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Study on the mechanism of salt-processed alismatis rhizoma (*Alisma plantago- aquatica subsp. orientale* (sam.) sam.) based on UPLC-Q-TOF-MS, pattern analysis, and transcriptome.

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Supplementary data

Table S1. Retention times and MS/MS data of compounds identified in AR, SAR by UPLC-Q-TOF-MS

NO.	t_R/min	([M+H]$^+$/[M+Na]$^+$/[M+NH$_4$]$^+$) theoretical	([M+H]$^+$/[M+Na]$^+$/[M+NH$_4$]$^+$) experimental	δ/ppm	Pattern	Formula	MS/MS	Compound	Change index

1	7.21	221.190 5	221.190 1	-1.8	$[M+H]^+$	$C_{15}H_{24}O$	221.188 6, 203.180 1, 161.133 6, 147.116 2, 133.099 5, 105.069 9	alismoxide	0.990
2	8.01	235.169 8	235.169 7	-0.4	$[M+H]^+$	$C_{15}H_{22}O_2$	157.1009		
3	8.72	503.337 3	503.336 5	-1.6	$[M+H]^+$	$C_{30}H_{46}O_6$	525.318 8, 485.328 1, 467.306 2, 431.281 4, 413.272 8, 395.254 3	alismanol O	
4	9.31	535.327 1	535.324 6	-4.7	$[M+H]^+$	$C_{30}H_{46}O_8$	499.305 2, 445.259 5, 429.263 7, 411.252 8, 385.093 6		
5	10.06	503.337 3	503.339 3	4	$[M+H]^+$	$C_{30}H_{46}O_6$	525.315 9, 503.327 9, 485.328 1, 467.318 0，449.296 4, 431.282 8, 413.269 4, 395.259 2		
6	10.07	221.190 5	221.191 1	2.7	$[M+H]^+$	$C_{15}H_{24}O$	203.179 8, 161.132 5, 147.119 1, 133.102 5	Alismoxide isomer	0.832
7	11.10	505.352 9	505.352 8	-0.2	$[M+H]^+$	$C_{30}H_{48}O_6$	527.334 7, 505.353 1, 487.342 2, 469.330 7, 451.320 2, 415.284 5, 397.274 1	16-oxo alisol A	0.710
8	11.57	431.279 7	431.279 6	-0.2	$[M+H]^+$	$C_{26}H_{38}O_5$	453.261 7, 431.280 7, 413.269 6, 395.261 3, 149.023 3		0.757
9	12.09	529.3529	529.3544	2.8	$[M+H]^+$	$C_{32}H_{48}O_6$	529.349 5, 511.334 8, 469.342 1, 451.322 4, 397.273 1	alismaketone C 23-acetate isomer	1.021
10	13.12	517.316 5	517.316 5	0	$[M+H]^+$	$C_{30}H_{44}O_7$	517.315 7, 499.303 6, 467.311 6, 445.259 0		0.769
11	14.40	487.342 3	487.341 5	-1.6	$[M+H]^+$	$C_{30}H_{46}O_5$	487.338 9, 469.330 5,	alisol C	0.913

							451.322 2, 433.310 6, 415.284 8	isomer	
12	14.82	219.174 9	219.174 4	-2.3	$[M+H]^+$	$C_{15}H_{22}O$	219.172 8, 201.164 3		
13	15.39	487.342 3	487.342 3	0	$[M+H]^+$	$C_{30}H_{46}O_5$	469.333 1, 451.321 2, 379.276 7, 337.251 6	dihydroxy-24-diacetyl alisol O	0.814
14	15.99	487.342 3	487.342 9	1.2	$[M+H]^+$	$C_{30}H_{46}O_5$	509.325 4, 487.343 5, 469.332 9, 451.322 1, 433.312 3, 415.285 6, 397.274 7	alisol C	0.878
15	16.41	471.347 4	471.347 6	0.4	$[M+H]^+$	$C_{30}H_{46}O_4$	471.344 7, 453.342 5, 381.276 6, 339.266 2	16,23-oxido-alisol B	0.588
16	16.69	529.350 5	529.350 3	-0.4	$[M+Na]^+$	$C_{30}H_{50}O_6$	529.349 2, 507.310 6, 471.340 3, 453.335 4	13,17-epoxy-alisol A	0.955
17	17.17	561.327 0	561.343 0	0.5	$[M+H]^+$	$C_{32}H_{48}O_8$	543.349 4		
18	18.12	487.342 3	487.339 4	-6	$[M+H]^+$	$C_{30}H_{46}O_5$	469.330 7, 451.322 9, 397.276 0, 353.248 3	dihydroxy-24-diacetyl alisol O isomer	0.814
19	18.42	489.358 0	489.357 9	-0.2	$[M+H]^+$	$C_{30}H_{48}O_5$	489.357 1, 471.344 9, 453.335 6, 399.290 6, 381.277 6	13,17-epoxy-alisol B	0.643
20	18.96	415.284 8	415.286 0	2.9	$[M+H]^+$	$C_{26}H_{38}O_4$	397.274 9, 379.262 3, 361.252 5, 337.249 1, 301.142 0		0.755
21	19.53	559.327 1	559.327 1	0	$[M+H]^+$	$C_{32}H_{46}O_8$	581.312 3, 559.328 2, 499.306 6, 481.297 5, 445.258 5		1.216

22	20.22	553.350 5	553.350 6	0.2	$[M+Na]^+$	$C_{32}H_{50}O_6$	553.349 8, 531.364 2, 513.359 0, 495.347 1, 435.325 9, 417.315 3, 381.279 3	23-acetate alisol N	1.839
23	21.76	369.243 0	369.242 9	-0.3	$[M+H]^+$	$C_{24}H_{32}O_3$	391.226 4, 369.243 4, 351.267 1, 301.141 9		1.135
24	22.31	547.363 5	547.363 7	0.4	$[M+H]^+$	$C_{32}H_{50}O_7$	569.345 1, 551.333 1, 529.357 5, 511.340 4, 451.319 9, 435.327 0, 381.279 1	16-oxo-alisol A-23-acetate	1.404
25	22.69	529.352 9	529.353 3	0.8	$[M+H]^+$	$C_{32}H_{48}O_6$	551.335 8, 529.354 1, 511.342 9, 469.332 5, 451.322 0, 433.311 0, 415.285 9	23-acetate alisol C	1.275
26	23.87	471.347 4	471.347 1	-0.6	$[M+H]^+$	$C_{30}H_{46}O_4$	493.329 1, 471.347 1, 453.336 3, 399.289 3, 381.277 7	11-deoxy-alisol C isomer	2.300
27	24.16	547.363 5	547.364 3	1.5	$[M+H]^+$	$C_{32}H_{50}O_7$	511.341 1, 451.321 6, 397.274 4	16β-hydroperoxy alisol B 23-acetate	0.370
28	24.72	513.358 0	513.359 3	2.5	$[M+H]^+$	$C_{32}H_{48}O_5$	513.366 6, 495.357 1, 471.352 5, 453.336 9, 435.327 9, 399.303 7, 381.277 9	11-deoxy-alisol C 23-acetate isomer	0.635
29	25.89	471.347 4	471.346 8	-1.3	$[M+H]^+$	$C_{30}H_{46}O_4$	493.330 5, 453.338 2, 399.291 1, 381.280 1	11-deoxy-alisol C isomer	1.675
30	26.17	513.355 6	513.357 2	3.1	$[M+Na]^+$	$C_{30}H_{50}O_5$	513.355 0, 453.335 6, 435.325 1, 383.294 6,	alisol A	3.929

							365.284 5, 339.268 9		
31	26.78	515.373 6	515.372 8	-1.6	$[M+H]^+$	$C_{32}H_{50}O_5$	515.372 0, 497.370 5, 437.343 9, 419.331 9, 339.269 1	23-acetate alisol B isomer	1.188
32	27.11	529.352 9	529.352 5	-0.8	$[M+H]^+$	$C_{32}H_{48}O_6$	551.331 5, 529.348 7, 511.337 4, 469.333 8, 451.322 2, 397.274 1	alismaketone C 23-acetate	0.649
33	27.72	503.337 3	503.337 6	0.6	$[M+H]^+$	$C_{30}H_{46}O_6$	525.319 2, 503.337 7, 485.327 1, 467.315 9, 431.280 1, 413.269 3	20-hydroxyanisole C	1.146
34	28.11	529.352 9	529.353 2	0.6	$[M+H]^+$	$C_{32}H_{48}O_6$	551.332 5, 529.353 4, 511.342 0, 469.340 9, 451.319 9, 397.273 9	alismaketone C 23-acetate isomer	1.052
35	28.53	545.347 8	545.347 0	-1.5	$[M+H]^+$	$C_{32}H_{48}O_7$	545.345 6, 527.335 9, 509.327 7, 485.321 4, 467.313 4, 449.299 8, 413.269 1	12-Hydroxy-16-oxo-alisol A-24-actetate	0.743
36	28.72	531.368 6	531.368 3	-0.6	$[M+H]^+$	$C_{32}H_{50}O_6$	553.350 2, 513.355 0, 495.346 1, 453.333 2, 435.326 1, 399.291 1, 381.279 8	24-acetate alisol F	1.105
37	28.89	511.342 3	511.341 6	-1.4	$[M+H]^+$	$C_{32}H_{46}O_5$	511.342 5, 493.334 6, 451.321 8, 433.312 8, 381.281 3	Alisol L-23-actetate	0.949
38	28.91	555.366 2	555.365 2	-1.8	$[M+Na]^+$	$C_{32}H_{52}O_6$	555.361 3, 533.325 3, 515.369 6, 497.360 7, 439.341 9, 383.294 1, 365.282 8	24-acetate alisol A	1.199

39	29.16	473.363 1	473.362 5	-1.3	$[M+H]^+$	$C_{30}H_{48}O_4$	495.344 6, 383.295 6, 365.283 6, 339.267 3	alisol G isomer	1.106
40	29.52	513.358 0	513.357 8	-0.4	$[M+H]^+$	$C_{32}H_{48}O_5$	535.340 3, 513.357 7, 453.336 6, 435.326 1, 399.288 6	11-deoxy-alisol C 23-acetate	1.183
41	29.88	527.337 3	527.337 0	-0.6	$[M+H]^+$	$C_{32}H_{46}O_6$	527.337 5, 509.324 8, 497.363 1, 467.316 0, 453.336 4, 437.340 2		0.686
42	30.19	545.347 8	545.347 9	0.2	$[M+H]^+$	$C_{32}H_{48}O_7$	567.329 4, 545.348 4, 485.327 3, 467.317 1, 431.282 7, 413.368 3	23-acetate alisol M	1.638
43	30.45	471.347 4	471.346 6	-1.7	$[M+H]^+$	$C_{30}H_{46}O_4$	493.328 5, 471.345 7, 453.337 9, 435.326 8, 399.289 3, 381.278 4	24-deacetyl alisol O	1.038
44	30.71	497.363 1	497.362 6	-1	$[M+H]^+$	$C_{32}H_{48}O_4$			0.765
45	30.86	531.368 6	531.368 1	-0.9	$[M+H]^+$	$C_{32}H_{50}O_6$	531.369 3, 513.356 3, 495.346 7, 453.336 5, 435.326 0, 399.288 7, 381.280 8	24-acetate alisol F isomer	0.733
46	31.23	473.363 1	473.363 1	0	$[M+H]^+$	$C_{30}H_{48}O_4$	473.362 4, 455.352 1, 437.341 2, 383.294 3, 365.284 3, 339.268 3	alisol B	1.409
47	31.63	473.363 1	473.363 3	0.4	$[M+H]^+$	$C_{30}H_{48}O_4$	473.368 0, 455.358 0, 437.341 9, 383.294 3, 365.283 1, 339.268 2	alisol B isomer	
48	32.24	529.352 9	529.355 3	4.5	$[M+H]^+$	$C_{32}H_{48}O_6$	529.348 6, 511.340 5, 451.319 2, 397.271 7, 379.269 3	16-oxo-11-anhydroalisol A 24-acetate	1.119
49	32.51	513.358 0	513.357 8	-0.4	$[M+H]^+$	$C_{32}H_{48}O_5$	513.357 7, 495.346 8,	alisol O	1.600

							453.340 9, 435.325 0,		
50	32.86	513.358 0	513.358 3	0.6	$[M+H]^+$	$C_{32}H_{48}O_5$	513.357 7, 495.344 5, 453.335 2, 435.325 1, 381.278 2	alisol O isomer	
51	33.73	515.373 6	515.373 1	-1	$[M+H]^+$	$C_{32}H_{50}O_5$	537.354 7, 515.367 0, 497.363 5, 479.352 8, 437.341 5, 419.331 4, 383.293 0, 339.267 0	23-acetate alisol B isomer	0.648
52	34.13	515.373 6	515.373 9	0.6	$[M+H]^+$	$C_{32}H_{50}O_5$	537.355 8, 515.374 3, 497.362 8, 479.352 6, 437.342 4, 419.331 6	23-acetate alisol B	0.865
53	34.93	513.358 0	513.357 6	-0.8	$[M+H]^+$	$C_{32}H_{48}O_5$	513.360 0, 495.351 6, 453.333 0, 435.323 4, 399.240 1, 381.271 4	alisol O isomer	
54	35.52	497.363 1	497.363 8	1.4	$[M+H]^+$	$C_{32}H_{48}O_4$	497.361 8, 453.335 8, 437.342 2, 419.331 9, 381.279 8, 362.283 8, 339.270 1, 301.142 4		0.793
55	35.81	455.352 5	455.351 9	-1.3	$[M+H]^+$	$C_{30}H_{46}O_3$	455.354 9, 437.342 0, 419.327 6, 383.294 0, 365.283 5, 341.284 0	alisol I	0.845
56	36.28	498.394 7	498.394 5	-0.4	$[M+NH_4]^+$	$C_{32}H_{48}O_3$			0.939
57	36.97	513.358 0	513.360 1	4.1	$[M+H]^+$	$C_{32}H_{48}O_5$	513.359 7, 495.340 7, 453.337 3, 435.328 8, 381.278 4, 363.268 8	alisol O isomer	0.556
58	37.35	513.358 0	513.357 4	-1.2	$[M+H]^+$	$C_{32}H_{48}O_5$	495.346 9, 453.335 9, 435.328 4, 381.277 1	alisol O isomer	
59	37.90	471.347 4	471.348 3	1.9	$[M+H]^+$	$C_{30}H_{46}O_4$	453.334 3, 435.323 3, 399.236 5, 381.237 2	11-deoxy-alisol C	
60	38.07	497.363 1	497.362 1	-2	$[M+H]^+$	$C_{32}H_{48}O_4$	437.342 1, 419.328 6,		0.653

							399.241 6, 381.277 3, 313.272 3		
61	38.81	497.363 1	497.362 9	-0.4	$[M+H]^+$	$C_{32}H_{48}O_4$	497.364 8, 453.334 0, 435.332 5, 399.282 0, 381.279 4, 339.274 6, 313.272 9		0.843
62	39.81	499.378 7	499.378 9	0.4	$[M+H]^+$	$C_{32}H_{50}O_4$	521.360 5, 499.378 7, 481.368 2, 439.357 5, 421.346 7	11-deoxy-alisol B 23-acetate	0.856
63	40.15	499.378 7	499.378 6	-0.2	$[M+H]^+$	$C_{32}H_{50}O_4$	521.359 2, 499.370 5, 481.343 2, 439.355 8, 421.355 0	11-deoxy-alisol B 23-acetate isomer	0.750

(Note: The change index > 1 indicates that the peak area increases after salting, and < 1 indicates that the peak area decreases after salting)

Type 1: Alisol O

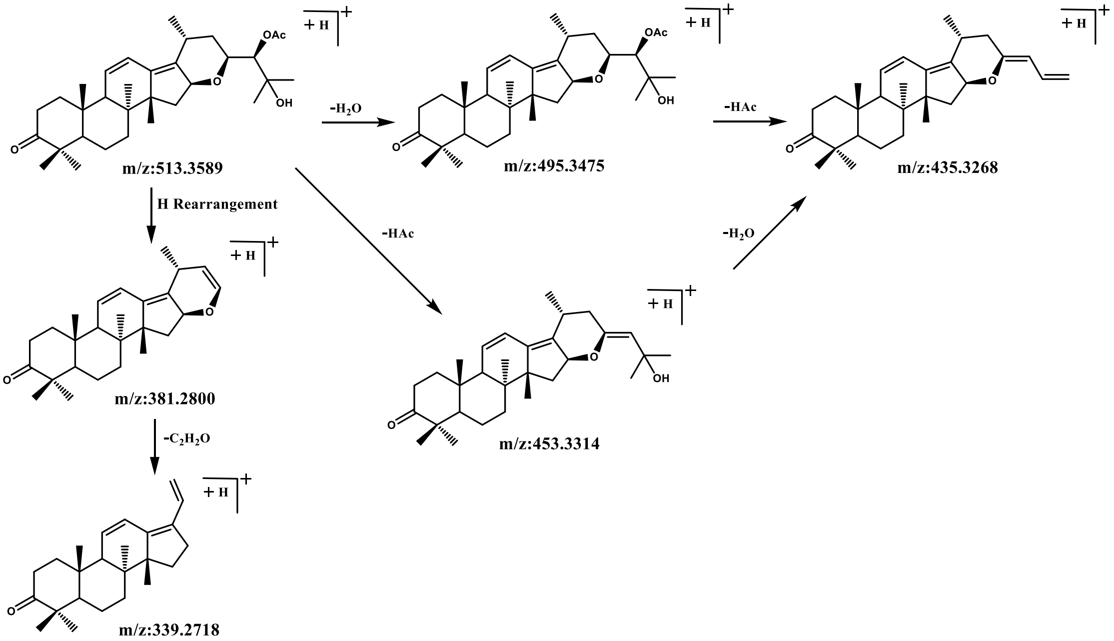

Figure S1. The fragmentation process of alisol O in positive ion mode

Type 2: 23-acetate alisol C

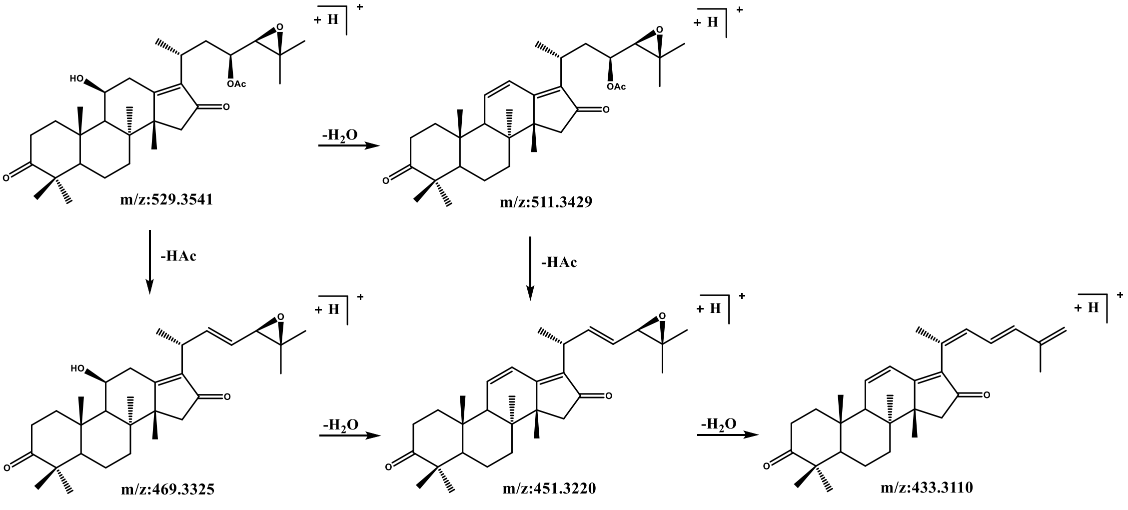

Figure S2. The fragmentation process of 23-acetate alisol C in positive ion mode

Type 3: 23-acetate alisol B

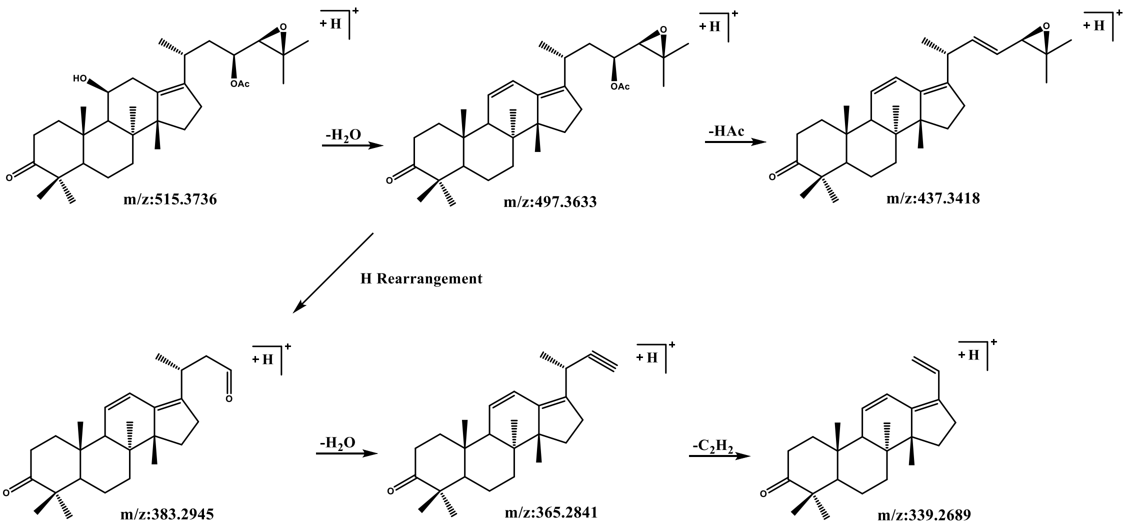

Figure S3. The fragmentation process of alisol B 23-acetate in positive ion mode

Type 4: Alismoxide

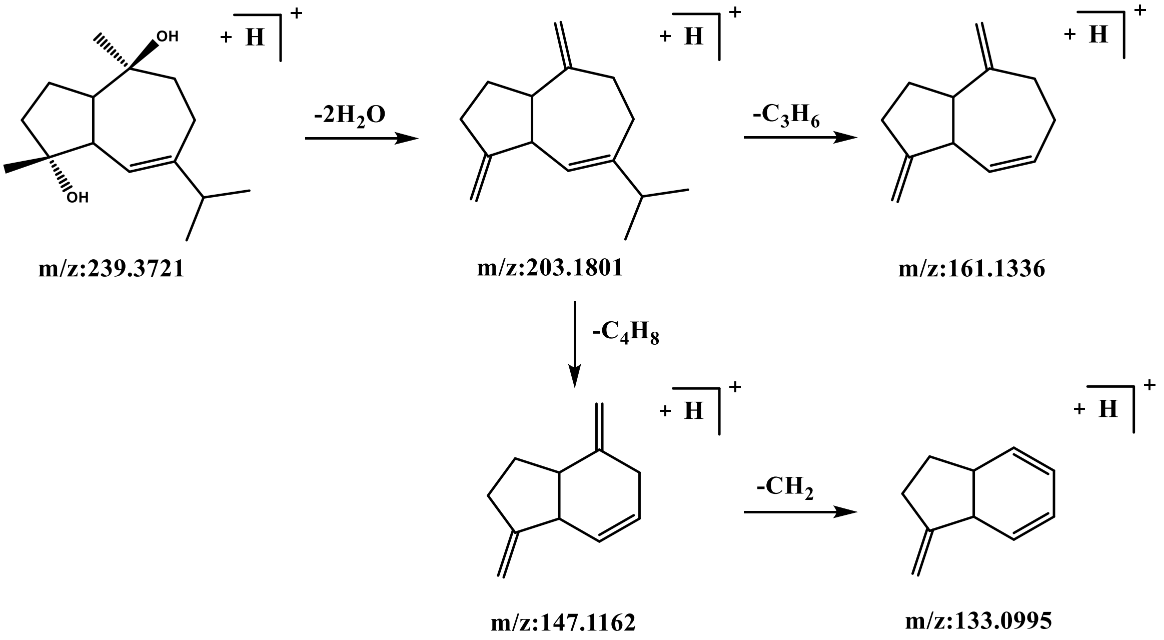

Figure S4. The fragmentation process of alismoxide in positive ion mode

Type 5: Alismaketone C 23-acetate

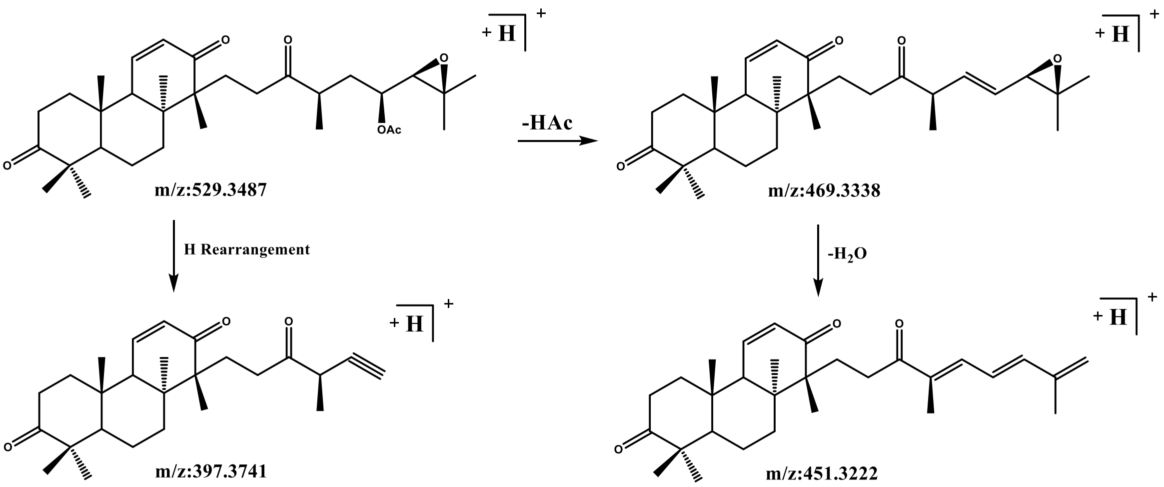

Figure S5. The fragmentation process of alismaketone C 23-acetate in positive ion mode

Type 6: 13,17-epoxy-alisol A

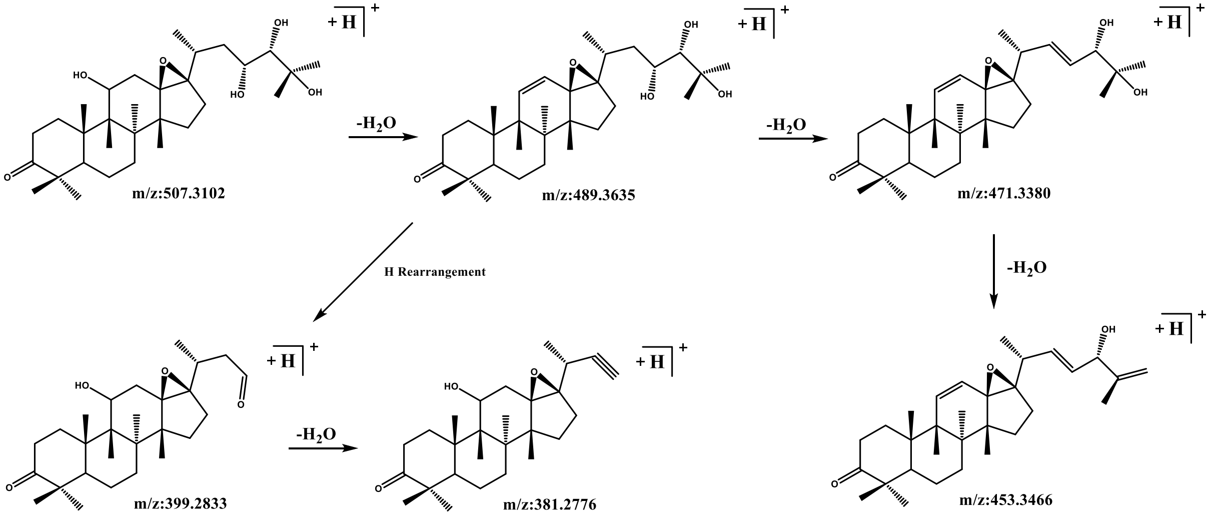

Figure S6. The fragmentation process of 13,17-epoxy-alisol A in positive ion mode

Table S2. Gene entries and gene names shared by biological processes in GO enrichment analysis of AR and SAR

Gene entry	Gene name
cell activation	ADORA2A, AIF1, BST2, C1QA, CD2, CD4, CD6, CD8A,

	CD74, CLU, COL3A1, CX3CR1, FCER1G, FCGR3A, FLT3, IL2RB, ITGA4, ITGAL, LCK, LCP1, LCP2, LEPR, LFNG, CD180, LYL1, PLEK, PRF1, PTPRC, CCL5, SELPLG, SLC11A1, SPN, TLR2, VCAM1, TSPAN32, IKZF1, IKZF3, KLRK1, LAT, RGCC, SASH3, APBB1IP, CLEC7A, FERMT3, THEMIS
positive regulation of immune response	C1QA, C1QB, C1QC, C1R, C1S, C3, C3AR1, C7, CD4, CD8A, CD74, CLU, CTSS, FCER1G, FCGR1A, FYB1, NCKAP1L, INPP5D, LCK, LCP2, CFP, PTPRC, CCL5, SLC11A1, TLR2, KLRK1, RGCC, TLR7, SLC15A3, TLR8, SASH3, MYO1G, CLEC7A, KLHL6, CMTM3, THEMIS
inflammatory response	ADORA2A, AIF1, C1QA, C3, C3AR1, CD6, CD68, CLU, CCR5, CNR2, CSF1R, CX3CR1, CYBB, DPEP1, FCGR1A, FCGR3A, FOLR2, FOS, HMOX1, ITGAL, CD180, PTN, CCL5, SLC11A1, TLR2, TNFRSF1B, VCAM1, LY86, CXCL13, STAB1, LAT, TLR7, TLR8, CLEC7A, PLD4, IL31RA
immune effector process	C1QA, C1QB, C1QC, C1R, C1S, C3, C7, CD2, CD8A, CD74, CLU, CX3CR1, FCER1G, FCGR1A, FCGR3A, IL2RB, INPP5D, ITGAL, LCP1, LFNG, CD180, CFP, PRF1, SLC11A1, SPN, KLRK1, LAT, RGCC, TLR8, APBB1IP, MYO1G
regulation of cell activation	ADORA2A, AIF1, CD2, CD4, CD6, CD74, CNR2, FCER1G, FCGR3A, NCKAP1L, HMOX1, INPP5D, LCK, PLEK, PTPRC, RAC2, CCL5, SPN, TNFRSF1B, VCAM1, ZBTB16, LAPTM5, TSPAN32, CD300A, IKZF3, KLRK1, LAT, SASH3, CLEC7A, CYGB, IL31RA, PIK3R6
positive regulation of phosphorylation	AIF1, C3, CD4, CD6, CD74, CLU, CSF1R, CX3CR1, FCGR1A, FLT3, HCLS1, NCKAP1L, LCP2, LEPR, PLAUR, PTPRC, CCL5, SLC11A1, TNFRSF11A, LAT, RGCC, AGAP2, IL31RA, PIK3R6, FGD2, TMEM119, NCF1
positive regulation of cytokine production	AIF1, C3, C3AR1, CD2, CD4, CD6, CD74, CLU, CSF1R, CYBB, FCER1G, FCGR3A, HMOX1, PTPRC, SLC11A1, SPN, TLR2, LAPTM5, KLRK1, RGCC, TLR7, TLR8, SASH3, CLEC7A
cell-cell adhesion	CD2, CD6, CDH11, CX3CR1, ITGA4, ITGAD, ITGAL, ITGAX, PLEK, PTPRC, RAC2, CCL5, SELPLG, SPN, VCAM1, NRXN1, PTPRU, TSPAN32, PCDH12, CADM3, FERMT3, HMCN1, LRG1, CRB2
regulation of immune effector process	BST2, C3, CD74, CX3CR1, FCGR1A, NCKAP1L, HMOX1, CFP, PTPRC, RAC2, TNFRSF1B, LAPTM5, CD300A, KLRK1, TLR7, SASH3, CLEC7A, SVEP1, PIK3R6, NCF1
extracellular matrix organization	COL1A1, COL1A2, COL3A1, COL12A1, CTSS, DPT, LCP1, LOXL1, LOXL2, MMP2, ADAMTSL2, FBLN5, OLFML2B, FKBP10, SMOC2, ADAMTS12, HMCN1
ossification	CDH11, COL1A1, COL1A2, COL6A1, VCAN, FHL2, TNC, IGFBP3, MMP2, PTN, SNAI1, CLEC3B, ZBTB16, TNFRSF11A, MRC2, ADAMTS12, TMEM119

Table S3. Gene entries and gene names shared by molecular functions in GO enrichment analysis of AR and SAR

Gene entry	Gene name
calcium ion binding	AIF1, C1R, C1S, CDH11, VCAN, ADGRE1, LCP1, LOXL2, PRF1, CLEC3B, TRPM2, NRXN1, FBLN5, STAB1, PCDH12, HPCAL4, DNAH7, FKBP10, SMOC2, SVEP1, HMCN1, CRB2
extracellular matrix structural constituent	AEBP1, CD4, COL1A1, COL1A2, COL3A1, COL6A1, COL6A2, COL12A1, VCAN, DCN, DPT, TNC, LAMA2, FBLN5, HMCN1
integrin binding	COL3A1, ITGA4, ITGAD, ITGAL, ITGAX, LCP1, PTN, VCAM1, ITGBL1, FBLN5, FERMT3
protein homodimerization activity	AOX1, BST2, CD4, CSF1R, FCER1G, Hmox1, PLEK, CCL5, SLC11A1, ZBTB16, FBLN5, ICZF3, CADM3, GIMAP7, FIBIN
carbohydrate binding	CD69, VCAN, LOXL2, PTN, CLEC3B, MRC2, CLEC10A, KLRK1, CLEC7A, CLEC2L, CLEC12A, FUOM
G protein-coupled receptor binding	ADORA2A, C3, CX3CR1, CCL5, WNT2B, PTCH2, CXCL14, CXCL13, CNRIP1, RTP4
glycosaminoglycan binding	VCAN, DCN, PTN, PTPRC, TLR2, CLEC3B, CXCL13, STAB1, SMOC2
metallopeptidase activity	AEBP1, DPEP1, MMP2, ADAM12, CPXM1, ADAMTS12, HTRA3
fibronectin binding	CTSS, IGFBP3, ITGA4, MMP2
pattern recognition receptor activity	TLR2, TLR7, TLR8, CLEC7A
immunoglobulin receptor activity	TLR2, TLR7, TLR8, CLEC7A
oxidoreductase activity, acting on the CH-NH3 group of donors, oxygen as acceptor	LOXL1, LOXL2, VCAM1

Table S4. Common gene entries and gene names of cell composition in GO enrichment analysis of AR and SAR

Gene entry	Gene name
extracellular matrix	AEBP1, C1QA, C1QB, C1QC, CLU, COL1A1, COL1A2, COL3A1, COL6A1, COL6A2, COL12A1, VCAN, CTSS, DCN, DPT, TNC, LAMA2, LOXL1, LOXL2, CD180, MMP2, CFP, CLEC3B, WNT2B, ADAMTSL2, LAMC3, FBLN5, OLFML2B, SMOC2, ADAMTS12, HMCN1
secretory granule membrane	BST2, C3AR1, CD53, CD68, CYBB, FCER1G, NCKAP1L, ITGAL, ITGAX, IRAG2, PLAUR, PTPRC, SLC11A1, TLR2, TNFRSF1B, TRPM2, LILRB3, CD300A, CLEC12A
lytic vacuole	BST2, C3, C3AR1, CD68, CD74, CFTR, COL6A1, VCAN,

	CTSS, DCN, IRAG2, PRF1, SLC11A1, TRPM2, LAPTM5, TLR7, SLC15A3, TLR8, NCF1
cell-cell junction	CD2, CD53, CDH11, LCP2, PTPRU, LAT, PCDH12, MXRA8, CADM3, HMCN1, PARD6G, CRB2, THEMIS
membrane raft	BST2, CD2, CD4, CD8A, HMOX1, INPP5D, LCK, LCP2, PTPRC, SELPLG, TLR2, TNFRSF1B, LAT, BAALC, PLVAP
endocytic vesicle	CD4, CD74, CFTR, CTSS, CYBB, FCGR1A, GRIA3, HCLS1, RAC2, SLC11A1, TLR2, STAB1, TLR7, PLD4, NCF1
cell-substrate junction	FHL2, TNC, ITGA4, LCP1, PLAUR, PTPRC, RAC2, RPLP2, ITGBL1, MRC2, CORO2B, APBB1IP, PARVG, FERMT3, HMCN1
protein complex involved in cell adhesion	TNC, ITGA4, ITGAD, ITGAL, ITGAX, LAMA2, PLAUR, ITGBL1, TSPAN32
collagen trimer	C1QA, C1QB, C1QC, COL1A1, COL1A2, COL3A1, COL6A1, COL6A2, COL12A1
basement membrane	TNC, LAMA2, LOXL1, LOXL2, SMOC2, HMCN1
immunological synapse	CD6, CD37, CD53, LCK, LAT
phagocytic cup	AIF1, LCP1, ARHGAP25, MYO1G
complement component C1 complex	C1QA, C1QB, C1QC

Table S5. Different regulated gene items in AR and SAR in GO enrichment analysis

	AR	SAR
Biological processes	response to bacterium, positive regulation of response to external stimulus, regulation of defense response, cell population proliferation, leukocyte migration, regulation of leukocyte migration, cell-matrix adhesion, leukocyte cell-cell adhesion, cell junction disassembly	cellular response to cytokine stimulus, positive regulation of cell migration, chemotaxis, vasculature development, negative regulation of immune system process, positive regulation of cell death, regulation of angiogenesis, myeloid leukocyte activation, integrin-mediated signaling pathway
Molecular functions	enzyme activator activity, cytokine binding, actin binding, MHC protein binding, collagen binding, SMAD binding, proteoglycan binding, molecular sequestering activity	kinase binding, immune receptor activity, growth factor binding, actin filament binding, SH3 domain binding, coreceptor activity, heme binding, phosphatidylinositol 3-kinase binding
Cell composition	side of membrane, neuronal cell body, actin cytoskeleton, phagocytic vesicle,	external side of plasma membrane, apical part of cell, secretory granule lumen, blood

	cytoplasmic side of plasma membrane, uropod, endolysosome	microparticle, microvillus, platelet dense granule lumen, phosphatidylinositol 3-kinase complex, class IB

Table S6. Enrichment and analysis of pathways and genes of the same regulated signal in AR and SAR by KEGG（Top 20）

Pathway	Gene name
Cell adhesion molecules	CD2, CD4, CD6, CD8A, VCAN, ITGA4, ITGAL, PTPRC, SELPLG, SPN, VCAM1, NRXN1, CADM3
PI3K-Akt signaling pathway	COL1A1, COL1A2, COL6A1, COL6A2, CSF1R, FLT3, TNC, IL2RB, LAMA2, TLR2, LAMC3, PIK3R6
Osteoclast differentiation	CSF1R, FCGR1A, FCGR3A, FHL2, FOS, LCK, LCP2, TNFRSF11A, LILRB3, NCF1
Platelet activation	CSF1R, FCGR1A, FCGR3A, FHL2, FOS, LCK, LCP2, TNFRSF11A, LILRB3, NCF1
Hematopoietic cell lineage	CD2, CD4, CD8A, CD37, CSF1R, FCGR1A, FLT3, ITGA4
Natural killer cell mediated cytotoxicity	CD2, CD4, CD8A, CD37, CSF1R, FCGR1A, FLT3, ITGA4
Yersinia infection	CD4, CD8A, FOS, FYB1, ITGA4, LCK, LCP2, RAC2, LAT
Malaria	GYPC, ITGAL, TLR2, VCAM1, KLRK1
Leukocyte transendothelial migration	CYBB, ITGA4, ITGAL, MMP2, RAC2, VCAM1, NCF1
Pathways in cancer	CSF1R, FLT3, FOS, HMOX1, IL2RB, LAMA2, MMP2, RAC2, RXRG, WNT2B, ZBTB16, PTCH2, LAMC3
Regulation of actin cytoskeleton	CSF1R, FLT3, FOS, HMOX1, IL2RB, LAMA2, MMP2, RAC2, RXRG, WNT2B, ZBTB16, PTCH2, LAMC3

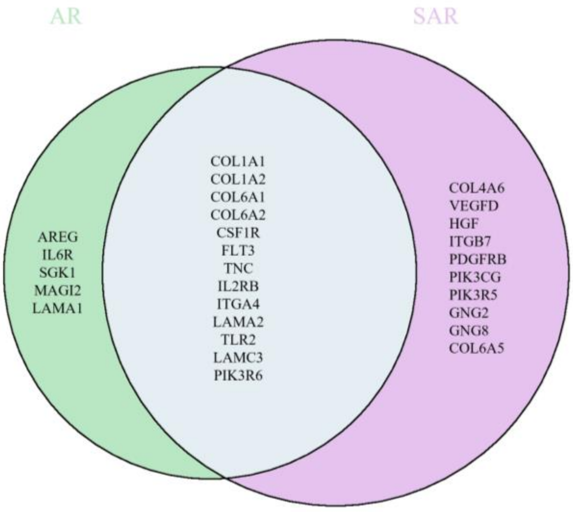

Figure S7. Wayne diagram of regulated genes involved in PI3K-Akt signaling pathway between AR and SAR

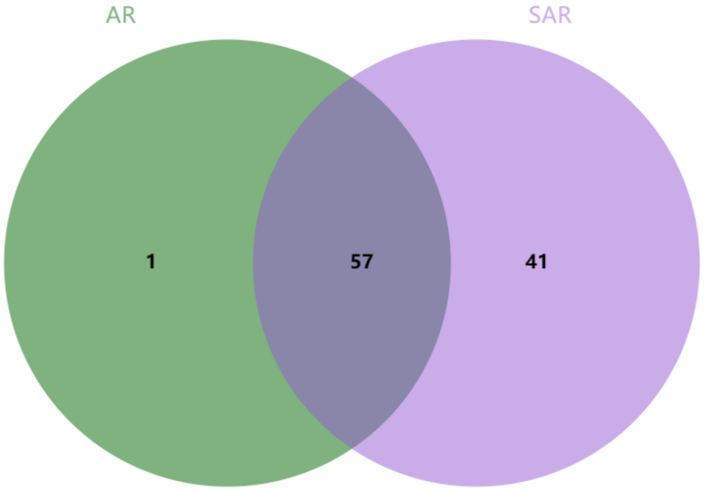

Figure S8. Wayne diagram of KEGG enrichment analysis pathway between AR and SAR

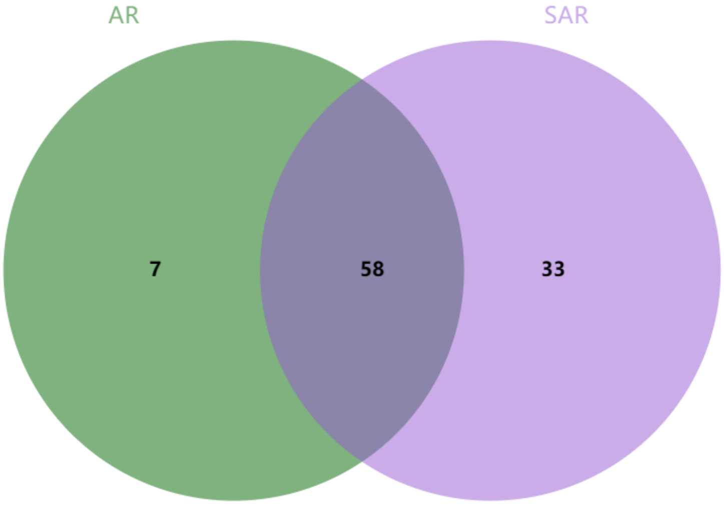

Figure S9. KEGG analysis of common pathway genes Wayne diagram of AR and SAR （Top 20）

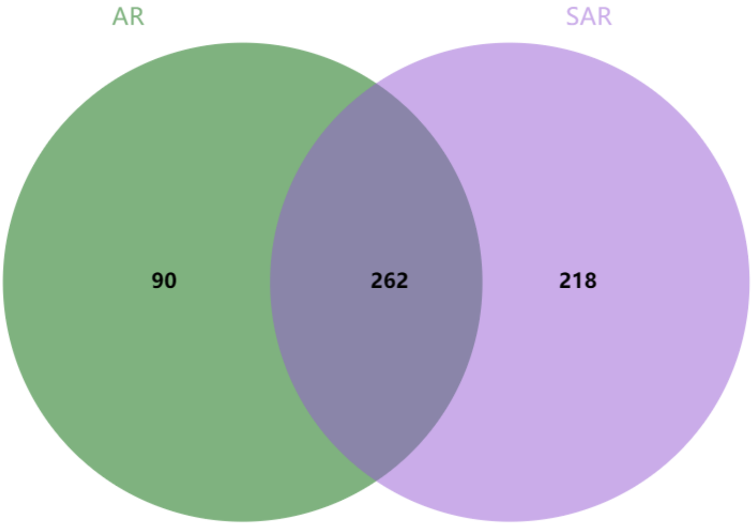

Figure S10. Wayne diagram of up-regulated genes in AR and SAR