EDITORIAL

NEUROTOXINS FROM *CONUS MUSICUS* (FAMILY CONIDAE)

In this issue of the journal, there is an article by Balamurgan *et al.* on the neuropharmacological effects of the crude venom extract of *Conus musicus* in mice. The toxins from this species of cone snail are collectively referred to as conotoxins. These are small peptide toxins, typically 12-30 amino acids with a high density of disulphide bonds. They are potent neurotoxins. There have been over 30 recorded cases of human envenomation by cone shell species. Members of Conidae family do not predate upon humans but will sting if disturbed.

The conotoxins are divided into alpha, mu, delta and omega. Much of the studies reported in the literature are on alpha, mu and omega conotoxins. Much more is known about the structure and biological activity of these compounds than the authors have presented in the article. Alpha conotoxins target nicotinic ligand gated channels. Mu conotoxins target voltage gated sodium channels while omega conotoxins target voltage gated calcium channels.

Currently, there are over 50 patents on different conotoxins. For example, patent number 6489298 filed in the USA on June 29, 2000 and accepted on December 3, 2002 refers to Contulakin-G analogue and the uses thereof. This alpha conotoxin is a glycosylated peptide and the claimed invention is directed to its use in therapeutics for anti-seizure, anti-inflammatory, anti-shock, anti-thrombus, hypotensive, analgesic, anti-psychotic, Parkinson's disease, gastrointestinal disorders, depressive states, cognitive dysfunction, anxiety, tardive dyskinesia, drug dependency, panic attack, mania, irritable bowel syndrome, diarrhoea, ulcers, gastrointestinal tumor, among others. Patent number 6465541 refers to another alpha conotoxin. It was issued in the USA on July 24, 2001 and the claimed invention is with regard to possible use in cardiovascular disorders, gastric motility disorders, urinary incontinence, nicotinic addiction, mood disorders and small cell lung carcinoma. Patent number W009954350A1 issued on October 28, 1999 is on novel omega conotoxin whose claimed invention relates to use in calcium channel blockade, analgesia, enhancement of opiate analgesia, treatment of schizophrenia, stimulant induced psychoses, hypertension, inflammation and diseases that may cause bronchoconstriction. Details regarding other patents on conotoxins are readily available in literature. The most common biological activities cited in these patents are analgesia, neurologic and psychiatric disorders, and neuromuscular blockade (muscle relaxants).

The first conotoxin approved by FDA in 2000 is ziconotide. It is administered by intrathecal route in patients with severe chronic pain. More conotoxin drugs are likely to come into the market. However, considering that many patents on conotoxins were filed more than 10 years ago, there is indication of possible problems in formulating them into stable dosage forms. Peptide drugs are generally unstable and difficult to synthesize in the laboratory. Extracting them from natural sources may be prohibitively expensive. There are generally suitable analgesics, antipsychotics and muscle relaxants which make it difficult to justify development of expensive alternatives with no obvious advantages. More important is the fact that peptides can only be administered parenterally since they are unstable when given orally. This is a great disadvantage in treatment of chronic illness since hospitalisation can only be for a limited period.

Editorial-in-Chief