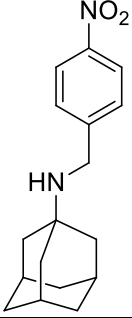
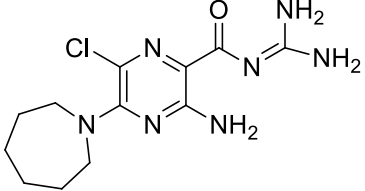
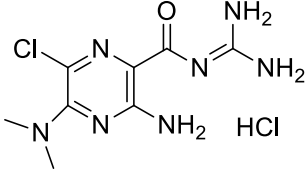
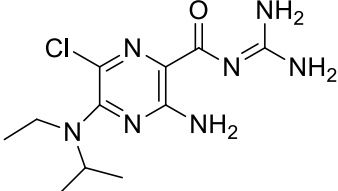
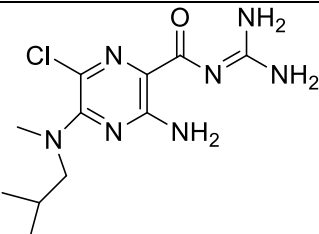
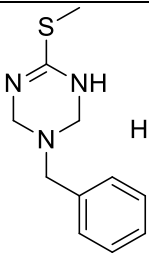
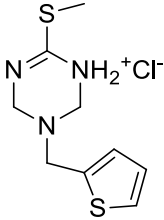
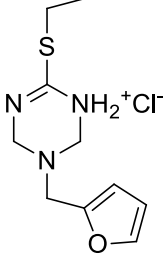
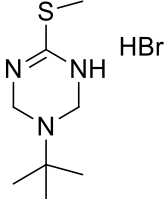
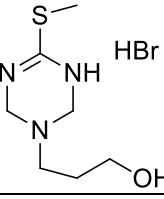
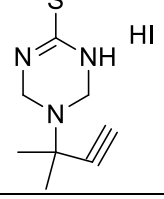
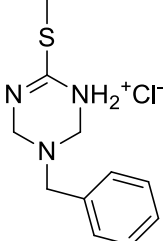
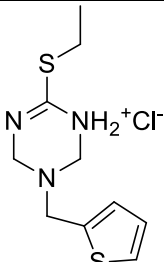
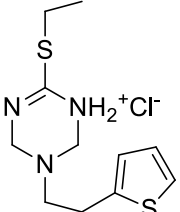
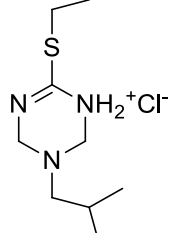
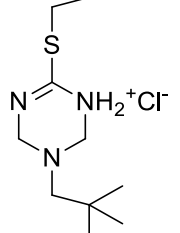
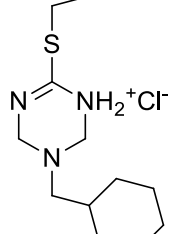
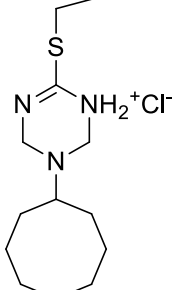


Table S1. Activity of hexamethylene amiloride and triazine analogs in the TEVC assay

Compound name (ID)	Structure	% inhibition at 100 μ M in TEVC		
		WT	S31N	V27A
N-(4-nitrobenzyl)adamantan-1-amine (4)		43.5 \pm 0.5	15.9 \pm 0.2	9.7 \pm 0.3
Hexamethylene amiloride (14)		89.9 \pm 0.7	17.6 \pm 0.8	11.3 \pm 1.2
5-(<i>N,N</i> -Dimethyl)amiloride hydrochloride (20)		23.3 \pm 1.9	0	0
5-(<i>N</i> -Ethyl- <i>N</i> -isopropyl)amiloride (21)		47.3 \pm 0.5	5.8 \pm 0.6	0
5-(<i>N</i> -Methyl- <i>N</i> -isobutyl)-amiloride (22)		55.7 \pm 1.0	1.1 \pm 1.1	2.1 \pm 2.1
3-benzyl-6-(methylthio)-1,2,3,4-tetrahydro-1,3,5-triazine hydroiodide (18)		4.5 \pm 2.3	3.4 \pm 1.7	0

6-(methylthio)-3-(thiophen-2-ylmethyl)-1,2,3,4-tetrahydro-1,3,5-triazin-1-ium chloride (23)		8.1 ± 1.7	1.6 ± 1.6	2.9 ± 1.3
6-(ethylthio)-3-(furan-2-ylmethyl)-1,2,3,4-tetrahydro-1,3,5-triazin-1-ium chloride (24)		17.9 ± 2.8	1.9 ± 1.6	3.1 ± 2.6
3-(tert-butyl)-6-(methylthio)-1,2,3,4-tetrahydro-1,3,5-triazine hydrobromide (25)		13.3 ± 1.5	7.4 ± 1.2	0
3-(4-(methylthio)-5,6-dihydro-1,3,5-triazin-1(2H)-yl)propan-1-ol hydrobromide (26)		5.5 ± 0.9	4.2 ± 1.0	11.9 ± 1.0
3-(2-methylbut-3-yn-2-yl)-6-(methylthio)-1,2,3,4-tetrahydro-1,3,5-triazine hydroiodide (27)		17.0 ± 1.9	4.1 ± 0.2	1.8 ± 1.8
3-benzyl-6-(ethylthio)-1,2,3,4-tetrahydro-1,3,5-triazin-1-ium chloride (28)		5.4 ± 1.6	4.4 ± 0.7	1.1 0.8
6-(ethylthio)-3-(thiophen-2-ylmethyl)-1,2,3,4-tetrahydro-1,3,5-triazin-1-ium chloride (29)		6.7 ± 1.4	6.1 ± 1.2	5.1 ± 0

<p>6-(ethylthio)-3-(2-(thiophen-2-yl)ethyl)-1,2,3,4-tetrahydro-1,3,5-triazin-1-ium chloride (30)</p>		<p>1.1 ± 1.1</p>	<p>8.1 ± 1.0</p>	<p>5.5 ± 1.4</p>
<p>6-(ethylthio)-3-isobutyl-1,2,3,4-tetrahydro-1,3,5-triazin-1-ium chloride (31)</p>		<p>1.2 ± 0.6</p>	<p>3.1 ± 0.5</p>	<p>0.3 ± 0.3</p>
<p>6-(ethylthio)-3-neopentyl-1,2,3,4-tetrahydro-1,3,5-triazin-1-ium chloride (32)</p>		<p>4.7 ± 1.3</p>	<p>2.9 ± 0.4</p>	<p>0.6 ± 0.6</p>
<p>3-(cyclohexylmethyl)-6-(ethylthio)-1,2,3,4-tetrahydro-1,3,5-triazin-1-ium chloride (33)</p>		<p>63.9 ± 2.0</p>	<p>6.4 ± 0.8</p>	<p>0</p>
<p>3-cyclooctyl-6-(ethylthio)-1,2,3,4-tetrahydro-1,3,5-triazin-1-ium chloride (34)</p>		<p>89.7 ± 0.4</p>	<p>7.4 ± 0.9</p>	<p>2.7 ± 1.1</p>