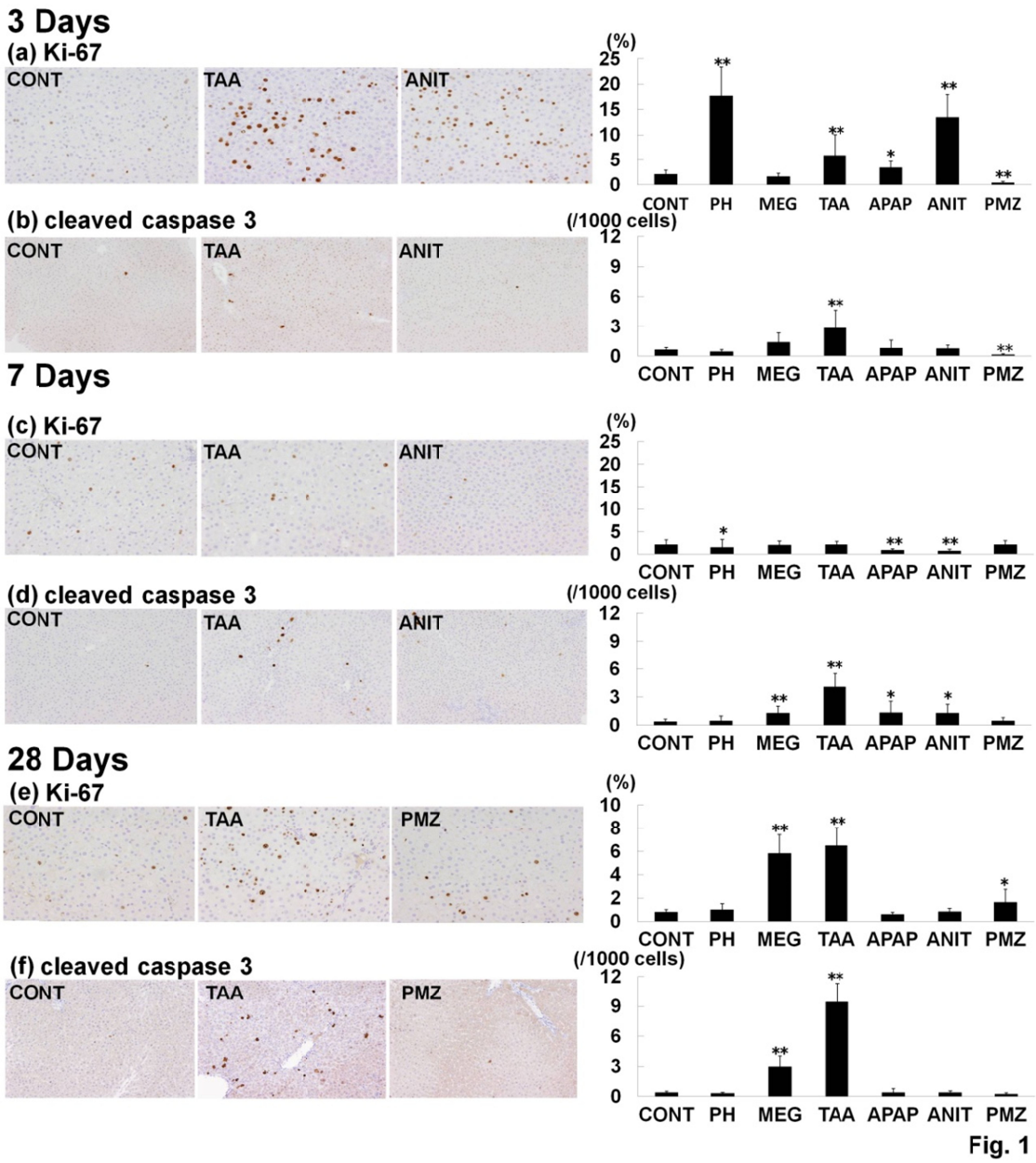

Fig. 1. Distribution of Ki-67$^+$ and cleaved caspase 3$^+$ cells in the liver in rats after 3, 7 or 28 days from the start of treatment. Photomicrographs show distribution of Ki-67$^+$ and cleaved caspase 3$^+$ cells in the liver of the representative cases from untreated controls and animals treated with TAA or ANIT (a, b, c, d) and treated with TAA or PMZ (e and f). The graph show positive cell ratios of hepatocytes per total cells counted in 10 animals in each group. Values represent mean + SD. (a) Ki-67 (after 3 days), (b) cleaved caspase 3 (after 3 days), (c) Ki-67 (after 7 days), (d) cleaved caspase 3 (after 7 days), (e) Ki-67 (after 28 days), (f) cleaved caspase 3 (after 28 days). *,** $P < 0.05$, 0.01 vs. untreated controls (Dunnett's or Steel's test).

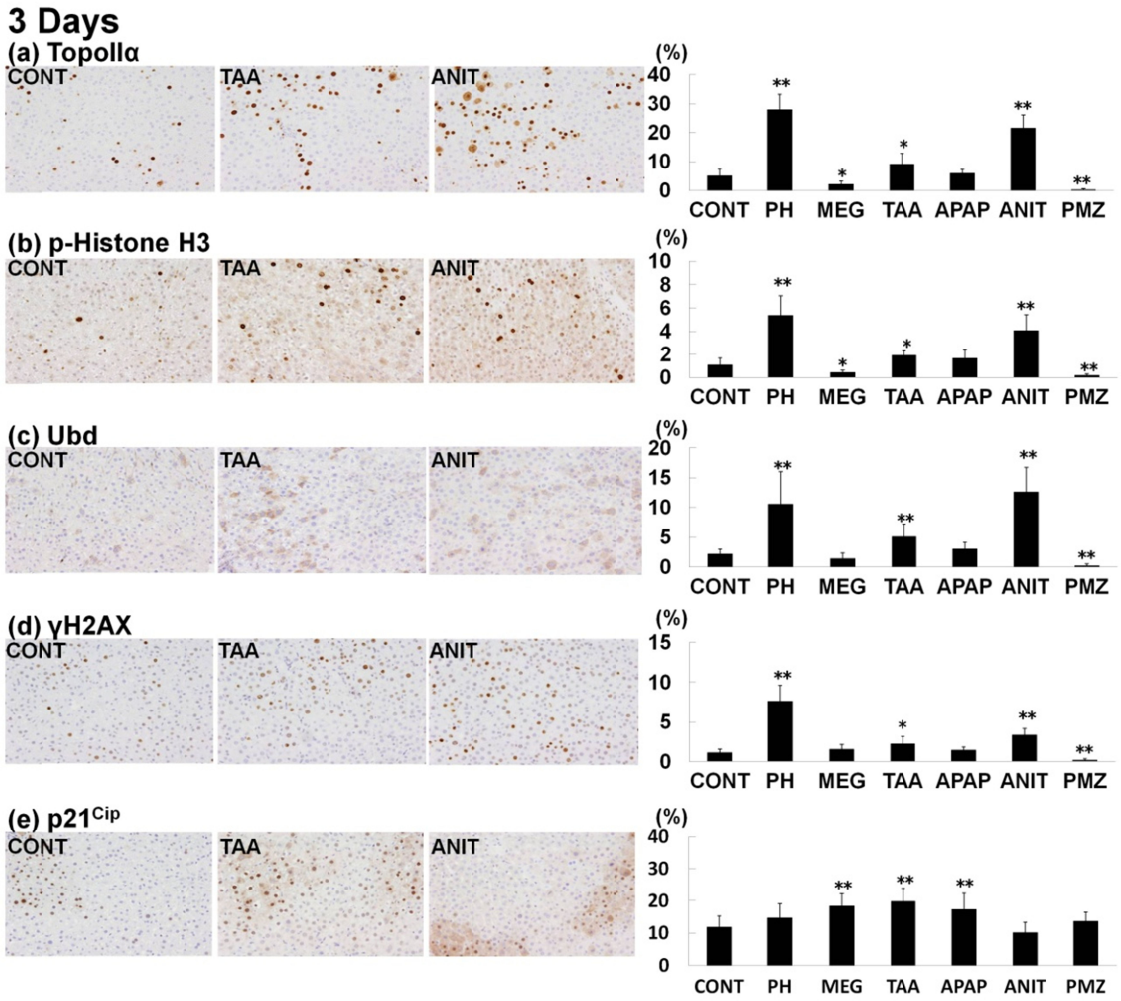

Fig. 2

Fig. 2. Distribution of TopoIIα^{+}, p-Histone H3^{+}, Ubd^{+}, γH2AX^{+} and p21^{Cip1+} cells in the liver in rats after 3 days from the start of treatment. Photomicrographs show distribution of TopoIIα^{+}, p-Histone H3^{+}, Ubd^{+}, γH2AX^{+} and p21^{Cip1+} cells in the liver of the representative cases from untreated controls and animals treated with TAA or ANIT. The graph show positive cell ratios of hepatocytes per total cells counted in 10 animals in each group. Values represent mean + SD. (a) TopoIIα, (b) p-Histone H3, (c) Ubd, (d) γH2AX, (e) p21^{Cip1}. *,** $P < 0.05$, 0.01 vs. untreated controls (Dunnett's or Steel's test).

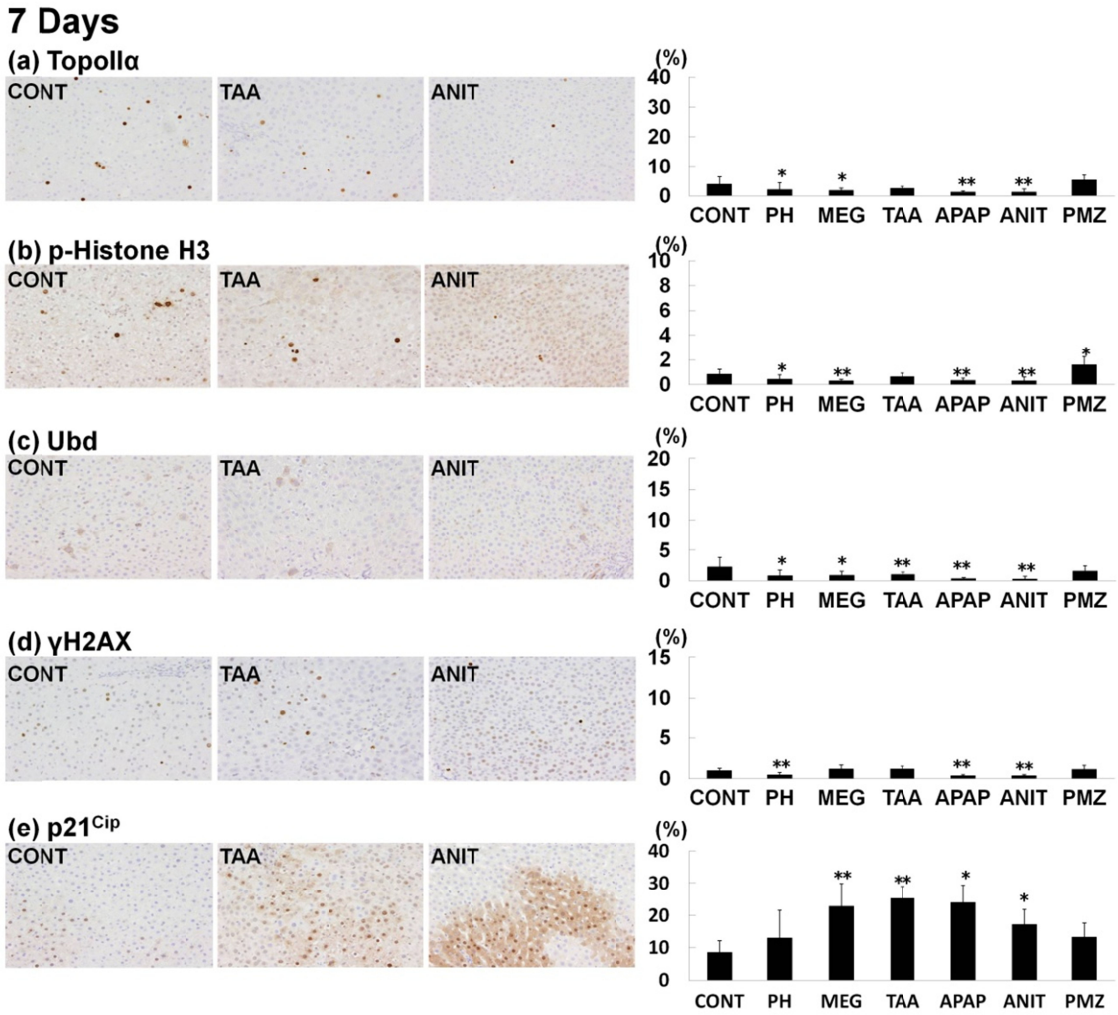

Fig. 3

Fig. 3. Distribution of TopoIIα^{+}, p-Histone H3^{+}, Ubd^{+}, γH2AX^{+} and p21^{Cip1+} cells in the liver in rats after 7 days from the start of treatment. Photomicrographs show distribution of TopoIIα^{+}, p-Histone H3^{+}, Ubd^{+}, γH2AX^{+} and p21^{Cip1+} cells in the liver of the representative cases from untreated controls and animals treated with TAA or ANIT. The graph show positive cell ratios of hepatocytes per total cells counted in 10 animals in each group. Values represent mean + SD. (a) TopoIIα, (b) p-Histone H3, (c) Ubd, (d) γH2AX, (e) p21^{Cip1}. *,** $P < 0.05$, 0.01 vs. untreated controls (Dunnett's or Steel's test).

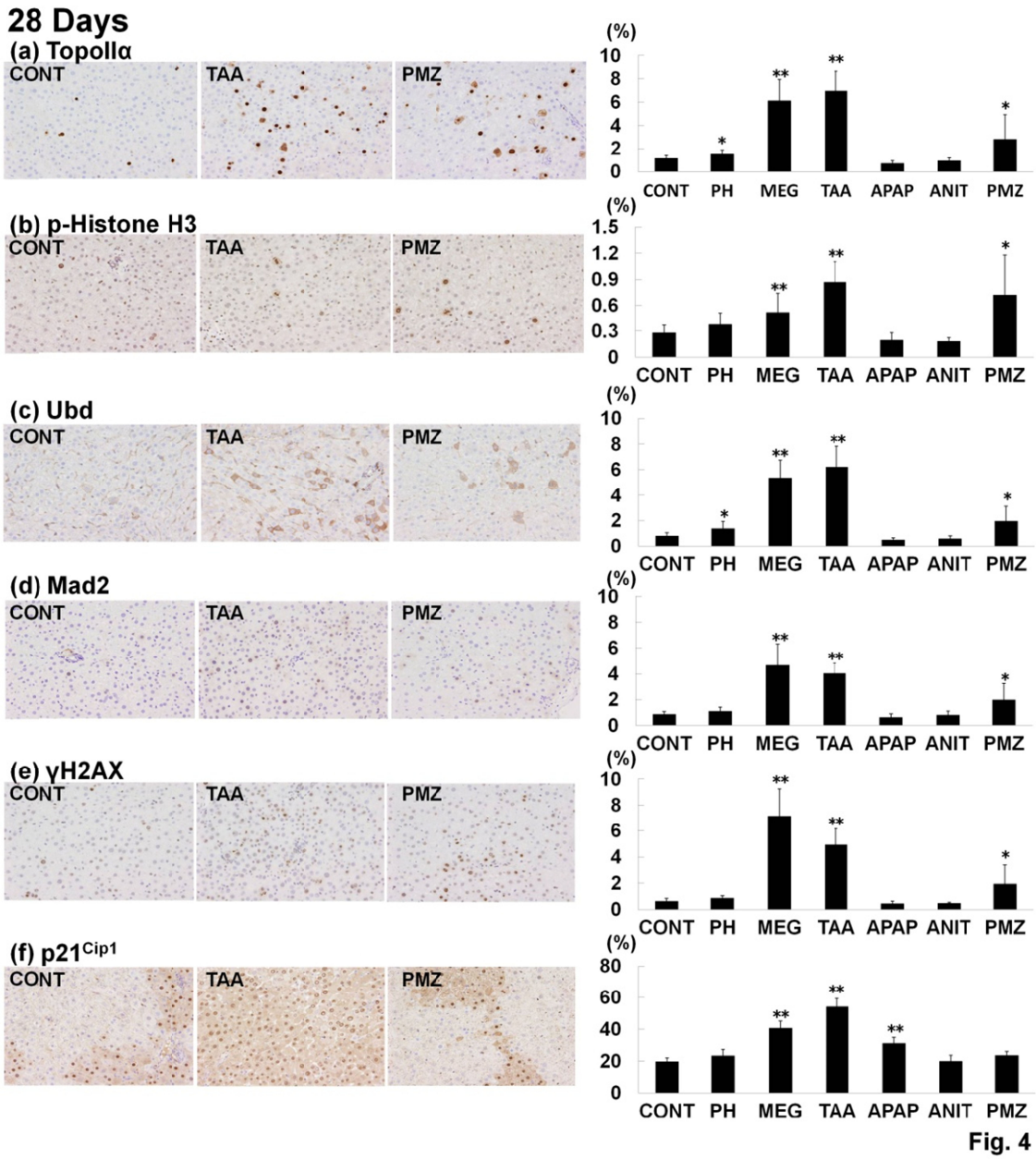

Fig. 4. Distribution of TopoIIα^{+}, p-Histone H3^{+}, Ubd^{+}, Mad2, γH2AX^{+} and p21^{Cip1+} cells in the liver in rats after 28 days from the start of treatment. Photomicrographs show distribution of TopoIIα^{+}, p-Histone H3^{+}, Ubd^{+}, γH2AX^{+} and p21^{Cip1+} cells in the liver of the representative cases from untreated controls and animals treated with TAA or PMZ. The graph show positive cell ratios of hepatocytes per total cells counted in 10 animals in each group. Values represent mean + SD. (a) TopoIIα, (b) p-Histone H3, (c) Ubd, (d) Mad2, (e) γH2AX, (f) p21^{Cip1}. *,** $P < 0.05$, 0.01 vs. untreated controls (Dunnett's or Steel's test).

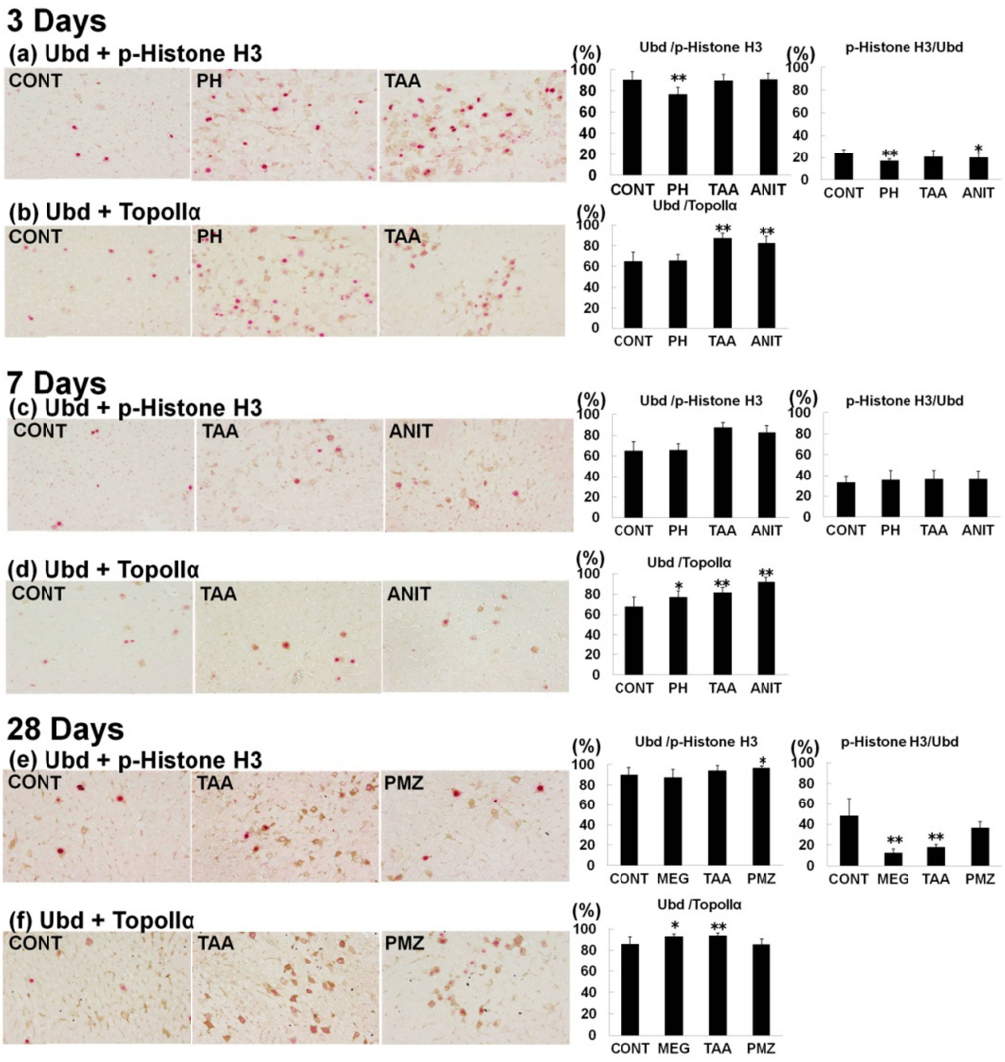

Fig. 5

Fig. 5. Distribution of immunoreactive cell population of p-Histone H3 co-expressing Ubd (Ubd/p-Histone H3), Ubd co-expressing p-Histone H3 (p-Histone H3/Ubd) or TopoIIα co-expressing Ubd (Ubd/ TopoIIα) in the liver rats after 3, 7 or 28 days from the start of treatment. Photomicrographs show distribution of Ubd/p-Histone H3, p-Histone H3/Ubd, Ubd/ TopoIIα in the liver in untreated controls and animals treated with TAA or ANIT (a, b) and treated with TAA or ANIT (c, d) and treated with TAA or PMZ (e, f). Immunoreactivety of Ubd (cytoplasm) and p-Histone H3 (nucleus) or TopoIIα (nucleus) is visualized as brown and red, respectively. The graphs show Ubd-positive cell ratio (%) of proximal hepatocytes per total cells immunoreactive with p-Histone H3 or TopoIIα, p-Histone H3-positive cell ratio (%) of proximal hepatocytes per total cells immunoreactive with Ubd counted in 10 animals in each group. Values represent mean + SD. (a) Ubd/p-Histone H3 or p-Histone H3/Ubd (after 3 days), (b) Ubd/ TopoIIα (after 3 days), (c) Ubd/p-Histone H3 or p-Histone H3/Ubd (after 7 days), (d) Ubd/ TopoIIα (after 7 days), (e) Ubd/p-Histone H3 or p-Histone H3/Ubd (after 28 days), (f) Ubd/ TopoIIα (after 28 days). *,** $P < 0.05$, 0.01 vs. untreated controls (Dunnett's or Steel's test).