International Journal of Trend in Scientific Research and Development (IJTSRD)
Volume 6 Issue 5, July-August 2022 Available Online: www.ijtsrd.com e-ISSN: 2456 – 6470

Review on Chemistry of Poisons in Amphibian SMN

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ABSTRACT

Harms are normal in nature, where they frequently serve the organic entity in substance safeguard. Such toxins either are created a new or are sequestered from dietary sources or advantageous creatures. Among vertebrates, amphibians are prominent for the great many toxic specialists that are contained in granular skin organs. These mixtures incorporate amines, peptides, proteins, steroids, and both water-solvent and lipid-dissolvable alkaloids. Except for the alkaloids, most appear to be created de riovo by the land and water proficient. The skin of creatures of land and water contains numerous underlying classes of alkaloids already unhnown in nature. These incorporate the batra-chotoxins, which have as of late been found to likewise happen in skin and quills of a bird, the histrionicotoxins, the gephyrotoxins, the decahydroquinolines, the pumiliotoxins and homopumiliotoxins, epibatidine, and the samandarines. Some land and water proficient skin alkaloids are plainly sequestered from the eating routine, which comprises predominantly of little arthropods. These incorporate pyrrolizidine and indolizidine alkaloids from insects, tricyclic coccinellines from creepy crawlies, and pyrrolizidine oximes, probably from millipedes. The wellsprings of different alkaloids in land and water proficient skin, including the batrachotoxins, the decahydroquinolines, the histrionicotoxins, the pumiliotoxins, and epibatidine, are obscure. While it is conceivable that these are created again or by cooperative microorganisms, it shows up additional possible that they are sequestered by the creatures of land and water from at this point obscure dietary sources.

How to cite this paper: Lalit Pardhe | Santosh Waghmare | Dr. Hemant Kamble "Review on Chemistry of Poisons in Amphibian SMN" Published in International Journal of Trend in Scientific Research and Development (ijtsrd), ISSN: 2456-6470, Volume-6 | Issue-5, August 2022, pp.479-484, URL: www.ijtsrd.com/papers/ijtsrd50503.pdf

IJTSRD50503

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Toxic substances happen all through nature and are standard ticularly notable from plants, where they probably serve in synthetic guard against herbivores. Toxic substances can likewise act as toxins, which are brought into casualties by coelenterates; molluscs; different arthropods, including bugs, insects, and scorpions; gila beasts; and snakes, by a chomp or sting, or as poisons, for example, those delivered by microbes, dinoflagellates, and different microorganisms. Instances of toxins of plant beginning envelop a large number of substances, including numerous alkaloids; different terpenes and steroids, some of which happen as saponins; and strange optional metabolites, for example, the trichothecenes, pyrethroids, and dianthrones (1, 2). One more extensive variety of probably guarded substances happen in mama rine spineless creatures, including steroid and terpenoid sapogenins, tetrodotoxins, an assortment of polyether poisons, and alkaloids (3, 4). Harms likewise happen in earthly spineless creatures and vertebrates, where they act as compound safeguards by bugs and different arthropods (5, 6), by fish (7), and by creatures of land and water (8). As of late, a harmful alkaloid was portrayed from the skin and quills of a bird (9), where it presents some insurance against predation by people. Substance safeguards can be coordinated either against hunters or against microorganisms. The current paper is worried about the synthetic nature, beginning, and capability of toxins present in land and water proficient skin. A large number of the substances in creatures of land and water could all the more likely be classified as "toxic" as opposed to "harmful," despite the fact that at sufficiently high measurements these mixtures would be harms.

Frogs and lizards have been considered harmful creatures for quite a long time and without a doubt most of creatures of land and water have now been found to contain toxic and once in a while noxious

substances in their skin discharges (8). The sort of organically dynamic substance found in creatures of land and water seems to have phylo-hereditary importance. Hence, indole alkylamines are commonly present in undeniable levels in bufonid frogs of the sort Bufo, phenolic amines in leptodactylid frogs, vasoactive peptides in an extraordinary assortment in hylid frogs, especially of class Phylomedusa (10), and bufadienolides in parotoid organs and skins of bufonid amphibians of the variety Bufo as well as in skin of related bufonid genera Atelopus and likely Dendrophryniscus and Melanophryniscus (11). The water-solvent alkaloid tetrodo-poison happens in newts of the family Salamandridae, amphibians of the brachycephalid variety Brachycephalus and the bufonid class Atelopus, and presently in one frog types of the dendrobatid sort Colostethus (12). Lipophilic alkaloids have been tracked down just in lizards of the salamandrid sort Salamandra,- in frogs of the dendrobatid genera Phyllobates, Dendrobates, Epipe-dobates, and Minyobates, the mantellid variety Mantella and the myobatrachid family Pseudophryne, and in amphibians of the bufonid class Melanophryniscus. In excess of 70 different genera from 11 land and water proficient families don't have skin alkaloids. The dissemination of different lipophilic alkaloids in creatures of land and water is given in Table 1 and designs are displayed in Fig. 1.

The beginning and capability of toxins and harmful substances found in creatures of land and water are just to some degree known. The elevated degrees of amines, including such notable biogenic amines as serotonin, receptor, and tyramine and subsidiaries thereof, tracked down in skin of different frogs and frogs (8), without a doubt are combined by the land and water proficient itself. They are put away in granular skin organs for emission upon assault by a hunter, whereupon their notable aggravation properties on buccal tissue would work well for in compound protection. The elevated degrees of vasoactive peptides, for example, bradykinin, sauvagine, physaelaemin, caer-ulein, bombesin, dermorphins, and so on, probably likewise serve in protection against hunters, albeit many, including the mama gainins, have high action as antimicrobials (13) and consequently could likewise act as a substance guard against microorgan-isms. Skin emissions from one hylid frog are utilized in "hunting enchantment" people customs by Amazonian Indians; such discharges contain numerous vasoactive peptides (10) and a peptide, adeno-regulin, that can influence focal adenosine receptors (14). The peptides of frog skin are blended by the land and water proficient and for sure extra peptides are being reasoned in light of cDNAs for their antecedents (15). The different hemolytic proteins of specific creatures of land and water are unquestionably of endogenous beginning. The steroidal bufadienolides seem, by all accounts, to be combined from cho-lesterol by the bufonid amphibians (16). It has been proposed that fundamentally comparable and harmful lucibufagins of fireflies may additionally be created by the bug from dietary cholesterol (17).

Table 1. Occurrence of lipid-soluble alkaloids in amphibians

Family and genus	SAM	BTX	HTX	PTX-A class			DHQ	Izidine alkaloid				Epi	Pseudophry
				PTX	aPTX	hPTX		3,5-P	3,5-I	5,8-I	1,4-Q		
Salamandridae													
Salamandra	+	–	–	–	–	–	–	–	–	–	–	–	–
Dendrobatidae													
Phyllobates	–	+	+	+	–	–	+	–	+	–	–	–	–
Dendrobates	–	–	+	+	+	+	+	+	+	+	+	–	–
Epipedobates	–	–	+	+	+	–	+	–	–	+	+	+	–
Minyobates	–	–	–	+	+	–	+	–	–	+	+	–	–
Mantellidae													
Mantella	–	–	–	+	+	+	+	+	+	+	+	–	–
Myobatrachidae													
Pseudophryne	–	–	–	+	+	–	–	–	–	–	–	–	+
Bufonidae													
Melanophryniscus	–	–	–	+	+	+	+	+	+	+	+	–	–

SAM, samandarines; BTX, batrachotoxins; HTX, histrionicotoxins; PTX, pumiliotoxins; aPTX, allopumiliotoxins; hPTX, homopumiliotoxins; DHQ, 2,5-disubstituted decahydroquinolines; 3,5-P, 3,5-disubstituted pyrrolizidines; 3,5-I and 5,8-I, disubstituted indolizidines; 1,4-Q, 1,4-disubstituted quinolizidines; Epi, epibatidine; Pseudophry, pseudophrynamines. With the exception of 3,5-P and 3,5-I, these alkaloids are not known to occur in arthropods (see text). Histrionicotoxins may occur in *Minyobates* and *Mantella*, but the evidence is not conclusive.

Phyllobates species from Panama and Costa Rica contain However, harmful cardenolides in ruler butterflies seem to either just follow measures of batrachotoxin or for certain be sequestered from milkweed plants by the hatchlings (18). The populations of Phyllobates lugubris no perceptible sums. compound protective qualities of the profoundly harmful bufadienolides Batrachotoxins are exceptional steroidal alkaloids, which were are because of impacts on layer Na+/K+-ATPase.unknown somewhere else in nature until the new disclosure of The beginning of tetrodotoxins in creatures of land and water and higher or-homobatrachotoxin at low levels in skin

and plumes of a ganisms stays puzzling. Hence, puffer fish brought up in hatch-Papua New Guinean bird of the class Pitohui (9). In the eries don't contain tetrodotoxin (19), and probable biosynthetic dendrobatid frogs, three significant alkaloids are available — to be specific, forerunners are not integrated into tetrodotoxin with newts batrachotoxin, homobatrachotoxin, and a substantially less harmful (20). Taking care of nontoxic puffer fish with tetrodotoxin does not possible forerunner, batrachotoxinin A. The last option, when taken care of to bring about sequestration, yet taking care of harmful ovaries from wild nontoxic hostage raised P. bicolor utilizing tidied natural product flies, is puffer fish does (19). A bacterial beginning for tetrodotoxin has accumulated into skin organs however isn't changed over completely to the more been proposed, yet such a source neglects to make sense of the reality that toxic esters batrachotoxin and homobatrachotoxin (25). Sanctum one Central American types of amphibian of the class Atelopus drobatid frogs of another variety wouldn't eat the batracho-contains predominantly tetrodotoxin; another Central American spe-toxinin-tidied organic product flies. Batrachotoxins depolarize nerve and cies contains mostly chiriquitoxin, which is a remarkable but muscle by unambiguous opening of sodium channels; the sodium basically comparative poison; but another contains mainly channels of the Phyllobates species are heartless toward the activity zetekitoxin, which is another exceptional, most likely structurally of batrachotoxin (22). related poison (see ref. 12). Chiriquitoxin, while related Further assessment of concentrates of dendrobatid frogs over construction to tetrodotoxin, contrasts in the carbon skeleton (21).nearly thirty years prompted the portrayal of almost 300 The substance cautious ascribes of tetrodotoxin are expected to alkaloids, addressing about 18 primary classes (see ref. 23). bar of voltage-subordinate sodium channels and hence Several classes stay obscure in nature besides in frog skin discontinuance of neuronal and muscle activity.(see Table 1), and their starting point stays dark considering The beginning of the lipophilic alkaloids in dendrobatid frogs, relatively late tracking down that frogs of the dendrobatid genera caused by the perception that the frogs, which are used Dendrobates and Epipedobates, as Phyllobates, don't have by Colombian Indians to harm blow darts, when raised in skin alkaloids when brought up in imprisonment (26). The dissemination of imprisonment contain none of the poisonous batrachotoxins present in the different alkaloids of creatures of land and water is relevant to any spec-wild-got frogs (22), still needs to be researched. In contrast, ulation with regards to their starting point (see Table 1).the harmful samandarines from fire lizards are available in The purported pumiliotoxin A class of "dendrobatid alka-the skin organs of the lizard through numerous ages of loids" is at this point known exclusively in nature from frog/frog skin. The sustain in bondage (G. Habermehl, individual communication).class comprises of alkaloids with either an indolizidine (pumilio-The different lipophilic alkaloids of creatures of land and water all have marked toxins and allopumiliotoxins) or a quinolizidine (homopu-action on particle channels and subsequently through such impacts would miliotoxins) ring, for each situation with a variable alkylidene side serve really as synthetic guards, despite the fact that some have chain. The pumiliotoxin A class happens in skin of all of the somewhat low toxicity. amphibian genera that contain lipophilic alkaloids with The batrachotoxins were the five star of special alkaloids exception of the fire lizards, which contain just saman-to be portrayed from skin concentrates of frogs of the familydarines. Despite a wide dissemination in the alkaloid-Dendrobatidae (see ref. 23 for a survey of land and water proficient alka-containing frogs, there are species as well as populaces of frogs loids). Batrachotoxin was identified in just five species of that have no pumiliotoxin A class alkaloids or just follow dendrobatid frogs and these frogs were then named the amounts. Individuals from pumiliotoxin A class are dynamic poisons monophyletic family Phyllobates, situated to a limited extent on the presence with consequences for sodium and maybe calcium channels and of batrachotoxins (24). Notwithstanding, levels of batrachotoxins along these lines, would work well for in protection against hunters.vary extensively, with the Colombian Phyllobates terribilis Histrionicotoxins address one more significant class of dendro-containing almost 1 mg of batrachotoxins per frog, while the batid alkaloids. They contain a novel spiropiperidine ring fairly more modest Phyllobates bicolor and Phyllobates aurotae-framework and side chains with acetylenic, olefinic, and allenic nia, likewise from the tropical jungles of the Pacific versant in gatherings. Histrionicotoxins stay known in nature just from Colombia, contain 10-overlap lower skin levels (8). The two dendrobatid frogs of the general Phyllobates, Dendrobates, and Epipedobates. They are presumably missing in the minuscule dendrobatid Decahydroquinolines happen in skin of all the frog/amphibian genera frogs of the family Minyobates. Histrionicotoxins were identified that have lipophilic alkaloids with the sole special case of the in a solitary Madagascan frog of the mantellid sort Mantella Australian myobatrachid frogs of the family Pseudophryne that (27) got through the pet exchange however have not been recognized contain just (al1o)pumiliotoxins and a progression of indole alka-in any concentrates of a few Mantella animal categories gathered in Mada-loids one of a kind in nature to this family of frogs — to be specific, the gascar (28).

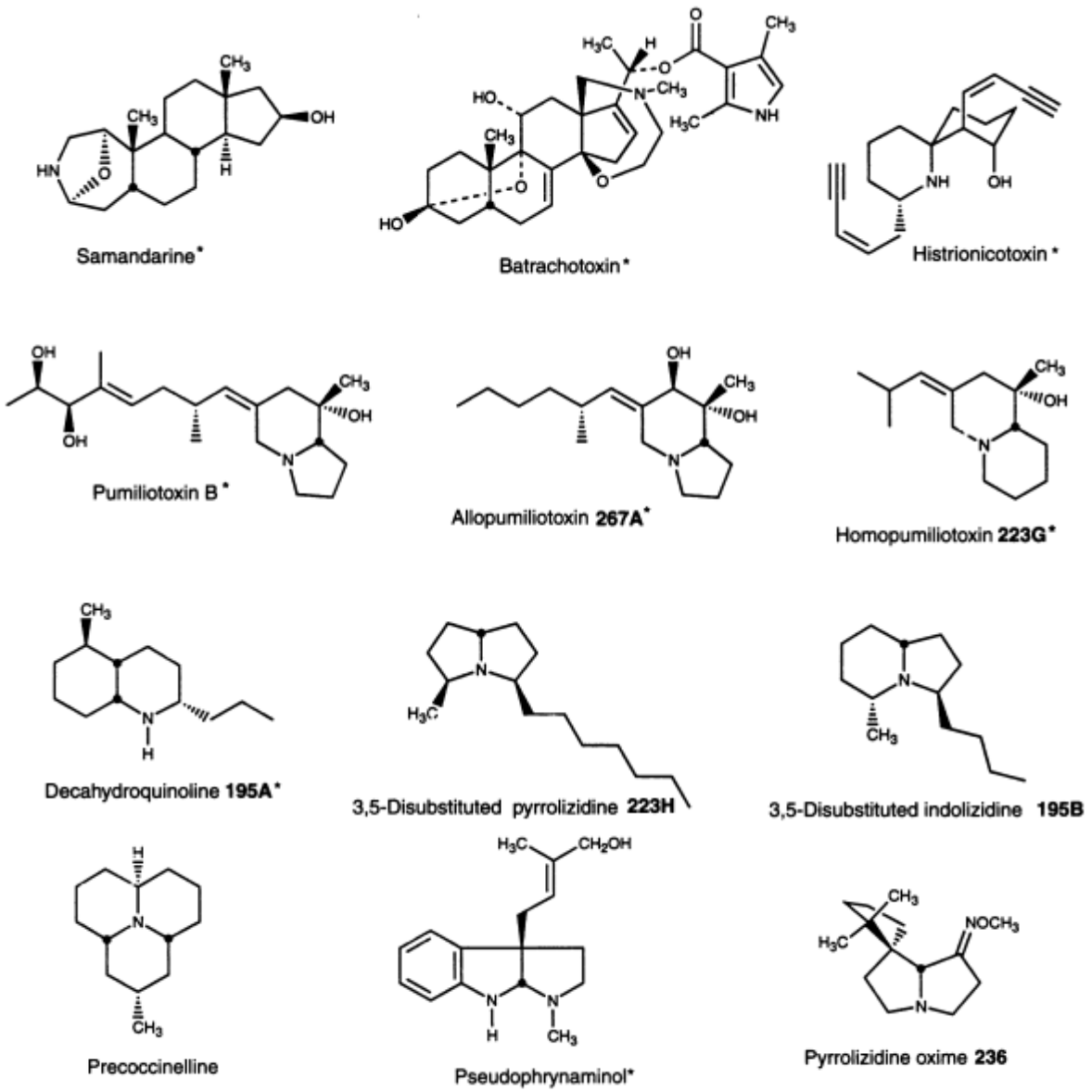

FIG. 1. Structures of lipophilic amphibian alkaloids. Alkaloids indicated by asterisks represent structural classes that have not been detected in nature except in amphibians and, in the case of batrachotoxins, in one species of bird (9).

Histrionicotoxins don't happen in that frame of mind of the pseudophrynamines (29). above dendrobatid frog genera or in all populaces of a single A series of basic bicyclic alkaloids could be considered to species (8). Their event inside populaces of a species make up a significant "izidine" class of alkaloids in the dendrobatid on a solitary little island can differ from undeniable levels to none. and different frogs. These incorporate the 3,5-disubstituted pyrroli-The decahydroquinolines are the third significant class of cave zidines, the 3,5-disubstituted and 5,8-disubstituted indoli-drobatid alkaloids actually known exclusively from frog/amphibian skin. zidines, and the 1,4-disubstituted quinolizidines. The 3,5-disubstituted pyrrolizidines and the 3,5-disubstituted indoliz-idines are not exceptional to frogs, having been accounted for from subterranean insects (see ref. 6). Subterranean insects in this manner address an expected dietary hotspot for such alkaloids in dendrobatid and different frogs. To be sure, taking care of examinations with subterranean insects of the class Monomorium that contain a 3,5-disubstituted indolizidine and a 2,5-disubstituted pyrro-lidine brought about an exceptional particular gathering, into the skin of the dendrobatid frog Dendrobates auratus, of the indolizidine yet not of the pyrrolidine (25). It ought to be noticed that some dendrobatid frogs in all actuality do contain critical levels in skin of such 2,5-disubstituted pyrrolidines and of 2,6-disubstituted piperidines, neither of which seems, by all accounts, to be sequestered into skin, by D. auratus. The 5,8-disubstituted indolizidines and 1,4-disubstituted quinolizidines stay at this point obscure in nature besides from frog/amphibian skin (Table 1).

There are likewise various alkaloids portrayed from skin concentrates of dendrobatid frogs that have a somewhat restricted dispersion inside the numerous species that have been inspected and are at this point known exclusively from frog skin. The tricyclic gephyrotoxins happen alongside the more generally disseminated histrionicotoxins in a couple of animal categories and populaces of dendrobatid frogs (8).

The tricyclic cyclopenta[b]quinoli-zidines happen in just a single animal types, a little Colombian frog Minyobates bombetes (30). The strong nicotinic pain relieving epibatidine happens just in four dendrobatid types of the variety Epipedobates tracked down in Ecuador (31).

Two classes of dendrobatid alkaloids have likely dietary sources. The first are the pyrrolizidine oximes (32), whose carbon skeleton is indistinguishable from that of nitropolyzonamine, an alkaloid from a little millipede (33). To be sure, raising the dendrobatid frog D. auratus in Panama on leaf-litter arthro-cases, assembled week by week, brought about skin levels of the pyrroli-zidine oxime 236 significantly higher than levels in wild-gotten frogs from the leaf-litter site (34). The second are the tricyclic coccinelline alkaloids that have been tracked down in a few frogs/frogs. The coccinellines happen as protective substances in different little creepy crawlies (see ref. 6). In this way, bugs address a potential dietary hotspot for coccinelline-class alkaloids in frog/amphibian skin. For sure, the creepy crawly alkaloid precoccinelline is a critical alkaloid in the skin of D. auratus brought up in Panama on leaf-litter arthropods (34). Different alkaloids that were tracked down in skin of D. auratus raised on leaf-litter arthropods are three other tricyclic alkaloids, maybe of the coccinelline class however of obscure construction, two 1,4-disubstituted quinolizidines, a gephyrotoxin, a decahydroquinoline, and a few histrion-icotoxins. Except for the pyrrolizidine oxime 236, skin levels of the different alkaloids in the hostage raised frogs were low contrasted with levels of alkaloids in wild-gotten frogs from the leaf-litter assortment site or from the parental supply of D. auratus on a close by island (34). Individual variety in wild-gotten frogs seems critical, which convolutes the examinations. Notwithstanding, the absence of any pumiliotoxins and the generally low levels or nonappearance of decahydroquinolines and histrionicotoxins in the hostage raised frogs recommends that dietary hotspots for these alkaloids have been missed in the worldview utilizing huge channels from leaf filter .In summary, poisons used in chemical defense are wide-spread in nature. In amphibians, the defensive substances seem to be elaborated by the amphibian in the case of amines, peptides, proteins, bufadienolides, and the salamander alka- loids of the samandarine class. For the tetrodotoxin class of water-soluble alkaloids, the origin is unclear, but symbiotic bacteria have been suggested for marine organisms (4). For the dendrobatid genera Phyllobates, Dendrobates, and Epipe- dobates, which in the wild contain skin alkaloids, have highly productive frameworks for collecting specifically into skin different dietary alkaloids (25, 34). An organic framework for sequestration of alkaloids for synthetic safeguard finds prece-dence in the exchange of pyrrolizidine alkaloids from plants through aphids to ladybug scarabs (35). Collection of cantharidins in muscle of ranid frogs in the wake of benefiting from bugs has been recorded (36). Frogs of the dendrobatid class Colostethus, which in the wild don't contain skin alkaloids, don't aggregate dietary alkaloids (25).

The recommendation that all alkaloids tracked down in skin organs of dendrobatid frogs and utilized in substance guard against pred-ators have a dietary beginning prompts many inquiries. In the first place, the profile of alkaloids has been viewed in many cases as normal for an animal groups or a populace. In this way, either the frameworks liable for sequestration of alkaloids vary in selectivity among various species as well as populaces of dendrobatid frogs or the little arthropod fauna introducing itself and utilized as an eating routine by various species or potentially populaces shifts even inside a little island. The last option shows up more probable. It was noticed that the dendrobatid frogs brought on leaf litter up in Panama imparted more alkaloids to a populace of D. auratus from the leaf-litter site than they did with the parental populace from a close by island (34). The subsequent significant inquiry concerns what little bugs or different arthropods contain such poisonous as well as unpalatable alkaloids as the batra-chotoxins, the pumiliotoxins, and the histrionicotoxins, the decahydroquinolines, the 5,8-disubstituted indolizidines, the 1,4-disubstituted quinolizidines, and epibatidine. It is comment capable that such little, apparently tacky arthropods stand out of scientists. Whether frogs purpose on sequestering guarded alkaloids search out such prey is un-known. As to the frogs/amphibians from the Madagascan family Mantellidae, the Australian family Myobatrachidae and the South American sort Melanophryniscus of the family Bufonidae, which additionally contain a large number of the dendrobatid alka-loids, it is obscure whether sequestering frameworks are available or even whether hostage raised frogs will need skin alkaloids. In the event that such frameworks are available, it is momentous from a developmental outlook that such irrelevant heredities of amphibians/frogs have freely evolved frameworks for sequestering alkaloids into skin organs from an eating routine of little, probably poisonous bugs for use by the frog/frog in substance protection.

REFERENCES

[1] Whittaker, R. H. & Feeny, P. P. (1971) Science 171, 757-770.

[2] Balandrin, M. F., Klocke, J. A., Wurtele, E. S. & Bollinger, W. H. (1985) Science 228, 1154-1160.

[3] Scheuer, P. J. (1990) Science 248, 173-177.

[4] Yasumoto, T. & Murata, M. (1993) Chem. Rev. 93, 1897-1909.

[5] Eisner, T. & Meinwald, J. (1966) Science 153, 1341-1350.

[6] Jones, T. H. & Blum, M. S. (1983) Alkaloids: Chemical and Biological Perspectives (Wiley, New York), Vol. 1, pp. 33-84.

[7] Tachibana, K. (1988) Bioorg. Mar. Chem. 2, 124-145.

[8] Daly, J. W., Myers, C. W. & Whittaker, N. (1987) Toxicon 25, 1023-1095.

[9] Dumbacher, J. P., Beehler, B. M., Spande, T. F., Garraffo, H. M. & Daly, J. W. (1992) Science 258, 799-801.

[10] Erspamer, V., Melchiorri, P., Erspamer, G. F., Montecucchi, P. C. & De Castiglione, R. (1985) Peptides 6, 7-12.

[11] Flier, J., Edwards, M. W., Daly, J. W. & Myers, C. W. (1980) Science 208, 503-505.

[12] Daly, J. W., Gusovsky, F., Myers, C. W., Yotsu-Yamashita, M. & Yasumoto, T. (1994) Toxicon 32, 279-285.

[13] Bevins, C. L. & Zasloff, M. (1990) Annu. Rev. Biochem. 59, 395-414.

[14] Daly, J. W., Caceres, J., Moni, R. W., Gusovsky, F., Moos, M., Jr., Seamon, K. B., Milton, K. & Myers, C. W. (1992) Proc. Natl. Acad. Sci. USA 89, 10960-10963.

[15] Richter, K., Egger, R., Negri, L., Corsi, R., Severini, C. & Kreil, G. (1990) Proc. Natl. Acad. Sci. USA 87, 4836-4839.

[16] Porto, A. M. & Gros, E. (1971) Experientia 27, 506.

[17] Eisner, T., Wiemer, D. F., Haynes, L. W. & Meinwald, J. (1978) Proc. Natl. Acad. Sci. USA 75, 905-908. 4

[18] Brower, L. P., van Zandt Brower, J. & Corvino, J. M. (1967) Proc. Natl. Acad. Sci. USA 57, 893-898.

[19] Matsui, T., Hamada, S. & Konosu, S. (1981) Bull. Jpn. Soc. Sci. Fish. 47, 535-537.

[20] Shimizu, Y. & Kobayashi, M. (1983) Chem. Pharm. Bull. 31, 3625-3631.

[21] Yotsu, M., Yasumoto, T., Kim, Y. H., Naoki, H. & Kao, C. Y. (1990) Tetrahedron Lett. 31, 3187-3190. 22. Daly, J. W., Myers, C. W., Warnick, J. E. & Albuquerque, E. X. (1980) Science 208, 1383-1385.

[22] Daly, J. W., Garraffo, H. M. & Spande, T. F. (1993) in The Alkaloids, ed. Cordell, G. A. (Academic, San Diego), Vol. 43, Chap. 3, pp. 185-288.

[23] Myers, C. W., Daly, J. W. & Malkin, B. (1978) Bull. Am. Mus. Nat. Hist. 161, 307-365.

[24] Daly, J. W., Secunda, S. I., Garraffo, H. M., Spande, T. F., Wisnieski, A. & Cover, J. F., Jr. (1994) Toxicon 32, 657-663.

[25] Daly, J. W., Secunda, S. I., Garraffo, H. M., Spande, T. F., Wisnieski, A., Nishihira, C. & Cover, J. F., Jr. (1992) Toxicon 30, 887-898.

[26] Daly, J. W., Highet, R J. & Myers, C. W. (1984) Toxicon 22, 905-919.

[27] Garraffo, H. M., Caceres, J., Daly, J. W., Spande, T. F., Andriamaharavo, N. R. & Andriantsiferana, M. (1993) J. Nat. Prod. 56, 1016-1038.

[28] Daly, J. W., Garraffo, H. M., Pannell, L. K & Spande, T. F. (1990) J. Nat. Prod. 53, 407-421.

[29] Spande, T. F., Garraffo, H. M., Yeh, H. J. C., Pu, Q. -L., Pannell, L. K. & Daly, J. W. (1992) J. Nat. Prod. 55, 707-722.

[30] Spande, T. F., Garraffo, H. M., Edwards, M. W., Yeh, H. J. C., Pannell, L. & Daly, J. W. (1993) J. Am. Chem. Soc. 114, 3475- 3478.

[31] Tokuyama, T., Daly, J. W., Garraffo, H. M. & Spande, T. F. (1992) Tetrahedron 48, 4247-4258.

[32] Meinwald, J., Smolanoff, J., McPhail, A. T., Miller, R. W., Eisner, T. & Hicks, K. (1975) Tetrahedron Lea. 2367-2370.

[33] Daly, J. W., Garraffo, H. M., Spande, T. F., Jaramillo, C. & Rand, A. S. (1994) J. Chem. Ecol. 4, 943-955. 35. Witte, L., Ehmke, A. & Hartmann, T. (1990) Natunvissenschaften 77, 540-543.

[34] Eisner, T., Conner, J., Carrel, J. E., McCormick, J. P., Slagle, A. J., Gans, C. & O'Reilly, J. C. (1990) Chemoecology 1, 57-62.