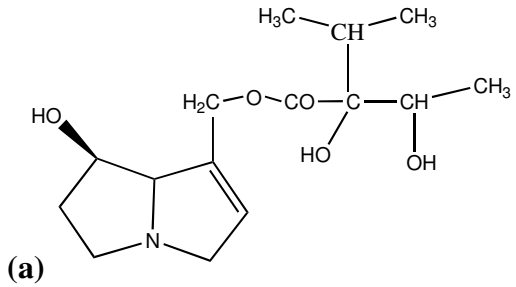
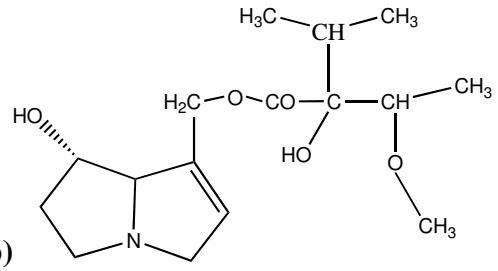
Figure 1: Representative pyrrolizidine alkaloid (PA) structures and their relative toxicity

Retronecine monoesters (a) display the lowest toxicity to 14-day-old rats. Heliotridine monoesters (b) are two to four times as toxic as the retronecine monoesters, while diesters of both retronecine and heliotridine are 4 times as toxic as corresponding monoesters. The most toxic PAs are the macrocyclic diesters (c). The N-oxide forms (d) of each pyrrolizidine alkaloid are non-toxic, but are readily converted to the toxic parent base in the gut [22,23].



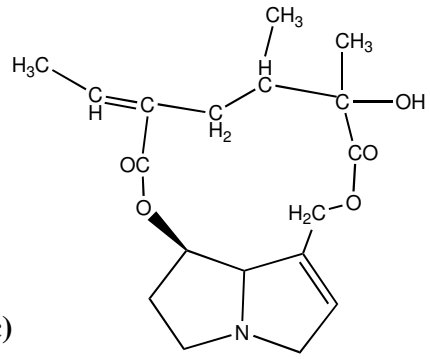
(a)

Retronecine monoester
(lycopsamine/intermedine)



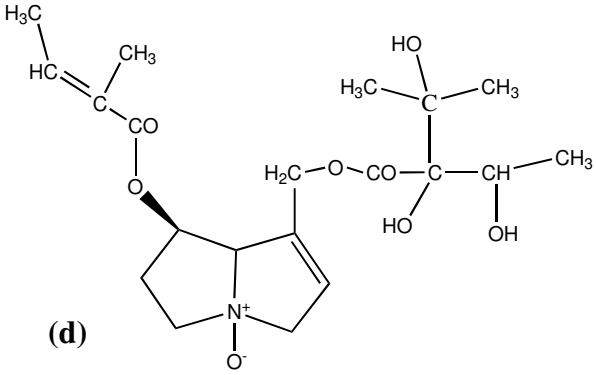
(b)

Heliotridine monoester
(heliotrine)



(c)

Macrocyclic retronecine diester
(senecionine)



(d)

N-oxide of retronecine diester
(echmidine N-oxide)

Adapted from: TRENDS IN PHARMACOLOGICAL SCIENCES, Vol 23, D. Rode, *Comfrey toxicity revisited*, pp 497-499, 2002 with permission from Elsevier.