MINI-REVIEW

KAMBÔ: an Amazonian enigma

Vidal Haddad Junior¹,* and Itamar Alves Martins²

¹Department of Dermatology, Botucatu School of Medicine, São Paulo State, Brazil
²Department of Zoology, Taubaté University, Taubaté, São Paulo State, Brazil

*Correspondence to: Vidal Haddad Junior, E-mail: vidal.haddad-junior@unesp.br, Tel: +55 14 3880 1259

Received: 25 April 2020 | Revised: 25 May 2020 | Accepted: 25 May 2020 | Published: 26 May 2020

© Copyright The Author(s). This is an open access article, published under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0). This license permits non-commercial use, distribution and reproduction of this article, provided the original work is appropriately acknowledged, with correct citation details.

ABSTRACT

The secretions of the Giant Monkey Frog Phyllomedusa bicolor are used by populations in the Amazon regions (mainly the indigenous Katukinas and Kaxinawás). The so-called “toad vaccine” or “kambô” is applied as a medication for infections and to prevent diseases, and also as physical and mental invigorator, and analgesic. Since the 1980s, researchers and companies have been interested in the composition of these secretions. Phyllomedusin, phyllokinin, caerulein and sauvagine are the polypeptides in these secretions that can cause intense effects on smooth muscles, vessels provoking, nausea and vomiting, arterial hypotension, flushing, palpitations, nausea, vomiting, bile secretion and angioedema. These actions are similar to bradykinin. However, the feeling of well-being and improvement of motor skills described by the users seems to be associated with dermorphine, caerulein or deltorphin – peptides with analgesic properties – and their affinity for the opiate receptor systems. Caerulein is a peptide that increases digestive secretions. Phyllomedusin and Phyllokinin lead to blood pressure and digestive effects. Sauvagine release corticotropin and mimics the physiological reactions of exposure to stress. Deltorphins and dermorphins have high affinity for the opiate receptor system and can lead to analgesia. The fame acquired by the therapy motivated the use by individuals from urban areas worldwide, without safety considerations. While in indigenous communities, there is an entire cultural tradition that provides relative safety to the application, however, the extension of use to individuals from urban areas worldwide is a problem, with reports of severe adverse effects and deaths. Undoubtedly, the skin secretions of the Phyllomedusa genus contain substances of intense pharmacological action and that can lead to research for therapeutic uses, but control over their application in rituals outside the forest is needed due the risks presented.

KEYWORDS: Frog venoms, amphibians, indigenous medicine, pharmacological and toxicological phenomena, toxinology

INTRODUCTION

Toads, frogs and tree frogs are animals present in the folklore and culture of almost all places where they exist. Although they are associated with rainfall and fertility, part of this presence is associated with the fact that they produce or accumulate toxic substances, capable of promoting their defense and causing serious poisoning in predators. Toad poisons most often cause manifestations similar to digitalic poisoning, being represented in the Mayan, Chinese and Vietnamese cultures, in addition to playing an important role in Europe in the Middle Ages, where they were associated with potions and recipes from alchemists and witches. In Brazil, the muiraquitã is an amulet of a green stone shaped like a frog or toad that is found in watercourses and is considered to bring luck to those who find it. The kambô, which also is a green tree frog, is associated with healing rituals in the Amazon rainforest, rituals that have spread to urban centers around the world.

An old legend from the Amazon region says that once many Indians from the village of Kaxinawá once got seriously ill
and the shaman was unable to do anything to cure them with the herbal medications. In one of his rituals using ayahuasca, the shaman received a message to enter the forest and there he found a deity holding a green frog. The shaman was shown how to shave the frog’s back and remove a whitish secretion, which should be applied to patients. The shaman used these secretions successfully and since it became a routine in the Kaxinawá and many other tribes. The different names for this treatment in the various tribes include kambô in Katuquinas, ‘kambu in Kaxinawás, and kampu or kempô in other tribes. (Lima et al, 2006; Venâncio and Melo-Sampaio, 2010).

The tree frog *Phyllomedusa bicolor* is a species of Amazonian tree frog belonging to the family Phyllomedusidae, which has eight genera: *Agalychnis* (14 spp.); *Callimedusa* (6 spp.); *Cruziohyla* (3 spp.); *Hylomantis* (2 spp.); *Phasmahyla* (8 spp.); *Phrynomedusa* (6 spp.); *Phyllomedusa* (16 spp.); *Pithecopus* (11 spp.). The *Phyllomedusa* genus, as well as others in this family, arouses great interest in the substances that it secretes in the skin for its defense. The *P. bicolor* or Giant Monkey Frog secretions are considered medicinal, being used routinely by indigenous populations in Amazon regions (Lima et al, 2006; Venâncio and Melo-Sampaio, 2010). The animals vocalize to demarcate territory at the time of mating when they are captured to extract skin secretions. The indigenous Amazonian ethnic groups Katukinas and Kaxinawás use as a medication for infections and as a physical and mental invigorator the so-called “toad vaccine”, which has the names of kambô or kampô. This medication is obtained by the natives of these ethnic groups and some others indigenous communities by extracting and applying

---

**Figure 1.** Geographic distribution of *Phyllomedusa bicolor* in the Amazonian basin. Map BerkeleyMapper/AmphibiaWeb. 2020. <http://amphibiaweb.org> University of California, Berkely, CA, USA.
cutaneous secretions from the tree frog *P. bicolor* and from some other species (in lesser quantities) in order to obtain analgesic and antibiotic effects. This also gives the application a preventive character of diseases, according their culture. The white or yellowish secretion extracted from the back of the batrachians is dehydrated and reduced to a paste (or “vaccine”), which is applied to the skin and quickly absorbed by the body. The name kambô is used in general for the tree frog that provides the secretion, for the obtained secretion and for the method of inoculation of the substances in humans, in addition to denominating the ritual itself. The method is widely used by these indigenous communities, which credit the secretions of the eliminating of bodily impurities, the property of preventing illnesses and physical and psychic stimuli (increase of mood and elimination of “panema” or suffering of the mind) (Lima, 2005; Lima and Labate, 2007).

**TOXINOLOGY**

Since the 1980s, several researchers and companies have been interested in the active ingredients present in the cutaneous secretion of *P. bicolor* and other species of the genus. Phyllomedusin, phyllokinin, caerulein and sauvagine are polypeptides cause intense effects in smooth muscles vessels: nausea, vomiting, arterial hypotension, flushing, palpitations, nausea, vomiting, bile secretion and angioedema. The actions of them are similar to bradykinin. However, the feeling of well-being and improvement of motor skills described by the users seems to be associated to the dermorphine, caerulein or deltorphin, peptides with analgesic properties and affinity for the opiate receptor systems. Caerulein is a peptide that increasing digestive secretions. Phyllomedusin and Phyllokinin lead to blood pressure and digestive effects. Sauvagine release corticotropin and mimics the physiological reactions of exposure to stress. Deltorphins and dermorphins have high affinity to the opiate receptor system and can lead to analgesia (Tokuyama et al, 1969; Daly et al, 1992, Negri et al, 1992; Daly et al, 1993; Lacombe et al, 2000; Leite et al, 2005). The fame acquired by the therapy motivated the application of the secretion by individuals from urban areas in other regions of the country and worldwide, initially without any control and with the risks inherent to the use of several pharmacologically active substances.

With the dissemination and intense and little-proven application of therapy, ANVISA (National Health Surveillance Agency of Brazil) prohibited any form of use, trade, distribution or advertising of kambô as a medicine outside the villages (Resolution - RE nº 8), situation that currently stands (Lima and Labate, 2008). The illegal removal of secretions and frogs from villages and the country can be detected by a specific test (MALDI-TOF), developed by the Federal Police of Acre State, Brazil (Gomes et al, 2013). The tree frog is identified by its vocalization in the trees. When captured, it is immobilized and has their poisonous secretion scraped from the back with a stick. The frog is later released. The secretion is applied on the arm of male individuals and on the calves of women. The shaman makes small punctual burns in sequence with the tip of a stick or incandescent vine (“titica”) and these serial and sequential inoculations are the entrance to the secretion, already hydrated again, which increases its viscosity and gives it an aspect of paste. This paste is applied in the exulcerations caused by the burns (Figure 3). The dose depends on the shamans and the patient. These healers themselves warn of the misuse of kambô, which in inexperienced hands can cause serious problems. With the potent actions of the substances demonstrated, it seems clear that use outside the tribes is very dangerous (den Brave et al, 2014; Hesselink, 2018; Labate and Lima, 2020).
In 2008, a 52-year-old trader, out of the four people receiving this treatment, died at a businessman’s home after receiving kambô. The ‘toad vaccine’ in this case had been brought from the state of Acre (den Brave et al, 2014; Hesselink, 2018; Labate and Lima, 2020). Another reported death of a 42-year-old man, chronic consumer of Kambô, found dead near a small box labeled ‘Kambô sticks’ is likely to have been caused due to kambô. The individual had no history of any diseases and the toxicological screening was negative for ethanol and other drugs. Phyllocaerulein, phyllokinin, and deltorphin A were isolated from the Kambô sticks but, only deltorphin A was detected in his blood sample. (Aquila et al, 2018). Leban and colleagues (2016) reported a 34-year-old man that was admitted to hospital due to icterus, skin itching, weakness, and pain in the upper abdomen. The patient had not previously consumed a significant amount of alcohol, but had performed the ritual of Kambô, using poison from *P. bicolor* to maintain abstinence of drinking, smoking, and with the aim to ‘purify his body’. It seems that often damage to the liver occurs after activation of the various peptides and organic compounds in medicaments used in natural medicine (Pogorzelska and Lapinski, 2017). Yet another report of adverse effects occurred in a 32-year-old female with severe protracted vomiting after the application of the Kambô ‘vaccine’, with a degree of hyponatremia of 116mmol/l, which is severe enough to cause a seizure. The authors commented that the peptides dermorphin and deltorphin act as agonists of the μ- and δ-opioid receptors, respectively, which may result in symptoms of opioid toxicity and the opioid-mediated stimulation of the chemoreceptor trigger zone has been shown to induce nausea and vomiting (Kumachev et al, 2018). Li et al (2018) reported a patient who was attended in an emergency department with prolonged symptoms of vomiting, flushing, facial swelling, altered mental status, and intense agitation requiring chemical restraints, twenty-two hours after a Kambô ritual, which configures a prolonged time of the poison’s actions, a fact not commonly observed in the ritual (Li et al, 2018). In 2018, Roy et al described a 33-year-old Caucasian female, who was brought to the local emergency room by the police with signals of psychedelic psychosis. She had no significant psychiatric history prior to this incident and she claimed that she uses the kambô toxin up to nine times per month. She presented with characteristics of paranoia, anxiety, bizarre delusions, labile mood, and panic attacks. As part of her treatment plan, the patient was started on risperidone and she gradually improved after nine days in the hospital psychiatry unit (Roy et al, 2018).

In addition to the clinical implications, the use of toad vaccine also poses problems for the law-enforcement authorities; since such products are sold as natural products, the users considers them as safe to consume, while in reality these may lead to serious and harmful effects on the user, and even death. (Folha de São Paulo Agency, 2008; Menocchi, 2008). “There is no research that ensures the use of the toad vaccine for the aforementioned indications; therefore, the patient who consumes the product is subject to serious and unknown health problems”, says the Anvisa ordinance, published on 30th April, 2004. Technical advice of Anvisa and the sanitary legislation further preaches that any input that you are not aware of the origin of, and which has no guarantee of therapeutic efficacy, the recommendation is that it should not be used.

CONCLUSIONS

Although widespread, the habit of using the ‘kambô’ does not yet have safe methods of application, which can result in serious health risks for the users. There is an entire
cultural tradition in indigenous communities that provides relative safety to its application, but the extension of its use to urban areas worldwide, without previous profound knowledge of the applicators, has been increasing resulting in serious side effects, including deaths. Undoubtedly, the skin secretions of the Phyllomedusa genus contain substances of intense pharmacological action and that may have therapeutic potential, but the control over their application in rituals outside the in indigenous settings is needed due to the intense risk posed by their use.

ACKNOWLEDGMENTS

We thank Professor Dr Marcelo Menin, UFAM, for the image of Phyllomedusa bicolor and Ariadne Mendes Vidal Haddad for the illustration of the application of kambô.

COMPETING INTERESTS

None declared.

REFERENCES

Aquilà I, Gratteri S, Sacco MA, et al. 2018. The biological effects of Kambo: is there a relationship between its administration and sudden death? J Forensic, 63, 965-968.

Daly JW, Caceres J, Moni RW, et al. 1992. Frog Secretions and Hunting Magic in the Upper Amazon: identifcation of a peptide that interacts with an adenosine receptor. Proc Natl Acad Sci USA, 89, 10960-10963.

Daly JW, Garraffo H, Martin S and Tolda F. 1993. Amphibian alkaloids. In: Cordell GA. (Ed.) The Alkaloids: Chemistry and Pharmacology, Academic Press, California, USA, 1st. edition, pp.193-194.

den Brave PS, Bruins E and Bronkhorst MWGA. 2014. Phyllomedusa bicolor skin secretion and the Kambô ritual. J Venom Anim Toxins incl Trop Dis, 20, 40.

Folha de São Paulo Agency. 2008. Homem morre após aplicar no corpo produto a base de veneno. (Man dies after applying poison-based product to body). Folha de São Paulo Newspaper. Available at: https://www1.folha.uol.com.br/fsp/cotidian/ff2504200826.htm. Accessed on 17/05/2020.

Gomes CS, Silva Jr RC, Ambrosio J, Maldaner AO, Souza MB and Bloch Jr C. 2013. Identificação de Secreção do Sapo Kambô (Phyllobates aurotaenia) Utilizando MALDI-TOF. (Identification of Kambô Frog (Phyllobates aurotaenia) Secretion Using MALDI-TOF). Braz J Forensic Sciences, Medical Law and Bioethics, 14, 191-252.

Hesselink JMK. 2018. Kambô: A Shamanic Medicine - Personal Testimonies. JOJ Case Stud, 8, 555739.

Kumachev A, Zipursky JS, Weinerman AS and Thompson M. 2018. Poisoning from the Kambô ritual. CJEM, 2, 1-3.

Labate BC and Lima EC. Medical Drug or Shamanic Power Plant: The Uses of Kambô in Brazil. Available at https://pontourbe.revues.org/2384?lang=pt (Journal of the Urban Anthropology Nucleus the São Paulo University). Accessed on 17/05/2020. DOI https://doi.org/10.4000/pontourbe.2384.

Lacombe C, Cifuentes-Díaz C, Dunia I, Aubert-Thomay M, Nicolas P and Amiche M. 2000. Peptide secretion in the cutaneous glands of South American tree frog Phyllomedusa bicolor: an ultrastructural study. Eur J Cell Biol, 79, 631-641.

Leban V, Kozelj G and Brvar M. 2016. The syndrome of inappropriate antidiuretic hormone secretion after giant leaf frog (Phyllo- medusa bicolor) venom exposure. Toxicon, 120, 107-109.

Leite JRSA, Silva LP, Rodrigues MIS, et al. 2005. Phyllopestins: A novel class of anti-bacterial and anti-protozoan peptides from the Phyllomedusa genus. Peptides, 26, 565-573.

Li K, Horng H, Lynch K and Smollin CG. 2018. Prolonged toxicity from Kambo cleansing ritual. Clin Toxicol, 2, 1-2.

Lima AP, Magnusson WE, Menin M, et al. 2006. Guia de Sapos da Reserva Adolpho Ducke - Amazônia Central (Guide to the frogs of Reserva Adolpho Ducke - Central Amazonia). Editora INPA, Manaus, Brazil, 2nd edition.

Lima EC. 2005. Kampu, kampo, kambô: o uso do sapo-verde entre os Katukina. (Kampu, kampo, kambô: the use of the green frog among the Katukina): Revista do IPHAN, 32, 254-267.

Lima EC and Labate BC. 2007. Remédio da Ciência e Remédio da Alma: Os usos da secreção do Kambô (Phyllomedusa bicolor) nas cidades. (Science Remedy and Soul Remedy: the uses of Kambô (Phyllomedusa bicolor) secretion in cities). Campos, 8, 71-90.

Lima EC and Labate BC. 2008. A expansão urbana do kampo (Phyllomedusa bicolor): notas etnográficas. (Urban expansion of kampo (Phyllomedusa bicolor): ethnnographic notes) In: Labate BC et al (org) Drogas e cultura, novas perspectivas (Drugs and culture, new perspectives). Editora da Universidade Federal da Bahia, Salvador, pp. 315-344.

Menocchi S. 2008. Investigada morte de homem que tomou ‘vacina do sapo’. (Investigated death of man who took ‘frog vaccine’). Estado de São Paulo Newspaper. Available at: https://www1.estadao.com.br/noticias/geral,investigada-morte-de-homem-que-tomou-vacina-do-sapo,162933. Accessed on 17/05/2020.

Negri L, Espenamer GF, Severini RL, Potenza P and Melchiorri EV. 1992. Dermorphin-related peptides from the skin of Phyllomedusa bicolor and their amidated analogs activate two µ opioid receptor subtypes that modulate antinociception and catalepsy in the rat. Proc Natl Acad Sci USA, 89, 7203-7207.

Pogorzelska J and Lapinski TW. 2017. Toxic hepatitis caused by the excretions of the Phyllomedusa bicolor frog - a case report. Clin Exp Hepatol, 3., 33-34.

Roy R, Baranwal A and Espiridion ED. 2018. Can overuse of Kambô cause psychosis? Cureus, 10, e2770.

Tokuyama T, Daly JW and Witkop B. 1969. “The structure of batrachotoxin, a steroidial alkaloid from the Colombian arrow poison frog, Phyllobates aurotaenia, and partial synthesis of batrachotoxin and its analogs and homologs”. J Am Chem Soc, 91, 3931-3938.

Venâncio NM and Melo-Sampaio PR. 2010. Reproductive behavior of the giant leaf frog Phyllomedusa bicolor (Anura: Hylidae) in the western Amazon. Journal of Herpetology, 9, 63-67.