In anesthetized open-chest dogs aconitine, at doses that did not produce cardiac arrhythmia, did not affect prostaglandin E (PGE) and $PGF_{2\alpha}$ efflux into coronary sinus blood but increased PGE and $PGF_{2\alpha}$ efflux at doses that produced arrhythmia. The increased $PGF_{2\alpha}$ efflux in cardiac arrhythmia was not affected by antiarrhythmics. Thus, prostaglandins appear to be released in cardiac arrhythmia and the increased PGE efflux during arrhythmia may be a protective mechanism against sympathetic influences [89].

3.3.3 Analgesic Effects

Three widely occurring alkaloids in aconite roots, mesaconitine, aconitine, and hypaconitine, showed analgesic activity in mice [90]. An investigation on the contribution of central monoamines and the opiate receptor to mesaconitine-induced analgesia showed that the analgesic action of intracerebral mesaconitine was dose dependent, indicating that its activity is elicited through the central nervous system. Levallorphan did not affect the analgesic activity of mesaconitine, suggesting that its activity is not mediated via the opiate receptor. Thus, the analgesic activity of mesaconitine is closely related to responses involving the central catecholaminergic system, particularly the noradrenergic system [91].

Mesaconitine-induced antinociception could be significantly potentiated by cyclic adenosine monophosphate (cAMP). The phosphodiesterase inhibitor theophylline also significantly potentiated mesaconitine-induced antinociception. Furthermore, mesaconitine-induced antinociception was markedly increased by isoproterenol, a β-adrenoceptor agonist, and reduced by propranolol, a β-adrenoceptor antagonist. Apparently, the antinociceptive action of mesaconitine is potentiated through cAMP and occurs via stimulation of the central β-adrenergic system [92].

Lappaconitine [93], *N*-deacetyllappaconitine, *N*-deacetylranaconitine, and *N*-deacetylfinaconitine [94] all exhibited a strong analgesic activity in animal experiments. The median analgesic dose (ED_{50}) of lappaconitine in mice after i.p. administration was found to be 3.5 mg/kg. An anesthesia test on rabbit cornea revealed that the surface anesthetic potency of lappaconitine was eight times stronger than that of cocaine. Local anesthetic effects on sciatic nerve block in mice were five times those of cocaine; in the intracutaneous wheal test in the guina pig lappaconitine was found to be about equally active [94].

It is interesting to note that aconitine could be used as an agent to induce a writhing syndrome in mice, thus providing a suitable model system for assessing aspirin-like analgesic activity. The writhing appeared quickly and was of greater frequency and longer duration than that caused by other agents. Orally administered, nonnarcotic analgesics antagonized the aconitine-induced writhing more selectively than did narcotic analgesics. Potencies of some nonnarcotic analgesics tested decreased in the following order: acetylsalicylic acid, phenylbutazone, amidopyrine, phenacetin, sodium salicylate [95].

3.3.4 Antiinflammatory Activity

Aconite alkaloids, obtained from the extract of *A. carmichaeli* roots, inhibited the increased vascular permeability induced by acetic acid in mouse peritoneal cavity