Fig.S1 (a) HE staining morphology of liver tissue in normal, model and geniposide-treated group of mouse under microscope (×200). (b)–(g) The biochemical indexes analysis of mouse, including AST, ALT, GSH, MDA, TG and γ-GT in normal, model and geniposide-treated group. Compared with the control group, " * " represent a significant difference (P<0.05); "** " represent extremely difference (P<0.01). Compared with the model group, "#" represent a significant difference (P<0.05); "## " represent extremely difference (P<0.01). C: control group; M: model group; G: geniposide-treated group.
Fig. S2 The result of TUNEL in situ terminal apoptosis and CASSASE-3 positive expression in normal, model and geniposide-treated group. (a) and (c) shows TUNEL in situ terminal apoptosis; (b) and (d) shows positive expression for CASSASE-3. Compared with the control group, "*" represent a significant difference (P<0.05); "**" represent extremely difference (P<0.01). Compared with the model group, "#" represent a significant difference (P<0.05); "##" represent extremely difference (P<0.01). C: control group; M: model group; G: geniposide-treated group.
Fig.S3  UPLC-Q/TOF-MS total ion chromatogram of blood samples from the control, model group and geniposide-treated group in positive and negative ion mode. C: control group; M: model group; G: geniposide-treated group.
**Fig.S4** (a) KEGG global metabolic network related with geniposide against ALD. Metabolite-metabolite (b) and metabolites-gene (c) interaction network associated with geniposide therapeutic effect on ALD mouse.
Table S1  Changes of metabolites of ALD animals after geniposide treatment.

| No. | Rt(min) | Ion form | m/z   | Proposed compound        | Formula | Trend in model | HMDB   | Regulated by Geniposide |
|-----|---------|----------|-------|--------------------------|---------|----------------|--------|-------------------------|
| 1   | 0.62    | M-H      | 191.02| isocitric acid            | C6H8O7  | ↓              | HMDB00193 | *                        |
| 2   | 0.74    | M-H      | 131.08| Ornithine                 | C5H12N2O2 | ↑             | HMDB00214 | *                        |
| 3   | 0.87    | M+H      | 175.12| Arginine                  | C6H14N4O2 | ↑             | HMDB00517 | *                        |
| 4   | 1.06    | M+H      | 147.11| Lysine                    | C6H14N2O2 | ↑             | HMDB00182 | *                        |
| 5   | 1.27    | M-H      | 169.04| Uric acid                 | C5H4N4O3 | ↑             | HMDB00289 | *                        |
| 6   | 1.43    | M-H      | 243.06| Uridine                   | C9H12N2O6 | ↓             | HMDB00296 | *                        |
| 7   | 1.60    | M+H      | 215.02| Citric acid               | C6H8O7  | ↑             | HMDB00094 | *                        |
| 8   | 1.76    | M-H      | 131.05| Asparagine                | C4H8N2O3 | ↓             | HMDB33780 | *                        |
| 9   | 2.47    | M+H      | 205.10| Tryptophan                | C11H12N2O2 | ↓             | HMDB13609 | *                        |
| 10  | 2.72    | M-H      | 212.00| Indoxyl sulfate           | C8H7NO4S | ↓             | HMDB00682 | *                        |
| 11  | 3.02    | M-H      | 136.06| Adenine                   | C5H5N5  | ↓             | HMDB00034 | *                        |
| 12  | 3.21    | M+H      | 145.06| Glutamine                 | C5H10N2O3 | ↓             | HMDB00641 | *                        |
| 13  | 3.36    | M+H      | 181.07| Glucose                   | C6H12O6  | ↑             | HMDB00122 | *                        |
| 14  | 3.68    | M+H      | 144.08| N,N-dimethylglycine       | C8H11N   | ↑             | HMDB00120 | *                        |
| 15  | 4.89    | M+H      | 116.07| Proline                   | C5H9NO2  | ↑             | HMDB03411 | *                        |
| 16  | 5.06    | M-H      | 285.21| Hexadecanedioic acid      | C16H30O4 | ↑             | HMDB00672 | *                        |
| 17  | 5.52    | M+H      | 184.10| Carnitine                 | C7H15NO3 | ↓             | HMDB00062 | *                        |
| 18  | 5.88    | M-H      | 514.28| Taurocholic acid          | C26H45N7O7 | ↓             | HMDB00036 | *                        |
| 19  | 6.05    | M+H      | 265.17| Oxodecanoic acid          | C14H26O3 | ↓             | HMDB10730 | *                        |
| 20  | 6.14    | M+H      | 488.30| Glycocholic acid          | C26H43N6O | ↑             | HMDB00138 | *                        |
| 21  | 6.29    | M-H      | 87.01 | Pyruvic acid              | C3H4O3  | ↓             | HMDB00243 | *                        |
| 22  | 6.41    | M+H      | 166.08| Phenylalanine             | C9H11NO2 | ↑             | HMDB00159 | *                        |
| 23  | 6.52    | M-H      | 345.21| Corticosterone            | C21H30O4 | ↑             | HMDB01547 | *                        |
| 24  | 6.64    | M+H      | 353.24| Prostaglandin E2          | C20H32O5 | ↑             | HMDB01220 | *                        |
| 25  | 6.75    | M+H      | 300.29| Sphingosine               | C18H37N2O2 | ↓            | HMDB00252 | *                        |
| 26  | 6.86    | M+H      | 327.23| Arachidonic acid          | C20H32O2 | ↑             | HMDB01043 | *                        |
| 27  | 7.15    | M-H      | 520.34| LysoPC(18:1)              | C26H52N07P | ↓             | HMDB02815 | *                        |
| 28  | 7.60    | M-H      | 508.34| LysoPC(17:0)              | C25H52N07P | ↓             | HMDB12108 | *                        |
| 29  | 7.71    | M-H      | 482.32| LysoPC(15:0)              | C23H48N07P | ↓            | HMDB10381 | *                        |
| 30  | 7.83    | M-H      | 282.28| Oleamide                  | C18H35NO | ↑             | HMDB02117 | *                        |
| 31  | 7.99    | M-H      | 494.33| LysoPC(16:0)              | C24H50N07P | ↓             | HMDB10382 | *                        |
| 32  | 8.11    | M+H      | 321.24| 8-HETE                   | C20H32O3 | ↓             | HMDB04679 | *                        |
| 33  | 8.27    | M-H      | 253.22| Palmitoleic acid          | C16H30O2 | ↑             | HMDB03229 | *                        |