Alkaloids of Anuran Skin: Antimicrobial Function?

Cyrus Macfoya, Douglas Danosus a, Raj Sandit a, Tappey H. Jonesb, H. Martin Garraffoc, Thomas F. Spande c, and John W. Dally c, *

a Biology Department, American University, Washington, D. C., USA
b Laboratory Chemistry, Virginia Military Institute, Lexington, Virginia 24450-0304, USA
c Laboratory of Bioorganic Chemistry, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, DHHS Bethesda, Maryland 20892-0820, USA. E-mail: jdaly@nih.gov

* Author for correspondence and reprint requests

Z. Naturforsch. 60c, 932–937 (2005); received May 24/July 5, 2005

A variety of alkaloids, most of which occur or are structurally related to alkaloids that occur in skin glands of dendrobatid poison frogs, were assayed for antimicrobial activity against the Gram-positive bacterium Bacillus subtilis, the Gram-negative bacterium Escherichia coli and the fungus Candida albicans. Certain pyrrolidines, piperidines and decahydroquinolines, perhydro-histrionicotoxin, and a synthetic pumiliotoxin were active against B. subtilis. Only 2-nonylpiperidine was active against E. coli. One pyrrolidine, two piperidines, two decahydroquinolines, and the synthetic pumiliotoxin were active against the fungus C. albicans. The results suggest that certain of the skin alkaloids of poison frogs, in addition to being noxious to predators, may also benefit the frog through protection against skin infections.

Key words: Alkaloids, Antibiotics, Antifungals

Introduction

A wide range of biologically active substances are present in skin of amphibians, and include peptides, biogenic amines, bufadienolides, tetrodotoxins, and lipophilic alkaloids (Daly, 1995; Daly et al., 1987). The peptides, amines and bufadienolides are produced by the amphibian, while most of the lipophilic alkaloids are derived unchanged from dietary sources (Daly, 2003). Many such substances in frog skin appear to serve in defense against predation, while others, in particular the peptides, have antimicrobial activity and serve in defense against skin infections. Indeed, a host of antibiotic peptides have been reported from frog skin (Bevins and Zasloff, 1990; Rinaldi, 2002). Antimicrobial activity also has been proposed for alkaloids (Habermehl and Preusser, 1969; Preusser et al., 1975). However, Gram-positive bacteria are present on skin of the European fire salamander (Bettin and Greven, 1986), a species with saminarine alkaloids in the skin. Frogs of certain genera of the families Dendrobatidae, Bufonidae, Mantellidae and Myobatrachidae are characterized by the presence of lipophilic skin alkaloids, which in most cases are sequestered into skin glands unchanged from alkaloid-containing arthropods (Daly, 2003). Most such alkaloids would be merely bitter and unpleasant to predators, but some are quite toxic, consonant with protection against predators and allowing for the bright, aposomatic coloration of the diurnal dendrobatid and mantellid poison frogs. Neither biologically active amines nor peptides, including antimicrobial peptides, have been reported for alkaloid-containing dendrobatid (Ersparser et al., 1986; Rosegghini et al., 1986) or, apparently, mantellid frogs. The bufonid toads (Melanophryniscus) have, in addition to skin alkaloids (Garraffo et al., 1993), both amines (Cei et al., 1968) and bufadienolide-like steroids (Flier et al., 1980). Apparently, no peptides have been detected. The myobatrachid frogs (Pseudophryne) do have amines and peptides (Roseghini et al., 1976; Simmaco et al., 1990), in addition to the skin alkaloids (Daly et al., 1990; Ersparer et al., 1985; Smith et al., 2002). Whether or not the skin alkaloids of the poison frogs could serve as antimicrobials and, thus, in lieu of peptides, protect such frogs against infection needed to be investigated. A select group of available compounds, related to ten of the over twenty structural alkaloid classes found in frog skin, were assayed against two bacteria and a fungus. Certain of these showed antibacterial and/or antifungal activity.