and 5–20 g/kg, respectively. Alkaline phosphatase was elevated in mice but lowered in rats after treatment with raw aconite root or mesaconitine. Pathological examination showed a slight focal cell infiltration in the liver of some mice treated with raw aconite root and mesaconitine. No pathologic change was observed in mice treated with processed aconite root at a daily dose of 1 g/kg [81].

Both respiratory depression in rabbits and heart fibrillation in guinea pigs caused by aconitine were antagonized by i.v. infusion of calcium chloride. Atropine counteracted the antagonistic effect of calcium choride on respiratory depression caused by large doses of aconitine [82]. Hydrocortisone was effective in treatment of *A. brachypodum* poisoning in rabbits [83].

Toxic effects of aconitine are mainly seen in the nervous system, effecting first excitation and then inhibition of the vagus and sensory nerves.

Aconitine also acts directly on cardiac muscle. Symptoms of intoxication include systemic paralysis, nausea, and vomiting, followed by dizziness, palpitation, intolerance of cold, irritability, delirium, hypotension, arrhythmia, shock, and coma. The common abnormal electrocardiographic signs include arrhythmia, ventricular tremor, atrioventricular block, and myocardial damage [84].

The toxicity of aconitine and nine analogues was tested in mice. High toxicity appeared to be associated with the presence of both an acetyl and a benzoyl group [85]. With respect to the toxicity of the roots of eight *Aconitum* species, that of those characterized by a lack of diester alkaloids and containing mainly C_{20} aminoalcohols or monoesterified C_{19} diterpene alkaloids, is comparatively low. In mice, i.v. LD_{50} values were 1600–3400 mg/kg. By contrast, the toxicity of those species containing diester bases, with an acetoxy residue at C-8 and benzoyloxy or anisoyloxy residues at C-14, is very high. The *Aconitum* species that contain mainly an aminoalcohol of C_{19} diterpene alkaloids display intermediate toxicity with LD_{50} values of 210–260 mg/kg [86].

Aconitine exhibits a noncompetitive, inhibitory effect on pig heart aconitase in vitro. This suggests a possible molecular basis for the toxic and pharmacologic actions produced in experimental animals by aconitine [87].

3.3.2 Arrhythmic Effects

Aconitine, mesaconitine, beiwutine, hypaconitine, 3-acetylaconitine, and deoxyaconitine administered i.v. to anesthetized rats induced arrhythmia. The potency of arrhythmia induction was of the order: beiwutine > mesaconitine > aconitine > 3-acetylaconitine > hypaconitine > deoxyaconitine [80]. Aconitine caused cardiac arrhythmia in mice. It can be used in experimental arrhythmia models to screen for antiarrhythmic drugs. The arrhythmia caused by aconitine was counteracted by i.v. administration of calcium [88]. Thus, when aconitine-induced arrhythmia is used to screen for antiarrhythmic effects of crude extracts, e.g., herbal drugs, interference from calcium that might be present in the extracts should be considered. Beiwutine appeared to be superior to aconitine in producing experimental arrhythmia for drug screening, since beiwutine administered i.v. to anesthetized rats caused arrhythmia but had little effect on blood pressure [80].

The arrhythmic activity of aconite alkaloids can be correlated with the presence of a benzoyl ester group; such compounds have been shown to be effective in inducing arrhythmia [85].