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# Bufo toxins: A boon or bane?

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## Abstract
Parotid glands of toads are not for the secretion of saliva. However they rather plays a vital role to keep them safe from the hunting predators. The secretion is basically a milky color toxin which provokes neurological, haematological, cardiotoxic etc. signs in intoxicated animals and can even be fatal. The so called deadliest toxin has been widely used in traditional Chinese therapy for a number of ailments. Recent research has proved the toxin posses cardiotonic, analgesic, sedative, anti-tumour and antimicrobial activity.

**Keywords:** Bufo toxins, boon, neurological, haematological

## Introduction
In amphibians, secretion from skin plays a vital role in maintaining physiological functions of the skin and also helps to get rid of predators as a defense mechanism [1]. When threatened parotid glands of toad belonging to genus *Bufo*, secretes a toxic steroid lactones, Bufotoxin commonly known for its life threatening action. Pharmacologically these milky color fluid is neurotoxic, hemotoxic, or cardiotoxic to mention a few [2]. The active ingredients in bufotoxin are 5-MeO-DMT, bufagins, bufalin, bufotalin, bufotenin, bufothionine, epinephrine, norepinephrine, and serotonin etc. The parotid glands actually secrete a compound called bufonin, which is a weaker poison but as soon as it comes in contact with air it gets oxidized a to form a bufadienolide called Bufotalin [$C_{34}H_{46}O_{10}$] which imparts a milky appearance to the toad secretions [3]. All species of Bufo toad secretes these substances however the quantity of individual ingredient varies depending on the species of the *Bufo* genus. For instance, the concentration of bufadienolides (digitaloid) is highest amongst *Bufo marinus and Bufo viridis* [4]. This review briefly describes the life threatening toxicity as well as its therapeutic application activity of toad toxins belonging to genus *Bufo*.

## Chemistry
Secretion from toad is achieved from both glandular and mucous gland. Secretion from the former is more toxic than the latter. Grandular gland secretion contains chemicals that can be broadly classified into Biogenic amines, Bufadienolides, alkaloids, steroids, peptides and proteins [5]. More than 80 types of Bufadienolides (other than peptides and amines) are found in the secretion (glandular) of toads along with Bufotoxin, Bufotenine and Bufagin [6-8]. Among bufadienolides the most common are Bufalin, Bufogenin, Bufotalin, Cinobufagin, Marinobufagin, Resibufagin bufadienolides. Serotonin, Histamine and Bradykinin are some of the common amines isolated from the toad skin [9].

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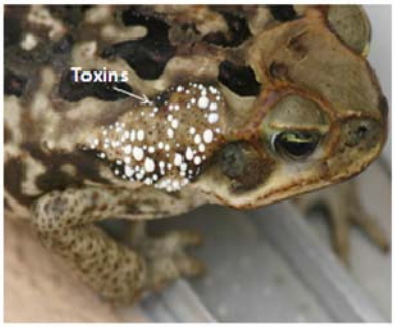

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**Signs of poisoning**

Since dogs and cats are frequent victim of bufotoxin poisoning so the clinical symptoms described here restricts to only these two species. Signs of intoxication may begin immediately after exposure or may be exhibited after 15 minutes. The intoxicated animals exhibits neurological signs like tremor, convulsion and ataxia with brick red mucous membrane, rapid respiration and vomition. ECG of affected dog revealed sinus arrthymia (mostly sinus tachycardia}. Experimentally tested dogs when fed with oral Bufo marinus toxin also revealed ventricular fibrillation. Although few cases of hypokelemia has been reported but on a large scale affected dogs showed hyperkelemia and this can be correlated to the blockade of sodium-potassium ATPase in the heart which results in accumulation of excess potassium in the serum [10].

**Line of treatment**

Most of the cases recover with usual treatment of poisoning such as oral lavage, fluid therapy, activated charcoal and sometimes propanolol and lidocaine to treat cardiac arrthymia During the past decades, the Galenical preparation, Chan su (dried toad venom) was tremendously used as an aphrodisiac however that trend could not be continued for long as cases of four men using the toxin as an aphrodisiac was found to be dead soon after its use. The report from medical test astonished the investigating officer and everyone present there. As per reports the cause of death was digoxin toxicity which was never prescribed for them. After proper analaysis the level of Bufotoxin was quite high in the victim's tissue which was the culprit for cardiac arrhythmia, action similar to cardiac glycosides toxicity. It was then inferred that if the toxicity signs resembled the toxicity of digitatis than the same substance in lower dose could be used to mimic the action of digitalis [11]. Bufotoxin has occupied a wide space in tradition Chinese therapy as it is still extensively used as an anesthetic (topical), extracted from Chinese toad Bufo bufo gargarizans Gantor (or Bufo melanostictus).

**Pharmacological implications**

**Cardiotonic activity**

Bufogenings shows akin action to cardiac glycosides. They inhibit sodium-potassium ATPase in the cardiac myocytes similar to digitalis. Blocking of the ATPase leads to drastic increase of sodium ion within the cardiac myocyte which subsequently stimulates opening of the sodium calcium exchange pump. This mechanism leads to uncontrolled accumulation of calcium in the cells (sodium is expelled out in exchange of calcium). The entire process ends up in cardiac arrhythmia. Apart, bufogenin also exerts local anaesthetic action by blocking sodium channel.

These compound can be used to enhance tonicity of the cardiac muscles just like digitalis. Such compounds can also be used in treatment of hypertension and congestive heart failure [12].

**Analgesic and sedative action**

Experimentally bufalin increases hepatic-blood circulation, which decreases amount of stagnating blood thereby decreasing pain. As analgesic, aspirin (prescribed for pain of unknown orign) and morphine (for neurological pain) are commonly used worldwide. However the miraculous benefit of aspirin as well of morphine comes with certain side effects. In such scenario, bufalin can be of potential use in pain-relief, anxiety diminishing and sleep induction. It can also be use for the treatment of rheumatic arthritis instead of aspirin. Bufagin as a local anesthetic is 30 to 60 times more potent than cocaine and the duration of analgesia is prolonged by causing very slow release of Acetylcholine (Ach) from the nerve ending [13]

**Antitumour action**

In vitro studies revealed certain bufadienolides exhits anti neoplastic activity. Bufalin have been found to exert anti-cancerous properties on leukemia cells lines by halting the growth and initiating apoptosis. Apoptosis in human-leukemia cells is due to altering expression of apoptotic genes c-myc and bcl-2. This action resembles the mechanism of topoisomerase inhibitors. Dried toad skin is tremendously used to prepare Cinobufacini (Huachansu), which has been proved as an effective therapy for treating various cancers in china. Cinobufacini works by a numbers of mechanism viz. apoptosis induction, inhibition of angiogenesis specially in tumour cells and distruption of cell cycle [14].

**Antimicrobial activity**

Almost all living creatures by birth or by virtue of evolution develops an effective defence system to fight against the disease causing organisms. Toad toxin in not excluded in this scenario, the secretion from the skin glands keep microbes especially bacteria away from the toad body as a defense mechanism. The secreted toxins helps toads to inhabit in environment dominated by pathogenic microbes which otherwise cause diseases like Red Leg Syndrome and Salmonellosis. The compound, telocinobufagin (a bufadienolides) has been found to inhibit growth of Staphylococcus aureus and Escherichia coli in vitro. Most of the antimicrobial compound are protein in nature and are characterised by their relatively small size (20-46 amino acid residues), basic nature (lysine- or arginine-rich), and amphipathic properties. Probably the first antibiotic proteins isolated from the toad secretions are Bombinans and BLPs (bombinin-like proteins) [15].

**Conclusion**

Toad toxin although posses harmful or sometimes even life threatening effect on the body of the victim it has acted as a very good and effective source of drug from time immorial. This can be inferred to the well known early Galenical preparation, Chang Su. The dried skin components has been successfully used in the treatment as analgesic, painkiller, sedative, antimicrobial, cardiotonic and antitumour activity. These creatures have been found to be of potential significance in the therapy however the rapid destruction of their habitats does raises question to supply these compounds in the same flow. In fact there could be possibility of new emerging diseases in the absence of such crucial creature in the ecosystem.

| Common bufadienolides isolated from skin of toad | |
|---|---|
| Arertobufagin | Resibufogenin |
| Arawbufagin | Cinobufotalitoxin |
| Hemisuberate | Desacetylcinobufotalin |
| Arenobufotoxin | Gamabufotalin |
| Argentinogenin | Gamabufotalitoxin |
| Bufalin | Hellebrigain |
| Bufalin | Hdlebritoxin |
| Hemisuberate | Marinobufagin |
| Bufalitoxin | Marinoic Acid |
| Cinobufotalin | Marinosin |
| Bufotalin | Resibufagin |
| Bufotalinin | Resibufaginol |
| Bufotalone | Vulgarobufotoxin |
| Cinobufagin | Tdocinobufagin |
| Cinobufagin | Resibufotoxin |
| Cinobufagino | Cinobufotoxin |
| Reference: Steyn and Heerden 1998 | |

**References**


1. Sakate M, Lucas D. Toad envenoming in dogs: effects and treatment. J Venom Anim Toxins. 2000; 6(1):52-62.
2. Noble GK. The Biology of the Amphibia, 1 st Ed. (New York: McGraw-Hill Book Co.). 1931.
3. Brubacher JR. Efficacy of digoxin specific Fab fragments (Digibind) in the treatment of toad venom poisoning. International Immunopharmacology. 2011; (3):342-349.
4. Toledo RC, Jared C. Cutaneous granular glands and amphibian venoms. Comp Biochem Phys A. 1995; 111(1):1-29.
5. Clarke BT. The natural history of amphibian skin secretions, their normal functioning and potential medical applications. Biol Rev Camb Philos Soc. 1997; 72(3):365-79.
6. Steyn PS, Heerden FR. Bufadienolides of plant and animal origin. Nat. Prod. Rep. 1998; 15:397-413.
7. Morris C. (ed) Academic Press: Dictionary of Science and Technology (London: Academic Press Inc.). 1992.
8. Hoiberg DH, Pappas T, Mackenzie MR. Encyclopædia Britannica 2002-Delux Edition. (USA: Encyclopædia Britannica Inc.). 2002.
9. Basir YJ, Knoop FC, Dulka J, Conlon MJ. Multiple antimicrobial peptides and peptides related to bradykinin and neuromedin N isolated from skin secretions of the pickerel frog, Rana palustris; Biochim. Biophys. Acta. 2000; 1543:95-105.
10. Eubig PA. Bufo species toxicosis: Big toad, big problem. Toxicology Brief. 2001. Retrived from https://aspcapro.org/sites/default/files/j-bufotoadtoxicity.pdf
11. Jing Y, Ohizumi H. Selective inhibitory effect of bufalin on growth of human tumor cells in vitro: association with the induction of apoptosis in leukemia HL-60 cells; Jpn. J. Cancer Res. 1994; (85):645-651.
12. Brown JAC. Analgesia, Digitalis, Morphine and Aspirin; in Pears Pocket Medical Encyclopaedia (ed) A M H Bennett (London: Little, Brown and Company). 2001.
13. Dasa M, Mallick BN, Dasgupta SC, Gomes A. A sleep inducing factor from common Indian toad (Bufo melanostictus, Schneider) skin extract; Toxicon. 2000; 38:1267-1281.
14. Watabe M, Masuda Y. The cooperative interaction of two different signaling pathways in response to bufalin induces apoptosis in human leukemia U937 cells; J. Biol. Chem. 1996; 271:14067-14072.
15. Nicolas P, Mor A. Peptides as weapons against microorganisms in the chemical defense system of vertebrates; Annu. Rev. Microbiol. 1995; 49:277-304.