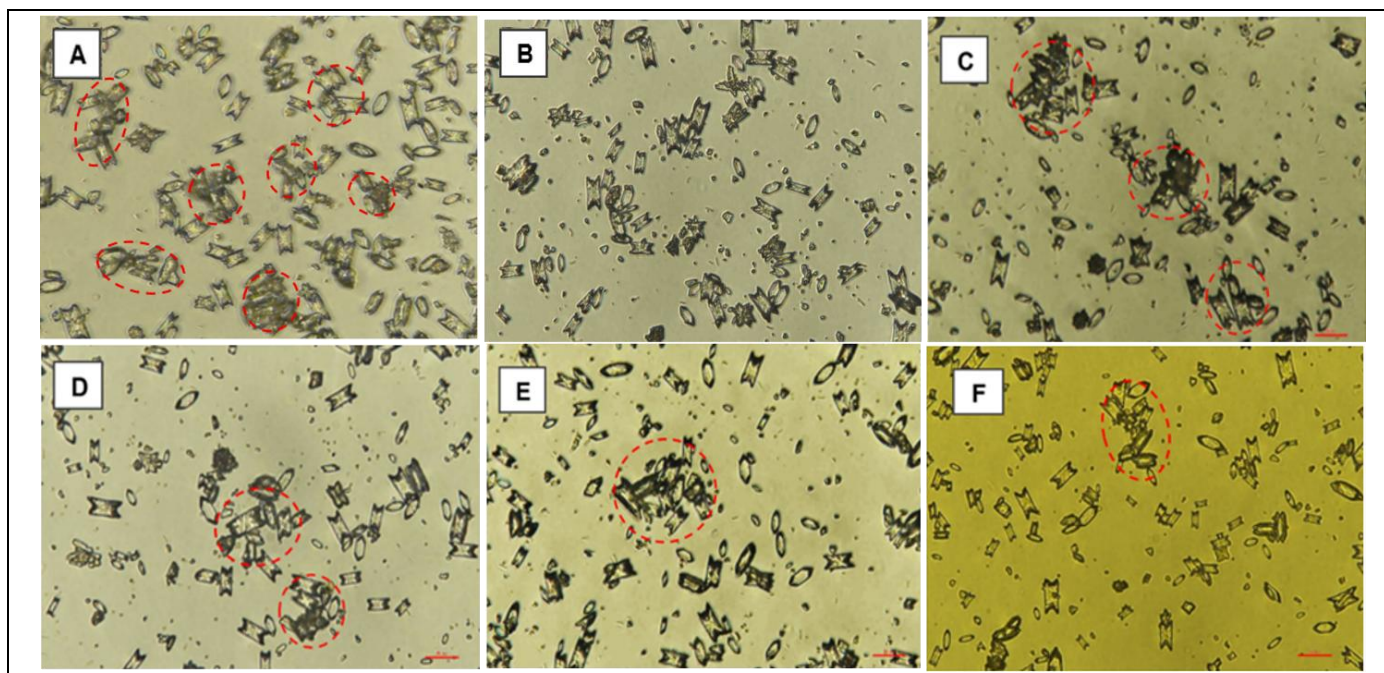


Figure S6 Effect of cystine on crystal aggregation. a (Negative control, 0 μg/mL); b (78.125 μg/mL); c (156.25 μg/mL); d (312.5 μg/mL); e (625 μg/mL); f (1250 μg/mL). Aggregated COM crystals, which were derived from three or more individual crystals, tightly joined together and it was indicated by the dashed circle. The scale bar was 100 μm for all captured images

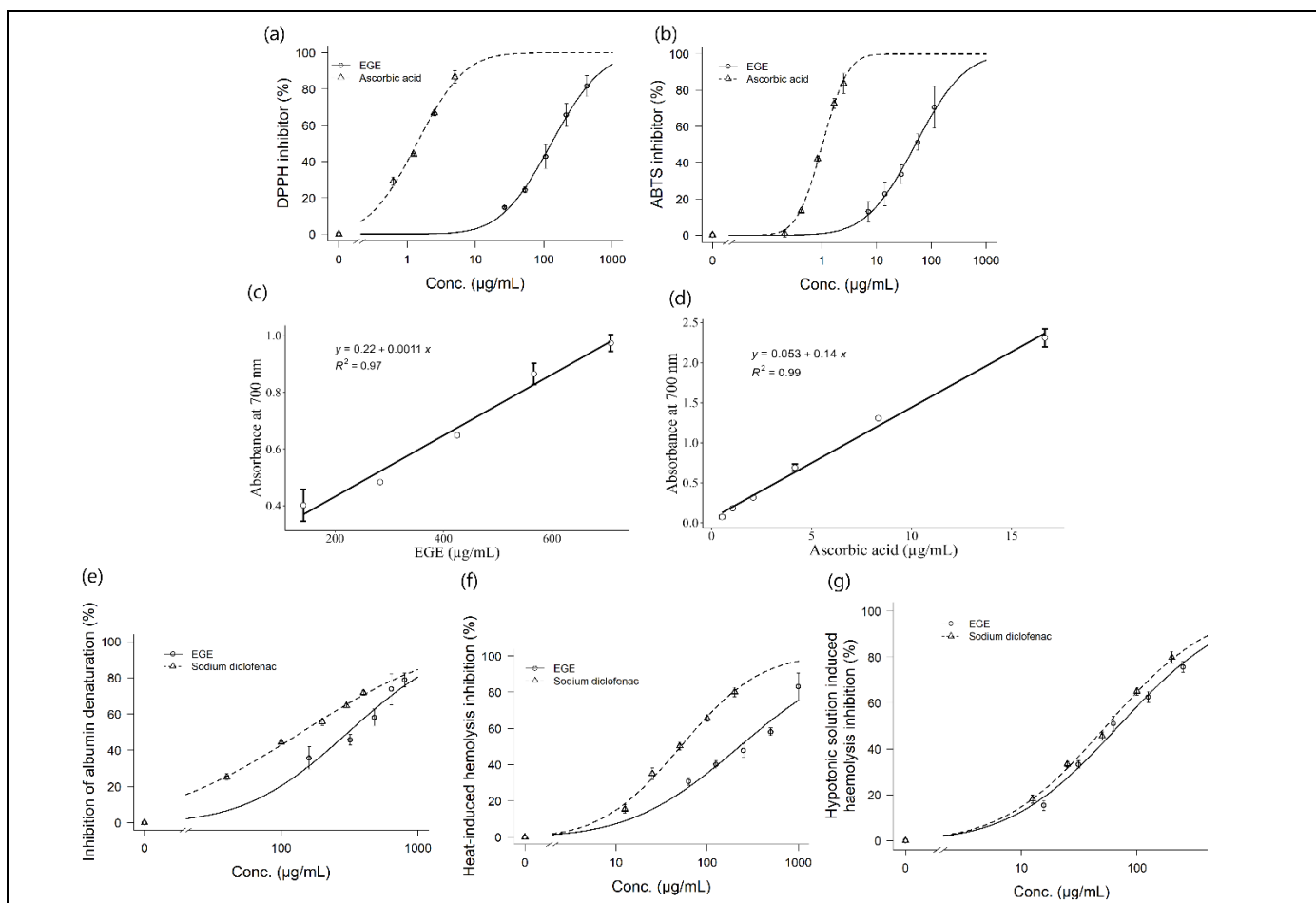


Figure S7 *In vitro* antioxidant and anti-inflammatory activities of EGE. (a) DPPH free radical scavenging activity of EGE and ascorbic acid, (b) ABTS radical cation scavenging activity of EGE and ascorbic acid, (c-d) Reducing power of EGE and ascorbic acid, (e) Inhibition of albumin denaturation (e), heat-induced hemolysis (f), and (g) hypotonic solution-induced haemolysis of EGE and diclofenac sodium