Bioactive Marine Alkaloids

Abstract
The chapter deals with bioactive marine alkaloids. The chemistry and biological activities of pyridoacridines, pyrroloacridines, indoles, β-carbolines, pyrroles, isoquinolines, and tyrosine derived alkaloids have been discussed and reviewed.

1. Introduction
The alkaloids are generally defined as naturally occurring basic nitrogenous compounds. Majority of this class of compounds display biological activity. The reviewers\(^1\) of marine alkaloids have, therefore, included amino acids, purines, primidines and their nucleosides, peptides, nitrogenous marine toxins, guanidine etc. under marine alkaloids. The chemistry and biological activities of marine toxins, nucleosides and peptides have been dealt separately in Chapters 7, 8 and 10, respectively. The chemistry and biological activities of the bioactive marine alkaloids for convenience have been discussed and reviewed.

2. Pyridoacridine Alkaloids
Marine pyridoacridine alkaloids have been the subject of intense study due to their significant biological activities.\(^4\)\(^{13}\) Over 75 pyridoacridine alkaloids have been isolated and characterized from marine source and it is expected that more of these alkaloids will be isolated in future. Almost all known pyridoacridine alkaloids are reported to have significant cytotoxicity. The compounds of this group also display several specific biological properties, such as inhibition to topoisomerase II,\(^12\)\(^ {14}\) antiHIV activity,\(^15\) Ca\(^{2+}\) release activity,\(^16\) metal chelating properties\(^17\) and intercalation of DNA property.
Pyridoacridines have a common tetracyclic heteroaromatic parent-pyrido [4,3,2-m,n]acridine (1) system. They are distributed across several phyla of marine invertebrates which are an intriguing fact, and it needs further investigation. One possibility is that in the biosynthesis of these alkaloids probably symbiotic microbes are involved, but it has not yet been tested. Marine pyridoacridine alkaloids have been reviewed extensively.18-23

2.1 Occurrence and Chemical Properties

Pyridoacridines have been isolated from marine sponges, tunicates, anemone and molluscs which are often ornately decorated with bright colors and patterns. Tropical tunicates (ascidians) in particular are generally richly pigmented in colors which vary from yellow to deep red, orange, blue and purple. It is often found that pyridoacridines isolated from such tunicates are the pigments (zoochromes) responsible for their coloration. Pyridoacridines act as a pH indicator. The indicator properties is correlated with the presence of at least two basic pyridine like nitrogen and is probably associated with electronic perturbations of an extended chromophore with charge-transfer properties. Simple indicator properties are absent in the less basic iminoquinones, such as cytodytin-A (2) and diplamine (3). Alkaline solution of the free base generally appears orange or red, while in acidic solution they are green-blue to purple. Some quaternary ammonium alkaloids, like petrosamine (4), are deep blue or purple salts.

Pyridoacridines are generally obtained as microcrystalline solids with melting points above 300°C. They have also been isolated as hydrochloride salts. Few pyridoacridines are found to be optically active. The optical activity of these compounds is due to the presence of additional asymmetric side chain. The majority of pyridoacridine alkaloids have planar heterocyclic system.

Because of variability in oxidation states of the heterocyclic nucleus, pyridoacridines exhibit facile redox reactions. For example, the iminoquinone substructure (5) in many alkaloids is easily reduced by NaBH₄. Partially saturated nitrogen containing rings in pyridoacridines are easily aromatized by air oxidation (auto oxidation) upon storage or heating in solution. Although